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IACC Strategic Plan 2026–2028

A New Federal Framework for Autism

WORKING DRAFT — SUBJECT TO ERRORS AND REVISION

Contents

Executive Summary

The 2026–2028 IACC Strategic Plan builds on the work of prior Strategic Plans, but it is organized to do something those plans were not designed to do. Across successive planning cycles, prior Plans documented community concerns, synthesized the state of the science, identified persistent gaps, broadened attention to co-occurring conditions and transition-age youth, and sustained federal focus on autism. That record defines the priorities on which this Plan depends and to which it remains accountable; it is carried forward, not set aside.

What has changed is the nature of the problem those priorities describe. Autism can no longer be addressed adequately as either a research topic or a single service category. It was identified in approximately 1 in 31 (32.2 per 1,000) children aged 8 years across the 16 communities in the CDC ADDM Network's 2022 surveillance year, up from approximately 1 in 150 in surveillance year 2000, a change that reflects greater awareness, expanded screening and ascertainment, and changes in surveillance sites and methodology as well as any change in underlying occurrence, and it reaches across research, surveillance, diagnosis, clinical care, co-occurring conditions, education, coverage, disability services, housing, employment, safety, aging, and civil rights. A problem of that scope requires a plan that can connect evidence to authority, authority to agency responsibility, and responsibility to measurable deliverables. This Plan is written to make those connections explicit.

Two facts explain why a plan built only on priorities is no longer sufficient. The first concerns how federal responsibility for autism is distributed. The authorities needed to serve individuals with autism or those who provide care for them are divided among agencies that operate largely as separate activities rather than as a coordinated strategy: NIH generates and validates scientific evidence; FDA governs regulatory science; HRSA supports translation and workforce capacity; CMS addresses coverage and implementation within its authority; and CDC, ACL, the Department of Education, the Department of Defense, and others act within their respective jurisdictions. No single agency holds the full set of authorities, and no standing mechanism carries a promising finding from discovery through validation, regulatory review, coverage analysis, and clinical adoption. The result is not too little activity but too little movement from activity to usable products.

The second fact concerns measurement. The 2024 Government Accountability Office review found that federal autism coordination only partially followed leading practices for accountability, that IACC Strategic Plans generally had not translated goals into measurable objectives against which progress could be judged, and that reporting tended to describe activities rather than track outcomes. A plan that only restates priorities cannot answer a finding of that kind.

The Statutory Mandate

The Autism CARES Act of 2024 gives this analysis statutory form. Congress did more than reauthorize federal autism activities, including the Interagency Autism Coordinating Committee, through September

30, 2029; it materially strengthened the federal autism framework in ways that respond directly to concerns autistic people, families, caregivers, clinicians, and other members of the public have raised for years. The Act requires federal planning to account for the entire population of autistic individuals across the lifespan, including those with co-occurring conditions and the full range of services and supports needed to ensure safety and promote well-being. Federal planning can no longer be confined to early childhood, conventional research portfolios, or narrow diagnostic categories. It must reach across the lifespan, from the prenatal period and early childhood through the transition to adulthood, adulthood, and later life, and it must account for families, caregivers, and clinical care.

Congress made that broader mandate concrete. It expressly expanded the NIH research agenda to include co-occurring conditions, caregiver supports, services and supports across the lifespan, dissemination and implementation, safety and well-being, and the full population of individuals with autism. It identified specific fields for federal attention, among them co-occurring conditions, developmental-behavioral pediatrics, endocrinology, and gerontology, and it strengthened public engagement while requiring clearer reporting on mental health, the transition to adulthood, expenditures, implementation, duplication, and outcomes. These were not incidental adjustments; together they establish a congressional agenda that anticipates a federal response beyond what has previously occurred.

Congress also changed the relationship between strategic planning and the NIH budget. The Committee must develop and update a Strategic Plan that includes proposed budgetary requirements and recommendations to reduce unnecessary duplication, and, under the Autism CARES Act of 2024, for fiscal years 2026 through 2029 the NIH Director must then prepare an annual budget estimate for NIH autism-related initiatives “pursuant to” that Plan. The Secretary and the Committee must be given a reasonable opportunity to comment on that estimate, but neither may change it, and the Director submits it directly to the President for review and transmittal to Congress. The Committee therefore does not write the estimate or control its contents, yet its role is not ornamental, because the Strategic Plan is meant to come first and the estimate to follow from it.

Read together with the Committee’s public membership, its public meetings, and its responsibility to improve the integration of public feedback, that sequence creates a pathway for community priorities to move from public input, through the Strategic Plan, and into the federal budget process. The Act’s legislative sponsor, Representative Chris Smith, described the new professional-judgment, or “bypass,” budget as a means of giving the autism community a comprehensive account of priority research areas and the resources needed to improve quality of life. The estimate is therefore not simply an internal NIH exercise; it is intended to make visible the relationship among public priorities, the Strategic Plan, federal research choices, and requested resources.

The record reviewed for this Plan indicates, however, that the federal research portfolio has not uniformly kept pace with the agenda Congress enacted. Adult and later-life health, co-occurring medical and mental health conditions, communication, caregiver supports, implementation research, and outcomes for people with complex or high support needs remain underdeveloped or disconnected from practice. The question this raises is not simply whether more studies are needed, but whether federal priorities, budgets,

research infrastructure, and accountability mechanisms now reflect the population and outcomes Congress directed the system to address. When major parts of that agenda remain behind, the resulting gap is not only scientific; it is a gap between the public planning and accountability process Congress created and the federal priorities that are meant to follow from it.

None of this enlarges the Committee's authority. The Autism CARES Act does not convert the Interagency Autism Coordinating Committee from an advisory body into an operating agency: under its authorizing statute the Committee monitors federal autism activities, convenes federal and nonfederal participants, evaluates progress, advises the Secretary of Health and Human Services, recommends coordinated action, and reports. No part of this Plan should be read as authorizing the Committee to direct, compel, or supervise the operations of other departments and agencies, to obligate funds, or to create obligations enforceable against any agency.

The distinction between recommendation and decision governs the entire Plan. The Committee identifies problems, assesses jurisdiction and capacity, proposes deliverables, and specifies how progress can be measured, while the Secretary and the authorized departments and agencies make the operational, regulatory, grantmaking, coverage, enforcement, and budget decisions, each within its own statutory authority and subject to available appropriations. Where this Plan names a lead or supporting agency, that designation reflects the Committee's assessment of which agency is best positioned by jurisdiction and capacity to carry the action forward. It is not evidence that the named agency has concurred, has been consulted, or has committed resources. A recommendation does not become binding because it identifies an agency, cites an authority, proposes a deliverable, or sets a target date. Where implementation depends on a state's election of an optional Medicaid pathway, the Plan may recommend adoption but cannot compel it, because that decision rests with the state.

This Plan does more than identify new federal priorities. Many of its recommendations provide practical means for carrying out responsibilities Congress has already assigned to the Secretary, the Director of NIH, CDC, HRSA, and the Interagency Autism Coordinating Committee. The surveillance agenda supports required child and adult epidemiology; the diagnostic agenda supports screening, workforce, and diagnostic-capacity responsibilities; the communication and mental-health domains support newly specified technical-assistance and reporting duties; the lifespan domains supply the information needed for reports on transition, home- and community-based services, and community participation; and the whole-of-plan register provides a common structure for monitoring implementation, expenditures, outcomes, and progress toward the Strategic Plan. These connections do not make every recommendation legally required; they show where the Plan offers an actionable method for fulfilling duties that already exist.

The April 2026 Recommendations: First Actions Under the Mandate

The Committee has already begun to exercise its role under the Autism CARES Act of 2024 . At its April 28, 2026 meeting, the Committee adopted four recommendations and transmitted them to the Secretary: clarification of EPSDT obligations regarding clinical assessment, co-occurring conditions, and safety risks for

children with autism; HRSA clinical guidance on structured review of systems, reduction of diagnostic overshadowing, and clinical safety assessment; adoption of a standardized functional designation of profound autism for research and policy purposes; and safety measures addressing the urgent risks associated with wandering and elopement. The Secretary has received these recommendations, and evaluation and avenues for implementation are ongoing. Consistent with the distinction that governs this Plan, the decisions they call for rest with the Secretary and the authorized agencies, each acting within its own authority.

How the Plan Is Organized

Because the Act frames progress in terms of measures, duplication reduction, and budget, the Plan organizes its recommendations by the federal action each area requires rather than by subject alone, according to how mature the evidence is. Where genuine scientific uncertainty remains, the action is discovery: a research investment with a defined endpoint. Where evidence exists but has not reached practice, the task is to close the distance between a finding and its use, through validation, regulatory science, coverage analysis, workforce preparation, and implementation research, with the recommendation identifying the responsible agencies and their respective roles.

Where existing authority already supports action, the recommendation is to act now, with a deliverable and a date. This calibration guards against two opposite failures: treating every priority as though it needs more study, which defers action already warranted, and treating early findings as ready for wide adoption, which commits resources ahead of the evidence. To keep it auditable, each major recommendation records the problem, the evidence stage, the category of federal action, the lead and supporting agencies, the relevant authority, the deliverable, the timeline, and, where feasible, the outcome measures—so that later Committees, the agencies, Congress, and the public can judge whether an action moved and whether it produced measurable improvement.

The Scientific Foundation

Part II supplies the evidentiary ground for these judgments while taking care not to overstate what is settled, because the calibration just described depends on stating the evidence accurately. On occurrence, the CDC ADDM Network's consistent, records-based case-finding makes its serial estimates comparable over time, and the share of children with profound autism—minimal or no functional speech and who require continuous care—has risen alongside the broader trend. Because autism has no observable moment of biological onset, incidence cannot be measured directly, and birth-cohort prevalence serves as its practical proxy. The Plan weighs the leading explanations for the rise—greater awareness, earlier identification, diagnostic substitution, broadened criteria, and prior under-recognition—and concludes that each is likely partly true but that none, alone or together, accounts for the full magnitude of prevalence increase. The Plan does not claim to have resolved whether a true increase in incidence has occurred; it treats that question as a federal research priority because the answer determines the future demand on health, education, and long-term support systems.

On heterogeneity, the evidence is directive rather than merely descriptive. Co-occurring conditions are the norm rather than the exception—more than 90% of individuals diagnosed with autism also have at least one medical, developmental, or psychiatric condition—and the clinical variation rests on biological variation across genetic, immune, metabolic, mitochondrial, gastrointestinal, and synaptic systems. The Plan therefore adopts no singular theory of autism causality, phenotype, trajectory, intervention, treatment, or care, and it rejects any population-wide approach that assumes uniformity where the evidence demonstrates substantial heterogeneity. Any framework that infers universal causality, a universal phenotype or developmental course, or a uniformly appropriate intervention, treatment, or care model fails to account adequately for the varied pathways, co-occurring conditions, functional profiles, and support needs represented within autism. Read correctly, this variation is not a set of competing theories of autism but evidence that autism arises through multiple pathways, which is why the Plan favors stratified investigation and, where clinically indicated, subgroup-specific care over undifferentiated approaches. The same reasoning identifies neurodevelopmental regression as a national priority: a clinically recognizable event, a subset of which has identifiable and treatable contributors, that too often fails to trigger an organized medical response. As evidence continues to mature, the Plan keeps clinical and coverage claims tied to validated findings rather than to plausible but unconfirmed mechanisms—the discipline that governs the therapeutic agenda described next.

Two Federal Systems: Translation and Navigation

The central design choice of this Plan is to meet a structural problem with coordinated federal capacity rather than with another round of separate programs. Two gaps recur. The federal government does not reliably move scientific findings into validated, usable care, and it does not reliably help people find and obtain the services to which they are entitled or record whether they did. The Plan proposes one federal system for each gap, and gives them comparable weight: the National Autism Precision Therapeutics Initiative (NAPTI) for translation, described in this section, and Autism.gov for navigation and public accountability, described in the section that follows.

Both are proposals that would require designated leadership, agency participation, technical capacity, and appropriations or reallocation to stand up. NAPTI is designed to carry science into practice. It would not be a new institute but a distributed effort built on existing NIH networks, Autism Centers of Excellence, clinical research sites, federal data assets, regulatory expertise, and agency implementation programs, organized so that no single research domain has to rebuild its own registry, assay platform, recruitment network, outcome system, or regulatory pathway. Its proposed governance follows the division of federal authority: a Secretary-designated National Autism Coordinator would convene the participating agencies, coordinate their contributions, and compile their reported milestones; NIH would lead operations through a coordinating-center and cooperative-network structure; FDA would co-lead regulatory science for contexts of use, biomarker qualification, and endpoints; and CDC, AHRQ, HRSA, CMS, ACL, and the Department of Defense would participate according to jurisdiction.

What makes NAPTI more than a coordinating label is a set of explicit evidence gates that hold each finding to the standard its intended use requires before it advances. A plausible mechanism is not a confirmed biomarker; an analytically valid assay is not yet a clinically useful test; a signal in a selected cohort is not a population-wide result or recommendation; and a short trial signal is not a clinical recommendation. A finding progresses from discovery through analytic validation, clinical validation, clinical investigation, regulatory review, and implementation only when the evidence for the next step is in hand, and each step yields a defined product—a harmonized or distinct phenotype, an assay standard, a qualified context of use, a multisite protocol, an evidence review, or an implementation package.

Autism.gov: Federal Navigation and Public Accountability

If NAPTI is the system for moving science into validated care, Autism.gov is the system for moving people to the care and services already available to them and for showing, publicly, whether the Plan is being carried out and how the federal system is addressing autism. It is proposed as a trusted federal front door that integrates existing federal resources rather than duplicating them, developed under HHS direction. Its premise is that fragmentation is experienced most acutely not in the research portfolio but at the point of use, where an autistic person or family confronts a set of programs organized by agency and authority rather than by need. Autism.gov is designed to reorganize that experience around the person. It would present life-stage and user-journey navigation built around how autistic people and families actually move through the system (screening and diagnosis, early intervention, school-age services, the transition to adulthood, adult health and employment, and aging) rather than around the federal boundaries that currently divide those functions. Existing federal platforms, including alzheimers.gov, cancer.gov, VA.gov, and HIV.gov, provide useful models for an integrated, user-centered federal portal.

On that foundation the portal would carry several substantive functions. A benefits and eligibility router would help users identify and pursue the major pathways for which they may qualify—Medicaid and CHIP, EPSDT, IDEA Parts C and B, SSI and SSDI, home- and community-based services waivers, housing assistance, respite, and vocational rehabilitation—while making clear that the tool guides users toward the right door and does not itself make eligibility determinations, which remain with the responsible agencies. A standardized state-by-state services map would let a user in any state see the major coverage, waiver, education, diagnostic, family-support, protection-and-advocacy, and housing resources available there, presented in a comparable format. Diagnostic-access and workforce visibility would surface wait times, provider capacity, tele-assessment availability, and disparities, to the extent reliable data can be developed. Caregiver and lifespan resources would consolidate respite, housing, crisis support, and transition planning in one place. And the site would be built to federal plain-language, accessibility, multilingual, and AAC-accessible standards, so that autistic people, Nonspeakers and other communication-diverse users, families, providers, and users with limited English can use it directly rather than through an intermediary.

The IACC Implementation Dashboard is the accountability component of Autism.gov, not the whole of it. It would map each Strategic Plan recommendation to its responsible agency, the authority under which it

proceeds, the category of federal action, the deliverable, its current status, the key performance indicators, the barriers encountered, and the next reporting date. In doing so the dashboard makes the Plan legible against the same Recognition–Access–Stabilization framework the domains use: it can show not only that guidance issued or a demonstration launched, but whether identified needs are being met with delivered services and whether those services produce durable outcomes—the direct federal response to the GAO finding that reporting described activities rather than progress toward results.

Governance would follow the same jurisdictional discipline applied throughout the Plan. The HHS Office of the Secretary, through the National Autism Coordinator, would serve as coordinating lead; GSA and USAGov, or comparable federal digital-service capacity, would develop and maintain the platform; and CMS, HRSA, CDC, the Department of Education, ACL, HUD, SSA, DOL, and DOJ's Civil Rights Division would contribute content and data according to their own authorities. No office would compel a peer agency; participation rests on each agency's jurisdiction and on the coordinating role the Act assigns. Implementation would proceed in phases rather than at once: first, governance, a content inventory, and user research with autistic people and families; then a public beta offering core navigation and the state services map; then the benefits router with expanded multilingual and diagnostic-access resources; and finally the full dashboard with standardized agency and state reporting.

The Therapeutic Agenda

Within that framework, Part IV sets out eleven Priority Therapeutic Domains. Each is an evidence-calibrated research and translation agenda for a defined subgroup, not a claim that every proposed mechanism or intervention is established, and the ten fall into three groups.

The first concerns neural, pharmacologic, and network biology: Neurotransmission, Neural Circuit Function, and Neuropsychopharmacology (Domain 1); Autonomic Dysfunction (Domain 7); Sleep and Circadian Regulation (Domain 8); Epilepsy and Network Excitability (Domain 9); Motor Planning, Praxis, Sensorimotor Integration, and Apraxia (Domain 10); and Adaptive Trial Design, Treatment Endpoints, and Repurposed Medications (Domain 11). Its aim is to move broad, unevenly supported prescribing and testing toward safer, subgroup-defined practice and toward outcomes measured as function, while ensuring that treatable epilepsy is not missed and that network findings are not over-read.

The second concerns immune, metabolic, and gastrointestinal biology: Immune, Autoimmune, and Inflammatory Biology (Domain 2); Folate Metabolism and One-Carbon Biology (Domain 3); Gastrointestinal Biology, Microbiome Function, and Nutrition (Domain 4); and Mitochondrial, Redox, and Metabolic Function (Domain 6). Its aim is to secure standard-of-care recognition and treatment of established conditions now, where clinically indicated, while advancing assay harmonization, biomarker validation, and confirmatory trials before broader clinical or coverage claims are made.

The third is a single integrating domain—Neurodevelopmental Regression, Functional Trajectory, and Health Stabilization (Domain 5)—which organizes an immediate, structured clinical response to regression

while building evidence about trajectory change on a shared record, and so connects the therapeutic agenda to the lifespan agenda that follows.

The Implementation Agenda

Part V turns from what should be discovered and translated to what can be delivered now under existing authority, applying a single measurement approach so the Plan does not accumulate more indicators than any federal system can populate. Every domain reports against the same three tiers: Recognition, whether a need is identified; Access, whether an identified need is met by a service actually delivered rather than authorized on paper; and Stabilization, whether the delivered service produces durable function, safety, and participation. A screen without access is not an outcome, and access without stabilization is not a result. Each deliverable also carries a burden tier that sets its sequence: Tier 1 work rests on existing authority—guidance, coverage clarifications, and technical assistance—and needs staff time rather than new money, so it moves first; Tier 2 work is gated by budget through grant and demonstration mechanisms agencies already run; and Tier 3 work requires capacity the responsible agency is not staffed to carry and must be staged, resourced, and assigned to a capable lead. Federal deliverables, which have accountable owners and dates, are reported separately from state-adoption outcomes, which can be tracked, measured and encouraged but not necessarily compelled.

The substance of Part V is carried by nine Life Course Domains that largely follow the arc of a life and rest, wherever possible, on existing statutory authorities, including IDEA, Medicaid, EPSDT, home- and community-based services, and civil-rights protections, rather than on authorities not yet enacted. The agenda begins with timely, equitable, and technology-enabled diagnosis, which establishes the measurable accountability model adopted by later domains, and then turns to special education and IDEA implementation, where national baselines for funding and missed services must precede the setting of defensible targets.

From there, the Plan addresses communication access for nonspeaking and minimally speaking autistic individuals as a federal quality-of-care priority, together with co-occurring mental health conditions, crisis care, and suicide prevention through systems designed to respond immediately while generating evidence for safer and more durable care. The adult domains address housing supply, transportation, supported living, and caregiver succession for autistic adults, including those with complex support needs; caregiver stabilization, respite, navigation, and family support so that public systems do not continue to rely on unsupported families as their hidden infrastructure; and employment, workforce participation, and workplace supports across the full range of functional profiles. The lifespan arc concludes with older autistic adults, aging, and later-life health, where needs will grow as successive birth cohorts enter later life.

Four commitments discipline all nine domains and keep the agenda from narrowing to the populations easiest to serve. Federal policy must reach the full population, including autistic people with profound autism, minimal speech, and complex medical or high support needs and those with intellectual disability, and as well as those with subtler or more precisely scoped presentations.

Communication access is treated as a condition of equitable care, a basic civil right, and the Plan preserves the term Nonspeaker for autistic individuals who do not develop functional spoken language or whose speech is minimal or unreliable. Complex medical or support needs are addressed directly rather than deferred. And the domains are built to operate within existing statutory authority, so that most first-year deliverables are Tier 1 actions the responsible agencies can carry out without new appropriations.

The Intended Result

Taken together, these choices are meant to move federal autism activity from fragmented programs and activity reporting toward coordinated action, public accountability, and the reliable translation of evidence into 21st century science and care. The mechanisms that would produce that shift are placed deliberately across the Plan rather than gathered into a single closing chapter: the implementation logic and duplication review in Part I, the evidence gates and common outcomes in Part III, and the Recognition–Access–Stabilization measures and burden tiers in Part V, made public through Autism.gov.

The Plan attempts to provide correspondingly concrete measures. For each major recommendation, a reader should be able to identify a responsible agency, a deliverable, a timeline, a budgetary requirement, and an outcome measure, and to determine from public reporting whether that commitment was met. Above that record of federal deliverables sits the test that ultimately matters: whether autistic people, across the full range of the lifespan and of support needs, are identified earlier, receive the services and supports clinically indicated for them, and remain stable in health, function, communication, safety, and participation. The Committee's role is unchanged—it monitors, convenes, advises, recommends, and reports—while the authorized departments and agencies act within their authority. In short, this is a plan for federal agencies, not from federal agencies. The proposed framework allows Congress, agencies, and the public to assess both the Committee's recommendations and agency implementation against a visible record.

While this Plan focuses on meeting the needs and challenges of the autism community, the Committee also acknowledges the unique perspectives, gifts, and exceptional abilities that individuals with autism contribute to our community and the world.

Preface

Process, Scope, Methodology, and Evidentiary Boundaries

This Preface explains how the working Strategic Plan Draft was assembled, what materials informed it, what materials remained unavailable, and how those limits should shape the way its recommendations are read.

The committee's process was informed by 6 core values including urgency, action, translation, lifespan inclusion, scientific excellence, and reducing symptom suffering and barriers. The process was also informed by the following mission statement:

The purpose of the IACC Strategic Plan for Autism Research, Services, and Policy is to accelerate progress toward improving the lives of autistic individuals and their families through scientific discovery, translation, and action. The Plan will emphasize the translation of research into effective interventions, clinical care, services, supports, and prevention strategies that maximize outcomes, improve quality of life, promote safety, communication, and well-being, and reduce the most serious adverse outcomes experienced by autistic individuals and their families. Consistent with the Autism CARES Act of 2024, the Plan will advance research related to causes, prevention, screening, diagnosis, interventions, clinical care, treatment, and access to services and supports across the lifespan, while ensuring that research reflects the full varied life experiences of autistic individuals, including those with co-occurring conditions and the full range of support needs.

Our drafting process did not have the benefit of a complete institutional record or formal handoff from the prior planning cycle, it drew largely on publicly available materials that could be independently located and reviewed. That constraint does not diminish the work performed, but it does make it necessary to distinguish what the Plan can establish on its own from what still requires agency records, costing, concurrence, and verification.

Purpose and Scope of This Working Strategic Plan

This document is a strategic synthesis and federal implementation framework: it sets priorities, maps them to federal functions and authorities, and defines how progress should be measured. It is not a systematic review, a clinical guideline, a benefit or eligibility determination, an agency rule, a budget score, or a statement of interagency concurrence. Where it recommends action by a department or agency, it does so as a **recommendation** to the Secretary of Health and Human Services and to the responsible agencies, to be carried out within their own discretion and statutory authority, subject to available appropriations. Rather, its purpose is to convert a large and uneven evidence base into coordinated federal action that can be tracked, evaluated, and revised as a single body of work rather than as a collection of separate activities.

The scope spans the autism lifespan and to better capture the full discovery-to-implementation continuum: the scientific foundation (Part II), the translational infrastructure proposed as the National Autism Precision Therapeutics Initiative (Part III), priority therapeutic and clinical domains (Part IV), federal navigation and lifespan supports including Autism.gov (Part V), and the accountability framework that governs implementation and updates (Part VI). The scope conditions set out in this Preface apply to each of those Parts.

Relationship to Existing Statutory Responsibilities

This Plan does not assume that every recommendation requires new authority; in many places it offers a practical way to carry out responsibilities Congress has already assigned under Part R of the Public Health Service Act and related provisions. Part II's surveillance agenda supports the Secretary's responsibilities for child and adult epidemiology, the diagnostic agenda supports screening, diagnostic-tool, workforce, and reporting responsibilities, and the communication and mental-health domains support newly specified technical-assistance and reporting duties. The transition, housing, community-mobility, employment, and caregiver recommendations can supply the information needed to evaluate whether people are living, working, and participating in their communities, while Autism.gov can support federal duties and statutory obligations to make program information available and establish a mechanism to receive public input. Part VI, in turn, supplies a common structure for sequencing considerations, monitoring implementation, expenditures, duplication, and outcomes.

These connections matter, but they also have limits: they do not make every recommendation legally required, enlarge the Committee's authority, or convert a proposed implementation mechanism into a statutory mandate or agency binding directive. What they establish is narrower and possibly more useful, showing where the Plan can help the Secretary and the responsible agencies carry out existing duties in a more coordinated, measurable, and publicly visible way while also advancing a more comprehensive approach to addressing the needs of autism stakeholders. The detailed statute-to-Plan crosswalk may be found in Part VI or the authority appendix, where it can be maintained as the Plan is updated.

Method: From Record to Recommendation

The Plan was developed through research and synthesis of the existing federal record, drawing largely on public comments, prior Strategic Plans, stakeholder responses to Requests for Information issued during earlier planning cycles, and the input and expertise of federal and public members, with reliance throughout on sources that could be independently located and reviewed. Each major recommendation moves through the same sequence: it identifies the problem, states the maturity of the supporting evidence, identifies the category of federal action required, maps that action to the agency positioned by jurisdiction and capacity to lead it, specifies the anticipated federal deliverable, and defines how progress and outcomes should be measured. This sequence is deliberate, because it keeps observation, interpretation, recommendation, implementation mechanism, and measurable outcome distinct, so that a

reviewer can see where the evidence ends, where federal judgment begins, and where agency verification is still required.

The same discipline governs the movement from science to policy. The Plan distinguishes scientific findings ready for translation from those that require replication; discovery signals from validated or cohort specific biomarkers; and distinguishes both from demonstrated clinical utility and deployable federal products. The Plan does not recommend advancing any finding beyond the stage its evidence supports. This evidence-gate logic, developed in Part III and applied across Part IV, is the mechanism by which the Plan avoids overstating what current science supports while supporting a directive to better incorporate a scientifically advanced precision-based cohort approach to autism.

Source Hierarchy and Evidentiary Treatment

The Plan draws on several classes of source, weighted according to their authority and their fitness for the claim being made. Enacted law and statutory text, including the Autism CARES Act of 2024 and the Committee's authorizing statute at 42 U.S.C. § 280i-2, govern questions of federal authority and obligation. Independent oversight findings, principally the 2024 Government Accountability Office report GAO-24-106446, establish the accountability problem the Plan is designed to address. Publicly available federal program, research-portfolio, and surveillance materials inform the assessment of federal activity to the extent those materials could be located and verified. Peer-reviewed scientific literature supports the biological and clinical claims in Parts II through IV, and the specific studies are collected, with citations and links, in the Appendix. Published public and community input, including the 2023–2024 IACC Request for Information on co-occurring conditions, identifies needs and priorities, and established federal implementation frameworks and comparator public portals helped to inform the design of proposed infrastructure.

Because the drafting process was not provided the most recent 2024 Strategic Plan or a complete agency record, the Plan was assembled from the public and published materials the drafters could independently locate: enacted federal law and legislative text; the 2024 GAO report; the publicly available NIH RCDC federal research-portfolio, surveillance, and program information; peer-reviewed scientific literature; published results of public-input mechanisms, including the 2024 Request for Information; the last publicly available IACC Strategic Plan (2012-2023) and public information about established federal portals and implementation frameworks used as comparators.

For clarity, the 2024 Strategic Plan was not available to the full Committee during the drafting process, although it was expected to become available. In the recommendations below, we identify materials that would support the Committee's future work but, because they were unavailable within the drafting timeframe, could not inform the development of this Plan.

Where sources diverge, the Plan gives precedence to statute on matters of authority, to peer-reviewed evidence on matters of science, and to oversight findings on matters of accountability, and it states when a claim rests on preliminary or methodologically distinct analysis rather than settled evidence.

Community and Lived-Experience Input

Autistic individuals, families, and caregivers informed the Plan's understanding of need and priority. The 2024 IACC Request for Information on co-occurring conditions, which produced 1,254 respondents and 8,778 response entries, is used in Part I to document the distance between frequently reported needs and federal response. Community input of this kind, especially when consistent, is treated as authoritative evidence of what individuals and families experience and prioritize, but it is not, by itself, treated as establishing scientific causation or clinical efficacy, which are questions the Plan supports resolving through evidence of lived-experience, scientific literature, investigation, and the evidence gates. Holding both propositions at once, that lived experience defines the problems worth solving and that efficacy must still be demonstrated, is essential to a plan meant to be both responsive and defensible.

Future Considerations for Effective IACC Work

Under the Autism CARES Act of 2024, the IACC is charged with monitoring autism-related federal activities across the government. It is our recommendation, in order to more effectively fulfill this obligation, that the Committee have access to relevant materials such as agency budget priorities or budget submissions; agency strategic, operating, or implementation plans; current program inventories and status reports; internal evidence reviews; program-office cost estimates; negotiated interagency agreements or decision records; agency comments or concurrence; complete state-by-state program and eligibility data; or unpublished datasets and proprietary records. Additional information may include documentation describing the full scope of autism-related actions agencies are pursuing, or which may have been rejected, modified, or deferred, or where agencies believe efforts are duplicative.

Scientific Uncertainty, Heterogeneity, and Evidence Maturity

The Plan treats autism as biologically and clinically heterogeneous, arising through multiple interacting pathways in which genetic susceptibility, immune, metabolic, microbial, and environmental influences, and developmental timing combine differently across individuals. It does not assert a single cause, and it does not treat contributing factors as singularly causal as an autism-wide finding. However, findings are characterized in terms of associations, probabilities, and subgroups rather than universal claims, and the strength of each claim is matched to the maturity of its evidence. Discovery-stage findings are identified as such and are not presented as ready for routine clinical use; areas of genuine uncertainty are named rather than resolved by assertion. This treatment is a feature of the Plan's scientific credibility, not a hedge, and it is applied consistently through the evidence-gate and discovery-translation-implementation logic that structures Parts II through IV.

Agency Authority, Appropriations, Costing, and Implementation Status

The Plan is careful about what its recommendations do and do not establish. Agency assignments represent the Committee's recommendations and its mapping of functions to statutory jurisdiction and

capacity based on publicly available data; they do not represent negotiated commitments or agency concurrence. Dollar figures throughout the Plan are order-of-magnitude planning ranges intended to convey relative scale and sequencing; they are not appropriations, Office of Management and Budget scores, or agency cost estimates, and each should be replaced by a program-office costing before it is treated as implementation-ready. Implementation status is not presented as verified where agency data or concurrence were not available; the accountability framework in Part VI further defines how status is to be reported, by whom, and with what treatment of missing data, precisely so that activity is not mistaken for outcome and unverified status is not mistaken for confirmed progress.

Limitations, Evidence Cutoff, and Updates

This is an in-progress working draft prepared for structured revision and wider community input and is subject to change. The material herein is largely derived from a longstanding public record. Its evidence cutoff is the date of the current revision recorded at the end of the document, so that materials and developments after that date are not reflected, and the sources consolidated in the Appendix were verified only as of that cutoff. Its principal limitation is not simply the passage of time but the absence of an efficient institutional handoff and the agency records needed to verify current priorities, implementation status, duplication, costs, and feasibility, all of which require review against the responsible agencies' own records before appropriation or implementation. Consistent with the Autism CARES Act of 2024 and the accountability framework in Part VI, the Plan is intended to be corrected and updated as better information becomes available, with each update distinguishing recommendations that are completed, in progress, modified, deferred, and not advanced. Stating these limits does not weaken the Plan; it identifies the work that remains before its recommendations can be treated as a verified federal implementation record.

Part I

A New Federal Framework for Autism

IACC Strategic Plan

July 2026

From Priorities to Implementation: The Federal Autism Enterprise

The United States has entered a new era in autism. What was once treated as a relatively uncommon neurodevelopmental condition affecting a limited number of children is now one of the nation's major public health, health care, disability, education, workforce, housing, economic, and social-policy challenges —with implications that extend across the life course.

The numbers make the case. Autism now affects approximately 1 in 31 children in the 2014 birth cohort, up from 1 in 150 in 2000 — a trajectory that reflects a rising, lifelong demand for services that federal and state systems were not built to meet. Children face delays in accessing diagnosis and treatment, with approximately 70% experiencing delayed entry to early intensive behavioral intervention — delays associated with significantly worse educational outcomes. The educational system is straining to respond to increasingly diverse individual needs. Growing numbers of individuals are presenting for care across the life course, including transition-age and adult populations, where they encounter long waitlists — averaging 8 years for autism waiver services in some states — and limited options. As of 2024, more than 700,000 people nationally were on waiting lists for Medicaid home- and community-based services. As successive birth cohorts reach adulthood — often as aging parents can no longer sustain lifelong caregiving — need is growing fastest where capacity is scarcest: the shortage of supported housing for adults with moderate-to-high support needs is but one example. These delays and gaps in access have measurable consequences: youth with autism and unmet mental health needs have 58% higher odds of emergency department utilization, and racial and ethnic minorities face significantly lower odds of receiving waiver services despite equal or greater need. Whether the underlying occurrence of autism has been rising, rather than being better recognized, is a question Part II takes up directly, and one the Plan does not presume to have answered.

This Plan is written for that reality. It does not treat autism as a narrow research topic or restricted to a predominant service category. It treats autism as a federal enterprise problem requiring discovery, translation, implementation, coordination, information dissemination, and accountability. A central question is no longer only what should be studied or what program should be funded. It is what should be studied, what should be translated, what should be implemented, which agencies should lead, which authorities should be used, what deliverables should result, and how the public should know whether federal action has improved health, communication, function, safety, independence, and quality of life. Those functions need to be integrated within a framework continuum, which is what this Plan intends to offer.

Previous IACC Strategic Plans contributed to establishing a historic foundation by defining national priorities, broadening attention to neurodivergent populations and transition-age youth, incorporating co-

occurring conditions into the federal agenda, expanding consideration of equity and disparities, and creating a public record of the challenges associated with autism. That record establishes the longstanding aspirations on which this Plan builds. It also shows why a different kind of federal planning is now required.

Successive Strategic Plans, public comments, research summaries, clinical reports, and stakeholder testimony have repeatedly identified concerns about contributing factors, diagnosis, co-occurring conditions, communication access, regression, safety, workforce capacity, housing, employment, caregiver stability, transition planning, aging, and the translation of research into care and services. Too often, these priorities have remained priorities alone. They have been documented and reaffirmed without being consistently translated into agency-specific responsibilities, defined deliverables, measurable objectives, implementation timelines, performance indicators, budget alignment, or a public response. Without translation and implementation, a significant portion of the autism community faces suffering, morbidity, higher mortality, and reduced quality of life.

The 2024 Government Accountability Office report provides independent support for this conclusion. While recognizing important advances in federal coordination, GAO found that existing autism activities only partially incorporated leading practices for defining common outcomes and ensuring accountability. Strategic Plan goals had not been translated into measurable objectives against which achievement could be evaluated, and reporting mechanisms largely described activities rather than tracking progress toward intended outcomes. These findings do not suggest that federal agencies lack commitment. They show that the planning architecture has not consistently provided the operational structure needed to evaluate implementation or measure success.

This Plan therefore adopts a different organizing principle. It is a federal implementation framework. Scientific discovery remains indispensable, but discovery alone is not sufficient, especially if it is too narrowly focused. Going forward discovery should be more diversified, with an emphasis on emerging biological and translational domains highlighted later in this plan. Evidence must be evaluated according to maturity and matched to the appropriate federal response: discovery, translation, or implementation. Treating every priority as though it requires additional research delays action that may already be warranted. Treating early-stage findings as ready for broad implementation creates the opposite risk. The purpose of the discovery-translation-implementation structure is to align federal action with evidence maturity, implementation readiness, and public need.

A federal response of this kind must match the extent of need represented across the spectrum and across life. No single agency, program, or scientific discipline can meet that challenge alone. Autism requires an interconnected federal enterprise spanning biomedical research, public health surveillance, health care financing, regulatory science, workforce development, disability policy, education, employment, housing, emergency preparedness, civil rights, benefits, transportation, nutrition, family stability, and community living. NIH, CDC, HRSA, CMS, ACL, FDA, the Department of Education, and other federal partners each hold essential authorities. None holds the full set of authorities needed to address the needs of autistic individuals and their families.

Viewed separately, these responsibilities can appear fragmented. Viewed together, they form a single federal pathway from evidence to daily life. A discovery supported by NIH may require replication,

validation, standardized measures, regulatory evaluation, workforce education, clinical guidance, coverage policy, implementation support, quality measurement, and public dissemination before it changes routine care. A finding about diagnostic delay may require surveillance modernization, clinical training, state technical assistance, Medicaid implementation, school coordination, and public navigation before it changes access. The same principle applies to housing, employment, communication access, transition planning, caregiver support, safety, and aging services.

The coordination problem is structural: authorities, funding streams, expertise, and responsibilities are distributed across departments and operating divisions. Scientific findings may remain within the research enterprise. Clinical guidance may develop separately from reimbursement policy. Workforce education may not reflect emerging evidence. Surveillance systems, quality measures, public navigation, and implementation activities may evolve in parallel rather than as components of a unified strategy. No family should be expected to navigate that fragmentation without an accessible and coherent public structure.

The success of the Plan should not be measured simply by number of grants awarded, publications produced, or meetings convened. Those may be necessary steps, but they are not the final outcome. Success should be measured by whether federal action produces earlier recognition, stronger understanding of contributing factors, appropriate care for co-occurring conditions, improved access to specialty care, better coordinated services, more effective translation of discovery, reduced preventable morbidity and mortality, greater functional stability, and improved quality of life across the life course. But every one of those goals rests on a prior question that remains unanswered: how much of the rising prevalence reflects a true increase in incidence — a question that bears on every projection, every resource decision, and every priority in this Plan.

From Discovery to Translation: Matching Federal Action to Evidence Maturity

Scientific maturity changes the appropriate focus of federal action. Advances in genetics, immunology, metabolism, neuroimmunology, maternal-fetal biology, environmental health, systems biology, data science, biomarker development, artificial intelligence, and precision medicine now permit investigation of biologically defined subgroups and modifiable pathways that were not feasible when prior plans were developed. The objective of a mature research enterprise is not simply to continue generating knowledge in areas already well developed. It is to determine how existing knowledge should be integrated, validated, translated, implemented, evaluated, and expanded in ways that measurably improve health and functional outcomes.

Discovery remains indispensable. But discovery is one component of a broader translational continuum. Unless new knowledge progresses through validation, clinical investigation, regulatory science, workforce education, reimbursement policy, implementation, and longitudinal outcome assessment, many advances remain confined to the research literature without producing corresponding improvements in clinical care, public health practice, services, safety, or quality of life.

This Plan therefore distinguishes among three different kinds of federal action.

Discovery priorities address questions for which important scientific uncertainty remains. These recommendations seek to generate new knowledge regarding biological mechanisms, contributing factors,

biomarkers, therapeutic targets, clinical trajectories, subgroup differences, or interventions before broader translation or implementation is appropriate.

Translation priorities address areas in which evidence has matured beyond basic discovery but has not yet been consistently incorporated into clinical practice, public health systems, coverage policy, regulatory pathways, workforce training, quality measurement, or service delivery. These recommendations focus on evidence synthesis, assay harmonization, multicenter validation, comparative effectiveness, regulatory science, clinical guidance, workforce education, surveillance modernization, and dissemination.

Implementation priorities address circumstances in which sufficient statutory authority, evidence, or federal infrastructure already exists, but coordination, accountability, operational guidance, coverage, technical assistance, public navigation, or consistent execution remains incomplete. These recommendations frequently involve interagency coordination, demonstration programs, state guidance, reimbursement policy, quality improvement, data interoperability, public reporting, and technical assistance.

A recommendation directed toward novel biomarker discovery should not be expected to produce the same federal product, or be evaluated using the same measures, as one directed toward existing evidence for clinician education, Medicaid implementation, communication access, housing policy, caregiver support, or public navigation. Each recommendation should carry expectations appropriate to its stage of development.

The practical purpose of this structure is to prevent two failures at once. The first failure is treating every unmet need as though it requires more research, even when existing authority or evidence already supports federal action. The second failure is treating promising but preliminary findings as though they are ready for broad implementation before validation, safety review, clinical guidance, workforce capacity, coverage policy, or outcome measurement exists. Both errors slow progress and can weaken accountability.

When any portion of this pathway is absent, progress slows regardless of the quality of the underlying science. The role of this Plan is to make that pathway explicit: what is known, what remains uncertain, what should be validated, what should be translated, what should be implemented, who should lead, what product should result, and how the public should know whether the federal autism enterprise has produced meaningful improvement.

Rebalancing the Portfolio: Gaps, Duplication, and Budget Alignment

The federal autism research portfolio should now be evaluated not only by how much activity it supports, but by whether that activity is distributed across the full discovery-to-implementation pathway and aligned with the scale, complexity, and unmet needs of the autism population. The question is not whether basic science should continue. It should. The question is whether the current portfolio gives sufficient weight to the areas most likely to produce diagnostic, therapeutic, clinical, service, safety, and life course benefit.

An internal Committee analysis of FY2025 RCDC-based portfolio analysis indicates that NIH autism-related funding remains concentrated toward the upstream end of the research pipeline. In one project-level analysis of 617 unique FY2025 autism projects (622 NIH RCDC autism grants, minus 5 duplicates) totaling approximately $339 million, genetics, and genomics accounted for 38.5% of funding, basic neuroscience for 14.5%, clinical research and phenotyping for 19.4%, intervention and treatment development for 13.9%, services and supports for 6.4%, epidemiology and population health for 1.3%, environmental factors for 5.8%, and infrastructure, methods, and workforce for 0.3%. Only 12.8% of funding had a primary co-occurring condition focus, while 61.1% had no specific co-occurring condition focus. (See Appendix, “Method of Record 1.”)

This distribution reveals a translation gap. As part of the same analysis of FY2025 NIH RCDC autism grants, found that approximately 40% of funding sits in molecular and animal-model research, while only 12% reaches intervention testing or services, and intervention testing alone accounts for roughly 6%. The highest-stakes daily-life concerns receive sparse investment: suicidality, aggression, feeding, self-injury, and wandering or elopement were represented by very small numbers of projects. This preliminary project-level classification is distinct from the broader NIH autism categorical-spending estimate used in the funding-comparison table; RCDC categories and portfolio classification methods should be interpreted according to their stated methodology and limitations. (See Appendix, “Method of Record 1.”)

The imbalance is not solely a matter of research stage; it also reflects research focus. A separate internal Committee analysis first classified FY 2025 RCDC autism projects according to whether they addressed etiology (causation) and then further categorized the etiologic projects by the type of causal factor investigated. Of the $184 million identified as etiologic research, $119 million supported exclusively genetic research, $39 million gene–environment research, $21 million exclusively non-genetic research, and $5 million epigenetic research. In that classification, for every dollar NIH invested in pure non-genetic autism research, it invested nearly six dollars in pure genetic research. A related translational-distance analysis found that 88% of autism research funding sat in discovery stages, while delivery-stage research accounted for 12%. (See Appendix, “Method of Record 2.”)

These analyses track with an NIH Funding Portfolio analysis by Autism Speaks which, using a 2024 CARES Act framework, found that for FY 2024, 80% of research budget dollars touched on foundational, basic science.

These findings should not be read as an argument against genetics, neuroscience, animal models, or basic biology. Nor should they be read as an argument against mechanistic discovery. Rather, they support a more diversified discovery portfolio that preserves genetic research while deliberately broadening the focus to include emerging biological domains such as immune function, the microbiome, mitochondrial and cellular metabolism, and their relevance to both core autism features and co-occurring conditions. They should be read as an argument against allowing repeated upstream activity to substitute for strategic progress or to outpace translation into clinical validation, implementation, and measurable public benefit. The portfolio should distinguish between research that fills an unanswered mechanistic gap, research that repeats a well-developed line of inquiry without a clear translational endpoint, and research that is positioned to generate a federal product such as a validated biomarker, clinical trial infrastructure,

evidence review, care pathway, quality measure, regulatory pathway, coverage analysis, workforce curriculum, service model, or public health implementation tool.

The same gap appears in community input. The 2024 IACC Request for Information on co-occurring conditions produced 1,254 respondents and 8,778 response entries. Respondents repeatedly identified sleep disorders, gastrointestinal conditions, pain, ADHD, anxiety, depression, suicidality, sensory processing, aggression or self-injury, EDS or hypermobility, dysautonomia/POTS, immune conditions, feeding disorders, communication barriers, service access problems, insurance barriers, and provider knowledge gaps. Yet the analysis found that the 2023 Strategic Plan's formal recommendations did not name any biological condition as a funding target with a quantitative metric or deadline; even domains mentioned frequently in narrative were often not converted into directive federal action.

The precision-medicine language in prior planning illustrates the problem. References to biomarkers, subgroups, and precision medicine are useful only if they are attached to the federal mechanisms required to make them real: targeted RFAs or NOFOs, assay harmonization, validation milestones, FDA engagement where appropriate, CMS coverage analysis where reimbursement is implicated, clinical-practice pathways, workforce training, and public reporting. Without those mechanisms, precision-medicine terminology remains aspirational rather than operational.

Rebalancing therefore requires a formal gap-and-duplication review. The annual autism portfolio review should identify not only what NIH and other agencies fund, but what distinct federal purpose each activity serves. It should ask whether funded work is producing new discovery, translational infrastructure, clinical validation, implementation tools, or measurable outcomes. It should identify areas of possible duplication or low-yield repetition, including repeated descriptive studies without implementation products, repeated pilot projects that do not mature into trials or guidance, repeated discovery investments without validation pathways, and clinical, regulatory, coverage, or workforce follow-through.

GAO's findings reinforce this need. GAO found that NIH-supported autism coordination only partially followed leading practices related to accountability, and that IACC Strategic Plans generally had not described how progress related to goals. GAO also found that the Office of National Autism Coordination lacked written procedures for reviewing federal autism information for potential duplication. GAO now reports that HHS provided finalized procedures for monitoring potential duplication in July 2025. The remaining task is to use those procedures publicly to identify where duplication exists, where funding remains misaligned, and where high-need gaps require RFAs, NOFOs, evidence reviews, interagency initiatives, or implementation products.

The Autism CARES Act of 2024 further strengthens this obligation by requiring the Strategic Plan to include proposed budgetary requirements and recommendations to prevent unnecessary duplication, while also directing the NIH Director to prepare annual autism budget estimates for FY2026 through FY2029 pursuant to the Strategic Plan. Portfolio analysis is therefore no longer solely an exercise in describing current investment. It is part of the statutory process through which future federal priorities, funding, and implementation are evaluated.

Rebalancing is about shifting the allocation among existing resources. An open question remains: are the Federal Government and NIH spending enough on autism? Does the total allocation itself need to

increase? There are many ways to approach this question. One economic one is to compare the spending on a condition to its economic burden.

Economic burden and societal cost estimates are not fully comparable across conditions. They differ in the years they describe, in the methods used to value informal care and lost productivity, and in whether they measure costs attributable to a condition or total costs incurred by people living with it. Dollars may not be adjusted to a common year. The comparisons below are therefore illustrative rather than definitive.

In FY2024, NIH invested approximately $3.86 billion in research on Alzheimer's disease and related dementias. The estimated annual economic cost of Alzheimer's and other dementias is roughly $797 billion — approximately $384 billion in direct health and long-term care costs, plus an estimated $413 billion in the value of unpaid family caregiving. Expressed as a ratio of NIH investment to annual economic cost, Alzheimer's and related dementias receive about 0.48%. In the same year, NIH invested approximately $305 million in autism research against an estimated annual economic cost of approximately $461 billion — a ratio of about 0.07%, or roughly seven cents in research for every $100 in annual economic cost. Autism's burden-adjusted research investment is therefore roughly one-seventh that of Alzheimer's. Funded at Alzheimer's investment-to-burden ratio, annual NIH autism research would be approximately $2.2 billion. This comparison likely understates the disparity. The $797 billion figure counts all care costs for people living with dementia, not only the costs attributable to dementia itself; a narrower accounting would widen, not narrow, the gap. While the cost definitions are not directly comparable, the estimates nevertheless provide a reasonable basis for assessing the direction and approximate magnitude of the disparity.

Asthma offers a second comparison. In FY2024, NIH invested approximately $270 million in asthma research—an amount roughly similar to its investment in autism research—against an estimated annual economic cost of approximately $82 billion, the most recent national estimate, based on 2013 data. The investment-to-burden ratio for asthma is approximately 0.33%, roughly five times the corresponding ratio for autism. If autism research were funded at the same investment-to-burden ratio as asthma, annual NIH funding would be approximately $1.5 billion.

The parallel between autism and dementia goes beyond budget figures. Emerging data point to the possibility that individuals with autism, and particularly those with profound autism, may be at increased risk for dementia. The two populations also converge on need and then diverge sharply in duration. More than one in four children with autism meet criteria for profound autism, a group requiring 24-hour access to a caregiver — a support intensity that likewise characterizes much of the dementia population. But dementia is overwhelmingly a condition of later life. Profound autism is present from early childhood and persists across the lifespan. Lifetime estimates reflect the asymmetry: the total lifetime cost of care for a person living with dementia is estimated at approximately $400,000, while the lifetime cost of supporting an individual with autism and co-occurring intellectual disability has been estimated at $2.4 million. The largest components of that cost in adulthood are not medical treatment but residential care and lost productivity — precisely the domains where federal capacity is thinnest.

Comparisons should not be treated as rigid funding formulas. Conditions differ in prevalence, biology, mortality, available treatments, prevention pathways, private-sector investment, and research maturity.

But research investment compared to annual economic cost provides a reasonable burden-adjusted benchmark. Autism's federal research investment relative to its economic burden stands out as an outlier.

This is not an argument for increasing funding without discipline. Increased funding without portfolio correction would risk expanding the same imbalance. The point is that autism research is both underfunded and misaligned relative to the scope of need and to the realities of stakeholders, expressed in decades of IACC public comments and responses to RFIs. Budget growth should be linked to specific objectives.

The federal autism enterprise should therefore conduct an annual portfolio and budget-alignment review. That review should identify which areas are over-concentrated, which are duplicative or low-yield, which high-need areas remain underfunded, which projects are positioned to produce usable federal products, and what level of investment is required to move priority domains from discovery to translation to implementation. Rebalancing should not mean abandoning discovery. It should mean funding discovery, translation, and implementation at levels proportionate to the scale of autism and organized around measurable improvements in health, function, communication, safety, independence, caregiver stability, and quality of life.

Recommendation Structure and Plan Architecture

This Plan is organized as a coordinated federal implementation strategy. Every major life course recommendation in this Plan follows a common structure. Each identifies the problem being addressed, the maturity of the supporting evidence, the category of federal action required, the lead federal agency, supporting agencies whose participation is necessary, existing statutory or regulatory authority where applicable, the anticipated federal deliverable, implementation timeline, measurable output indicators, meaningful outcome measures where feasible, subgroup and equity considerations, dependencies or limitations, and a mechanism for public reporting.

This structure does not expand the statutory authority of the IACC. It strengthens the Committee's advisory role by making recommendations specific enough to inform implementation, evaluation, budget alignment, future planning, and public accountability in better alignment with the CARES Act. A recommendation does not become binding because it names a lead agency, identifies an authority, proposes a deliverable, or establishes a timeline. It becomes a more useful federal planning tool.

The same questions should be asked across the Plan. What problem is being addressed? What evidence exists? Is the barrier scientific uncertainty, failed translation, or failed implementation? Which agency is positioned to lead? Which agencies must participate? What authority supports the action? What federal product should result? How will progress be measured? How will autistic individuals and families know that the action changed something that matters?

Part I establishes the organizing logic of the Plan: the federal autism enterprise, the discovery-translation-implementation sequence, the three categories of federal action, the common recommendation structure, and the accountability posture that governs the recommendations that follow.

Part II establishes the scientific and public health foundation. It addresses autism epidemiology, heterogeneity, contributing factors, developmental timing, biological complexity, co-occurring conditions, and neurodevelopmental regression. Its purpose is not to provide an exhaustive scientific review. Its purpose is to establish the evidentiary basis for federal action and to explain why the next phase of federal planning must account for subgroups, mechanisms, biological states, functional needs, and longitudinal trajectories.

Part III establishes the translational infrastructure. It introduces the National Autism Precision Therapeutics Initiative as the proposed national framework for biomarker-informed therapeutic development, multicenter clinical investigation, shared data standards, regulatory coordination, implementation science, and longitudinal outcome evaluation. NAPTI is the mechanism through which discovery biology can move into validated biomarkers, stratified clinical investigation, regulatory pathways, clinical care, and measurable improvements in health and function.

Part IV applies that framework to priority therapeutic and clinical domains. Each domain identifies the state of evidence, remaining gaps, translational readiness, agency roles, deliverables, and outcome-oriented performance indicators. The purpose is to determine which domains remain discovery questions, which are ready for validation or clinical investigation, and which require implementation tools, guidance, coverage analysis, workforce training, or quality measurement.

Part V addresses federal navigation, diagnostic access, and life course supports. It begins with Autism.gov as the federal front door for navigation and accountability, then addresses diagnostic modernization, special education, mental health and suicide prevention, communication access, housing, caregiver supports, employment, aging, and other systems that determine whether autistic individuals and families can use the care, services, and protections that federal policy promises. Autism.gov should not function only as an informational website. It should operate as a public navigation, coordination, and accountability platform that makes agency responsibilities, implementation milestones, research opportunities, clinical guidance, public resources, and deliverables visible in one place.

Part VI establishes the concluding accountability framework: how implementation should be monitored, progress evaluated, agencies coordinated, and public reporting conducted, and how future updates should distinguish among recommendations that are completed, in progress, require modification, or have not advanced. Its purpose is to ensure that evaluation occurs throughout the planning cycle, rather than becoming a retrospective description at its conclusion.

Three threads run through the entire Plan. NAPTI supplies the translational infrastructure connecting evidence to priority domains and functional outcomes. Autism.gov supplies the public interface and accountability dashboard that makes federal responsibility visible. The common recommendation structure applies across every domain and support system, so that a recommendation about biological mechanisms and a recommendation about housing are written, assigned, and measured with the same discipline.

Taken together, the Plan describes a single pathway: what is known, what must be built, what individuals and families can use, what supports surround them across life, and how the public can hold the federal enterprise accountable. The purpose is to provide the Secretary of Health and Human Services, federal agencies, Congress, stakeholders, and the public with a coherent implementation framework capable of translating scientific knowledge into coordinated federal action and measurable improvements in health, function, communication, independence, safety, quality of life, and lifelong outcomes.

The objective of this Strategic Plan is not to replace the scientific achievements of previous decades, but to build upon them. Earlier investments created the knowledge base necessary for today's opportunities in biomarker development, precision medicine, implementation science, regulatory pathways, clinical guidance, and integrated systems of care. The next phase of federal leadership should ensure that these advances are translated into measurable improvements in health, function, communication, safety, independence, and quality of life.

Part II — Discovery Biology and the Case for Precision Translation

Part II establishes the scientific foundation for the strategy that follows. Autism is heterogeneous and biologically complex. Genetic findings identify susceptibility, developmental context, and biologically relevant pathways rather than a fixed or unitary cause. For the past two decades, federal autism research has placed substantial emphasis on genetics while comparatively underinvesting in other emerging biological and clinical domains. Recent research and clinical observations suggest that these areas may also play important roles in autism and hold significant potential for near-term scientific advances, therapeutic development, and improved clinical care. This section identifies and highlights several of these priority areas that warrant substantially increased federal investment.

There is substantial agreement among both researchers and scientific studies that autism is not singularly caused by genes or environment, but that rather the function and nature of each contribute substantially. Moreover, the heterogeneity from individual to individual suggests that no single answer will apply to all. Therefore, casting a wider net with a more diversified research agenda is most likely to help the most individuals.

In addition to its biological underpinnings, developmental timing shapes whether biological vulnerability becomes lasting change. Accordingly, neurodevelopmental regression should be treated as a clinically identifiable, developmentally timed, and biologically informative event that makes the need for precision infrastructure visible which this Part II further highlights.

Understanding Autism: Epidemiology, Heterogeneity, and Contributing Factors

Part I established the organizing framework for a modern federal autism enterprise by defining the relationship between scientific discovery, translation, implementation, and measurable public outcomes. It argued that the principal challenge facing the federal government is no longer simply generating knowledge but determining how existing and emerging evidence should be translated into coordinated federal action that improves health, communication, function, safety, independence, and quality of life across the life course.

Part II establishes the scientific and public health foundation upon which those actions are built. Its purpose is not to provide a comprehensive review of autism research or to catalog every biological hypothesis that has been proposed over the past several decades. Rather, it examines the current state of scientific knowledge through the lens of federal decision-making. The central question is not simply what is known about autism, but what the evidence means for surveillance, research prioritization, clinical translation, implementation, and long-term federal planning.

The chapters that follow build this scientific foundation in sequence. They examine autism as a heterogeneous neurodevelopmental condition; evaluate the interacting genetic, biological, developmental, and environmental factors that shape individual outcomes; establish neurodevelopmental regression as a clinically informative developmental phenotype; and demonstrate why this evidence requires a

coordinated federal strategy for precision translation. Together, they provide the scientific rationale for the translational infrastructure, implementation priorities, and federal actions presented in the remainder of this Strategic Plan. For federal planning, the implication is direct: that surveillance, research portfolios, clinical translation, and implementation systems should be organized around biologically and clinically meaningful subgroups, developmental timing, co-occurring conditions, and measurable outcomes rather than diagnosis alone.

Autism Epidemiology and Public Health

The federal response to autism must begin with an accurate understanding of the population it is intended to serve. Epidemiology provides more than estimates of prevalence; it defines the scale of need, characterizes patterns of health and disability across the population, identifies disparities in diagnosis and access to care, and informs decisions regarding research investment, workforce development, clinical infrastructure, public health surveillance, and service delivery. As autism prevalence has continued to increase over successive birth cohorts, one question has become central to all of these: how much of that increase reflects a true increase in incidence. The answer determines not only how many individuals require services, but also whether existing federal systems are adequately equipped to meet current and future demand.

After more than two decades of rising birth-cohort prevalence, the federal enterprise must begin to answer the question directly: how much of the dramatic rise in autism is real? Autism identification in the United States has risen from approximately 1 in 150 children in 2000 to 1 in 31 in 2022—a roughly fivefold increase. A 1996 CDC prevalence study in metropolitan Atlanta, using the active surveillance methods that would become the basis for the ADDM Network, found a prevalence of approximately 1 in 300. A contemporaneous CDC investigation in Brick Township, New Jersey, conducted in response to community concern, found a full-spectrum prevalence of 6.7 per 1,000 (1 in 150) among children aged 3–10 in 1998—a figure the ADDM Network would confirm at the national level in its first surveillance year (2000). Across its surveillance years, the ADDM Network has applied a consistent active case-finding framework—the same age group, the same records-based ascertainment—making its serial estimates far more comparable over time than counts drawn from clinical or administrative sources. Over that same period, profound autism—minimal or no functional speech and/or IQ below 50—rose from 2.7 per 1,000 in 2000 to 4.6 per 1,000 in 2016.

If the rise reflects, even in part, a true increase in incidence, demand on health care, education, housing, and long-term supports will keep growing beyond what current planning anticipates, and the search for contributing and modifiable causes becomes urgent. Because autism has no directly observable moment of biological onset and because of a host of other factors, incidence is challenging to measure directly; birth-year prevalence—the cumulative share of a birth cohort identified by a fixed reference age—is its practical proxy. Although several explanations have been offered for why the rise might not represent a true increase, none appears able to fully account for its magnitude.

Greater awareness and earlier identification clearly affect when children are identified, but may not fully explain the number ultimately identified. Age at diagnosis has fallen even as cumulative birth-cohort prevalence has continued to climb; awareness finds children sooner without raising the total a cohort ultimately reaches. Diagnostic substitution, the relabeling of children from other categories, would require those categories to fall in step. Intellectual disability (ID) prevalence has remained stable, and, where directly measured, autism with co-occurring ID has risen rather than fallen. The one study attributing even a quarter of the increase to substitution assumes that rate rather than deriving it from the data. Broadened diagnostic criteria would predict that each revision of the manual admitted more children; applied to the same children, successive criteria in fact identify slightly fewer, and the rise both precedes and outlasts every criteria change.

