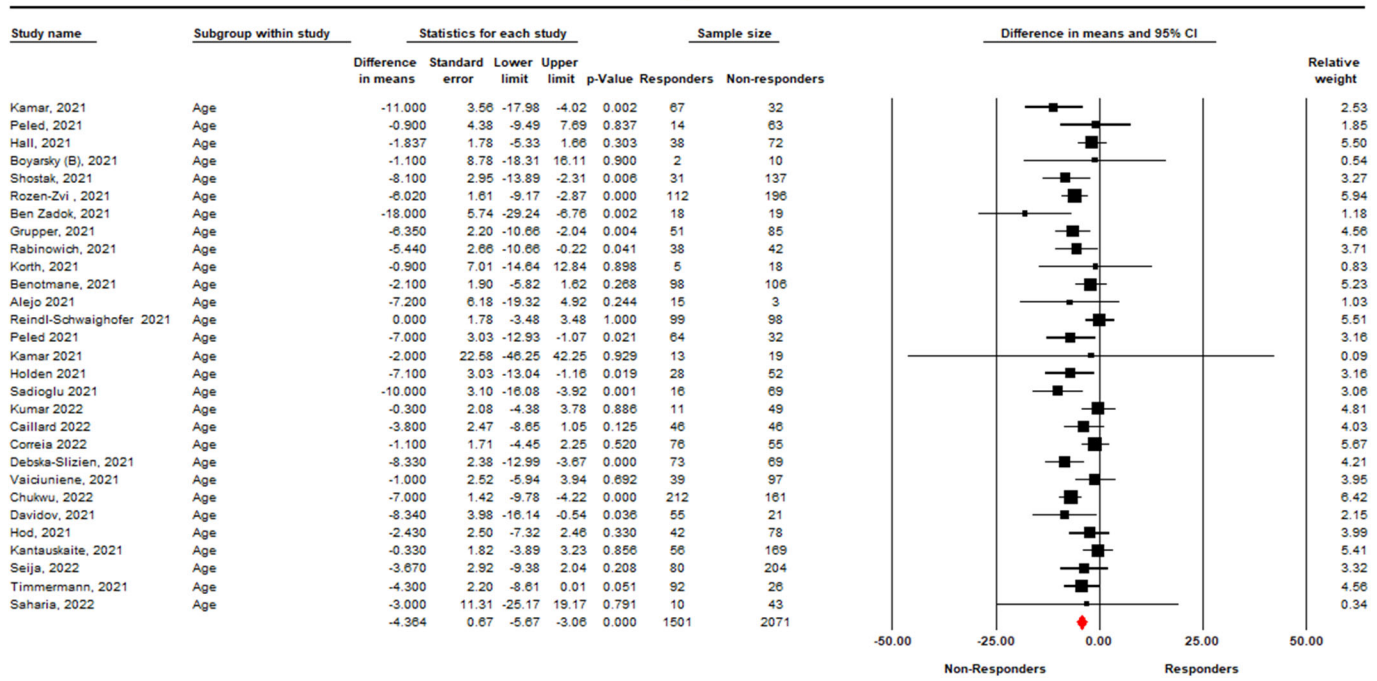


Figure S1. Forest Plots of Studied Risk Factors

Age



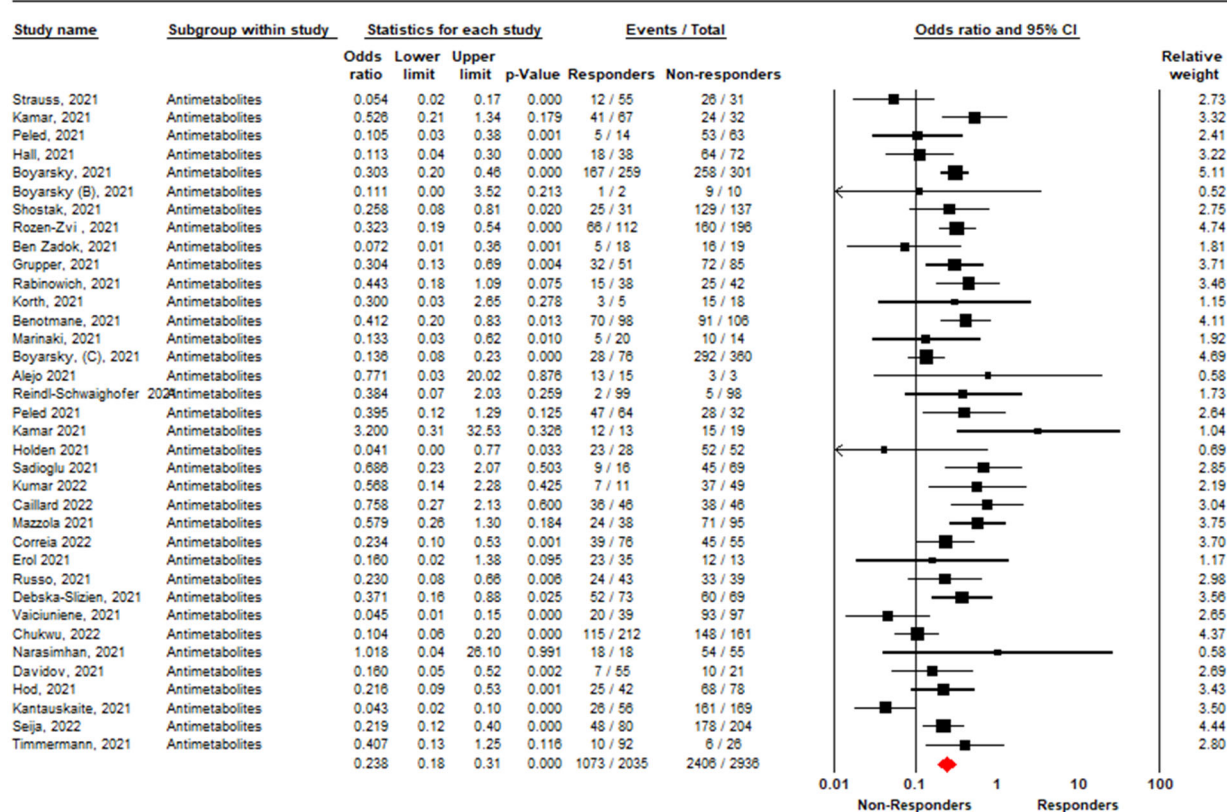
Heterogeneity: $\tau^2=4.94$; $Q=50.05$, $df=28$, $P=0.006$; $I^2=44\%$

#Studies: 29 #Patients: 3572 #Response: 1501

#Diff in mean (95%CI): -4.363 (-5.67 to -3.06) $P < 0.001$

The pooled mean difference of all 29 studies considering age showed that younger age significantly improves the response to vaccine (MD=-4.364, p-value<0.001). The mean age of the vaccine responders was 4.364 years younger than non-responders. Lower age is associated with higher vaccine response. The result showed moderate heterogeneity (p-value=0.006, $I^2=44\%$). The