**Subgroup analysis – sample method, urine (1) vs other (0, 2, 3)**

**Meta-analysis (after removing the papers)**

**Stored in the *results* Excel document, *meta\_analysis* sheet, and the forest plot *forestplot\_strongeffect\_ur.pdf*, *forestplot\_strongeffect\_ot.pdf*, and *forestplot\_average\_ur.pdf, forestplot\_average\_ot.pdf***

**Strong effect - urine**

**Random Effects Model:** Provides an OR of 1.2482 with a 95% CI [0.9921; 1.5705], indicating a positive association that approaches statistical significance (p=0.0585), with a slightly broader CI to account for heterogeneity.

**Heterogeneity Assessment**

Tau^2 (0.1539) and Tau (0.3924) estimate the variance among true effect sizes, indicating substantial between-study variability.

I^2 (79.8%): A high percentage of total variation across studies is due to heterogeneity rather than chance, highlighting significant differences in study outcomes.

H (2.23): Confirms significant heterogeneity, suggesting the observed variance is more than twice what would be expected from sampling error alone.

**Test for Heterogeneity**

**Q statistic (74.43) with 15 degrees of freedom and a p-value < .0001** strongly indicates significant heterogeneity among the included studies, justifying the use of a random effects model over a common effect model.

The meta-analysis demonstrates a statistically significant moderate positive association across the included studies in the common effect model, with a slightly less significant result in the random effects model. The presence of substantial heterogeneity, evidenced by the high I^2 value and the significant Q test, suggests that the effect sizes vary significantly across different study settings or populations.

The random effects model, which provides a slightly lower OR than the common effect model, is more appropriate given the significant heterogeneity among the studies. This model adjusts for the variability in effect sizes, offering a more nuanced interpretation of the overall effect that considers differences among the studies.

Given the observed heterogeneity, readers should consider the specific contexts of the individual studies when interpreting the overall effect size. The significant overall effect suggests a genuine association, but the variability among studies underscores the need for cautious interpretation and further investigation into the sources of heterogeneity.

**Average Effect - urine**

**Random Effects Model**: Provides an OR of 1.1566 with a 95% CI [0.9561; 1.3992], suggesting a positive association that is not statistically significant (p=0.1343), with a broader CI reflecting the variability in effect sizes across studies.

**Heterogeneity Assessment**

Tau^2 (0.0933) and Tau (0.3055) estimate the variance among true effect sizes, indicating substantial between-study variability.

I^2 (76.9%): A high percentage of the total variation across studies is due to heterogeneity rather than chance, highlighting significant differences in study outcomes.

H (2.08): Confirms significant heterogeneity, suggesting the observed variance is more than twice what would be expected from sampling error alone.

**Test for Heterogeneity**

**Q statistic (64.84) with 15 degrees of freedom and a p-value < .0001** strongly indicates significant heterogeneity among the included studies, justifying the use of a random effects model over a common effect model.

The meta-analysis demonstrates a statistically significant moderate positive association across the included studies in the common effect model, with a less significant result in the random effects model due to accounting for heterogeneity. The presence of substantial heterogeneity, as evidenced by the high I^2 value and the significant Q test, suggests that the effect sizes vary significantly across different study settings or populations.

The random effects model provides a more nuanced estimate of the overall effect size, considering the significant heterogeneity among the studies. Despite the broader confidence interval and the lack of statistical significance in the random effects model, the trend toward a positive association remains, though it should be interpreted with caution due to the variability among study results.

Given the observed heterogeneity, readers should consider the specific contexts of the individual studies when interpreting the overall effect size. The results suggest a genuine association, but the variability among studies underscores the need for cautious interpretation and further investigation into the sources of heterogeneity.

**Strong effect – Other**

**Common Effect Model and Random Effects Model:** Both models yield an identical OR of 1.9956 with a 95% CI [1.4101; 2.8243], statistically significant with a z-score of 3.90 and a p-value < 0.0001. This indicates a strong and statistically significant positive association across the included studies, suggesting that the exposure or intervention is associated with an increased odds of the outcome.

**Heterogeneity Assessment**

Tau^2: Estimated at 0, with a confidence interval ranging from 0.0000 to 1.6115. This indicates no estimated between-study variance, suggesting that any observed differences among study outcomes could be attributed to sampling variability rather than actual heterogeneity.

I^2: 0.0%, with a confidence interval from 0.0% to 89.6%. The point estimate suggests no heterogeneity, but the wide confidence interval indicates uncertainty about the extent of heterogeneity.

H: The value of 1.00 (with a CI from 1.00 to 3.10) further suggests that the observed variance is as expected under the sampling error alone, though the confidence interval allows for potential heterogeneity.

**Test for Heterogeneity**

**Q statistic (0.44) with 2 degrees of freedom and a p-value of 0.8036** indicates no significant heterogeneity among the included studies. This finding supports the similarity of the common and random effects model results.

The meta-analysis demonstrates a strong and statistically significant positive association across the three studies analyzed, with an overall effect size suggesting that the exposure or intervention is associated with nearly double the odds of the outcome. The absence of significant heterogeneity, as indicated by the Q test and tau^2 estimate, suggests that the study results are consistent across the studies included.

However, the limited number of studies (k=3) and the wide confidence interval for I^2 caution against overinterpreting the homogeneity of effects. The wide confidence interval for I^2, extending up to 89.6%, highlights the potential for substantial heterogeneity that this small sample of studies might not adequately represent. Therefore, conclusions drawn from this meta-analysis should be considered in light of its limitations, including the small number of studies and the potential for underestimated heterogeneity. Further research, incorporating more studies, could provide a more comprehensive assessment of the effect size and its consistency across different populations and settings.

**Average Effect – Other**

**Common Effect Model and Random Effects Model:** Both models yield an identical OR of 1.9142 with a 95% CI [1.3526; 2.7090], statistically significant with a z-score of 3.66 and a p-value of 0.0002. This indicates a strong and statistically significant positive association across the included studies.

**Heterogeneity Assessment**

Tau^2: Estimated at 0, suggesting no between-study variance and, therefore, no heterogeneity among the study outcomes beyond what can be attributed to sampling error.

I^2: 0.0%, indicating no heterogeneity among the studies. However, the confidence interval for I^2 stretches up to 89.6%, reflecting the uncertainty about the extent of heterogeneity due to the small number of studies.

H: The value of 1.00 supports the absence of significant heterogeneity, although the confidence interval (up to 3.10) allows for the possibility of heterogeneity.

**Test for Heterogeneity**

Q statistic (0.62) with 2 degrees of freedom and a p-value of 0.7333 suggests no significant heterogeneity among the included studies, supporting the similarity of the common and random effects model results.

The meta-analysis demonstrates a strong and statistically significant positive association across the three studies analyzed, with an overall effect size suggesting that the exposure or intervention is associated with nearly double the odds of the outcome. The absence of significant heterogeneity, as indicated by both tau^2 and the Q test, supports the consistency of the effect across studies.

However, the limited number of studies (k=3) and the wide confidence interval for I^2 caution against overinterpreting the homogeneity of effects. The confidence interval for I^2, reaching up to 89.6%, highlights potential for substantial heterogeneity not captured by this analysis. Therefore, while the findings indicate a significant positive association, they should be interpreted with caution, considering the small sample size and potential for underestimated heterogeneity. Further research incorporating more studies could provide a more comprehensive understanding of the effect size and its consistency across different populations and settings.