The proffered explanation that most resists direct test, and that therefore requires the most careful consideration, is that of diagnostic oversight: the claim that autistic individuals existed at today's rates in earlier decades but went uncounted, so that current figures reflect the discovery of a previously hidden population rather than a real increase. The arithmetic of this claim deserves scrutiny. If today's rate of approximately 1 in 31 reflects the true underlying rate, and the measured rate in 2000 was 1 in 150, then roughly 80% of all autistic children in earlier cohorts would have gone unidentified. It is plausible—even likely—that a portion of that unidentified share comprises individuals with subtler presentations who may not have been diagnosed with autism. But better recognition of milder cases cannot, by itself, account for the full magnitude of the change. Contemporary data indicate that 25–30% of individuals with autism are minimally verbal, and a substantial proportion have diagnosed intellectual disability. These are not subtle presentations. Proportionally applied to earlier cohorts, the diagnostic-oversight hypothesis requires that large numbers of children with profound functional impairment—limited or no speech and requiring intensive daily support—would have gone undetected. That would require not just missed diagnoses, but missing systems: an entire generation of individuals who needed intensive, lifelong support passing through pediatric care, schools, and communities without recognition. This hypothesis is not readily supported by available evidence.

None of this proves that the entire rise in prevalence is driven by a true increase in incidence. Each explanation offered for the increase is likely partly true: awareness has improved, access to diagnosis has widened, and individuals with milder core symptoms may well have been missed in earlier years. And these factors may act synergistically. But because these explanations cannot fully account for the rise, and because the answer carries enormous implications, the federal enterprise must be oriented toward resolving the question.

The rising autism trend has not unfolded in isolation. Over the same decades, a range of chronic and immune-mediated conditions of childhood has risen as well. The incidence of type 1 diabetes in children has climbed roughly 2–3% per year globally, with US prevalence among youth rising about 45% between 2001 and 2017. Childhood food and environmental allergies have increased substantially: food allergy now affects on the order of 8–10% of children in Western countries, and allergic rhinitis and atopic dermatitis have risen globally. Pediatric inflammatory bowel disease has risen sharply worldwide, and US prevalence

more than doubled—from about 33 to 77 per 100,000—between 2007 and 2016. Autism itself has been increasingly linked to a range of immune changes, from maternal immune activation in pregnancy to neuroinflammation and altered immune profiles in autistic individuals. These parallel trends warrant cautious interpretation but raise a question this Plan takes seriously, addressed in Contributing Factors and Causality: whether shared or overlapping vulnerabilities involving immune function may contribute to these concurrent patterns.

There are other important questions that counting alone cannot answer. Knowing how many individuals meet diagnostic criteria says little about who they are, what they need, or what drives their symptoms. Autism is profoundly heterogeneous. Co-occurring conditions are the norm rather than the exception: over 90% of autistic children have at least one medical, developmental, or psychiatric condition—gastrointestinal disorders, sleep disturbance, epilepsy, ADHD, and anxiety among the most common—and these drive health care utilization, complicate treatment, and reduce quality of life, particularly among those with the highest support needs. This clinical variation rests on biological variation—genetic, immune, metabolic, mitochondrial, gastrointestinal, and synaptic—best read not as competing theories of autism but as evidence that it arises through multiple convergent mechanisms whose contributions differ across individuals.

Yet current surveillance captures diagnostic status far more completely than this clinical or biological detail. Severity is inadequately tracked: profound autism, non-speaking and minimally speaking individuals, regressive autism, and adolescents and adults across the life course remain poorly characterized, as do the co-occurring conditions that most affect health, cost, and quality of life, the extent of undiagnosed autism and misdiagnosis, and recent shifts in who is being identified. These are not scientific unknowns awaiting discovery; they are gaps that surveillance design and intentional analysis can close, and they are not peripheral—they determine whether federal data systems can identify subgroups with distinct needs and support translational research.

More granular, biologically informed data would also make the search for causes more fruitful, giving mechanistic research better-defined populations to study rather than a single undifferentiated diagnosis. Future federal investments should therefore support epidemiologic approaches capable of integrating clinical phenotyping, longitudinal observation, molecular biomarkers, environmental assessment, genomic information, health services research, and real-world outcomes. Surveillance should emphasize characterization alongside enumeration; the biological mechanisms at issue are taken up in Contributing Factors and Causality. Epidemiology can serve as the bridge between population health and translational science.

Federal Priorities for Autism Epidemiology and Population Characterization

Federal autism epidemiology should now be organized around two linked tasks: determining how much of the observed rise in autism reflects a true increase in incidence, and characterizing the autism population with sufficient clinical, developmental, biological, and functional detail to guide research, services, and implementation. The priorities below translate these tasks into broad constructs for agency consideration,

identifying potential actions, deliverables, and performance indicators to be refined through methodological review, feasibility assessment, and implementation planning. We recognize these priorities would incur additional appropriations beyond current levels, our recommendation is an additional $30M additional investment to better ascertain autism epidemiology.

Priority 1.1 — Evaluate the observed increase using data already in hand

Much can be learned about the increase in autism from existing federal data, without establishing new surveillance systems. This priority focuses those data on a central question—how changes in diagnostic timing, identification, and underlying occurrence may each have contributed to observed trends—through a coordinated series of analyses that compare autism occurrence over time while holding the underlying population, geographic area, or administrative system as constant as possible.

Lead Agency: CDC / NCBDDD (ADDM Network), with the U.S. Department of Education (IDEA data) and the California Department of Developmental Services.

Deliverable: A suite of analyses using existing data —

1. Core decomposition. Birth-year-prevalence and age-at-diagnosis (time-to-event) analysis of the ADDM Pooled Dataset (birth cohorts 1992–2018), separating changes in the probability of diagnosis from changes in true birth-year prevalence.
2. Metropolitan Atlanta (MADDSP). Compile and analyze the MADDSP autism time series for birth years 1986–2014, comparing ASD trends with other developmental disabilities for the birth cohorts in which comparable data are available and evaluating diagnostic substitution, including ASD–intellectual disability overlap, through the latest available comparable cohort.
3. California (ADDM × CDDS). Assess the feasibility of site-level linkage or aggregate comparison of California ADDM and CDDS data, subject to applicable authority and data-use agreements. Where feasible, compare trends within overlapping geographic areas and document differences in definitions, ascertainment, population coverage, and available data.
4. Historical reconstruction and triangulation. Compare modern ADDM estimates with earlier published estimates from Wisconsin (Treffert 1970), Utah (Ritvo et al. 1989), Missouri (Hillman et al. 2000), and other locations where geographic correspondence can reasonably be assessed. Treat these comparisons as triangulation and sensitivity analyses—not as directly commensurable prevalence series—and explicitly document differences in case definition, ascertainment, and population.
5. National contextual comparison. Conduct descriptive comparisons of ADDM and IDEA data at corresponding state and national levels, explicitly accounting for differences in purpose, eligibility, age, geography, and ascertainment rather than treating them as directly commensurable prevalence estimates.

KPI: Independent methodological and feasibility review completed within 12 months; core ADDM analysis initiated within 24 months; and supporting same-place analyses undertaken as data access, funding, and comparability permit.

Priority 1.2 — Strengthen and expand ADDM surveillance

Lead Agency: CDC / NCBDDD.

Deliverable: Implement, as feasible, enhancements to the ADDM surveillance model

6. Continue current records-based ADDM surveillance at all sites for age-4 and age-8 cohorts.
7. Restore active surveillance at selected sites with independent case determination and a validation component using independent clinical assessment to quantify sensitivity, specificity, and rates of undiagnosed autism and misdiagnosis. These sites should also extend surveillance to age 16 to identify undiagnosed adolescents, characterize transition-age outcomes, and evaluate the added value of continued age-based follow-up.
8. Develop and test standardized, feasible definitions for developmental regression, language and communication status, profound autism, co-occurring conditions, and adaptive functioning and expand these data elements across sites.
9. Develop and implement a phased plan to restore multi-disability tracking—including ID, CP, and ADHD alongside ASD—with the surveillance definitions and resources needed to evaluate diagnostic substitution and compare trends across conditions.
10. Conduct focused analysis of the reversal in racial/ethnic and socioeconomic prevalence patterns assessing the extent to which observed changes reflect improved identification, differential exposure, or other factors.
11. Expand access to the ADDM Pooled Dataset to qualified external investigators, consistent with applicable site agreements and data-source restrictions.

KPI: Validation protocol, standardized expanded-data definitions, and resource plan completed within 18 months; active surveillance with expanded data elements implemented at ≥4 selected sites by the 2029 cycle; validation study completed within 36 months; and first age-16 estimates published by 2032.

Priority 1.3 — Build prospective incidence measurement into a larger investigation of contributing factors

Improving prospective measurement of temporal changes in autism occurrence requires following successive birth cohorts. That measurement should be incorporated into a larger federal investigation of

contributing factors—one designed to track biomarkers, developmental trajectories, environmental exposures, and co-occurring medical conditions from birth. Such a cohort could strengthen prospective estimates of incidence while generating the biological and exposure data needed to investigate causation.

Lead Agency: NIH (NICHD lead, with NIEHS, NIMH) in coordination with CDC.

Deliverable: Following formal power, representativeness, and feasibility analyses, establish or build upon existing pregnancy- and birth-cohort infrastructure for a multisite prospective cohort. Sample size, number of sites, enrollment waves, and follow-up intervals should be determined by the analyses and be sufficient to evaluate temporal trends and prespecified subgroups. The cohort should incorporate standardized developmental assessments, maternal and neonatal biospecimens, environmental-exposure assessment, and medical-record linkage where permitted.

KPI: Formal study-design, power, representativeness analyses, and budget requirements completed within 18 months; initial enrollment initiated within five years; and the timing of subsequent waves and comparative estimates established by the approved study protocol.

Domain 2: Characterizing the Autism Population

Priority 2.1 — Linkage of surveillance to biological and environmental data

Lead Agency: NIH (NIEHS lead, with NICHD, NIMH) in coordination with CDC.

Deliverable: At sites participating in ADDM and compatible pregnancy or birth cohorts, assess the legal, technical, and operational feasibility of person-level or appropriately aggregated linkage of de-identified data. Where feasible and permitted, pilot linkage to selected high-priority data sources, including genomic data, newborn-screening biospecimens, environmental-exposure databases, claims, registries, hospital data, and maternal health records.

KPI: Feasibility and governance assessments completed at three or more sites within 24 months; at least one linkage pilot initiated within 36 months where approvals and data permit; and subsequent data-access and publication timelines established from the pilot findings.

Priority 2.2 — Life Course prevalence: adolescents, young adults, and adults

Lead Agency: CDC / NCBDDD in coordination with ACL (Administration for Community Living), CMS, SSA, and the Department of Education.

Deliverable: Develop and implement a coordinated federal strategy to produce the first methodologically sound estimates of autism prevalence beyond childhood. No existing federal system measures autism prevalence among adults, leaving the nation unable to project the scale of services, housing, healthcare, and support the growing population will require. This priority has two components—

12. Longitudinal follow-up of individuals previously identified by ADDM at age 8 and/or 16, focusing on functional status in young adulthood, co-occurring conditions, and the needs of individuals with profound autism across the life course with attrition and the resulting limits on prevalence inference reported explicitly.
13. A cross-agency feasibility assessment of linked administrative data and population-based screening approaches, followed by phased pilots in defined geographic areas where data access and linkage quality are sufficient.

KPI: Cross-agency feasibility and methods plan completed within 24 months; two or more ADDM sites conducting young-adult follow-up by 2029; and a timetable for federal adult-prevalence estimates established on the basis of data availability and methodological review.

Federal Priorities for Autism Epidemiology: The actions and timelines summarized below are planning constructs and remain subject to methodological review, feasibility assessment, data access, governance approval, agency authority, and available appropriations.

Lead Agency	Deliverable	Key Performance Indicator
Domain 1 — How Much of the Rise Is Real		
CDC (NCBDDD), with Dept. of Education (IDEA) and California DDS	Core analysis. Subject to independent methodological review of the assumptions, data requirements, and interpretive limits, analyze birth-year prevalence and age at diagnosis in the ADDM Pooled Dataset to estimate how changes in the timing and probability of diagnosis may have contributed to observed birth-cohort trends.	Independent methodological and feasibility review completed within 12 months; core ADDM analysis published within 24 months; and supporting analyses completed within 18–24 months as data access and comparability permit.
NIH (NICHD lead, with NIEHS, NIMH), with CDC	As part of a larger investigation of autism causation and contributing factors, establish or build upon multisite pregnancy- and birth-cohort infrastructure following formal power, representativeness, and feasibility analyses. Sample size, number of sites, enrollment waves, and follow-up intervals should be determined by those analyses and support temporal-trend and prespecified subgroup analyses.	Formal study-design, power, and representativeness analyses completed within 18 months; initial cohort enrolled with 24-month assessments within five years; and subsequent enrollment waves and comparative incidence estimates completed according to the approved protocol, with a target of first comparative estimates within 10 years.
CDC (NCBDDD)	Enhanced ADDM surveillance: current records-based surveillance at ages 4	Validation protocol, standardized expanded-data definitions, and resource

Lead Agency	Deliverable	Key Performance Indicator
	and 8; active surveillance restored at ≥4 selected sites with independent case determination and a validation component; age-16 coverage; standardized expanded data elements; phased restoration of multi-disability tracking; analysis of racial, ethnic, and socioeconomic patterns; and expanded Pooled Dataset access consistent with applicable agreements.	plan completed within 18 months; active surveillance with expanded data elements implemented at ≥4 selected sites by the 2028 cycle; validation study completed within 36 months; and first age-16 estimates published by 2031.
Domain 2 — Characterizing the Population Across the Life Course		
NIH (NIEHS lead, with NICHD, NIMH), with CDC	At sites participating in ADDM and compatible pregnancy or birth cohorts, assess the legal, technical, and operational feasibility of person-level or appropriately aggregated linkage. Where feasible and permitted, pilot linkage to selected biological, environmental, clinical, and administrative data sources.	Feasibility and governance assessments completed at ≥3 sites within 24 months; at least one linkage pilot initiated within 36 months where approvals and data permit; and an initial methods or environmental-exposure analysis completed within 48 months.
CDC (NCBDDD), with ACL, CMS, SSA, U.S. Dept. of Education	Develop and implement a coordinated federal strategy to produce the first methodologically sound estimates of autism prevalence beyond childhood, combining longitudinal follow-up of ADDM-identified cohorts with linked administrative-data analysis and phased population-based screening in defined geographic areas.	Cross-agency methods and linkage plan completed within 18 months; ≥2 ADDM sites conducting young-adult follow-up by 2029; and the first federal adult-autism prevalence estimate published within 36 months using methods established through the plan.

Heterogeneity as the Organizing Principle

Heterogeneity is the organizing feature of autism biology, and it should also be the organizing feature of the federal autism enterprise. The diversity within the autistic population is not a complication to be controlled away. It is the structure that determines which findings replicate, which interventions work, and for whom.

Large cohort studies, case-control investigations, and clinical trials have generated substantial insight into genetics, neurodevelopment, behavior, and epidemiology. Yet the diversity within study populations has

repeatedly complicated interpretation. Biological signals that are robust within a defined subgroup may become attenuated or undetectable when measured across heterogeneous populations. Therapeutic effects that are meaningful for one subset may appear inconsistent when assessed without reference to the biological differences that distinguish those who respond from those who do not. Heterogeneity has therefore come to be understood not as a peripheral source of complexity but as the central consideration in study design, data interpretation, clinical translation, and federal planning.

Advances in genomics have identified hundreds of genes associated with autism susceptibility, encompassing both rare variants of large effect and complex polygenic contributions. These findings establish that no single genetic architecture accounts for autism. Different combinations of inherited and de novo variation may converge on overlapping neurodevelopmental phenotypes through distinct biological mechanisms. Heterogeneity arises not only from inherited variation but also from the developmental context within which that variation is expressed. That context includes maternal immune biology, placental function, mitochondrial resilience, epigenetic regulation, and environmental influence.

Beyond genetics, evidence from immunology, developmental neuroscience, gastroenterology, metabolism, neurophysiology, and systems biology has expanded the understanding of autism as a condition involving multiple interacting physiological systems. These findings do not imply that every discovery mechanism is present in every individual, but rather that autism encompasses numerous partially overlapping biological pathways whose contributions vary across clinically meaningful populations.

Recognition of these differences reshapes how the scientific literature should be read. Apparent inconsistencies among studies frequently reflect differences in cohort composition rather than contradictory biology, and investigations enrolling predominantly syndromic autism, profound autism, regressive autism, minimally speaking individuals, intellectually able adults, or children with prominent gastrointestinal or immune manifestations may reasonably observe different biological findings despite studying individuals who all satisfy the same behavioral diagnostic criteria—an autism diagnosis. Variation in age, developmental stage, sex, environmental exposure, co-occurring conditions, medication use, and outcome measures can likewise shape observed associations, so that the operative question is not whether a given finding is associated with autism, but in which populations that finding is relevant, reproducible, and clinically meaningful.

Behavioral diagnosis remains essential for clinical identification and access to services, but it provides limited insight into underlying biology or likely treatment response. A more precise account of any autistic population therefore integrates behavioral characterization with molecular, physiological, developmental, and clinical features, in the expectation that no single marker will define autism broadly and that combinations of complementary measures are required to distinguish meaningful subgroups. Precision in the language used to describe populations follows from the same logic, since broad comparisons between autism and controls are frequently inadequate to the questions now being asked, and a study population is

better specified by developmental stage, cognitive profile, communication status, medical comorbidity, regression history, and genetic findings than by diagnosis alone.

Heterogeneity extends beyond biology to encompass developmental trajectory and health outcome. Some autistic individuals require lifelong intensive support while others achieve substantial functional independence, communication ranges from fluent language to lifelong minimal or absent functional speech, and intellectual functioning, adaptive skills, educational attainment, employment, physical health, psychiatric comorbidity, and quality of life vary widely, differences that determine which services are needed, which outcomes matter, and which agencies must act. These same differences bear directly on therapeutic research, because interventions organized around broad diagnostic enrollment may fail to detect effects confined to biologically defined populations, whereas stratification and mechanism-matched outcomes, now well established in oncology, rare disease, and immunology, improve the ability to identify meaningful effects while limiting exposure to interventions unlikely to help a given individual.

Recognizing heterogeneity supplies a framework capable of integrating diverse observations into a coherent model of neurodevelopment in which multiple developmental pathways converge upon shared behavioral characteristics while remaining distinguishable through underlying biology, developmental history, or treatment response. Understood in this way, heterogeneity is not an obstacle to progress but the foundation on which precision medicine, targeted therapeutics, and individualized care responsibly rest, and it directly shapes the examination of contributing genetic, biological, and environmental factors that follows.

Contributing Factors and Causality

Autism is heterogeneous in its biology and its causation. The accumulated evidence supports a model in which autism arises through multiple interacting developmental pathways involving varying combinations of genetic susceptibility, biological vulnerability, environmental influence, and developmental timing. This complexity reflects not the unknowability of causation but the likelihood that autism encompasses numerous etiologic and pathogenic processes converging upon overlapping neurodevelopmental phenotypes, and it establishes developmental timing as central rather than incidental.

Neurodevelopment proceeds through tightly coordinated sequences of cellular proliferation, migration, synaptogenesis, circuit refinement, immune maturation, metabolic programming, and microbiome development. Because these processes unfold within specific developmental windows, timing matters. An exposure or biological event that occurs during a sensitive window may carry consequences that the same event would not produce later in development. Its impact may also differ across individuals, depending on genetic susceptibility, immune and metabolic resilience, cumulative biological stress, and remaining physiological reserve.

The relevant question is therefore not merely whether genes or environment contribute to autism, but how genetic susceptibility, and other biological domains, such as environmental exposures, immune

activation, metabolic capacity, microbial ecology, and developmental timing interact across critical periods to influence risk, phenotype, severity, trajectory, and long-term outcome.

Gene-discovery efforts have identified more than one hundred autism risk genes—commonly cited as 102 genes at a Bayesian false-discovery rate (FDR) ≤ 0.1, narrowing to 78 at FDR ≤ 0.05 and 26 at a Bonferroni-corrected (family-wise error rate ≤ 0.05) threshold. Common variation of small effect carries the majority of population-level risk, while rare coding variants explain only a minority of clinical cases. Even using today's most advanced tools, no specific genetic cause is identified in 75-85% percent of people with ASD, underscoring how much of ASD remains unexplained by identifiable genetic findings.

In many cases the risk genes identified converge on a limited set of biological processes, including chromatin modification, synapse structure and function, and neurogenesis in developing excitatory neurons of the human mid-gestational cortex.

That convergence is one reason a strategy confined to gene discovery would remain incomplete. The developmental pathways through which these genes act are modified by immune, metabolic, microbial, and environmental inputs. Federal strategy should therefore support gene discovery and genetic interventions where needed, but also emphasize penetrance, expression, developmental context, modifiable pathways, and translation into clinically meaningful subgroups.

The strength of the genetic contribution is frequently misread, and the distinction between heritability and genetic determinism is worth stating plainly. Twin and family studies indicate that autism is substantially heritable. This establishes that genetic variation accounts for a large share of the variance in autism liability across the population under present conditions. However, twin studies suffer from a number of methodological, widely acknowledged assumptions and biases that tend to push estimates of genetic contribution up. Moreover, heritability, is a population-level statistic about the distribution of a trait. It is not a statement about the origin of autism in any individual. It neither implies that autism can be read from the genome nor that developmental and environmental context are immaterial.

High heritability can be fully consistent with incomplete penetrance, variable expressivity, gene–environment interaction, and outcomes that remain modifiable. It coexists with two familiar observations: individuals carrying similar pathogenic variants may follow markedly different developmental courses, and many autistic individuals have no identifiable monogenic explanation. Heritability therefore establishes that genetic susceptibility is real and substantial—without establishing that genes are equivalent to autism or that they determine its expression.

This distinction matters. A strategy that treated autism as a fundamentally genetic condition to be resolved through gene discovery would misread both the biology and the opportunity, because the most consequential questions concern what modifies susceptibility, what governs penetrance and severity, and which pathways remain open to intervention.

Among the most developed of those modifying influences are the interactions between maternal health and fetal neurodevelopment. Investigations of maternal immune activation have associated infection,

inflammation, autoimmune disease, obesity, and metabolic dysfunction with altered fetal brain development under defined circumstances, with a maternal interleukin-6 and interleukin-17A axis among the more consistently implicated pathways and one large Swedish cohort reporting an approximately thirty percent increase in autism likelihood following severe maternal infection, associations whose magnitude varies across populations and which describe elevated likelihood rather than individual causation.

Maternal autoantibody reactivity is among the most advanced candidate biomarkers in autism, and the pathway from mechanistic observation to analytical validation illustrates the sequence that a federal biomarker qualification program could support. Independent of the maternal literature, postmortem neuropathology has documented innate neuroinflammation, including microglial and astroglial activation with elevated MCP-1 and TGF-β1 across cortex, white matter, and cerebellum.

Prenatal and early-life environmental exposures, considered collectively as the exposome, interact with genetic risk in part through effects on the maternal microbiome and immune system that can influence offspring neurodevelopment—illustrated by maternal microbiome effects on offspring microglia and by the dependence of maternal interleukin-17A effects on specific commensal bacteria. These are best understood as likely contributing factors.

What binds biological domains together is not a single autism-specific discovery but a well-established feature of human physiology, namely that these systems reciprocally act on one another rather than in isolation, for example immune signaling can alter cellular metabolism, microbial metabolites affect immune development, neurotransmission, and cellular energetics, genetic variation modifies the response to environmental exposure, and so on.

A perturbation in one system therefore may propagate to others rather than remaining contained, and this reciprocal interaction is the durable core of the systems account. The recurrent observation that independent metabolomic, immunologic, mitochondrial, microbial, and physiologic lines of evidence implicate the same domains is consistent with such an interacting system, and one large metabolomic study offered an integrating hypothesis in which the purine network was the most-changed of fifty pathways, but convergence of this kind is necessary rather than sufficient, since shared confounding and common upstream causes can produce the same appearance, and the weight of the systems account rests on the established biology of cross-system interaction rather than on co-occurrence alone.

Causation in autism is, on this account, heterogeneous, developmental, and conditional rather than uniform, and it is better resolved by determining which mechanisms operate in which populations, under what developmental circumstances, and through which pathways than by seeking a single universal explanation, an orientation consistent with the broader course of biomedical science in which conditions once considered uniform are increasingly understood as collections of biologically distinct subtypes.

An Integrated Developmental Systems Framework

Autism looks different from person to person, and its contributing factors interact rather than act alone. This points to an integrated developmental systems view: *autism emerges when several factors combine—biological susceptibility, the timing of development, environmental exposures, and how the body adapts to them.* This fits a broader shift across developmental biology, immunology, and systems medicine toward seeing complex conditions as the result of interacting systems, not single causes.

Development begins within a biological context established by inherited and acquired characteristics, which shape resilience and susceptibility without determining outcome and govern how an individual responds to later physiological and environmental challenge. As development proceeds, individuals encounter biological exposures and physiological stressors that vary in timing, duration, intensity, and cumulative burden. While in many individuals the adaptive response to these events resolves without lasting consequence, in others, particularly during sensitive windows, it may exceed available physiological resilience or interact with preexisting vulnerability in ways that alter developmental trajectory.

This framework also elevates resilience and recovery to the same standing as risk. The biology that allows some individuals to recover after immune, metabolic, seizure, sleep, or gastrointestinal destabilization, and the physiology that restores homeostasis after transient disturbance, are as informative for prevention and treatment as the mechanisms of vulnerability themselves. Simply stated—the *key idea is adaptive capacity—how well the body restores balance.* Because its systems are linked, overwhelming that capacity sets off a coordinated response rather than a series of separate failures. So a problem found in one system isn't necessarily a standalone defect or the cause of autism. It may be one piece of a larger reaction, and its significance can vary from one group of people to another.

Viewed through this lens, the biological domains presented throughout the remainder of the Strategic Plan are neither competing explanations for autism nor an implication that every mechanism is present in every individual. They are interacting physiological systems whose contributions vary across biologically and clinically defined populations. Organizing the federal enterprise around these interconnected systems provides an opportunity to consider biologically integrated processes.

Implications for Federal Action

Translating this science responsibly requires that federal claims be held to the standard the evidence can bear. Findings should be communicated in terms of well-established peer reviewed research, associations, probabilities, and subgroups rather than universal causation or cure. Established evidence should be distinguished from investigational evidence in every clinical recommendation. The safety, dignity, and priorities of autistic individuals and their families should remain central to research and implementation.

These commitments are not a constraint upon ambition. They are the condition of credibility. A strategy that overstates causal certainty or promises resolution beyond the evidence forfeits the trust on which sustained federal effort depends.

Within that discipline, the evidence sorts federal responsibility according to maturity. Where the issue is not scientific uncertainty but the failure to recognize and treat established co-occurring conditions, the task is immediate implementation under existing standards of care. Recognition and management of established immune, autoimmune, allergic, immunodeficiency, gastrointestinal, seizure, sleep, psychiatric, and autonomic conditions in autistic individuals should not be delayed or overlooked because an autism diagnosis is present.

Where domains such as immune function, the microbiome, mitochondrial function, and cellular metabolism remain incompletely understood, the federal response should be sustained research investment, rigorous evaluation, and development of the evidence needed to determine their relevance to core autism features, co-occurring conditions, and treatment response.

Where biomarkers and biologically defined subgroups are reproducible, the task is validation and qualification. Where mechanisms remain investigational, the task is disciplined evaluation before clinical adoption. A mature strategy neither defers established care pending further study nor advances investigational mechanisms ahead of the evidence that would justify them. Holding each finding to its appropriate stage is the discipline on which the credibility of the whole rests.

No single agency can address heterogeneity of this scope, and progress depends on coordination among the agencies responsible for basic science, clinical research, public health surveillance, healthcare delivery, regulatory evaluation, and implementation, each acting within its statutory mission toward a common translational purpose. The principal challenge is no longer determining whether autism has a single cause. It is directing existing and emerging knowledge into biologically defined populations that can be recognized clinically, characterized reliably, and served precisely. Those populations provide the basis for the translational infrastructure introduced in Part III and for the Priority Therapeutic Domains addressed in Part IV, several of which correspond directly to the immune, metabolic, folate, gastrointestinal, autonomic, sleep, and regression pathways described here.

Success should ultimately be measured not by the volume of research produced but by its translation into usable federal products and measurable health outcomes. Those products include validated biomarkers, standardized clinical evaluation for relevant cohorts, biologically stratified care, clinical guidance, quality measures, implementation tools, and reductions in preventable developmental disability and untreated co-occurring illness among autistic individuals across the life course.

Neurodevelopmental Regression: A National Priority for Precision Medicine, Early Intervention, and Therapeutic Development

Scientific Rationale

Neurodevelopmental regression represents one of the most clinically significant and biologically informative phenomena in autism research. It is characterized by the loss of previously acquired language, social communication, adaptive, or motor skills after a period of apparently typical or near-typical development. It is a frightening and distressing experience for families, and clinical observations consistently document behavioral indicators of acute distress in the individuals themselves, including new-onset irritability, sleep disruption, self-injurious behavior, and loss of engagement. Regression occurs in 30 to 40 percent of autistic children,[1] most commonly during the second year of life and is associated in many studies with greater developmental impairment, increased support needs, higher rates of co-occurring medical conditions, and poorer long-term functional outcomes. Yet there remains no standardized federal framework for identifying, evaluating, documenting, or studying this population.

For decades, regression has often been treated as a historical pattern of symptom onset rather than as a biologically important developmental event. Clinical care remains variable, definitions differ across studies, surveillance systems do not consistently distinguish regressive from non-regressive autism, and medical evaluation following developmental skill loss is not standardized. As a result, one of the most informative phenotypes in autism has remained fragmented across research disciplines and inconsistently addressed in clinical practice.

The scientific case for elevating regression is straightforward. Regression identifies a developmental transition during which measurable change is occurring. Unlike studies performed years after developmental trajectories have stabilized, prospective investigation before, during, and after regression can evaluate biological processes as they unfold. This includes immune activation, mitochondrial function, cellular metabolism, electrophysiology, neuroimaging, microbiome composition, metabolomics, transcriptomics, environmental exposures, and other pathways that may change during the period when skills are lost or recovery begins.

Current evidence does not support treating regression as a single subtype or a single mechanism. Rather, regression should be understood as a clinical phenotype that may arise through different pathways in different children. Genetic susceptibility, immune dysregulation, mitochondrial dysfunction, altered redox biology, purinergic signaling, synaptic remodeling, epileptiform activity, gastrointestinal dysfunction, maternal immune activation, environmental susceptibility, and gene-environment interactions may each be relevant for some populations. That regression marks a biologically distinguishable population is not a theoretical claim. In young children, observed elevations in circulating inflammatory cytokines were concentrated predominantly among autistic children with regression and were associated with greater behavioral impairment.[2] These findings indicate that this subgroup can be identified using existing methods and that the principal barrier to its systematic characterization is the absence of a coordinated federal framework.

Emerging preclinical work demonstrates that these pathways are not competing explanations but interacting ones. A recent study established that a genetic vulnerability in *SHANK3* that produces no

observable phenotype on its own in mice becomes behaviorally penetrant following a single systemic immune challenge, that the resulting impairment is accompanied by measurable synaptic and neuroinflammatory change, and that it is partially reversible with anti-inflammatory treatment.[3] Critically, the effect was selective rather than global, sparing some behavioral domains entirely and varying by sex, which indicates that even within a single genotype and a single trigger the phenotype is not uniform.

The relationship among these pathways can be described more precisely, and in a way the current evidence supports without asserting a cause. Biological contributors to regression appear to operate at three distinguishable levels, and separating them clarifies both what should be measured and when. The first consists of factors that establish a child's threshold capacity to maintain physiological stability, including genetic variants affecting metabolic, immune, and redox regulation, prenatal maternal immune activation, maternal autoantibodies, brain autoantibodies, and cumulative early-life environmental burden. These factors do not necessarily produce regression on their own; they instead influence how much physiological or immunological stress a developing system can absorb.

The second consists of acute stressors encountered against that baseline, including infection, inflammatory or immune triggers, and periods of elevated metabolic demand. Such stressors may exert disproportionate influence on the developing brain when they occur during the second year of life, a period in which microglial, mitochondrial, and synaptic systems are converging on rapid developmental change.

The third level, and the one most neglected in current research, consists of the processes that determine whether the system returns to its prior state once the initiating stressor has resolved. This is the domain of the cell danger response framework and healing cycle, in which the metabolic shift from defense back to growth is understood as an actively regulated transition rather than a passive return to baseline.[4] In a system with adequate reserve, inflammatory signaling subsides, cellular metabolism returns to growth, and development resumes along its prior trajectory. In a system without that reserve, the response instead becomes self-sustaining, and the sequence by which it does so is increasingly well characterized.

Sustained inflammatory signaling maintains microglia in an activated state. Neuroglial activation and an active neuroinflammatory response were first demonstrated in the brain tissue and cerebrospinal fluid of individuals with autism two decades ago, and that finding has since been extended by independent postmortem, transcriptomic, and in vivo imaging methods.[5] Activated microglia shift their metabolism from oxidative phosphorylation toward glycolysis, consuming energy and generating oxidative stress that further constrains mitochondrial output, a reprogramming that Toll-like receptor 4 signaling is itself sufficient to induce.[6] Mitochondrial dysfunction and altered redox status are independently well documented in autism.[7] Constrained mitochondria in turn release mitochondrial DNA, extracellular ATP, and reactive oxygen species that function as damage-associated molecular patterns, recruiting further immune activation through Toll-like receptor 9, the NLRP3 inflammasome, and cGAS-STING signaling.[8] Each link in this sequence is independently established. The closed cycle they describe is a synthesis rather than a demonstrated finding, and whether it operates as such in the developing human brain during regression is precisely the question that prospective investigation is required to answer.

Each cycle diverts resources from growth, and the diversion is not metabolically neutral, because synaptic refinement, language acquisition, and social learning are among the most energetically expensive processes a two-year-old undertakes.

Impaired pruning and disrupted gut-immune signaling then feed back into the same loop as additional sources of inflammatory input, so that the system is not merely failing to recover but is actively regenerating the conditions of its own dysregulation. Repeated stressors encountered before the prior cycle has completed produce a stacking of incomplete healing rather than a series of independent insults. [9] The clinical signature of this closure is escalation, in which each subsequent illness, exposure, or metabolic challenge produces a larger and more prolonged response than the one preceding it, and the child's baseline settles progressively lower after each event rather than returning to where it began.

Developmental timing is central to this analysis. Regression most often emerges during a period of rapid synaptic remodeling, microglial participation in circuit refinement, immune maturation, expansion of microbial diversity, and increasing metabolic demand associated with brain growth. This timing does not establish causation, but it provides a biologically plausible context in which physiological stressors may interact with differential susceptibility and adaptive capacity. A child may carry biological vulnerability without regressing; a stressor may occur without long-term developmental consequence; and the same event may have different implications depending on developmental timing, baseline physiology, and the capacity to restore homeostasis. This also explains why comparable exposures produce divergent outcomes in different children, because outcome depends on the interaction of susceptibility, timing, and resolution capacity rather than on the exposure considered in isolation. Federal research should therefore determine which mechanisms are operative in which children, under what developmental circumstances, and with what implications for diagnosis, prognosis, treatment, and recovery.

This perspective also clarifies the relationship between regression and clinical care. Current practice often treats developmental skill loss as an expected variation within autism, resulting in inconsistent medical evaluation and missed opportunities to identify treatable co-occurring conditions. Regression should instead trigger timely, clinically appropriate assessment based on presentation, including neurological, metabolic, immunological, genetic, gastrointestinal, sleep, and electrophysiological evaluation when indicated. Standardizing this response would improve diagnostic consistency, facilitate earlier recognition of medically significant conditions, and create the infrastructure needed for biomarker-guided studies.

The scientific and clinical implications are therefore linked. Regression provides a defined developmental event for mechanistic investigation, a stratification variable for precision therapeutic research, and a care-coordination signal for timely medical evaluation. Its importance does not depend on assuming a single causal pathway. It depends on recognizing that developmental skill loss is clinically consequential, biologically informative, and insufficiently addressed by the current federal autism research and care infrastructure.

A National Neurodevelopmental Regression Initiative

The federal autism research enterprise should establish neurodevelopmental regression as a cross-cutting scientific priority spanning epidemiology, developmental neuroscience, clinical investigation, biomarker development, surveillance, implementation science, and therapeutic translation. The objective should not be to create another isolated research program. It should be to create a common framework through which existing federal agencies can coordinate complementary responsibilities around a shared phenotype, common definitions, harmonized data elements, and measurable deliverables. Because regression is biologically heterogeneous, that framework must treat it as a stratified phenotype from the

outset, with mechanism-specific characterization built into study design rather than reconstructed after the fact. The tasks below follow from that requirement.

The first federal task is standardization and cohort identification. A national regression initiative should establish a common case definition and phenotyping protocol that captures age of onset, tempo of skill loss, developmental domains affected, antecedent medical events, febrile or infectious contexts, seizure or epileptiform features, sleep disruption, gastrointestinal symptoms, immune or autoimmune features, metabolic concerns, prior developmental trajectory, prenatal history, and recovery or stabilization over time. Without this foundation, studies conducted across different sites and populations cannot be reliably compared, pooled, or translated into clinical guidance, and the field will continue to generate findings that do not replicate because the populations under study were never biologically comparable.

The second task is prospective investigation. Federal research should support longitudinal regression cohorts with harmonized clinical phenotyping, serial biospecimen collection, integrated multi-omic analyses, environmental exposure assessment, neurophysiological evaluation, and shared data resources. These cohorts should be designed to evaluate biological changes before, during, and after regression whenever possible, rather than relying primarily on retrospective characterization after developmental change has stabilized.

The third task is biomarker and trial readiness. Regression should be incorporated into biomarker development, enrichment strategies, and precision trial design. This does not mean that all children with regression should be grouped together for therapeutic testing. It means that regression should be used as an entry point for identifying biologically defined subgroups, including immune-mediated, metabolic, mitochondrial, epileptiform, genetic, gastrointestinal, post-infectious, or other clinically meaningful profiles that may require different interventions and endpoints. The value of this approach lies in identifying such profiles as they emerge, rather than years after developmental change has stabilized and the biological signal has faded. Antipurinergic therapy offers the clearest existing illustration of what mechanism-matched intervention looks like in practice, having been developed from an explicit metabolic hypothesis and tested in a population in which regression is common.

The fourth task is clinical implementation. Federal agencies should support clinician education, care-pathway development, and quality measures so that developmental regression prompts timely evaluation rather than being attributed automatically to the underlying autism diagnosis. This implementation work should be coordinated with the therapeutic domain on regression, recovery, and health stabilization, which addresses prompt recognition, standard-of-care workup, treatable causes, and trial readiness.

Agency responsibilities should align with existing statutory roles. NIH should support prospective longitudinal cohorts, biomarker discovery, mechanistic studies, and biomarker-informed trials. CDC should incorporate standardized regression definitions into surveillance and expand approaches capable of characterizing developmental trajectories rather than diagnostic status alone. FDA should advise on biomarker qualification, enrichment strategies, endpoints, and pediatric safety considerations for regression-directed trials. HRSA should support clinician education and diagnostic care pathways. CMS should ensure access to appropriate medical evaluation for Medicaid-enrolled individuals with suspected regression and support quality measures for timely workup. AHRQ should evaluate evidence on diagnostic pathways, treatable causes, and care standards.

Success should be measured by concrete outputs: a standardized regression case definition, harmonized phenotyping protocol, shared common data elements, prospective cohorts, validated or candidate biomarkers, clinically meaningful endpoints, coordinated trials, diagnostic care pathways, and measurable reductions in delayed evaluation, lost-to-follow-up, and preventable developmental morbidity among children who experience regression.

Budget Architecture: The National Neurodevelopmental Regression Initiative

The National Neurodevelopmental Regression Initiative shall integrate environmental exposure science with genetic, epigenetic, immune, metabolic, mitochondrial, neurological, and functional-trajectory research. Environmental investigation should address prenatal, perinatal, and early-childhood exposures; physiologic stressors; cumulative mixtures; developmental timing; and biological measures of exposure. Genetic research should focus on susceptibility, resilience, gene–environment interaction, and pathway-specific response rather than duplicating broad autism gene-discovery portfolios. Prospective designs should determine which combinations of exposure, biological susceptibility, developmental timing, and recovery capacity are associated with regression and subsequent functional trajectory.

NDR component area	FY2028
Prospective rapid-response cohort, serial biospecimens, and functional trajectories	$7M
Immune, cytokine, purinergic, microglial, and inflammasome mechanisms	$12M
Environmental exposures and developmental exposome	$7M
Mitochondrial, redox, metabolic, and GI–immune mechanisms	$10M
Genetics, mitochondrial genetics, epigenetics, and gene–environment interaction	$7M
Assay harmonization, replication, and reference methods	$7M
Target-engagement and proof-of-mechanism studies	$7M
Total	**$57M**

Environmental research priorities

Prenatal, perinatal, and early-childhood exposure timing

Air pollution, pesticides, metals, endocrine-active chemicals, and water contaminants

Maternal health, placental biology, infection, medications, diet, and nutritional status

Acute infectious, inflammatory, or metabolic stressors preceding regression

Cumulative exposures and mixtures rather than one-chemical-at-a-time studies

Biological measures of exposure through metabolomics, adductomics, epigenomics, and validated exposure biomarkers

Protective environments and factors associated with recovery and resilience

Studies should not depend strictly on retrospective parental recall. They should combine medical records, geospatial data, prospectively collected specimens, validated or recorded exposure measures, and prespecified causal-inference methods.

Genetics priorities

Rare variants, copy-number variants, and polygenic susceptibility

Mitochondrial DNA and nuclear genes governing mitochondrial function

Immune, purinergic, inflammasome, redox, metabolic, synaptic, and ion-channel pathways

Epigenetic and transcriptional responses associated with exposure and regression timing

Family-based and trio analyses where useful

Gene–environment and gene–physiologic-stress interactions

Genetic factors associated with resilience, recovery, or treatment response

The central question should not be simply, *"Which genes are associated with autism?"* It should be:

Which genetic and epigenetic characteristics alter susceptibility or resilience to defined environmental, infectious, inflammatory, or metabolic stressors, and how do those interactions affect the onset, severity, persistence, or reversibility of neurodevelopmental regression?

Transition to Precision Infrastructure

Neurodevelopmental regression illustrates the broader requirement for the next phase of federal autism strategy. It is clinically identifiable, developmentally timed, biologically heterogeneous, and potentially actionable, which makes visible the central point developed in the sections that follow: the infrastructure needed to study regression responsibly is the infrastructure needed to translate autism science more broadly into precision therapeutics, clinical guidance, and measurable health outcomes. The National Autism Precision Therapeutics Initiative should function as the federal mechanism for moving from heterogeneous biology and developmentally timed phenotypes to validated biomarkers, stratified clinical investigation, regulatory coordination, implementation science, and longitudinal outcome evaluation.

Part III — Precision Infrastructure and the National Translational Enterprise

Part III establishes a proposed shared infrastructure through which the priorities in this Plan can move from discovery to validation, clinical investigation, implementation, and measurable public benefit. It does not create a new institute, displace investigator-initiated science, or presume that every biological finding is ready for clinical use. It creates a disciplined pathway for determining what is reproducible, in whom it matters, what evidence is still missing, and which federal product should follow.

Why a National Translational Infrastructure Is Required

The scientific problem is heterogeneity; the federal problem is fragmentation. NIH, FDA, CDC, AHRQ, HRSA, CMS, ACL, the Department of Defense, and other agencies each hold part of the discovery-to-implementation pathway, but no standing mechanism presently carries promising autism findings across assay harmonization, prospective validation, regulatory consultation, multisite trials, implementation science, coverage analysis, workforce translation, and long-term outcomes. The result is not a lack of activity. It is the absence of an accountable progression from activity to usable federal products.

The 2024 GAO findings provide the independent foundation for this architecture. GAO identified weaknesses in accountability, progress measurement, and duplication review across the federal autism enterprise. Congress then strengthened the governing obligation. Under 42 U.S.C. § 280i-2(b)(1) and (5), the Committee must monitor autism research and, to the extent practicable, services and supports across relevant federal departments; include proposed budgetary requirements; and recommend how federal activities can avoid unnecessary duplication. The annual portfolio map, evidence-stage review, and public milestone reporting described below are the operational response to those duties, not optional additions to the Plan.

The same statute expressly identifies the Department of Defense among the federal agencies serving autistic individuals. DoD’s Congressionally Directed Medical Research Programs Autism Research Program, administered through Defense Health Agency Research and Development, has funded autism research since 2007 and currently supports areas that overlap this Plan, including novel therapeutics, heterogeneous clinical expression, environmental risk, diagnosis and service access, healthcare delivery, life course transition, and co-occurring pain, sleep, gastrointestinal, inflammatory, mental-health, attention, and seizure conditions. DoD should therefore participate as a research partner and portfolio contributor, while DHA, the Military Health System, and TRICARE participate in military-family research or implementation only within their respective authorities.

The National Autism Precision Therapeutics Initiative

The National Autism Precision Therapeutics Initiative (NAPTI) is the proposed federal translational infrastructure for precision autism science and implementation. It is a distributed enterprise built on existing NIH networks, Autism Centers of Excellence, clinical research sites, federal data assets, regulatory expertise, and agency implementation programs. Its purpose is to make shared capabilities available across priority domains so that each domain does not recreate its own registry, assay platform, recruitment network, outcome system, or regulatory pathway.

Function	Assignment
Executive sponsor	Secretary-designated National Autism Coordinator, positioned to convene and obtain implementation attestations across agencies.
Operational lead	NIH, using a coordinating-center and cooperative-network structure.
Regulatory-science co-lead	FDA, for contexts of use, biomarker qualification, endpoints, enrichment, pediatric safety, and evidentiary sequencing.
Core participating agencies	CDC, AHRQ, HRSA, CMS, ACL, DoD/CDMRP, and other departments or operating divisions according to statutory role.
Implementation vehicle	Build on Autism Centers of Excellence and other established NIH and federal networks; create shared cores rather than a new institute or duplicative stand-alone programs.
Public accountability	Autism.gov IACC Implementation Dashboard, with quarterly milestone updates and annual agency attestations.

Evidence Gates: Discovery Is Not Implementation

NAPTI should apply explicit evidence gates. A plausible mechanism is not a confirmed biomarker; an analytically valid assay may not yet be a clinically useful test; a subgroup signal—or biomarker in a selected cohort is not a population-wide result; and a short trial signal needs validation before becoming a clinical recommendation. Progression should occur when the evidence required for application has been met.

Stage	Threshold for progression	Principal federal product
Discovery	Biologically plausible signal with reproducible methods and a defined population or presentation.	Replication plan, harmonized phenotype, and decision whether continued discovery is warranted.
Analytic validation	Reliable measurement across laboratories, specimens, platforms, and preanalytic conditions.	Assay standard, quality controls, reference materials, and reporting language.

Stage	Threshold for progression	Principal federal product
Clinical validation	Prospective association with a defined state, prognosis, or treatment response in the intended population.	Defined context of use, sensitivity and specificity, calibration, subgroup performance, and limitations.
Clinical investigation	Intervention rationale, safety basis, trial-ready population, endpoints, and comparator.	Multisite protocol, adaptive or pragmatic design where appropriate, and prespecified go/no-go criteria.
Regulatory and evidence review	Evidence adequate for FDA, AHRQ, professional guidance, or coverage consideration within each agency's authority.	Qualification, approval or labeling where warranted, evidence review, clinical guidance, or coverage analysis.
Implementation and outcomes	Mature evidence plus a delivery pathway, workforce, financing, and measurement plan.	Implementation package, quality measures, access tracking, and durability-qualified person-level outcomes.

Eight Shared Enterprise Capabilities

1. Portfolio Alignment and Duplication Review

Create a cross-agency portfolio map that assigns every major investment to an evidence stage, population, domain, intended federal product, and decision point. The map should identify gaps, low-yield repetition, complementary replication, and projects that require a pathway to validation rather than another descriptive cycle.

2. Harmonized Phenotyping and Common Data Elements

Maintain a modular core covering developmental history, regression and trajectory, communication, intellectual and adaptive function, co-occurring conditions, medication and intervention exposure, biological sex, environmental context, support needs, and outcomes. Domain modules should add specificity without fragmenting the common architecture.

3. Biospecimen, Assay, and Reference-Methods Platform

Standardize collection, processing, storage, quality control, inter-laboratory comparison, reference materials, and reporting for candidate immune, metabolic, folate, microbiome, autonomic, neurophysiologic, and other measures. No candidate assay should move into clinical or coverage recommendations solely because it is available.

4. Biomarker Validation and Regulatory Science

Select candidate biomarkers through transparent readiness criteria; define intended contexts of use; conduct prospective validation in relevant and, when required, unselected populations; and engage FDA early on qualification, enrichment, endpoints, pediatric safety, and evidentiary thresholds.

5. Multicenter Precision Trial Network

Provide reusable contracting, recruitment, consent, safety, pharmacy, data, and endpoint infrastructure for adaptive, platform, pragmatic, and confirmatory trials. Inclusion of profound autism, intellectual disability, minimal or no functional speech, regression, epilepsy, and medical complexity should be designed in unless scientifically or ethically unjustified.

6. Real-World Evidence and Longitudinal Outcomes

Use interoperable registry modules and appropriate claims, EHR, surveillance, and participant-reported data to measure safety, access, health stability, functional trajectory, participation, caregiver burden, and durability. The registry should be a shared architecture, not a collection of disease-siloed registries.

7. Implementation, Coverage, and Workforce Translation

When evidence is mature, connect AHRQ review, HRSA training, CMS coverage and quality work, CDC surveillance, ACL service systems, ED and other departmental programs, and professional partners. Guidance and coverage should follow evidence, not substitute for it.

8. Public Reporting, Data Access, and Course Correction

Report milestones, negative and null findings, validation failures, discontinued lines, data availability, agency decisions, and outcome trends through Autism.gov. The public record should show not only what was funded, but what advanced, what did not, and why.

Common Outcome Architecture

Every domain should report against the same outcome sequence while retaining domain-specific measures. This prevents activity counts from being mistaken for impact and allows cross-domain learning when several biological or clinical states coexist in the same person.

- Change, decline, condition, or unmet need identified against a defined baseline.
- Clinically indicated workup or evidence-stage evaluation completed.
- Treatable contributor, clinically meaningful state, or validated subgroup characterized.
- Indicated intervention, care pathway, or research protocol delivered within a defined interval.
- Function, health, communication, safety, or participation measured directly.

- Health stabilized and further deterioration or avoidable morbidity reduced over a defined follow-up period.
- Indicated care or support covered, accessible, and actually delivered.

Sequenced Federal Workplan

Time	Enterprise deliverable	Decision significance
Within 12 months	Governance charter, statutory and agency-role crosswalk, portfolio and duplication-review method, detailed costing, privacy and data-governance plan, and domain-prioritization criteria.	Authorizes disciplined design before large-scale launch.
Within 18 months	Funding opportunity or cooperative agreement; coordinating-center solicitation; core specifications for phenotyping, assays, outcomes, trials, and public reporting.	Creates a single national architecture rather than parallel domain infrastructures.
Within 24 months	Coordinating center and foundational cores operational; priority biomarker and trial-readiness portfolio selected; agency implementation agreements executed.	Moves the enterprise from planning to shared operations.
Within 36 months	Multicenter pilots active in the highest-readiness domains, including at least one validation program, one precision trial, and one implementation demonstration.	Tests the infrastructure before expansion.
Within 5 years	Prospective validation decisions, trial and implementation results, public outcome reporting, and a formal continue/modify/stop decision for each priority line.	Makes course correction a required product.

Budget and Portfolio Alignment

The planning range is approximately $10–20 million for design and initial coordination; $75–125 million annually for launch; and $150–250 million annually at mature scale, subject to NIH and OMB costing. These amounts sit within—not automatically in addition to—the broader federal research and NAPTI envelope

proposed in Part I. The annual budget estimate should show which existing investments can be aligned, which new capabilities require funding, and which duplicative or low-yield activities should be modified or discontinued.

Budget growth should be gated. The design phase should establish cost, authority, governance, privacy, and scientific-selection rules. Launch funding should follow completed core specifications. Mature-scale funding should follow evidence that the network can recruit representative cohorts, harmonize measures, complete multisite studies, release usable data, and produce decisions rather than simply expand activity.

Executive Dashboard Measures

Autism.gov should display a limited executive set. Domain workplans may retain secondary and diagnostic measures, but the public dashboard need not reproduce every technical indicator, but publicly funded research findings should be made available.

Category	Executive measures
Portfolio and statutory alignment	Share of federal autism investment mapped to evidence stage and intended product; funding directed to identified gaps; duplicative or low-yield lines modified; annual budget estimate tied to the Plan.
Infrastructure readiness	Sites activated; adoption of common data elements; assay proficiency; representative recruitment; time to data availability.
Biomarker progression	Candidates entering analytic validation; candidates completing prospective clinical validation; FDA contexts of use established; candidates discontinued for failure to meet thresholds.
Trial execution	Multisite protocols launched; recruitment and retention; inclusion of high-support and medically complex participants; completion against prespecified timelines and safety standards.
Translation and access	Evidence reviews, guidance, quality measures, or coverage analyses completed; time from mature evidence to federal product; covered access among people with an indicated need.
Health and function	Durability-qualified change in health stability, communication, adaptive function, participation, safety, emergency use, hospitalization, quality of life, and caregiver demands in defined populations.
Transparency and course correction	Quarterly milestone reporting; data and protocol availability; annual agency attestations; public continue/modify/stop decisions; negative and null results reported.

Relationship to Parts IV and V

NAPTI carries the shared scientific and translational infrastructure. Part IV identifies the domains that use that infrastructure according to evidence maturity. Part V uses a parallel implementation discipline for services and life course systems. To preserve credibility, each area is limited to four consolidated federal products and four executive performance indicators.

Part IV — Priority Therapeutic Domains

Part IV applies the shared translational framework to eleven biologically and clinically relevant, interconnected systems. These are also domains repeatedly identified by stakeholders through years of public comment and advocacy—areas marked by significant morbidity that have received inadequate clinical and research attention despite their effect on quality of life and health care utilization. Each domain identifies its distinct biology or implementation problem, locates itself on the translational continuum, assigns federal leads, and specifies deliverables and outcome-oriented performance indicators mapped to the common outcome architecture. The domains do not describe distinct or competing theories of autism; each concerns defined subgroups and the interventions that help them.

Recommended NIH architecture

These figures describe two instruments with different legal foundations, and the distinction governs how each should be read. The Part IV domain-directed portfolio expresses planning targets for allocating the existing, institute-funded autism research base across mechanistic priorities; it recommends how funds already appropriated to and flowing through the National Institutes of Health should be steered, and it requires no new authority to implement. The Protected Neurodevelopmental Regression Initiative, by contrast, represents new directed funding established and sustained through dedicated authorization and appropriation, so that its resources remain insulated from year-to-year institute discretion. The combined figure of $327 million accordingly denotes the portion of the portfolio addressed by this plan's targets together with its single new protected line, and it should not be read as the total federal autism research budget or as a request for $327 million in new appropriations.

Translational coordination under the NAPTI framework is resourced within the Part IV domain-directed portfolio and is described in full in Part III of this plan. It is not carried here as a separate administrative line, and its omission from the architecture total is deliberate rather than an oversight.

Component	FY2028
Part IV domain-directed portfolio	**$270M**

NIH Part IV and NDR architecture (plan-directed portion)	**$327M**

Weighted Part IV portfolio

These should be planning targets, not inflexible congressional earmarks.

Part IV domain	Base portfolio target	Priority rationale
1. Neurotransmission and neural circuits	$30M	Circuit function, excitation/inhibition, synaptic signaling, and treatment targets
2. Immune, autoimmune, inflammatory, and microglial biology	$45M	Highest mechanistic priority; cytokines, immune-cell states, purinergic signaling, inflammasomes, microglia, maternal immune biology
3. Folate and one-carbon biology	$15M	FRAA assays, cerebral folate biology, methylation and redox interactions
4. GI biology and microbiome	$30M	Mucosal biology, microbial metabolites, enzyme function, pain, feeding, and immune–metabolic interactions
5. NDR functional trajectory and stabilization	$10M	Continuing projects; supplemented by the separate $57M NDR Initiative
6. Mitochondrial, redox, metabolic, and endocrine biology	$45M	Highest mechanistic priority; bioenergetic reserve, metabolic stress, redox signaling, metabolism, recovery failure, and endocrine function
7. Autonomic dysfunction	$10M	Heart-rate variability, orthostatic physiology, thermoregulation, GI and stress-response integration
8. Sleep and circadian regulation	$15M	Sleep disruption as both contributor and measurable modifier of functional trajectory

9. Epilepsy and network excitability	$20M	Seizures, sleep EEG, epileptiform activity, regression, and functional outcomes
10. Motor planning, praxis, and sensorimotor function	$15M	Motor phenotype, communication access, functional measurement, and inclusive endpoints
11. Adaptive trials, endpoints, biomarkers, and repurposed therapeutics	$35M	Moves findings through validation, target engagement, and controlled investigation
Part IV total	**$270M**	

Priority Therapeutic Domain 1: Neurotransmission, Neural Circuit Function, and Neuropsychopharmacology

Strategic Objective

Determine which interventions directed toward neurotransmission, neural-circuit function, and neuropsychopharmacology improve clinically meaningful outcomes in defined autistic subgroups, and translate that evidence into safer prescribing, biomarker-informed therapeutic trials, and person-level outcomes that matter in daily life.

This domain has two distinct purposes. The first is immediate: improve the safety, monitoring, and evidence base for medications already used to treat recognized co-occurring psychiatric, neurologic, behavioral, sleep, attention, and regulatory conditions in autistic individuals. The second is translational: develop biomarker- and phenotype-informed neural-circuit trials that identify which interventions help which subgroups, under what clinical circumstances, and with what durable functional benefit.

This domain does not define autism itself as a medication target. Medication use should be tied to a recognized clinical indication, a defined neural-circuit hypothesis, or a biomarker- or phenotype-supported trial design. Functional endpoints include communication, adaptive functioning, emotional regulation, attention, sleep, sensory regulation, learning, participation, caregiver demands, health stability, and quality of life.

Domain Scope

Neural-circuit function is one part of autism-relevant biology. It intersects with sleep, epilepsy, autonomic regulation, gastrointestinal symptoms, immune activity, metabolism, sensory processing, medication exposure, and developmental timing. Domain 1 carries the medication and neural-circuit portion of the portfolio while coordinating with adjacent domains when another mechanism is primary.

The federal task is practical: make current prescribing safer and more measurable, reduce low-value or unsafe polypharmacy, evaluate common medication strategies through autism-relevant comparative-effectiveness designs, validate stratification tools before routine use, and test candidate neural-circuit interventions in defined populations rather than broad diagnostic samples.

Current State of Evidence

Current prescribing is clinically important but unevenly supported

Many pharmacologic interventions are already widely used in autism-related care, primarily for co-occurring psychiatric, neurologic, behavioral, sleep, attention, and regulatory conditions. Some medications have evidence for specific indications. Many prescribing decisions still rely on extrapolation,

clinician experience, family preference, payer constraints, trial-and-error sequencing, or limited subgroup data.

This creates two linked needs: better comparative-effectiveness evidence for medication strategies in autism-relevant subgroups, and better safety surveillance for long-term exposure, adverse events, emergency utilization, hospitalization, metabolic effects, sedation, behavioral activation, and interactions with epilepsy, sleep disruption, gastrointestinal disease, intellectual disability, minimal or no functional speech, and complex medical conditions.

Medication safety and polypharmacy are implementation-ready priorities

Medication safety does not need to wait for discovery biology. Participating systems can begin now by documenting the clinical indication for each medication, baseline function and target symptoms, communication and support needs, adverse-event risk, metabolic monitoring, drug interactions, seizure and sleep considerations, and the plan for follow-up or deprescribing when benefit is not demonstrated.

The term "polypharmacy" should not be used as a blunt count of medications. The measurable concern is low-value, unsafe, duplicative, or poorly monitored medication use. Federal reporting should therefore track guideline-concordant prescribing, structured medication review, deprescribing when appropriate, adverse-event monitoring, and person-level outcomes after medication optimization.

Neural-circuit therapeutics require better stratification

Research has identified multiple neural systems that may contribute to communication, attention, learning, sensory processing, emotional regulation, adaptive function, and behavior, including excitatory and inhibitory signaling, monoaminergic pathways, neuropeptide signaling, synaptic function, network regulation, and neurophysiologic activity. A plausible neural mechanism does not establish benefit in a broad autism population.

Future studies should reduce broad diagnostic enrollment when an intervention is expected to act through a specific mechanism. Cohorts should be defined by developmental phenotype, communication status, intellectual functioning, co-occurring epilepsy, sleep profile, autonomic features, medication history, pharmacogenomic factors, relevant medical comorbidities, and neurophysiologic measures when clinically indicated. Regulators should establish guidelines and approval pathways that address the substantial heterogeneity of the autism population.

Outcomes must measure function, not only symptom reduction

Medication and neural-circuit trials should not rely only on narrow symptom scales. Federal studies should include communication, adaptive function, educational or vocational participation, sleep stability, emotional regulation, sensory tolerance, safety, caregiver demands, health stability, and quality of life.