sensitivity analysis was performed (Figure 2, below) and a random effect model was used to show the results are robust.

Antimetabolites



Heterogeneity: $\tau^2=0.30$; $Q=81.54$, $df=35$, $P<0.001$; $I^2=57\%$

#Studies: 36 #Patients: 4971

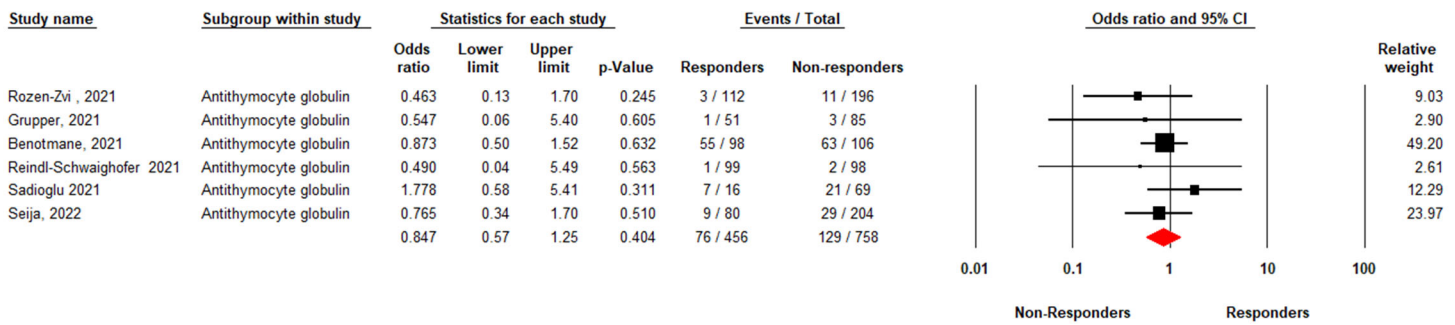
#Responders: 1073/2035 #Non-responders: 2406/2936

#OR (95%CI): 0.238 (0.18 to 0.31) $P < 0.001$

The pooled mean difference of 36 studies considering antimetabolites showed that taking less antimetabolites significantly improves the response to vaccine (OR=0.238, p-value<0.001). Those who showed a response to the vaccine have received 76.6% less antimetabolites than who did not show a response.

