alzheimer's association

UNIVERSITY OF GOTHENBURG

The Alzheimer's Association quality control program

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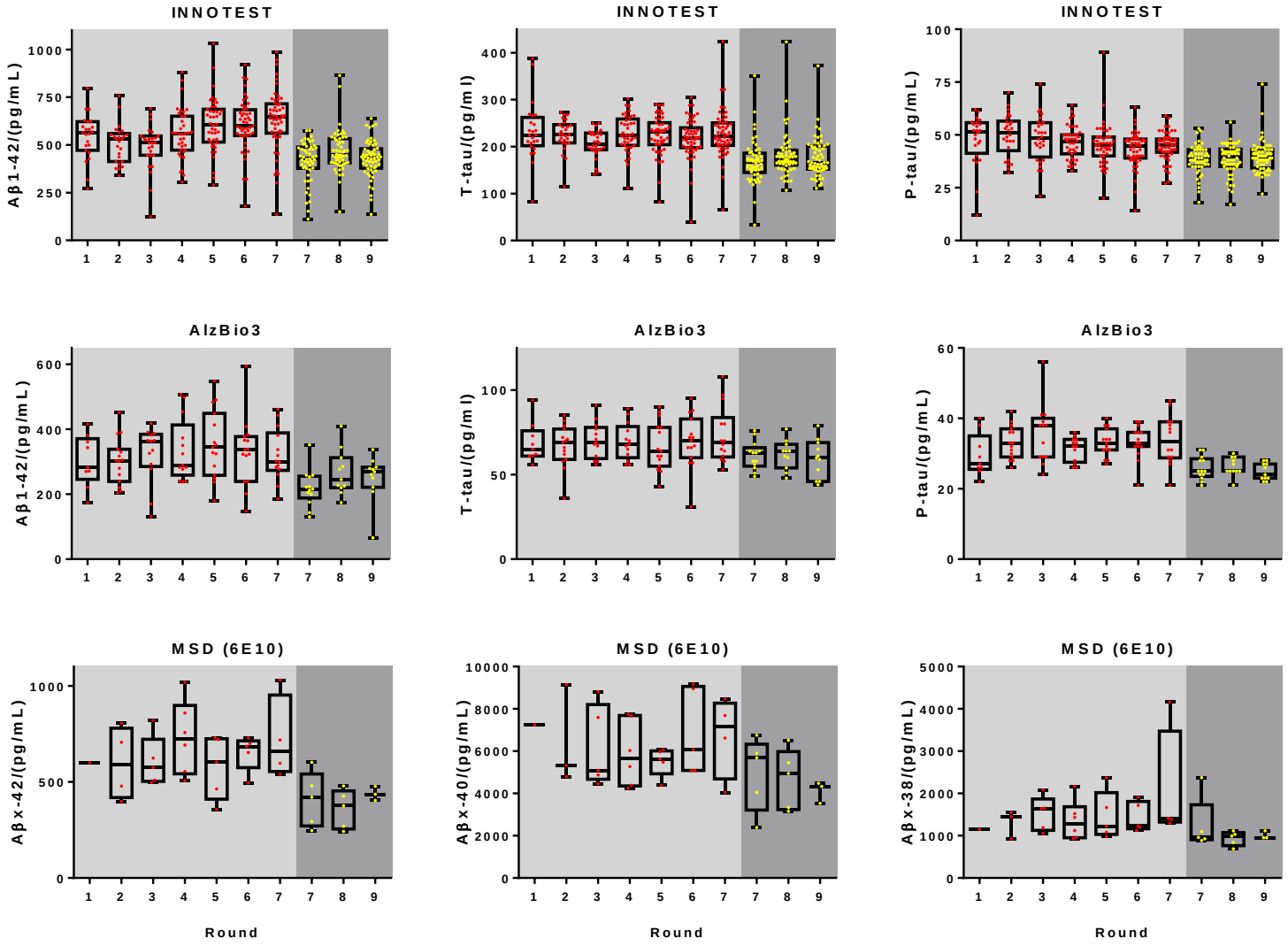
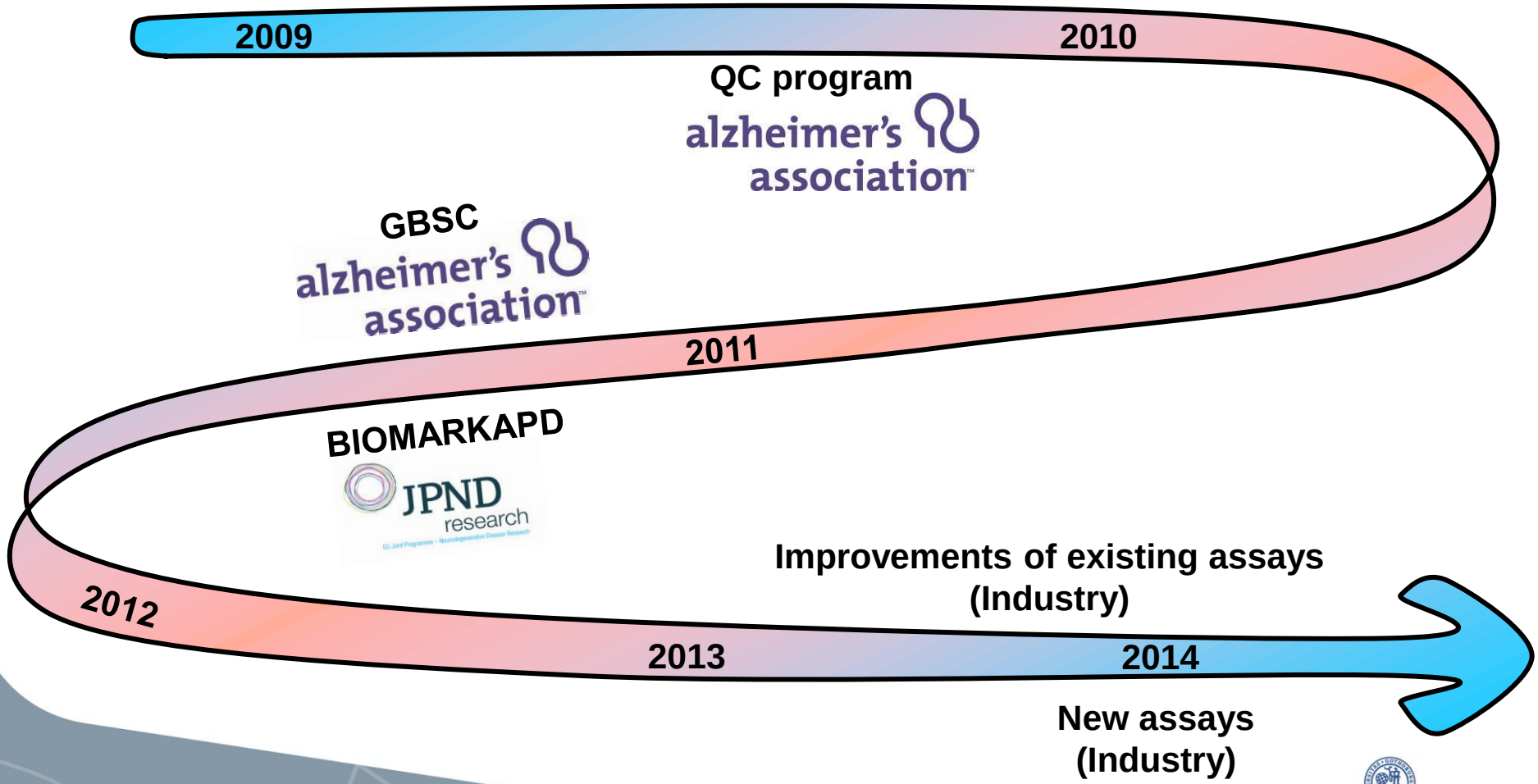
QC program facts

