**Exercises - Day 2 - Workshop on Dose-Response Meta-Analysis**

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**Group 1: Binary outcome**

**Intended Learning Outcomes:**

* Estimate and interpret meta-analysis of non-linear dose-response
* Use a quadratic function and restricted cubic spline function
* Conduct statistical inference (test, confidence) about the non-linear dose-response
* Compute and interpret common measures for quantifying statistical heterogeneity
* Conduct subgroup analyses and apply meta-regression models

**Part I: Non-linear dose-response curves based on aggregated data**

Let’s continue with the aggregated dose-response data from 12 studies investigating the association between body mass index (BMI) measured and the odds of fractures.

**Part I: Non-linear dose-response meta-analysis based on aggregated data**

1. **Quadratic function.** In a dose-response model, use a quadratic function to model the effect of BMI on the odds ratio of fractures.
2. Based on the estimated meta-analytical model, is there any strong indication against a simpler linear trend? What is the result of the test for the overall effect of BMI on the odds ratio?
3. Independenlty of the test result, visualize the estimated dose-response function (odds ratio) with a 95% confidence interval using 25 kg/m^2 as referent.
4. **Restricted cubic spline function.** In a common-effect dose-response model, use restricted cubic splines with 3 knots at fixed percentiles (10th, 50th, 90th) of the overall distribution of BMI to model the effect of BMI on the odds ratio.
5. Based on the estimated meta-analytical model, is there any strong indication against a simpler linear trend? What is the result of the test for the overall effect of BMI on the odds ratio?
6. Independenlty of the test result, visualize the estimated dose-response function (Odds Ratio) with a 95% confidence interval using 25 kg/m^2 units as referent.

**Part II: Quantify the statistical heterogeneity and its impact**

1. Compute and interpret common measures of heterogeneity, such as the Q statistic and Q test, estimate of between-study heterogeneity, and I2, for the meta-analysis of linear trend.
2. Present graphically the observed heterogeneity in linear trend and its implication in terms of mean predicted linear trend, as well as predicted linear trend for a new study.
3. Repeat Questions 1-2 for meta-analysis of non-linear dose-response. Contrast the findings.
4. Consider the study-level covariate *z*. Is there any differential dose-response curve depending on the level of *z*? Perform a subgroup or meta-regression analysis, and present the predicted mean curves conditional on the levels of *z*.