The result showed moderate heterogeneity (p-value<0.001, $I^2=57\%$). The sensitivity analysis was performed (Figure 2, below) and a random effect model was used to show the results are robust.

Antithymocyte globulin



Heterogeneity: $\tau^2=0.0$; $Q=2.95$, $df=5$, $P=0.71$; $I^2=0\%$

#Studies: 6 #Patients: 1214

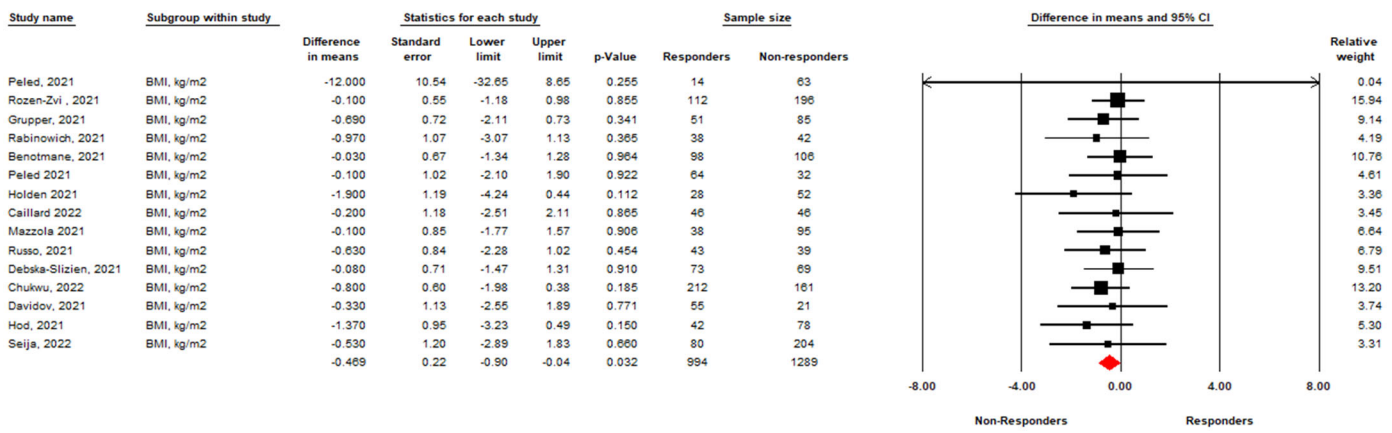
#Responers: 76/456 #Non-responders: 129/758

#OR (95%CI): 0.847 (0.57 to 1.25) P = 0.404

The weighted odds ratio of all 6 studies taking antithymocyte globulin exposure into consideration is 0.847, antithymocyte globulin exposure has no significant effect on the pooled odds of vaccine immune response (pooled p-value=0.4)

The estimated heterogeneity of the model (τ^2) is 0.00 and the percentage of variation across the effect sizes that is due to heterogeneity rather than chance (I^2) is 0% (p-value=0.708)

Body Mass Index



Heterogeneity: $\tau^2=0.0$; $Q=5.75$, $df=14$, $P=0.97$; $I^2=0\%$

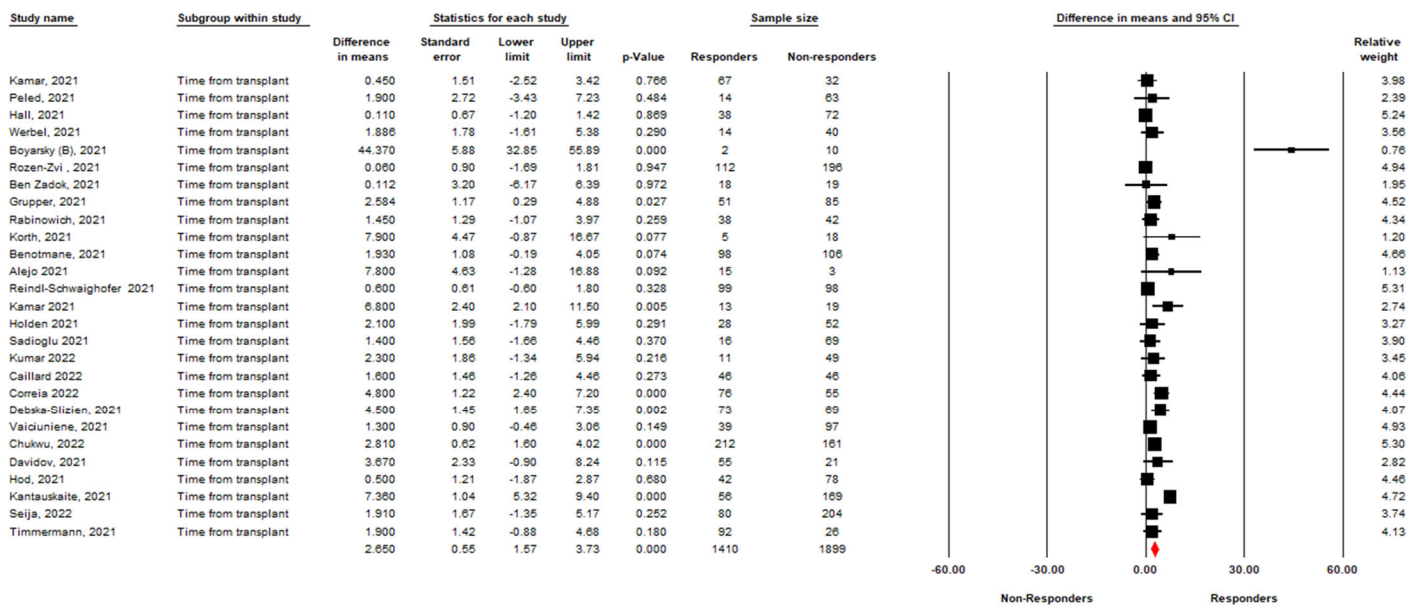
#Studies: 15 #Patients: 2283 #Response: 994