- Initiated 2009 and 98 laboratories are now listed in the database.
- Three rounds/year with three samples: two unique and one longitudinal.
- Presently three different assay platforms by two companies (Innogenetics and MesoScaleDiscovery).
- Coordinated from Neurochemistry Laboratory in Mölndal, Sweden and is sponsored by The Alzheimer's Association.
- Two publications:
  Mattsson, N. et al, Alzheimer's & Dementia 2011;7:386-395
  Mattsson, N. et al, Alzheimer's & Dementia 2013;9:251-261

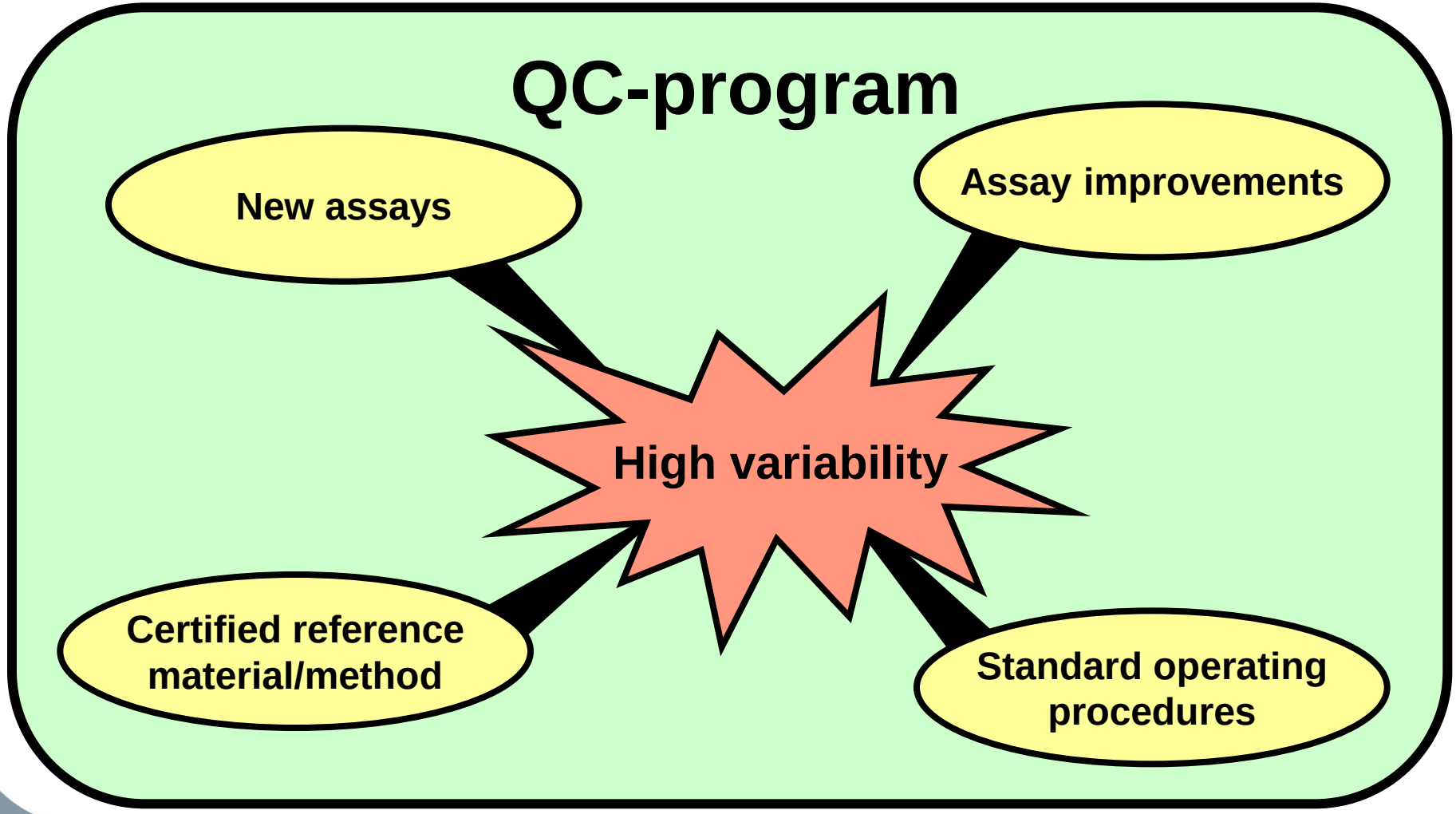
Results (QC-L)


INNOTEST
Aβ1-42/(pg/mL)
INNOTEST
T-tau/(pg/ml)
INNOTEST
P-tau/(pg/mL)
AlzBio3
Aβ1-42/(pg/mL)
AlzBio3
T-tau/(pg/ml)
AlzBio3
P-tau/(pg/mL)
MSD (6E10)
Aβx-42/(pg/mL)
MSD (6E10)
Aβx-40/(pg/mL)
MSD (6E10)
Aβx-38/(pg/mL)
Round
Round
Round

Past, present, and future



The big picture



Funding

- The first four years have been funded by a generous grant from an anonymous donor to the Alzheimer's Association.
- Future funding is not yet clear.

