University of Gothenburg External QC Program Supported by GBSC and DxA for blood-based Alzheimer's disease biomarkers

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1 Introduction

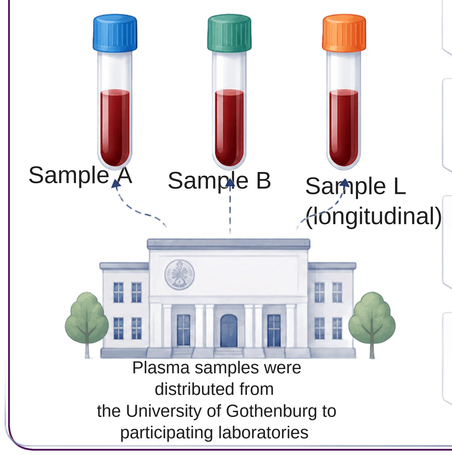


Blood-based biomarkers are increasingly used for Alzheimer's disease (AD) management, yet substantial variability remains across studies and laboratories

To address this, a global external quality control (QC) program for blood biomarkers was established, building on the Alzheimer's Association CSF QC program.

The program estimates inter-assay and inter-laboratory variability and monitors batch-to-batch assay variation for key biomarkers: NfL, GFAP, Aß40, Aß42, p-tau181 and p-tau217.

2 Methodology



Plasma samples were distributed from the University of Gothenburg to participating laboratories

Three rounds (Feb, May, Oct) were distributed at once, once per year.

Participating laboratories analyzed samples using commercially available kits.

Data from rounds 32-48 were analyzed to assess variability and longitudinal trends.

Coefficient of variation (CV%) for samples A, B, and L were calculated for each assay, biomarker and platform.

3 Results

Participation grew from 7 laboratories in the first round to 74 laboratories overall.

Fully automated platforms increased over time.
In the final round (48):

- Lumipulse (n = 54)
- Simoa (n = 27)
- Cobas (n = 5)
- MSD (n = 2)



Most frequently analyzed biomarkers in final round (48):

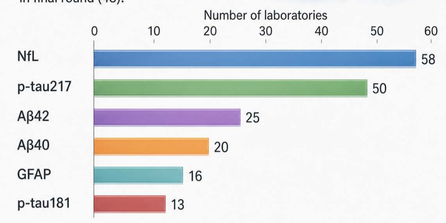
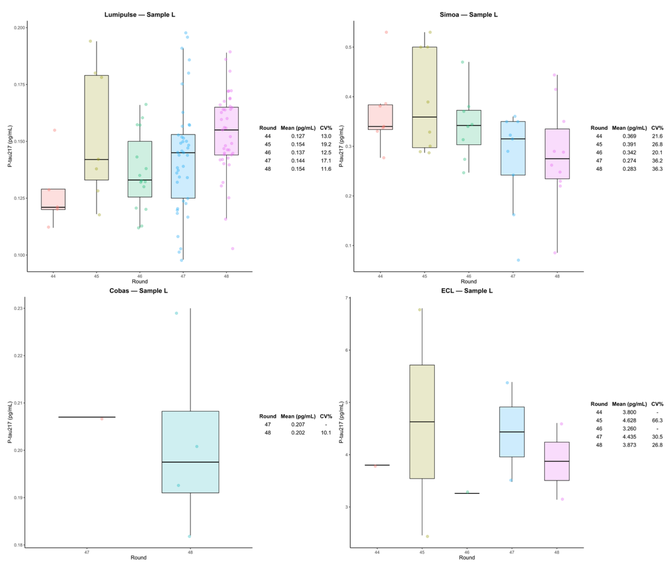


Figure 1. Number of laboratories analyzing each biomarker in the final round (48).

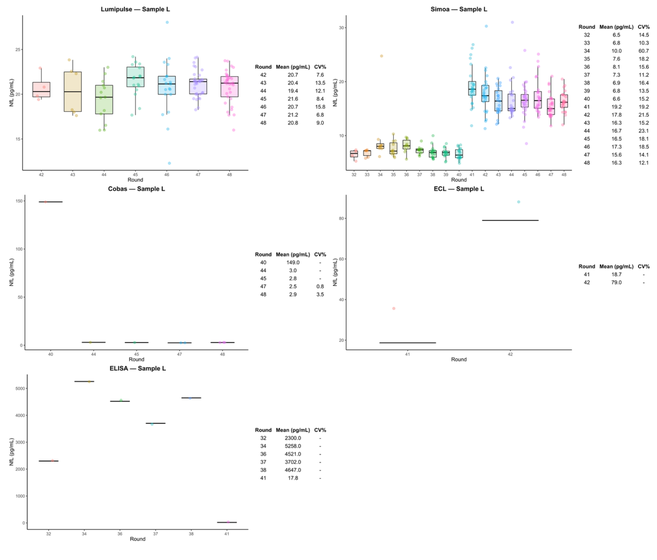
3 Results

Variablity in plasma p-tau217



Inter-laboratory CVs% for p-tau217
Sample A: Lumipulse 6.9–20%, Simoa 18–37%, Cobas 19%, MSD 33–70%
Sample B: Lumipulse 11–19%, Simoa 15–37%, Cobas 6.8%, MSD 5.0–83%
Longitudinal sample (L): Lumipulse 12–19%, Simoa 20–36%, Cobas 10%, MSD 27–66%

Variablity in plasma NfL



Inter-laboratory CVs% for NfL
Sample A: Lumipulse 5.6–18%, Simoa 6.8–94%, Cobas 1.0–4.6%
Sample B: Lumipulse 8.2–25%, Simoa 12–40%, Cobas 0.8–2.1%
Longitudinal sample (L): Lumipulse 6.8–16%, Simoa 11–61%, Cobas 0.8–3.5%

5 Conclusion

Variability persists
Despite increasing adoption of blood-based AD biomarkers, considerable variability persists between laboratories using the same assay and analytical platform, with lower variability observed for fully automated platforms.

Automated platforms show lower variability
This within-assay variability may be influenced by differences in laboratory-specific analytical procedures and sample handling, but could also reflect inherent assay-related factors.

Need for harmonization of workflows
These findings highlight the need for improved harmonization of laboratory workflows to reduce within-assay variability.

QC programs ensure assay performance
At present, cross-assay comparisons remain challenging due to the lack of commutable reference materials, underscoring the importance of quality control programs in monitoring assay-specific performance prior to broader clinical implementation.

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Future Directions

- Expansion to additional international laboratories.
- Inclusion of BD-tau and other emerging blood biomarkers.
- Inclusion of Siemens, Abbott, and Beckman Coulter analytical platforms.
- Continued monitoring of longitudinal assay performance and harmonization across laboratories.