#Diff in mean (95%CI): -0.469 (-0.9 to -0.04) $P = 0.032$

The weighted mean difference of all 15 studies taking BMI into consideration is -0.469 with a pooled standard error of 0.219, responders have 0.469 lower pooled BMI mean difference compared to non-responders (pooled p-value=0.032). Lower BMI is associated with higher vaccine response.

The estimated heterogeneity of the model (τ^2) is 0.00 and the percentage of variation across the effect sizes that is due to heterogeneity rather than chance (I^2) is 0% (p-value=0.972)

Time from transplant

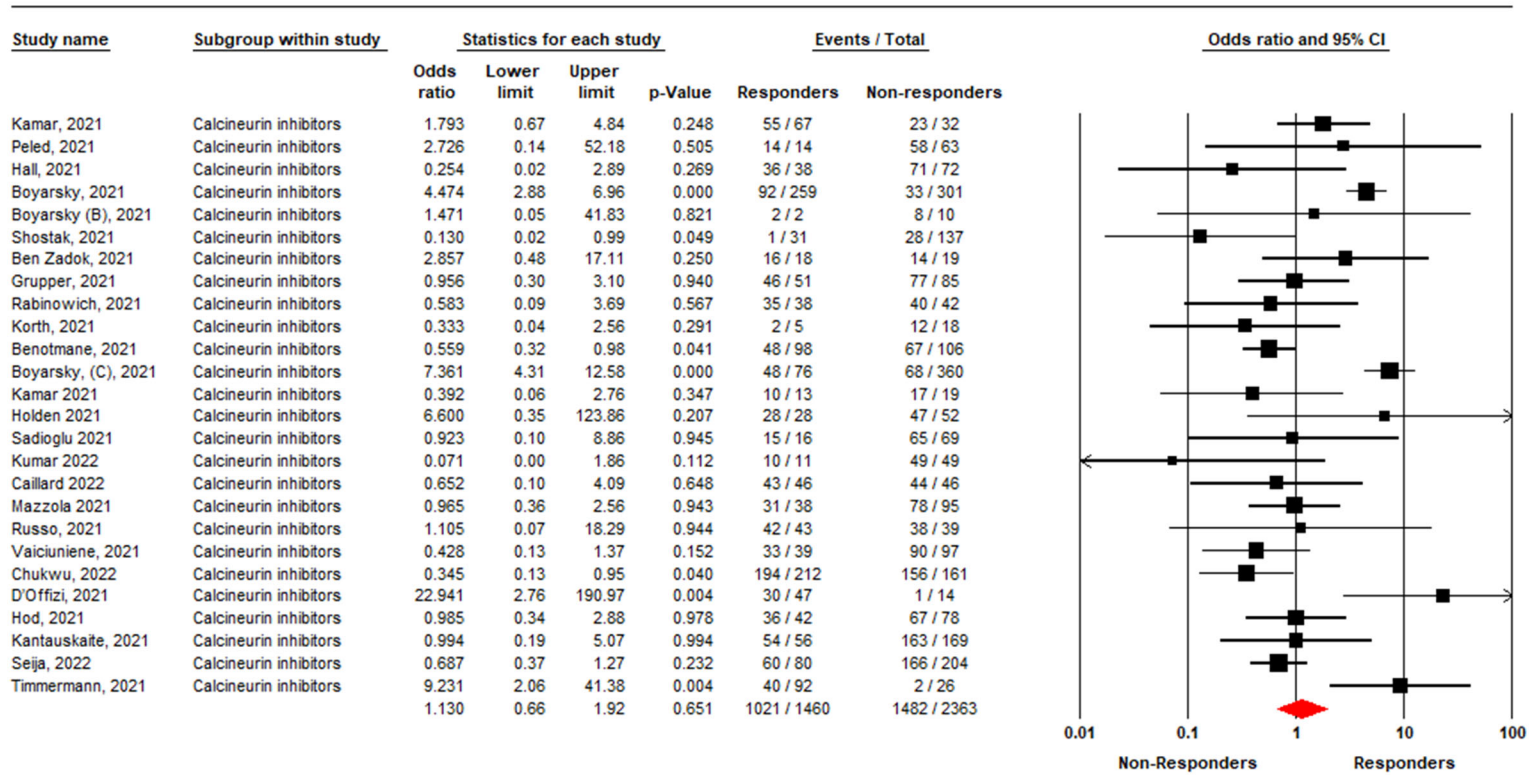


#Studies: 27 #Patients: 3309 #Response: 1410
 #Diff in mean (95%CI): 2.65 (1.57 to 3.73) P < 0.001

The weighted mean difference of all 27 studies taking the time from transplant into consideration is 2.65 years with a pooled standard error of 0.551, the pooled mean difference in time from transplant shows that responders have 2.65 higher years from transplant compared to non-responders (pooled p-value<0.001) higher time from transplant is associated with higher vaccine response.