CSF biomarker variability in the Alzheimer's Association quality control program

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Background

The cerebrospinal fluid (CSF) biomarkers amyloid-b 1-42 (Ab42), total-tau (T-tau), and phosphorylated-tau (P-tau) are increasingly used for Alzheimer's disease (AD) research and patient management. However, in addition to significant differences between platform-specific commercial assay kit results, there are large variations in biomarker measurements between and within laboratories. One goal with the Alzheimer's Association quality control has been to identify the sources for the variabil prerequisite for attempting to decrease their co thereby improve the reproducibility in the meas

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Method

Data from the first nine rounds of the Alzheime Association QC program was used. In each round, three pools of CSF samples (one longitudinal and two unique) were analyzed by participating laboratories for tau and Aβ proteins by single analyte enzyme-linked immunosorbent assays (ELISA), a multiplexing xMAP assay (both from Innogenetics) or an immunoassay with electrochemiluminescence detection (Meso Scale Discovery; MSD).

Results

Figure 1 shows the results for the longitudinal sample and the large variabilities in determining the analytes concentrations are apparent. Coefficients of variation (CV) between the laboratories were around 20-30%, while the between lot CV ranged from approximately 0-20% (Figure 2). Longitudinal within-laboratory CV was 5-19%. Interestingly, longitudinal within-laboratory CVs differed considerably between biomarkers at individual laboratories, suggesting that a component of the variability was assay-dependent.

A detailed analysis of the results has recently been published (1).

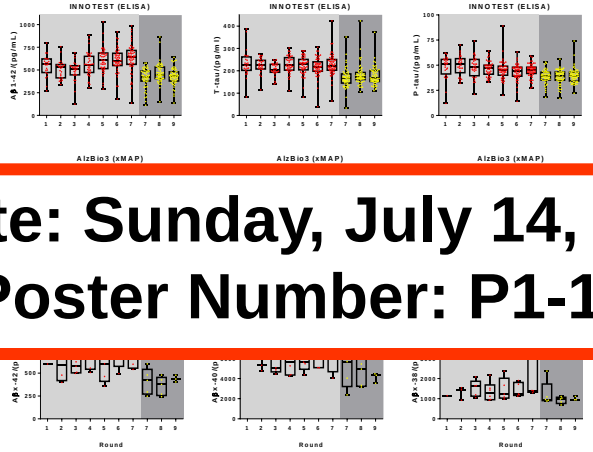

Figure1. Results of the longitudinal QC sample for the first nine rounds of the Alzheimer Association QC program. At round seven a new sample was introduced and the switch is highlighted by a change in both symbol and background colors. The number of participating laboratories were 84.

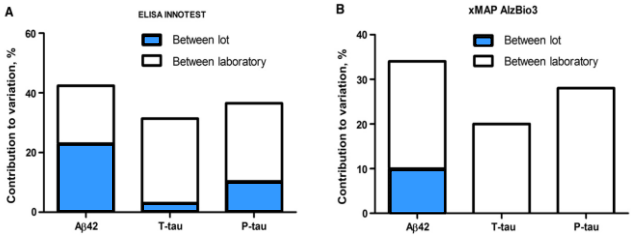

Figure2. Relative contribution of between lot and between laboratory to the total variability for INNOTEST and AlzBio3.

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Conclusions

Despite attempts to reduce the overall variability of CSF AD biomarker measurements it remains too high to allow assignment of universal cutoff values for a specific intended use, even for laboratories using the same commercially available assay. Thus, each laboratory must ensure longitudinal stability (lot consistency) in their measurements and use internally qualified cutoff levels.

nt effects have a significant influence on ecially for Ab42. Further standardization of edures and improvement of kit ncluding adoption of a universal reference kely increase the usefulness of CSF AD researchers and clinicians.

cturers acknowledge the problem with the roducibility and both companies that part in the QC program actively work to improve their assays.

Work is also in progress to introduce the AD biomarkers on fully automated systems, which has the potential to dramatically reduce both the within and between laboratory variability.

Take home message

The high between-lab variabilities for the AD biomarkers remain a problem. However, the future carry hope that the imprecisions will be reduced due to improvements of present, and introduction of new assays.

Acknowledgement

A generous grant from an anonymous donor to the Alzheimer's Association supported this study.

Reference

(1) Mattsson, N. et al (2013) CSF biomarker variability in the Alzheimer's Association quality control program. Alzheimers Dement 9, 251-61.

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