**Subgroup analysis – nation Case control vs Cross sectional**

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

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

**Strong effect – Case control**

**Random Effects Model**: Provides an OR of 1.3978 with a 95% CI of [1.1185; 1.7467]. This model, accounting for between-study variability, suggests a slightly stronger association than the common effect model but with a wider CI, reflecting greater uncertainty due to heterogeneity.

**Heterogeneity Assessment**

Tau^2 (0.1375) and Tau (0.3707) estimate the variance among true effect sizes, indicating significant between-study variability.

I^2 (81.9%): A high percentage of the total variation across studies is due to heterogeneity rather than chance, suggesting considerable differences in study outcomes.

H (2.35): Confirms substantial heterogeneity, indicating the total variance is more than twice what would be expected from sampling error alone.

**Test for Heterogeneity**

Q statistic (71.69) with 13 degrees of freedom and a p-value < 0.0001 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, with both common and random effects models indicating a genuine effect. However, the presence of substantial heterogeneity, as evidenced by the I^2 statistic and the Q test, suggests that the effect sizes vary significantly across different settings or populations.

The random effects model provides a more accurate estimate of the overall effect size, considering the significant heterogeneity among the studies. This model's adjusted OR is higher than that of the common effect model, reflecting a potentially stronger association when accounting for 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 significant overall effect suggests a true association, but the variability among studies underscores the need for cautious interpretation and further investigation into the sources of heterogeneity.

**Average Effect – Case control**

**Random Effects Model**: an OR of 1.2757 with a 95% CI [1.0528; 1.5458]. This model accounts for heterogeneity among the studies and also indicates a statistically significant moderate positive association, albeit with a slightly wider CI reflecting the variability in effect sizes across studies. The p-value of 0.0130 confirms the statistical significance of this effect.

**Heterogeneity Assessment**

Tau^2 (0.0932) and Tau (0.3053) estimate the variance among the true effect sizes, suggesting a considerable level of between-study variability.

I^2 (79.2%): Indicates a high proportion of the total variability in study estimates is due to heterogeneity rather than chance, highlighting substantial differences in study outcomes.

H^2 (2.19): Confirms significant heterogeneity, suggesting the observed variance is over twice what would be expected from sampling error alone.

**Test for Heterogeneity**

Q statistic (62.43) with 13 degrees of freedom and a p-value < 0.0001 strongly indicates significant heterogeneity among the included studies, supporting the use of the random effects model over the common effect model.

The meta-analysis demonstrates a statistically significant moderate positive association across the included studies, with both the common and random effects models showing a genuine effect. However, 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, providing a slightly higher 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 accurate 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 true association, but the variability among studies underscores the need for cautious interpretation and further investigation into the sources of heterogeneity.

**Strong effect – Cross-sectional**

**Random Effects Model**: an OR of 0.9869 with a broader 95% CI [0.5876; 1.6574], also indicating no significant overall effect when heterogeneity is accounted for. The near-zero z-score (-0.05) and high p-value (0.9601) reinforce the lack of statistical significance.

**Heterogeneity Assessment**

Tau^2 (0.1152) and Tau (0.3394) measure the estimated variance among true effect sizes, suggesting a moderate level of between-study variability.

I^2 (31.7%): Indicates a moderate proportion of the total variation across studies is due to heterogeneity rather than chance. However, this value also suggests that a substantial part of the variation can be attributed to sampling variability.

H^2 (1.21): Further supports the presence of moderate heterogeneity, indicating the observed variance is slightly higher than expected from sampling error alone.

**Test for Heterogeneity**

Q statistic (5.86) with 4 degrees of freedom and a p-value of 0.2102 suggests that the heterogeneity among the included studies is not statistically significant. This result implies that the variability in study outcomes may largely stem from sampling error or within-study variation.

The meta-analysis, involving 5 studies, indicates no statistically significant overall effect of the intervention or exposure under study, as demonstrated by both the common and random effects models. The absence of a significant effect suggests that, on average, the intervention or exposure does not significantly alter the odds of the outcome compared to the control.

The observed moderate heterogeneity (I^2=31.7%) and the non-significant Q test for heterogeneity indicate that while there is some variation among study outcomes, this variability is not substantial enough to impact the overall effect estimate significantly. However, the wide confidence intervals, especially in the random effects model, highlight the uncertainty surrounding the effect size estimates, suggesting that the true effect could range from a slight protective effect to a moderate increase in odds.

Given the limited number of studies and the presence of moderate heterogeneity, these results should be interpreted with caution. Further research, potentially including more studies or a more in-depth examination of the sources of heterogeneity, may be needed to draw more definitive conclusions about the effect of the intervention or exposure.

**Average Effect – Cross sectional**

**Random Effects Model**: an OR of 0.9869 with a broader 95% CI [0.5876; 1.6574], also indicating no significant overall effect when heterogeneity is accounted for. The near-zero z-score (-0.05) and high p-value (0.9601) reinforce the lack of statistical significance.

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