- The Biofluid Based Biomarker PIA has 3 Work groups: Saliva, Context of Use, and Reference Ranges.
- The Reference Ranges WG performed a literature search and compiled a list of the pre- and analytical variables to understand the cofounding factors and their study variability.
- Reference Ranges WG has 22 members and Michelle Mielke is the Chair. Goals are:
    1. Identify and decide on a few promising biofluids based markers that can be used at the general physician level
    2. Compare/contrast study sample collection, assays, populations
    3. Establish 'normal ranges'
    4. Decide on how best to move forward
    5. Identify studies interested in donating samples
- Created a checklist comprised of sample collection, assay information (analytical and clinical) tested checklist on 4 recent papers on amyloid beta and shared with the group.
- Pre-analytical variables- 13 variables based on literature and experts of the group, i.e. time of collection, fasting status, tube types, needle size and location of draw, freeze-thaw cycles, etc. In the 4 papers they reviewed there wasn't much description of pre-analytical variables.
- Assay methodology and biochemical process variables

    Ex. quantitative, calibration standards used, assay sensitivity, assay specificity, etc.
- For the Assays (including clinical performance) and statistical analysis variable the WG looked at intended context of use, dependent variable, independent variable.
- Study population: sample size, age, sex, diet, gestation, medications, no-AD comorbidities.
- Insights from this exercise are: comprehensive pre-analytical variables are lacking in original research studies; the purpose of those original research studies were not designed to study pre-analytical/analytical variables; study of these variables require a specific design. Also learned, study results are due to many factors such as patient population. Can perform a Round Robin to measure assay method and performance difference.
- Should the standardized protocol be applicable to all promising AD blood biomarkers? The most promising biomarkers are NfL, p-tau, t-tau, then amyloid beta.
- Questions posed by the WG:
    1. Should the standardized protocols be analyte and/or method specific?
    2. If so, what blood analytes and methods should these standardized protocols include?
    3. Can we establish best pre-analytical protocols form the literature or do we need to test them in new studies?

        Henrik Zetterberg suggested to design a study for a gold standard from sample collection and nBT/1 0 3ngT 11.04 Tf1 0 0 1 144.02 419.71 Tm0 g0 G[Fo)-2(r t)-2(

Sid O' Bryant commented that standardization might be unlikely. Some of the protocols used from the research wont translate to clinical. Ex. Quest Diagnostics parameters around markers can vary.

Henrik suggested to design a study where they mimic Quest Diagnostic procedures and compare that to what the group determines is the gold standard.

Sid will ask Quest Diagnostics for their protocol and Michelle will work with Sid. Henrik will send the publication in DaDM on comparison of transport to the GBSC and SABB. Charlotte Teunnison volunteered to participate and will do in parallel the same for amyloid.

This will be a comparison of an ultimate protocol vs. real world protocol.

Preview of Vision for Round Robin Testing of Blood Samples as part of QC Program Expansion – Kaj Blennow

- Primary aim is to examine how the assays compare, how tightly they correlate to measure Aβ42 and Aβ40.
- 70 individual plasma samples comparing ~ 10 different methods.
- Plan to have the results by March and would like to present at AAIC 2019.
- Would like to expand the QC for blood, they will take on labs that are focused on blood but it is has to be assays that are generally available. They will need 3-4 labs that are using the same assay for participation.

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- Goals of the meeting are to: 1.) Gather hard data and the literature available; 2.)