WP09, Rachel Robinson:

Welcome to the next presentation in the Work Package 9 RECAP Summer School series. As you have already had the opportunity to understand how to create a combine large datasets, the harmonization process, and the differences between one stage and two stage IPD meta-analyses from my colleagues, I will now present some actual findings from an IPD meta-analysis using these methods on ADHD in preterm born children.

This presentation will take a look at the findings of a 1 stage IPD meta-analysis on ADHD symptoms, as well as the results compared to a Finnish register study. We will also consider how the risks of ADHD pertains to all degrees of prematurity. In our IPD we used data from 8 different cohorts that come from 5 different countries. In total we analyzed data from 1385 preterm and 1633 term-born adult, who rated their ADHD symptoms using validated scales in adulthood. The population-based register study uses data from nationwide registers in Finland and comprised 36962 adults who were born preterm and 684739 who were born at term. We followed them from the age 18 and older and identified any hospital treatment or outpatient visit in public specialized care with ADHD as the primary or subsidiary diagnosis. Finally, we will consider the practical implications of these results.

We performed a 1 stage IPD meta-analysis because it takes full advantage of the available data from individual participants without needing to perform additional intermediate steps. The one stage use of random effects allows you to account for within-cohort clustering. The one stage also provides the possibility to immediately see the effects of covariates, which is more time consuming to assess in a two stage. Furthermore, it avoids the assumption of normally distributed study effect estimates with known variances that are usually made in the second stage of the two-stage approach. Finally, we chose the one stage analysis because overall it also allows greater flexibility of parameter specification over the two-stage approach.
In the register study we used log-binomial regression analysis.
In our one stage and register study data analyses, we adjusted for participant age, sex and parental education.
We tested the interactions with sex, as male dominance in childhood symptoms and disorder have been observed. Studies have also shown demonstrated that men and women no longer differ in adulthood in ADHD symptoms in disorder, while other studies have reported that women may experience more symptoms and risk of diagnosis.
We also tested parental education, as low parental education is a risk factor for preterm birth and ADHD symptoms, we wanted to see if the risk was highest in those born preterm to parent's with the lowest education and vice versa.

IPD Meta-Analysis Results
This forest plot show the results across the 8 clinical cohorts using their overall total ADHD symptoms score, which indicates that preterms do not differ in the total number of ADHD symptoms compared to term borns.

IPD Meta-Analysis Results
The same is seen when we look at the inattention and hyperactivity/impulsivity subscales – ultimately no differences between preterm and terms borns.

IPD Meta-Analysis Results
We also analyzed whether preterm and term borns differed in clinically relevant symptoms, in other words, whether or not the participant would likely to obtain a probable clinical ADHD diagnosis, according to the symptom scale manuals.
Here you can see that preterm and term born adults did not differ in ADHD symptoms that were above this clinical cutoff.
Finnish Register study

HOWEVER; when we look at the results from the register study, we see that in the Finnish population-based register study, preterm adults are in fact statistically significantly more likely to obtain a primary or subsidiary diagnosis of ADHD at 18 years of age or older.
Clearly, these are conflicting findings and we need to dig a bit deeper to understand why this might be the case.

When we study different degrees of preterm birth and categorize them in groups, we see in the IPD meta-analyses of the clinical cohorts that extremely preterms had higher risk of probable clinical ADHD in self reports.
The register study shows a similar pattern but the risk is significant in the very preterm group; in the EPT group the relaitve risk is also higher, but the p-value is 0.07; the reason why we do not see a significant difference in theEPT group, is because we only have 10 cases with ADHD in the Ept group.
The figures here show the preterm only analyes, IPD of clinical cohorts on the left panel and the register study on the right panel.
In both analyses, gestational age was associated significantly with risk of ADHD. As you can see, the risk of ADHD above clinical cutoff in self-reports in adulthood and the risk of obatining an ADHD diagnosis in adulthod increase by each declining week of gestation.

When we compared preterm and term born adults in self-reported symptoms in general, we found no differences. This is in conflict with the finding that they are more likely to obtain an ADHD diagnosis in adulthood.
However, those who were born at the lower end of the gestational age spectrum were more likely to have scores that were above the clinical cutoff in the self-reported symptoms and were also more likely to obtain and ADHD diagnosis. This suggests that those preterms born earlier may not have outgrown from ADHD until adulthood.