For some interventions, the most meaningful effect may be functional augmentation. A medication or neural-circuit intervention may increase a person's ability to benefit from communication supports, occupational therapy, behavioral services, educational programming, vocational training, or community participation. That possibility should be tested directly rather than inferred from symptom change.

Translational Status

Component	Translational status	Federal task
Medication treatment for recognized co-occurring conditions	Implementation-ready. Evidence-limited for some conditions/populations. Standards of care for otherwise diagnosed conditions should apply.	Improve comparative-effectiveness evidence, prescribing guidance, medication review, safety monitoring, and quality measures.
Medication safety and polypharmacy surveillance	Implementation-ready	Use the NAPTI Real-World Evidence and Outcomes Registry as the shared module for utilization, adverse events, emergency use, hospitalization, monitoring, and long-term outcomes.
Biomarker- and phenotype-informed neural-circuit therapeutics	Validation to precision-trial stage	Use defined cohorts, candidate biomarkers, adaptive designs, subgroup endpoints, and FDA-aligned contexts of use.
Adaptive trial methods and endpoint development	Infrastructure-ready	Create reusable templates for enrichment, response-adaptive designs, platform methods, safety monitoring, and functional endpoints.
Therapeutic augmentation of communication and participation	Translation-ready	Test whether targeted interventions increase the benefit of communication, educational, behavioral, occupational, vocational, or community supports.
Next-generation neural-circuit mechanisms	Discovery to validation	Continue mechanism refinement and biomarker development before broad clinical implementation.

Knowledge and Implementation Gaps

- Commonly used medication strategies have not been evaluated consistently across autism-relevant subgroups, ages, clinical contexts, and outcome domains.
- Medication combinations, long-term exposure, adverse events, metabolic effects, emergency utilization, hospitalization, and real-world outcomes are not tracked with sufficient consistency.
- Trials often enroll diagnostically heterogeneous samples even when the intervention is expected to work only in a defined biological or clinical subgroup.
- Neural-circuit biomarkers, pharmacogenomic predictors, EEG or other neurophysiologic measures, and digital endpoints remain incompletely validated for routine clinical use.
- Outcome measures often emphasize symptom change without measuring communication, adaptive capacity, participation, health stability, caregiver demandsand quality of life.
- Individuals with profound autism, intellectual disability, minimal or no functional speech, epilepsy, regression, and complex medical conditions remain underrepresented in medication and neural-circuit studies.
- Implementation has not kept pace with practice: medications are widely prescribed, but national guidance, clinician education, monitoring expectations, and quality measures remain uneven.

Priority Federal Translation Agenda

Initiative 1: Comparative-Effectiveness and Prescribing Quality

Lead agency: AHRQ. Supporting agencies: NIH, HRSA, CMS.

AHRQ, with NIH, HRSA, and CMS, should establish a coordinated comparative-effectiveness initiative for medications commonly used in autism-related care. The initiative should evaluate medication strategies for attention, hyperactivity, irritability, anxiety, emotional dysregulation, aggression, self-injury, sleep disturbance, and related co-occurring conditions. It should identify which strategies improve which outcomes, in which subgroups, and with what safety profile.

This initiative should clarify when medication is being used to treat a recognized co-occurring condition rather than autism itself. It should support future prescribing guidance, clinician education, Medicaid and EPSDT implementation, deprescribing guidance when benefit is not demonstrated, and quality measures that distinguish access from outcomes.

Initiative 2: Medication Safety and Real-World Outcomes Module

Lead agency: CDC. Supporting agencies: CMS, AHRQ, NIH.

CDC, with CMS, AHRQ, and NIH, should develop a medication safety and outcomes module within the shared NAPTI Real-World Evidence and Outcomes Registry rather than creating a parallel registry. The module should track medication utilization, clinical indication, baseline function, adverse events, metabolic

monitoring, sedation, behavioral activation, polypharmacy risk, emergency utilization, hospitalization, school or work participation where available, caregiver demands, and patient- or caregiver-reported outcomes.

The module should be designed for quality improvement and public accountability. It should identify high-risk medication combinations, gaps in monitoring, discontinuation patterns, access barriers, and subgroup differences in benefit or harm. Medicaid-linked analyses should be used where feasible, with appropriate privacy protections and stratification by age, communication status, intellectual disability, epilepsy, sleep disruption, complex medical conditions, race, ethnicity, geography, and payer.

Initiative 3: Biomarker-Informed Neural-Circuit and Adaptive Trial Program

Lead agencies: NIH and FDA. Supporting agencies: CDC, AHRQ.

NIH and FDA should support multicenter neural-circuit therapeutic studies using harmonized phenotyping, common data elements, candidate biomarkers, adaptive methods, and biologically or clinically defined enrollment. Candidate stratification variables should include developmental phenotype, communication status, intellectual functioning, sleep profile, epilepsy, autonomic features, medication history, pharmacogenomic factors, relevant medical comorbidities, and neurophysiologic measures when clinically indicated.

Federal autism therapeutic development should accommodate the vast biological heterogeneity in individuals with autism. Two complementary approaches will assist in that.

First: Trial Design - Incorporate adaptive trial methods when scientifically appropriate. These may include response-adaptive randomization, enrichment strategies, platform trials, Bayesian methods, and sequential multiple-assignment randomized trials. Adaptive methods should be used to improve efficiency, reduce unnecessary participant exposure, identify treatment-responsive cohorts, and support decision-making when subgroup effects are likely.

Second: Clinical endpoints. FDA should provide guidance on the types of evidence that would support approval, expanded indications, or labeling for treatment-responsive subgroups when scientifically justified. FDA should also support the development, qualification, and use of clinically meaningful endpoints and outcome measures that capture improvements in co-occurring conditions, functional abilities, quality of life, and other outcomes that matter to autistic individuals and their families.

Initiative 4: Functional Augmentation of Communication and Participation

Lead agency: NIH. Supporting agencies: AHRQ, HRSA, CMS.

Federal studies should evaluate whether medication-related or neural-circuit interventions increase an individual's ability to benefit from communication supports, educational programming, behavioral services, occupational therapy, vocational training, self-care supports, or community participation. This initiative should not promote medication for its own sake. It should test whether targeted interventions improve participation, learning, communication, health stability, safety, and daily function in defined subgroups.

Studies should measure both the intervention and the support it is intended to augment. For example, if an intervention is hypothesized to improve attention, regulation, or sleep so that a person can use AAC, participate in therapy, or remain in school or work, those downstream outcomes should be pre-specified and measured over a defined follow-up window.

Agency Actions

Agency	Priority actions
NIH	Fund biomarker development, neural-circuit therapeutic trials, functional augmentation studies, adaptive trial infrastructure, and coordination with sleep, epilepsy, autonomic, metabolic, gastrointestinal, immune, and regression domains when relevant.
FDA	Advise on biomarker qualification, endpoint development, adaptive trial design, enrichment strategies, digital or neurophysiologic measures, pediatric safety, and regulatory science for neural-circuit-directed interventions.
AHRQ	Lead comparative-effectiveness reviews, implementation science, prescribing evidence synthesis, deprescribing evidence review, and evaluation of real-world medication strategies.
HRSA	Develop clinician education, prescribing and deprescribing guidance dissemination, workforce training, and integration of medication safety and functional outcome guidance into primary care, developmental, psychiatric, neurologic, and community settings.
CMS	Support coverage alignment, Medicaid implementation, EPSDT clarification where applicable, quality measures, access evaluation, medication monitoring, and publicly financed care models that distinguish indicated care from broad medication use.
CDC	Support longitudinal surveillance and the medication safety/outcomes module within the NAPTI Real-World Evidence and Outcomes Registry,

Agency	Priority actions
	including utilization, adverse events, polypharmacy, emergency use, hospitalization, and long-term outcomes.
DoD / CDMRP Autism Research Program	Support high-risk, high-impact and translational autism research responsive to annual CDMRP areas, including therapeutics, treatment outcomes, heterogeneity, and co-occurring mental-health or neurologic conditions; use NAPTI data and outcome standards where applicable.

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Complete an AHRQ evidence review and specify national baseline measures for indication-based prescribing, structured medication review, deprescribing when appropriate, metabolic and adverse-event monitoring, and person-level functional outcomes.	AHRQ	NIH; CDC; HRSA; CMS; FDA; DoD/CDMRP
18–24 months	Pilot the medication-safety and real-world-outcomes module within the shared NAPTI registry and publish reusable FDA-aligned templates for enrichment, adaptive protocols, pediatric safety, and functional endpoints.	CDC and NIH	FDA; AHRQ; CMS; HRSA
24–36 months	Launch pragmatic medication studies and at least one biomarker- or phenotype-informed neural-circuit trial that includes communication-diverse and medically complex participants when scientifically appropriate.	NIH and AHRQ	FDA; CDC; CMS; HRSA; DoD/CDMRP
3–5 years	Report subgroup-specific comparative-	AHRQ and NIH	FDA; CDC; HRSA; CMS

Phase	Consolidated federal product	Accountable lead	Supporting partners
	effectiveness, safety, access, deprescribing, and functional-augmentation results and translate mature findings into federal prescribing, monitoring, and coverage guidance.		

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Percentage of participating systems documenting indication, baseline function, target outcomes, safety risks, and a monitoring or deprescribing plan for medication use.
- Median time from an identified medication need or safety concern to structured review and covered, delivered follow-up.
- Change in guideline-concordant prescribing and rates of adverse events, metabolic complications, emergency use, hospitalization, and treatment discontinuation after medication optimization.
- Durability-qualified change in communication, adaptive function, participation, sleep, emotional regulation, health stability, caregiver demands, or quality of life in defined treatment-responsive subgroups.

Implementation Standards

- Medication use should be tied to a recognized clinical indication, a documented treatment target, or a biomarker- or phenotype-supported research protocol; autism alone should not be treated as the medication indication.
- Safety monitoring should include adverse events that may be difficult to report verbally, including sedation, agitation, akathisia-like activation, sleep disruption, appetite or weight change, seizure change, gastrointestinal effects, pain expression, motor change, and loss of participation.
- Biomarkers, pharmacogenomic predictors, EEG or neurophysiologic measures, and digital endpoints should have defined contexts of use before they guide routine clinical care.
- Real-world evidence for medication safety should be collected through the shared NAPTI registry architecture so that this domain does not create duplicative infrastructure.
- Research and implementation should include high-support and communication-diverse autistic individuals unless exclusion is scientifically or ethically justified.

- Success should be measured by access, safety, function, health stabilization, and quality of life, not by medication exposure, trial launch, or symptom-score change alone.

Translational Readiness Assessment

Domain 1 spans implementation, validation, and discovery. Current medication use for recognized co-occurring conditions is implementation-ready but evidence-limited; the immediate federal work is comparative effectiveness, safer prescribing, deprescribing when appropriate, monitoring, coverage alignment, and quality measurement. Medication safety and polypharmacy surveillance are also implementation-ready and should proceed through the shared NAPTI Real-World Evidence and Outcomes Registry.

Biomarker-informed neural-circuit interventions remain at the validation and precision-trial stage. Next-generation neural-circuit mechanisms remain discovery-to-validation. The federal objective is to move from broad medication use and broad trials toward documented indications, safer prescribing, better subgroup definition, adaptive trials where appropriate, and measurable improvement in function, participation, health stability, and quality of life.

Priority Therapeutic Domain 2: Immune, Autoimmune, and Inflammatory Biology

Strategic Objective

Determine which immune, autoimmune, inflammatory, and neuroimmune phenotypes carry clinical significance in autistic individuals; ensure that established immune and neuroimmune conditions are recognized and managed according to existing standards of care; and advance only those immune-related biomarkers, mechanisms, or subgroups that are mature enough for validation, qualification, or precision therapeutic study.

This domain concerns defined subgroups, not immune-directed treatment across the autism population. The federal objective is to distinguish standard medical care from investigational immune biology, reduce diagnostic overshadowing when immune or neuroimmune illness is clinically indicated, validate reproducible immune phenotypes, and determine whether biomarker-defined interventions improve health stability, function, developmental trajectory, participation, or quality of life in specific subgroups.

Scientific Rationale

Immune, autoimmune, inflammatory, and neuroimmune findings in autism now support a more disciplined federal posture than either broad dismissal or broad clinical adoption. The evidence points to clinically meaningful subgroups, but it does not support a universal immune explanation of autism or unstratified immune-directed treatment.

The domain spans the developmental continuum. Relevant questions include maternal immune biology, placental immune signaling, maternal autoantibodies, fetal susceptibility, postnatal immune dysregulation, recurrent infection, primary immunodeficiency, allergy, mast-cell disease, autoimmunity, inflammatory gastrointestinal disease, post-infectious neuroimmune presentations, neuroinflammation, and immune-triggered functional decline or regression. These questions differ in maturity and therefore require different federal actions.

The immediate implementation issue is straightforward: when an autistic person has clinical evidence of an established immune, autoimmune, allergic, immunodeficiency, inflammatory gastrointestinal, post-infectious, or acute neuroimmune condition, autism should not delay evaluation, referral, treatment, coverage, or follow-up. The translational science issue is narrower: which immune biomarkers and mechanisms are reproducible enough to identify subgroups, stratify trials, and support safe therapeutic testing.

Current State of Evidence

Established immune and neuroimmune conditions require standard medical care

Primary immunodeficiency, autoimmune disease, allergic disease, mast-cell disease, inflammatory gastrointestinal disease, autoimmune encephalitis, post-infectious neuroimmune presentations, and related conditions have diagnostic and specialty-care pathways independent of autism. When clinical

features support evaluation, autistic individuals should receive the same indicated workup, referral, treatment, and monitoring as any other patient.

An immediate federal and healthcare priority is correcting diagnostic overshadowing. Abrupt regression, loss of adaptive function, sudden neuropsychiatric deterioration, severe anxiety or obsessive-compulsive symptoms, catatonia-like deterioration, movement abnormalities, restrictive eating, sleep collapse, seizure-like changes, episodic unresponsiveness, aggression, self-injury, or marked personality change may have behavioral, psychiatric, neurological, gastrointestinal, metabolic, medication-related, environmental, infectious, inflammatory, autoimmune, or neuroimmune contributors. The pathway should require structured differential evaluation, not a presumption that the change is autism or a presumption that it is immune-mediated. Appropriate clinical history, presentation, laboratory testing, and examination is needed.

Prenatal and maternal immune biology is promising but requires causal and safety sequencing

Maternal immune activation, maternal autoimmune disease, allergic and inflammatory conditions, maternal metabolic inflammation, placental immune dysfunction, infection, and maternal brain-reactive autoantibodies have been associated with altered fetal neurodevelopment under defined biological and temporal conditions. These pathways are important because they connect maternal physiology, fetal susceptibility, placental biology, immune signaling, developmental timing, and later neurodevelopmental outcome.

Federal work in this area should separate three questions: recognition and treatment of established maternal medical conditions; causal and susceptibility research using prospective and genetically informed designs; and prevention or risk-reduction intervention. Prenatal or postnatal immunomodulation should advance toward clinical investigation and implementation when confirmed evidence of susceptibility, biomarker selection, maternal-fetal safety, and outcome evidence justify that step.

Postnatal immune phenotypes define subgroups, not a universal mechanism

Postnatal findings include altered innate and adaptive immune responses, cytokine and chemokine differences, immune-cell activation, impaired immune regulation, recurrent infection, allergic disease, autoimmunity, immune-mediated gastrointestinal disease, mast-cell features, and post-infectious destabilization. These findings vary across cohorts and should not be interpreted as universal or as competing explanations for autism.

Their importance lies in clustering within clinically meaningful presentations, including developmental regression, fluctuating function, severe sleep disruption, episodic neuropsychiatric deterioration, seizures or epileptiform activity, gastrointestinal inflammation, recurrent illness, allergic or autoimmune disease, and treatment-responsive immune phenotypes. The federal question is which phenotypes are reproducible, clinically meaningful, and treatment-relevant.

Neuroinflammation and glial biology remain translationally relevant but context-dependent

Microglia and astrocytes regulate synaptic refinement, neurotransmitter balance, cellular metabolism, extracellular signaling, and immune surveillance. Evidence in defined autism populations suggests that

microglial activation, astrocytic stress, cytokine and chemokine signaling, blood-brain-barrier signaling, myeloid-lineage dysregulation, mitochondrial stress, redox imbalance, and immune-metabolic feedback may influence neural-network function or functional fluctuation.

These findings should be handled as dynamic immune-metabolic states, not as static proof of inflammation or as a basis for broad treatment. The most useful federal work will link neuroimmune measures to specific presentations, timing, genetic susceptibility, treatment response, safety, and longitudinal function.

Autoantibodies and immune biomarkers require harmonized assays and translation of defined contexts of use

Maternal brain-reactive autoantibodies, folate receptor-alpha autoantibodies, anti-neuronal or basal-ganglia-associated antibodies, systemic autoimmune markers, thyroid autoimmunity, cytokine and chemokine panels, and functional immune-reactivity measures have been reported in defined subgroups. Some findings may be pathogenic, some may be stratification biomarkers, some may indicate broader immune dysregulation, and some may be incidental.

The federal task is to identify where translational findings should be disseminated—and for which sub-populations—while distinguishing emerging categories through assay harmonization, reference thresholds, specimen handling standards, clinical correlation, prospective cohorts, mechanistic study, biomarker qualification, and biomarker-informed trials. No immune biomarker should be treated as a general autism biomarker without a defined context or cohort.

Recovery, resilience, and fever-responsive change deserve direct study

Not all individuals exposed to infection, fever, inflammatory illness, immune activation, medication changes, or other physiologic stressors experience the same outcome. Recovery, compensation, fever-responsive improvement, restoration of homeostasis, and vulnerability to relapse may reveal mechanisms of resilience and reversibility. Federal studies should measure both risk and recovery because both are necessary for prevention, stabilization, and therapeutic development.

Federal research should support standardized cytokine and immune-response profiling in clinically defined autism cohorts, including both baseline and stimulated immune assays. Priority analytes should include inflammatory, regulatory, innate immune, Th1/Th2/Th17, chemokine, and interferon-related markers, with harmonized specimen collection, processing, assay platforms, reference ranges, and replication across sites. These assays should not be used as stand-alone diagnostic tests, but as part of a broader immune phenotyping strategy linked to clinical features, co-occurring medical conditions, regression history, infection burden, treatment response, and longitudinal outcomes.

Translational Readiness

Domain 2 spans implementation, biomarker validation, causal research, and precision therapeutic development. Federal action should follow evidence maturity rather than treating all immune hypotheses as equally ready for clinical use.

Component	Translational status	Federal task
Established immune, autoimmune, allergic, immunodeficiency, inflammatory gastrointestinal, post-infectious, and acute neuroimmune conditions	Implementation-ready	Improve recognition, referral, coverage, clinical guidance, clinician education, and follow-up under existing standards of care.
Acute immune-mediated or neuroimmune destabilization evaluation	Implementation-ready with pathway support	Define clinical triggers, differential workup, referral pathways, urgent red flags, and follow-up expectations without assuming every presentation is immune-mediated.
Immune biomarkers, including maternal autoantibody patterns, folate receptor-alpha autoantibodies, anti-neuronal markers, cytokine/chemokine panels, and functional immune-reactivity measures	Validation-to-qualification stage	Harmonize assays, define intended contexts of use, validate analytic and clinical performance, and engage FDA early.
Maternal immune biology, susceptibility, prevention, and resilience	Causal and safety research stage	Use prospective, sibling, family, genetically informed, and causal-inference designs before prevention claims or pregnancy intervention.

Component	Translational status	Federal task
Immune-triggered regression and immune-metabolic neuroinflammatory subgroups	Discovery-to-validation	Use genetic, clinical, immune, metabolic, and longitudinal measures to define reproducible subgroups and candidate mechanisms.
Immune-directed therapeutic interventions	Precision-trial stage only in defined subgroups	Test interventions only where biologic rationale, biomarker or clinical subgroup definition, safety parameters, and meaningful outcomes support controlled evaluation.

Knowledge and Implementation Gaps

- Established immune and neuroimmune conditions may be missed when acute change, regression, sleep collapse, seizure-like events, pain, gastrointestinal inflammation, recurrent illness, or neuropsychiatric deterioration is attributed to autism without indicated medical evaluation.
- Clinical systems lack a consistent pathway for evaluating abrupt immune-mediated or neuroimmune destabilization while maintaining a broad differential diagnosis.
- Immune assays vary across laboratories, specimens, thresholds, timing, and interpretation, limiting replication, clinical correlation, biomarker qualification, and multicenter trials.
- Several immune findings have plausible biological rationale but remain vulnerable to cohort variation, confounding, inconsistent laboratory methods, and limited outcome measurement.
- Maternal immune biology and prevention research require stronger causal designs, susceptibility markers, and maternal-fetal safety evidence before any intervention claims are made.
- Immune biology interacts with mitochondrial function, redox biology, folate metabolism, gastrointestinal physiology, autonomic regulation, sleep, epilepsy, and regression, but studies do not consistently measure those cross-domain contributors.
- High-support, nonspeaking, intellectually disabled, medically complex, rural, racially and ethnically diverse, and late-diagnosed autistic individuals remain underrepresented in immune studies and clinical pathways.
- Health-system data are not yet organized to report referral timeliness, indicated workup completion, characterized immune contributors, access attainment, and health stabilization in defined immune cohorts.

Priority Federal Translation Agenda

Federal action should proceed through four coordinated initiatives. The initiatives use existing agency authority, existing cohorts, the NAPTI shared cores, CDC surveillance, CMS administrative data, and the NAPTI Real-World Evidence and Outcomes Registry rather than creating a new stand-alone immune infrastructure.

Initiative 2.1: Clinical Recognition and Standard-Care Access for Established Immune and Neuroimmune Conditions

Lead agencies: HRSA, CMS. Supporting agencies: AHRQ, CDC, NIH, ACL.

HRSA, CMS, and AHRQ should translate existing standards of care into practical autism-competent recognition, referral, and follow-up guidance for established immune, autoimmune, allergic, immunodeficiency, inflammatory gastrointestinal, post-infectious, and acute neuroimmune conditions. The guidance should clarify that this initiative is not autism-specific immune treatment, even if treatment impacts core symptoms associated with autism. It is a diagnostic-overshadowing and access initiative that ensures autistic individuals receive indicated medical care when the clinical presentation supports it.

The guidance should identify clinical triggers for evaluation, urgent red flags, specialty referral pathways, medication and infection review, pain and gastrointestinal review, seizure and sleep considerations, and follow-up intervals. CMS should clarify coverage and quality expectations for indicated evaluation and treatment, including EPSDT applicability for Medicaid-enrolled children and access pathways for adults where federal authority permits.

Initiative 2.2: Acute Neuroimmune Destabilization Evaluation Pathway

Lead agencies: HRSA, AHRQ, CMS. Supporting agencies: NIH, CDC, SAMHSA.

Federal partners should develop a structured clinical and diagnostic pathway for abrupt regression, sudden functional loss, episodic neuropsychiatric deterioration, catatonia-like change, severe restrictive eating, movement abnormalities, seizure-like changes, severe sleep collapse, aggression or self-injury with acute onset, or marked personality change. The pathway should require broad differential evaluation before attribution to autism, behavior, psychiatric illness, or immune disease.

The pathway should draw on existing frameworks for autoimmune encephalitis, PANS/PANDAS where clinically applicable, post-infectious neuroimmune syndromes, seizure and ESES evaluation, catatonia, metabolic decompensation, inflammatory gastrointestinal disease, infection, medication effects, pain, sleep disruption, and environmental destabilization. It should specify when urgent referral is indicated and when standard outpatient evaluation is sufficient.

Initiative 2.3: Immune Biomarker Harmonization, Validation, and Qualification

Lead agencies: NIH, FDA. Supporting agencies: AHRQ, CDC, CMS, DoD.

NIH and FDA should define a shortlist of candidate immune biomarkers and intended contexts of use. Priority candidates may include maternal autoantibody-related reactivity patterns; folate receptor-alpha autoantibodies coordinated with the folate domain; post-infectious, anti-neuronal, or basal-ganglia-

associated markers in acute presentations; functional immune-reactivity measures; and compound signatures for immune-triggered regression subgroups that combine clinical phenotype, genetic vulnerability, immune activation, and longitudinal change.

The first task is harmonization. Federally supported studies should adopt common data elements, specimen-handling standards, assay methods, reporting language, reference thresholds where available, and clinical-correlation requirements. FDA engagement should begin before large additional investments so that studies generate evidence suitable for biomarker qualification or defined research use.

Initiative 2.4: Maternal Immune Biology, Susceptibility, Resilience, and Precision Therapeutic Discovery

Lead agency: NIH. Supporting agencies: FDA, CDC, HRSA, AHRQ.

NIH should support causal and mechanistic studies that determine which maternal, fetal, host, genetic, immune, metabolic, autoimmune, infectious, allergic, and environmental factors influence susceptibility to maternal immune activation, maternal autoantibody-related risk, and postnatal immune-triggered regression or functional decline. Designs should include large scale mechanistic and treatment studies using maternal immune activation animal models, prospective pregnancy cohorts, sibling and family comparisons, genetically informed analyses, existing pediatric cohorts, defined genetic registries, and causal-inference methods where possible.

Mechanistic work should evaluate candidate intervention points such as placental antibody transfer, cytokine and chemokine cascades, microglial priming, blood-brain-barrier signaling, mitochondrial and redox stress, inflammasome activation, and immune-mediated synaptic dysfunction. Therapeutic studies should advance only in biomarker-defined or clinically defined subgroups, with clear safety parameters and meaningful outcomes. Prenatal immunomodulation should not move beyond research planning before susceptibility confirmation and safety evidence justify that step.

Agency	Priority actions
HRSA	Lead clinician education on immune and neuroimmune diagnostic overshadowing, clinical trigger recognition, referral pathways, acute destabilization guidance, and primary-care and specialty dissemination.
CMS	Clarify coverage and quality expectations for indicated evaluation and management of recognized immune and acute neuroimmune conditions, including EPSDT where applicable; support access-attainment and time-to-care measures.
AHRQ	Anchor recognition and acute-evaluation guidance in existing specialty standards; conduct evidence reviews on diagnostic pathways, referral,

Agency	Priority actions
	comparative effectiveness, and health-services implementation.
NIH	Lead susceptibility, mechanism, biomarker, maternal immune biology, immune-triggered regression, resilience, and biomarker-defined therapeutic research through existing cohorts and NAPTI shared cores.
FDA	Advise on immune biomarker qualification, intended contexts of use, enrichment strategies, endpoint selection, pediatric safety, maternal-fetal safety, and biomarker-defined trial design.
CDC	Support surveillance and data linkage for immune-related health outcomes, infection burden, emergency utilization, hospitalization, regression context, and longitudinal outcomes using existing systems and shared NAPTI measures.
ACL	Support functional, participation, caregiver-demands, and community-living outcome alignment where immune-related stabilization affects daily support needs or caregiver stability.
SAMHSA	Coordinate where acute neuroimmune or immune-mediated presentations overlap with crisis, catatonia-like deterioration, psychiatric emergency care, or behavioral-health referral pathways.
DoD / CDMRP Autism Research Program	Support innovative mechanistic and translational research on inflammation, immune biology, environmental risk, and biologically defined co-occurring conditions consistent with annual CDMRP priorities and appropriations.

Agency Actions

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish presentation-driven recognition and referral guidance for established immune, autoimmune, allergic, immunodeficiency, inflammatory, post-infectious, and acute neuroimmune conditions while preserving a broad differential diagnosis.	HRSA and AHRQ	CMS; CDC; NIH; SAMHSA; ACL
18–24 months	Adopt a federal immune common-data-element and assay-harmonization package, including specimen handling, analytic standards, reporting language, candidate contexts of use, and a shortlist of biomarkers for prospective validation.	NIH and FDA	CDC; AHRQ; CMS; DoD/CDMRP
24–36 months	Pilot acute-destabilization pathways and initiate prospective maternal, postnatal, resilience, and immune-target studies using harmonized phenotyping and longitudinal outcomes.	NIH and HRSA	FDA; CDC; AHRQ; CMS; SAMHSA; DoD/CDMRP
3–5 years	Complete analytic and clinical validation decisions for priority biomarkers and advance only biomarker- or clinically defined intervention trials that meet causal, safety, and regulatory thresholds.	NIH and FDA	AHRQ; CDC; HRSA; CMS

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Adoption and workup-completeness rates for immune and acute-neuroimmune recognition pathways in participating clinical systems.

- Median time from predefined clinical trigger to indicated evaluation and from a characterized contributor to covered, delivered treatment and follow-up.
- Number, percentage, and dollar value of federally supported immune discovery and translational studies using harmonized assays, common data elements, intended contexts of use, and inclusive subgroup reporting.
- Diagnostic yield, health stabilization, adverse events, and durability-qualified functional outcomes after indicated immune or neuroimmune care in defined subgroups.

Implementation Standards

- Established immune, autoimmune, allergic, immunodeficiency, inflammatory gastrointestinal, post-infectious, and acute neuroimmune conditions should be evaluated and treated according to applicable medical standards when clinically indicated, regardless of autism diagnosis.
- Clinical guidance should preserve a broad differential diagnosis. Acute change should not be attributed automatically to autism, psychiatric illness, behavior, or immune disease without indicated evaluation and assessment.
- Immune-directed interventions should not be promoted for broad autism populations. Controlled evaluation should be limited to biomarker-defined or clinically defined subgroups with symptom parameters and meaningful outcomes.
- Maternal immune and prevention research should distinguish treatment of established maternal medical conditions from investigational prenatal immunomodulation; pregnancy interventions require causal, biomarker, and safety evidence.
- Biomarker reporting should specify the assay, specimen, threshold, timing, subgroup, and intended context of use or symptom correlation. No immune biomarker should be described as a general autism biomarker unless evidence supports that claim.
- Immune-domain reporting should use shared NAPTI cores, CDC surveillance, CMS administrative data, and the NAPTI Real-World Evidence and Outcomes Registry rather than creating duplicative stand-alone infrastructure.
- Functional improvement should be measured directly, durability-qualified, linked to whether a treatable contributor or biological state was characterized and treated, and not characterized as cure.

Translational Readiness Assessment

This domain spans the full continuum. Recognition and management of established immune, autoimmune, allergic, immunodeficiency, inflammatory gastrointestinal, post-infectious, and acute neuroimmune conditions are implementation-ready. The federal task is to reduce diagnostic overshadowing, improve referral and coverage, and measure whether indicated care is actually delivered.

Immune biomarker work is validation-to-qualification. The next federal step is assay harmonization, common data elements, intended contexts of use, analytic and clinical validation, and FDA engagement before broad clinical claims. Maternal immune biology, immune-triggered regression, neuroinflammatory

mechanisms, and resilience biology remain causal and mechanistic research priorities unless a specific subgroup and context of use have matured further.

Immune-directed therapeutic development should remain targeted. Interventions such as intravenous immunoglobulin, anti-inflammatory strategies, microglial-modulating approaches, or other immunomodulatory interventions should be evaluated only where biologic rationale, biomarker or clinical subgroup definition, safety parameters, and meaningful outcomes support controlled study. The federal priority is to work through existing authority and shared infrastructure toward measurable improvements in health, function, participation, and quality of life, not to expand immune-directed treatment across the autism population.

Priority Therapeutic Domain 3: Folate Metabolism and One-Carbon Biology

Strategic Objective

Advance folate metabolism and one-carbon biology as a biomarker-defined therapeutic domain, with near-term priority on cerebral folate transport, folate receptor alpha autoantibody assay harmonization, and confirmatory leucovorin trials in defined subgroups, while keeping broader methylation, redox, and cofactor-support strategies within a stricter validation framework.

This domain concerns defined subgroups, not broad folate, methylation, or one-carbon supplementation across autism. The federal objective is to determine which individuals have measurable folate-transport or one-carbon pathway abnormalities, which biomarkers reliably identify them, which interventions improve clinically meaningful outcomes, and what evidentiary threshold is required before federal guidance, coverage, or regulatory action is appropriate.

Scientific Rationale

The regulatory record, and the Committee's position on it.

On March 10, 2026, the Food and Drug Administration approved expanded use of Wellcovorin (leucovorin calcium) for cerebral folate transport deficiency in adult and pediatric patients with a confirmed pathogenic variant in the folate receptor 1 gene. The agency did not approve leucovorin for autism. This Plan endorses the distinction: a confirmed genetic indication should not be extrapolated to a broader diagnostic population or to an autoantibody-defined hypothesis that has not completed prospective validation.

This Plan does not recommend leucovorin as a treatment for autism, population-level folate-receptor-autoantibody screening, clinician treatment guidance, or coverage determination in advance of confirmatory evidence. Initiative 3.2 is the federal response to the evidence gap: determine prospectively, using harmonized assays and pre-specified outcomes, whether a folate-transport-defined subgroup exists within autism and whether it responds durably and safely to folate-transport-directed therapy.

Three populations must remain distinct to determine whether outcomes are cohort dependent.

Population	Definition	Federal evidentiary status
FOLR1-related cerebral folate transport deficiency	Cerebral folate deficiency with a confirmed pathogenic FOLR1 variant.	FDA-approved leucovorin indication as of March 10, 2026. Ultra-rare; not an autism indication.
Cerebral folate deficiency from	Low cerebrospinal-fluid 5-methyltetrahydrofolate associated with	Recognized neurologic or metabolic condition requiring specialist evaluation;

Population	Definition	Federal evidentiary status
other etiologies	another genetic, mitochondrial, or clinically established cause, or an unresolved mechanism.	not covered by the FOLR1-specific approval unless the labeled criteria are met.
Folate-receptor-alpha-autoantibody-associated transport disruption	Binding or blocking autoantibodies, with or without documented central folate deficiency.	Candidate subgroup. Assays are not harmonized; the relationship to central folate availability and prospective treatment response remains unresolved. This is the population Initiative 3.2 is designed to characterize.

The existing evidence is suggestive. A small single-site randomized trial reported improved verbal communication over twelve weeks, with a larger signal among children positive for folate-receptor-alpha autoantibodies; retrospective analyses are consistent with a biomarker-response relationship but have not established one. The evidence is sufficient to justify a confirmatory federal trial. The FDA recently determined it was not currently sufficient for population-wide testing, broad clinical use, or characterization of leucovorin as a general autism treatment.

The recommended evidentiary sequence is therefore: assay harmonization; prospective subgroup definition; adequately powered multisite confirmation; FDA-aligned interpretation; and then, if efficacy and safety thresholds are met, treatment guidance and coverage analysis.

Current State of Knowledge

Cerebral folate transport is the near-term translational use case

Folate receptor alpha transports 5-methyltetrahydrofolate into the brain, and low central nervous system 5-methyltetrahydrofolate is the defining feature of cerebral folate deficiency. Folate receptor alpha autoantibodies may interfere with this transport pathway and may help identify a subgroup for whom folate-transport-directed therapy is biologically plausible.

This does not establish leucovorin as a general autism treatment. It supports the narrower conclusion that folate-transport biomarkers may identify a treatment-responsive subgroup and that confirmatory, adequately powered, multicenter trials are warranted.

Folate receptor alpha autoantibody testing requires harmonization before implementation

The central implementation barrier is not only whether the pathway is biologically plausible. It is whether the relevant assays are standardized, reproducible, and clinically interpretable. Folate receptor alpha autoantibody testing has varied across studies in method, specimen handling, thresholds, reporting, and interpretation. Without assay harmonization, multicenter trials, FDA biomarker qualification, coverage policy, and clinical guidance will remain difficult to operationalize.

Assay harmonization should therefore be the foundational near-term deliverable for Domain 3. Federal work should establish assay type, specimen requirements, reference thresholds, quality-control procedures, reporting language, analytic validity standards, clinical interpretation guardrails, and repeat-testing criteria when clinically or analytically justified.

Leucovorin evidence should be advanced through biomarker-defined confirmation

Leucovorin has the strongest translational rationale where there is evidence of cerebral folate transport disruption, folate receptor alpha autoantibody positivity, or clinically established cerebral folate deficiency. The next federal action is not general dissemination as an autism treatment. It is a confirmatory trial program that tests whether biomarker-defined subgroups show durable improvement in communication, adaptive function, participation, health stability, and quality of life, with safety monitoring and subgroup reporting.

Trial design should distinguish binding and blocking folate receptor alpha autoantibodies, CSF folate status where clinically available, age, language level, developmental profile, seizure history, medication use, co-occurring metabolic or mitochondrial findings, and baseline communication and adaptive function. Dosing, formulation, adherence, adverse events, and durability should be captured consistently.

Binding and blocking autoantibodies may help predict response but need prospective validation

Binding folate receptor alpha autoantibody titers may help predict response, but the current evidence should be treated as early validation rather than clinical certainty. Prospective studies should determine whether binding or blocking autoantibodies, CSF folate measures, soluble folate-binding proteins, one-carbon metabolites, redox markers, or pharmacogenomic factors improve subgroup definition and treatment prediction beyond clinical phenotype alone.

Broader one-carbon, methylation, and cofactor strategies remain earlier stage

One-carbon metabolism intersects with methylation, transsulfuration, glutathione metabolism, oxidative stress, mitochondrial function, and redox biology. These intersections are biologically important, but they do not justify broad clinical recommendations for methylation support, folate supplementation, or cofactor combinations without validated biomarkers, defined enrollment criteria, safety monitoring, and outcomes that matter to patients and families.

The domain should use one-carbon biology as a mechanistic and stratification framework, not as a general supplementation agenda. Methylation-related interventions, cofactor combinations, and broader supplement strategies should be evaluated only when enrollment is tied to biochemical, genetic, functional, or clinical evidence of pathway disruption.

Translational Status

Domain 3 spans near-translation, validation, implementation-to-validation, and discovery-to-validation. Federal action should start where the evidence is most mature while preventing broader supplementation claims from outrunning the data.

Component	Translational status	Federal task
Cerebral folate transport and leucovorin response in defined subgroups	Near-translation	Harmonize assays, conduct confirmatory multicenter trials, standardize endpoints, monitor safety, and engage FDA on biomarker qualification.
Folate receptor alpha autoantibody testing	Validation required	Standardize assay methods, specimen requirements, thresholds, interpretation, quality control, repeat-testing criteria, and reporting language.
Binding and blocking folate receptor alpha autoantibodies as response biomarkers	Early validation	Confirm predictive value in prospective controlled studies and define contexts of use before clinical or coverage reliance.
Cerebral folate deficiency recognition and referral	Implementation-to-validation	Clarify when testing, neurology or metabolic referral, CSF folate evaluation, treatment consideration, and follow-up are indicated.
Broader one-carbon, methylation, and cofactor-support strategies	Discovery-to-validation	Require biomarker-defined enrollment, safety monitoring, and meaningful outcomes; avoid general clinical recommendations until evidence matures.
Redox, glutathione, mitochondrial, and immune overlap	Cross-domain validation	Align folate-pathway measures with the metabolic, redox, immune, and mitochondrial domains to reduce duplication and clarify subgroup biology.
Coverage and access pathways	Evidence-linked implementation	Align CMS coverage assessment with validated assays, clinically indicated evaluation, and biomarker-defined

Component	Translational status	Federal task
		treatment evidence; avoid directed coverage before evidence thresholds are met.

Knowledge and Implementation Gaps

- Assay inconsistency: Folate receptor alpha autoantibody testing is not yet harmonized across laboratories, methods, specimen handling, thresholds, reporting language, or interpretation.
- Limited confirmatory trial evidence: Existing controlled studies are promising but remain limited by sample size, site concentration, follow-up duration, and outcome heterogeneity.
- Regulatory and coverage pathways are not settled: FDA, CMS, HRSA, and AHRQ need a shared evidence sequence for assays, biomarker qualification, endpoint standards, labeling questions, and coverage assessment.
- Biomarker-response relationships require prospective validation: Binding and blocking folate receptor alpha autoantibodies, CSF folate measures, soluble folate-binding proteins, one-carbon metabolites, redox markers, and pharmacogenomic factors need evaluation in controlled studies.
- Safety and dosing need consistency: Leucovorin and related interventions require standardized dose, formulation, adherence, adverse-event, seizure, sleep, GI, medication-interaction, and durability monitoring.
- Outcome measures need standardization: Communication, adaptive function, irritability, sleep, seizure burden, movement symptoms, attention, participation, caregiver-reported function, safety, and quality of life should be measured consistently across studies.
- Broad supplementation can outrun evidence: Methylation and one-carbon support strategies risk clinical uptake before subgroup definition, dosing, safety monitoring, and outcomes are established.
- Cross-domain biology can create redundancy: Folate, glutathione, mitochondrial function, immune biology, and redox balance overlap. Domain 3 should focus on folate and one-carbon mechanisms while coordinating with the metabolic/redox and immune domains.
- High-support and communication-diverse populations must be included: Trials and cohorts should include nonspeaking, minimally speaking, intellectually disabled, high-support, medically complex, regressive, rural, racially and ethnically diverse, late-diagnosed, and adult participants when scientifically appropriate.

Priority Federal Translation Agenda

Initiative 3.1: Folate Receptor Alpha Autoantibody Assay Harmonization

Lead agencies: NIH, FDA. Supporting agencies: CDC, CMS, AHRQ.

Federal agencies should establish standardized methods for folate receptor alpha autoantibody testing, including assay type, specimen requirements, thresholds, reporting language, quality control, analytic validity, clinical interpretation, and repeat-testing criteria. This is the precondition for credible multicenter trials, biomarker qualification, clinical guidance, and coverage policy.

Initiative 3.2: Confirmatory Multicenter Leucovorin Trial in Biomarker-Defined Subgroups

Lead agency: NIH. Supporting agencies: FDA, HRSA, CMS, AHRQ.

NIH should fund an adequately powered, multicenter, biomarker-defined trial of leucovorin in autistic individuals with evidence of folate transport disruption. Enrollment should be based on harmonized biomarkers, with stratification by binding and blocking folate receptor alpha autoantibodies, CSF folate status where clinically available, age, language level, developmental profile, seizure history, medication use, and relevant metabolic or mitochondrial findings.

The trial should not be framed as a general autism treatment trial. It should be framed as a precision therapeutic trial for a defined folate-transport subgroup, with standardized communication, adaptive-function, participation, safety, and quality-of-life endpoints.

Initiative 3.3: Cerebral Folate Deficiency Recognition, Referral, and Clinical Guidance

Lead agencies: HRSA and AHRQ. Supporting agencies: NIH, FDA, and CMS.

At 24 months, clinician material should be limited to differential recognition: established cerebral folate deficiency, when neurologic or metabolic referral is indicated, and how biomarker-indicated evaluation differs from unstratified folate or supplement use. It shall not recommend leucovorin for autism or treatment based solely on an unharmonized autoantibody result.

Any guidance addressing treatment in a folate-transport-defined autism subgroup is sequenced behind Initiative 3.2 and belongs only in the five-year deliverable if confirmatory evidence and regulatory review support it.

Initiative 3.4: One-Carbon, Methylation, and Redox Stratification Studies

Lead agency: NIH. Supporting agencies: AHRQ, FDA, CDC.

NIH should support studies that evaluate one-carbon metabolism, methylation capacity, transsulfuration, glutathione metabolism, redox balance, and related cofactor biology in defined subgroups. This work should coordinate with the mitochondrial, metabolic, redox, and immune domains and should avoid creating a parallel supplement agenda without validated stratification.

The priority is to identify which biochemical patterns are reproducible, clinically meaningful, treatment-responsive, and safe to target. Studies should use biomarker-defined enrollment, standardized outcome measures, medication and supplement exposure tracking, and durability follow-up.

Initiative 3.5: NLRP3 Inflammasome as a Cross-Domain One-Carbon/Immune Stratification Target

Lead agency: NIH. Supporting agencies: FDA, AHRQ, CDC.

NIH should support mechanistic and biomarker studies evaluating the NLRP3 inflammasome as a shared node linking one-carbon metabolism, transsulfuration, glutathione redox status, mitochondrial function, and innate immune activation in defined subgroups. The transsulfuration arm of one-carbon biology generates cysteine, the rate-limiting precursor for glutathione, and glutathione redox balance is a direct regulator of NLRP3 activation. The transsulfuration enzyme cystathionine β-synthase restrains microglial NLRP3 activation through glutathione-dependent redox control, and glutathione efflux acts as a necessary switch for NLRP3 activation, establishing a mechanistic bridge between one-carbon flux and innate immune activation (Mou et al., 2023; Zhang et al., 2021).

This initiative should not be framed as an NLRP3-directed treatment program or as a rationale for anti-inflammatory or supplement intervention absent validated biomarkers. Its purpose is to determine whether NLRP3-linked redox and immune measures improve subgroup definition, coordinate the folate/one-carbon domain with the metabolic/redox and immune domains, and reduce duplication across domains. Any move toward intervention should require biomarker-defined enrollment, safety monitoring, and clinically meaningful outcomes consistent with the standards applied to Initiative 3.4.

Agency Actions

Agency	Priority actions
NIH	Fund assay harmonization, biomarker-defined leucovorin trials, folate-transport studies, one-carbon pathway cohorts, endpoint development, and cross-domain studies with mitochondrial, redox, metabolic, and immune biology.
FDA	Advise on biomarker qualification, intended contexts of use, enrichment strategy, endpoint selection, pediatric safety, labeling questions, and regulatory requirements for folate-transport-defined indications.
AHRQ	Conduct evidence reviews distinguishing cerebral folate deficiency, folate receptor alpha autoantibody-positive subgroups, leucovorin trials, safety evidence, and broader one-carbon or methylation interventions.
HRSA	Develop clinician education that distinguishes biomarker-indicated folate-

Agency	Priority actions
	transport evaluation from unstratified supplementation and supports appropriate referral, safety monitoring, and follow-up.
CMS	Evaluate coverage evidence for validated folate receptor alpha autoantibody testing, clinically indicated CSF folate evaluation, biomarker-indicated treatment pathways, and access-attainment reporting once evidence thresholds are met.
CDC	Support longitudinal outcome tracking for biomarker-defined folate-transport cohorts, safety signals, service access, real-world implementation patterns, and linkage to the NAPTI Real-World Evidence and Outcomes Registry rather than a stand-alone folate registry.

This combined agenda begins at 12 months because assay harmonization, evidence review, and referral-guidance work are actionable through existing NIH, FDA, AHRQ, HRSA, CMS, and CDC authorities. Clinical and coverage guidance should follow validated evidence rather than precede it.

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Complete folate-receptor-alpha autoantibody assay comparison, evidence review, specimen and reporting standards, and an FDA consultation defining the evidentiary pathway for any proposed biomarker context of use.	NIH and FDA	AHRQ; CDC; DoD/CDMRP
18–24 months	Publish clinician material limited to	HRSA and AHRQ	FDA; NIH; CMS

Phase	Consolidated federal product	Accountable lead	Supporting partners
	differential recognition of established cerebral folate deficiency, appropriate neurologic or metabolic referral, and the distinction between indicated evaluation and unstratified supplement use; it shall not recommend leucovorin for autism.		
24–36 months	Launch a multicenter confirmatory trial in prospectively defined folate-transport subgroups using harmonized assays, prespecified functional outcomes, adequate safety monitoring, and FDA consultation.	NIH	FDA; AHRQ; CDC; DoD/CDMRP
3–5 years	Report trial and biomarker-validation results; only if prespecified thresholds are met, develop treatment guidance, regulatory strategy, and coverage analysis for the validated subgroup.	NIH and FDA	AHRQ; HRSA; CMS; CDC

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Availability and adoption of harmonized folate-transport assays and common data elements in federally supported studies.
- Enrollment, retention, safety-monitoring completeness, and subgroup diversity in the multicenter confirmatory trial.
- Progress toward a defined FDA biomarker context of use and completion of prespecified trial efficacy and safety thresholds.
- Durability-qualified functional and health outcomes in prospectively defined subgroups, with no population-wide treatment or screening claim.

Implementation Standards

- Domain 3 should not be framed as a broad folate, methylation, one-carbon, or supplement strategy for autism. Every clinical or research claim should identify the subgroup, biomarker, intervention, endpoint, and evidence maturity.
- Assay harmonization is the first dependency. Multicenter trials, biomarker qualification, coverage assessment, and clinician guidance should not rely on inconsistent laboratory methods, thresholds, or reporting language.

- Leucovorin studies should enroll biomarker-defined or clinically defined folate-transport subgroups and should not be described as general autism treatment trials.
- Clinical guidance should distinguish established cerebral folate deficiency or biomarker-indicated folate-transport evaluation from investigational methylation, redox, or cofactor-support strategies.
- Coverage policy should follow validated testing, clinically indicated evaluation, and evidence-defined treatment pathways. Coverage-directed recommendations should not precede assay validation or confirmatory evidence.
- Broader one-carbon, methylation, redox, and cofactor-support interventions should require biomarker-defined enrollment, safety monitoring, dose and formulation clarity, and clinically meaningful outcomes before guidance is considered. For example, the transsulfuration enzyme cystathionine β-synthase restrains microglial NLRP3 inflammasome activation through glutathione-dependent redox control, illustrating a direct mechanistic bridge between one-carbon/transsulfuration flux and innate immune activation (Mou et al., 2023)
- Functional improvement should be measured directly, durability-qualified, linked to whether a folate-transport state was characterized and treated, and never characterized as cure.
- Studies should include high-support and underrepresented populations whenever scientifically appropriate, including nonspeaking and minimally speaking individuals, people with intellectual disability, medically complex individuals, people with regression history, rural populations, racially and ethnically diverse groups, adults, and late-diagnosed individuals.
- Folate-domain reporting should use shared NAPTI cores, harmonized data elements, and the Real-World Evidence and Outcomes Registry rather than creating duplicative stand-alone infrastructure.

Translational Readiness Assessment

Within its defined subgroup, cerebral folate transport-directed therapy is one of the most advanced biomarker-linked opportunities in the therapeutic portfolio. The near-term work is assay harmonization, confirmatory multicenter trials, endpoint standardization, biomarker qualification, safety monitoring, and careful clinical guidance.

The current evidence may not support broad folate, methylation, one-carbon, or cofactor-support recommendations across autism. Broader one-carbon, methylation, redox, and cofactor-support strategies remain at a validation stage and should move into federal clinical or coverage guidance with confirmed biomarkers, defined enrollment criteria, safety evidence, and clinically meaningful outcomes.

The practical federal objective is to prevent two errors at once: failing to advance a plausible biomarker-defined treatment pathway where evidence is comparatively mature, and allowing broader supplement claims to outrun the validation needed for responsible policy. Domain 3 should therefore move quickly on assay harmonization and confirmatory trial readiness while keeping clinical and coverage claims tied to validated evidence.

Priority Therapeutic Domain 4: Gastrointestinal Biology, Microbiome Function, and Nutrition

Strategic Objective

Establish gastrointestinal health as a core clinical and translational priority in autism by improving recognition and treatment of gastrointestinal pain, feeding and nutrition risk, malabsorption, motility concerns, and standard gastrointestinal disease, while advancing disciplined biomarker-defined research on gut-brain axis interaction microbiome function, mucosal immune activation, microbial metabolites, digestive enzyme activity, intestinal barrier biology, diet-responsive physiology, and microbiome-directed interventions.

This domain has two linked but distinct federal tasks. The first is pragmatic and implementation-ready: autistic children and adults with reflux, constipation, diarrhea, bloating, abdominal pain, feeding restriction, post-meal escalation, night waking, visible distention, undigested food, growth or weight concerns, or unexplained irritability should receive timely medical evaluation and follow-up. These symptoms should not be attributed by default to autism, sensory behavior, noncompliance, or psychiatric presentation when gastrointestinal pain or dysfunction may be contributing.

The second task is translational and less mature. Microbiome composition, microbial enzymatic activity, mucosal immune signaling, intestinal permeability, short-chain fatty acid balance, aromatic amino acid metabolites, digestive enzyme activity, and diet-responsive physiology may identify clinically meaningful subgroups. These hypotheses require harmonized measurement, biomarker-defined enrollment, controlled trials, safety monitoring, and outcomes tied to pain, sleep, stooling, feeding, health stability, participation, and other quality of life outcomes in addition to core symptoms.

Scientific Rationale

Gastrointestinal problems are very common in individuals in ASD, with some estimates as high as 80% - suggesting possible mechanistic links. Interactions between the gut and brain (the gut-brain axis) are increasingly being documented in the scientific research literature and the medical community.

Gastrointestinal dysfunction can be a major determinant of pain, sleep, feeding, behavior, communication, learning, and participation. In autistic individuals with limited speech or unreliable symptom reporting, the same outward behavior may reflect communication difficulty, environmental mismatch, psychiatric distress, seizure activity, medication effects, or gastrointestinal pain. Federal policy should make gastrointestinal pain visible enough that it is evaluated rather than assumed.

The implementation problem is immediate. Constipation, reflux, diarrhea, abdominal pain, motility disorders, feeding disorder, malabsorption, nutritional deficiency, celiac disease, eosinophilic disease, inflammatory gastrointestinal disease, medication effects, and clinically significant pain already have ordinary standards of care. The federal task is to make those standards reliably accessible to autistic individuals, including people with sensory, communication, motor, cognitive, and support needs.

The research problem is narrower and less mature. Microbiome function, microbial metabolites, mucosal immune activation, barrier biology, digestive enzyme activity, diet-responsive physiology, FMT, and microbiota transfer therapy may define clinically meaningful subgroups, but they require harmonized phenotyping, biomarker-defined enrollment, controlled trials, safety monitoring, and durability-qualified outcomes before they can support federal guidance beyond established care.

Current State of Knowledge

Gastrointestinal symptoms can present as behavior, sleep disruption, or functional loss

Gastrointestinal pain may present as irritability, aggression, self-injury, withdrawal, sleep disruption, feeding refusal, post-meal escalation, abdominal pressing, toileting change, loss of participation, or apparent behavioral deterioration. These signs are nonspecific, but they are not clinically meaningless. In individuals with limited speech or limited interoceptive awareness, behavior may be the only pain signal and, GI pain should be considered and evaluated.

The clinical implication is direct: structured gastrointestinal history, pain assessment, stooling review, feeding and nutrition review, medication review, and referral when indicated should be part of autism-related care when symptoms suggest gastrointestinal burden. Misinterpreting gastrointestinal pain as behavior alone delays diagnosis and can prolong physiologic stress.

Standard gastrointestinal and nutrition care is ready for implementation now

Recognized gastrointestinal conditions, feeding disorders, malabsorption, nutritional deficiency, celiac disease, eosinophilic disease, inflammatory bowel disease, reflux, constipation, motility concerns, medication-related gastrointestinal effects, and clinically significant pain should be evaluated and managed under existing standards of care. The federal problem is not the absence of basic medical standards. It is inconsistent recognition, referral, access, follow-up, and quality measurement for autistic individuals.

Nutrition requires the same discipline. Restricted intake, food selectivity, weight change, growth concerns, micronutrient deficiency, dehydration risk, allergy, intolerance, and feeding disorder should trigger appropriate dietitian, feeding-team, gastroenterology, or other clinical referral. Medically indicated nutrition care should be distinguished from generalized autism dietary claims.

Microbiome and mucosal findings justify targeted research, not broad clinical adoption

Microbiome studies have reported altered microbial ecology in some autistic cohorts, but findings vary by age, diet, medication exposure, antibiotic history, geography, methods, and gastrointestinal phenotype. The more useful question is not only which organisms are present, but what the microbial community is doing: short-chain fatty acid production, aromatic amino acid metabolism, sulfur metabolism, bile acid metabolism, ammonia production, barrier effects, and mucosal immune tone.

Mucosal immune activation, barrier dysfunction, intestinal permeability, microbial metabolites, and gut-derived vagal nerve and inflammatory signaling should be studied together with clinical symptoms, stooling, feeding, pain, sleep, behavior, medication exposure, and diet. These findings should prompt better phenotyping and controlled studies, not over-diagnosis or unstratified treatment.

FMT, digestive enzymes, and diet-responsive interventions require evidence-matched sequencing

FMT and microbiota transfer therapy are in the controlled-trial stage. Open-label and observational findings justify rigorous testing, but they do not support framing FMT or microbiota transfer therapy as a general autism intervention yet. Trials should enroll defined subgroups with significant gastrointestinal symptoms, confirmed dysbiosis, inflammatory or IBD-like features, or metabolomic evidence of gut-derived physiologic burden, and should include donor screening, adverse-event monitoring, microbial and metabolomic endpoints, durability assessment, and long-term follow-up.

Digestive enzyme activity and maldigestion are legitimate research priorities, especially in individuals with bloating, undigested food, diarrhea, constipation, feeding refusal, restricted diets, suspected malabsorption, or post-meal distress. Targeted enzyme interventions should be tested in defined symptomatic or biochemically plausible subgroups. Valid endpoints should include relief of pain, bloating, stool abnormalities, feeding disruption, sleep disturbance, and post-meal distress, in addition to evaluation of core autism symptoms.

Dietary intervention research should distinguish medically indicated nutrition care from broader autism-directed dietary claims. Comparative-effectiveness work should measure benefit, potential harm, nutritional adequacy, adherence burden, caregiver demands, subgroup response, microbial and metabolomic effects, and durability.

Translational Status

Component	Translational status	Next federal action
Standard gastrointestinal evaluation and treatment	Implementation-ready	Improve symptom recognition, referral, access, pain assessment, follow-up, and quality measurement.
Feeding, nutrition, malabsorption, and deficiency care	Implementation-ready	Improve access to dietitians, feeding teams, gastroenterology, motility evaluation, and medically indicated nutrition support.
GI pain, post-meal flare, and symptom measurement in limited-communication populations	Development-to-validation	Develop and validate measures usable in clinical care, quality programs, surveillance, and trials.
Microbiome	Discovery-to-validation	Funding of large scale microbiome

Component	Translational status	Next federal action
taxa, metagenomic function, and microbial metabolites		studies that harmonize sequencing, metabolomics, stool collection, diet tracking, medication exposure, and longitudinal sampling.
Mucosal immune activation and barrier dysfunction	Biomarker-validation stage	Study calprotectin, lactoferrin, zonulin or other barrier markers, permeability, immune cell patterns, and clinical outcomes together.
Digestive enzyme activity and maldigestion	Early validation-to-precision trial	Profile enzyme activity, diet context, stool findings, permeability, and post-meal symptoms; test targeted interventions in defined subgroups.
FMT and microbiota transfer therapy	Controlled-trial stage	Support for biomarker-defined, safety-monitored trials in GI-symptomatic, dysbiotic, inflammatory, or gut-metabolic subgroups.
Dietary and nutrition interventions	Comparative-effectiveness stage	Evaluate benefits, harms, nutritional adequacy, adherence burden, caregiver demands, and subgroup response.

Knowledge and Implementation Gaps

- GI pain can go under-detected when distress, sleep disruption, feeding refusal, agitation, self-injury, or withdrawal is interpreted as behavior without medical review.
- Clinical systems do not consistently use autism-appropriate GI symptom, pain, stooling, feeding, and post-meal flare measures, especially for individuals with limited communication.
- Access to gastroenterology, motility evaluation, dietitians, feeding teams, and malabsorption workup varies by geography, payer, age, communication profile, and support need.
- Microbiome and metabolomic studies lack consistent stool collection, sequencing, diet tracking, medication and antibiotic documentation, symptom measures, and longitudinal follow-up.
- Mucosal immune and barrier markers require standardized interpretation and clinical correlation before they can guide care or trial enrollment.
- Digestive enzyme activity, maldigestion, protein digestion, carbohydrate intolerance, and post-meal physiologic flares are undermeasured in autism GI studies.
- FMT and microbiota transfer therapy require controlled, biomarker-defined, safety-monitored trials before any broad clinical or coverage recommendation.

- Dietary research often fails to separate medically indicated nutrition care from generalized autism dietary claims..
- Individuals with profound autism, intellectual disability, minimal or no functional speech, feeding disorders, regression, and complex medical conditions carry high GI burden but remain underincluded in research and quality measurement.

Priority Federal Translation Agenda

Federal action should be ordered by evidence maturity. Standard gastrointestinal and nutrition care should move through implementation now. Pain and symptom measurement should move from development to validation. Microbiome, mucosal, metabolite, enzyme, FMT, and diet-responsive hypotheses should move through harmonized measurement, biomarker-defined cohorts, controlled trials, and evidence thresholds before clinical adoption.

Initiative 4.1: Standard-of-Care GI Recognition, Pain Assessment, and Nutrition Access

Lead agencies: HRSA, CMS, AHRQ. Supporting agencies: NIH, CDC.

HRSA, CMS, and AHRQ should establish autism-specific implementation guidance for recognizing gastrointestinal pain, referring for evaluation, treating standard GI disease, addressing feeding and nutrition risk, and following symptoms over time. The guidance should address constipation, reflux, abdominal pain, diarrhea, bloating, motility disorders, food selectivity, feeding refusal, undigested food, growth or weight concerns, suspected malabsorption, inflammatory or immune-mediated disease, medication effects, sleep disruption linked to GI symptoms, and pain behaviors in limited-communication individuals.

CMS should evaluate access to gastroenterology, nutrition, feeding services, motility evaluation, indicated testing, and follow-up in Medicaid and other publicly financed care. Quality measures should focus on documented symptom assessment, completed referral when indicated, follow-up after evaluation, and access-attainment for covered, delivered care.

Initiative 4.2: GI Symptom, Pain, and Post-Meal Flare Measurement

Lead agencies: NIH, AHRQ. Supporting agencies: HRSA, CDC.

