ALS GLOBAL RESEARCH INITIATIVE (AGRI)

Building a Global Open Science Resource to Accelerate ALS Biomarker Discovery

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ALS Global Research Initiative
POWERED BY TARGET ALS

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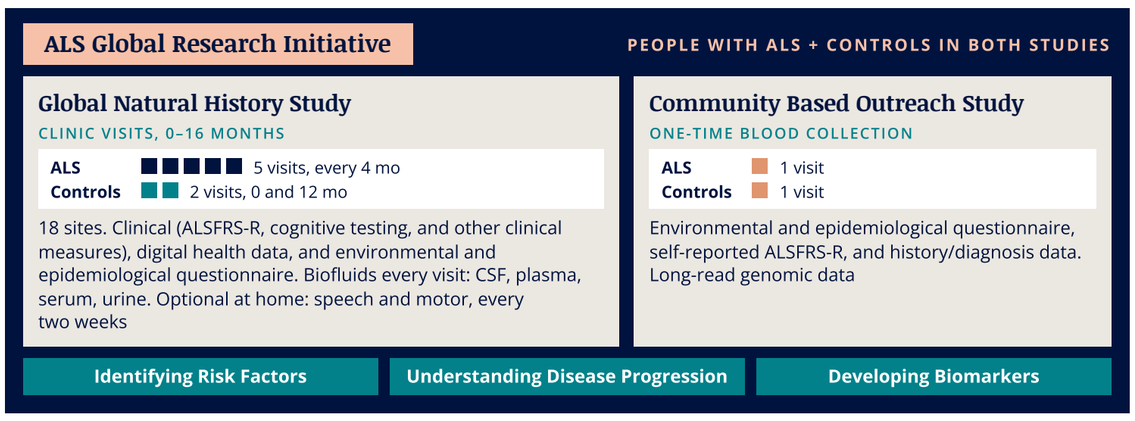
Background

To accelerate discovery and therapeutic development, Target ALS launched the ALS Global Research Initiative (AGRI), an international effort generating deeply characterized clinical, molecular, and environmental datasets and sharing them through the Target ALS Data Engine, an open science research platform. AGRI integrates two complementary observational studies: the Global Natural History Study (GNHS), a longitudinal study collecting clinical data and biospecimens from people living with ALS and healthy controls, and a community outreach study (CBOS) conducting one time visits to capture environmental exposures and long read genomic data. Together, AGRI aims to build the most inclusive and comprehensive global data set to study disease risk, progression, and therapeutic targets.

Methods

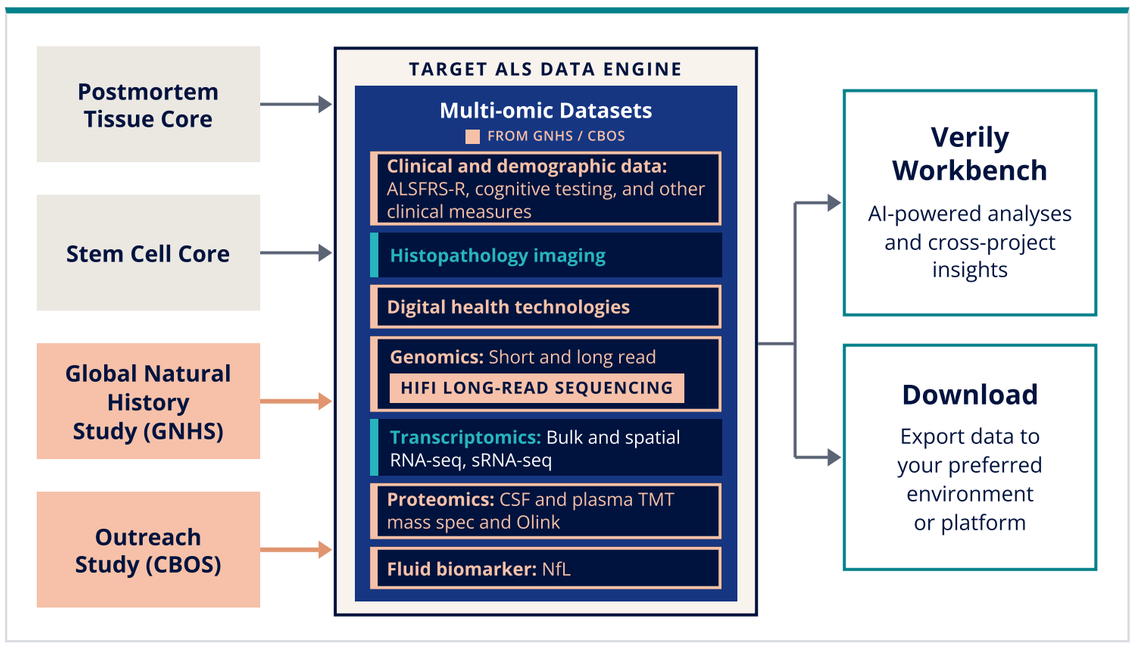
AGRI comprises two complementary observational studies. The Global Natural History Study (GNHS) follows participants with ALS at 18 international sites every four months for up to 18 months, collecting ALSFRS-R scores, cognitive testing, digital health measures, and blood, urine, and cerebrospinal fluid for whole genome sequencing, proteomics, and neurofilament light (NfL) assays. The Community Based Outreach Study (CBOS) adds single-visit assessments of environmental exposures and long-read genomic data. All datasets are harmonized and linked before release through the Target ALS Data Engine for academic and industry researchers.

