

Before	After
<p>We assessed homoscedasticity between treatments and over time. Our main analysis compared, for the former, the outcome variability between Treated (T) and Control (C) arms at the trial end. For the latter, we compared the variability between Outcome (O) and its Baseline (B) value for the treated arm.</p> <p>To distinguish between random variability and heterogeneity, we fitted a random mixed effects model using the logarithm of the variance ratio at the end of the trial as response with the study as random effect and the logarithm of the variance ratio at baseline as fixed effect (17).</p>	<p>We assessed homoscedasticity between treatments and over time. Our main analysis compared, for the former, the outcome variability between Treated (T) and Control (C) arms at the trial end. For the latter, we compared the variability between Outcome (O) and its Baseline (B) value for the treated arm.</p> <p>To distinguish between the random sampling variability and heterogeneity, we fitted a random-effects model using the logarithm of the outcome variance ratio at the end of the trial as response with the study as random effect and the logarithm of the variance ratio at baseline as fixed effect (17).</p> <p>The main fitted model for between-arm comparison was:</p> $\log\left(\frac{V_{OT}}{V_{OC}}\right)_i = \mu + s_i + \beta \cdot \log\left(\frac{V_{BT}}{V_{BC}}\right)_i + e_i$ <p>with <math>s_i \sim N(0, \tau)</math> and <math>e_i \sim N(0, v_i)</math></p> <p>Where <math>V_{xx}</math> represent the variances of the outcome in each arm (<math>V_{xT}</math>, <math>V_{xC}</math>) at the end of the study (<math>V_{OT}</math>, <math>V_{OC}</math>) and at baseline (<math>V_{BT}</math>, <math>V_{BC}</math>). The parameter <math>\mu</math> is the averaged variance ratio across all the studies; <math>s_i</math> represents the heterogeneity between-study effect associated to study <math>i</math> with variance <math>\tau^2</math>; <math>\beta</math> is the coefficient for the linear association with the baseline variance ratio; and <math>e_i</math> represents the intra-study random error with variance <math>v_i^2</math>.</p> <p>The parameter <math>\mu</math> represents a measure of the imbalance between the variances at the end of the study, which we call heteroscedasticity.</p> <p>The estimated value of <math>\tau^2</math> provides a measure of heterogeneity, that is, to what extent the value of <math>\mu</math></p>

<p>An analogous model was employed to assess the homoscedasticity over time, as such a model allows the separation of random allocation variability from additional heterogeneity.</p>	<p>is applicable to all studies. The larger <math>\tau^2</math> is, the less the homogeneity.</p> <p>The percentage of variance explained by the differences among studies in respect to the overall variance is measured by the <math>I^2</math> statistic. That is:</p> $I^2 = \frac{\tau^2}{\tau^2 + \nu^2}$ <p><math>\nu^2</math> is the expected value of the error variance</p> <p>An analogous model was employed to assess the homoscedasticity over time.</p> <p>As there is only one available measure for each study, both sources of variability cannot be empirically differentiated: (i) within study or random or that one related to sample size; and (ii) heterogeneity. In order to isolate the second, the first was theoretically estimated using the Delta method –as explained in Sections V and VI of <i>Supplementary material</i></p>
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