NIH and AHRQ should support development and validation of GI symptom, pain, stooling, feeding, and post-meal flare measures that work across communication levels and support needs. Measures should include caregiver observation, stooling patterns, feeding changes, abdominal distention, post-meal behavioral flares, sleep disruption, pain behaviors, medication exposure, diet context, functional decline, and objective clinical findings where available.

These tools should be usable in care, comparative-effectiveness research, microbiome trials, FMT and MTT trials, dietary studies, enzyme studies, surveillance, and quality programs. They should be designed to reduce diagnostic overshadowing rather than merely add another research scale.

Initiative 4.3: Integrated Microbiome, Metabolite, Mucosal, Enzyme, and Diet Biomarker Program

Lead agency: NIH. Supporting agencies: CDC, FDA, AHRQ.

NIH should support large-scale integrated biomarker studies that measure microbial taxa, metagenomic function, microbial metabolites, stool inflammatory markers, barrier or permeability markers, immune markers, digestive enzyme activity, diet, medication and antibiotic exposure, stooling, pain, sleep, feeding, and functional outcomes across a broad cross section of geographically and ethnically diverse individuals. The purpose is to move beyond the broad statement that the microbiome differs in autism and determine whether reproducible gut-metabolic, mucosal-immune, enzyme, or diet-responsive signatures identify subgroups with clinically meaningful treatment targets.

Common data elements should be coordinated with the NAPTI Harmonized Phenotyping and Common Data Elements Core and the Real-World Evidence and Outcomes Registry rather than creating a separate GI registry. This allows GI outcomes to be compared with sleep, immune, metabolic, autonomic, regression, and medication domains where symptoms overlap.

Initiative 4.4: Controlled Precision Trials and Evidence Reviews

Lead agencies: NIH, FDA, AHRQ. Supporting agencies: HRSA, CMS, CDC.

NIH and FDA should support rigorous controlled trials of FMT, microbiota transfer therapy, microbiome-directed interventions, and targeted enzyme interventions in defined subgroups. Enrollment should be based on significant GI symptoms plus relevant clinical or biomarker evidence, not autism diagnosis alone. Trials should include adverse-event monitoring, donor screening where applicable, pediatric safety controls, microbial and metabolomic endpoints, GI symptoms, pain, stooling, sleep, feeding, durability, and person-level functional outcomes.

AHRQ should conduct comparative-effectiveness reviews of standard GI management, diet and nutrition interventions, digestive enzyme interventions, and microbiome-directed therapies. Reviews should distinguish standard care for recognized GI and nutrition conditions from investigational autism-directed claims. HRSA and CMS should use the results to update clinician education, coverage analysis, and quality-measure pilots only where the evidence supports that step.

Agency Actions

Agency	Priority actions
NIH	Fund GI pain and symptom-measure development, integrated microbiome-metabolome-mucosal-enzyme-diet cohorts, biomarker harmonization, FMT/MTT trials, digestive enzyme studies, dietary subgroup studies, and mucosal barrier research. Coordinate shared measures through NAPTI rather than a standalone GI infrastructure.
FDA	Advise on FMT/MTT trial design, donor screening, microbiome-directed

Agency	Priority actions
	product regulation, endpoint selection, pediatric safety, digestive enzyme intervention pathways, digital or biomarker measure qualification where relevant, and long-term safety monitoring.
AHRQ	Conduct comparative-effectiveness reviews of standard GI management, diet and nutrition interventions, digestive enzyme interventions, and microbiome-directed therapies; distinguish medically indicated care from investigational claims; identify trial-ready questions.
HRSA	Develop clinician education on GI pain recognition, post-meal flares, feeding and nutrition risk, standard GI referral, enzyme and maldigestion awareness, limited-communication pain assessment, and diagnostic overshadowing.
CMS	Evaluate coverage and access to gastroenterology, nutrition, feeding services, motility evaluation, indicated testing, and follow-up; support quality measures for symptom assessment, completed referral, timely treatment, and access-attainment.
CDC	Support surveillance or registry-linked tracking of GI comorbidity, feeding and nutrition risk, pain burden, emergency utilization, hospitalization, microbiome intervention safety, disparities in access, and longitudinal outcomes using existing systems where feasible.
DoD / CDMRP Autism Research Program	Support innovative research on gastrointestinal conditions, pain, healthcare delivery, and treatment outcomes consistent with annual CDMRP priorities and shared NAPTI standards.

Key Performance Indicators

Indicators map to the common outcome architecture. The first set of measures address recognition, workup, timing, and access. Additional measures track research infrastructure, inclusion, and diagnostic yield; evidence generation, health stabilization, functional improvement, and durability in defined subgroups; and whether federally supported research continues to advance discovery in GI and microbiome biology.

- Percentage of participating clinical systems using structured GI symptom, pain, stooling, feeding, and post-meal flare assessment with referral triggers for limited-communication and high-support populations.
- Percentage of individuals with reported GI symptoms or pain behaviors who receive indicated evaluation or completed referral to gastroenterology, nutrition, feeding, motility, malabsorption, or related services.

- Median time from reported GI symptoms, pain behaviors, or post-meal flares to indicated evaluation, and median time from a characterized GI contributor to initiation of the indicated care pathway.
- Availability and adoption of validated GI symptom, pain, and post-meal flare measures for individuals with minimal or no functional speech, intellectual disability, or complex medical conditions.
- Access-attainment rate: proportion of individuals with an indicated GI, nutrition, feeding, motility, or malabsorption need who receive covered, delivered evaluation, treatment, and follow-up in participating systems.
- Number and percentage of federally supported GI, microbiome, nutrition, enzyme, FMT/MTT, or diet studies using harmonized common data elements and integrated stool, serum, urine, diet, medication, immune, and outcome measures.
- Inclusion of individuals with profound autism, intellectual disability, minimal or no functional speech, feeding disorders, regression, rural residence, racial or ethnic minority status, and complex medical conditions in GI care models, research cohorts, and trial reporting.
- Diagnostic yield of structured GI assessment: proportion of behaviorally presenting, sleep-disrupted, feeding-disrupted, or unexplained-decline cases in which evaluation identifies a treatable gastrointestinal, nutrition, feeding, motility, malabsorption, or pain contributor.
- Controlled precision-trial progress for microbiome-directed therapy, FMT/MTT, digestive enzyme, or diet-responsive subgroups, reported with predefined enrollment criteria, safety thresholds, durability windows, and GI-specific as well as functional endpoints.
- Health and functional stabilization after treatment of an identified GI disease, nutrition problem, feeding disorder, malabsorption, motility condition, or pain source, including change in pain, stool burden, sleep disruption, feeding safety, irritability, self-injury where linked to pain, participation, emergency utilization, hospitalization, caregiver burden, and quality of life, reported by subgroup and durability window.
- GI/microbiome discovery portfolio: number and percentage of federally supported GI- and microbiome-domain studies examining gastrointestinal biology, microbiome function, microbial metabolites, mucosal immune signaling, digestive enzyme activity, intestinal barrier biology, diet-responsive physiology, candidate targets, or system-level interactions in relation to core autism features, co-occurring conditions, regression, developmental trajectory, or treatment response.

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish autism-competent guidance for	HRSA and AHRQ	CMS; NIH; CDC

Phase	Consolidated federal product	Accountable lead	Supporting partners
	recognizing gastrointestinal pain, feeding and nutrition risk, constipation, reflux, diarrhea, malabsorption, motility concerns, and other established disease requiring standard evaluation.		
18–24 months	Validate practical symptom, pain, stooling, feeding, and post-meal measures for people across communication levels and adopt harmonized microbiome, metabolite, mucosal, enzyme, diet, medication, and antibiotic data elements.	NIH and AHRQ	CDC; FDA; HRSA; DoD/CDMRP
24–36 months	Launch controlled, safety-monitored studies of microbiome-directed, nutrition, diet-responsive, or digestive-enzyme interventions only in defined clinical or biomarker subgroups, accompanied by comparative evidence review.	NIH and AHRQ	FDA; CDC; CMS; HRSA; DoD/CDMRP
3–5 years	Report diagnostic yield, access, safety, nutritional adequacy, symptom change, and functional outcomes; translate only mature findings into clinical or coverage guidance.	AHRQ and NIH	FDA; HRSA; CMS; CDC

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Percentage of participating systems using structured GI, pain, feeding, and nutrition assessment with indicated referral completion.
- Median time from reported symptoms or pain behavior to evaluation and from a characterized contributor to covered, delivered care.
- Number, percentage, and dollar value of federally supported GI and microbiome discovery and translational studies using harmonized collection, diet, medication, clinical-phenotype, safety, and functional-outcome standards.
- Change in pain, GI symptoms, nutritional status, sleep, behavior, communication, participation, emergency use, and caregiver burden after treatment of an identified condition.

Translational Readiness Assessment

Domain 4 has an implementation-ready clinical core and a validation-stage translational frontier. Standard gastrointestinal care is ready now when the issue is recognized disease, pain, constipation, reflux, diarrhea, feeding restriction, malabsorption, nutritional deficiency, motility concern, inflammatory disease, medication effect, or clinically indicated evaluation. The federal task should be to support consistent recognition, referral, access, follow-up, and quality measurement.

Microbiome function, microbial metabolites, mucosal immune activation, barrier biology, digestive enzyme insufficiency, FMT/MTT, and diet-responsive subgroups require disciplined validation. The necessary federal products are harmonized symptom and biomarker measures, defined enrollment criteria, controlled trials, long-term safety monitoring, and outcome measures that show whether pain, sleep, feeding, stooling, health stability, participation, and quality of life improve in the subgroup expected to respond.

The practical federal objective is threefold: identify testable links and therapeutic targets connecting gastrointestinal biology, the microbiome, autism-related features, and co-occurring conditions; stop missing treatable gastrointestinal and nutrition problems; and build a credible evidence base for precision GI, microbiome, enzyme, and diet-responsive interventions in defined autistic subgroups.

Priority Therapeutic Domain 5: Neurodevelopmental Regression, Functional Trajectory, and Health Stabilization

Strategic Objective

Establish a national clinical and translational pathway for neurodevelopmental regression and clinically significant functional loss in autism that ensures prompt recognition, indicated diagnostic evaluation, follow-up after loss of skills or function, health stabilization, and mechanism-directed studies of functional trajectory in coordinated, biomarker-defined populations.

When regression or substantial functional loss occurs, the health system should recognize the change, document the prior baseline, complete the indicated evaluation, identify treatable contributors where present, deliver the appropriate care pathway, prevent loss to follow-up, and measure whether health, function, communication, safety, and participation stabilize or improve over time. The response should be organized around the regression event itself, whether the immediate contributor is seizure-related, metabolic, immune-mediated, infectious, sleep-related, gastrointestinal, medication-related, psychiatric, environmental, or not yet defined.

This domain does not treat regression as a single mechanism or as proof of any one biological explanation. It translates the broader Neurodevelopmental Regression (NDR) scientific platform into a practical clinical response, quality program, and functional-trajectory evidence system.

Scientific Rationale

Neurodevelopmental regression marks the loss of previously acquired developmental, language, communication, social, behavioral, motor, adaptive, sleep, feeding, toileting, or participation capacity. The standalone NDR priority establishes the science: the heterogeneous biology, possible contributors, case definition, phenotyping standards, and biospecimen framework. Domain 5 owns the clinical response, follow-up pathway, quality measures, and functional-trajectory endpoints that follow from that science.

The federal task is twofold. First, clinical systems must reliably identify and evaluate regression or substantial functional loss when it occurs, including in autistic children, adolescents, and adults whose changes may otherwise be attributed to autism itself. Second, mechanism-directed studies must use NDR phenotyping and biomarker standards to determine which subgroups show stabilization, return toward pre-decline baseline, preserved function, or improved participation after specific, indicated interventions.

The purpose is operational. When a person loses skills or function, the system should not wait for a complete mechanistic explanation before acting. It should trigger an organized, indicated diagnostic pathway; identify treatable contributors where present; coordinate specialty care; support families and caregivers during follow-up; and track whether health and function stabilize, worsen, or improve over defined follow-up windows.

Current State of Knowledge

Regression is clinically recognizable but inconsistently acted upon

Regression is often reported by families, caregivers, clinicians, educators, and support staff, but the response remains variable. Some individuals receive timely neurologic, metabolic, immunologic, infectious, gastrointestinal, sleep, medication, psychiatric, developmental, or general medical evaluation. Others experience delayed workup, fragmented referrals, or no structured follow-up after the initial loss is documented.

This is not only a research gap. It is an implementation failure. Autism can create diagnostic overshadowing, in which new loss of language, communication, adaptive function, sleep stability, motor capacity, continence, feeding, behavior regulation, safety, or participation is treated as part of the baseline condition rather than as a change requiring evaluation.

A subset of regression has identifiable and treatable contributors

Some regression presentations overlap with established clinical pathways in neurology, sleep medicine, metabolic medicine, immunology, infectious disease, gastroenterology, psychiatry, pain medicine, and general pediatrics or adult medicine. Examples include seizures or sleep-activated epileptiform activity, electrical status epilepticus in sleep, metabolic decompensation or mitochondrial vulnerability, immunodeficiency disorder, acute inflammatory or post-infectious deterioration, severe sleep disruption, pain, gastrointestinal disease, medication adverse effects, catatonia-like deterioration, and other destabilizing medical conditions.

A meaningful subset of regression warrants prompt medical evaluation because treatable contributors may be present. When such contributors are present, delay can reduce the opportunity for stabilization, symptom relief, return toward the prior baseline, or prevention of prolonged unresolved decline. The pathway should therefore measure timing, referral completion, treatment initiation, and longitudinal outcome rather than only whether a regression history was recorded.

Undefined regression requires a common care and research language

Many regression presentations remain mechanistically unclear after initial evaluation. For these cases, the immediate need is not speculation. The immediate need is a standardized clinical history, timing record, tempo description, trigger documentation, developmental and functional trajectory, safety assessment, objective outcome measures, and biospecimen collection where appropriate. These elements should align with the NDR case definition and phenotyping protocol so that clinical care, quality measurement, surveillance, and trials build from the same record.

The clinical pathway and the NDR scientific platform should remain distinct but interoperable. NDR supplies the common language for phenotype, timing, biospecimen standards, and longitudinal trajectory. Domain 5 applies that language to care coordination, referral completion, quality measurement, follow-up, and trial readiness.

Functional trajectory and stabilization must be measured directly

Regression research often focuses on onset and cause. The health system also needs to measure what happens after the regression event. Families and clinicians need to know whether sleep stabilizes, seizures improve, pain decreases, feeding improves, behavior becomes safer, hospitalizations decline, adaptive function returns, communication improves, and the person regains participation in school, work, therapy, family life, or community settings.

These outcomes are not secondary to the research agenda. They determine whether the clinical response matters. Federal programs should measure stabilization, continued decline, partial return toward pre-decline baseline, substantial return toward baseline, recurrence, and access to indicated care over defined follow-up windows. Graded improvement should be reported as a longitudinal trajectory, not as cure and not as a binary claim.

Translational Status

Domain 5 has three linked tracks that should be kept separate but coordinated. The clinical-response track can move now. It does not require consensus on a single mechanism of regression. It requires a practical standard that loss of previously acquired skill or function is a clinical change warranting documentation, indicated evaluation, follow-up, and care coordination.

Track	Readiness	Primary purpose	Federal product
Clinical recognition, indicated workup, and stabilization	Implementation-ready for many components	Recognize regression or major functional loss, complete an indicated standard-of-care workup, reduce missed treatable contributors, prevent loss to follow-up, and connect the person to care.	National care pathway, clinician and family tools, referral standards, coverage clarification, quality measures, and follow-up benchmarks.
NDR-aligned functional-trajectory measurement	Implementation-to-validation	Use common history, timing, baseline, follow-up, and outcome measures so clinical care and research produce comparable	Common data elements, fixed follow-up windows, graded functional-trajectory classifications, stabilization endpoints, and quality-measure specifications.

Track	Readiness	Primary purpose	Federal product
		data.	
Mechanism-directed functional-trajectory studies	Discovery-to-validation	Test targeted interventions in defined regression subgroups while using shared functional and stabilization endpoints.	Biomarker-defined studies coordinated with NDR and the immune, epilepsy, metabolic, sleep, gastrointestinal, autonomic, and medication domains; FDA-aligned endpoint and safety guidance.

Knowledge and Implementation Gaps

- No uniform trigger for clinical response: Regression does not consistently activate a structured diagnostic and follow-up pathway across primary care, developmental pediatrics, neurology, psychiatry, sleep medicine, gastroenterology, metabolic medicine, immunology, or adult medicine.
- Diagnostic overshadowing remains common: Loss of function may be attributed to autism rather than treated as a new clinical event requiring evaluation.
- Workup is uneven: Access to EEG, sleep evaluation, metabolic testing, immune or inflammatory evaluation, gastrointestinal assessment, medication review, pain assessment, psychiatric evaluation, and specialty referral varies by geography, insurance, age, and clinician awareness.
- Follow-up is poorly defined: Many individuals are evaluated once but not tracked longitudinally for stabilization, recurrence, return toward baseline, unresolved decline, caregiver strain, safety, or participation.
- Outcomes are not standardized: Trials and clinical programs often measure symptoms or behavior without consistent functional-trajectory, health-stabilization, and access-attainment endpoints.
- Research and care pathways are disconnected: Mechanistic regression studies may collect high-quality data while clinical systems fail to translate regression recognition into timely care.
- Adults and high-support populations are underprotected: Individuals with minimal or no functional speech, intellectual disability, complex medical conditions, late diagnosis, or adult functional decline may be least able to communicate change and least likely to receive a structured response.

Priority Federal Translation Agenda

Federal action should follow evidence maturity. The first task is implementation: make regression or major functional loss an actionable clinical event. The second task is quality measurement: track whether the indicated evaluation, referral, follow-up, and care pathway actually occur. The third task is research: coordinate biomarker-defined studies through NDR and the relevant therapeutic domains so mechanism-directed claims are tested in the right subgroup.

Initiative 5.1: National Regression Recognition and Indicated Diagnostic Pathway

Lead agencies: HRSA, AHRQ, CMS.

Partner agencies: NIH, CDC, FDA.

Federal agencies should develop and disseminate a national care pathway for recognition, documentation, indicated diagnostic evaluation, referral, and follow-up after neurodevelopmental regression or substantial functional loss in autistic individuals. The trigger should be observable and functional: loss or substantial decline in language, communication, motor
motor function (including fine and gross motor skills) or new onset of stereotypies,tics, or other atypical m otor behaviors, social engagement, adaptive behavior, behavioral regulation, sleep stability, feeding, toileting, school or work participation, safety, or another previously acquired capacity.

The pathway should specify the minimum clinical history and baseline documentation while allowing clinical judgment based on age, acuity, presentation, recurrence, and comorbidities. It should include medication review, medical review of systems, safety assessment, family-facing recognition materials, urgent red flags, and referral criteria for neurologic, sleep, metabolic, immune, infectious, gastrointestinal, psychiatric, pain, medication-related, or general medical evaluation when indicated. Medical assessment should consider differential diagnosis associated with regression. The goal is not to make every child or adult receive every test. The goal is to prevent regression from being dismissed, delayed, or handled without a coherent clinical pathway.

Initiative 5.2: Regression Follow-Up and Health Stabilization Quality Program

Lead agencies: CMS, HRSA, AHRQ.

Partner agencies: CDC, NIH.

Federal agencies should create a quality and implementation program to reduce delayed workup, incomplete referral, loss to follow-up, and unresolved health destabilization after regression is reported. The program should define follow-up intervals, track completion of indicated referrals, measure time from identified contributor to indicated care, and report stabilization outcomes across sleep, seizures, pain, feeding, gastrointestinal distress, hospitalization, safety, adaptive function, communication, and participation.

CMS should identify coverage and access barriers affecting EEG, sleep medicine, metabolic genetics, immunology, gastroenterology, pain evaluation, behavioral health, medication review, care coordination, and related follow-up. HRSA should disseminate clinician and family-facing tools. AHRQ should anchor pathway and quality measures in available evidence and identify where evidence is insufficient but action is still warranted under standard clinical care.

Initiative 5.3: NDR-Aligned Biomarker-Defined Functional-Trajectory and Stabilization Studies

Lead agencies: NIH, FDA.

Partner agencies: CDC, HRSA, CMS, AHRQ.

NIH and FDA should support coordinated studies and trials that test mechanism-directed interventions in defined regression subgroups while using shared functional-trajectory and stabilization endpoints. These studies should use NDR phenotyping and biospecimen standards, predefine the clinical or biomarker subgroup, and coordinate with the relevant therapeutic domain. Immune-mediated regression studies should sit scientifically within the Immune Domain; seizure-related studies should coordinate with epilepsy and neurology priorities; metabolic and mitochondrial studies should coordinate with the metabolic domain; sleep, gastrointestinal, autonomic, and medication-related presentations should coordinate with their respective domains.

Participants should not be enrolled into mechanistic studies as a substitute for clinical evaluation. Trial design should ensure that the indicated standard-of-care workup has been completed or is being completed, that FDA input informs enrichment and endpoints where regulated products are involved, and that outcomes measure stabilization, recurrence, participation, and return toward pre-decline baseline at fixed follow-up intervals.

Agency Actions

Agency	Priority actions
NIH	Fund regression cohort studies, biomarker-defined functional-trajectory studies, and longitudinal outcome studies using NDR standards; require coordination with immune, metabolic, epilepsy, sleep, gastrointestinal, autonomic, medication, and other relevant domain programs when those mechanisms are being tested; support inclusion of high-support, minimally speaking, nonspeaking, intellectually disabled, medically complex, and adult populations where scientifically appropriate.
FDA	Advise on enrichment, endpoints, pediatric and adult safety, recurrence outcomes, durability windows, and clinically meaningful functional-improvement or stabilization measures for regression-related trials and regulated products.
HRSA	Develop clinician education, family-facing recognition tools, referral pathways, and training resources for primary care, developmental pediatrics, neurology, psychiatry, sleep medicine, gastroenterology, community providers, and adult-care settings.
AHRQ	Conduct evidence reviews on diagnostic evaluation, treatable contributors, care coordination, follow-up models, functional-trajectory measures, stabilization outcomes, and implementation strategies after regression or major functional loss.
CMS	Address coverage and access barriers for indicated evaluation and follow-up, including neurology, EEG, sleep, metabolic genetics, immune, gastrointestinal, behavioral health, pain evaluation, medication review, care coordination, and related services; support quality measures for evaluation

Agency	Priority actions
	timing, referral completion, follow-up, and access attainment.
CDC	Support surveillance of regression incidence, timing, triggers, recurrence, evaluation patterns, service connection, and longitudinal outcomes using harmonized definitions when available; link reporting to existing surveillance and outcomes infrastructure rather than creating a separate registry unless later evidence justifies it.
DoD / CDMRP Autism Research Program	Support prospective or mechanistic regression research when responsive to annual CDMRP priorities, using the national regression definition, trajectory measures, and shared biospecimen standards.

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Adopt a national regression case definition, developmental-baseline and trajectory data set, presentation-driven evaluation standard, and clinician-facing recognition and urgent-referral pathway.	NIH, CDC, HRSA, and AHRQ	CMS; FDA; DoD/CDMRP
18–24 months	Establish prospective multicenter regression cohorts with serial biospecimens, harmonized phenotyping, fixed follow-up intervals, and linkage to the relevant immune, metabolic, epilepsy, sleep, GI, autonomic, and medication domains.	NIH	CDC; FDA; AHRQ; DoD/CDMRP
24–36 months	Pilot the clinical pathway and quality measures in participating health systems and initiate mechanism-directed studies in prospectively defined regression subgroups.	HRSA, CMS, and NIH	AHRQ; CDC; FDA
3–5 years	Report time to evaluation and care, diagnostic yield, health stabilization, continued decline, and partial or substantial return toward baseline by subgroup and	NIH and AHRQ	CDC; HRSA; CMS; FDA

Phase	Consolidated federal product	Accountable lead	Supporting partners
	durability window.		

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Percentage of regression or substantial functional-loss events documented against a prior baseline and receiving the indicated workup.
- Median time from recognized loss to indicated evaluation and from a characterized contributor to covered, delivered care.
- Enrollment, biospecimen completeness, subgroup representation, and cross-domain data completeness in prospective regression cohorts.
- Graded trajectory at fixed follow-up: continued decline, no change, stabilization, partial return toward baseline, or substantial return toward baseline.

Implementation Standards

- The pathway should be indicated, not universal. Regression should trigger clinical response, but the specific workup should follow age, presentation, acuity, recurrence, clinical red flags, and comorbidities.
- Change should be measured against the person's own prior baseline, not against a generic developmental norm alone.
- Standard clinical care should not be delayed while mechanism-directed research is pending.
- Mechanism-directed studies should not substitute for clinical evaluation, specialty referral, or follow-up after regression is reported.
- Functional improvement should be reported by domain, subgroup, and durability window. It should not be described as cure or as a universal expected outcome.
- High-support, limited-communication, intellectually disabled, medically complex, racially and ethnically diverse, rural, late-diagnosed, and adult populations should be included in design, evaluation, and outcome reporting where scientifically and ethically appropriate.

Translational Readiness Assessment

Regression recognition, baseline documentation, indicated diagnostic evaluation, referral completion, and treatable-contributor follow-up are implementation-ready. The main barriers are inconsistent recognition, diagnostic overshadowing, access, timing, payer coverage, and loss to follow-up, not the absence of a single regression mechanism.

Functional-trajectory and stabilization measurement is at early validation and needs harmonization across clinical programs, quality measures, surveillance, and trials. Biomarker-defined functional-trajectory studies remain discovery-to-validation and depend on NDR phenotyping standards and coordination with the immune, metabolic, epilepsy, sleep, gastrointestinal, autonomic, medication, and related domains. The practical federal objective is to make regression trigger an organized response now while building credible evidence about trajectory change on the shared NDR record.

Priority Therapeutic Domain 6: Mitochondrial, Redox, Metabolic Function, and Endocrine Biology

Strategic Objective

Advance mitochondrial, redox, metabolic, endocrine, and neuroendocrine biology as an integrated research and precision-therapeutic domain for autistic individuals with measurable abnormalities, while ensuring timely recognition and standard care for primary mitochondrial disease, established metabolic disorders, endocrine disease, and medication-related metabolic or endocrine complications.

This domain concerns identifiable metabolic subgroups, not a mitochondrial, redox, purinergic, or supplement-based explanation of autism broadly. The federal question is whether measurable bioenergetic impairment, oxidative stress, altered redox capacity, impaired fatty-acid oxidation, carnitine insufficiency, purinergic-signaling abnormalities, or related stress vulnerabilities contribute to health instability, regression risk, fatigue, weakness, seizure susceptibility, gastrointestinal burden, developmental trajectory, or treatment response in defined subgroups.

Scientific Rationale

Cellular energy metabolism is a plausible and testable therapeutic target because the brain, immune system, gastrointestinal tract, skeletal muscle, and autonomic system are highly energy-dependent. In some autistic individuals, mitochondrial and redox findings may reflect reduced physiologic reserve, altered stress response, impaired recovery after illness, intolerance of fasting or exertion, fatigue, poor endurance, regression vulnerability, seizure-threshold changes, or broader health instability— features consistent with impaired cellular energy metabolism. This domain also includes endocrine and neuroendocrine physiology. Research should examine thyroid, adrenal, glucose-regulatory, growth, pubertal, reproductive, and stress-response pathways; their interaction with immune, environmental, circadian, gastrointestinal, and autonomic systems; and their relevance to neurodevelopmental regression, co-occurring conditions, functional trajectory, and treatment response.

The relevant biology includes oxidative phosphorylation, electron-transport-chain activity, ATP generation, lactate and pyruvate metabolism, lactate-to-pyruvate ratio, fatty-acid oxidation, acylcarnitine profiles, organic acids, carnitine status, glutathione balance, reactive oxygen species, nitrosative stress, metabolomics, and downstream effects on inflammation, neuronal excitability, autonomic function, and cellular resilience.

Mitochondrial and redox findings should be treated as measurable biology in defined subgroups, not as a basis for broad or unstratified supplementation. A prudent federal strategy is to identify reproducible metabolic phenotypes, harmonize biomarkers, test interventions in biochemically defined cohorts, and measure outcomes that matter clinically.

Current State of Knowledge

Primary mitochondrial disease and secondary dysfunction require different responses

A subset of autistic individuals has primary mitochondrial disease or another recognized metabolic disorder. That situation is a medical-care and access problem before it is a precision-autism research problem. These individuals require appropriate metabolic genetics evaluation, standard diagnostic workup, clinical management, emergency or illness planning, medication and nutrition review, and follow-up under established medical standards.

A larger group may show secondary mitochondrial dysfunction, redox imbalance, or abnormal metabolic stress responses without meeting criteria for a primary mitochondrial disorder. This group is most relevant to precision therapeutic development. The key task is to determine which abnormalities are stable, clinically meaningful, treatment-responsive, and linked to outcomes such as fatigue, stamina, regression stability, seizures, sleep, gastrointestinal function, adaptive capacity, hospitalization, or quality of life.

Autistic individuals may develop the same thyroid, pituitary, adrenal, pancreatic, growth, pubertal, reproductive, bone-mineral, and other endocrine conditions as the general population. Autism should not delay clinically indicated evaluation of abnormal growth, weight change, excessive thirst or urination, hypoglycemia, menstrual disturbance, early or delayed puberty, temperature intolerance, unexplained fatigue, changes in blood pressure, electrolyte abnormalities, galactorrhea, bone-health concerns, or other endocrine signs. Clinical testing should follow established endocrine standards and the individual presentation rather than an autism-specific universal panel.

Redox biology is a candidate stratification system, not a treatment indication by itself

Reduced glutathione, altered oxidized-to-reduced glutathione ratio, elevated oxidative stress markers, impaired antioxidant capacity, and nitrosative stress have been reported in subsets of autistic individuals for decades. These findings may matter because redox capacity influences mitochondrial function, immune regulation, cellular redox homeostasis and biotransformation, synaptic physiology, and response to physiologic stress.

They also require careful interpretation. A low glutathione ratio, elevated oxidative marker, or abnormal metabolomic signature may be meaningful in one subgroup and nonspecific in another. Biomarker thresholds, specimen handling, illness timing, medication exposure, supplement exposure, diet, age, and laboratory method all affect interpretation. Federal guidance should therefore require analytic consistency when redox measures are used for trial enrollment, care pathways, or coverage decisions.

Metabolic vulnerability may be stress-responsive

Some metabolic abnormalities are most visible during physiologic stress: fever, infection, fasting, dehydration, exertion, anesthesia, seizure activity, sleep disruption, gastrointestinal illness, or inflammatory activation. A person may appear metabolically stable at baseline but destabilize during acute

illness. That pattern is clinically important because it can affect emergency planning, regression evaluation, hospitalization risk, and recurrent decompensation.

Federal studies should distinguish transient metabolic perturbation from persistent dysfunction. Both may matter, but they require different study designs. Baseline biomarker panels alone may miss stress-responsive physiology unless longitudinal sampling, illness context, acute-care data, and recovery trajectory are captured. Patient cell line mitochondrial function can also be evaluated ex-vivo under normal and induced stress conditions.

Supportive interventions need subgroup evidence and safety monitoring

Interventions used or proposed in mitochondrial, redox, or metabolic medicine, such as L-carnitine, coenzyme Q10, N-acetylcysteine, taurine, glutathione-directed strategies, riboflavin or other mitochondrial cofactors, targeted nutrition strategies, and related mechanism-supported approaches have plausible rationales in selected contexts. Some are already used clinically, but the evidence remains uneven because studies often enroll broad autism populations, use inconsistent biomarkers, combine multiple agents, or rely on short-term outcomes.

The operational question is specific: which intervention helps which subgroup, based on which biochemical profile, at what dose, with what safety monitoring, and with what measurable improvement in health, function, or stability. Multi-agent protocols should not be treated as self-explanatory evidence; trials should isolate components or justify combinations prospectively.

Emerging metabolic therapies require sequencing before broad testing

Ketogenic and other metabolic therapies may be appropriate under established indications, such as specific seizure contexts, and may have investigational relevance for defined metabolic subgroups. Outside of established indications, they should move through mechanistic study, early safety evaluation, biomarker-defined enrollment, and endpoint development before broader clinical testing.

This caution is especially important in autism, where feeding restriction, gastrointestinal disease, nutritional deficiency, medication use, epilepsy, sleep disruption, and complex care needs may alter the risk-benefit profile of metabolic interventions. Purinergic-signaling approaches and other emerging cellular-stress interventions should remain within controlled, safety-monitored research until subgroup, mechanism, dose, durability, and adverse-event evidence justify movement to later stages.

Purinergic signaling connects cellular stress, metabolism, and immune response but remains investigational in autism.

Extracellular ATP can function as a danger signal through P2X and P2Y receptors, including pathways involving P2X7, microglial signaling, calcium flux, and inflammasome activation. CD39 converts extracellular ATP and ADP toward AMP, and CD73 converts AMP to adenosine, shifting signaling toward adenosine receptors and potential resolution pathways. Federal research should measure extracellular purines, ectonucleotidase activity, receptor function, downstream immune and metabolic effects, and recovery over time in defined populations. The pathway should be tested rather than treated as an established universal mechanism or an immediate indication for antipurinergic treatment.

Translational Status

Component	Translational status	Federal task
Primary mitochondrial disease and recognized metabolic disorders	Implementation-ready	Improve recognition, access to metabolic genetics, emergency and illness planning, standard care, and follow-up.
Clinical triggers for metabolic evaluation	Implementation-ready with pathway support	Create referral guidance and clinician education for regression after illness, recurrent decompensation, fatigue, exercise intolerance, motor weakness, seizures, vomiting, failure to thrive, unexplained lactic acidosis, multisystem involvement, or family history.
Secondary mitochondrial dysfunction and redox imbalance	Biomarker-validation stage	Harmonize metabolic and redox measures; define clinically meaningful and reproducible subgroups.
Stress-responsive metabolic vulnerability	Discovery-to-validation	Use longitudinal and acute-illness sampling to distinguish transient perturbation from persistent dysfunction and to support emergency planning when indicated. Test patient mitochondrial function in ex-vivo cell lines under normal and metabolic stress conditions.
Mitochondrial and redox supportive interventions	Precision-trial stage	Test in biochemically defined cohorts with standardized outcomes, isolated or justified components, and systematic safety monitoring.
Emerging metabolic and purinergic-signaling therapies	Early validation	Conduct mechanistic and early-phase safety studies before broad clinical testing or coverage guidance.
Metabolic real-world outcomes	Implementation-to-validation	Track metabolic phenotypes, interventions, safety signals, regression

Component	Translational status	Federal task
		context, emergency utilization, hospitalization, recovery time, and long-term outcomes through shared NAPTI infrastructure.

Knowledge and Implementation Gaps

- Broad enrollment weakens interpretation: trials that enroll unselected autistic populations are unlikely to identify effects limited to biochemically defined subgroups.
- Biomarker variability: lactate, pyruvate, lactate-to-pyruvate ratio, acylcarnitines, organic acids, carnitine status, glutathione measures, oxidative stress markers, and metabolomic signatures vary by specimen handling, clinical state, diet, medication exposure, supplement exposure, illness, and laboratory threshold.
- Case definitions are inconsistent: studies use different definitions for primary mitochondrial disease, secondary mitochondrial dysfunction, redox imbalance, metabolic vulnerability, stress-responsive decompensation, and treatment-responsive metabolic phenotype.
- Stress physiology is undermeasured: many studies rely on baseline markers and miss illness-related, fasting-related, seizure-related, anesthesia-related, or regression-associated metabolic destabilization.
- Interventions are often combined: multi-agent supplement protocols make it difficult to determine which component is responsible for benefit, harm, or no effect.
- Safety monitoring is uneven: metabolic interventions can affect sleep, appetite, gastrointestinal function, seizure threshold, behavior, weight, hydration, and medication interactions.
- Access to metabolic evaluation is inconsistent: autistic individuals with fatigue, regression, seizures, motor weakness, exercise intolerance, feeding problems, or illness-related decompensation may not receive timely metabolic genetics evaluation.
- Emergency planning is not routinely captured: individuals with recurrent decompensation risk may not have documented sick-day, fasting, anesthesia, hydration, medication, nutrition, or emergency-department plans.
- Real-world outcome tracking is fragmented: metabolic phenotypes, indicated care, intervention exposure, safety, recovery time, hospitalization, and functional outcomes should report through the shared NAPTI real-world evidence and outcomes architecture rather than through isolated registries.

- Endocrine phenotypes are insufficiently characterized: National autism cohorts do not consistently capture thyroid disease, diabetes and glucose dysregulation, growth, puberty, reproductive health, prolactin, bone health, or adrenal and neuroendocrine conditions.
- Developmental timing is undermeasured: Hormone concentrations and their meaning vary by age, pubertal stage, time of day, menstrual status, pregnancy, menopause, illness, and sleep.
- Medication effects are difficult to separate from intrinsic biology: Metabolic and endocrine adverse effects require baseline and longitudinal measurement.
- Environmental and endocrine interactions remain uncertain: Endocrine-active exposures require validated exposure measures, developmental timing, mixture analysis, and gene–environment designs.
- Communication differences can obscure endocrine symptoms: Pain, menstrual symptoms, thirst, fatigue, temperature intolerance, weakness, and other changes may be communicated through behavior or functional decline

Priority Federal Translation Agenda

Priority 1: National Metabolic and Redox Biomarker Harmonization

Lead agencies: NIH, FDA.

Supporting agencies: CDC, AHRQ, CMS.

Federal agencies should establish harmonized protocols for mitochondrial, redox, and metabolic biomarker collection, processing, reporting, and interpretation. Priority markers should include lactate, pyruvate, lactate-to-pyruvate ratio, alanine, acylcarnitine profiles, plasma amino acids, urine organic acids, carnitine status, glutathione measures, oxidative and nitrosative stress markers, metabolomics, and clinically indicated genetic testing.

The goal is comparable, reproducible measures that can identify subgroups, support multicenter trials, guide safety monitoring, and distinguish primary metabolic disease from secondary or stress-responsive dysfunction.

Priority 2: Access to Standard Metabolic Evaluation and Emergency Planning

Lead agencies: HRSA, CMS.

Supporting agencies: NIH, AHRQ, CDC.

Autistic individuals with clinical features suggestive of mitochondrial disease, recognized metabolic disorder, or recurrent metabolic vulnerability should have access to appropriate metabolic evaluation. Clinical triggers may include developmental regression after illness, recurrent decompensation, unexplained fatigue, exercise intolerance, motor weakness, seizures, episodic vomiting, failure to thrive, unexplained lactic acidosis, abnormal movement, multisystem involvement, anesthesia sensitivity, fasting intolerance, or family history suggesting metabolic disease.

Federal implementation should focus on clinician education, referral pathways, emergency and illness planning, medication and nutrition review, and coverage for indicated testing and specialty evaluation. This is standard medical care where established disease or recognized clinical triggers are present.

Priority 3: Biomarker-Defined Trials of Mitochondrial and Redox Support

Lead agency: NIH.

Supporting agencies: FDA, AHRQ, CDC.

NIH should fund biomarker-informed trials of mitochondrial and redox supportive interventions in biochemically defined subgroups. Candidate interventions may include L-carnitine, coenzyme Q10, N-acetylcysteine, taurine, glutathione-directed strategies, riboflavin or other mitochondrial cofactors, targeted nutrition strategies, or other mechanism-supported approaches.

Trials should define enrollment by metabolic or redox profile, specify the intervention and dose, justify any combination protocol, monitor safety, and use outcomes that reflect the reason the intervention is being tested. Relevant outcomes include fatigue, stamina, muscle strength, sleep stability, seizure burden, gastrointestinal tolerance, adaptive functioning, regression stability, emergency utilization, hospitalization, school or community participation, caregiver burden, and quality of life.

Priority 4: Stress-Responsive Metabolic Vulnerability Program

Lead agency: NIH.

Supporting agencies: CDC, HRSA, CMS.

Federal research should examine metabolic changes during physiologic stress, not only at baseline. Studies should capture illness, fever, fasting, dehydration, seizures, anesthesia, sleep disruption, gastrointestinal illness, inflammatory activation, medication changes, and regression context. The purpose is to determine whether some individuals have episodic metabolic vulnerability that becomes clinically visible only during stress.

The program should support longitudinal sampling, emergency-department and hospitalization data, caregiver-reported decompensation patterns, recovery trajectories after acute illness, and linkage to clinically indicated emergency or sick-day protocols.

Priority 5: Comparative-Effectiveness and Evidence Threshold Review

Lead agency: AHRQ.

Supporting agencies: NIH, FDA, HRSA, CMS.

AHRQ should conduct comparative-effectiveness reviews of mitochondrial, redox, purinergic-signaling, diet-based metabolic, and other metabolic interventions used in relevant autistic populations. Reviews should distinguish standard care for diagnosed metabolic disease from investigational use in autism-related subgroups. They should also evaluate evidence quality, safety, subgroup definition, dosing, component attribution, durability, outcomes, and readiness for clinical guidance or coverage consideration.

The review should support a staged evidence framework: coverage and implementation for established metabolic disease and recognized clinical indications; coverage-with-evidence-development or trial enrollment for promising biomarker-defined interventions; research-only status for early metabolic, redox, or purinergic approaches that lack validated subgroups or adequate safety evidence.

Priority 6: Endocrine and Neuroendocrine Health, Measurement, and Longitudinal Research

Lead agencies: NIH and HRSA.
Supporting agencies: FDA, CMS, AHRQ, CDC.

Federal agencies should establish a coordinated endocrine and neuroendocrine research and clinical-recognition program. HRSA should disseminate clinical recognition and referral tools for established endocrine conditions, including thyroid disease, diabetes and glucose dysregulation, abnormal growth or puberty, reproductive and menstrual conditions, medication-related endocrine effects, and other clinically indicated presentations. CMS should evaluate barriers to covered testing, specialty referral, and follow-up within its authority.

NIH should support longitudinal research on thyroid–mitochondrial interactions, insulin and glucose regulation, HPA-axis and stress-response physiology, pubertal and reproductive transitions, neuroendocrine–immune signaling, metabolic medication effects, and endocrine contributors to regression or functional change. Measurement protocols should account for age, pubertal stage, time of day, illness, sleep, diet, medication, body composition, and reproductive status.

Environmental research should coordinate with the NDR exposome workstream to investigate endocrine-active exposures and developmental timing. Genetic research should examine mitochondrial, metabolic, endocrine, and stress-response susceptibility and gene–environment interactions without duplicating broad autism gene-discovery programs.

Routine endocrine screening of every autistic person is not the objective. The objectives are timely recognition of established disease, valid characterization of endocrine subgroups, and determination of whether endocrine or neuroendocrine physiology modifies health stability, regression, recovery, or treatment response.

Agency Actions

Agency	Priority actions
NIH	Fund metabolic and redox phenotyping, investigational mechanistic research to identify therapeutic targets, biomarker standardization, stress-responsive metabolic studies, biomarker-defined trials, longitudinal cohorts, and subgroup-specific outcome measurement through shared NAPTI infrastructure.
FDA	Advise on biomarker qualification, contexts of use, enrichment strategies, endpoints, pediatric safety, trial design, and regulatory pathways for metabolic, redox, endocrine, and purinergic-signaling interventions where

Agency	Priority actions
	applicable.
AHRQ	Conduct comparative-effectiveness reviews of mitochondrial, redox, purinergic-signaling, ketogenic, diet-based, and other metabolic interventions, with attention to subgroup evidence, safety, component attribution, and outcome quality.
HRSA	Develop clinician education on metabolic red flags, referral pathways, standard care for recognized mitochondrial or metabolic disease, endocrine instability, emergency planning, and avoidance of broad unstratified supplementation.
CMS	Evaluate access to metabolic genetics, biochemical testing, indicated therapies, emergency planning, care coordination, and quality measurement for Medicaid-enrolled autistic individuals with documented clinical triggers or recognized metabolic disease.
CDC	Support surveillance and real-world outcome capture of metabolic phenotypes, interventions, safety signals, regression context, emergency utilization, hospitalization, recovery time, and longitudinal health and function outcomes through existing data systems and the NAPTI outcomes architecture.

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish harmonized metabolic, mitochondrial, redox, specimen, preanalytic, and interpretation standards that distinguish primary mitochondrial disease, secondary dysfunction, and research-stage signatures.	NIH and FDA	CDC; AHRQ; DoD/CDMRP
18–24 months	Issue presentation-driven referral and emergency-planning guidance for clinically indicated metabolic evaluation, fasting or	HRSA and AHRQ	CMS; NIH

Phase	Consolidated federal product	Accountable lead	Supporting partners
	illness vulnerability, medication risk, and known mitochondrial disease.		
24–36 months	Launch biomarker-defined trials of metabolic or redox support and prospective studies of stress-responsive vulnerability using prespecified safety, seizure, illness, and functional outcomes.	NIH	FDA; AHRQ; CDC; DoD/CDMRP
3–5 years	Complete comparative-effectiveness and evidence-threshold reviews and report which biomarkers, clinical phenotypes, and interventions merit continued development, guidance, or discontinuation.	AHRQ and NIH	FDA; HRSA; CMS; CDC

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Adoption of harmonized metabolic, redox and research-grade endocrine measurement standards and clinically appropriate referral pathways.
- Median time from a metabolic decompensation or endocrine trigger concern to indicated evaluation, emergency planning, and covered follow-up.
- Number, percentage and dollar value of mitochondrial, redox, metabolic function, and endocrine discovery and translational trials using biomarker-defined enrollment, formulation and dose clarity, safety monitoring, and inclusion of medically complex participants.
- Change in metabolic stability, glucose regulation, growth or pubertal concerns, medication-related complications, illness-related decompensation, emergency use, fatigue, seizures, sleep, adaptive function, participation, and caregiver burden in defined subgroups.

Implementation Standards

- Standard care for recognized mitochondrial disease and established metabolic disorders should proceed now and should not wait for autism-specific biomarker validation.
- Secondary mitochondrial dysfunction, redox imbalance, and stress-responsive metabolic vulnerability should be evaluated through harmonized measures, defined clinical contexts, and subgroup-specific outcomes.
- Metabolic and redox interventions should not be framed as broad autism treatments or broad supplement recommendations.

- Trials should enroll biochemically defined participants, specify dose and component attribution, monitor safety systematically, and measure outcomes that match the biological rationale for treatment.
- Emergency and illness planning should be included when recurrent decompensation risk is documented, especially around fever, fasting, dehydration, exertion, anesthesia, seizures, gastrointestinal illness, or inflammatory activation.
- Outcome reporting should distinguish clinical access, biomarker validation, trial enrollment, safety, and person-level health or functional change.

Translational Readiness Assessment

This domain spans implementation, biomarker validation, precision trials, and early discovery. Recognized primary mitochondrial disease and established metabolic disorders are implementation-ready and require access, clinician education, emergency planning, and standard care now. Secondary mitochondrial dysfunction, redox imbalance, and stress-responsive metabolic vulnerability are ready for disciplined biomarker harmonization, longitudinal study, and enriched trials. Supportive interventions and emerging metabolic or purinergic-signaling therapies should move forward only in biochemically defined cohorts with safety monitoring and clinically meaningful endpoints.

The federal objective is practical: identify the individuals whose biology shows measurable metabolic vulnerability; ensure standard care when recognized disease or clinical triggers are present; test interventions only in the individuals whose biochemical profile supports that approach; and measure whether health stability, function, recovery time, and quality of life improve over defined follow-up intervals.

Priority Therapeutic Domain 7: Autonomic Dysfunction

Strategic Objective

Establish autonomic dysfunction as a clinically meaningful and measurable therapeutic domain in autism by improving recognition of dysautonomia, orthostatic intolerance, postural orthostatic tachycardia syndrome, thermoregulatory disturbance, sweating abnormalities, gastrointestinal motility disturbance, and stress-recovery dysregulation, while developing objective autonomic measures that can support defined cohorts, pragmatic trials, and clinical outcome tracking.

This domain separates two federal tasks. Recognized autonomic disorders and clinically meaningful autonomic symptoms require timely medical evaluation, referral, standard care, coverage review, and follow-up now. Autonomic physiology as an autism-relevant biomarker remains at the validation stage and should not be treated as a universal autism mechanism or as a broad clinical test without defined contexts of use.

Scientific Rationale

The autonomic nervous system regulates heart rate, blood pressure, temperature, sweating, digestion, sleep-wake transitions, arousal, stress response, recovery, and adaptation to posture, exertion, sensory load, illness, and emotional demand. When autonomic regulation is unstable, the clinical presentation can look behavioral even when the driver is physiologic.

Autonomic symptoms can include dizziness, presyncope, syncope, tachycardia, exercise intolerance, temperature dysregulation, abnormal sweating, fatigue, postural worsening, gastrointestinal dysmotility, poor recovery after illness, sensory overload, sleep instability, anxiety-like distress, irritability, aggression, self-injury, feeding difficulty, or reduced participation. These symptoms should not be attributed automatically to anxiety, behavior, sensory intolerance, or autism when autonomic dysfunction may be contributing.

The evidence base is important but uneven. Studies have reported autonomic differences in subsets of autistic individuals, including heart rate, heart-rate variability, respiratory sinus arrhythmia, electrodermal activity, and sympathetic arousal, but findings vary by age, task, anxiety, medication exposure, gastrointestinal symptoms, sleep, sensory state, and measurement method. Whether these autonomic differences represent a trait feature of autism or are better explained by co-occurring anxiety, constipation, psychoactive medication, or methodological variability remains an open question, and the evidence is further limited by small sample sizes, heterogeneous protocols, and low certainty ratings, particularly in populations with co-occurring intellectual disability. That variability supports a precision approach: clinically defined physiology, repeated measurement, subgroup-specific outcomes, and careful separation of autonomic dysfunction from anxiety, pain, medication effects, constipation, sleep loss, dehydration, or task-related arousal.

The federal posture should be narrow and useful. Autonomic physiology should improve subgroup recognition, clinical care, measurement, and trials; it should not become another universal theory of autism.

Current State of Knowledge

Autonomic symptoms can be clinically significant

Orthostatic intolerance, postural tachycardia, presyncope, syncope, heat intolerance, abnormal sweating, fatigue, palpitations, nausea, motility disturbance, exercise intolerance, and poor recovery after illness or exertion can substantially impair daily function. In autistic individuals with limited communication, these symptoms may present as refusal, agitation, withdrawal, collapse, aggression, self-injury, school avoidance, work avoidance, or sudden loss of tolerance for ordinary demands.

Autonomic evaluation should be part of the differential when symptoms cluster around posture, exertion, heat, hydration, meals, sleep disruption, illness, medication changes, pain, or sensory load. This is especially important for individuals with connective-tissue features, hypermobility, chronic gastrointestinal symptoms, fatigue, recurrent unexplained distress, or post-illness decompensation. Although no population-based study has established the prevalence of POTS or orthostatic intolerance specifically in autistic individuals, clinical observation across developmental pediatrics, neurology, and cardiology settings suggests that these presentations may be underrecognized in this population, and formal epidemiologic investigation is warranted.

Clinical pathways should be presentation-driven

The clinical response should not be broad autonomic screening for every autistic person. It should be a structured response when the presentation fits. Clinician-facing materials should help primary care, developmental pediatrics, cardiology, neurology, gastroenterology, psychiatry, emergency care, and rehabilitation providers know when to document orthostatic symptoms, obtain orthostatic vitals, review hydration and medications, assess pain and gastrointestinal contributors, and refer for cardiology, neurology, autonomic, rehabilitation, sleep, or related evaluation when indicated.

This work does not require a new autism-specific theory of dysautonomia before clinicians act on recognized symptoms. It requires better recognition, referral, coverage, and follow-up for presentations that already meet standard medical concern thresholds.

Physiologic measures are promising but not yet harmonized

Autonomic physiology can be measured through resting heart rate, heart-rate variability, respiratory sinus arrhythmia, electrodermal activity, skin conductance, blood pressure and blood-pressure variability, orthostatic vitals, tilt-table testing when clinically indicated, pupillometry, temperature, sweating, sleep physiology, and wearable sensor data. Each measure captures part of the system. None is sufficient alone.

The field needs harmonized protocols. Studies should document resting conditions, posture, task demand, time of day, sleep status, hydration, caffeine or stimulant exposure, psychotropic medication, gastrointestinal symptoms, pain, anxiety state, pubertal status, menstrual cycle when relevant, recent illness, and device or sensor characteristics. Without this context, autonomic data will remain difficult to interpret, reproduce, or use for trial stratification.

Wearable and remote measures need clinical-utility guardrails

Wearable and remote tools may be valuable because autonomic dysfunction often fluctuates across real-world settings. A brief clinic measure may miss patterns that families see at home, school, work, therapy, transportation, meals, sleep, or recovery after illness.

These tools should be developed as clinical and research supports, not surveillance devices. Federal validation should require accuracy against reference measures, sensory tolerability, wearability, privacy protection, consent and data-governance standards, missing-data rules, caregiver burden assessment, clinician interpretability, and evidence that the data can change evaluation, care, trial stratification, or outcome measurement. A wearable signal is not useful merely because it can be collected. Current evidence for wearable autonomic monitoring in autism is limited to small pilot and feasibility studies; no wearable tool has been validated against reference autonomic measures at scale in autistic populations, including those with sensory sensitivities or intellectual disability.

Autonomic dysregulation interacts with other domains

Autonomic arousal can intensify anxiety, sensory over-responsivity, sleep disruption, gastrointestinal symptoms, pain expression, medication sensitivity, and emotional dysregulation. The direction of causality may vary. Anxiety can drive autonomic activation; pain, constipation, reflux, dehydration, orthostatic intolerance, sleep loss, medication effects, and inflammatory illness can also drive anxiety-like distress.

Federal studies should therefore collect autonomic measures alongside sleep, GI symptoms, pain, sensory load, medications, hydration, nutrition, activity, seizure burden, anxiety, menstrual cycle when relevant, and functional participation. Autonomic dysfunction should not be studied as a stand-alone variable detached from the clinical context that shapes autonomic state.

Intervention endpoints should match the physiology being treated

Autonomic-directed care may include standard management of recognized disorders, such as hydration, salt when clinically appropriate, compression, physical reconditioning, medication review, treatment of contributing pain or GI disease, sleep stabilization, and pharmacologic therapy when clinically indicated. Other approaches, including paced breathing, biofeedback, vagal or arousal-regulation strategies, sensory-environment modification, activity pacing, and stress-recovery supports, require stronger autism-specific evidence. Heart-rate-variability biofeedback and related arousal-regulation approaches remain at the proof-of-concept stage in autism.

The endpoint should not be a generic claim of improved autism symptoms. The endpoint should match the physiology: fewer presyncope or syncope episodes, improved orthostatic tolerance, reduced tachycardia burden, better sleep continuity, improved GI motility or meal tolerance, improved recovery after exertion or illness, lower distress during transitions, reduced self-injury or aggression linked to physiologic overload, increased school or work participation, and lower caregiver burden.

Translational Status

Knowledge and Implementation Gaps

- Autonomic symptoms are underrecognized: dizziness, tachycardia, heat intolerance, sweating changes, fatigue, presyncope, postural worsening, GI dysmotility, and poor recovery after stress may be missed or attributed to behavior.
- Clinical pathways are inconsistent: autistic individuals with suspected dysautonomia do not reliably receive orthostatic vitals, medication review, cardiology, neurology, autonomic, rehabilitation, GI, sleep, or related evaluation when indicated.
- Measurement is not standardized: HRV, RSA, EDA, pupillometry, blood-pressure variability, and wearable data are collected using inconsistent protocols and interpreted without adequate clinical context.
- Thresholds are not validated: the field lacks autism-relevant thresholds that distinguish clinically meaningful autonomic dysfunction from anxiety, medication effects, pain, constipation, sleep loss, dehydration, or task-related arousal.
- Limited-communication populations are under-included: individuals who may benefit most from objective physiologic measures are often excluded from autonomic and wearable studies.
- Wearable tools require stronger validation: accuracy, sensory tolerability, privacy, consent, missing-data rules, caregiver burden, and clinical interpretability must be addressed before broad use.
- Trials are not yet physiologically targeted: autonomic regulation interventions rarely enroll participants based on defined autonomic profiles or measure physiology-matched outcomes.
- Outcomes are often too generic: studies should measure orthostatic tolerance, tachycardia burden, pre-syncope, recovery time, sleep, GI symptoms, participation, emergency use, and caregiver burden rather than broad autism symptom change alone.

Priority Federal Translation Agenda

Priority 1: Clinical Recognition and Standard Care for Dysautonomia

Lead agencies: HRSA, CMS, AHRQ

Supporting agencies: NIH, CDC

Federal agencies should establish clinician-facing guidance for recognizing autonomic symptoms in autistic individuals and referring for appropriate evaluation when indicated. The guidance should address orthostatic intolerance, POTS, syncope, pre-syncope, tachycardia, abnormal sweating, thermoregulation, exercise intolerance, fatigue, GI dysmotility, hydration sensitivity, medication effects, pain contributors, sleep disruption, and post-illness decompensation.

This priority is standard-care implementation. It should not require clinicians to accept a broad autism-specific dysautonomia theory before evaluating recognized symptoms.

Priority 2: Autonomic Measurement Harmonization Program

Lead agencies: NIH, FDA

Supporting agencies: CDC, AHRQ

NIH and FDA should establish harmonized methods for autonomic measurement in autism research and trials. Priority measures should include resting heart rate, HRV, RSA, EDA, skin conductance, blood-pressure variability, orthostatic vitals, pupillometry, temperature, sweating, sleep physiology, and wearable physiology.

Protocols should require documentation of posture, time of day, sleep, hydration, medication exposure, stimulant use, pain, GI symptoms, anxiety state, recent illness, pubertal status, menstrual cycle when relevant, and task context. The goal is not to create a single autonomic score. The goal is to make autonomic data reproducible, interpretable, and useful for subgroup definition and trial design.

Priority 3: Wearable and Remote Physiology Validation

Lead agency: NIH

Supporting agencies: FDA, CDC, AHRQ, HRSA

Federal studies should validate wearable and remote tools that capture autonomic physiology in real-world settings. Tools should be evaluated in individuals across communication levels, support needs, sensory profiles, ages, sex, co-occurring medical conditions, and residential or school/work contexts.

Validation should include accuracy against reference measures, wearability, sensory tolerability, battery life, missing data, privacy, consent, caregiver burden, clinician interpretability, and whether the data predict clinically meaningful events such as postural symptoms, sleep disruption, GI flares, physiologic distress, school or work refusal, emergency visits, or recovery after illness. Wearable measures should not be scaled as monitoring tools unless they have a defined clinical or research purpose.

Priority 4: Pragmatic Trials of Autonomic-Directed Care

Lead agencies: NIH, AHRQ

Supporting agencies: FDA, HRSA, CMS

Federal agencies should support pragmatic trials of autonomic-directed care in defined subgroups. Interventions may include standard dysautonomia management, hydration and salt strategies when appropriate, compression, physical reconditioning, medication review, sleep and pain stabilization, GI

treatment, pharmacologic therapy when clinically indicated, biofeedback, paced breathing, arousal-regulation strategies, sensory-environment modification, and activity pacing.

Enrollment should be based on clinical autonomic features, validated physiologic measures, or both. Outcomes should include orthostatic tolerance, tachycardia burden, presyncope, fatigue, sleep continuity, GI symptoms, distress during transitions, self-injury or aggression linked to physiologic overload, school or work participation, emergency utilization, and caregiver burden.

Priority 5: Autonomic Physiology Across Sleep, GI, Pain, Sensory, Medication, and Illness Contexts

Lead agency: NIH

Supporting agencies: CDC, AHRQ, HRSA

Autonomic data should be interpreted with the clinical context that shapes autonomic state. Federal studies should evaluate autonomic physiology alongside sleep, gastrointestinal symptoms, pain, sensory exposure, hydration, nutrition, menstrual cycle when relevant, medications, physical activity, seizure burden, acute illness, and functional participation.

This program should determine whether autonomic measures help identify the physiology behind recurrent distress, sleep disruption, post-meal flares, sensory overload, fatigue, school or work avoidance, post-illness decompensation, or episodic functional decline. The goal is better clinical explanation and better matching of intervention to presentation.

Agency Actions

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish presentation-driven recognition and referral guidance for orthostatic intolerance, POTS, syncope, thermoregulatory disturbance, sweating abnormalities, gastrointestinal dysmotility, and post-illness decompensation.	HRSA and AHRQ	CMS; NIH; CDC
18–24 months	Adopt harmonized autonomic protocols covering posture, hydration, sleep,	NIH and FDA	CDC; AHRQ; DoD/CDMRP

Phase	Consolidated federal product	Accountable lead	Supporting partners
	medication, pain, GI symptoms, anxiety state, illness, sex-specific variables, device characteristics, and clinically appropriate reference measures.		
24–36 months	Validate wearable and remote physiology tools for accuracy, tolerability, privacy, missing-data performance, caregiver burden, clinical interpretability, and defined research or clinical utility.	NIH	FDA; CDC; AHRQ; HRSA; DoD/CDMRP
3–5 years	Complete pragmatic trials of autonomic-directed care in defined phenotypes and report physiology-matched health, participation, safety, and quality-of-life outcomes.	NIH and AHRQ	FDA; HRSA; CMS

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Adoption of autonomic trigger guidance and completion of indicated orthostatic, medication, hydration, pain, GI, sleep, or specialty evaluation.
- Median time from trigger to evaluation and from a characterized autonomic contributor to covered, delivered care.
- Percentage of federally supported autonomic and wearable studies meeting harmonization, accuracy, tolerability, privacy, inclusion, and clinical-utility standards.
- Change in orthostatic tolerance, tachycardia burden, presyncope, fatigue, sleep, GI symptoms, recovery, participation, emergency use, and caregiver burden in defined phenotypes.