Figure 1. AGRI Framework Model



Nine modalities, one open science resource

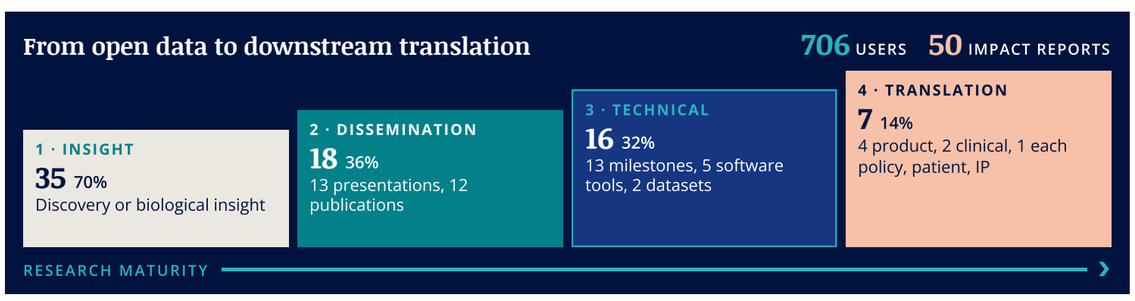
Figure 2. AGRI data flow through the Target ALS Data Engine



Explore the Data Engine
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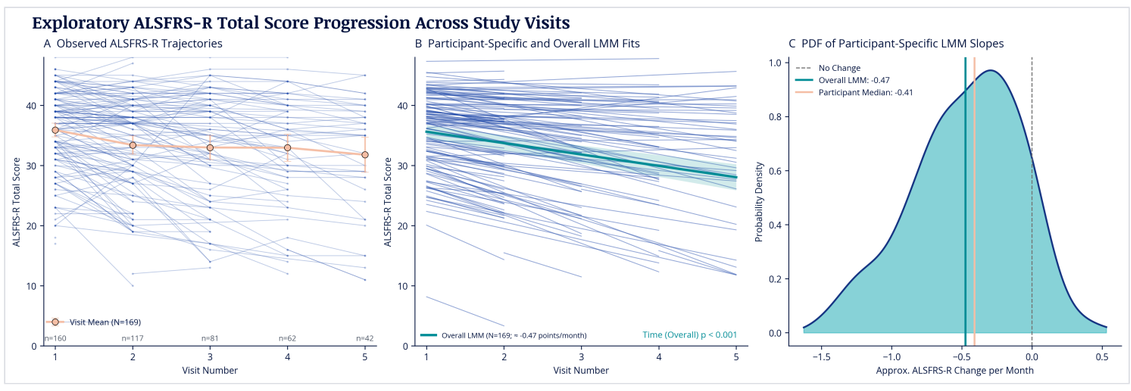
Figure 3. Reported research and impact from Target ALS Data Engine users



Results

To date, 398 participants have enrolled in the Global Natural History Study (GNHS) and 101 in the Community Based Outreach Study (CBOS). AGRI has generated longitudinal clinical, digital health, and molecular datasets, with more than 56,000 biofluid samples collected in the biorepository. GNHS data span nine modalities, and nearly 60% of participants (169 of 283) have contributed four or more data types. ALSFRS-R scores are available for 169 participants, 133 of whom have scores from two or more visits documenting change over time. Among the 208 participants with whole-genome sequencing, 29% have a non-European research-derived ancestry classification (single non-European ancestry ≥70%, dual ancestry, or multiple ancestry).

