Supplementary Online Content

Skillbäck T, Rosén C, Asztely F, Mattsson N, Blennow K, Zetterberg H. Diagnostic performance of cerebrospinal fluid total tau and phosphorylated tau in Creutzfeldt-Jakob disease: results from the Swedish Mortality Registry. *JAMA Neurol*.
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eMethods. Biochemical measurements and statistical analysis

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods.

Biochemical Measurements

The coefficients of variation (CVs) of the assays for T-tau and P-tau were determined by analysing records of measurements of internal control samples that are routinely carried out at the lab at Mölndal at least twice a week. Control samples are kept in frozen aliquots and reused until depleted and then exchanged. Standard deviations of the averages of all measurements from each control sample were calculated and an average of these standard deviations was used to represent a CV for every analysis.

For T-tau seven different low, and six different high controls were used. The low controls measured standard deviations of 8.04%, 8.69%, 10.94%, 8.66%, 9.67%, 9.88% and 9.01%, resulting in a mean CV of 9.27%. The high controls measured standard deviations of 19.41%, 4.57%, 7.56%, 13.95%, 10.73% and 9.62%, resulting in a mean CV of 10.97%. The total average of the T-tau measurements was calculated to 10.35%.

For P-tau seven different low, and seven different high controls were used. The seven low controls measured standard deviations of 9.06%, 8.22%, 9.20%, 11.79%, 8.54%, 11.68% and 11.04%, giving a mean CV of 9.94%. The high controls measured standard deviations of 9.80%, 15.49%, 8.91%, 9.30%, 8.47%, 8.85% and 9.38%, giving a mean CV of 10.03%. The total average of the P-tau measurements was calculated to 10.19%.

No measureable longitudinal drift was registered for any of the analyses.

Statistical Analysis

The associations between biomarker levels and possible confounding demographic factors (age and sex) were tested by non-parametric statistics (Spearman correlation and Mann-Whitney U test). Group comparisons of age, biomarker levels and survival were done by Mann-Whitney U and T-test. The associations between diagnosis (dichotomous) and biomarker levels were tested by logistic regression, adjusted for age and sex. The associations between biomarker levels and age, sex and survival were tested by multiple regressions. Biomarker accuracies were calculated as sensitivity, specificity and LR+. The sensitivity was the proportion that tested positive among all true positives (according to the Swedish mortality registry), the specificity was the proportion that tested negative among all true negatives and the LR+ was calculated by sensitivity / (1 − specificity). In addition to using previously defined cut-offs, we determined novel biomarker cut-offs using the Youden index. The Youden index for a cut-off is defined by its sensitivity + specificity -1. Statistical significance was determined at $p < 0.05$.