Implementation Standards

- Evaluation should be presentation-driven. Autonomic workup should be triggered by defined clinical patterns rather than applied as universal screening across autism.
- Standard care should proceed when recognized autonomic disorders, orthostatic intolerance, POTS, syncope, thermoregulatory disturbance, or related clinical presentations meet ordinary medical concern thresholds.

- HRV, RSA, EDA, pupillometry, blood-pressure variability, and wearable measures should not be treated as broad autism biomarkers until methods, thresholds, reliability, and contexts of use are validated.
- Wearable and remote tools should be developed as clinical and research supports, not surveillance devices. Validation must include privacy, consent, sensory tolerability, missing-data standards, caregiver burden, and clinical utility.
- Outcomes should match the physiology being treated and should not be reported as nonspecific improvement in autism symptoms.
- Studies and quality measures should include people with limited communication, intellectual disability, high support needs, complex medical conditions, and underrepresented demographic groups when scientifically and ethically appropriate.
- Reporting should distinguish symptom recognition, diagnostic evaluation, characterized autonomic contributor, delivered care pathway, access attainment, and person-level health or participation change.

Translational Readiness Assessment

Autonomic dysfunction spans implementation and validation. Recognized dysautonomia, orthostatic intolerance, POTS, syncope, thermoregulatory disturbance, GI dysmotility, post-illness decompensation, and related clinical presentations are implementation-ready when they meet standard medical criteria. The federal priority for these presentations is recognition, referral, coverage, standard care, and follow-up.

Autonomic physiology as an autism-relevant biomarker remains at the validation stage. Objective measures require harmonized methods, clinical context, repeated measurement, reliability testing, sensory-tolerable collection, privacy safeguards, and defined contexts of use before pragmatic trials enroll individuals whose symptoms and physiology justify autonomic-directed care. The practical aim is to make physiologic distress visible earlier and match intervention to autonomic phenotype rather than to behavior alone.

Priority Therapeutic Domain 8: Sleep and Circadian Regulation

Strategic Objective

Reduce the health, functional, and family burden of sleep disturbance in autistic individuals by making evidence-informed sleep assessment and first-line sleep care part of routine autism-related health care; improving recognition of treatable medical contributors; and advancing comparative-effectiveness trials, objective sleep measurement, circadian phenotyping, and prospective pediatric safety monitoring where the evidence base remains incomplete.

Scientific Rationale

Sleep disturbance is one of the most common and clinically consequential health problems affecting autistic individuals, and it is also one of the most practical therapeutic targets. Reviews of sleep in autism describe high rates of insomnia, delayed sleep onset, night waking, reduced sleep duration, parasomnias, circadian rhythm disturbance, and co-occurring primary sleep disorders, with effects that extend into daytime behavior, learning, family functioning, and caregiver burden (Hillman, Estes, and Chen 2024; Diaz-Roman et al. 2018).

Sleep should not be treated as an ancillary quality-of-life issue. Many individuals with autism experience chronic sleep disruption lasting years — and its effects cascade across the household, eroding caregiver health, sibling well-being, and family stability. Poor sleep can worsen irritability, aggression, self-injury, anxiety, inattention, seizure vulnerability, pain sensitivity, gastrointestinal symptoms, adaptive functioning, and participation in school or employment.,. It also creates a recurring diagnostic problem: symptoms driven or worsened by sleep disruption may be interpreted as behavioral noncompliance, psychiatric escalation, or developmental inevitability rather than as treatable physiology.

The federal task is not to establish that sleep matters. That point is already settled. The task is to make sleep assessment and treatment reliable, accessible, measurable, and sequenced around the presentation. Sleep disturbance in autism may reflect behavioral or environmental factors, circadian timing, melatonin biology, primary sleep disorders, pain, gastrointestinal disease, epilepsy, medication effects, anxiety, autonomic instability, or other medical contributors. A credible care pathway keeps all of these possibilities visible rather than treating every sleep problem as behavioral insomnia.

The practical organizing principle for this domain is straightforward: determine why the person is awake before escalating treatment.

Current State of Knowledge

Sleep disturbance is common, consequential, and treatable

The clinical literature supports sleep as a core health domain in autism rather than a secondary concern. Meta-analytic and clinical reviews describe substantial sleep disturbance across subjective and objective measures, with common findings including reduced sleep duration, prolonged sleep latency, frequent night waking, lower sleep efficiency, and circadian timing differences.

Sleep assessment should be expected in autism-related care, especially when a child, adolescent, or adult presents with irritability, aggression, self-injury, anxiety, attention problems, regression-like functional loss, seizures, worsening gastrointestinal symptoms, daytime fatigue, school disruption, or loss of participation. These presentations should trigger clinical inquiry into sleep timing, sleep duration, awakenings, breathing, movement, pain, reflux, medications, seizure-like events, and circadian pattern.

Behavioral sleep care and melatonin are ready for wider implementation

Behavioral sleep education, parent- or caregiver-mediated sleep strategies, environmental modification, structured routines, initiation or increase of exercise/physical activity, and clinically appropriate melatonin have the strongest near-term implementation relevance. Controlled studies and reviews support melatonin for sleep-onset insomnia in autistic children, particularly where delayed sleep onset or circadian timing is part of the presentation.

Implementation should not mean indiscriminate use. Melatonin guidance should address indication, timing, dose, formulation, response tracking, adverse effects, interactions with seizure disorders or other medications, and discontinuation or reassessment. Behavioral and environmental sleep care and education on the positive effects of exercise and physical activity on sleep should be accessible before or alongside medication when clinically appropriate, and pharmacologic escalation should not substitute for evaluation of medical contributors.

Medical contributors must be actively evaluated

Sleep disruption in autism is often treated as insomnia before the underlying drivers are fully assessed. That approach misses treatable contributors. Gastrointestinal discomfort, reflux, constipation, food-related symptoms, pain, epilepsy, nocturnal seizures, obstructive sleep apnea, restless sleep, iron-related contributors when clinically indicated, autonomic instability, medication effects, and anxiety can all present as bedtime resistance, prolonged sleep latency, night waking, early waking, or daytime dysregulation.

Federal guidance should support practical screening and referral pathways, including when to consider polysomnography, neurology evaluation, gastrointestinal evaluation, pain assessment, medication review, ferritin or iron-related evaluation when clinically indicated, and treatment of primary sleep disorders under existing pediatric, adult, neurology, and sleep-medicine standards.

Objective sleep and circadian measures should support care and trials

Sleep assessment still relies heavily on caregiver report, sleep diaries, and clinical history. Those sources are essential, but they are incomplete, especially for nonspeaking individuals, people with limited interoceptive communication, individuals who sleep separately from caregivers, and patients whose night waking, movement, respiratory symptoms, seizures, or autonomic changes are not reliably observed. Actigraphy, validated wearable-derived measures, sleep diaries, caregiver report, video-supported observation where appropriate, and clinically indicated polysomnography should each have defined roles.

Objective measures should not replace clinical judgment. They should make sleep problems easier to identify, quantify, and follow over time. They should also make trials more credible by reducing reliance on broad behavior ratings that may improve for reasons unrelated to sleep.

Circadian dysregulation is an important line of inquiry where delayed sleep onset, irregular sleep-wake timing, seasonal sensitivity, light sensitivity, melatonin timing differences, or response to melatonin is present. Circadian findings should not be treated as self-executing clinical biomarkers. They become useful when they inform timing, dosing, sequencing, environmental light intervention, or referral decisions that improve sleep and daytime functioning.

Pharmacologic use requires stronger pediatric safety and durability evidence

Melatonin occupies a different evidentiary position from newer or more sedating pharmacologic approaches. Melatonin has controlled-trial and review support for sleep-onset problems in autistic children, while many other pharmacologic sleep aids are used off label with limited long-term pediatric safety, durability, and comparative-effectiveness data. However, efficacy is variable and effects can fade with time. Long-term pediatric safety data remain limited; the AAN practice guideline notes concern about potential suppression of the hypothalamic-gonadal axis, and the longest controlled follow-up to date — a two-year open-label extension — found no detrimental effects on growth or pubertal development but does not resolve uncertainty beyond that interval.

The federal plan should avoid treating off-label sleep medication use (e.g. clonidine, trazodone) as settled care simply because it is common. Where medications are studied, trials and prospective follow-up should measure sleep, daytime functioning, adverse effects, durability, discontinuation, seizure-related interactions, psychiatric-medication interactions, endocrine or pubertal considerations where clinically relevant, caregiver-relevant outcomes, and reasons for treatment failure. Clinical experience suggests that off-label agents can produce meaningful improvements in sleep and family quality of life for individuals who do not respond to melatonin alone; the intent is not to withhold these options but to generate the comparative-effectiveness, safety, and durability data needed to guide their use more reliably.

Translational Status

Area	Readiness	Practical implication
Behavioral sleep education and environmental sleep supports	Implementation-ready	Embed in routine care, clinician education, Medicaid-supported care coordination, and family-facing supports.
Melatonin for sleep-onset insomnia and circadian-delay presentations	Implementation-ready with continued safety monitoring	Use through clinical guidance that addresses indication, timing, formulation, dose, response tracking, adverse effects, and reassessment.
Primary sleep disorders, including obstructive sleep	Standard-of-care pathway	Recognize and refer using existing pediatric, adult, neurology, and sleep-medicine standards.

Area	Readiness	Practical implication
apnea and restless sleep presentations		
Medical-contributor evaluation	Implementation-ready in indicated presentations	Evaluate pain, GI disease, epilepsy, medication effects, anxiety, autonomic symptoms, iron-related contributors when indicated, and other drivers before escalating treatment.
Objective sleep measurement, actigraphy, and wearable-derived measures	Validation-to-implementation	Define clinical and trial contexts of use, especially for limited-communication individuals; validate accuracy, acceptability, missing data, and interpretability.
Circadian biomarkers and timing interventions	Validation stage	Measure circadian biology when it can inform treatment timing, sequencing, light exposure, dosing, or referral decisions.
Newer or sedating pharmacologic sleep aids	Trial and prospective-follow-up stage	Require pediatric safety, durability, comparative-effectiveness, adverse-event, and interaction data before broader federal guidance encourages use.

Knowledge and Implementation Gaps

- Sleep assessment is not consistently embedded in autism-related care, even when daytime symptoms suggest sleep disruption.
- Behavioral sleep interventions and melatonin are not implemented evenly across settings, payers, ages, and provider types.
- Clinicians often lack practical pathways for distinguishing insomnia from pain, gastrointestinal disease, epilepsy, obstructive sleep apnea, restless sleep, autonomic dysregulation, anxiety, medication effects, or circadian delay.
- Comparative-effectiveness evidence remains limited for intervention selection, sequencing, combination approaches, and durability.
- Objective sleep measures are not yet standardized for clinical use or trials in autistic individuals with limited communication.

- Circadian markers require clearer clinical contexts of use before they are used to guide care.
- Long-term pediatric safety and durability data remain limited for many pharmacologic sleep aids used off label.
- Outcomes often focus on sleep latency or duration without adequately measuring daytime irritability, aggression, self-injury, seizure burden, learning, participation, caregiver sleep, and family functioning.

Priority Federal Translation Agenda

Priority 8.1: National Sleep Recognition and Standard Care Implementation

Lead agencies: HRSA, CMS, AHRQ

Supporting agencies: NIH, CDC

Federal agencies should support a national effort to make sleep assessment a routine part of autism-related health care. This should include practical screening questions, referral triggers, care pathways, and family-facing materials that help distinguish behavioral insomnia from treatable medical contributors.

Implementation materials should be usable in primary care, developmental-behavioral pediatrics, neurology, psychiatry, sleep medicine, gastrointestinal clinics, school-linked health settings, and Medicaid-supported care coordination. The goal is not to create another specialty silo. The goal is to ensure that sleep is recognized early, evaluated appropriately, treated when indicated, and followed over time.

Priority 8.2: Comparative-Effectiveness Review and Sequencing Trials

Lead agencies: AHRQ, NIH

Supporting agencies: FDA, HRSA, CMS

AHRQ and NIH should support a coordinated comparative-effectiveness agenda for sleep interventions in autism. The program should compare behavioral sleep education, environmental intervention, melatonin, circadian timing strategies, medical evaluation and treatment of contributors, primary sleep-disorder treatment, and selected pharmacologic approaches where justified by safety and clinical need.

Trials should evaluate sequencing. For example, studies should test whether outcomes differ when behavioral sleep intervention is delivered before melatonin, alongside melatonin, or after medical contributors are addressed. Trials should also examine whether subgroups defined by sleep-onset delay, night waking, epilepsy, gastrointestinal symptoms, pain, autonomic symptoms, anxiety, medication exposure, intellectual disability, communication profile, or age respond differently.

Priority 8.3: Objective Sleep Measurement and Limited-Communication Assessment

Lead agencies: NIH, CDC, FDA

Supporting agencies: AHRQ, HRSA

Federal agencies should support validation of objective and caregiver-reported sleep measures suitable for autistic individuals across communication profiles. Actigraphy, wearable-derived sleep measures, sleep diaries, caregiver report, video-supported observation where appropriate, and polysomnography should each have defined roles.

This work should be especially attentive to people who cannot reliably report fatigue, pain, reflux, restless sleep, nightmares, nocturnal seizures, or internal arousal. Validated measures should be usable in clinical care, quality programs, pragmatic trials, and longitudinal follow-up, and should capture outcomes that matter to patients and families.

Priority 8.4: Circadian Biology, Melatonin, and Pediatric Safety Monitoring

Lead agencies: NIH, FDA

Supporting agencies: CDC, AHRQ, HRSA

NIH and FDA should support a focused circadian and pediatric safety program. This should include melatonin timing, formulation, dose-response, durability, adverse effects, discontinuation, pubertal and endocrine considerations where clinically relevant, interactions with seizure disorders and other medications, and prospective safety monitoring for sleep interventions commonly used in autistic children.

Circadian studies should connect measurement to clinical decisions. Dim-light melatonin onset, sleep timing, light exposure, actigraphy, temperature rhythm, and related measures should be studied when they can inform treatment selection, timing, sequencing, or environmental light intervention. Newer or sedating sleep medications should move through controlled or prospective follow-up designs before federal guidance treats them as broadly established.

Priority 8.5: Sleep Comorbidity Integration Program

Lead agencies: NIH, AHRQ

Supporting agencies: HRSA, CMS, CDC

Sleep should be integrated with other relevant health domains. Gastrointestinal symptoms, pain, epilepsy, autonomic dysregulation, anxiety, medication effects, iron-related restless sleep presentations, and primary sleep disorders should be built into sleep assessment pathways and trial designs.

This approach reflects how autistic individuals present clinically. If a child or adult is awake because of reflux, constipation, nocturnal seizures, orthostatic symptoms, medication activation, pain, anxiety, obstructive sleep apnea, or restless sleep, the sleep intervention must identify and address that driver rather than escalating treatment as if all insomnia has the same cause.

Agency Actions

Agency	Priority actions
NIH	Fund comparative-effectiveness and sequencing trials; support objective sleep-measure validation, circadian phenotyping, melatonin timing and formulation studies, pediatric safety monitoring, and cross-domain sleep studies involving GI, pain, epilepsy, autonomic, medication, and mental-health contributors.
AHRQ	Conduct comparative-effectiveness reviews of behavioral sleep care, melatonin, circadian strategies, primary sleep-disorder treatment, selected

Agency	Priority actions
	pharmacologic approaches, and treatment of medical contributors; develop implementation guidance for intervention selection and sequencing.
HRSA	Develop clinician education and implementation resources for sleep assessment and management in autistic individuals; include medical contributors, primary sleep disorders, referral triggers, melatonin guidance, and follow-up; integrate sleep guidance into federally funded autism, maternal-child health, and primary-care training programs.
CMS	Evaluate coverage and access barriers for sleep evaluation and treatment, including polysomnography when clinically indicated; support quality measures for documented sleep screening, referral, treatment initiation, follow-up, and Medicaid care models that include sleep assessment as part of broader health stabilization.
FDA	Provide guidance on endpoints for pediatric sleep trials in autistic populations; advise on melatonin formulation, dosing, timing, adverse-event monitoring, durability, and safety; clarify evidentiary expectations for wearable-derived sleep measures and regulated sleep-intervention products when used in trials.
CDC	Improve surveillance of sleep disturbance in autistic children, adolescents, and adults; track associations with behavioral crises, seizures, educational participation, health care utilization, caregiver sleep loss, and family burden; support public health materials explaining when sleep disturbance should prompt clinical evaluation.
DoD / CDMRP Autism Research Program	Support sleep and co-occurring-condition research, treatment-outcome studies, and military-family-relevant healthcare delivery research consistent with annual CDMRP priorities.

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish autism-competent sleep recognition, behavioral sleep care, medical	HRSA and AHRQ	CMS; NIH; CDC

Phase	Consolidated federal product	Accountable lead	Supporting partners
	differential, medication review, and indicated sleep-specialty referral guidance across the life course.		
18–24 months	Adopt objective and limited-communication sleep measures and a pediatric safety-monitoring framework for melatonin, psychotropic medication, respiratory risk, epilepsy, and other common clinical contexts.	NIH and FDA	CDC; AHRQ; DoD/CDMRP
24–36 months	Launch comparative-effectiveness and sequencing studies of behavioral, circadian, melatonin, medical, and selected pharmacologic approaches in clinically defined subgroups.	NIH and AHRQ	FDA; HRSA; CMS; DoD/CDMRP
3–5 years	Report durable sleep, safety, daytime function, communication, behavior, school or work participation, health utilization, and caregiver outcomes and translate mature findings into guidance.	AHRQ and NIH	FDA; CDC; HRSA; CMS

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Percentage of participating systems completing structured sleep assessment, medical differential review, and indicated referral or treatment.
- Median time from clinically significant sleep concern to covered evaluation and care, stratified by age, geography, communication status, and payer.
- Adoption of objective sleep measures and completeness of pediatric and long-term safety monitoring in federally supported studies.
- Change in sleep continuity, daytime alertness, seizures where relevant, communication, behavior, participation, emergency use, and caregiver sleep burden.

Implementation Standards

- Sleep assessment should be routine when daytime symptoms, medical instability, regression-like change, seizures, GI symptoms, pain, or loss of participation suggest sleep disruption.

- Sleep treatment should be sequenced around presentation and should not escalate pharmacologically before reasonable evaluation of medical contributors.
- Behavioral and environmental sleep care, melatonin guidance, primary sleep-disorder referral, and medical-contributor evaluation should be accessible across communication profiles, ages, support needs, and payer systems.
- Objective measures should support clinical judgment and trial credibility, not replace history, caregiver observation, or individualized assessment.
- Sleep outcomes should include daytime function, health stability, caregiver sleep, family burden, and participation, not sleep duration or latency alone.

Translational Readiness Assessment

Sleep and circadian regulation has a strong implementation core. Behavioral sleep care, environmental sleep supports, melatonin for appropriate sleep-onset or circadian-delay presentations with continued safety monitoring, and evaluation of primary sleep disorders are ready for wider clinical implementation. The federal priority is to make those elements consistent, accessible, measurable, and connected to follow-up.

Comparative effectiveness, objective measurement, circadian phenotyping, and pediatric pharmacologic safety require additional work through structured trials, validation studies, and prospective follow-up rather than informal expansion of off-label practice. The distinguishing federal objective is to determine why the person is awake before escalating treatment.

Priority Therapeutic Domain 9: Epilepsy and Network Excitability

Strategic Objective

Ensure timely recognition, evaluation, and standard-of-care treatment of epilepsy in autistic individuals, while advancing a focused research agenda on subclinical epileptiform activity, sleep-potentiated epileptiform discharges, electrical status epilepticus in sleep, altered network excitability, and seizure-associated developmental or functional decline in defined presentations.

Domain 9 has two tracks that should remain distinct. Clinical seizures, suspected seizures, recognized epileptic encephalopathies, seizure safety, and epilepsy follow-up are implementation-ready standard care. Subclinical epileptiform activity, sleep-potentiated discharges, electrical status epilepticus in sleep, and network-excitability biomarkers require defined clinical contexts, standardized protocols, and outcome validation before they are used to justify broad intervention.

Scientific Rationale

Epilepsy is one of the most serious co-occurring medical conditions in autism. It is associated with elevated morbidity, increased health-system burden, developmental vulnerability, cognitive and behavioral decline in some individuals, and epilepsy-related mortality, including sudden unexpected death in epilepsy. Reviews consistently describe a higher epilepsy burden in autistic populations — approximately **12% across the spectrum** and **21–24% in those with co-occurring intellectual disability**, compared with 0.8% in the general population — with risk influenced by intellectual disability, genetic conditions, developmental history, age, and clinical ascertainment (Lukmanji et al., 2019; Hirota and King, 2023; Tuchman and Jeste 2015; Besag 2017; Zarakoviti et al. 2022).

The clinical obligation is immediate. Autistic individuals with seizures should receive the same standard neurology evaluation and treatment available to anyone with epilepsy. Autism should not delay recognition, EEG evaluation, neurology referral, antiseizure treatment, safety counseling, rescue-medication planning when indicated, or follow-up. This is especially important for individuals with limited communication, intellectual disability, complex motor presentations, sleep disruption, behavioral change, or episodes that are misread as attention, anxiety, refusal, stereotypy, aggression, self-injury, or psychiatric escalation.

The research obligation is narrower. Autism is associated with questions that ordinary epilepsy care does not settle: the clinical significance of interictal or subclinical epileptiform activity, the role of sleep-potentiated epileptiform discharges, the management of electrical status epilepticus in sleep, and the relationship between network excitability, regression, and functional loss. These questions matter, but they require discipline. Abnormal EEG findings do not automatically explain autism, and not every behavioral change is seizure-related.

The federal strategy should therefore close access gaps in established epilepsy care now while supporting rigorous studies to determine when EEG abnormalities, sleep EEG findings, seizure burden, and network-excitability measures change clinical decisions and improve outcomes when treated.

Current State of Knowledge

Clinical epilepsy care is implementation-ready

Diagnosis and treatment of clinical seizures are governed by established neurology standards. The federal problem is not lack of basic epilepsy treatment. The problem is uneven recognition, delayed referral, incomplete follow-up, and inconsistent adaptation for communication and support needs. In autism, seizure recognition may be delayed when events are subtle, nocturnal, behaviorally complex, or difficult to distinguish from stereotyped movement, inattention, catatonia-like features, panic, pain behavior, sleep events, medication effects, or autonomic episodes.

Seizure recognition is harder when communication is limited

A person who cannot describe aura, confusion, nocturnal events, headache, fatigue, sensory change, postictal symptoms, or loss of time may present only with unexplained distress, aggression, self-injury, sleep disruption, regression-like change, episodic shutdown, sudden falls, staring spells, or new loss of skills. Clinical pathways should support careful history, caregiver video review when available, event characterization, neurology referral, EEG when indicated, sleep EEG when clinically triggered, and follow-up after abnormal or inconclusive results.

Epilepsy risk is heterogeneous

Epilepsy in autism is not evenly distributed. Reviews identify multiple risk modifiers, including intellectual disability, female sex in some studies, genetic or syndromic etiologies, developmental delay, regression history, and age-related patterns of seizure onset (Zarakoviti et al. 2022; Tuchman and Jeste 2015). Federal programs should not treat epilepsy as a uniform autism feature. They should support risk-informed recognition, referral, monitoring, and outcome measurement.

EEG abnormalities require clinical context

Epileptiform activity can occur in autistic individuals with or without clinically recognized seizures. Reviews describe elevated rates of EEG abnormalities in some ASD cohorts, but estimates vary substantially by sample, age, sleep recording, intellectual disability, referral setting, and EEG method (Spence and Schneider 2009; Milovanovic and Grujicic 2021). The translational issue is whether a specific EEG finding changes care. Some findings identify epilepsy or an epileptic encephalopathy requiring treatment. Others may be incidental, nonspecific, or of uncertain functional significance. Federal research should define contexts of use: which EEG patterns, in which clinical presentations, at which developmental periods, and with which outcomes justify treatment or monitoring.

Sleep EEG is clinically important in selected presentations

Sleep can reveal epileptiform activity not captured during wake recordings, and sleep-potentiated patterns are relevant when regression, nocturnal events, language loss, developmental plateau, fluctuating function, treatment-resistant sleep disruption, or unexplained functional decline is present. Electrical status epilepticus in sleep and related epileptic encephalopathy concepts are clinically important because epileptiform activity during sleep can contribute to cognitive, language, behavioral, or developmental deterioration in defined contexts (Tuchman 2006; Milovanovic and Grujicic 2021). This does not mean every autistic child needs a sleep EEG. It means federal care pathways should specify when sleep EEG is clinically indicated and when a waking EEG is insufficient.

Language loss and ESES/CSWS require specific attention

Language loss deserves particular attention because Landau-Kleffner syndrome and related sleep-dependent epileptic encephalopathy presentations can be mistaken for autism-related language regression. Daytime EEG may miss relevant sleep-dependent temporal epileptiform activity. Federal materials should identify sudden or fluctuating language loss, nocturnal events, morning confusion or irritability, regression, and functional decline with neurologic features as referral triggers, while avoiding universal screening recommendations unsupported by evidence.

Network excitability is a plausible mechanism, but not a clinical shortcut

Altered excitation-inhibition balance, synaptic signaling, ion channels, and network-level physiology are recurring themes in autism and epilepsy research. Experimental and clinical reviews describe overlapping biology between autism and epilepsy, including genetic and circuit mechanisms that can affect neuronal excitability (Stafstrom and Benke 2015; Zahra et al. 2022). That science should not become a loose label for every regression, agitation, sleep problem, or behavioral crisis. Studies should connect electrophysiology, seizure history, sleep findings, genotype where relevant, developmental course, medication exposure, and longitudinal outcomes.

Regression and epilepsy overlap in clinically important subgroups

The relationship among autism, epilepsy, epileptiform activity, and regression remains clinically important and incompletely resolved. Reviews and clinical studies describe overlap between epileptic encephalopathies, language or behavioral regression, and autistic features, but they also emphasize heterogeneity and uncertainty (Tuchman 2006; Tuchman and Jeste 2015; Nie et al. 2023). When a child, adolescent, or adult loses skills, develops new seizures, shows episodic decline, or develops new aggression or self-injury with neurologic features, seizure and EEG evaluation should be part of the indicated clinical workup. Research should determine whether seizure control, treatment of sleep-potentiated epileptiform activity, or other network-directed interventions improve functional trajectory in defined presentations.

Safety counseling and SUDEP prevention require adaptation

Seizure safety counseling, SUDEP education, medication-adherence support, rescue-medication planning, nighttime supervision planning, and school or residential seizure action plans are ordinary components of epilepsy care. They must be adapted for communication profile, intellectual disability, wandering risk, sleep arrangements, supervision needs, caregiver capacity, and emergency response. SUDEP reviews emphasize that uncontrolled seizures and generalized tonic-clonic seizures are major risk factors, supporting the need for seizure control, counseling, and follow-up (Friedman 2022; Wicker and Cole 2021).

Translational Status

Knowledge and Implementation Gaps

- Seizures are under-recognized: Events may be missed when autistic individuals have limited communication, intellectual disability, nocturnal events, episodic shutdown, or behaviorally complex presentations.
- Access is uneven: Neurology, EEG, sleep EEG, antiseizure medication management, rescue-medication planning, and epilepsy follow-up vary by geography, payer, age, and disability profile.
- EEG pathways are inconsistent: Care pathways do not consistently specify when suspected regression, language loss, episodic behavioral change, nocturnal events, morning confusion, or sleep disruption should prompt EEG or sleep EEG.
- Abnormal EEG results are not always actionable: Clinical interpretation, follow-up, and treatment thresholds are not consistently defined after abnormal or equivocal EEG findings.
- Subclinical epileptiform activity remains uncertain: The functional significance of interictal or subclinical epileptiform activity is unresolved in many presentations.
- ESES/CSWS evidence needs autism-relevant outcomes: Treatment thresholds for sleep-potentiated epileptiform activity and electrical status epilepticus in sleep need standardized identification, treatment documentation, and longitudinal functional outcome measurement.
- Language-loss presentations can be missed: Landau-Kleffner syndrome and related sleep-dependent epileptic encephalopathy presentations may be missed when language loss is attributed to autism without adequate sleep-based EEG evaluation.
- Safety counseling is not consistently adapted: SUDEP counseling, seizure action plans, rescue-medication education, medication adherence, and emergency planning are not consistently tailored to communication profile, supervision needs, and caregiver capacity.
- Trials often use narrow endpoints: Studies rarely measure whether seizure or EEG-directed care changes language, cognition, adaptive function, behavior, sleep, participation, hospitalization, injury, or caregiver burden.
- High-support populations remain under included: Nonspeaking and minimally speaking individuals, people with intellectual disability, profound autism, high support needs, regression, and complex medical comorbidity are often excluded despite high clinical burden.

- Network excitability is not yet clinically operational: Research has not consistently connected electrophysiology, seizure history, sleep findings, genotype, biologic contributors, treatment response, and pragmatic clinical decisions.

Priority Federal Translation Agenda

Priority 1: Epilepsy Recognition and Access Initiative

Lead agencies: HRSA, CMS. Supporting agencies: AHRQ, CDC, NIH.

Federal agencies should support a national effort to improve seizure recognition and epilepsy care access for autistic individuals. The initiative should include clinician education, caregiver-facing materials, event-characterization tools, referral pathways, and quality measures for primary care, developmental-behavioral pediatrics, psychiatry, neurology, emergency care, school-linked health settings, residential settings, and Medicaid care coordination. The objective is not to label every difficult event as a seizure. The objective is to reduce missed neurologic disease and ensure timely access to standard epilepsy care when clinical concern is present.

Priority 2: EEG and Sleep EEG Care Pathways for Selected Presentations

Lead agencies: HRSA, AHRQ. Supporting agencies: CMS, NIH, CDC.

Federal partners should support practical care pathways for EEG and sleep EEG evaluation in autistic individuals. These pathways should clarify when EEG is indicated, when sleep EEG should be considered, how caregiver videos can support triage, how EEG modality should match the concern, and how results should be interpreted in clinical context. Referral triggers should include suspected seizures, nocturnal events, developmental regression, sudden or fluctuating language loss, suspected Landau-Kleffner syndrome, ESES/CSWS concern, unexplained episodic behavioral change, catatonia-like deterioration, sudden loss of adaptive skills, morning confusion or irritability, and sleep disruption with neurologic features.

Priority 3: Subclinical Epileptiform Activity and ESES/CSWS Clinical Utility Program

Lead agency: NIH. Supporting agencies: FDA, AHRQ, HRSA, CMS.

NIH should support coordinated studies of subclinical epileptiform activity, sleep-potentiated epileptiform discharges, ESES/CSWS, and seizure-associated regression in autistic individuals. Studies should use standardized EEG and sleep EEG protocols, clear clinical phenotypes, repeated developmental and functional measures, and careful treatment documentation. The central question is clinical utility: which EEG findings predict decline, which are incidental, which presentations improve with treatment, and which outcomes change when epileptiform activity is reduced.

Priority 4: Network Excitability and Biologic Context Studies

Lead agency: NIH. Supporting agencies: FDA, CDC, AHRQ.

Federal research should connect electrical instability to targeted biologic contributors only when the clinical pattern supports that evaluation. Relevant contexts may include illness-triggered seizures, fever- or temperature-sensitive events, fasting or exertion sensitivity, cyclic vomiting or unexplained fatigue, refractory seizures, puberty-related worsening, catamenial patterns, regression after sleep disruption, medication-related worsening, immune or inflammatory flares, ion-channel findings, or neurologic change after metabolic stress. This program should not recommend broad, untethered panels for every autistic person.

Priority 5: Seizure Management and Functional-Trajectory Trials

Lead agencies: NIH, AHRQ. Supporting agencies: FDA, CMS, HRSA.

Federal agencies should support trials and evidence reviews evaluating whether optimized seizure management or treatment of defined EEG presentations changes outcomes beyond seizure frequency. Outcomes should include language, cognition, adaptive function, behavior, sleep, participation, hospitalization, injury, safety, and caregiver burden. Trials should report results by defined presentation, baseline function, EEG pattern, seizure type, developmental history, communication profile, intellectual disability, medication exposure, and durability window. Functional change should be reported as observed trajectory, not as a general or guaranteed treatment result.

Priority 6: SUDEP, Safety, and Family-Centered Epilepsy Education

Lead agencies: CDC, HRSA. Supporting agencies: CMS, NIH.

Federal partners should improve epilepsy safety education for autistic individuals and families. Materials should address seizure observation, event documentation, rescue medication when indicated, medication adherence, nocturnal seizures, SUDEP counseling, sleep safety, wandering risk, school and residential seizure action plans, emergency response, and follow-up. The education agenda should be practical and adapted for communication profile, support needs, supervision structure, and caregiver capacity.

Agency Actions

Agency	Priority actions
DoD / CDMRP Autism Research Program	Support seizure, epilepsy, network-excitability, and treatment-outcome research consistent with annual CDMRP priorities and standardized electrophysiology and functional outcomes.

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish autism-adapted seizure-recognition, neurology referral, EEG and sleep-EEG indication, safety, rescue-medication, seizure-action-plan, and SUDEP education pathways.	HRSA, AHRQ, and CDC	CMS; NIH; DoD/CDMRP
18–24 months	Adopt standardized EEG, sleep-EEG, ESES/CSWS, seizure-type, developmental-trajectory, treatment-documentation, and functional-outcome data elements.	NIH	FDA; CDC; AHRQ; DoD/CDMRP
24–36 months	Launch clinical-utility studies of subclinical or sleep-potentiated epileptiform activity and trials testing whether optimized seizure or defined EEG-directed care changes functional trajectory.	NIH and AHRQ	FDA; HRSA; CMS; DoD/CDMRP
3–5 years	Report access, diagnostic yield, seizure control, safety-plan completion, hospitalization, injury, functional trajectory, and the contexts in which EEG findings do or do not change care.	NIH and AHRQ	CDC; FDA; HRSA; CMS

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Median time from seizure concern or neurologic deterioration to neurology evaluation and clinically appropriate EEG modality.
- Percentage of confirmed epilepsy or treatable EEG presentations receiving indicated treatment, safety counseling, action planning, and covered follow-up.

- Percentage of federally supported studies using standardized electrophysiology, phenotype, treatment, inclusion, and functional-outcome standards.
- Change in seizure-related hospitalization, injury, emergency use, sleep, language, adaptive function, participation, safety, and caregiver burden in defined presentations.

Implementation Standards

- Autism should not delay standard epilepsy evaluation, treatment, safety counseling, or follow-up when seizures or epileptic encephalopathy are suspected or confirmed.
- EEG and sleep EEG pathways should be presentation-driven. Referral triggers should be explicit, but universal EEG or sleep EEG screening should not be implied.
- Abnormal EEG findings should be interpreted in clinical context and paired with follow-up. An abnormal tracing alone should not be treated as a complete treatment plan.
- Network-excitability language should remain tied to defined electrophysiology, phenotype, and outcome measures, not used as a broad explanation for behavior, regression, or autism.
- Functional outcomes should be measured directly, durability-qualified, and reported by subgroup; improvement should not be characterized as cure or as a guaranteed result.
- Safety materials should be accessible to families, schools, residential providers, and clinicians and adapted for communication profile, supervision needs, medication adherence, wandering risk, and emergency planning.
- Studies should include the populations most affected by epilepsy burden, including nonspeaking and minimally speaking individuals, people with intellectual disability, profound autism, high support needs, regression, and complex medical conditions.

Translational Readiness Assessment

Epilepsy and network excitability spans established clinical care and autism-specific validation questions. Clinical seizure recognition, neurology referral, EEG evaluation when indicated, antiseizure treatment, rescue-medication planning when appropriate, seizure safety counseling, SUDEP education, and follow-up are ready for implementation. The federal priority is to make access timely and equitable, especially for individuals whose communication or behavior makes seizures harder to recognize.

The autism-specific network-excitability agenda - subclinical epileptiform activity, sleep-potentiated discharges, ESES/CSWS, suspected Landau-Kleffner presentations, and regression-related EEG questions - remains at the validation and trial stage except where standard neurologic care already applies. These questions should be studied through standardized protocols, defined clinical contexts, and functional outcomes that show whether the EEG or network finding identifies a treatable contributor to loss of function. The practical aim is to prevent missed epilepsy while avoiding over-interpretation of EEG findings that do not yet have established clinical utility.

Priority Therapeutic Domain 10: Motor Planning, Praxis, Sensorimotor Integration, and Apraxia

Strategic Objective

Improve communication, self-care, feeding, mobility, agency, and safety for autistic individuals whose functional limitations are shaped by motor planning, praxis, motor speech, oral-motor function, coordination, gait, handwriting, posture, endurance, or motor-access needs. Federal action should expand access to clinically indicated services now while building better differential assessment, standardized measures, and comparative-effectiveness evidence for autism-relevant motor interventions.

This domain treats motor access as a practical condition of care. Occupational therapy, physical therapy, speech-language pathology, feeding therapy, assistive technology, adaptive equipment, and durable medical equipment should not wait for autism-specific motor biomarkers when the need is clinically indicated. At the same time, federal research should determine which motor and communication-access interventions work best, for whom, and with what durable effect.

Scientific Rationale

Motor planning and praxis affect the ability to plan, sequence, initiate, coordinate, and adapt movement. These capacities shape communication, feeding, handwriting, dressing, hygiene, mobility, play, school participation, work participation, safety, and access to augmentative and alternative communication. When motor planning is impaired, a person may know what they want to do but be unable to initiate, sequence, sustain, or coordinate the movement needed to do it.

These capacities depend on sensorimotor integration, the process by which the nervous system combines sensory input (proprioceptive, vestibular, tactile, visual, auditory, and interoceptive) with motor commands to plan, execute, and refine movement. This is a well-established neuroscientific construct mediated by cortical-cerebellar and cortical-striatal circuits that neuroimaging research consistently shows are altered in autistic individuals. However, most neuroimaging and sensorimotor studies have excluded individuals with intellectual disability or profound autism, leaving the highest-support-needs population essentially unstudied.

This distinction matters clinically. Motor difficulty can be misread as refusal, lack of comprehension, low motivation, anxiety, aggression, cognitive incapacity, treatment resistance, or noncompliance. Similarly, impulsive motor behaviors, including bolting, unsafe movement, and self-injurious behavior, should not automatically be interpreted as intentional noncompliance. Meta-analytic data demonstrate a significant inhibitory control deficit in autism, and evidence implicates autonomic dysregulation, sensory overload, and pain as additional neurophysiologic contributors. However, the causal pathways from autonomic dysregulation and sensory overload to specific impulsive motor behaviors remain incompletely characterized and require further study. For nonspeaking and minimally speaking autistic individuals, motor access may determine whether the person can use speech, gesture, pointing, eye gaze, switches,

typing, touch screens, handwriting, feeding supports, adaptive equipment, or AAC. If the motor demand is not recognized, the person's competence and needs may be underestimated.

Motor differences are widely reported in autism, including impairments in balance, gait, coordination, fine-motor control, imitation, praxis, postural control, visual-motor integration, oral-motor function, and speech-motor planning. Large cohort analyses, meta-analyses and reviews support motor impairment as common and clinically relevant in autistic children, but measurement remains inconsistent and motor needs are still under-recognized in diagnosis, treatment planning, and research design.

The term "whole body apraxia" is increasingly used within the autism community and by some occupational therapists to describe the observation that motor-planning difficulty in profound autism often extends beyond speech to affect limb movement, self-care, feeding, mobility, and functional independence simultaneously. This is not a standardized clinical diagnosis; the established literature describes these presentations using region-specific classifications (limb apraxia, oral apraxia, childhood apraxia of speech) or the broader constructs of dyspraxia and motor-planning impairment. However, the underlying clinical concern — that apraxia in autism is not confined to speech and affects the entire body — is supported by studies demonstrating that praxis deficits in autism span gestural, postural, and whole-body domains.

This domain should not collapse all limited speech, functional difficulty, or behavioral presentation into apraxia only. It should create a practical pathway for identifying when motor planning, praxis, motor speech, oral-motor function, coordination, endurance, posture, pain, seizure activity, catatonia-like deterioration, medication effects, sensory avoidance, co-occurring conditions or environmental mismatch is contributing to loss of access.

Current State of Knowledge

Motor planning is a functional access issue

The most important policy point is simple: motor ability, alongside and reciprocally regulated by sensorimotor processing, can determine whether an autistic person can use the services and supports already offered to them. A person may need communication support, but also need postural support, switch access, eye-gaze access, motor-initiation support, reduced fine-motor load, adaptive seating, vagal support, or a different response format before the communication support is usable.

The intervention target is access to action. The outcome is not only an improved motor score. It is improved ability to communicate, eat safely, move safely, participate, complete self-care, use AAC, demonstrate comprehension, and reduce avoidable distress.

Differential assessment is essential

Motor functional limitations in autism may arise from multiple sources, and sensorimotor processing differences can compound or drive difficulties across the full range of motor function — not only motor planning, but also coordination, balance, gait, postural control, fine-motor control, feeding, oral-motor function, endurance, and motor initiation. A functional limitation may reflect dyspraxia, sensorimotor integration deficits, weakness, hypotonia, hypermobility, interoceptive differences, sensory avoidance,

pain, anxiety, catatonia-like deterioration, seizure activity, sleep disruption, gastrointestinal discomfort, medication effects, intellectual disability, language comprehension, fatigue, or environmental mismatch. More than one may be present, and atypical sensory processing may alter the expression of any of them.

Assessment should therefore ask what movement or motor function is affected, what breaks down, when the breakdown occurs, whether the difficulty is consistent across contexts, and whether performance changes with fatigue, pain, dysregulation, sensory load, interoceptive state, postural support, time pressure, or multi-step motor sequencing. A range of co-occurring medical conditions should also be considered.

Differential assessment is essential Speech-motor impairment is likely a major and under-recognized contributor to limited speech

Nonspeaking and minimally speaking autistic individuals have motor impairment at higher rates and greater severity than those who speak. Eighty-eight percent of autistic children are at risk for motor impairment, with risk increasing alongside language, cognitive, and functional impairment (Bhat 2021). Fine motor skill predicts speech intelligibility in minimally verbal but not verbal autistic children, suggesting motor output is a functional bottleneck for speech production in the population most affected. Direct analysis of low and minimally verbal autistic individuals has found evidence of motor speech disorder — including reduced intelligibility, impaired coordination and consistency, and articulatory deficits — with patterns consistent with apraxia of speech (Maffei et al. 2024). Clinical studies have also identified motor-impaired subgroups with oral-motor and expressive language deficits out of proportion to receptive language — the pattern expected when motor output, not comprehension, is the primary barrier.

Other factors can contribute to limited speech, including verbal auditory agnosia, intellectual disability affecting symbolic language development, joint attention deficits, and social-communication impairment itself. More than one factor may be present in a given individual. The practical clinical and research question remains whether speech-motor, oral-motor, language, hearing, cognitive, motor-initiation, sensorimotor integration, sensory, or medical factors — or a combination — are limiting communication, and federal guidance should support assessment capable of distinguishing these contributors. But the dominant clinical and research risk in this population is not overdiagnosis of speech-motor impairment; it is systematic failure to recognize, assess, and treat it.

Praxis, dyspraxia and sensorimotor function are measurable but not routinely assessed

Praxis difficulties have been demonstrated in autistic children, including impaired performance and recognition of skilled gestures, motor planning differences, and difficulties with imitation and gesture production. Studies suggest that dyspraxia can be measured more efficiently than traditional lengthy praxis batteries, but these measures are not yet embedded in routine autism characterization or federal data standards. Dyspraxia in autism is associated with poorer social, communicative, and behavioral outcomes, reinforcing the clinical importance of routine assessment. Motor initiation — the ability to begin a planned movement — may be independently impaired, so that failure to act is misread as refusal or

incomprehension rather than a motor-access barrier. Similarly, inhibition, or the ability to stop or suppress motor movements may also be independently impaired, resulting in actions that may appear impulsive, repetitive, noncompliant or may be misunderstood as non-compliance or cognitive ability.

Sensory processing and sensorimotor integration can also be assessed using standardized clinical tools — including the Sensory Profile, Sensory Processing Measure, and related instruments — that are already in use in autism research and clinical practice. However, these measures are rarely integrated with motor assessment, and sensorimotor integration measures validated specifically for autistic populations with intellectual disability or minimal speech remain limited. Autonomic measures such as heart rate variability and electrodermal activity can index physiologic contributors to motor dysregulation but are not yet part of routine clinical or research characterization.

The federal role is to standardize practical measures, not to require a single theory of motor dysfunction. Motor phenotyping should include limb praxis, oral praxis, speech-motor planning, fine- and gross-motor coordination, visual-motor integration, motor imitation, postural control, gait, motor initiation, motor sequencing, motor learning, feeding, handwriting, adaptive self-care, sensory processing profile, sensorimotor integration, and AAC motor access.

Motor access affects research inclusion and assessment validity

Many autistic individuals with minimal or no functional speech, intellectual disability, profound autism, regression, or complex medical needs are excluded from research because study procedures require reliable speech, pointing, writing, imitation, sustained sitting, device use, or rapid compliance. This exclusion can be methodological rather than scientifically necessary.

Federal studies should use adaptive protocols when possible: flexible response formats, modified testing environments, extended administration time, caregiver-assisted contextual data, home-based or remote options, and outcome measures that do not require reliable motor output. A person's inability to point, speak, or perform on command should not be mistaken for lack of comprehension.

Translational Status

Component	Readiness	Federal task
Clinically indicated OT, PT, speech-language pathology, feeding therapy, assistive technology, adaptive equipment, and durable medical equipment	Implementation-ready	Improve recognition, referral, coverage, delivery, and follow-up without waiting for autism-specific motor biomarkers.
Differential assessment	Implementation-ready with	Develop practical trigger lists, assessment

Component	Readiness	Federal task
of motor planning, praxis, motor speech, oral-motor function, coordination, posture, gait, pain, seizures, medication effects, sensory factors, co-occurring medical conditions, and catatonia-like deterioration	pathway support	prompts, referral guidance, and clinician education.
Motor-access assessment for assistive technology and device operation	Implementation-ready with evidence-building	Integrate motor-access assessment into communication access and device-selection pathways.
Standardized autism-relevant motor phenotyping	Validation stage	Define common data elements and measures usable across age, language level, intellectual disability, support need, and motor output.
Digital, kinematic, wearable, speech-motor, and motor-access measures	Validation stage	Define contexts of use, sensory tolerability, privacy protections, missing-data standards, and links to functional outcomes.
Intervention selection and sequencing for praxis, motor learning, speech-motor, feeding, handwriting, adaptive function, AAC access, and assistive technology	Comparative-effectiveness stage	Test interventions in defined motor and communication-access profiles using pragmatic designs and meaningful endpoints.
Adaptive research designs that reduce exclusion based on motor output	Implementation-to-validation	Require accessible procedures and outcome measures that separate comprehension from speech, pointing, writing, imitation, and sustained sitting demands.

Knowledge and Implementation Gaps

- Motor planning, praxis, and motor-access needs are not consistently assessed in autism care.
- Functional limitations are often attributed to behavior, cognition, anxiety, or noncompliance before motor access is evaluated.
- Speech-motor impairment is not reliably distinguished from language comprehension, expressive language, oral-motor weakness, hearing, sensory factors, or broader motor-initiation difficulty.
- Standardized motor and praxis measures are not routinely used across federally funded autism studies.
- Individuals with minimal or no functional speech, intellectual disability, profound autism, regression, motor impairment, or medical complexity remain underrepresented in research.
- Cognitive and receptive-language assessments often require motor output, which can underestimate language comprehension and decision-making capacity.
- Evidence is limited on which OT, PT, speech-motor, motor-learning, feeding, handwriting, adaptive-function, and AAC-access interventions work best for defined profiles.
- Digital and kinematic motor measures are promising but need validation against clinically meaningful outcomes before broad use.
- Coverage and access barriers limit medically necessary motor, communication, feeding, mobility, and assistive-technology supports.
- Long-term outcomes for these populations —adaptive function, participation, injury risk, service access, and caregiver demands — are not systematically tracked over time.
- Referral pathways to OT, PT, speech-language pathology, and assistive-technology services are inconsistent, and referral completion is not measured.

Priority Federal Translation Agenda

Priority 1: Functional Access and Clinically Indicated Services

Lead agencies: HRSA, CMS, AHRQ. Supporting agencies: NIH, ACL, ED/OSEP.

Federal policy should make clear that recognized motor, speech-motor, feeding, oral-motor, coordination, mobility, handwriting, and assistive-technology needs warrant timely evaluation and support. Clinically indicated occupational therapy, physical therapy, speech-language pathology, feeding therapy, adaptive equipment, assistive technology, and durable medical equipment should not be delayed because autism-specific motor biomarkers remain underdeveloped.

This is the implementation core of the domain. A child who cannot access a device because of motor planning, posture, gaze control, switch activation, fine-motor difficulty, or fatigue does not need a research biomarker before the access problem is addressed. An adult who cannot complete self-care, write, feed safely, ambulate safely, or communicate symptoms needs functional assessment and support.

Following analysis of Medicaid access barriers, CMS should issue guidance clarifying coverage of medically necessary motor, feeding, mobility, and assistive-technology supports, including EPSDT obligations and medical-necessity criteria.

Priority 2: Differential Assessment and Referral Pathways

Lead agencies: HRSA, AHRQ. Supporting agencies: CMS, NIH, ED/OSEP.

HRSA and AHRQ should support practical pathways for recognizing motor planning, praxis, apraxia, dyspraxia, motor speech, feeding, oral-motor, handwriting, postural, gait. These pathways should help clinicians distinguish motor-access problems from behavior, cognition, language comprehension, dysarthria, catatonia-like deterioration, seizure-related change, pain, sleep disruption, sensory avoidance, anxiety, medication effects, and environmental mismatch.

The pathways should be usable in primary care, developmental-behavioral pediatrics, neurology, rehabilitation medicine, psychiatry, OT, PT, speech-language pathology, feeding clinics, schools, and Medicaid care coordination. They should also support referral when loss of function suggests neurologic, medical, pain-related, or catatonia-like contributors.

Priority 3: Standardized Motor Phenotyping and Measurement Validation

Lead agencies: NIH, FDA. Supporting agencies: CDC, AHRQ.

NIH should support a common data-element set for autism motor studies, covering limb praxis, oral praxis, speech-motor planning, fine- and gross-motor coordination, visual-motor integration, imitation, postural control, gait, motor initiation, motor sequencing, motor learning, feeding, handwriting, adaptive self-care.

Measures should be usable across age, language level, intellectual disability, communication profile, and support need. Digital, kinematic, wearable, speech-motor, and motor-access measures should advance only with defined contexts of use, sensory tolerability, privacy protection, missing-data standards, and comparison with functional outcomes.

Priority 4: Comparative-Effectiveness and Pragmatic Intervention Research

Lead agencies: AHRQ, NIH. Supporting agencies: HRSA, CMS, ACL, ED/OSEP.

AHRQ and NIH should support pragmatic studies of OT, PT, speech-language pathology, speech-motor intervention, praxis intervention, motor-learning approaches, feeding and oral-motor supports, handwriting and visual-motor interventions, adaptive-function intervention, assistive technology, and environmental modification.

Outcomes should include self-care, feeding safety, handwriting or alternative access to instruction, mobility, safety, participation, injury risk, caregiver demands, and quality of life. Impairment-level improvement matters, but it is not enough. The question is whether the person gains access to action, communication, and daily life.

In addition to intervention trials, CDC and ACL should support longitudinal tracking of communication access, adaptive function, participation, injury risk, service access, and caregiver demands over time, so that real-world outcomes for these populations are measured rather than assumed.

Priority 5: Inclusive Research Design and Assessment Bias Reduction

Lead agencies: NIH, AHRQ, CDC. Supporting agencies: ACL, ED/OSEP, HRSA.

Federally funded studies should be designed to include autistic individuals with minimal or no functional speech, intellectual disability, profound autism, regression history, motor impairment, and medical complexity when scientifically and ethically appropriate. This requires adaptive procedures, not just broader recruitment language.

NIH, AHRQ, CDC, ACL, and ED/OSEP should support methods that separate comprehension from motor output where possible. Receptive-language and cognitive assessment should include options that reduce speech, gesture, pointing, writing, and fine-motor demands. Otherwise, research may continue to underestimate the abilities and needs of the people most affected.

Agency Actions

Agency	Priority actions
NIH	Fund motor-planning, praxis, speech-motor, motor-learning, sensorimotor integration; support standardized outcome measures; conduct pragmatic and comparative-effectiveness studies in defined autistic subgroups; investigate how sensory processing, autonomic nervous system dysregulation, and impaired inhibitory control affect motor planning, motor initiation, motor inhibition, and adaptive function; require inclusion of individuals with profound autism, regression, and medical complexity. Federal levers include RFAs/NOFOs, cooperative agreements, NAPTI network studies, common data elements, and longitudinal cohorts.
FDA	Engage where regulated devices, digital motor measures, wearable movement metrics, sensorimotor assessment tools, speech-motor tools, diagnostics, or software tools require validation. Advise on endpoints, contexts of use, pediatric safety, device validation, and regulatory pathways when applicable.
AHRQ	Conduct evidence and comparative-effectiveness reviews on motor-planning and praxis assessment, sensorimotor integration interventions, OT, PT, SLP motor-speech interventions, feeding/oral-motor supports, handwriting and visual-motor supports, adaptive-function interventions, and implementation-relevant evidence thresholds.
HRSA	Develop clinician-education and implementation resources on recognition of motor-planning impairment, apraxia, dyspraxia, motor speech disorders, sensory contributions to motor difficulty, feeding/oral-motor needs, referral

Agency	Priority actions
	pathways, and differentiation from behavioral presentations, cognition, language comprehension, dysarthria, catatonia, seizure-related deterioration, autonomic dysregulation, sensory overload, pain, medication effects, or noncompliance. Levers include LEND, DBP, MCHB programs, Family-to-Family Health Information Centers, clinician modules, and technical assistance.
CMS	Evaluate Medicaid access to OT, PT, SLP, assistive technology, durable medical equipment, feeding therapy, sensory integration services, and medically necessary motor-access supports; assess EPSDT implementation barriers, quality-measure opportunities, managed-care issues, provider availability, and state variation. Following its access-barrier analysis, CMS should issue guidance clarifying coverage of medically necessary motor, feeding, mobility, and assistive-technology supports for Medicaid-enrolled autistic individuals — including EPSDT obligations, medical-necessity criteria, and at least one access-related quality measure for Medicaid and managed-care oversight.
CDC	Support surveillance or registry-linked tracking of motor impairment, sensorimotor function, communication access, adaptive function, feeding difficulty, injury risk, participation, service access, and long-term outcomes where feasible. Levers include public-health indicators, registry partnerships, and longitudinal data standards.
ACL	Evaluate functional outcomes, independence, caregiver demands, community participation, respite need, assistive-technology access, self-care, mobility, sensory-motor support needs, and quality-of-life effects across the life course. Levers include DD Act networks, caregiver-support programs, community-living measures, and functional-outcome evaluation. Training and guidance for direct support professionals on recognizing motor-planning impairment as distinct from cognitive limitation, supporting communication access, and identifying unmet medical needs in nonspeaking individuals.

Key Performance Indicators

Indicators map to the common outcome architecture. The first set of measures address identification, workup, referral, and covered access. Additional measures capture inclusion and measurement infrastructure, and diagnostic yield and functional outcomes.

- Percentage of participating clinical systems using a motor-access and differential-assessment pathway for motor planning, praxis, motor speech, feeding, oral-motor, handwriting, posture, gait, assistive-technology, or durable-medical-equipment needs.
- Median time from documented motor, feeding, speech-motor, oral-motor, mobility, handwriting, or self-care concern to indicated evaluation.

- Percentage of individuals with an indicated motor or communication-access need who receive completed referral or service connection for OT, PT, speech-language pathology, feeding therapy, assistive technology, adaptive equipment, or durable medical equipment.
- Access-attainment rate: proportion of individuals with an indicated motor-access or communication-access need who receive covered, delivered services or equipment, with denials, prior-authorization delays, and time to delivery reported separately.
- Number and percentage of federally funded studies using standardized motor-planning, praxis, motor-speech, feeding, oral-motor, handwriting, and adaptive-function, including adaptive procedures that reduce motor-output exclusion.
- Inclusion rate of individuals with minimal or no functional speech, intellectual disability, profound autism, regression history, motor impairment, feeding difficulty, and complex medical conditions in motor and communication-access research.
- Diagnostic yield of structured differential assessment among presentations meeting motor-access trigger criteria, including the proportion in which motor planning, speech-motor, feeding, pain, seizure-related, catatonia-like, medication-related, sensory, or environmental contributors are identified and addressed.
- Functional access outcome: change from baseline in self-care, feeding safety, mobility, handwriting or alternative access to instruction, participation, injury risk, avoidable distress, caregiver demands, or quality of life after indicated motor-access intervention, reported by profile and follow-up interval.

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish differential-assessment and referral guidance distinguishing motor-planning, speech-motor, neuromuscular, orthopedic, sensory, cognitive, language, pain, medication, and environmental contributors to functional access.	HRSA and AHRQ	CMS; ED/OSEP; ACL; NIH
18–24 months	Adopt standardized motor and sensorimotor phenotyping and validate motor-minimized assessment methods that reduce motor-output demands so that cognition, receptive language, and literacy can be assessed in people whose abilities	NIH	FDA; AHRQ; CDC; DoD/CDMRP

Phase	Consolidated federal product	Accountable lead	Supporting partners
	may be obscured by motor or speech demands.		
24–36 months	Launch comparative-effectiveness and pragmatic studies of clinically indicated occupational, physical, speech-motor, assistive-technology, motor-learning, and environmental supports in defined profiles, including individuals with profound autism.	NIH and AHRQ	HRSA; CMS; ED/OSEP; ACL
3–5 years	Report access, assessment validity, functional communication, self-care, mobility, participation, safety, and caregiver outcomes and translate mature findings into service and research standards.	AHRQ and NIH	HRSA; CMS; ED/OSEP; ACL

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Percentage of participating systems using differential motor-access assessment and completing indicated specialty or therapy referrals.
- Median time from documented motor-access concern to covered evaluation, assistive technology, therapy, or environmental support.
- Adoption and validity of standardized motor phenotyping and motor-minimized assessments in federally supported studies.
- Change in communication access, self-care, mobility, educational or vocational participation, safety, and caregiver demands in defined motor profiles.

Translational Readiness Assessment

Motor planning, praxis, sensorimotor differences, and apraxia combine immediate access needs with longer-term measurement work. Access to recognized clinical services is implementation-ready. Autistic individuals should not wait for autism-specific motor biomarkers before receiving clinically indicated OT, PT, speech-language pathology, feeding therapy, assistive technology, adaptive equipment, durable medical equipment, or motor-access support.

The evidence-building work is also necessary. Autism-specific claims about motor-planning interventions, speech-apraxia prevalence, digital motor biomarkers, and subgroup response require stronger phenotyping, validated measures, and pragmatic trials. The federal objective is practical: implement access

where the need is already clear and build the measurement base needed to make motor intervention more precise and appropriately individualized.

Priority Therapeutic Domain 11: Adaptive Trial Design, Treatment Endpoints, and Repurposed Medications for a Heterogeneous Population

Strategic Objective

Establish a federal pathway for evaluating new and repurposed treatments in autism that accommodates biological heterogeneity. This includes trial designs capable of detecting and confirming benefit in subgroups and treatment-responsive populations, endpoints suited to the condition, and a structured route for converting off-label clinical experience into reviewable evidence and, where warranted, label support.

When a treatment shows a credible signal of benefit for some individuals with autism, the federal system should be able to determine whether the treatment reliably benefits a subgroup or treatment-responsive population, evaluate it under a design suited to that question, measure outcomes that matter with instruments fit for the condition, and—where the evidence supports it—translate the result into labeling that improves clinician awareness, prescribing confidence, and access. The response should be organized around the evaluation problem itself, whether the candidate is a novel agent or an approved drug.

Scientific Rationale

Addressing the preceding therapeutic domains in autism depends on access to adequate treatment, and the problem of autism's heterogeneity is inseparable from how new and repurposed treatments are evaluated. Few treatments have been investigated specifically in autism or carry a formal autism indication, and many medications are used widely off label without adequate data.

Autism's heterogeneity – both biological and phenotypical - addressed earlier in this Plan, has a direct consequence for treatment evaluation. A drug with a plausible mechanism may help some individuals whose autism arises from that mechanism while doing little for the rest. In an all-comers trial, benefit in responders washes out against non-responders at the group level, and a treatment that genuinely helps a meaningful subgroup can fail to reach statistical significance. This is not a reason to dismiss such signals; it is a reason to evaluate them differently.

Evaluation is further constrained by measurement. Autism has few validated clinical endpoints; those that exist are largely observer-based behavioral instruments not designed to capture short-term change, and there are no established biomarkers for rapid, objective assessment of treatment response. Symptoms also fluctuate with setting and overtime, so a single point of measurement is inherently noisy. Taken together, heterogeneity and outcome assessment challenges make autism trials harder to design, harder to interpret, and more expensive to run than trials in conditions with objective endpoints making the incentive gap for off-patent, repurposed drugs more acute, since sponsors cannot recover trial costs through market exclusivity.