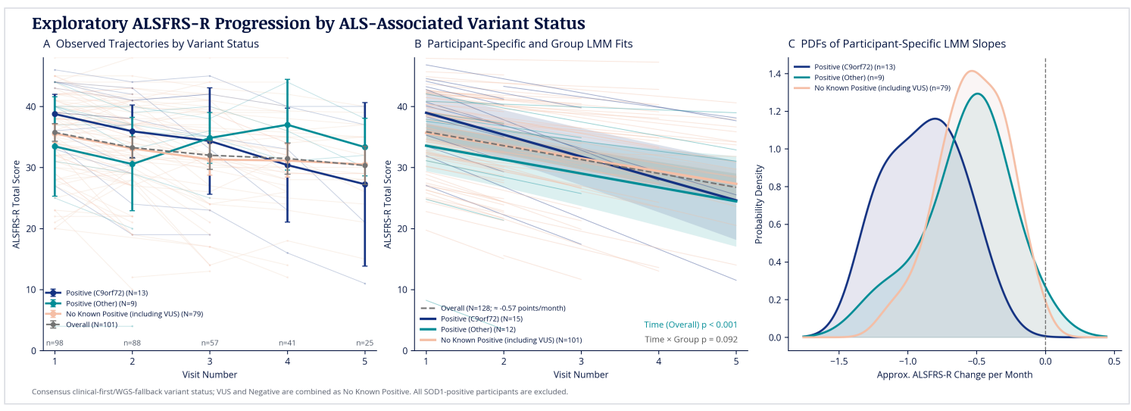
Figure 4. ALSFRS-R total score progression across study visits



ALSFRS-R declined significantly over time across the full cohort (≈ -0.47 points/month, p < 0.001), with wide between-participant variability in individual slopes (median -0.41 points/month).

Overall slope differs from Figure 5 because Figure 5 excludes SOD1-positive participants and uses a different analytic sample.

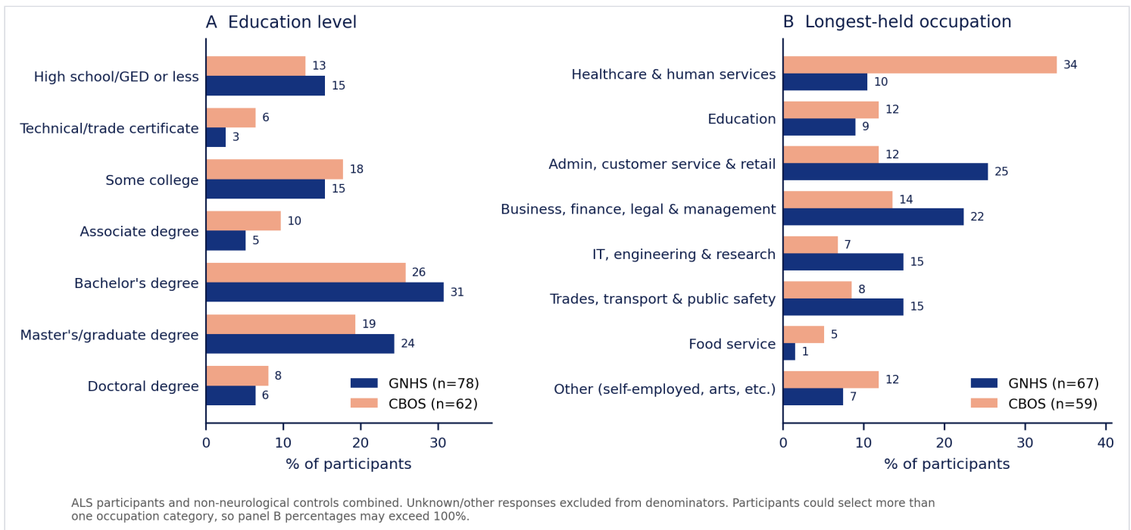
Figure 5. ALSFRS-R progression by ALS-associated variant status



Participants with a C9orf72 expansion trended toward faster ALSFRS-R decline than other groups, but the Time × Group interaction was not significant (p = 0.092), while the cohort overall declined significantly (≈ -0.57 points/month, p < 0.001).

Panel A reflects participants with observed scores; Panels B and C include participants contributing to LMM estimation (≥2 visits) [confirm criteria]. SOD1-positive participants are excluded.

Figure 6. Education and occupational history. GNHS and CBOS capture complementary educational and occupational backgrounds; AGRI's recent global expansion will further broaden this diversity for exposure-informed biomarker discovery.



ALS participants and non-neurological controls combined. Unknown/other responses excluded from denominators. Participants could select more than one occupation category, so panel B percentages may exceed 100%.

Conclusion

AGRI aligns with the Target ALS commitment to collaborative, open science. By integrating longitudinal clinical measures, multi-omic profiles (whole genome sequencing, quantitative proteomics, NfL), and digital health data from an ancestrally diverse international cohort, and releasing them to academic and industry investigators through the Target ALS Data Engine, AGRI provides a shared infrastructure for biomarker discovery, characterization of clinical and molecular heterogeneity, and therapeutic target identification.