Current State of Knowledge

No approved treatments for core symptoms

Risperidone and aripiprazole are approved for irritability associated with autism, not for core social-communication or restricted and repetitive features. There are no FDA-approved treatments for the core symptoms of autism, despite decades of research and a large affected population.

Conventional all-comers trials are a poor fit

Because autism almost certainly comprises biologically distinct subgroups, treatments evaluated across broadly defined populations tend to show diluted or null effects even where a real subgroup benefit exists. In some conditions, established biomarkers allow patient stratification into subgroups, however biomarkers in autism have not been well-established. As a result, promising signals may be dismissed at the group level on statistical grounds rather than re-examined through designs capable of confirming effects in treatment-responsive populations.

Endpoints and measurement are underdeveloped

Outcome assessment relies on subjective, observer-dependent instruments that were not built to detect short-term change, with no validated biomarkers to provide faster or more objective readouts. Setting-dependent variability adds noise, forcing larger and costlier trials to detect valid signals.

Off-label use has outpaced the evidence

Many medications are prescribed off-label for autism-related symptoms and co-occurring conditions, often on the basis of small studies with limited replication and short follow-up. Individuals with intellectual disability, minimal speech, epilepsy, self-injury, or medical complexity are frequently underrepresented, and trials seldom stratify by phenotype or biomarker.

Label gaps have clinical consequences

Autism has no defined medical specialty, so families see pediatricians, neurologists, or psychiatrists with varying familiarity with the scattered treatment literature. Without label support, even a clinician aware of a promising drug can face institutional and reimbursement barriers to prescribing it, and what a child is offered depends heavily on which clinician the family happens to see.

Translational Status

This domain has four linked tracks that should be kept separate but coordinated.

The trial-design and endpoint track is not yet guidance-ready: the field has not settled which designs and endpoints fit autism’s heterogeneity, so the near-term task is to build that knowledge through an FDA led working groups.

The endpoint and biomarker track requires sustained development and validation. FDA should define the characteristics and evidentiary standards needed for regulatory use, while NIH supports the underlying research through targeted funding mechanisms.

Label expansion for approved drugs can proceed now under existing authority.

Real-world evidence on off-label use can be captured through existing surveillance and registry infrastructure.

Knowledge and Implementation Gaps

- No trial-design framework for heterogeneity: All-comers trials dilute subgroup benefit, studies rarely stratify by phenotype or biomarker, and there is no autism-specific guidance on designs suited to the condition.
- Endpoints and biomarkers are lacking: Outcome measurement depends on subjective, setting-sensitive instruments, with no validated biomarkers for objective or short-term assessment, or patient stratification.
- No route from signal to label: Credible signals remain scattered across small studies, clinical experience, and off-label use, with no clear pathway to reviewable evidence. Generic-drug economics remove the usual commercial incentive to generate it with autism specific features increasing trial costs.
- Few autism-specific labeled options: Approved indications are limited to irritability; nothing is approved for the core features of autism, leaving most treatment decisions without label support.
- Small and inconsistent trials: Many repurposed medications being used only have small, studies with limited replication and inconsistent outcomes.
- Severe and profound autism are underrepresented: Individuals with intellectual disability, minimal speech, epilepsy, self-injury, or medical complexity are often excluded from or difficult to include in trials.
- Off-label use is untracked: Widely prescribed medications lack adequate autism-specific data and are not captured in systematic safety or outcome surveillance.

Priority Federal Translation Agenda

Federal action should follow evidence maturity. The near-term task is to build the knowledge the field lacks —convening the expertise needed to define trial designs and endpoints suited to autism—while signaling where existing flexibilities may be used in the interim and identifying promising repurposing candidates. The medium-term tasks are providing clear guidance that encourages trials from academic and commercial sponsors, prioritizing identified repurposing candidates, and funding targeted trials that include the populations most often left out. The continuing task is real-world evidence: capture how these drugs are used and what happens when they are.

Initiative 11.1: FDA-led Working Groups and Workshops on Trial Designs for a Heterogeneous Population

Lead agency: FDA.

Partner agencies: NIH, AHRQ.

FDA should convene a working group and workshop of internal and external experts and stakeholders to identify the trial designs best suited to autism's heterogeneity and determine what evidence could support approval or labeling for a subgroup or treatment-responsive population. Adaptive, enrichment, and responder-enrichment approaches should be central to this work. The knowledge needed to write definitive guidance does not yet exist in settled form; the immediate task is to build it. Given the scale of autism, the absence of any approved treatment for its core symptoms, and the very high rates of co-occurring conditions and disabling symptoms, this work should proceed with urgency and on a defined timeline, with the explicit goal of converting the group's conclusions into FDA guidance as quickly as the evidence allows.

In parallel, FDA and NIH should support development and validation of endpoints and biomarkers fit for autism and its co-occurring conditions, so that treatment response can eventually be measured more objectively and over shorter windows than current observer-based instruments allow.

Initiative 11.2: Development and Validation of Treatment Endpoints and Biomarkers

Lead agency: FDA.

Partner agencies: NIH, AHRQ.

FDA should lead a parallel effort to define the characteristics and evidentiary standards required for endpoints and biomarkers fit for autism and its co-occurring conditions. NIH should support their development and validation through targeted funding mechanisms, such as cooperative agreements or other coordinated funding opportunities, with continuing FDA involvement to help ensure that resulting measures are suitable for regulatory use. AHRQ should assess the validity and comparative performance of current and candidate outcome measures.

Initiative 11.3: Interim Use of Existing Trial-Design Flexibilities

Lead agency: FDA.

Partner agencies: NIH.

Pending the definitive guidance to be informed by Initiative 11.1, FDA may determine that certain flexibilities already used in rare-disease drug development—adaptive designs, enrichment, and responder-enrichment approaches—are applicable to autism trials now, and could signal where sponsors may use them in the interim. These tools are already established; what is not yet settled is how best to apply them to autism's heterogeneity. Any interim use should be revisited once Initiative 11.1 yields more definitive, autism-specific standards.

Initiative 11.4: Repurposed-Medication Prioritization and Label-Expansion Pathway

Lead agency: FDA.

Partner agencies: AHRQ, NIH.

FDA should designate autism as a priority area for drug repurposing and pursue label expansion for approved drugs where the safety profile is well established and the published literature shows a credible signal of benefit in autism or an autism subgroup. This is consistent with existing FDA mechanisms for updating labeling of older drugs on the basis of accumulated evidence and systematic review of publicly available science. AHRQ should organize, score, and prioritize candidates from the existing review literature; the point is not to endorse any single list but to mine a literature deep enough to warrant organized federal attention.

There are already many medications widely used off label in autism. Systematic reviews exist in the scientific literature that list those and attempt to rank by strength of evidence. Further examples are cited in the References: Repurposed Drugs at the end of this document.

Where credible signals exist but the economics of off-patent drugs remove the incentive to generate confirmatory evidence, FDA should identify the incentive and evidence-generation options available under existing authority; and potential novel mechanisms to encourage evidence generation and repurposing in priority areas.

Initiative 11.5: Targeted, Subgroup-Stratified Trials and Real-World Evidence Infrastructure

Lead agency: NIH.

Partner agencies: FDA, AHRQ, CMS, CDC.

NIH should fund trials, preferably multi-site, of high-priority repurposed agents that include strategies to predefine and stratify subgroups where possible, or to identify apparent responders and confirm efficacy using enrichment, responder enrichment, or adaptive designs where appropriate. AHRQ should anchor candidate selection and evidence thresholds; FDA input should inform enrichment and endpoints where regulated products are involved.

In parallel, CDC and CMS should support real-world evidence infrastructure of medication-use and adverse-event registries, common data elements, and polypharmacy tracking so that off-label prescribing and its outcomes are captured through existing surveillance where possible. CMS should identify coverage and reimbursement barriers to guideline-consistent use of approved and label-expanded medications.

Agency Actions

Agency	Priority actions
FDA	Convene a working group and workshops of internal and external experts and stakeholders to define adaptive, enrichment, and responder-enrichment trial designs suited to autism; lead a parallel effort to define the characteristics and evidentiary standards required for endpoints and biomarkers suitable for regulatory use; convert the resulting conclusions into guidance on an accelerated timeline and disseminate it to research and industry; signal where existing rare-disease flexibilities may be used in the interim; designate

Agency	Priority actions
	autism a priority area for drug repurposing; and pursue label expansion for approved drugs with established safety and a credible autism signal; and identify available and potential incentive and evidence-generation mechanisms for off-patent drugs in priority areas.
NIH	Fund trials suited to autism heterogeneity of high-priority repurposed agents and support endpoint and biomarker development and validation through targeted funding mechanisms, such as cooperative agreements or other coordinated funding opportunities; encourage inclusion of severe and profound autism, intellectual disability, minimal-speech, medically complex, and adult populations where safe and scientifically appropriate.
AHRQ	Systematically review, score, and prioritize repurposing candidates from the existing literature; specify evidence thresholds for subgroup benefit; assess the validity of current and candidate outcome measures.
CMS	Identify coverage and reimbursement barriers to guideline-consistent use of approved and label-expanded medications; support quality and outcome tracking for treated populations.
CDC	Support surveillance of medication use, off-label prescribing patterns, adverse events, and polypharmacy through existing infrastructure, using harmonized data elements when available.

Consolidated Federal Implementation Compact

The compact below organizes the domain's existing time-bounded deliverables and agency assignments into the accountable federal workplan used throughout Part IV.

Phase	Consolidated federal product	Accountable lead	Supporting partners
18 months	FDA working group and workshops convened and charged on a defined	FDA; AHRQ	NIH

Phase	Consolidated federal product	Accountable lead	Supporting partners
	timeline. Interim signaling of existing trial-design flexibilities usable now. Parallel FDA-led endpoint and biomarker effort initiated. Systematic prioritization of repurposing candidates initiated by AHRQ. Autism designated a priority area for drug repurposing.		
24 months	Working group identifies candidate adaptive, enrichment, and responder-enrichment designs suited to autism. Priority endpoint and biomarker development needs are identified and targeted funding is initiated. Label-expansion pathway defined, with at least one candidate advanced toward label review where safety and evidence support it.	FDA; NIH	AHRQ
3 years	FDA guidance on trial designs and regulatory expectations for endpoints issued and disseminated to research and industry. At least one subgroup-stratified multisite trial of a repurposed agent initiated, with meaningful inclusion of severe and profound autism. Medication-use and adverse-event registry operational through existing infrastructure. Consensus outcome measures for autism treatment trials issued.	FDA; NIH; CDC	AHRQ; CMS
5 years	Public reporting on guidance adoption, label expansions, subgroup-stratified trial results, off-label use and outcomes, and inclusion of severe and profound autism in federally funded treatment trials.	FDA; NIH; CDC	AHRQ; CMS

Executive Performance Indicators

These four measures constitute the executive accountability set and retain the trial-design, endpoint, repurposing, trial-inclusion, real-world-evidence, and access measures specified for this domain.

- Convening of FDA-led trial-design and endpoint/biomarker working groups on defined timelines; issuance and uptake among academic investigators and industry sponsors of adaptive and enrichment guidance and fit-for-purpose endpoint standards; and number of candidate endpoints or biomarkers advanced to a defined readiness stage.
- Number of repurposing candidates systematically reviewed, scored, and prioritized against defined evidence thresholds; designation of autism as a priority repurposing area; and number of label expansions pursued and achieved.
- Number of subgroup-stratified multisite trials of repurposed agents initiated, by condition; proportion of federally funded autism treatment trials using enrichment or adaptive designs or predefined subgroups; and proportion meaningfully including individuals with intellectual disability, minimal speech, epilepsy, self-injury, or medical complexity.
- Operational status of medication-use and adverse-event surveillance and number of medications and individuals captured, including polypharmacy; and reduction in coverage or reimbursement barriers for approved and label-expanded medications, with median time to access.

Implementation Standards

Named medications are illustrative, not endorsements; naming a drug reflects its wide off-label use and its evidence gap, not a recommendation to prescribe it.

- Trials should be designed for heterogeneity, evaluating effects in predefined subgroups or treatment-responsive populations rather than relying solely on all-comers analyses where the science warrants.
- Endpoints should be fit for autism and for setting-dependent variability; a single subjective, single-setting measurement should not be the sole basis for a conclusion.
- Repurposing should be safety-first, prioritizing drugs with established safety profiles and tracking adverse events, interactions, and polypharmacy.
- Severe, profound, intellectually disabled, minimal-speech, medically complex, and adult populations should be included in design, evaluation, and outcome reporting where safe and scientifically appropriate.
- Medication research is additive and should not divert from behavioral, developmental, communication, and family-support interventions; the objective is to reduce suffering and treat co-occurring conditions, not to erase autism.

Translational Readiness Assessment

The near-term, implementation-ready levers are label expansion for approved drugs with established safety and credible signals, which uses existing FDA authority, and real-world evidence infrastructure, which can be built on existing surveillance. Trial-design and endpoint standards are not yet guidance-ready: the field has not settled which designs and endpoints fit autism, so the working group is the necessary first step, with the explicit aim of converting its conclusions into guidance quickly. Targeted

subgroup-stratified or responder-enriched trials and endpoint and biomarker development are discovery-to-validation and depend on sustained research investment.

The principal barriers are the absence of a settled design-and-endpoint framework, the misalignment between generic-drug economics and trial costs, and persistent inclusion gaps—not an absence of candidate treatments. The practical federal objective is to make the evaluation system fit autism's heterogeneity so that credible signals can be tested in the right populations and, where warranted, converted into labeling that improves clinical awareness, prescribing confidence, and access.

Part V — Federal Navigation, Diagnostic Access, and Life Course Supports

Part V shifts from the discovery-and-translation template used in Part IV to an implementation template. Where Part IV domains progress from Scientific Rationale through Translational Status to a Translation Agenda, Part V sections begin from a Statement of Need and Core Objectives and add Implementation Standards, reflecting that these priorities are principally about deploying and scaling existing authorities, services, and infrastructure rather than maturing new biology.

Precision biology and translational infrastructure improve health only when autistic people and their families can find, reach, and sustain the services they are entitled to across the life course. Part V addresses the federal systems that determine daily stability — from the moment a family first worries about a toddler, through diagnosis, education, mental health and crisis care, housing, caregiving, employment, and later-life health. These are implementation-ready priorities that operate through existing statutory authority, paired with the evidence-building work needed to make each system more precise and durable.

What binds these domains together is not a single program but a shared problem of navigation and accountability. Autism services in the United States are delivered through a complex, multi-agency system that families, autistic individuals, and providers consistently describe as fragmented and overwhelming. Information is scattered across CMS, HRSA, CDC, ED, ACL, HUD, SSA, DOL, DOJ, and fifty-plus state systems, and both the 2021–2023 IACC Strategic Plan and GAO-24-106446 identify the same twin failures: weak linkage from screening to services, and insufficient public tracking of progress toward federal goals. Part V therefore opens by establishing the connective infrastructure — Autism.gov — that makes every subsequent section usable, and then proceeds through the life course sections in the order a life unfolds: diagnosis first, then education, then the adult and later-life supports.

Throughout Part V, profound autism and I/DD are treated as distinct, non-equivalent categories that may co-occur in some individuals but should not be presumed to do so. Profound autism is a functional subgroup within autism, defined here by minimal or no functional spoken communication and the need for continuous support; intellectual disability is neither required nor presumed. I/DD is a broader service and policy category defined on different grounds. Federal recommendations, data, and outcome reporting should identify the populations separately and characterize co-occurrence only when directly established.

Autism.gov: The Federal Front Door for Autism Navigation and Accountability

Autism.gov is the organizing federal infrastructure for the entire life course subject area, not a detached web page appended to it. It is proposed as a single, official federal portal developed with the direction and support of HHS that serves as the trusted front door for autism-related information, navigation, eligibility pathways, state services, civil-rights information, and — most consequentially — public accountability for IACC Strategic Plan implementation. It is designed to integrate existing federal resources rather than

duplicate them, and to connect the domains that this Part addresses: diagnostics, special education, mental health and crisis care, housing, caregiver supports, employment, aging, and the civil-rights protections that run through all of them.

The rationale is documented rather than speculative. Families and autistic adults describe service navigation as overwhelming and fragmented, and that fragmentation contributes directly to lost-to-follow-up after positive screens, delayed access to services, and inequitable outcomes. The IACC Strategic Plan calls for better tracking from screening through intervention; GAO-24-106446 found that federal autism coordination lacks clear, public mechanisms for tracking progress against goals. A single, well-designed.gov domain is the most direct federal response to both findings.

What Successful Federal Portals Demonstrate

Autism.gov does not need to be invented from first principles. Four established federal portals each solve part of the problem, and Autism.gov should adapt their proven design principles to a lifelong condition that spans developmental, medical, educational, housing, employment, caregiver, aging, and civil-rights domains.

Federal portal	Proven design principle	Application to Autism.gov
VA.gov	Organizes complex benefits around life events and user journeys rather than agency structure, with benefits routing built into the experience.	Life-stage navigation and a benefits and eligibility router that reflect how families actually experience autism services, not how agencies are organized.
HIV.gov / AHEAD	Combines authoritative education with a transparent public dashboard that tracks national goals at state and local levels.	The flagship IACC Implementation Dashboard, offering clear, goal-oriented public tracking of Strategic Plan progress.
Alzheimers.gov	Provides caregiver-focused, practical guidance alongside research-participation tools.	Caregiver- and family-centered resources for respite, crisis support, transition, and life course planning.
Cancer.gov	Serves as the authoritative central source across a condition continuum, segmented by audience.	One trusted, plain-language source of autism information organized for caregivers, autistic adults, providers,

Federal portal	Proven design principle	Application to Autism.gov
		researchers, and state systems.

Core Functions

The portal's functions are prioritized for realism — high-value, maintainable features first, expanding over time — and each integrates existing platforms rather than building parallel systems.

Life-stage and journey navigation. Users select their situation ("I am worried about my toddler," "My child screened positive," "We are waiting for diagnosis," "Transitioning to adulthood," "I am an autistic adult seeking employment or services," "I need respite," "I need housing or HCBS"), mirroring the journey-based design of VA.gov and Alzheimers.gov.

Benefits and eligibility router. A guided tool that routes users toward likely programs — Medicaid/CHIP, EPSDT, IDEA Part C and B, SSI/SSDI, HCBS waivers, housing vouchers, Lifespan Respite, vocational rehabilitation — without making final eligibility determinations, modeled on VA.gov's benefits tools.

State-by-state services map. Standardized entries for every state and territory covering Medicaid autism coverage, HCBS waiver names and waitlist status, Part C and B contacts, LEND/DBP sites, family-to-family health information centers, protection-and-advocacy agencies, and housing resources, beginning with high-priority data and expanding.

IACC Implementation Dashboard — the flagship accountability feature. Every IACC Strategic Plan recommendation is mapped to a responsible agency, statutory authority, federal action, deliverable, status, key performance indicators, implementation barriers, and next report date, supplying the transparency GAO-24-106446 found missing. HIV.gov's AHEAD dashboard is the clearest model.

Diagnostic access and workforce visibility. State and regional metrics on diagnostic wait times, provider capacity, tele-assessment availability, and disparities, integrated with the diagnostic-access agenda that opens the life course sections below.

Caregiver and life course support resources. Practical guidance on respite, housing pathways, crisis support, and transition planning, modeled on the Alzheimers.gov caregiver sections.

The portal is built on a small set of design principles drawn from those comparables: user journeys over agency structure; transparency and accountability; a caregiver- and family-centered tone; a single trusted, authoritative source; integration first to minimize cost and duplication; and a phased, maintainable roadmap. Its interfaces should meet federal plain-language and accessibility standards, with multilingual and AAC-accessible design where appropriate so that autistic adults, communication-diverse users, and non-English-speaking families can use it directly.

Governance, Milestones, and Accountability

Lead: HHS Office of the Secretary / National Autism Coordinator, with authority to coordinate across agencies. **Platform development:** GSA, using TTS, USAGov, or comparable current federal digital-service capacity to provide user-centered design, accessibility, and plain-language and multilingual support. **Content and data partners:** CMS (Medicaid, EPSDT, HCBS, waivers, appeals); HRSA (LEND/DBP, workforce, family-to-family centers); CDC (screening, early identification, ADDM data); ED (IDEA Part C and B); ACL (caregiver supports, respite, protection and advocacy); HUD (housing options); SSA and DOL (benefits, employment); and DOJ/OCR (civil rights, law-enforcement training, legal protections). The portal integrates the USAGov benefit-finder model and agency-specific content rather than creating new standalone systems. Authentication should be added only if needed to support secure personalized functions.

Timeframe	Milestone
6 months	Interagency memorandum of agreement executed; governance charter published; user research completed for priority journeys; high-level content inventory finished.
12 months	Public beta launched with core life-stage navigation and a basic state services map, with phased expansion toward coverage of all 50 states, DC, and territories; key federal agency pages integrated; plain-language and accessibility standards applied.
18 months	Benefits router live; diagnostic pathway guidance and caregiver resources expanded; Spanish-language version launched; initial diagnostic-access metrics published.
24 months	Full IACC Implementation Dashboard live; diffusion target of at least 30 states contributing standardized data; quarterly public analytics reporting begins, with missing state data identified transparently.

Timeframe	Milestone
4 years	Measurable improvements in family-reported ease of navigation, reductions in lost-to-follow-up after positive screens, and increased visibility of IACC progress, with ongoing iterative improvement based on user feedback.

Autism.gov is a practical, high-leverage investment that responds directly to documented navigation failures and accountability gaps. When paired with the diagnostic-access and closed-loop tracking agenda that follows, it creates a coherent federal entry point and accountability system for autism across the life course — the connective tissue for every section of Part V.

Common Measurement Framework and Implementation-Burden Taxonomy

The life course domains that follow share a small number of recurring measurement needs and one recurring risk. The risk is accumulation. When every domain writes its own full slate of indicators, the plan acquires more measures than any federal system can populate, and a dashboard that tracks everything ends up tracking nothing. This framework resolves that risk the way the NAPTI structure resolves it for research, by defining shared measurement infrastructure once and letting each domain inherit it rather than rebuild it. Two instruments do the work: a common indicator set that every domain draws from, and an implementation-burden taxonomy that keeps the plan honest about what each deliverable actually asks of an agency.

The common outcome architecture. Every domain organizes its indicators along one architecture. Recognition measures whether a need is identified. Access measures whether an identified need is met with a delivered service rather than an authorization on paper. Stabilization measures whether the delivered service produces durable function, safety, and participation. A screen without access is not an outcome, and access without stabilization is not a result. The three tiers hold across diagnosis, education, communication, mental health, housing, caregiving, employment, and aging, which is why the indicators below are written once and specified by each domain.

Common indicator set. Each domain inherits the following measures and specifies the touchpoints, populations, and data sources that apply to it. Domains reference these rather than restating them, and add only the indicators genuinely specific to their work.

Time from identified need to delivered service, measured at the touchpoints each domain defines.

Access-attainment: the share of people for whom an indicated service or support is actually delivered, not only authorized or referred.

Closed-loop referral completion, confirming the person reached the intended service.

Coverage integrity: the share of Medicaid, EPSDT, HCBS, and managed-care determinations that apply individualized, person-centered standards rather than categorical exclusions.

Workforce readiness: training adoption and competency completion in the domain's provider network.

Reduction in avoidable acute events, including emergency department use, psychiatric hospitalization, emergency placement, and crisis contact, attributable to unmet need in the domain.

Continuity across the transitions the domain touches, including pediatric-to-adult, school-to-adult, and aging transitions.

Transportation-related service disruption, a cross-cutting dependency that recurs in housing, employment, health care, and aging and is measured once here rather than scattered across domains.

Access variation and subgroup reporting: where statistically reliable and legally permissible, report headline indicators by geography, payer, language, rurality, race and ethnicity, sex, support need, communication status, and other relevant characteristics, with appropriate aggregation, suppression, and small-cell privacy protections.

Federal deliverables and state-adoption outcomes are measured differently. The plan distinguishes what federal agencies control from what depends on state election. A federal deliverable, such as issued guidance or a launched dashboard, has an accountable owner and a date. A state-adoption outcome, such as the number of states electing an optional Medicaid approach, can be measured and incentivized but cannot be compelled through this plan, and it should not sit on the same line as a federal deliverable. Indicators of the second kind are reported as diffusion measures, so that slow uptake reads as a signal for federal technical assistance rather than as a federal failure to deliver.

Implementation-burden taxonomy. Every deliverable in the domains that follow carries one of three burden levels. Naming the level is not bookkeeping. It is the difference between a deliverable an agency can execute this year and one that will stall for want of infrastructure the agency does not have.

Tier	What it requires	Sequencing
Tier 1 — Authority-based	Guidance, clarification, coverage and coding determinations, monitoring, and technical assistance. Needs staff time, not new money or new infrastructure.	Moves first.
Tier 2 — Fund-and-solicit	Appropriations or reallocation through granting mechanisms agencies already operate: demonstrations, competitive solicitations, evaluation contracts, and recognized apprenticeships.	Gated by budget, not by capacity.
Tier 3 —	Infrastructure, oversight, or sustained	Must be staged, resourced, and assigned

Tier	What it requires	Sequencing
Capacity-building	multi-site implementation the responsible agency is not staffed to carry: national data systems, cross-program record linkage, continuous demonstration oversight.	to a capable lead or an implementation partner.

Each domain closes its agenda with a short sequencing note that assigns its principal deliverables to these tiers and stages the Tier 3 work explicitly. Dollar figures throughout Part V are order-of-magnitude planning ranges meant to convey relative scale and sequencing rather than formal cost estimates; each should be replaced by a program-office costing before appropriation.

Life Course Domain I: Timely, Equitable, and Technology-Enabled Diagnosis

Strategic Objective

Compress the interval from developmental concern to completed diagnosis, appropriate medical evaluation, and service entry for autistic children and adults by making timely diagnostic work financially and operationally viable in primary and community care; preserving interdisciplinary and specialty expertise for complex presentations; and using emerging technologies only where they demonstrably extend competent clinical capacity. Diagnostic timeliness, diagnostic accuracy, and medically appropriate follow-up should advance as one accountable pathway.

Statement of Need

The diagnostic bottleneck remains one of the most measurable failures in the federal autism service system. In CDC's 2022 surveillance year, only 50.3 percent of 8-year-old children with autism and available evaluations had been evaluated by 36 months, and the median age of earliest known diagnosis among children with a diagnostic statement was 47 months. These figures represent lost developmental time and provide an unusually clear federal accountability baseline. GAO-24-106446 further found that federal autism coordination did not clearly track or report progress toward IACC goals; this domain therefore ties each major action to an accountable agency, timeframe, and measurable result.

The bottleneck is not solely a shortage of specialists. Payment and workflow often do not support the time, documentation, consultation, and follow-up needed to act on a positive developmental screen or complete a diagnostic evaluation. At the same time, an autism diagnosis may obscure gastrointestinal, immunologic, neurologic, metabolic, sleep-related, psychiatric, pain-related, or other findings that require condition-specific evaluation. Training more clinicians without correcting payment barriers, referral pathways, and diagnostic overshadowing will not create durable capacity.

The federal government already holds most of the necessary levers. Medicaid's Early and Periodic Screening, Diagnostic, and Treatment benefit provides a coverage foundation for children; Autism CARES programs support LEND and Developmental-Behavioral Pediatrics training; and HRSA's primary-care, rural-health, and workforce programs reach the settings where access gaps are greatest. During HRSA's July 2024–June 2025 reporting period, LEND trainees and faculty provided 169,070 diagnostic services and DBP trainees and faculty provided 33,561. The federal task is to connect and extend this infrastructure—not create a new entitlement or a large new delivery system.

Diagnostic and Coding Parity

The governing clinical principle is diagnostic and coding parity. Co-occurring and underlying conditions identified during evaluation should be documented and coded under the specific condition, symptom, or clinical finding involved, as they would be for any other patient. Autism should be recorded as relevant comorbid context, not used as a category that absorbs symptoms, suppresses appropriate diagnostic inquiry, or supports categorical denial of coverage. This is not a departure from existing standards but an application of them: the federal coding guidelines already require that diagnoses be reported at the highest level of specificity documented, that signs and symptoms not routinely associated with an established condition be coded when present, and that the record be reviewed to identify the specific conditions treated. Compliance with these guidelines is required for applicable HIPAA-covered diagnosis-code transactions and under relevant federal and payer program requirements.

A communication-adapted review of systems should be usable for speaking, nonspeaking, minimally speaking, and otherwise communication-disabled individuals and should incorporate caregiver information, augmentative and alternative communication, direct observation, changes in behavior or function, and prior records. It should guide medically indicated testing, consultation, and referral without creating a categorical, autism-wide testing entitlement and without delaying autism diagnosis and service entry until every co-occurring condition is resolved.

This principle applies with particular force to genetic and metabolic conditions. The Committee recommends genetic and metabolic evaluation, including whole genome sequencing where indicated, during or following an ASD diagnosis, and with particular urgency at the first onset of seizures, developmental regression, intellectual disability, dysmorphic features, congenital anomalies, or signs of possible metabolic compromise such as failure to thrive, lethargy, or hypotonia. This recommendation serves three connected purposes.

The first is the identification of genetic conditions. A meaningful subset of children with autism carry an identifiable genetic variant, and the presentations named above raise the probability that such a variant is present and clinically significant. Identifying it enables informed genetic counseling for the family and, in a growing number of conditions, opens precision treatment avenues that depend on knowing the underlying molecular cause.

The second is accurate differential diagnosis. Several conditions that present with autistic features are distinct disorders with their own trajectories and management, and some have treatment guidelines. When developmental skill loss, growth failure, or new seizures are absorbed automatically into the autism diagnosis, the opportunity to identify these conditions is lost. A structured evaluation ensures that regression and its accompanying features prompt a search for a specific cause rather than being recorded as a variation within autism.

The third is workforce readiness. The clinical value of the first two purposes is realized only if frontline clinicians can recognize when a presentation warrants evaluation and can initiate it without delay. HRSA should lead the development of training content that equips primary care and developmental clinicians to identify the genetic and metabolic red flags associated with autism, to initiate appropriate first-tier testing, and to refer efficiently for specialized sequencing, interpretation, and management. This positions recognition and the first steps of the workup in the primary care setting where children are actually seen, while reserving specialized interpretation for genetics and metabolic medicine, and it extends diagnostic capacity into the communities where access to genetics referral is currently most limited.

Core Objectives

- Remove payment, coverage, and utilization-management barriers that delay clinical action, diagnostic evaluation, specialist consultation, and medically indicated follow-up.
- Expand pediatric and adult diagnostic capacity through existing federal workforce, primary-care, rural-health, tribal-health, and autism-training programs.
- Establish a communication-adapted diagnostic and medical-evaluation protocol that recognizes co-occurring and underlying conditions and identifies cases requiring expedited specialty care.
- Preserve specialist expertise for complex, atypical, regressive, neurologically concerning, or diagnostically ambiguous presentations rather than requiring specialist entry for every evaluation.
- Reduce rural, tribal, frontier, minority-language, adult, and other medically underserved access gaps through targeted implementation in existing clinics and provider networks.
- Track the pathway from positive screen through clinical action, diagnosis, indicated medical evaluation, treatment or referral, and service entry.
- Evaluate emerging diagnostic technologies according to regulatory status, independent validation, transparency, clinical utility, subgroup performance, and the consequences of error.

Priority Federal Implementation Agenda

Implementation should begin with authority-based payment and clinical guidance, followed by targeted workforce and access investments and staged data integration. The incremental planning target is approximately $14 million in Year 1, $29 million in Year 2, and $40 million in Year 3. These amounts support guidance, protocol development, workforce supplements, tele-mentoring, limited implementation awards, evaluation, and data infrastructure; they do not replace payment for covered clinical services.

Initiative 1: Medicaid Payment, Coverage, and Diagnostic-Overshadowing Clarification

Lead: *CMS, with HRSA, AHRQ, state Medicaid agencies, and participating managed-care organizations; informed by relevant MACPAC analyses and recommendations.*

CMS should issue a State Health Official letter addressing payment and coverage policies that impede timely diagnosis and evaluation of co-occurring conditions. The guidance should clarify same-day preventive and separately identifiable problem-oriented services when a positive screen requires additional work; reinforce EPSDT follow-up and condition-specific coverage; identify recognized payment approaches for developmental testing, prolonged services, caregiver training, and inter-professional consultation; and require review of blanket edits, prior-authorization rules, denial patterns, and rates that make covered services practically unavailable. CMS should distinguish federal coverage obligations from optional state payment methodologies rather than prescribe one national billing model. The incremental planning target is $2 million in Year 1 and $3 million in Years 2 and 3.

Initiative 2: Review of Systems Clinical Protocol and Workforce Expansion

Lead: *HRSA, with AHRQ, CMS, CDC, and IHS; implementation through LEND and DBP programs, AHECs, Teaching Health Centers, health centers, and relevant professional organizations.*

HRSA should lead development and dissemination of common competency-based clinical guidance for autism evaluation and medical assessment across the life course, with AHRQ supporting evidence review, implementation evaluation, and quality-measure development. The guidance should identify core elements for developmental history, observation, differential assessment, review of systems, condition-specific documentation and coding, adult pathways, interprofessional consultation, and escalation of complex or regressive presentations.

Delivery should use programs already positioned for this work. LEND and DBP programs and the Autism CARES interdisciplinary training resource center should provide advanced faculty, curriculum, fidelity review, and complex-case consultation. AHECs, Teaching Health Centers, health centers, rural health clinics, and IHS, tribal, and urban Indian programs should extend training and mentored implementation into community settings. Pediatric and adult tele-mentoring should allow clinicians to retain responsibility for care while obtaining interdisciplinary consultation and expedited referral when needed. Competitive supplements or expanded-scope awards should be used before creating new administrative structures. The incremental planning target rises from $7 million in Year 1 to $21 million in Year 3.

Initiative 3: Rural, Tribal, Adult, and Underserved Implementation with Closed-Loop Accountability

Lead: *HRSA, IHS, CMS, and CDC, with ED/OSEP, AHRQ, state Medicaid and Title V programs, and participating health systems.*

Federal agencies should support a limited set of competitively selected implementations in the clinics and provider networks already serving rural, tribal, frontier, minority-language, adult, and medically underserved populations. Awards should finance workforce preparation, consultation access, workflow redesign, translation, data collection, and evaluation—not ordinary clinical services otherwise payable through coverage or existing grants. Existing HRSA rural-network mechanisms, AHECs, Teaching Health Centers, health centers, rural health clinics, and Indian health systems provide practical avenues without a separate hub structure.

CDC, CMS, HRSA, and ED should define a minimum data set that follows the pathway from screening and clinical action through diagnostic determination, medical review, indicated workup, treatment or referral, and service entry. Cross-system linkage among Medicaid, clinical, public-health, and IDEA Part C records is a legal and governance task as well as a technical one; it should begin with common definitions, model agreements, counsel, and a small number of jurisdictions. Aggregate reporting, sampled chart review, or validated manual follow-up should be used where individual linkage is not lawful or feasible. The incremental planning target rises from $4 million in Year 1 to $10 million in Year 3.

Initiative 4: Emerging Diagnostic Technology Evidence and Coverage Pathway

Lead: *FDA, AHRQ, CMS, and HRSA, with NIH, DoD/DHA, the National Autism Coordinator, and participating health systems.*

Emerging technologies may improve triage, structure observation, reduce administrative burden, or extend expertise, but commercial availability and narrow regulatory authorization should not be treated as general clinical validity. Technologies making diagnostic, risk-classification, or rule-out claims should be assessed for regulatory status, independent prospective validation, representative-population performance, false-positive and false-negative consequences, subgroup performance, transparency, reproducibility, clinical utility, and effects on diagnostic time and specialist referrals. The Strategic Plan does not endorse any individual product; it supports the responsible use of technological advances that can improve timely access and diagnostic accuracy.

A public register could report regulatory status, intended use, evidence category, and independent-validation status without federal endorsement or ranking. Autism.gov could serve as the public source for this information. To control cost, no more than two substantial independent prospective evaluations should be supported during the first three years unless additional funds are separately appropriated. The incremental planning target rises from $1 million in Year 1 to $6 million in Year 3.

Agency Actions

CMS. Lead Medicaid payment, coverage, utilization-management, and diagnostic-overshadowing clarification; identify and monitor payment and denial patterns that impede timely evaluation; reinforce EPSDT follow-up and condition-specific coverage; and participate in the common data set, underserved implementation, and evidence-to-coverage pathway for emerging technologies. (Initiatives 1, 3, 4)

HRSA / AHRQ. Develop the life course diagnostic and medical-evaluation protocol; expand competency-based training, tele-mentoring, fidelity review, and complex-case consultation through existing LEND, DBP, AHEC, Teaching Health Center, health-center, rural-health, and related programs; support targeted implementation; and conduct independent clinical-utility and evidence reviews. (Initiatives 1, 2, 3, 4)

CDC / IHS / ED-OSEP. Maintain national diagnostic-timeliness baselines; co-design tribal and underserved implementation; define common pathway measures; and support lawful linkage or validated aggregate follow-up across public-health, clinical, Medicaid, Title V, and IDEA Part C systems. (Initiatives 2, 3)

FDA / NIH / DoD-DHA. Clarify the regulatory and evidentiary status of emerging diagnostic technologies and support no more than two substantial independent prospective evaluations during the first three years, with representative-population, subgroup-performance, error-consequence, and clinical-utility requirements. (Initiative 4)

National Autism Coordinator. Convene the participating agencies, resolve cross-agency dependencies, align deliverables with the HHS Autism Services and Access Scorecard, and ensure that public reporting distinguishes federal deliverables from state adoption, covered clinical services, and technology-specific research milestones. (Initiatives 1–4)

Implementation Sequencing

Federal actions should proceed in a deliberate sequence. Within 12 months, CMS should issue payment and coverage clarification; HRSA and AHRQ should establish the protocol-development process and competency framework; CDC and participating agencies should define the minimum data set and baseline specifications; and FDA and AHRQ should publish the evidentiary framework for emerging technologies. By 24 months, workforce supplements, tele-mentoring, and targeted rural, tribal, adult, and underserved implementations should be operating; participating jurisdictions should have adopted lawful data-governance arrangements; and the first independent technology evaluation should be underway. By 36 months, agencies should report changes in diagnostic capacity, timeliness, medical-evaluation completion, referral and service entry, payment barriers, and access gaps; complete or report substantial progress on the limited technology evaluations; and identify which interventions warrant continuation, expansion, revision, or discontinuation.

The Year 3 incremental target of approximately $40 million is intentionally limited to federal guidance, protocol and curriculum development, workforce supplements, tele-mentoring, targeted implementation, data evaluation, and no more than two independent technology assessments. It does not finance ordinary

diagnostic visits, laboratory services, imaging, consultation, treatment, or other services payable through public or private coverage. State adoption should be reported as a diffusion measure, not represented as a federal deliverable fully within agency control.

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Federal Commitment	Lead	12-Month Deliverable	24-Month Deliverable	36-Month Deliverable / Outcome
Payment, coverage, and diagnostic-overshadowing clarification	CMS	State Health Official letter and review framework for payment, utilization management, and denial patterns	Initial state and managed-care implementation reporting	Reported changes in actionable payment barriers, denials, and timely follow-up
Clinical protocol and workforce expansion	HRSA / AHRQ	Life Course protocol, competency framework, and implementation-award design	Workforce supplements, tele-mentoring, fidelity review, and complex-case consultation operating	Increased evaluation capacity with reported diagnostic reliability, consultation use, and medically appropriate follow-up
Underserved implementation and closed-loop accountability	HRSA / IHS / CMS / CDC	Common minimum data set, governance models, and competitive implementation notice	Selected rural, tribal, adult, minority-language, and underserved implementations operating	Reported changes in timeliness, pathway completion, service entry, and access gaps
Emerging diagnostic technology evidence pathway	FDA / AHRQ / CMS / HRSA	Public evidentiary criteria and register design	First independent prospective evaluation underway and public status reporting initiated	No more than two evaluations completed or substantially advanced, with evidence-to-coverage findings reported

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Age and timeliness of evaluation and diagnosis, including the percentage of children evaluated by 36 months, median age of earliest known diagnosis, and the interval from documented concern or positive screen to diagnostic determination.
- Diagnostic capacity and equitable access, including wait times, completed pediatric and adult evaluations, geographic and language access, and the number of trained clinicians who subsequently perform evaluations with appropriate consultation and fidelity.
- Completion of the clinical pathway from diagnosis through communication-adapted medical review, indicated workup, treatment or referral, and entry into services, including escalation of complex, regressive, neurologically concerning, or diagnostically ambiguous presentations.
- Payment and operational barriers that make covered services practically unavailable, including denial and prior-authorization patterns, consultation access, and the proportion of participating sites demonstrating sustained improvement after implementation support ends.
- Technology-specific enrollment, accuracy, error, subgroup-performance, referral, and clinical-utility measures should remain visible in evaluation workplans and the public evidence register, but should not substitute for population-level diagnostic and service outcomes.

Implementation Standards

The initiatives should be incorporated into the HHS Autism Services and Access Scorecard and reported through the Autism.gov IACC Implementation Dashboard, with each federal deliverable mapped to its lead agency, authority, funding, implementation date, baseline, target, data source, and reporting frequency. Cross-agency accountability requires a National Autism Coordinator positioned to obtain meaningful attestations from CMS, HRSA, CDC, ED, IHS, and other participating agencies.

- Implementation must preserve adult pathways, effective communication, condition-specific clinical standards, and escalation for complex cases. Specialist referral should carry forward prior observations, records, and testing so patients are not required to begin again. HRSA-supported programs should report whether trained clinicians subsequently perform evaluations, use consultation, identify and appropriately evaluate co-occurring conditions, shorten wait times, improve service linkage, and maintain diagnostic reliability.
- Measures requiring cross-system linkage should be treated as developing implementation measures until the underlying authority, data quality, and attribution have been validated. Population-level diagnosis age and early evaluation remain the principal long-term outcomes. Training counts, diagnostic volume, communication-adapted review completion, claim denials, rural access, adult access, and technology enrollment should remain visible as secondary scorecard indicators, but training completion alone is not an outcome.

Translational Readiness Assessment

This domain has high near-term readiness because its first actions do not require a new national service-delivery structure. CMS can clarify payment and EPSDT expectations; HRSA can extend existing autism, workforce, primary-care, and rural-health programs; AHRQ can develop the clinical protocol and independent evidence reviews; IHS can co-design tribal implementation; and CDC can maintain national baselines and a common data structure. Participating practices can begin payment, workflow, training, and consultation changes while the more difficult cross-system data architecture is developed.

The central sequence is straightforward: make timely diagnosis and competent medical evaluation payable; prepare clinicians to perform them; preserve consultation and referral for complex cases; and measure whether patients move from screening to diagnosis, indicated workup, treatment, and services. This approach directs new federal resources toward the limited functions necessary to change practice while avoiding duplicative infrastructure and open-ended service obligations.

Life Course Domain II: Special Education, IDEA Implementation

Strategic Objective

Strengthen the timely delivery of a free appropriate public education to autistic students under the Individuals with Disabilities Education Act (IDEA) by improving fiscal accountability, workforce capacity, service-delivery transparency, and civil-rights enforcement — through existing IDEA authorities rather than a new federal entitlement.

Statement of Need

Children with disabilities are entitled to a free appropriate public education under IDEA, yet persistent underfunding, workforce shortages, inconsistent implementation, and limited civil-rights enforcement prevent many students from receiving services in a timely manner. IDEA established a Part B funding formula with a statutory maximum tied to 40 percent of national average per-pupil expenditure, but annual federal appropriations have remained well below that level, but the federal contribution remains well below that level, leaving school districts under growing fiscal pressure as the number of students requiring services rises. At the same time, shortages of teachers, school psychologists, speech-language pathologists, occupational therapists, physical therapists, and behavior specialists produce delayed evaluations, missed services, and larger caseloads, while families increasingly rely on dispute resolution to obtain services and the Office for Civil Rights manages a substantial complaint workload.

These challenges warrant coordinated federal leadership through the U.S. Department of Education, working with HHS where workforce development intersects with the health professions. Special education is the school-age counterpart to the diagnostic agenda above: timely evaluation and timely educational services are the same federal interest applied at successive points in a child's development.

For many families of autistic students, including students with profound autism, significant behavioral challenges, or other intensive support needs, the assigned public school cannot always provide timely evaluations, appropriate services, a suitable peer environment, or a program model matched to the child’s needs, and families increasingly turn to adversarial remedies — state complaints, mediation, due process, and OCR complaints — to secure services. Where authorized by state law, parent-directed school choice may provide a separate policy option: charter schools, private-school scholarships, education savings accounts, and micro-school or hybrid settings can offer families alternatives and reduce dependence on conflict-based remedies. Education savings accounts are especially relevant to autism, where a family may need a customized combination of tuition, therapies, behavioral supports, assistive technology, transportation, and curriculum rather than a single school placement. These options do not replace the public system’s obligation to offer a free appropriate public education; the rights and services associated with any particular placement remain governed by IDEA, Section 504, and applicable state law. The federal role is not to prescribe a delivery model but to ensure that families have transparent information, portable funding where state law permits, and comparable outcome and safety data across public, charter, private,

ESA, and micro-school settings, with continued oversight for nondiscrimination, fiscal integrity, and student safety.

Accountability also needs to reflect how these students actually progress. Students with profound autism and the most significant disabilities often make meaningful gains that standardized academic assessments cannot fully capture. While the alternate assessments required under the Every Student Succeeds Act (ESSA) remain essential, academic proficiency alone does not reflect growth in communication, adaptive behavior, functional independence, self-regulation, or transition to adulthood. Federal policy should encourage states to supplement existing systems with validated measures of student growth — progress toward IEP goals, communication and AAC development, adaptive behavior, inclusive participation, transition readiness, and family quality of life — reported alongside academic results rather than replacing them.

Core Objectives

- Restore progress toward the original IDEA funding commitment while improving expenditure transparency.
- Expand and retain the special education and related-services workforce needed to implement IDEA.
- Increase transparency and accountability in the delivery of IDEA services.
- Strengthen enforcement of IDEA and Section 504 protections.
- Support transparent parent-directed school-choice options where authorized by state law.

Priority Federal Implementation Agenda

Federal administrative responsibility for several functions in this domain is currently in transition. Deliverables are therefore identified by function rather than by office: accountable leads reflect the entity holding each function at the time of writing, and where responsibility shifts, the deliverable, its timeline, and its public reporting obligation should carry with it.

Initiative 1: IDEA Funding and Fiscal Accountability

Lead: Department of Education (OSERS/OSEP), reporting to OMB and Congress on IDEA appropriations and the funding gap.

Federal action should rely on existing IDEA monitoring authorities, technical assistance, competitive grants, and public reporting, with local educational agencies continuing to administer services. The Department should issue standardized fiscal-reporting guidance, publish district-level IDEA funding dashboards, report legal expenditures and mediation and due-process outcomes annually, and identify best-practice districts, leveraging IDEA Part B authorities, discretionary and personnel-preparation grants, and targeted appropriations where applicable. ED/OSEP should report to Congress and OMB on the IDEA funding gap and annual progress toward the statutory maximum under IDEA §611, expressed in relation to the 40-percent-of-national-average-per-pupil-expenditure benchmark.

Separately, and as a contingency only: should the Department of Education at some future point be closed, consolidated, or materially reduced, ED/OSEP should report to Congress and OMB on any resulting federal savings and identify those available for reinvestment in IDEA Part B — prioritizing autism services, high-cost disability categories, rural and underserved communities, workforce capacity, and parent-directed options — so the federal share makes measurable annual progress toward the statutory maximum under IDEA §611. Any such savings should be directed to students with disabilities rather than used to reduce support or weaken enforcement. This provision takes effect only if such a change occurs.

Initiative 2: Special Education Workforce Capacity

Lead: ED/OSEP and HRSA.

To expand and retain the workforce that implements IDEA, the federal agenda should expand personnel-preparation grants, increase scholarships and loan forgiveness tied to service commitments, support retention incentives, and publish annual workforce dashboards. HRSA participation reflects the overlap between education-sector and health-profession shortages — particularly for speech-language pathologists, occupational and physical therapists, and school psychologists — connecting this initiative to the diagnostic-workforce expansion earlier in Part V.

Initiative 3: IDEA Service Delivery and Accountability

Lead: ED/OSEP, with HHS.

The Department should develop common reporting specifications, publish an annual IDEA Performance Dashboard, disseminate best practices, and strengthen mediation guidance so that IEP services are delivered as written and missed services are visible and correctable, while states retain flexibility and report standardized metrics that allow national comparison. ED/OSEP should also encourage states to supplement ESSA accountability with a National Special Population Accountability Framework that preserves existing requirements while incorporating validated measures of student growth for students with the most significant disabilities — progress toward IEP goals, communication and AAC development, adaptive behavior, functional independence, social-emotional development, inclusive participation, transition readiness, supported-employment outcomes, and family quality-of-life indicators, drawing on existing resources such as the National Center on Educational Outcomes and National Core Indicators, reported through the Special Education Performance Dashboard alongside academic results.

Initiative 4: Civil-Rights Enforcement Capacity

Lead: Department of Education, Office for Civil Rights.

To strengthen enforcement of IDEA and Section 504 protections, OCR should restore staffing, publish complaint dashboards, establish complaint-resolution benchmarks, and issue compliance assistance, so that families experience consistent enforcement rather than resolution delays.

Initiative 5: Parent-Directed School Choice as a State-Dependent Policy Option

Lead: Because these programs are authorized and structured primarily under state law, the federal role should focus on transparency, technical assistance, nondiscrimination, safety, fiscal integrity, and

comparable outcomes—not on treating school choice as a core IDEA entitlement. ED/OSEP, in coordination with state education agencies and, where applicable, scholarship-administering organizations.
ED/OSEP should publish comparable state-level data on students with disabilities participating in charter schools, vouchers, education savings accounts, micro-schools, and parent-directed programs — including whether autism-specific funding weights are available, how funds may be used for related services, and whether participating providers meet nondiscrimination, child-safety, fiscal-integrity, and outcomes-reporting expectations — through the Special Education Performance Dashboard. ED/OSEP should identify leading autism scholarship and ESA models and provide technical assistance to states that choose to weight choice funding by disability intensity while preserving IDEA and Section 504 protections.

Agency Actions

ED (OSERS / OSEP). Lead IDEA fiscal accountability, workforce capacity, service-delivery transparency, and parent-directed school-choice data; issue standardized reporting guidance; publish the annual Special Education Performance Dashboard covering funding, workforce, evaluation timeliness, service delivery, dispute resolution, civil-rights enforcement, supplemental growth measures, and school-choice data; provide technical assistance to states; report to Congress and OMB on the IDEA funding gap and annual progress toward the statutory maximum under IDEA §611, expressed in relation to the 40-percent-of-national-average-per-pupil-expenditure benchmark. (Initiatives 1, 2, 3, 5)

ED / OCR. Enforce IDEA and Section 504; restore staffing, publish complaint dashboards, and set resolution benchmarks. (Initiative 4)

HRSA / HHS. Support special education and related-services workforce development where it intersects with the health professions. (Initiative 2)

Implementation Sequencing

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Issue standardized reporting guidance for IDEA funding, evaluation timeliness, workforce vacancies, services delivered as written, missed services, dispute resolution, and civil-rights enforcement.	ED/OSEP	ED/OCR; OMB; state education agencies
18–24 months	Launch an annual Special Education	ED/OSEP	ED/OCR; National

Phase	Consolidated federal product	Accountable lead	Supporting partners
	Performance Dashboard and technical-assistance package using comparable state measures while preserving state and local authority.		Autism Coordinator
24–36 months	Pilot supplemental growth and transition measures for students with the most significant disabilities and publish comparable data on publicly supported school-choice arrangements.	ED/OSEP	NCEO; state partners
3–5 years	Report national trends in evaluation, workforce capacity, service delivery, complaints, dispute resolution, transition readiness, and implementation of corrective action.	ED/OSEP and ED/OCR	OMB; National Autism Coordinator

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Evaluation timeliness, IEP service-delivery completion, and missed-service rates attributable to workforce or implementation failures.
- Vacancy, turnover, and caseload indicators for special educators, related-service professionals, and paraprofessionals.
- Complaint, mediation, due-process, corrective-action, and civil-rights resolution timeliness and outcomes.
- Student growth, communication, adaptive function, inclusive participation, transition readiness, and post-school connection for students across support levels.

Implementation Standards

The Department of Education should publish an annual Special Education Performance Dashboard summarizing IDEA funding, workforce capacity, evaluation timeliness, service delivery, dispute resolution, and civil-rights enforcement, with OSEP and OCR jointly reviewing national performance each year. These measures should be incorporated into an HHS/Department of Education autism services scorecard coordinated with the National Autism Coordinator and surfaced through the Autism.gov IACC Implementation Dashboard, so special education accountability is visible alongside the other life course domains. National baselines remain incomplete for missed IEP services attributable to staffing shortages,

workforce projections by discipline, and district-level litigation expenditures; establishing these is early-phase work.

Translational Readiness Assessment

Special education accountability is implementation-ready and relies on existing IDEA authorities rather than new programs or entitlements. Fiscal-reporting guidance, funding and complaint dashboards, and the Special Education Performance Dashboard can move first under current monitoring authority. Workforce expansion, school-choice transparency, and supplemental growth measures run through existing grant and reporting mechanisms. District-level funding and missed-services metrics require establishing national baselines before targets can be set and represent the domain's principal early-phase measurement work.

Life Course Domain III: Improving Communication and Access for Nonspeaking and Minimally Speaking Autistic Individuals

Throughout this domain, the term "Nonspeaker" refers to an autistic individual who does not develop functional spoken language or who has minimal or unreliable speech.

Strategic Objective

Ensure that autistic individuals across their life course, particularly Nonspeakers, can obtain individualized communication evaluation and appropriate supports without delay, while federal agencies build the measurement, subgroup-definition, comparative-effectiveness evidence, and precision health studies needed to determine which communication interventions and implementation strategies improve real-world outcomes, for whom, under what conditions, and for which communication profiles, with what durable effect.

This domain treats communication access as a health and functional priority. Access to speech-language pathology, occupational therapy, AAC evaluation, assistive technology—including emerging communication methods—and the modalities an individual is already using or may use is critical. Access refers to the ability to use an individual's preferred modality of communication across a variety of contexts and honoring their and their families' needs and preferences. At the same time, federal research should investigate which communication-access interventions work best, for whom, for which communication profiles and with what durable effect.

Statement of Need

Communication is a core determinant of health, safety, education, employment, community participation, and self-determination. The ability to express pain, symptoms, fear, preferences, needs, goals, consent, refusal, and ideas is not a peripheral developmental skill. It is a functional and health-related capacity that affects nearly every major outcome addressed in this Strategic Plan.

Communication challenges in autistic children can present very early, often appearing between 6 and 12 months of age, even before diagnosis. Early intervention, including pre-diagnostic support, can change the trajectory of communication development, and thus remains a research priority. For a substantial subset of these children, these early differences do not resolve. Approximately 25% to 30% of autistic children do not develop functional spoken language or remain minimally speaking beyond early childhood. These individuals are among the most underserved and underrepresented populations in autism research, despite often having among the highest support needs. Communication barriers also affect adults across the life course, including individuals whose speech is unreliable, limited under stress, disrupted by motor-planning problems, or insufficient for complex medical, educational, legal, employment, or community participation. Communication impairment is especially prevalent among individuals with profound autism — those who require continuous (24/7) support and have minimal or unreliable speech — so prioritizing this domain addresses two documented gaps at once: a major contributor to functional disability, and the underrepresentation of individuals with profound autism in autism research.

Effective communication depends on receptive language, expressive language, and pragmatic language which utilize motor skills, sensory/auditory processing, attention, memory, language learning, executive functioning, and other cognitive skills. Identification of communication abilities and needs, and subsequent interventions should account for these inter-dependencies. Because motor and sensory functioning directly shape speech production and the ability to use other communication methods, communication access cannot be separated from sensorimotor function. When a person cannot reliably respond through speech, pointing, imitation, or other motor-dependent output, observed performance can obscure actual language, literacy, and cognition. Nonspeakers frequently show floor effects on standardized assessment, so language, communication competence, and cognition may be systematically underestimated and symptoms may be attributed to autism rather than investigated — a form of diagnostic overshadowing. Motor-output barriers can mask communication ability, which is why communication access is inseparable from the sensorimotor foundations addressed in Priority Therapeutic Domain 10 (Motor Planning, Praxis, Sensorimotor Integration, and Apraxia).

Core Objectives

- Make communication, in all its forms, a named federal quality-of-care priority across the life course rather than a peripheral developmental skill.
- Guarantee individualized communication evaluation and access to appropriate supports.
- Build the definitions, phenotyping, and motor-minimized assessments needed to stop underestimating people whose ability is obscured by motor, sensory, or medical barriers.
- Determine, through precision health research, which communication interventions work best for which subgroups, under what conditions, and with what durability.
- Protect established access against categorical, method-based exclusions by anchoring federal policy in individualized effective-communication and reasonable-modification standards.
- Measure outcomes that matter in daily life, including the ability to report pain and symptoms, participate in health care, express consent or refusal, report safety concerns, and sustain participation and quality of life.

Current State of Evidence

Standard-of-care AAC — including picture-based systems, speech-generating devices, sign, and conventional aided and unaided approaches — shows positive effects on targeted communication outcomes, but the evidence is of low or very low certainty and focused largely on requesting in children, reflecting general challenges of generating high-certainty evidence for individualized communication interventions in heterogeneous populations. These systems rarely support the fuller range of communication — reporting pain, describing internal states, expressing safety concerns, participating in health care and other decisions — that full participation requires. Standard-of-care AAC does not meet the communication needs of all individuals with autism; many individuals and families report that conventional methods — including PECS, speech-generating devices, and sign language — have not produced functional communication, and that text-based methods provide access where standard approaches did not. Access

can be transformative for many and should not be delayed while federal research projects continue to investigate communication methods.

Text-based and letter-based communication approaches are used by a substantial and growing number of nonspeaking individuals who report meaningful benefit. While evidence is emerging, that *absence should not be represented or considered equivalent to proof of ineffectiveness or evidence of invalidity*.

These methods typically involve a trained communication partner — a person, often a parent, aide, educator, or clinician, who supports another individual's communication.

Federal research should investigate and develop approaches to support a fuller range of functional (reporting pain; describing internal states; expressing opinions, wants, needs and safety concerns; and participating in healthcare and other decisions) and nuanced communication using methods appropriate to each approach. Accomplishing these objectives should be an early priority for the federal research agenda, alongside preserving individual access to methods that are already in use by a given person while that research develops. While that evidence is developed, public programs should respect individualized decisions about communication methodology and should not impose categorical, method-based exclusions. *Communication access is a civil right and honoring it does not require any federal agency to endorse a specific method*.

As previously stated, effective communication relies on motor skills, sensory/auditory processing, autonomic regulation, attention, memory, language learning, executive functioning, and other cognitive skills. Understanding and accounting for the interactions of these skills is essential. The relationship between motor function and communication access requires particular federal attention. For some Nonspeakers, the limiting factor may not be language comprehension but rather the inability to initiate, sequence, coordinate, and execute the motor output that communication requires. Motor planning, fine-motor coordination, oral-motor function, pointing, reaching, eye gaze, typing, touch-screen use, postural control, autonomic function, and visual-motor integration all affect communication, and motor skills are significantly associated with communication in minimally speaking autistic children regardless of age, setting, or modality. Processing speed may be better preserved when motor demands are minimized and may decline as motor-output demands increase.

When assessment depends on motor output, cognitive ability, receptive language, literacy, or decision-making capacity may be obscured. This concern is not theoretical: motor-minimized and strength-informed assessments have shown that some minimally speaking autistic individuals classified as untestable or profoundly impaired by conventional instruments can perform within normal ranges when motor-output demands are reduced. Federal research should therefore examine whether current communication and cognitive assessment methods systematically underestimate Nonspeaking and other autistic individuals, especially those with motor-planning impairment, apraxia, epilepsy, regression history, autonomic dysregulation, pain, sleep disruption, gastrointestinal problems, or other co-occurring conditions. The

underlying motor mechanics are addressed in Priority Therapeutic Domain 10 (Motor Planning, Praxis, Sensorimotor Integration, and Apraxia).

Evidence Gaps

The field lacks consistent definitions of nonspeaking and minimally speaking autism, and lacks phenotyping, motor-minimized cognitive and receptive-language assessments, objective communication-access measures, and longitudinal outcomes that matter to individuals and families.

Federal research should move beyond narrow impairment measures and requesting behavior. Outcomes should include the ability to communicate pain and symptoms, participate in healthcare, express consent or refusal, report abuse or safety concerns, reduce frustration and dysregulation, decrease self-injury where communication barriers contribute, improve educational and community participation, support employment where feasible, reduce caregiver demands, facilitate independence, and improve quality of life.

The field should shift towards precision health interventions. Families, clinicians, educators, and payers are often forced to make decisions without adequate evidence comparing AAC modalities, speech-generating devices, picture-based systems, eye-gaze technology, text-based instruction, communication partner training, naturalistic developmental approaches incorporating AAC, and emerging technologies across defined subgroups. Beyond comparative-effectiveness research, studies should evaluate not only whether an approach works, but for whom, at what age or developmental stage, with what motor profile, with what level of support, in which settings, and with what durability.

A further gap concerns the interaction between communication and co-occurring conditions. Communication may be affected by epilepsy or subclinical seizure activity, sleep disruption, pain, gastrointestinal disease, feeding problems, dysautonomia, anxiety, sensory dysregulation, medication effects, neuromuscular conditions, neuroinflammation, mitochondrial dysfunction, or other treatable contributors. Federal studies should not treat these conditions only as covariates. They should test whether recognition and treatment of co-occurring conditions improve communication pillars (receptive, expressive, and pragmatic language) and how they impact access, communication reliability, participation, and safety.

A final gap concerns dyadic communication and communication partner support. Many communication methods develop within a relationship between the nonspeaking individual and a trained partner, caregiver, clinician, educator, or support professional. The field has not adequately studied how partner training, coaching, motor support, regulation, proximity, pacing, environmental structure, and fading of support affect communication outcomes over time.
Autonomic regulation may be central: autonomic dysregulation is documented in autism — reduced heart-rate variability and parasympathetic tone, and delayed recovery after stress — and can affect the volitional motor output on which communication depends. Emerging research on caregiver-child physiological co-regulation suggests that communication partners may help stabilize arousal and create conditions under which motor planning, volitional motor control and communication become more accessible. Federal

research should measure autonomic indicators — heart-rate variability, respiratory sinus arrhythmia, electrodermal activity, and pupillometry — in both the Nonspeaker and the partner during interaction, and test whether physiological synchrony predicts communication outcomes. This work should be designed to answer whether physiological co-regulation improves an individual's own communicative output.

Priority Federal Implementation Agenda

Initiative 1: Protection of Established Communication Access

Protect individualized access to communication methods already in use while research and technology development continues. Nonspeakers should not be categorically barred from using an AAC method, including but not limited to text-based methodologies, communication support, or communication partner arrangement in federally funded or public programs. Federally funded or public programs should support continued access to communication methods when individualized, experience-based evidence suggests the method is effective for them, including while broader research is underway. The federal standard is individualized assessment: whether the communication support is effective for the person, in the relevant setting, for the communication task at issue, and whether reasonable alternatives would provide equal access. This does not require any federal agency to endorse a particular AAC method, resolve scientific controversy, or fund services outside applicable program authority. HHS OCR should issue effective-communication guidance to this effect; CMS should apply the same individualized standard in Medicaid; and HHS should coordinate with DOJ and the Department of Education so that communication access follows the individual across settings.

Lead agencies: HHS OCR, with CMS, HRSA, DOJ, and the Department of Education.

Initiative 2: Improve Communication and Access to Services

Ensure that autistic individuals, including Nonspeakers, have access to comprehensive, individualized communication evaluation conducted by qualified professionals (including but not limited to speech-language pathologists, occupational therapists, and special education teachers) and to the full range of individually indicated communication approaches — occupational therapy, motor training, speech-language pathology, AAC evaluation, assistive technology, speech-generating devices, communication partner training, and text-based methods based on individualized assessment. Access should not be delayed or restricted to methods with completed randomized trials. Continual data tracking presents an opportunity to build evidence regarding the usability and efficacy of these approaches—that is, practice- and clinically based evidence—when evidence for this population is limited and methods already in use have been excluded from evidence reviews.

Lead agencies: CMS, with HRSA, Department of Education and AHRQ.

Initiative 3: Differential Assessment and Referral Pathways

Support practical pathways that help clinicians distinguish among the range of factors contributing to a communication challenge. Differential, adaptive, and appropriate assessments should consider motor-planning impairment, sensory factors, pain, seizure activity, medication effects, autonomic functioning, language comprehension, cognition, and environmental mismatch. This should trigger prompt, appropriate referral across primary care, developmental-behavioral pediatrics, neurology, speech-language pathology, occupational therapy, schools, and Medicaid care coordination tailored to the individual's needs.

Lead agencies: HRSA, with AHRQ, CMS.

Initiative 4: Common Data Elements and Motor-Minimized Assessment

Define a standardized communication-access common data-element (CDE) set for federally funded autism studies. Assessment CDEs might include a motor-access profile for communication (pointing, reaching, eye gaze, typing, touch-screen use, switch access), communication partner support level, oral-motor and speech-motor planning, fine-motor coordination, visual-motor integration, motor initiation and sequencing, physiological regulation during communication, and co-occurring conditions. Intervention CDEs might include AAC type and proficiency, text-based communication ability, support level and communication modality. Outcome CDEs should emphasize meaningful and functional endpoints and quality of life. CDEs rely on development and standardization of assessment tools that either don't rely on or can accommodate motor-planning impairment and minimize other task-based demands, so that receptive language, cognition, literacy, decision-making capacity, and individual strengths can be accurately evaluated. For example, conventional evaluation methods may not accurately assess Nonspeakers who cannot reliably demonstrate ability through speech, pointing, imitation, handwriting, or standard direct testing. This work should include adaptive research-design guidance so that Nonspeakers and those with profound autism, regression, motor impairment, or medical complexity are not excluded by protocol design. These CDEs could also be encouraged in the development of practice-based evidence.

Lead agencies: NIH (NIDCD, NICHD, NIMH, NINDS), with AHRQ.

Initiative 5: Precision Research

Support precision health studies within a given communication challenge domain (i.e., understanding language, expressing thoughts, or social communication) that are tailored to accommodate the unique needs and challenges of an individual. Studies should evaluate intensity, sequencing, and the scaffolding and fading of supports; how supports are introduced and adjusted at different stages of communication development; which individuals benefit most from which approaches; whether the quality of communication partner training predicts outcomes; caregiver feasibility; and potential adverse effects.

Outcomes should extend beyond requesting to communication function, generalization across home, school, healthcare, work, and community settings, durability, healthcare engagement, safety, self-determination, participation, quality of life, and caregiver burden. Studies should also test whether

treatment of co-occurring conditions — including epilepsy, subclinical seizure activity, gastrointestinal disease, pain, and sleep disruption — directly improves communication access or function.

This initiative also prioritizes precision research to understand which approaches work best, for whom, and under what conditions and might include comparing conventional AAC, speech-generating devices, eye-gaze systems, picture-based communication, sign-based approaches where appropriate, text-based communication instruction, communication partner training, naturalistic developmental approaches incorporating AAC, and emerging technology-assisted methods.

Lead agencies: NIH (NIDCD, NICHD, NIMH, NINDS), with AHRQ.

Initiative 6: The Motor-Communication Interface and Dyadic Development

Investigate how motor planning, motor initiation, sequencing, praxis, oral-motor and speech-motor function, fine-motor control, eye gaze, oculomotor function, postural support, visual-motor and sensorimotor integration, sensory processing, and autonomic regulation and co-regulation affect expressive communication, coordinated with research on the co-occurring conditions that may affect communication reliability. A central aim is to determine whether motor-output barriers contribute to systematic underestimation of language and cognition, and whether specialized communication instruction — including text-based methods — can reveal abilities not ascertainable through conventional assessment. Federal research should also investigate dyadic communication development — how communication develops over time between Nonspeakers and their communication partners, including the role of autonomic co-regulation. Motor and sensorimotor mechanics are addressed in Priority Therapeutic Domain 10 (Motor Planning, Praxis, Sensorimotor Integration, and Apraxia).

Lead agencies: NIH (NICHD, NINDS, NIMH, NIDCD).

Initiative 7: Leveraging Emerging Technology Across the Clinical and Research Pipeline

Evaluate emerging technological approaches — including eye tracking, motion capture, computational linguistic analysis, physiological monitoring, EEG, neural imaging, virtual reality, artificial-intelligence-assisted communication tools, and brain-computer interfaces where appropriate — for use in functional communication and as diagnostic tools, outcome measures, tracking tools, and as potential strategies for interventions.

Lead agencies: NIH (NICHD, NINDS, NIMH, NIDCD, NIBIB).

Agency Actions

NIH (NIDCD, NICHD, NIMH, NIBIB, NINDS).

Support the federal research initiative on improving communication and access for autistic individuals, including Nonspeakers, with standardized common data elements and adaptive research-design guidance; motor-minimized cognitive and receptive-language assessment tools; comparative-effectiveness studies of the full range of interventions, including text-based methods; motor-communication and dyadic-development research, including autonomic co-regulation; emerging technology-assisted communication and objective communication-access measures; and a longitudinal communication-outcomes system. Require inclusion of individuals with profound autism, regression, and medical complexity. (Initiatives 3–6)

AHRQ

Conduct comparative-effectiveness reviews and studies of communication-access interventions — including conventional AAC, speech-generating devices, eye-gaze systems, picture-based systems, text-based instruction, communication partner training, and emerging approaches — and identify the methodological adaptations needed to evaluate rigorously the approaches that have been underrepresented in or excluded from systematic review, including generalization across settings and partners, and durable functional outcomes. (Initiative 4)

HRSA

Develop, disseminate, and train clinicians through education, referral, and technical-assistance resources on recognizing communication-access barriers and distinguishing communication impairment from cognitive incapacity, language comprehension, motor-planning impairment, dysarthria, sensory dysregulation, pain, medication effects, or autism itself, with referral pathways for AAC evaluation, speech-language pathology, occupational therapy, motor assessment, assistive technology, communication partner training, and evaluation of co-occurring conditions. (Initiative 2)

CMS

Analyze Medicaid access barriers for communication-access needs — AAC evaluation, occupational therapy, speech-language pathology, assistive technology, speech-generating devices, dedicated-device requirements, school-home equipment barriers, managed-care variation, EPSDT implementation, and early-intervention limitations — identify state policies that categorically exclude communication methods, and issue guidance clarifying coverage of medically necessary communication-access supports and that Medicaid HCBS and self-directed budgets may not categorically exclude a method without an individualized, person-centered determination. (Initiative 1)

HHS Office for Civil Rights

Issue effective-communication guidance requiring individualized assessment of communication supports for Nonspeakers and establishing that a Nonspeaker may not be categorically barred from an AAC method

including text-based communication methods, communication support, or communication partner arrangement in a federally funded or public program, and addressing method-based exclusions. (Initiative 7)

HHS, with DOJ and the Department of Education

Coordinate to align federal communication-access expectations across healthcare, disability services, schools, community programs, and public accommodations, so that communication access follows the individual across settings and is not narrowed by fragmented funding streams or setting-specific exclusions, including appropriate cross-references addressing communication access under IDEA, AAC in schools, and assistive technology. (Initiative 7)

Implementation Sequencing

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish individualized communication-access and differential-assessment guidance covering AAC, assistive technology, speech and motor assessment, communication-partner support, and protection against categorical method-based exclusion.	HRSA, CMS, and HHS OCR	AHRQ; ED; DOJ
18–24 months	Adopt communication research and assessment tools including common data elements, motor-minimized assessment standards, and inclusive research-design requirements.	NIH and AHRQ	NIDCD; NICHD; NIMH; NINDS; NIBIB; ED
24–36 months	Launch precision health studies across communication modalities and support levels, including emerging text-based and technology-assisted approaches, including generalization, safety, and functional outcomes.	AHRQ and NIH	HRSA; CMS; ED; FDA where regulated technology is involved
3–5 years	Report access, generalization, healthcare communication, safety reporting, participation, self-determination, quality of	AHRQ and NIH	HHS OCR; HRSA; CMS; ED; DOJ

Phase	Consolidated federal product	Accountable lead	Supporting partners
	life, and caregiver burden and translate mature evidence into policy and practice.		

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Percentage of nonspeaking and minimally speaking individuals receiving a comprehensive individualized communication and motor-access evaluation and coverage for the selected support.
- Time from identified communication-access need to evaluation, device or method availability, partner training, and cross-setting implementation.
- Percentage of federally supported studies using motor-minimized assessment, reliability and generalization safeguards, inclusive enrollment, and meaningful communication outcomes beyond requesting.
- Change in the ability to report pain, symptoms, consent or refusal, abuse or safety concerns, and to participate across healthcare, education, work, home, and community settings.

Implementation Standards

- Nonspeakers, including AAC users, should be involved in design, testing, implementation, and evaluation.
- Every deliverable should span the life course. Pediatric-only communication policy is inadequate.
- Access should be tailored to the individual rather than categorical.
- Screening and evaluation should be paired with delivered supports and follow-up. A communication assessment without subsequent support is not an outcome.
- Communication impairment should be distinguished from cognitive incapacity, and communication access should follow the individual across health care, education, disability services, and community settings rather than being narrowed by fragmented funding.

Translational Readiness Assessment

Improving communication for individuals with autism, including Nonspeakers, spans access, implementation, comparative effectiveness, and discovery. Comprehensive communication evaluation and access to individualized communication supports are implementation-ready and should not be delayed or narrowed while the evidence base is built. Comparative-effectiveness research is needed to determine which communication-access interventions work best for defined subgroups and which supports produce durable gains that generalize across settings and partners. Discovery and testing work remain necessary for

objective measurement tools, motor-minimized assessments, emerging technologies, and study of the motor, autonomic, neurological, and regulatory systems that affect communication.

Life Course Domain IV: Co-Occurring Mental Health Conditions, Crisis Care, and Suicide Prevention

Strategic Objective

Ensure that autistic children, adolescents, adults, and older adults have timely access to autism-competent mental health recognition, support, treatment, crisis response, care coordination, and continuity of care across the life course.

Several therapeutic domains in this Plan address biological contributors to distress, destabilization, self-injury, sleep disruption, seizure activity, pain, autonomic arousal, medication effects, and functional decline. This section addresses the federal systems required to ensure that co-occurring mental health conditions and crisis presentations are recognized, treated, supported, and followed across the life course.

The purpose is practical. Autistic people should not have to become suicidal, hospitalized, expelled, arrested, excluded, or abandoned before systems recognize that mental health needs require competent care. Federal policy should make co-occurring mental health conditions and suicidality a named implementation priority within autism policy, with clear agency obligations, measurable access standards, and accountable continuity of care.

Statement of Need

Co-occurring mental health conditions are not peripheral to autism policy. Depression, anxiety, ADHD, trauma-related symptoms, obsessive-compulsive symptoms, substance use, irritability, aggression, self-injury, suicidal ideation, and crisis presentations can determine whether an autistic person can remain in school, participate in family and community life, work, communicate distress, avoid hospitalization, and remain safe.

Current systems are not consistently designed around autistic communication, sensory, cognitive, developmental, and support profiles. General mental health tools and crisis protocols may not account for literal interpretation of questions, alexithymia, atypical affect, masking, perseveration, shutdown, sensory overload, AAC use, intellectual disability, caregiver role, fear of disclosure, trauma history, or distress expressed through behavior rather than conventional self-report.

The implementation gap is not simply lack of awareness. It is the absence of enforceable access, coverage, training, crisis, and follow-up expectations across the federal systems that already touch autistic people: SAMHSA crisis and community mental health programs, CMS Medicaid and CHIP authority, HRSA workforce programs, NIH and AHRQ research and evidence translation, CDC surveillance, ED school guidance, DOJ and HHS OCR civil-rights authority, ACL disability programs, and ACF family support systems.

Core Objectives

- Make co-occurring mental health conditions and suicidality a named federal autism implementation priority.
- Build autism-adapted tools and service models that work across communication profiles, support levels, developmental stages, and service settings.
- Align Medicaid, CHIP, EPSDT, managed care, HCBS, CCBHC, school-based, crisis, and community mental health systems around autism-competent care.
- Make suicide prevention an explicit function of 988, mobile crisis, emergency departments, inpatient psychiatric settings, pediatric and adult primary care, schools, and community behavioral health.
- Require continuity of care after crisis, hospitalization, school exclusion, emergency department use, or transition from pediatric to adult systems.

Priority Federal Implementation Agenda

This agenda begins at 12 months because publishing the federal Autism Mental Health and Suicide Prevention Action Agenda relies on existing HHS, ONAC/IACC, and partner-agency coordination mechanisms that are already actionable.

Initiative 1: Autism Mental Health and Suicide Prevention Action Agenda

HHS, through the Office of the Secretary and the National Autism Coordinator, with consideration of IACC recommendations, should publish a federal Autism Mental Health and Suicide Prevention Action Agenda with agency-specific commitments, deadlines, funding mechanisms, data systems, and annual agency status reporting established within each participating agency's authority.

The agenda should cover depression, anxiety, ADHD, suicidality, trauma, serious emotional disturbance, behavioral crisis, self-injury, substance use, psychiatric hospitalization, medication safety, caregiver support, transition-age youth, adult mental health, and older adult mental health. It should function as the organizing federal implementation document rather than another statement of concern.

Lead agencies: HHS/National Autism Coordinator, with NIH, SAMHSA, CMS, HRSA, CDC, AHRQ, ED, DOJ, ACL, and ACF.

Initiative 2: Surveillance, Risk Identification, and Autism-Adapted Screening

CDC, NIH, SAMHSA, HRSA, CMS, and AHRQ should create a coordinated surveillance and screening strategy for co-occurring mental health conditions and suicidality in autism. Prevalence tracking alone is not enough. Federal data systems should be able to report diagnosed or suspected depression, anxiety, ADHD, serious emotional disturbance, self-injury, suicidal ideation, suicide attempts, psychiatric emergency visits, hospitalizations, substance use disorders, unmet mental health needs, and post-crisis follow-up.

The federal government should also support development and validation of autism-adapted suicide risk screening, assessment, safety planning, and follow-up protocols. Required products should include tools appropriate for youth, adults, AAC users, nonspeaking people, people with intellectual disability, people with high-support needs, and people whose distress is expressed through behavior rather than conventional self-report.

Lead agencies: CDC, NIMH, SAMHSA, AHRQ, CMS, HRSA.

Initiative 3: Crisis, 988, Emergency, Inpatient, School, and Civil-Rights Standards

SAMHSA, CMS, AHRQ, ED, DOJ, HHS OCR, CDC, HRSA, and NIH should establish federal standards for autism-competent crisis response across 988, mobile crisis, emergency departments, crisis stabilization, inpatient psychiatric settings, school crisis response, and post-crisis referral.

The standards should require concrete communication, sensory-informed de-escalation, AAC access, adapted safety planning, caregiver involvement when appropriate, privacy protections, safe re-entry after hospitalization, avoidance of unnecessary law-enforcement escalation, restraint and seclusion reduction, discharge planning, and referrals that actually accept autistic people. Crisis response should be routed to health-based care whenever possible, with disability accommodations treated as part of the standard of care.

Lead agencies: SAMHSA, CMS, AHRQ, ED/OSEP/OCR, DOJ, HHS OCR, HRSA, CDC.

Initiative 4: Coverage, Community Mental Health, Adult Access, and Family Stabilization

CMS, SAMHSA, ACL, HRSA, AHRQ, and ACF should align coverage and service-delivery systems so autism-competent mental health care is a covered, measurable, and accountable expectation. This includes screening, diagnosis, adapted psychotherapy, psychiatric consultation, medication management, crisis stabilization, intensive outpatient and partial hospitalization when needed, peer and family support, post-discharge follow-up, care navigation, and HCBS supports that prevent avoidable institutionalization.

CMS should clarify Medicaid, CHIP, EPSDT, managed care, and HCBS expectations for autism mental health care, including network adequacy standards that measure whether providers actually serve autistic people. SAMHSA and CMS should develop an autism-competent CCBHC and community mental health model. Federal policy should also address adult mental health access, transition out of pediatric and school systems, and family stabilization supports without implying family causation.

Lead agencies: CMS, SAMHSA, ACL, HRSA, AHRQ, ACF.

Initiative 5: Research, Comparative Effectiveness, Medication Safety, Workforce, and Practice Toolkits

NIH, AHRQ, HRSA, SAMHSA, FDA, CMS, and ED should build the evidence and workforce base for autism-competent mental health care. This includes research on mechanisms, risk prediction, prevention,

diagnosis, and treatment of depression, anxiety, ADHD, suicidality, trauma, self-injury, substance use, sleep-related psychiatric distress, emotion dysregulation, crisis recurrence, and intervention response.

The research agenda should include adapted CBT, DBT-informed approaches, caregiver-supported treatment, peer support, ADHD treatment in autism, antidepressant and anxiety-treatment response, suicide-specific interventions, crisis follow-up models, digital supports, integrated care models, medication safety, and deprescribing when medication burden exceeds benefit. AHRQ should produce evidence reviews and practice toolkits. HRSA and SAMHSA should require autism mental health competencies across relevant workforce programs.

Lead agencies: NIH/NIMH, AHRQ, HRSA, SAMHSA, FDA, CMS, ED.

Agency	Priority actions
HHS / NAC	Convene the federal action agenda, coordinate agency-authorized annual status reporting, and align autism mental-health priorities across research, services, surveillance, coverage, and civil-rights programs.
NIH / NIMH	Fund autism mental health research, adapted interventions, suicide-prevention tools, risk prediction, comparative effectiveness, medication safety, and inclusion of communication-diverse and high-support populations.
SAMHSA	Implement autism-competent 988, mobile crisis, CCBHC, community behavioral health, substance use, crisis stabilization, and grantee training expectations.
CMS	Issue Medicaid, CHIP, EPSDT, managed care, HCBS, CCBHC, and quality-measure guidance; require network adequacy, follow-up, access-attainment, and coverage reporting.

Agency	Priority actions
HRSA	Build workforce competencies through Autism CARES, LEND, Developmental-Behavioral Pediatrics, MCH, primary care, psychiatry, psychology, nursing, social work, and care coordination programs.
CDC	Expand surveillance for autism mental health, suicidality, self-harm, psychiatric emergency use, hospitalization, adult data, and state-level indicators.
AHRQ	Conduct evidence reviews, practice toolkits, implementation science, quality-improvement guidance, and comparative-effectiveness translation.
ED / OSEP / OCR	Issue school-based mental health, suicide-prevention, crisis-response, re-entry, discipline, and disability-accommodation guidance.
DOJ / HHS OCR	Address avoidable criminalization, restraint, seclusion, exclusion, disability discrimination, crisis-response accommodations, and health-based diversion.
ACL	Support adult access, family stabilization, caregiver navigation, disability systems coordination, peer support, and crisis-related family supports (joint with ACF).
ACF	Support adult access, family stabilization, caregiver navigation, disability systems coordination, peer support, and crisis-related family supports (joint with ACL).

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish an autism mental-health and suicide-prevention action agenda with adapted screening, differential assessment, crisis, 988, emergency, inpatient, school, and civil-rights standards.	SAMHSA and HRSA	CMS; CDC; NIH; AHRQ; ED; DOJ; HHS OCR
18–24 months	Establish surveillance and baseline measures for depression, anxiety, ADHD, suicidality, self-injury, crisis use, hospitalization, restraint, seclusion, and post-crisis follow-up across communication and support profiles.	CDC and SAMHSA	CMS; NIH; AHRQ; ED
24–36 months	Launch community-care, crisis-diversion, medication-safety, workforce, and comparative-effectiveness demonstrations with family stabilization and communication access built into the model.	SAMHSA, CMS, and AHRQ	HRSA; NIH; FDA; ACL; ACF; ED; DoD/DHA where applicable
3–5 years	Report access, symptom and functional outcomes, suicide attempts and deaths where measurable, crisis recurrence, emergency and inpatient use, coercive practices, and caregiver stability.	SAMHSA and CDC	CMS; AHRQ; HRSA; NIH; ED

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Percentage receiving autism-adapted mental-health screening, differential assessment, referral, and completed treatment when indicated.
- Time from identified risk or crisis to appropriate response, follow-up, and covered community care.
- Rates of suicide-related events, crisis recurrence, emergency use, hospitalization, restraint, seclusion, medication adverse events, and avoidable placement disruption.

- Durability-qualified change in mental health, safety, communication, participation, health stability, quality of life, and caregiver demands.

Implementation Standards

- Autistic people and families should be involved in testing, implementation, and evaluation, including people with intellectual disability, high-support needs, AAC users, nonspeaking people, adults, and people with lived experience of psychiatric crisis.
- Every deliverable should include relevant life course coverage. Pediatric-only policy is inadequate.
- Measurable access standards: wait times, provider availability, denial rates, out-of-network use, follow-up after crisis, and whether referred providers actually serve autistic people.
- Guidance should distinguish autism from co-occurring mental health conditions without separating people into disconnected systems. Diagnostic overshadowing should be treated as a quality failure.
- Federal reports should include funding accountability by agency, condition, age group, service setting, and research or service category.

Translational Readiness Assessment

Mental health recognition, access, safety, crisis response, adapted communication, follow-up, and coverage can be made accountable now, through existing statutory authority and without waiting for new autism-specific biomarkers.

The evidence-building component is real but bounded. Autism-adapted screening tools, suicide-prevention protocols, psychotherapy models, medication strategies, crisis follow-up models, and adult access models require validation and comparative-effectiveness evidence. The federal objective is to build systems that respond now while generating the evidence that makes care more precise, safer, and more durable.

Life Course Domain V: Housing Supply, Supported Living, and Caregiver Succession for Autistic Adults

Strategic Objective

Ensure that autistic adults with support needs, including those with profound autism, have access to safe, appropriate, sustainable housing and supported-living models that preserve civil rights, match support intensity, strengthen community participation, and prevent avoidable crisis, institutionalization, homelessness, or emergency residential displacement.

For autistic adults who cannot live independently, housing is not one service among many. It is the platform on which health care, daily support, workforce stability, safety, relationships, vocational opportunity, and community participation depend.

The federal problem is not only coordination of existing services. It is also the shortage of actual residential capacity. Rights, eligibility, and funding matter, but they do not create housing by themselves. Families cannot choose among options that do not exist, and adults with high support needs cannot be served by a system that has no available place for them to live.

Statement of Need

Adults with autism live across a wide range of support profiles. Some live independently with limited assistance. Others need daily support, overnight supervision, nursing, behavioral support, transportation, communication support, supported employment or day services, and help with personal care. A smaller but highly vulnerable population requires 24-hour support and cannot safely rely on ordinary independent living models.

Only about one in five autistic young adults in the United States has ever lived independently in the years after high school — the lowest rate among disability groups — and in a population-based cohort followed into early adulthood, roughly 37 percent required overnight care. Even among autistic adults without a diagnosed co-occurring intellectual disability, only about 25 percent live in their own households, with most living with family into at least middle age. When adults do live alone, they frequently depend on government assistance such as Supplemental Security Income to do so, meaning that "living alone" often does not mean living without support. The urgency of this challenge will only increase over time, as autism prevalence continues to rise and a growing number of autistic youth reach adulthood.

Within this population, adults with profound autism who require 24-hour support represent the most urgent case. Many other adults with autism require housing supports to varying degrees as well. For families providing this level of care, succession planning is a central and often unresolved concern: with many adults living with aging parents and limited residential capacity available, the question of who will provide care as caregivers age is one that current federal policy has largely left unaddressed.

The central problem is not merely that services are difficult to coordinate. It is that the housing supply itself is insufficient. For many families, eligibility on paper does not translate into an available, appropriate place to live, and coordination alone cannot solve a shortage of actual residential capacity. Federal policy should therefore move beyond helping systems manage existing scarcity and toward creating the conditions for new supply: more residential models, more providers and developers, more financing tools, and more public-private partnerships capable of producing housing at scale.

Even funded capacity depends on a workforce that is not there. The direct support professionals who make community living possible face a chronic and deepening shortage, with annual turnover of 40 to 50 percent in many settings, driven above all by low wages, limited benefits, and few paths for advancement. The President's Committee for People with Intellectual Disabilities warned in both its 2017 and 2024 reports that these shortages force residential providers to close, delay transitions out of family homes and institutions, and leave people on waiting lists despite available funding. Directors of autism-specific Medicaid waiver programs have identified workforce shortage and turnover among the greatest obstacles to service delivery, with 67 percent naming low salaries as the primary driver.

Addressing these gaps is not only a matter of capacity but of outcomes. Safe, appropriate, and stable housing is the platform on which health, safety, relationships, employment, community participation, and quality of life depend. Well-matched supported living reduces avoidable crises, hospitalizations, and emergency placements, and it allows autistic adults to live with greater stability, dignity, and connection. The measure of federal housing policy should be not only how many placements exist, but whether they improve the daily lives of the people they serve.

Core Objectives

- Make housing supply and supported living a named federal autism life course priority.
- Expand the range and capacity of residential models for adults with diverse support needs, including adults requiring 24-hour support.
- Align Medicaid HCBS, housing finance, transition planning, and caregiver-succession policy around stable adult living.
- Clarify that community integration is judged by lived outcomes, not physical configuration alone.
- Build the DSP workforce and provider capacity required to make supported living real.
- Measure whether housing and supported-living models improve stability, safety, community participation, health care use, caregiver succession, and long-term public cost.

Priority Federal Implementation Agenda

This agenda begins at 12 months because publishing the federal Housing Supply and Supported Living Action Agenda relies on existing HHS, ONAC/IACC, and partner-agency coordination mechanisms that are already actionable.

Initiative 1: Federal Housing Supply and Supported Living Action Agenda

Lead agencies: HHS Office of the Secretary/National Autism Coordinator, with ACL, CMS, HUD, ACF, DOJ, and HHS OCR

HHS, through the Office of the Secretary and the National Autism Coordinator, and informed by IACC recommendations, should publish a federal Housing Supply and Supported Living Action Agenda identifying concrete federal actions, agency responsibilities, data gaps, demonstration pathways, financing tools, and annual agency status reporting established within each participating agency's authority. The agenda should address adults across support levels, with explicit attention to individuals who require 24-hour support, nonspeaking or minimally speaking adults, adults with intellectual disability, adults with co-occurring medical or behavioral support needs, transition-age youth, and older autistic adults, and should recognize that housing need is not solved by a single model — federal policy should create the conditions for multiple high-quality models to be built, evaluated, and replicated.

Initiative 2: Regulatory Clarity on Community Integration, Choice, and Intentional Communities

Lead agencies: CMS, ACL, DOJ, HHS OCR, HUD.

CMS, working with ACL, DOJ, HHS OCR, and HUD, should issue clarifying guidance confirming that community integration is assessed by outcomes—connection, participation, and choice—and by actual operating conditions, rather than physical configuration alone; recognizing that thoughtfully designed intentional communities can satisfy integration requirements when chosen through person-centered planning and when they preserve dignity, autonomy, privacy, freedom from coercion, access to the broader community, and meaningful participation; and establishing a predictable national heightened-scrutiny framework so that states and providers understand compliance requirements before investing. Consistent with *Olmstead* and related civil-rights authorities, federal policy should reject institutional isolation and coercive placement while clarifying that disability-specific or intentional models are not disqualified by physical design alone and that heightened scrutiny should assess actual conditions and outcomes rather than categorically deter innovation.

Initiative 3: HCBS, Medicaid, Transition, and Caregiver-Succession Alignment

Lead agencies: CMS, ACL, ACF, HUD, SSA.

CMS, ACL, ACF, HUD, and SSA should align Medicaid HCBS, transition planning, benefits planning, and residential readiness around predictable adult need. HCBS remains the primary mechanism for the daily supports that make community living possible, but it generally pays for services rather than housing itself, and many families experience eligibility on paper without an available, appropriate place to live. Within existing authority, CMS should enable and encourage states to (a) adopt acuity-based reimbursement that reflects the staffing intensity high-support individuals require; (b) establish reserved-capacity or crisis set-asides so that a residential slot becomes available when an aging caregiver can no longer provide care; and (c) provide presumptive eligibility at the school-to-adult transition so that supports do not lapse at age-out.

In parallel, ACL, with CMS, and HUD should establish a standardized caregiver future-planning framework and tools, beginning in adolescence and no later than age 14, addressing residential readiness, succession and emergency planning, and financial and benefits planning, with particular attention to families whose primary caregivers are over 55. Caregiver work in this domain remains tied to residential planning, succession, and emergency backup; broader caregiver support and respite are addressed in the caregiver-supports section of the Plan.

Initiative 4: DSP Workforce and Provider Capacity Strategy

Lead agencies: DOL, ACL, CMS, HRSA, ED.

The direct support professional workforce is the constraint that ultimately caps residential supply. DOL, ACL, CMS, HRSA, and ED should develop a national DSP workforce and provider-capacity strategy. DOL, with ACL, should establish nationally recognized career pathways for direct support professionals — registered apprenticeships, competency-based training, stackable credentials, and advancement opportunities within direct-support roles. CMS, with ACL, should enable states to strengthen DSP recruitment and retention through payment-policy options — competitive wages, benefits, retention incentives, and reimbursement that reflects the complexity of supporting the highest-need individuals. Demonstration models should test workforce housing, shared supervision, team-based staffing, technology-enabled training, AI-assisted documentation, and remote supports where those tools improve safety and reduce administrative burden without replacing human care. Participating states should report direct-support-professional vacancy, turnover, retention, wage, supervision, and training indicators tied to supported-living capacity.

Initiative 5: Demonstration, Financing, Data, and Quality Outcomes for Supported Living Models

Lead agencies: ACL, HUD, CMS, ACF, Treasury, evaluation partners.

ACL and HUD's Community Planning and Development office should co-lead a funded demonstration initiative to build, evaluate, and compare supported-living models — at least 10 sites across rural, suburban, and urban areas — including small specialized homes, enhanced behavioral-support residences, supported apartments, intentional communities, farmstead or campus-based communities, clustered housing, technology-assisted supports, and hybrid models, with existing HUD resources braided in where available. In parallel, HUD, CMS, and ACL, with Treasury and congressional coordination where needed, should coordinate federal housing and financial incentives to expand residential supply — HUD Section 811 and other supportive-housing tools; project-based supportive housing; mixed-use and mixed-population developments that combine autism housing with affordable senior housing, workforce housing, healthcare access, and community amenities; LIHTC scoring preferences and basis boosts; tax-exempt bond financing; public-private partnerships; and braided Medicaid, housing, and philanthropic capital. Some housing-finance tools require congressional action or appropriations; the Plan states this plainly while directing HHS and partner agencies to use existing levers to create the evidence, guidance, and financing pathways needed for scale. The objective is not to fund isolated demonstration projects but to create a durable

marketplace for high-quality residential options, and evaluation should test whether integrated models reduce long-term per-person cost growth through transportation savings, shared infrastructure, team-based staffing, fewer emergency interventions, better workforce retention, and more proactive healthcare.

Agency Actions

HHS Office of the Secretary/National Autism Coordinator. Convene the federal housing and supported-living agenda, align agency responsibilities, and coordinate agency-authorized annual status reporting as part of autism life course implementation. (Initiative 1)

ACL. Lead disability-systems coordination, residential quality frameworks, caregiver-succession tools, state technical assistance, and supported-living demonstration design. (Initiatives 1–5)

CMS. Issue HCBS, waiver, managed-care, acuity-based payment, transition, quality-measure, Settings Rule, and residential-support guidance within existing authority. (Initiatives 2, 3, 4)

HUD. Coordinate housing resources, supportive-housing expertise, Section 811 alignment where available, mixed-population development, and demonstration support with HHS partners. (Initiatives 1, 5)

DOL. Develop DSP apprenticeship, credential, career-ladder, and workforce-development pathways. (Initiative 4)

HRSA / ED. Support workforce training, transition planning, and professional education relevant to supported living and high-support needs. (Initiative 4)

ACF / SSA. Support benefits planning, family transition planning, caregiver-succession tools, and coordination for families facing residential transition. (Initiative 3)

DOJ / HHS OCR. Ensure civil-rights guidance protects against institutional isolation while preserving informed choice and model-neutral evaluation. (Initiative 2)

Treasury. Support tax, bond, LIHTC, and public-private financing incentives for supportive-housing expansion, with congressional coordination where needed. (Initiative 5)

Implementation Sequencing

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish a federal housing and supported-living action agenda, regulatory clarification on community integration and informed choice, and a caregiver-succession planning framework.	HUD, ACL, and CMS	DOJ; HHS OCR; ACF; SSA
18–24 months	Establish national baseline measures for housing need, waitlists, provider capacity, direct-support workforce, caregiver age and succession risk, and residential instability.	HUD and ACL	CMS; ACF; DOL; SSA
24–36 months	Launch financing and service-model demonstrations spanning scattered-site, shared, family-supported, intentional-community, and other person-centered options with enforceable quality and rights protections.	HUD and CMS	ACL; ACF; Treasury/IRS; DOJ; HHS OCR
3–5 years	Report net housing capacity, time to placement, choice, stability, health and safety, community participation, workforce adequacy, caregiver succession, comparative cost and quality across supported-living models, and avoidable institutional or crisis placement.	HUD, ACL, and CMS	DOJ; ACF; DOL; SSA

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Net increase in appropriate supported-living capacity and reduction in time from documented need to stable placement.
- Percentage of individuals receiving informed choice among feasible settings and services, with documented rights, safety, and person-centered safeguards.
- Direct-support workforce vacancy, turnover, compensation, training, and continuity indicators in participating systems and adoption of recognized direct-support-professional apprenticeship and credential pathways.
- Housing stability, health and safety, community participation, avoidable crisis or institutional placement, and completed caregiver-succession planning.

Implementation Standards

- Autistic adults, families, providers, disability-rights organizations, state DD agencies, housing experts, and direct support professionals should have input regarding design, implementation, and evaluation.
- Federal guidance should preserve civil rights and informed choice while avoiding a default assumption that one physical model is inherently superior for every person.
- Housing and supported-living policy should be evaluated by lived outcomes: stability, safety, autonomy, participation, relationships, health access, support match, and quality of life.
- Caregiver-related measures in this section should remain focused on residential planning, succession, emergency backup, and transition continuity, not general caregiver-support policy.
- Federal reporting should distinguish services that support community living from capital and housing-supply mechanisms that create places to live.

Translational Readiness Assessment

Residential supply, HCBS alignment, workforce capacity, and caregiver succession are necessary for adult stability, and each can be advanced now through planning, guidance, financing pathways, workforce development, and accountable measurement rather than new science.

The demonstration and evaluation component compares supported-living models under real-world conditions. Federal demonstrations should determine which models work for which support profiles, how they are financed, how workforce stability is achieved, whether they reduce crisis-driven placements, and whether they improve safety, health access, participation, community connection, caregiver confidence, and long-term sustainability.

Life Course Domain VI: Caregiver Stabilization, Respite, Navigation, and Family Support

Strategic Objective

Ensure that family caregivers of autistic children, adolescents, adults, and older adults have practical support, timely respite, navigation, mental-health access, financial guidance, and transition assistance sufficient to sustain care without requiring crisis, exhaustion, or system failure before help becomes available.

Caregiver capacity is a load-bearing assumption beneath the autism service system. Diagnosis, therapy access, school implementation, medical follow-up, crisis prevention, HCBS use, housing transition, employment support, and aging-related planning all depend on families who can find the system, understand it, use it, and remain stable enough to continue care.

This section addresses caregiver stabilization directly. Housing policy must create places to live and supported-living capacity; caregiver policy must make sure families have respite, navigation, mental-health access, financial stabilization, peer support, and connection to the right federal or state pathway at the right time.

Statement of Need

Families often become the default care coordinators for autism because systems are fragmented. They manage diagnosis, therapies, school services, medical care, insurance, Medicaid, HCBS, safety, transportation, employment planning, crisis response, and adult transitions, often without a single accountable point of navigation. When support is delayed or difficult to access, the burden does not disappear. It shifts to the family.

Respite remains one of the clearest unmet needs. Routine respite can preserve family stability before crisis. Emergency respite is different. It is the short-notice, time-limited capacity needed when a caregiver is hospitalized, exhausted, temporarily unable to continue, or facing an acute family emergency. Most systems do not have this capability in a predictable form.

Caregiver mental health should also be treated as part of system stability, not as an afterthought. Screening alone is insufficient. Families need a pathway from identified strain to accessible support, peer connection, counseling or behavioral health care when needed, and follow-up that confirms the referral actually worked.

Financial strain is another destabilizing force. Families may face out-of-pocket costs, reduced employment, denied services, complex benefits rules, and uncertainty about ABLE accounts, SSI, Medicaid, HCBS, paid family caregiving, tax provisions, and other supports. The federal role is not to promise a new entitlement. It is to make existing pathways easier to understand, easier to access, and more consistently measured.

Core Objectives

- Make caregiver stabilization a named autism implementation priority across the life course.
- Build routine and emergency respite capacity for autistic people across support needs, with explicit attention to people with profound autism, and for people with I/DD
- Create a shared navigation backbone that connects families to diagnosis, services, respite, benefits, education, health care, transition, and aging resources.
- Make voluntary caregiver mental-health screening meaningful by pairing it with informed consent, an appropriate setting, referral capacity, access, and follow-up.
- Improve financial and benefits navigation, including existing Medicaid, SSI, ABLE, tax, and paid-family-caregiving pathways where available.
- Establish national baselines for caregiver strain, respite access, navigation failures, financial burden, and successful connection to supports.

Priority Federal Implementation Agenda

This agenda begins at 12 months because publishing the Autism and I/DD Caregiver Stabilization Action Agenda can rely on existing HHS and partner-agency coordination mechanisms.

Initiative 1: Autism and I/DD Caregiver Stabilization Action Agenda

HHS, through the Office of the Secretary and the National Autism Coordinator, and informed by IACC recommendations, should publish an Autism and I/DD Caregiver Stabilization Action Agenda with distinct attention to the needs of families supporting people with profound autism. The agenda should identify the federal products needed to support families across the life course: respite guidance, emergency respite models, family navigation tools, caregiver mental-health referral pathways, benefits navigation, financial-stabilization technical assistance, and agency-authorized public reporting.

The agenda should be built on existing caregiver infrastructure, including ACL's National Strategy to Support Family Caregivers, Lifespan Respite, No Wrong Door, Aging and Disability Resource Centers, Developmental Disabilities Act networks, HRSA training programs, Medicaid care coordination, and Autism.gov. The federal task is to make those systems usable for autism families.

Lead agencies: HHS/ONAC, IACC, ACL, CMS, HRSA, SAMHSA, CDC, ED, ACF, SSA, Treasury/IRS.

Initiative 2: Routine and Emergency Respite Capacity

ACL, CMS, and HRSA should strengthen respite capacity for autistic people across support needs—including people with profound autism—and for people with I/DD within the Lifespan Respite architecture and Medicaid pathways where available. Routine respite should be treated as a stabilizing support that helps families sustain care. Emergency respite should be treated as a distinct capability with defined activation criteria, trained provider capacity, response-time expectations, and follow-up.

Emergency respite should not require a family to exhaust ordinary respite first. It should be available for caregiver hospitalization, acute family emergency, imminent placement breakdown, or short-term inability to continue care safely. The purpose is not to replace housing, crisis care, or long-term services. The purpose is to prevent a temporary caregiving failure from becoming an avoidable institutional placement, emergency department boarding, psychiatric crisis, or family collapse.

Lead agencies: ACL, CMS, HRSA.

Initiative 3: Family Education and Navigation at Diagnosis and Major Transitions

HRSA, CDC, ACL, CMS, ED, and SSA should create a standardized Autism Family Education and Navigation Toolkit for use at diagnosis and major transition points. Families should not leave a diagnostic appointment, school transition meeting, hospital discharge, or adult-service eligibility encounter without clear next steps.

The toolkit should cover autism and developmental trajectory; early intervention; medical evaluation and co-occurring conditions; insurance, Medicaid, HCBS, and private coverage; IDEA and Section 504; communication access; safety and wandering; crisis planning; respite; caregiver well-being; benefits; adult-service eligibility; supported decision-making; employment and postsecondary options; and referral to housing, aging, and caregiver resources when relevant. Its housing function should be navigation: helping families reach the right housing pathway without turning caregiver support into a housing-supply program.

Lead agencies: HRSA, CDC, ACL, CMS, ED, SSA.

Initiative 4: Caregiver Mental Health, Peer Support, and Crisis Prevention

CMS, SAMHSA, HRSA, ACL, and ACF should make caregiver mental-health support a routine component of autism service systems. Voluntary screening, with informed consent, may be offered at appropriate clinical, care-coordination, or family-support contact points when privacy, referral capacity, and follow-up are available. Participating programs should specify who conducts the screening, how results are documented and protected, and whether follow-up is financed through the caregiver's own coverage, an applicable family-support benefit, grant funding, or another authorized source. Screening should not be a condition of services for the autistic person.

Support should include peer navigation, family support, counseling or behavioral health referral where clinically indicated, tele-behavioral health when local capacity is thin, and crisis planning for families under acute strain. The language should remain careful. Caregiver support is not a substitute for services owed to the autistic person, and it should not imply family causation. It is a stability support for the care environment that federal systems already rely on.

Lead agencies: CMS, SAMHSA, HRSA, ACL, ACF.

Initiative 5: Financial, Benefits, and Paid-Family-Caregiving Navigation

ACL, CMS, SSA, Treasury/IRS, and ACF should improve financial and benefits navigation for autism families using existing authorities. The federal role should include plain-language guidance, screening tools, technical assistance, and state-option clarity rather than promises beyond current law.

Navigation should address SSI, SSDI, Medicaid, CHIP, HCBS, ABLE accounts, relevant tax provisions, private insurance appeals, out-of-pocket cost relief where available, and paid family caregiving options under existing HCBS authorities when states elect to use them. This initiative should also measure financial strain because unmet cost burden can destabilize care, reduce employment, delay services, and increase crisis risk.

Lead agencies: ACL, CMS, SSA, Treasury/IRS, ACF.

Agency	Priority actions
ACL	Lead Lifespan Respite, National Strategy to Support Family Caregivers alignment, No Wrong Door/ADRC integration, DD Act network coordination, and caregiver navigation.
CMS	Clarify Medicaid, CHIP, HCBS, respite, care coordination, paid-family-caregiving, managed-care, and quality-measure options within existing authority.
HRSA	Integrate family navigation, caregiver education, and support competencies into Autism CARES, LEND, DBP, primary care, and workforce programs.
SAMHSA	Support caregiver mental-health referral pathways, peer support, crisis prevention, and behavioral health access.
CDC	Support baseline data, surveillance options, and family-facing public-health education at diagnosis and transition.

Agency	Priority actions
ED	Integrate caregiver navigation into school transition, IDEA, Section 504, and family engagement technical assistance.
SSA	Provide plain-language disability-benefits guidance and support transition-age benefits navigation.
Treasury / IRS	Provide plain-language guidance on ABLE accounts and relevant tax provisions.
ACF	Support family stabilization, family resource centers, navigation, and coordination for families under strain.

Agency Actions

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish a caregiver-stabilization action agenda, caregiver-strain and urgent-risk framework, routine and emergency respite guidance, and a life-stage navigation architecture for Autism.gov.	ACL and ACF	CMS; HRSA; SAMHSA; CDC; ED; SSA
18–24 months	Launch emergency-respite and closed-loop family-navigation pilots with defined activation, response, referral-completion, cultural and language access, and follow-up standards.	ACL, CMS, and HRSA	ACF; SAMHSA; state partners
24–36 months	Implement caregiver mental-health, peer-support, benefits, ABLE, tax, insurance,	ACL and ACF	CMS; SAMHSA; SSA; Treasury/IRS; ED

Phase	Consolidated federal product	Accountable lead	Supporting partners
	HCBS, paid-family-caregiving, and succession-navigation tools through existing federal and state infrastructure.		
3–5 years	Report respite capacity, emergency response, navigation completion, financial strain, caregiver mental-health access, family stability, and crises or placements averted.	ACL	ACF; CMS; HRSA; SAMHSA; CDC

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Availability, utilization, unmet need, and activation time for routine and emergency respite.
- Percentage of families completing referred services and benefits navigation rather than receiving information alone.
- Caregiver mental-health access, financial and benefits-navigation completion, and caregiver-reported stability.
- Reduction in emergency caregiving breakdown, unresolved navigation failures, avoidable crisis escalation, and avoidable placement disruption.

Implementation Standards

- Caregiver support should strengthen the care environment without substituting for services owed directly to autistic people.
- Family-facing tools should be plain-language, culturally responsive, accessible, and organized by life stage and support need.
- Screening should be paired with referral and follow-up. A screen without access is not an outcome.
- Housing-related caregiver succession should be coordinated with the housing agenda, while this section carries the broader respite, navigation, mental-health, financial, and transition-support work.
- Federal reporting should establish baselines before setting unrealistic targets in areas where national data are currently weak.

Translational Readiness Assessment

Families need respite, navigation, mental-health access, financial guidance, and transition support, and existing caregiver, disability, Medicaid, public-health, education, and benefits infrastructure can deliver these once it is coordinated more coherently.

The evidence-building task is practical: to determine which navigation models reduce loss to follow-up, which respite models prevent crisis escalation, which caregiver-support pathways improve stability, and which financial-navigation tools reduce avoidable strain. The aim is to stop relying on unsupported families as the system’s hidden infrastructure.

Life Course Domain VII: Employment, Workforce Participation, and Workplace Supports Across Functional Profiles

Strategic Objective

Ensure that autistic adolescents and adults have access to employment pathways, workplace accommodations, supported employment, vocational rehabilitation, transition services, technology supports, and retention strategies that match their strengths, support needs, communication profiles, and long-term goals.

Employment policy should not treat autistic people as a single workforce category. Some individuals need intensive supported employment, job coaching, day-to-work transition, transportation support, and HCBS-funded services. Others can perform competitive or professional work but lose jobs because of executive-function demands, sensory environments, social-communication mismatch, inflexible management practices, anxiety, burnout, or lack of accommodation. A credible federal strategy addresses both.

This section concerns autistic people's own employment access, retention, and advancement. Housing covers the workforce needed to staff supported living, and caregiver supports address the employment consequences of sustained caregiving. The federal objective here is to make work possible, sustainable, and meaningful for autistic people themselves.

Statement of Need

Employment is not only an economic outcome. It affects independence, daily structure, community participation, health coverage, social connection, self-determination, and long-term stability. Yet autistic people remain too often underemployed, unemployed, pushed out of work, or limited to programs that do not match their abilities.

The service system frequently separates people into two incomplete categories. Individuals with high support needs may be directed toward day programming without sufficient pathways to supported work, customized employment, or meaningful daily activity tied to skill development. Autistic adults with average or high cognitive ability may be assumed to need little support, even when workplace design, executive-function demands, sensory conditions, interview practices, disclosure concerns, and burnout create serious barriers.

Federal policy should therefore recognize two connected tracks. One track strengthens supported employment, customized employment, vocational rehabilitation, and day-to-work pathways for individuals who need substantial support. The other strengthens accommodations, management practices, flexible work design, federal hiring, postsecondary-to-work transition, and retention supports for individuals capable of competitive employment but vulnerable to workplace failure. The tracks should be connected, not hierarchical. The question is what support makes work sustainable for the person in front of the system.

Core Objectives

- Make autistic employment access, retention, and advancement a named federal implementation priority.
- Preserve and strengthen supported employment for people with high support needs.
- Modernize vocational rehabilitation and workforce programs for autistic people who need accommodations but may not qualify for intensive disability services.
- Improve employer practices around recruitment, interviewing, onboarding, supervision, sensory environment, communication, executive-function support, and flexible work.
- Build transition pathways from secondary school, postsecondary education, apprenticeships, day services, and HCBS supports into meaningful work.
- Measure employment quality, retention, advancement, accommodation use, burnout, underemployment, and sustained participation rather than job placement alone.

Priority Federal Implementation Agenda

This agenda begins at 12 months because publishing the federal Autism Employment and Workforce Participation Action Agenda relies on existing DOL, ED/RSA, ACL, OPM, EEOC, HRSA, and CMS authorities that are already actionable.

Initiative 1: Federal Autism Employment and Workforce Participation Action Agenda

DOL, ED/RSA, ACL, OPM, EEOC, HRSA, CMS, and HHS should publish a federal Autism Employment and Workforce Participation Action Agenda. The agenda should identify the distinct federal roles needed for supported employment, vocational rehabilitation, employer guidance, federal hiring, postsecondary transition, accommodations, technology supports, and retention.

The agenda should be explicit that job entry is not enough. Federal reporting should track whether autistic people obtain work, keep work, advance when they want to, receive accommodations, avoid preventable job loss, and have access to support when work begins to destabilize.

Lead agencies: DOL/ODEP, ED/RSA, ACL, OPM, EEOC.

Supporting agencies: CMS, HRSA, HHS, SAMHSA, SSA.

Initiative 2: Supported Employment, Customized Employment, and Day-to-Work Pathways

ACL, CMS, ED/RSA, and DOL should strengthen supported employment and customized employment for autistic people who need substantial support to obtain and sustain work. This includes people with intellectual disability, profound autism, minimal or no functional speech, complex communication needs, motor-access needs, behavioral support needs, transportation barriers, and co-occurring medical conditions.

Federal guidance should help states and providers align HCBS, vocational rehabilitation, school transition, supported employment, day services, and employment-first policy without assuming that every person follows the same path. Meaningful work may include competitive integrated employment, customized employment, supported self-employment, social enterprise, microenterprise, supported volunteering tied to skill development, or structured day-to-work transition. The key measure is not whether the person fits a predefined program. It is whether the person receives support that increases meaningful participation, choice, skill development, and stability.

Lead agencies: ACL, CMS, ED/RSA, DOL.

Initiative 3: Workplace Accommodation, Retention, and Advancement

DOL/ODEP, EEOC, the Job Accommodation Network, OPM, ED/RSA, and employer partners should develop autism-specific workplace accommodation, retention, and advancement tools. These should address recruitment, interviews, onboarding, communication norms, sensory environment, written instructions, predictable expectations, executive-function supports, flexible scheduling, remote or hybrid work where appropriate, performance feedback, conflict resolution, disclosure, and anti-discrimination protections.

This initiative should be especially clear about autistic adults who are capable of competitive work but repeatedly lose jobs because the workplace is not designed for their profile. The goal is not special treatment. The goal is accurate job matching, effective supervision, usable accommodations, and retention practices that allow qualified workers to perform.

Lead agencies: DOL/ODEP, EEOC, JAN, OPM.

Supporting agencies: ED/RSA, HRSA, SAMHSA.

Initiative 4: Postsecondary-to-Work, Apprenticeship, and Federal Hiring Pathways

ED, DOL, OPM, ACL, and SSA should strengthen transition from high school, postsecondary education, vocational training, apprenticeships, and disability services into employment. Too many autistic young adults leave school or college without a practical bridge to work, benefits counseling, accommodation planning, transportation, job coaching, or employer connection.

Federal partners should create transition models for autistic students and young adults entering the workforce, including those leaving special education, community college, four-year college, certificate programs, apprenticeships, supported employment, and day services. OPM and DOL should also test an autism hiring and retention pilot within the federal workforce, with attention to onboarding, supervision, accommodation, career advancement, and retention.

Lead agencies: ED, DOL, OPM.

Supporting agencies: ACL, SSA, ED/RSA, CMS.

Initiative 5: Technology, Coaching, Burnout Prevention, and Employment Quality

DOL, ED, NIH, SAMHSA, HRSA, ACL, and AHRQ should evaluate technology-enabled and human-supported employment tools that improve real-world work participation. These may include digital coaching, scheduling supports, task-management tools, communication supports, job-coaching platforms, AI-assisted organization tools, transportation coordination, and remote support when appropriate.

The evidence agenda should also address burnout, mental health, workplace trauma, job cycling, underemployment, and loss of employment after initially successful placement. Employment quality matters. Federal programs should measure whether the job is sustainable, whether supports are usable, whether the person can communicate needs, whether work improves or destabilizes health, and whether advancement is possible when desired.

Lead agencies: DOL, ED, NIH, SAMHSA, AHRQ.

Supporting agencies: HRSA, ACL, CMS.

Agency	Priority actions
DOL / ODEP	Lead autism employment agenda, employer guidance, demonstrations, accommodation dissemination, apprenticeship alignment, and workplace-practice modernization.
ED / RSA	Modernize vocational rehabilitation guidance, transition pathways, postsecondary-to-work supports, and VR access for autistic people across support profiles.
ACL	Coordinate supported employment, DD Act networks, day-to-work pathways, and community participation supports.
CMS	Clarify HCBS-supported employment, care coordination, transportation, and quality-measure options within existing authority.
EEOC	Support accommodation, non-discrimination, disclosure, hiring, retention, and workplace-rights guidance.

Agency	Priority actions
OPM	Develop federal hiring, onboarding, accommodation, retention, and advancement pilots.
JAN	Disseminate practical accommodation tools for autistic workers, managers, and HR offices.
SSA	Support benefits counseling, work incentives, and plain-language employment-related benefits guidance.
NIH / AHRQ / SAMHSA	Support research, evidence review, burnout prevention, mental-health considerations, and employment-quality measures.
HRSA	Integrate employment-related navigation and interdisciplinary training into relevant autism workforce programs.

Agency Actions

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish a federal employment action agenda, workplace-accommodation and retention toolkit, vocational-rehabilitation modernization guidance, and a federal-hiring pilot design.	DOL, ED, and OPM	ACL; EEOC; JAN; CMS
18–24 months	Establish comparable employment-quality, retention, accommodation, supported-employment, benefits-counseling,	DOL	ED; ACL; CMS; OPM; EEOC

Phase	Consolidated federal product	Accountable lead	Supporting partners
	transition, and preventable-job-loss measures.		
24–36 months	Launch supported and customized employment, postsecondary-to-work, apprenticeship, federal-hiring, coaching, technology-support, and burnout-prevention demonstrations across functional profiles.	DOL and ED	ACL; CMS; OPM; EEOC; NIH; AHRQ
3–5 years	Report job entry, retention, advancement, hours and earnings, accommodation implementation, health stability, supported-employment access, transition outcomes, and preventable job loss.	DOL	ED; ACL; CMS; OPM; EEOC

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Employment retention at 6, 12, and 24 months, with job quality, hours, earnings, advancement, and support intensity reported.
- Percentage receiving needed vocational rehabilitation, supported employment, benefits counseling, technology, coaching, or workplace accommodation.
- Percentage of transition plans producing a completed connection to vocational rehabilitation, workforce, postsecondary, or supported-employment systems.
- Reduction in unresolved accommodation failures, preventable job loss, job cycling, health destabilization, and exclusion of people with high support or communication needs.

Implementation Standards

- Employment policy should include autistic people across support levels and should not reserve workforce strategy only for those who can navigate competitive work without support.
- Supported employment, customized employment, and day-to-work pathways should be preserved while accommodation and retention supports are expanded for competitive and professional employment.
- Job placement alone is insufficient. Federal reporting should measure retention, advancement, accommodation implementation, job quality, health stability, and preventable job loss.

- Employment supports should coordinate with housing, caregiver supports, transition planning, communication access, motor access, mental health, and benefits counseling so that work support is connected to the services that make sustained participation possible.
- Autistic workers should be involved in program design and evaluation, including individuals with high support needs, communication differences, executive-function challenges, sensory needs, and lived experience of workplace failure or burnout.

Translational Readiness Assessment

Transition planning, vocational rehabilitation access, supported employment, accommodation guidance, federal hiring, employer training, and retention supports can all be improved now through coordination, guidance, demonstration, and measurement.

The evidence-building task is to learn which employment models work for which profiles. Federal partners should measure whether supported employment, accommodations, technology tools, job coaching, flexible work, employer training, and transition supports improve not only job entry, but retention, advancement, participation, health stability, and quality of life.

Life Course Domain VIII: Older Autistic Adults, Aging, and Later-Life Health

Strategic Objective

Ensure that autistic adults entering middle and older age have access to aging services, adult and geriatric health care, Medicare-covered preventive care, dementia and cognitive-change recognition, long-term services and supports, communication access, supported decision-making, safety protections, palliative care, and research that reflects how autism and co-occurring conditions affect later life.

The life course does not end at transition. Federal autism policy has historically concentrated on children, diagnosis, school services, and early intervention, while the first large cohorts identified under broader diagnostic criteria are now moving into middle and older age. Many older adults with autism were never diagnosed in childhood. Others have lived for decades with autism, intellectual disability, epilepsy, motor differences, psychiatric conditions, sensory needs, communication barriers, or complex medical histories that adult and geriatric systems are not prepared to recognize.

Later-life autism policy should start from a simple premise: aging does not erase autism, and autism does not remove the ordinary rights and needs of aging. The federal task is to make the aging system competent to receive autistic adults, to make adult and geriatric medicine competent to recognize baseline and change, and to build evidence about health, cognition, function, service needs, mortality, and quality of life across the aging window.

Statement of Need

Older autistic adults sit at the intersection of systems that often do not communicate. Autism systems may age out at school exit or young adulthood. Aging systems may not recognize autism, intellectual disability, sensory needs, communication differences, supported decision-making, or lifelong functional profiles. Medicare may become the primary health coverage for some people while Medicaid remains central for long-term services and supports. Families may still be providing daily care into the caregiver's own older age, even as the autistic adult also begins to experience age-related medical, cognitive, functional, or residential change.

The clinical problem is equally practical. A later-life change in behavior, sleep, gait, seizure pattern, mood, communication, self-care, pain expression, continence, medication tolerance, or daily function may be mislabeled as "just autism" unless clinicians have a baseline and know how change presents in autistic individuals and I/DD populations. Decline can be missed, and ordinary aging care can also be inaccessible when visits are not adapted for communication, sensory, motor, cognitive, or support needs.

A credible federal aging strategy should therefore connect five bodies of work: aging-network navigation; geriatric and adult-medicine competence; Medicare preventive care and cognitive-change recognition; research and surveillance; and later-life protections, supported decision-making, and palliative care.

Housing, caregiver supports, employment, communication access, and mental health remain necessary supports, but the aging section should carry the later-life health and aging-system architecture.

Core Objectives

- Make older autistic adults and autistic adults entering middle age a named federal life course priority.
- Integrate autism and I/DD competence into the federal aging network, including ADRC, No Wrong Door, Area Agency on Aging, and Older Americans Act infrastructure.
- Build an adult and geriatric workforce capable of receiving autistic adults from pediatric, developmental, neurology, psychiatry, primary-care, and disability-service systems.
- Adapt Medicare preventive care, cognitive-assessment pathways, dementia detection, medication review, and health-maintenance planning for autistic and I/DD beneficiaries.
- Establish a federal aging-in-autism research and surveillance agenda that includes cognition, dementia, cardiometabolic health, epilepsy, bone health, pain, sleep, reproductive and midlife health, cancer screening, palliative care, mortality, and quality of life.
- Protect older autistic adults from diagnostic overshadowing, neglect, exploitation, abuse, avoidable institutionalization, loss of autonomy, and exclusion from aging research and services.

Priority Federal Implementation Agenda

This agenda begins at 12 months because integrating autism and I/DD into the federal aging network relies on existing ACL, CMS, HRSA, and aging-network infrastructure that is already actionable.

Initiative 1: Autism and I/DD Integration into the Federal Aging Network

ACL, with CMS, HRSA, State Units on Aging, Area Agencies on Aging, ADRCs, No Wrong Door systems, DD Act networks, and Centers for Independent Living, should integrate autism and I/DD into the federal aging network. Existing aging access points should become usable for older autistic adults and families, rather than leaving them to rebuild navigation at each later-life transition.

This initiative should create an autism and I/DD aging line within federal aging infrastructure. ADRCs, No Wrong Door systems, and Area Agencies on Aging should be able to recognize autism and/or I/DD, connect people to benefits and long-term services and supports, make referrals to autism-competent health and community providers, identify caregiver-succession risk, and support future planning without defaulting to guardianship or crisis placement.

Lead agencies: ACL, CMS.

Supporting agencies: HRSA, HHS, DD Act networks, State Units on Aging, Area Agencies on Aging.

Initiative 2: Adult and Geriatric Workforce Competence for Neurodivergent Aging

HRSA, with CMS, ACL, NIH, LEND programs, Developmental-Behavioral Pediatrics networks, primary-care training programs, neurology, psychiatry, and the Geriatrics Workforce Enhancement Program, should

build adult and geriatric workforce competence for neurodivergent aging. Too many autistic adults remain attached to pediatric or developmental clinicians because adult systems have no clear destination prepared to receive them.

The workforce agenda should define what adult and geriatric clinicians need to know: autism across the life course; intellectual and developmental disability; communication access; sensory accommodations; motor and praxis differences; epilepsy; polypharmacy; mental health; pain recognition; sleep; autonomic and gastrointestinal issues; behavior change as possible medical signal; supported decision-making; caregiver participation with consent; and transition from pediatric to adult and geriatric care.

Lead agencies: HRSA, CMS.

Supporting agencies: ACL, NIH, AHRQ, SAMHSA, professional societies.

Initiative 3: Medicare Preventive Care, Cognitive-Change Detection, and Health Maintenance

CMS, with NIH/NIA, ACL, HRSA, AHRQ, and clinical partners, should adapt Medicare preventive-care and cognitive-assessment pathways so that autistic individuals and I/DD beneficiaries have a usable later-life health baseline. A baseline is not paperwork. It is the reference point that lets clinicians distinguish lifelong traits from new change.

The adapted approach should include functional baseline, communication method, sensory and motor access needs, decision-support preferences, usual behavior and daily function, seizure and sleep history, medication and antipsychotic review, pain and gastrointestinal review, fall and mobility risk, nutrition, dental and vision access, cancer screening, cardiometabolic risk, bone health, reproductive and midlife health where relevant, caregiver or supporter input with consent, and referral triggers when change is observed.

CMS should also support a population-appropriate dementia and cognitive-change pathway for autistic individuals and I/DD beneficiaries. The pathway should recognize that many standard cognitive instruments were not designed for people with lifelong communication, intellectual, motor, or adaptive differences. Screening should therefore emphasize change from the person’s own baseline, collateral observation when appropriate, functional change, medical rule-outs, medication effects, seizures, sleep disruption, depression, pain, sensory change, and environmental destabilization before attributing decline to dementia or autism.

Lead agencies: CMS, NIH/NIA.

Supporting agencies: ACL, HRSA, AHRQ, SAMHSA.

Initiative 4: Aging-in-Autism Research, Surveillance, and Evidence Infrastructure

NIH, with NIA as lead institute and NIMH, NICHD, NINDS, CDC, AHRQ, ACL, and CMS as partners, should establish an Aging-in-Autism Research Initiative. The scientific question is not settled. Autistic adults may show different aging trajectories depending on intellectual disability, epilepsy, co-occurring medical

conditions, sex, genetics, environmental exposures, health care access, social isolation, medication burden, and support history. Federal research should be designed to answer those questions rather than assume a single trajectory.

The research agenda should support prospective longitudinal cohorts beginning in midlife, harmonized functional and cognitive measures, health-system data linkage, Medicare and Medicaid analyses, brain-tissue and biospecimen infrastructure with older-adult metadata, and inclusion of nonspeaking, minimally speaking, intellectually disabled, high-support-needs, rural, racially and ethnically diverse, and late-diagnosed adults. It should include outcomes that matter in later life: cognitive change, dementia, pain, sleep, epilepsy, cardiometabolic disease, bone health, cancer screening, medication burden, mobility, falls, mental health, loneliness, abuse risk, residential transitions, palliative care, mortality, participation, and quality of life.

Lead agencies: NIH/NIA.

Supporting agencies: NIMH, NICHD, NINDS, CDC, AHRQ, ACL, CMS.

Initiative 5: Later-Life Safety, Supported Decision-Making, Palliative Care, and End-of-Life Access

ACL, CMS, DOJ, HRSA, SAMHSA, and HHS should ensure that older autistic adults are included in later-life safety, rights, decision-support, abuse-prevention, and palliative-care planning. Autistic adults with communication differences, intellectual disability, isolation, dependence on paid or family caregivers, psychiatric comorbidity, cognitive change, or complex medical needs may be at heightened risk of being misunderstood, ignored, over-controlled, under-treated, or moved into restrictive settings without adequate planning.

Federal guidance should support abuse and exploitation recognition, communication-accessible reporting, supported decision-making, advance-care planning, health-care proxies where appropriate, palliative-care and hospice access, grief and bereavement support, and end-of-life care adapted to sensory, communication, cognitive, motor, and relational needs. The goal is not to medicalize aging. The goal is to make ordinary later-life rights and services real for autistic people.

Lead agencies: ACL, CMS, DOJ.

Supporting agencies: HRSA, SAMHSA, HHS, state protection and advocacy systems.

Agency	Priority actions
ACL	Lead aging-network integration, ADRC/No Wrong Door coordination, Older Americans Act alignment, DD Act network connection, supported decision-making, elder-justice linkage, and aging-caregiver navigation.

Agency	Priority actions
CMS	Adapt Medicare preventive-care and cognitive-assessment pathways, coordinate Medicare/Medicaid interface, support LTSS access, clarify payment and quality pathways, and test adapted care models.
HRSA	Lead adult and geriatric workforce training, GWEP integration, LEND and continuing-education alignment, and transition-of-care standards.
NIH / NIA	Lead aging-in-autism research, longitudinal cohorts, cognitive aging, dementia, health trajectories, brain-tissue infrastructure, and biomarker/data standards for older adults.
NIMH / NICHD / NINDS	Support research on mental health, developmental trajectory, epilepsy, neurobiology, cognition, and co-occurring neurological conditions in aging autistic adults.
CDC	Evaluate options for adult and older-adult surveillance and health-system data linkage.
AHRQ	Support evidence reviews, quality measures, care-model evaluation, and patient-safety research for older autistic adults.
DOJ	Support disability-rights, Olmstead, elder-justice, abuse, neglect, exploitation, and communication-access protections.
SAMHSA	Address older-adult mental health, crisis, suicide prevention, substance use, trauma, and continuity of behavioral health care.
State Units on Aging /	Implement aging-network navigation, cross-training, referral, options

Agency	Priority actions
Area Agencies on Aging / ADRCs	counseling, future planning, and LTSS access support.

Agency Actions

Consolidated Federal Implementation Compact

The compact below is the accountable federal workplan for this area. More detailed initiative language remains as the scientific and operational rationale; it should not be read as creating additional stand-alone national deliverables.

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Publish autism and I/DD aging-navigation materials and adapted Annual Wellness Visit, baseline-function, medication-review, cognitive-change, dementia-referral, communication, and decision-support workflows.	ACL and CMS	HRSA; NIH; DOJ
18–24 months	Integrate autism and I/DD competence into existing geriatric and aging-network training and establish inclusive later-life research measures and recruitment standards.	HRSA, ACL, and NIH	CMS; aging and DD networks
24–36 months	Launch aging-in-autism research and care-model studies addressing multimorbidity, medication risk, cognition, mobility, seizures, sleep, pain, caregiver aging, residential transition, palliative care, and mortality.	NIH and CMS	ACL; HRSA; DOJ
3–5 years	Report aging-network adoption, preventive-care access, time to evaluation of change, treatable contributors, care continuity, safety, supported decision-making, quality of life, and later-life outcomes.	ACL, CMS, and NIH	HRSA; DOJ; state aging networks

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Percentage of aging-network and clinical sites using autism-competent navigation, preventive-care, medication-review, and cognitive-change workflows.
- Percentage of older autistic adults with documented baseline function, communication method, health risks, and decision-support preferences.
- Time from observed cognitive, behavioral, functional, mobility, sleep, seizure, mood, pain, or self-care change to appropriate evaluation and covered follow-up.
- Reduction in missed treatable contributors and preventable health or residential destabilization, with quality of life, autonomy, safety, and caregiver continuity reported.

Implementation Standards

- Older autistic adults should be included across support levels, communication profiles, cognitive profiles, residential settings, and diagnostic histories.
- Aging policy should measure change from the person's own baseline rather than assuming that new decline, distress, pain, medication toxicity, seizure activity, sleep disruption, or functional loss is part of autism.
- Medicare, Medicaid, aging services, disability services, and health-care systems should coordinate around the person rather than forcing families to reconstruct the system at every transition.
- Later-life services should protect autonomy, communication access, supported decision-making, safety, dignity, and continuity of care.
- Autistic older adults, including people with intellectual disability and complex communication needs, should be included in design, evaluation, governance, and outcome review.

Translational Readiness Assessment

Integrating autistic adults into the aging network, training geriatric clinicians, adapting preventive-care workflows, documenting baseline function, and protecting later-life rights can proceed now, before every question about autism and aging is resolved.

The research agenda is substantial: to define aging trajectories, risk profiles, protective factors, treatable contributors, and care models with enough precision to guide Medicare, Medicaid, geriatric practice, autism services, and aging policy. The organizing implementation goal is to stop treating older autistic adults as an exception that no system owns.

Life Course Domain IX: Transportation, Mobility, and Access

Strategic Objective

Ensure that autistic people across the full range of support needs can reliably reach health care, education, employment, day programming, housing, family and relationships, recreation, and community life through transportation that is safe, affordable, predictable, accessible, and matched to individual needs.

Transportation is the connective infrastructure that determines whether housing, health care, employment, day services, and community participation are available in practice. The governing principle should be to reduce unnecessary travel created by fragmented services while preserving the supported mobility required for individual choice and meaningful community access. Accordingly, this domain functions both as a distinct life course priority and as a cross-cutting implementation dependency for housing, health care, education, employment, HCBS, caregiver supports, and community participation; those domains should incorporate transportation access into their planning and outcome measures.

Statement of Need

Transportation barriers can make otherwise available services, supports, housing, employment, and community activities inaccessible in practice. Autistic people may encounter barriers involving availability, cost, rural distance, sensory demands, communication, motor planning, executive functioning, unpredictable service, and lack of trained accompaniment. People with profound autism or complex medical and safety needs may require door-through-door assistance, communication support, familiar drivers, medical preparedness, elopement safeguards, or continuous supervision.

Autism-specific transportation research remains limited and is concentrated primarily on driving, public transportation, and relatively independent community mobility. National data do not adequately represent autistic people living in supported settings or those requiring substantial assistance. Federal implementation should therefore proceed through existing transportation and disability authorities while building practical evidence about which models provide safe, reliable access across support needs.

Core Objectives

- Make transportation an operational component of HCBS, health, employment, transition, and day-service planning.
- Build and test a continuum of independent and supported transportation matched to individual needs.
- Measure completed access to chosen destinations, safety, reliability, caregiver burden, and quality of life rather than the existence of a transportation benefit or referral.

Priority Federal Implementation Agenda

This agenda uses CCAM as the federal coordinating mechanism, including its existing program inventory and fund-braiding guidance, and begins with authorities already available to DOT/FTA, ACL, CMS, DOL, and ED.

Initiative 1: Transportation in HCBS, Health, Employment, and Service Planning

CMS, ACL, HRSA, DOL, and ED should make transportation explicit in person-centered service, health and discharge, employment, transition, and day-service planning. Plans should specify chosen destinations, accompaniment, evening and weekend access, rural and backup needs, and whether trips are completed. CMS should incorporate unmet trips, reliability, missed care or work, beneficiary experience, and caregiver burden into HCBS quality oversight.

Federal guidance should apply a “reduce compulsory travel, preserve community access” standard so that fragmented systems do not impose avoidable travel while individuals retain reliable access to the broader community.

Lead agencies: CMS and ACL, coordinated with DOT/FTA through CCAM.

Supporting agencies: HRSA, DOL/ODEP, ED, DOJ, and SSA.

Initiative 2: Autism-Inclusive Mobility and Supported-Transportation Demonstrations

FTA and ACL, working with CMS and other CCAM partners, should issue autism-inclusive guidance and test models across support levels and geographic settings. Guidance should address driver assessment and travel training; booking and disruption information; telephone and digital access; mobility management; demand-responsive and door-through-door service; trained accompaniment; sensory and communication support; and medical and elopement safeguards.

Demonstrations and data collection should meaningfully include people with profound autism, intellectual disability, minimal or no functional speech, complex medical needs, continuous-supervision requirements, and people living in supported settings. Success should be measured by safe, reliable access to chosen destinations with the support required—not by withdrawal of support.

Lead agencies: DOT/FTA and ACL.

Supporting agencies: CMS, ACL/NIDILRR, HRSA, DOL, ED, CDC, BTS, and the U.S. Access Board.

Agency	Priority actions
DOT / FTA and ACL	Coordinate through CCAM; issue implementation guidance; support accessible and supported-mobility demonstrations.
CMS	Integrate operational transportation access into person-centered planning,

Agency	Priority actions
	HCBS quality oversight, and community-access expectations.
DOL and ED	Connect transportation to employment, vocational rehabilitation, school transition, postsecondary access, and day-to-work pathways.
ACL/NIDILRR and BTS	Evaluate models and build common autism-inclusive mobility data, including people in supported settings and those requiring substantial assistance.

Agency Actions

Consolidated Federal Implementation Compact

Phase	Consolidated federal product	Accountable lead	Supporting partners
12–18 months	Issue coordinated transportation and HCBS quality guidance for health, employment, transition, and day-service planning, including the “reduce compulsory travel, preserve community access” standard.	CMS, ACL, and FTA	HRSA; DOL; ED; DOJ
18–36 months	Launch autism-inclusive mobility and supported-transportation demonstrations across support levels and urban, suburban, and rural settings.	FTA and ACL	CMS; ACL/NIDILRR; FTA; HRSA
3–5 years	Report access, reliability, safety, missed services, compulsory travel, caregiver burden, and high-support outcomes.	FTA and ACL	CMS; BTS; DOL; ED; CDC

Executive Performance Indicators

These four measures constitute the executive accountability set. Technical measures may be retained in agency workplans as secondary indicators.

- Percentage of autistic people with an individualized mobility assessment and an operational transportation plan.
- Percentage able to reach health care, housing, employment or day activity, education, family, recreation, shopping, and other chosen destinations on the schedule required.
- Reduction in unmet, late, canceled, excessively long, or unsafe trips; missed care and work; and compulsory travel created by fragmented services.

- Availability and reliability of trained accompaniment, communication support, sensory accommodations, backup transportation, and door-through-door service for people with high support needs.

Implementation Standards

Transportation access should be measured by completed access to chosen destinations, not by the existence of a benefit, referral, route, vehicle, or service plan.

- Independent travel should not be the sole measure of success. Supported mobility, including continuous accompaniment when required, is a valid community-living support.
- Shared transportation should expand capacity without limiting individual scheduling or destination choice. Technology should protect privacy and supplement rather than displace necessary human support.

Translational Readiness Assessment

Implementation can begin now through existing federal coordination, person-centered planning, mobility-management funding, and demonstration authority. Evidence building should determine which independent and supported models work across support profiles and settings and establish common measures linking transportation to access, safety, participation, caregiver burden, public cost, and quality of life.

Part VI — Federal Accountability, Implementation Oversight, and Strategic Plan Updates

Part I of this Plan committed to a concluding accountability framework, a defined account of how implementation should be monitored, how progress should be evaluated, how agencies should coordinate, how public reporting should occur, and how future updates should distinguish recommendations that are completed, in progress, in need of modification, or not yet advanced. Part VI supplies that framework. It does not restate the scientific, therapeutic, or lifespan content of Parts II through V. Instead it defines the governance, register, status taxonomy, prioritization logic, reporting cadence, outcome discipline, budgetary posture, data-governance gates, and update mechanism that allow the recommendations of the preceding Parts to be tracked, evaluated, and revised as a single coordinated body of work rather than as separate and uncontrolled activities.

Purpose and Legal Posture

This chapter implements the accountability design described in Part I, and it does not enlarge the statutory authority of the Interagency Autism Coordinating Committee. Under its authorizing statute the Committee monitors federal autism activities, convenes federal and nonfederal participants, evaluates progress, advises the Secretary of Health and Human Services, recommends coordinated action, and reports. Each mechanism established below operates within that monitoring, evaluation, and recommendation function, and nothing in Part VI should be read as authorizing the Committee to direct, compel, or supervise the operations of other departments and agencies, to obligate funds, or to create obligations enforceable against any agency.

The distinction between recommendation and decision governs the entire chapter. The Committee identifies problems, assesses jurisdiction and capacity, proposes deliverables, and specifies how progress can be measured, while the Secretary and the authorized departments and agencies decide whether and how to act within their own statutory authority and subject to available appropriations. Where this Plan names a lead or supporting agency, that designation reflects the Committee’s assessment of which agency is best positioned by jurisdiction and capacity to carry the action forward, and it is not evidence that the named agency has concurred, has been consulted, or has committed resources, unless that concurrence is separately documented through the agency’s own processes. A recommendation does not become binding because it identifies an agency, cites an authority, proposes a deliverable, or sets a target date, and federal agency representatives serving as Committee members do not make a binding decision on behalf of their agencies by voting to advance a recommendation to the Secretary or an agency head.

A parallel distinction governs state and local outcomes. Many of the improvements this Plan seeks depend on adoption by states, territories, tribes, health systems, schools, and other entities the federal government does not direct, and where this framework measures state adoption or system uptake, those measures are diffusion indicators. They describe the spread of a federally supported practice, they can be encouraged, supported, and reported, and their absence is not a federal failure to perform. This governing clause controls the interpretation of every state-adoption, agency-reporting, and attestation reference elsewhere in this Plan. Where earlier Parts use directive verbs such as "require annual reporting," those references should be read as recommendations that the Secretary or responsible agency establish reporting within its own authority, and where earlier Parts refer to agency "attestations," those references mean self-reported administrative status statements rather than reporting the Committee itself imposes or legal certifications creating independent liability.

Governance and Foundational Dependencies

The accountability architecture described in this Plan depends on coordinating capacity that does not yet exist in the form the architecture assumes. The Plan refers throughout to a Secretary-designated National Autism Coordinator as the convener of cross-agency reporting, the sponsor of the National Autism Precision Therapeutics Initiative, and the steward of the public Autism.gov dashboard. That coordinating role already exists under federal law, but the expanded governance model proposed here, including placement at or through the HHS Office of the Secretary, dedicated staffing, delegated reporting responsibilities, and stewardship of the Autism.gov platform, remains contingent on Secretarial action, available resources, and interagency participation. Until those elements are established, the expanded role should be understood as a recommended governance structure rather than as an operating office, and the reporting functions that depend on it should be described as contingent.

The most consequential of these dependencies is organizational placement. For a coordinating role to compile and publish status information drawn from peer agencies of equal or greater standing, it must sit at a level of the Department from which such coordination is credible, and this Plan therefore recommends placement of the Coordinator at, or a reporting line through, the HHS Office of the Secretary. That placement is a foundational dependency recommended by the Plan rather than an accomplished fact, no statement in Parts II through V should be read as asserting that the relocation has occurred, and every description of the Coordinator convening agencies or obtaining status information assumes that this dependency has first been satisfied.

Even once established, the Coordinator's function remains coordinative rather than directive, in keeping with the recommendation-and-not-decision principle set out above. The Coordinator may request, coordinate, compile, and publish agency status information, and may convene agencies to align schedules, definitions, and reporting formats, but cannot compel a peer agency to act, to report, or to adopt a position absent authority delegated by the Secretary or conferred by statute. That limit is the legal reality within which the framework operates, and the framework is built to produce useful transparency through voluntary, jurisdiction-respecting coordination rather than through compulsion it does not possess.

The relationships among the principal actors follow from these limits. The Coordinator, supported by assigned staff, serves as the compiling and publishing point for whole-of-plan status information and supports the Committee's monitoring, evaluation, and recommendation functions. The National Autism

Precision Therapeutics Initiative and the operating agencies generate the underlying implementation activity and supply status information within their own authorities, Autism.gov is the public interface through which that information is displayed, the Office of Management and Budget exercises its established role in budget formulation, cost review, and clearance, and Congress exercises its appropriations and oversight authority. Part VI creates no new statutory office and transfers no agency's authority to the Coordinator; it defines how existing and recommended roles relate so that the Plan can be tracked coherently.

Whole-of-Plan Implementation Register

The scale of this Plan, encompassing its therapeutic domains, lifespan domains, and infrastructure initiatives across several dozen major recommendations, creates a specific accountability risk. Each domain may be tracked through its own separate dashboard, those dashboards may use inconsistent definitions and update on inconsistent schedules, and no single view may allow the Secretary, OMB, Congress, or the public to see the whole. The Plan has already warned that a dashboard tracking everything ends up tracking nothing, and the federal consequence is that accountability requires consolidation rather than proliferation. This framework therefore recommends one consolidated whole-of-plan implementation register covering every major recommendation across Parts II through V, in place of a set of independently maintained and uncontrolled dashboards.

The register is a controlled record. For each major recommendation it should capture, at minimum, a unique identifier, the Plan Part and domain in which the recommendation originates, the evidence stage of the underlying science or practice, the implementation-burden tier, the lead and supporting agencies as assessed by the Committee, the relevant statutory or regulatory authority where applicable, the category of federal action, the anticipated federal deliverable, the dependencies that must be resolved before the deliverable can proceed, the budgetary requirement and its funding posture, the baseline status of the associated measure, the key performance indicator or outcome measure, the target date, the current status expressed in the taxonomy defined below, the principal barrier or risk, the next action, and the next reporting date. Capturing these fields uniformly is what allows recommendations from different domains to be compared, sequenced, and reported with the same discipline.

The public Autism.gov implementation dashboard is the outward-facing view of this single register rather than a separate reporting system maintained on its own terms. The dashboard displays a curated, plain-language, accessible subset of the register suitable for public use, while the register itself remains the authoritative internal record from which the dashboard is generated. Maintaining this relationship prevents divergence between what agencies report internally and what the public sees, and it ensures that the accountability apparatus has one owner, one definition set, and one update cycle.

Status Taxonomy

A register is only as useful as the consistency of its status language, and this framework therefore defines a single set of status categories to be applied uniformly across every recommendation, so that "in progress" carries the same meaning in a therapeutic domain that it carries in a lifespan domain. The categories are as follows.

Not initiated: no federal action has begun.

Dependency unresolved: a foundational dependency, such as Coordinator placement, a data-governance approval, or an appropriation, must be resolved before the action can proceed.

Planning or design: the responsible agency is scoping, designing, or specifying the action.

Funded or solicited: funding has been identified or a solicitation has been issued.

In progress: the action is actively underway.

Implemented or operational: the federal deliverable exists or the federal action has occurred and is in ongoing operation.

Completed: the defined action is finished and no further federal activity is planned within this cycle.

Modified or superseded: the recommendation has been changed or replaced in light of new evidence or circumstances.

Deferred: the recommendation remains valid but has been postponed, with a stated reason.

Closed or no further action: the recommendation is retired, with a stated reason.

One distinction within this taxonomy is essential to the integrity of the whole framework. “Implemented” means that the federal deliverable exists or the federal action occurred, and it does not mean that the intended outcome has improved. Activity completion and outcome improvement are separate facts, reported separately: a guidance document issued, a solicitation released, or a dashboard launched is an implementation event, whereas whether autistic individuals and families experienced better access, function, stabilization, or safety as a result is an outcome question answered through the outcome measures defined below. Treating activity as evidence of outcome is the specific failure this taxonomy is designed to prevent.

Prioritization and Sequencing

Because each domain in this Plan sequences its own initiatives, the Plan as a whole can appear to treat nearly every recommendation as simultaneously first in line, which is not sequencing but rather the absence of whole-of-plan sequencing expressed in the language of sequencing. The federal consequence is that the Plan needs prioritization criteria operating across domains and not only within them. This framework establishes the following whole-of-plan criteria for relative prioritization: urgency and safety, population reach and unmet need, evidence maturity, existing authority, implementation burden, dependency readiness, data readiness, budgetary requirement, and expected measurable benefit. These criteria are applied to rank recommendations relative to one another, so that the register supports comparison across Parts rather than a collection of independent claims to priority.

Applying these criteria yields a defined near-term priority set, a limited group of recommendations identified for action in the current cycle and distinguished from the larger body of recommendations that remain valid but are sequenced for later phases. Identifying a near-term set does not deprioritize the remainder, and it makes the Plan usable for budgeting and oversight by naming what is to be pursued first and why. The near-term set should favor recommendations that rest on existing authority, address urgent safety needs, reach large or underserved populations, carry resolved dependencies and ready baselines, and can demonstrate measurable benefit within the cycle.

Two analytic frames already present in the Plan should be applied across all of Parts II through V rather than only where they were first introduced. The discovery-translation-implementation frame, which describes evidence maturity, and the Tier 1, Tier 2, and Tier 3 implementation-burden frame, which describes what a deliverable actually costs an agency in effort and capacity, should both be assigned to every major recommendation, including those in the National Autism Precision Therapeutics Initiative and the therapeutic domains, and not only to the lifespan domains where the burden tiers were first defined. Applying both frames uniformly is a labeling exercise using the register fields defined above, and it is what allows a reviewer to distinguish a low-burden action resting on existing authority from a high-burden action that requires new capacity.

The framework also separates recommendations by their funding and authority posture into three groups: actions that can proceed under existing authority and within current resources, actions that are appropriation-dependent and cannot proceed without new funds, and actions that require new statutory authority or new institutional capacity before they can begin. This separation prevents the Plan from presenting an appropriation-dependent or authority-dependent action as though it were ready to execute, and it aligns the prioritization criteria above with the budgetary discipline defined later in this chapter.

Reporting Cadence and Autism CARES Act Alignment

The reporting rhythm of this framework is aligned with the statutory expectations of the Autism CARES Act of 2024, enacted as Pub. L. No. 118-180, which reauthorizes the Committee and related programs through September 30, 2029 (see IACC, Autism CARES Act of 2024). Consistent with 42 U.S.C. § 280i-2(b)(6), the framework contemplates an annual update to the Summary of Advances and a biennial update to the Strategic Plan that reports progress toward its goals and the specific measures taken, and these annual and biennial products are the primary public reporting cycle for the whole-of-plan register. Quarterly operational updates are reserved for a limited set of active milestones, namely the recommendations in the near-term priority set that are actively in progress, rather than applied to every recommendation. Updating every recommendation quarterly would recreate the tracks-everything, tracks-nothing failure the register is meant to avoid and would impose a reporting burden disproportionate to its value for recommendations that are dependency-unresolved, deferred, or in early planning, so the quarterly cycle exists to keep genuinely active work visible between the annual and biennial products.

The framework also specifies the mechanics of compilation. Once established with the placement and resources described above, the National Autism Coordinator compiles the register and publishes the dashboard, each reporting product carries a stated data cutoff date so that readers know the period it describes, and compiled submissions are subject to basic quality checks for completeness, internal consistency, and correct use of the status taxonomy before publication. Where an agency does not submit a status update, or where a state does not contribute data, the missing information is shown as missing rather than inferred or silently omitted, and the reason is noted where known, because transparent treatment of missing data is itself an accountability feature.

Annual agency status submissions are administrative status statements, self-reported implementation updates that an agency provides on its own activities within its own authority. They are not legally binding certifications, and they should not be described using terms that imply a certification standard or

independent liability unless an agency separately establishes such a process under its own authority, consistent with the governing clause in the Purpose and Legal Posture section.

Autism.gov would also give NIH a practical way to carry out an obligation Congress has already assigned. Section 409C(d) of the Public Health Service Act requires the Director of NIH to provide a means for the public to learn about existing and planned NIH autism programs and activities and to submit comments about them, and Autism.gov would not create this obligation but would make it visible, accessible, and usable (42 U.S.C. § 284g(d)). The NIH portion of the portal should therefore provide current information about existing and planned autism activities, research participation opportunities, funding initiatives, and major program decisions, together with a clearly identified way for the public to provide input directly to NIH. That process should be accessible to speaking and nonspeaking autistic individuals, people who use augmentative and alternative communication, families, caregivers, providers, and individuals representing the full range of co-occurring conditions and support needs. The statutory responsibility remains with the Director of NIH, since a shared federal platform does not transfer NIH's responsibility for the accuracy of its information, its receipt and management of public comments, its privacy protections, or its records retention, and although Autism.gov can extend the same model of transparency and public engagement to other participating agencies, that broader role is a recommendation of this Plan while NIH's responsibility is already established in law.

Outcome and Baseline Discipline

Several of the Plan's performance indicators presuppose baselines that do not yet exist, among them a national measure of autism prevalence among adults, national baselines for missed special-education services, and workforce projections by discipline. An indicator that assumes a baseline the federal government has not established cannot report change against that baseline until the baseline exists, and the framework therefore requires that every key performance indicator be tagged by its measurement readiness as one of three states: baseline established, meaning trend reporting can begin now; baseline development required, meaning a defined baseline-establishment step must be completed before change can be reported; or not currently measurable, meaning the data the indicator would require are not collected by any existing federal system. Tagging indicators this way allows a reviewer to see at a glance which numbers are trend-ready and which remain aspirational pending a separate measurement step.

The framework also distinguishes among the kinds of things an indicator can measure, because conflating them overstates progress. Activity measures count federal actions taken, output measures count products produced, access measures capture whether individuals can reach a service or protection, stabilization or outcome measures capture whether health, function, communication, safety, or independence actually changed, and diffusion measures capture adoption by states and other non-federal entities. Each measure is labeled by type in the register, so that an increase in activity is not read as an improvement in outcome and diffusion is scored as adoption rather than as a federal deliverable. Where a Recognition, Access, and Stabilization structure is appropriate, capturing whether a condition is recognized, whether the individual can access appropriate evaluation and care, and whether the person's status stabilizes or improves against their own baseline, it should be used, because it ties measurement to the sequence in which care actually helps a person. That structure should not be forced onto discovery research, where the appropriate measures are scientific progress and translational readiness rather than clinical stabilization, since applying

clinically framed metrics to early-stage discovery would misrepresent both the science and the accountability picture.

Every reported measure should be accompanied by the information needed to interpret it: a brief methods note, the denominator on which a rate is calculated, the principal limitations, the recency of the underlying data, and disaggregation by relevant subgroups where the data permit and where small-cell disclosure risks are controlled. Measures reported without denominators, methods, or limitations invite misinterpretation and undermine the credibility of the accountability framework as a whole.

Budget and Appropriations Accountability

The Plan contains many dollar figures, most of them order-of-magnitude planning ranges rather than formal cost estimates. The Autism CARES Act of 2024 reauthorized specified autism programs at fixed annual authorization levels through FY 2029, and those authorizations are neither appropriations nor a source of funding for the additional initiatives proposed in this Plan, so budgetary accountability begins with classification. Each recommendation with a resource implication is assigned to one of four categories: actions that can be carried out within the current baseline, actions that are reallocation or administrative in nature and shift or repurpose existing resources, actions that require new appropriations, and actions that are contingent on new statutory authority. This classification is recorded in the register alongside each item's funding posture.

Two guardrails follow from this classification. First, the planning ranges stated in this Plan are neither appropriations nor formal budget scores, they convey relative scale and sequencing, and they must not be presented as committed funding. Second, before an appropriation-dependent or resource-intensive item is presented as implementation-ready, it should carry an agency-developed cost estimate, with Office of Management and Budget review as applicable, rather than only a planning range, and an item in either category that lacks such costing is not implementation-ready regardless of how well specified its deliverable may be.

Budgetary accountability also extends beyond launch. The recurring cost of major initiatives and of the infrastructure used to track them, including the National Autism Precision Therapeutics Initiative, Autism.gov, the consolidated implementation dashboard, registries, and the reporting systems that feed them, must be identified as sustainment and operations-and-maintenance cost, distinct from initial launch or design cost. Federal reporting systems and public dashboards have a well-documented tendency to go stale once initial funding and attention recede, and identifying sustainment cost while assigning an owner for post-launch continuity is what prevents the accountability infrastructure from becoming the first casualty of the next budget cycle.

Recommended Federal Autism Funding Levels

Fiscal Year 2028

The Autism CARES Act of 2024 authorizes $390.444 million in annual federal autism funding for each of fiscal years 2025 through 2029, comprising $306 million for the National Institutes of Health and the Interagency

Autism Coordinating Committee, $28.1 million for the Centers for Disease Control and Prevention, and $56.344 million for the Health Resources and Services Administration. This authorization establishes the baseline against which the Committee's recommendations are measured, and every figure in this section is offered as an addition to it rather than as a substitute for any existing program.

The recommendations divide into two instruments with distinct legal foundations. The Part IV domain-directed portfolio, delivered through the NAPTI translational framework, expresses planning targets for the mechanistic priorities that the existing institute-funded research base should advance, and it steers appropriated funds without requiring new authority. The National Neurodevelopmental Regression Initiative, by contrast, represents new directed funding that would be established and sustained through dedicated authorization and appropriation, so that its resources remain protected from year-to-year institute discretion. The recommended addition for the Centers for Disease Control and Prevention supports the surveillance and public health monitoring on which national prevalence and trend estimates depend.

Consistent with the Committee's coordinative authority, these are recommended levels rather than directed appropriations, and they are offered to guide the agencies and the Congress as annual budgets are developed. Taken together, the recommendations would raise total annual federal autism funding to $747.444 million, an investment commensurate with the scientific opportunities this plan describes and continuous with the Committee's practice of recommending funding sufficient to meet identified need.

Baseline and resulting recommended levels, by agency

Agency	Current Autism CARES Act authorization (annual, FY2025–2029)	Recommended addition (FY2028)	Resulting recommended level
NIH (including the IACC)	$306.000M	$327M	$633.000M
CDC	$28.100M	$20M	$48.100M
HRSA	$56.344M	$10M	$66.344M
Total	**$390.444M**	**$357M**	**$747.444M**

Recommended additions, by initiative

Recommended initiative	Agency	FY2028 addition
National Neurodevelopmental Regression Initiative (NDR)	NIH	$57M
NAPTI translational framework (Part IV domain-directed portfolio)	NIH	$270M
CDC autism surveillance and public health monitoring	CDC	$20M

Recommended initiative	Agency	FY2028 addition
HRSA diagnostics workforce training	HRSA	$10M
Total recommended addition		**$357M**

The NAPTI line delivers the Part IV domain-directed portfolio and corresponds to the $270 million Part IV architecture total presented in the body of this plan. Authorization figures reflect 42 U.S.C. § 280i-4 (Autism CARES Act of 2024), FY2025–2029; a dash indicates no recommended addition.

Privacy, Accessibility, and Data Governance Gates

Several of the Plan's most valuable research and service activities may involve sensitive data about a population that includes minors and individuals with intellectual disability, for whom heightened legal and ethical protections may apply, and those activities include record linkage among claims, electronic health records, surveillance, developmental-services records, and, in some initiatives, physiological monitoring. The framework establishes a sequencing gate: no record linkage, data-sharing arrangement, or public reporting involving sensitive data should proceed before the applicable privacy, security, civil rights, informed-consent, institutional-review, data-use, and disclosure-control requirements have been defined and approved by the responsible authorities. The gate is deliberately a precondition rather than a parallel workstream, because building technical infrastructure before the governance rules are approved creates civil rights and privacy exposure rather than a mere project-sequencing problem.

Accessibility is subject to comparable discipline. Accessibility commitments stated as design values must be expressed as measurable standards with their own indicators, including conformance with Section 508 and applicable Web Content Accessibility Guidelines criteria for public digital products, along with usability for augmentative and alternative communication and for multiple languages where applicable to the audience served. An accessibility commitment that carries no testable metric cannot be evaluated, and it should be recorded in the register with an explicit accessibility-conformance indicator rather than as an unmeasured aspiration.

Public reporting is governed by disclosure discipline. Any public release drawn from the register or its underlying data should apply appropriate aggregation and suppression controls to protect individuals in small cells, and it should disclose limitations rather than presenting incomplete data as complete. These controls apply with particular force to subgroup disaggregation, which is valuable for subgroup analysis but carries a re-identification risk that must be managed before publication rather than after.

Review, Escalation, and Plan Updates

The framework defines how barriers move upward for resolution. When a recommendation stalls on an unresolved dependency, a resource shortfall, or an interagency coordination problem the Coordinator cannot resolve at the working level, the barrier is escalated, together with the relevant register entry, to the

Secretary or to the leadership of the responsible agency, so that resolution is sought by an authority able to act. Escalation is a transparency and coordination mechanism, and it confers on neither the Committee nor the Coordinator any power to direct the resolution, only to surface the barrier to those who can.

The framework also defines how recommendations change over time. A recommendation may be modified when evidence or circumstances shift, superseded when a better approach replaces it, deferred when it remains valid but cannot be pursued now, or closed when it is no longer appropriate to pursue, and each such change is recorded in the register with a stated reason, so that the evolution of the Plan is visible rather than silent. The biennial Strategic Plan update is the formal occasion for reconciling these changes, since each update should distinguish recommendations that are completed, in progress, modified, deferred, and not advanced, and should explain why each falls where it does, which is precisely the distinction Part I promised this framework would make.

Because the accountability apparatus is itself a set of federal commitments with recurring cost, the framework includes a sunset and continuation review. The dashboards, register, and supporting infrastructure established for the 2026 to 2028 cycle should be reviewed at the close of the cycle, and again in relation to the authorization period running through 2029, to determine whether each element should continue, be modified, or be retired. This review prevents the indefinite accumulation of stale metrics and reporting obligations, and it ties the life of the accountability infrastructure to its demonstrated usefulness and to the statutory horizon within which the Committee operates.

Executive Accountability Scorecard

The chapter concludes with a concise whole-of-plan scorecard designed to measure implementation integrity rather than the volume of activity. A high count of actions taken is not by itself evidence that the Plan is working, so the scorecard emphasizes whether recommendations have owners and authority, whether appropriation-dependent items have been costed, whether foundational dependencies are resolved, whether reporting is timely, and whether outcomes rather than activities are improving. The measures below constitute the executive accountability set, while more detailed indicators, including baseline-readiness tags, Tier 1 launch rates, public dashboard currency, and accessibility conformance, remain in the whole-of-plan register and in agency workplans.

Accountability Measure	What It Verifies
Recommendations with assigned owner and authority	Share of major recommendations with a named lead agency and an identified statutory or regulatory authority.
Appropriation-dependent items costed	Share of appropriation-dependent recommendations carrying an agency-developed cost estimate, with OMB review as applicable, rather than only a planning range.
Unresolved dependencies	Count of recommendations held in dependency-unresolved status, including foundational dependencies such as Coordinator placement.
Timely reporting	Share of expected agency status submissions received by the stated data cutoff for the reporting cycle.

Accountability Measure	What It Verifies
Outcome measures showing improvement	Share of stabilization or outcome measures, as distinct from activity measures, demonstrating improvement against a defined baseline.

Read together, these measures answer the question Part I posed. They ask not whether the federal autism enterprise has been busy, but whether it has implemented what it committed to implement, with owners, authority, resources, and evidence of benefit, in a manner the Secretary, Congress, and the public can verify. The sources most directly relevant to the accountability posture of this Plan are the Autism CARES Act of 2024, enacted as Pub. L. No. 118-180 and summarized by the IACC, and the Government Accountability Office's 2024 review of federal autism coordination and monitoring, GAO-24-106446, whose findings on interagency coordination and monitoring this framework is designed to address.

Appendix A

Analysis of the FY2025 NIH Autism Research Portfolio (RCDC)

Methods of Record 1: Research Type, Co-occurring Condition Focus, & Translational Distance,

This document records the method that produced the classifications in the FY2025 NIH RCDC autism portfolio analysis. It describes the portfolio as constructed, the classification pipeline as executed, and each framework as applied. It is limited to fiscal year 2025 (FY2025) and to work actually performed.

1. Portfolio Construction and Data Sources

The portfolio comprised the National Institutes of Health (NIH) research projects officially classified as **Autism** for fiscal year 2025 by the NIH Research, Condition, and Disease Categorization (RCDC) system. The complete set of FY2025 RCDC–Autism projects was downloaded from NIH RePORTER.

The RCDC export identified each project and its funding but did not include the abstract or the public health relevance narrative (the project narrative). That text was therefore obtained from a separate NIH RePORTER extraction retrieved with "autism" as a **project term** — a broader query that returned full project text and yielded **1,624 studies**. This project-term extraction was cross-referenced to the RCDC dataset and matched by **project number**, with project title and principal investigator used as a secondary check, so that the abstract and public health relevance narrative could be attached to each FY2025 RCDC–Autism project. The project-term set was broader than the RCDC portfolio and served only as the source of narrative text; the analyzed portfolio remained the 617 RCDC–Autism projects.

The FY2025 RCDC–Autism export returned **622 project records**. Five were exact duplicates — identical in project number, title, PI, and amount, totaling $150,756 — and were flagged and excluded from every summary table. The remaining **617 unique projects** constituted the analyzed portfolio, representing **$339,053,143** in FY2025 NIH funding.

NIH RePORTER returned records at the funding-line and sub-project level rather than one row per grant, so the export contained **structural multiplicity**: multi-project center awards (P50, U54, U19) appeared as separate component rows, administrative supplements appeared alongside their parent award, and some grants appeared on more than one funding line. This structural multiplicity was **retained** as distinct records, because each was a separately funded effort; only exact-duplicate rows were removed. The portfolio was analyzed against a single, unambiguous denominator of 617 projects.

2. Classification Approach

All 617 projects were classified by an automated, rule-guided LLM pass that read each project's title, abstract, and public health relevance narrative and assigned categories by the framework's precedence rules — reproducible only approximately, and not a careful human read. The pass characterized what each project **stated** — its aims and methods — not its scientific quality, merit, or importance.

The frameworks were written as priority-ordered decision rules rather than as conceptual definitions, for a specific reason. Most grants satisfied several conceptual definitions at once, e.g., a project using a mouse model, molecular assays, and a human cohort matches three translational tiers simultaneously — and an LLM pass applying open-ended definitions to such a project could place it differently on repeated runs. Fixing the categories in a defined order, so that a project took the first one it qualified for, converted that unstable judgment call into a repeatable procedure. It also located where uncertainty remained.

On the single-label axes (Co-occurring Condition Focus, primary Research Type, and Translational Distance tier), each project received exactly one assignment, so project counts and dollars each partitioned the portfolio once and summed to 100% of the total. Multi-label tags — condition-domain tags and secondary research types — were counts only and were never dollar-weighted, so they reported additional footprint without disturbing the single-label partition.

3. The Classification Frameworks as Applied

3.1 Framework 1 — Co-occurring Condition Focus

This axis recorded whether, and how centrally, a project targeted one of the following **co-occurring condition** experienced by autistic people: intellectual disability, anxiety, ADHD, sensory concerns, depression, psychosis, epilepsy/seizures, immune/inflammation, autonomic, sleep, motor concerns, mortality/premature death, suicidality, gi/gastrointestinal issues, irritability, substance use, emotional dysregulation, aggression, self-injury, feeding/eating challenges, wandering/elopement, drowning, ocd/obsessive-compulsive, catatonia, self injury/safety. As applied, “condition” meant a co-occurring condition, symptom, health concern, or safety challenge; it did not encompass the core diagnostic features of autism themselves.

Each project received one classification: **Primary Condition Focus** (a co-occurring condition was named in the title or framed as the central target of the work); **Secondary Condition Focus** (the condition was a genuine, meaningful secondary objective or endpoint, not a one-line mention); or **No Specific Condition Focus** (no specific condition was an object of study, or a condition was named only in passing). Classification followed a strict evidence rule — a project was coded from what it actually studied and measured, not from background statements that its findings might someday prove relevant. A named genetic syndrome, by itself, did not earn a condition focus; the project qualified only when a specific condition was targeted (a tuberous-sclerosis epilepsy study was Primary; a Rett biomarker study for seizure prediction was Secondary).

Separately from the Primary/Secondary/No-Specific call, every specific co-occurring condition a project addressed was recorded as a **condition-domain tag** (multi-label, counts only, never dollar-weighted). These tags were reported both across all 617 projects and within the Primary Condition Focus subset, so the prevalence of each condition could be read against the number of projects that made it their central target.

3.2 Framework 2 — Research Type

Each project received one **primary research type**, which partitioned the portfolio’s projects and dollars exactly once across nine categories: Genetics & Genomics, Basic Neuroscience, Clinical Research & Phenotyping, Intervention & Treatment Development, Services & Supports, Epidemiology & Population Health, Environmental Factors, Syndromic Autism Research, and Infrastructure, Methods & Workforce. The primary type was assigned by a **two-pass procedure**,

on the principle that a category naming a mechanism should not override the project's actual purpose. For each project the project's title, abstract, and public health narrative were evaluated.

Pass 1 — purpose gate (first match wins): a project that developed, adapted, or tested a treatment for humans — including gene therapy, antisense oligonucleotides, and gene editing used therapeutically — was **Intervention & Treatment Development** (the delivery mechanism, genetic or otherwise, did not change the type); a project testing an environmental exposure, including gene-by-environment interaction, was **Environmental Factors**; a project delivering, organizing, financing, or improving a service or support was **Services & Supports**.

Pass 2 — subject-matter waterfall (applied only to the remaining "understand" studies, first match wins): Infrastructure/Methods/Workforce → Genetics & Genomics → Syndromic Autism Research → Epidemiology & Population Health → Clinical Research & Phenotyping → Basic Neuroscience. Genetics was placed high and was deliberately broad, capturing gene-driven syndrome work (e.g., SHANK3, MECP2, FMR1) and population genetics; the syndrome category held the clinical, behavioral, or phenotypic syndrome work that remained once gene-level work was claimed. Genetics & Genomics and Syndromic Autism Research were ultimately combined into a single category (Genetic and Genomics), since the waterfall's first-match logic meant a project's placement depended on whether it named a gene (e.g., FMR1) or a syndrome (e.g., Fragile X) rather than on a substantive difference in subject matter. Basic Neuroscience was assigned **last, by elimination — never by default**.

Each project could also carry **Secondary Research Types** (multi-label, counts only). These were reported as a research-type overlap table showing, for each primary type, the other domains a study also involved; funding was attributed to the primary type only and was never summed across the multi-label overlap.

3.3 Framework 3 — Translational Distance

Each project received one tier on the standard translational spectrum based on review of its title, abstract and public health narrative **T1 through T6**: T1 Molecular/Cellular Mechanisms, T2 Animal Models/Preclinical, T3 Human Biomarkers/Phenotyping, T4 Clinical Characterization/Natural History, T5 Intervention Development/Testing, and T6 Implementation/Services. The tier reflected the **furthest stage a project's own methods actually reached**, never the stage its significance or future-directions language aspired to.

A **system gate** served as the master tie-breaker. A project with a genuine human aim — a stated Specific Aim producing its own primary human data and outcome — was human-facing and eligible for T3–T6, with any accompanying animal or cell work recorded rather than pulling the tier down. A project whose data came only from molecules, cells, organoids, or animals was preclinical and capped at T1–T2; within that band, molecular/cellular study was T1 and whole-organism or organoid study was T2, and an intervention developed or tested only in animals remained T2. Within human-facing work, tiers were assigned by furthest activity reached (T6 > T5 > T4 > T3). Because human treatment testing sat at T5 and deployment of proven interventions at T6, the portfolio's "closest to patients" reading rested on the combined **T5-plus-T6 delivery-end share** — in FY2025, 99 projects. Center and multi-component grants received a single primary tier (the tier of the stated core aim, defaulting to the discovery end when genuinely mixed); dollars rode on that single tier only.

3.4 Autism Centrality (verification analysis)

Independently of the four frameworks, every project was classified for **autism centrality** — whether the project actually concerned autism — as a check on the RCDC categorization. Each project was assigned to one of four tiers:

Direct (534 projects), **Contextual** (57), **Syndromic route** (18), or **No stated autism content** (8), with a project-level count of autism mentions also recorded, and 80 records identified as center components. This verification confirmed that the large majority of the RCDC-tagged portfolio was directly about autism while making explicit the minority that entered through a syndromic route, appeared only contextually, or carried no stated autism content in its text.

4. Reliability and Confidence

Because the classification was an automated LLM pass rather than a human read, project-level tags at contested boundaries should be treated as approximate; the **aggregate shares are the dependable output**. Per-project classification confidence was recorded (see the scoring notes in §5).

The two ends of the translational spectrum were not equally certain. The delivery-end share (T5 plus T6) rested on a coarse, robust distinction — whether a project tested or deployed an intervention in humans — and was the primary driver of the analysis. The finer internal split at the discovery end (T1 – T4) involved closer judgment calls and carried more classification uncertainty. Repeated passes over the data produced only small variation in the aggregate shares, and what movement there was fell largely between adjacent discovery-end categories rather than across the discovery-versus-delivery line.

The priority-ordered rules improved reproducibility but did not eliminate judgment; the residual judgment concentrated in a small subset of projects at the discovery-end boundaries. However the primary distinctions between the delivery-end share and the broad discovery-versus-delivery comparison were stable.

FY2025 NIH Autism Research Portfolio (RCDC) — Analysis

617 analyzed projects · $339.1M total · funding rounded to $0.1M. ·

Research Type

Research Type	Funding	Share
Genetics & Genomics	$130.5M	38.5%
Clinical Research & Phenotyping	$65.9M	19.4%
Basic Neuroscience	$49.0M	14.5%
Intervention & Treatment Development	$47.0M	13.9%
Services & Supports	$21.8M	6.4%
Environmental Factors	$19.7M	5.8%
Epidemiology & Population Health	$4.2M	1.3%
Infrastructure, Methods & Workforce	$0.9M	0.3%
TOTAL	**$339.1M**	**100%**

Translational Distance:

Stage	Funding	Share
T1 Molecular and cellular	$31.3M	9.2%
T2 Animal models and preclinical	$104.9M	30.9%
T3 Human biomarkers and phenotyping	$36.1M	10.7%
T4 Clinical characterization and natural history	$124.3M	36.7%
T5 Intervention development and testing	$20.1M	5.9%
T6 Implementation and services	$22.3M	6.6%
Total	**$339.1M**	**100%**

Translational Distance: Groupings

Groupings	Funding	Share
Discovery subtotal (T1–T4)	**$296.7M**	**87.5%**
Preclinical subtotal (T1–T2)	**$136.2M**	**40.2%**
Middle subtotal (T3–T4) — harder calls	**$160.5M**	**47.3%**
Delivery subtotal (T5–T6)	**$42.4M**	**12.5%**

Note: T3 and T4 were frequently borderline. Classification used a keyword search of project text, not a narrative review, so the T3/T4 boundary — and the discovery/delivery line generally — is least certain in this middle band. The most robust contrast is between the unambiguous preclinical end (T1–T2, 40.2%) and the delivery end (T5–T6, 12.5%). Groupings do not add to 100% due to overlapping groupings.

Appendix B

Analysis of the FY2025 NIH Autism Research Portfolio (RCDC)

Methods of Record 2: Etiological Classification

This document records the method that produced the etiological classifications in the FY2025 NIH RCDC autism portfolio analysis, as contained in the accompanying results workbook. It is limited to fiscal year 2025 and to work actually performed. It is a companion to a separate Methods of Record document ("Method of Record 1") covering Co-occurring Condition Focus, Research Type, Translational Distance, and Heterogeneity Handling, applied to the same portfolio.

1. Portfolio and Scope

The portfolio is the same 617-project FY2025 RCDC–Autism analyzed portfolio described in Method of Record 1, representing $339,053,143 in FY2025 NIH funding. Duplicate handling and portfolio construction follow Method of Record 1 and are not repeated here.

2. Classification Approach

Each project in the portfolio was classified into exactly one of five etiological categories, regardless of its research type or translational stage, based on the project's stated framing of what causes autism spectrum disorder (ASD):

Category	Definition
Genetic	Project's primary framing identifies a genetic cause of ASD: specific risk genes, genetic variants, GWAS, copy number variants, or gene-editing models. Requires genetic-etiology language to be present.
Non-Genetic	Project's primary framing identifies a non-genetic cause: environmental exposures, immune or inflammatory mechanisms, or gut-microbiome pathways. This is a positively defined category requiring specific language to be present, not a default for projects that lack genetic framing.
Gene-Environment Interaction (GxE)	Project explicitly studies the interaction between genetic and environmental factors, or substantively addresses both without a single clear primary driver.
Epigenetic	Project's primary focus is an epigenetic mechanism (DNA methylation, histone modification, chromatin remodeling) without a clear upstream genetic or environmental driver.

Category	Definition
Unclassified	No etiological position taken. The project does not state a genetic, non-genetic, GxE, or epigenetic cause. This is the residual category and is common for projects concerned with treatment, services, phenotyping, or infrastructure.

Genetic and Non-Genetic are both positively defined categories: each requires the project's own title or abstract to state the relevant causal framing. A project with neither is Unclassified, which is the true residual and does not imply a non-genetic position.

2.1 Classification Method

Classification was performed using a rule-based text classifier applied to each project's title and abstract. The classifier searches for documented keyword and phrase patterns associated with each etiological category and applies a fixed set of precedence rules to resolve cases where a project's text matches more than one category's patterns. Specifically:

- If a project's text contains explicit gene-environment interaction language, it is classified GxE regardless of what other patterns match.
- If a project's text contains both genetic and non-genetic patterns without explicit GxE language, the project's title is checked for a primary framing; if the title favors one side, that side is used, otherwise the project is classified GxE.
- If a project's text contains epigenetic patterns together with a genetic or non-genetic driver, the project is classified by that driver. Epigenetic is used only when the text contains epigenetic patterns without an identifiable upstream genetic or environmental driver.
- If a project's text matches only one category's patterns, it receives that category.
- If a project's text matches no category's patterns, it is Unclassified.

The classifier is deterministic: the same title and abstract text will always produce the same classification. Every classification can be traced to the specific pattern(s) that produced it.

The full keyword lists, regular-expression patterns, and decision-rule documentation are available as a companion technical appendix upon request.

2.2 Human Review

Classification combined the automated method above with human review at two distinct points.

First, during development of the classification patterns, a set of projects flagged as ambiguous were reviewed and classified directly by a subject-matter reviewer, in parallel with the process of building and refining the pattern set itself. Fifteen projects, representing $12.9 million, were classified in this manner.

Second, following a full-portfolio run of the automated classifier, a targeted review of the highest-funded Unclassified projects was conducted to check for pattern gaps. This review identified four projects, representing $2,159,541 (0.6% of total portfolio funding), that had been classified Unclassified but whose text supported a positive etiological classification. All four were moved out of Unclassified and into a positive category; none involved a shift between Genetic and Non-Genetic. The specific shifts were:

Shift	Projects	Funding
Unclassified → Genetic	3	$1,648,000
Unclassified → Gene-Environment Interaction (GxE)	1	$511,541
Total	**4**	**$2,159,541**

In total, 19 of 617 projects (3.1% of the portfolio by count; 4.6% by funding) were classified with direct human review rather than solely by the automated pattern match. The net effect on the portfolio's aggregate etiological composition is small: the four-project correction described above represents 0.6% of total portfolio funding, and in every case moved a project from no stated etiological position to a positive one, rather than altering the balance between Genetic and Non-Genetic classifications.

3. Results

Across all 617 projects in the analyzed portfolio:

Category	Projects	Funding	% of Total
Genetic	240	$119,489,994	35.2%
Non-Genetic	35	$20,592,313	6.1%
Gene-Environment (GxE)	33	$38,763,537	11.4%
Epigenetic	3	$4,943,352	1.5%
Unclassified	306	$155,263,947	45.8%
Total	**617**	**$339,053,143**	**100.0%**

Among the 311 projects and $183,789,196 that take a position on cause (i.e., excluding Unclassified), the distribution is:

Category	Funding	% of Classified	Projects
Genetic	$119,489,994	65.0%	240
Gene-Environment (GxE)	$38,763,537	21.1%	33
Non-Genetic	$20,592,313	11.2%	35
Epigenetic	$4,943,352	2.7%	3
Total Classified	**$183,789,196**	**100.0%**	**311**

4. Comparability Note

This analysis and Method of Record 1 were applied to the same 617-project portfolio and adopt the same Translational Distance classification documented there. The two analyses use different classification frameworks

answering different questions: Method of Record 1's Research Type framework partitions the portfolio by primary subject matter (e.g., Genetics & Genomics, Syndromic Autism Research, Basic Neuroscience), while this Etiological analysis partitions the portfolio by etiological framing. The two frameworks are not designed to align category-for-category and should be read as complementary, not reconciled, views of the same portfolio.

Appendix C

Life Course Domain I: Timely, Equitable, and Technology-Enabled Diagnosis

Communication-Adapted Clinical Protocol (Contents)

The HRSA/AHRQ protocol should address: developmental surveillance and screening; diagnostic history, observation, differential assessment, and documentation; selection and use of validated instruments; identification of cases requiring interdisciplinary or specialty referral; communication-adapted history and review of systems for speaking, nonspeaking, minimally speaking, and otherwise communication-disabled patients; evaluation of pain, sleep disturbance, altered behavior, functional decline, regression, and acute change as possible clinical findings rather than presumed autism manifestations; indicated first-line workup and condition-specific referral; recognition of neurologic, gastrointestinal, immunologic, metabolic, endocrine, hematologic, genetic, sleep, psychiatric, motor, and sensory presentations; condition-specific documentation and coding; electronic and inter-professional consultation; culturally and linguistically appropriate assessment; adult diagnostic and medical-evaluation pathways; pediatric-to-adult transition; and appropriate use and limitations of technology-assisted assessment.

Escalation criteria requiring specialty referral: regression or loss of acquired skills; suspected seizures or focal neurologic findings; severe or unexplained sleep disturbance; significant, unexplained, or continued gastrointestinal symptoms; recurrent, prolonged, multiple, or unusual infections; metabolic or mitochondrial warning signs (low muscle tone, fatigue, lethargy, failure to thrive, abnormal growth); unexplained pain; acute or substantial behavioral or functional change; suspected genetic or syndromic conditions; significant motor or speech-motor impairment; complex psychiatric presentations; diagnostic ambiguity; and findings outside the clinician’s competence or scope.

Minimum Data Set (Fields)

Date and setting of developmental screening; screening result; date of clinical action or referral; date of initial diagnostic evaluation; date of completed diagnostic determination; diagnostic outcome; date of Early Intervention or IDEA referral; date services began; communication profile; date of communication-adapted review of systems; clinically indicated workup or consultation; completion or noncompletion of recommended evaluation; co-occurring conditions identified; treatment or referral initiated; denial and appeal experience; payer; rurality; race and ethnicity; primary language; biological sex; age; support level.

Collection of race, ethnicity, primary language, biological sex, and other individual characteristics is governed by the legal and validation conditions described under Initiative 3 and the KPI data-dependency note.

Technology Assessment Criteria

Technologies making diagnostic or rule-out claims should be assessed against: applicable regulatory status; independent prospective validation; performance in clinically representative populations; false-positive and false-negative consequences; subgroup performance; transparency and clinician reviewability; reproducibility; clinical utility; effects on diagnostic time; effects on specialist referrals; payer and workflow burden; and real-world performance in rural, underserved, pediatric, adult, and complex populations.

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Part I—A New Federal Framework for Autism

From Priorities to Implementation: The Federal Autism Enterprise

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Part II—Discovery Biology and the Case for Precision Translation

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Priority Therapeutic Domain 8: Sleep and Circadian Regulation

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Strategic Plan Part V, Life Course — References

Life Course Domain I: Timely, Equitable, and Technology-Enabled Diagnosis

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Life Course Domain IV: Co-Occurring Mental Health Conditions, Crisis Care, and Suicide Prevention

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Life Course Domain V: Housing Supply, Supported Living, and Caregiver Succession for Autistic Adults

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