The estimated heterogeneity of the model (τ^2) is 5.355 and the percentage of variation across the effect sizes that is due to heterogeneity rather than chance (I^2) is 78% (p-value<0.001)

Calcineurin inhibitors



#Studies: 26 #Patients: 3823

#Responders: 1021/1460 #Non-responders: 1482/2363

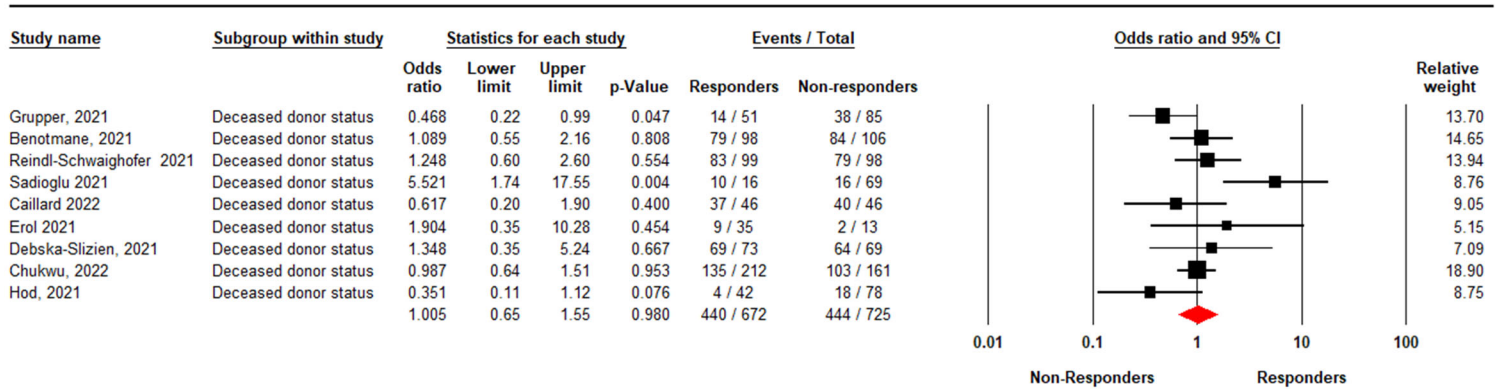
#OR (95%CI): 1.13 (0.66 to 1.92) P = 0.651

The weighted odds ratio of all 26 studies taking calcineurin inhibitors use into consideration is 1.13

The calcineurin inhibitors use at the time of vaccine administration have no significant effect on the pooled odds of vaccine response (pooled p-value=0.651)

The estimated heterogeneity of the model (tau2) is 1.195 and the percentage of variation across the effect sizes that is due to heterogeneity rather than chance (I2) is 79% (p-value<0.001)

Deceased donor status



Heterogeneity: $\tau^2=0.21$; $Q=17.32$, $df=8$, $P=0.027$; $I^2=53.8\%$

#Studies: 9 #Patients: 1397

#Responders: 440/672 #Non-responders: 444/725

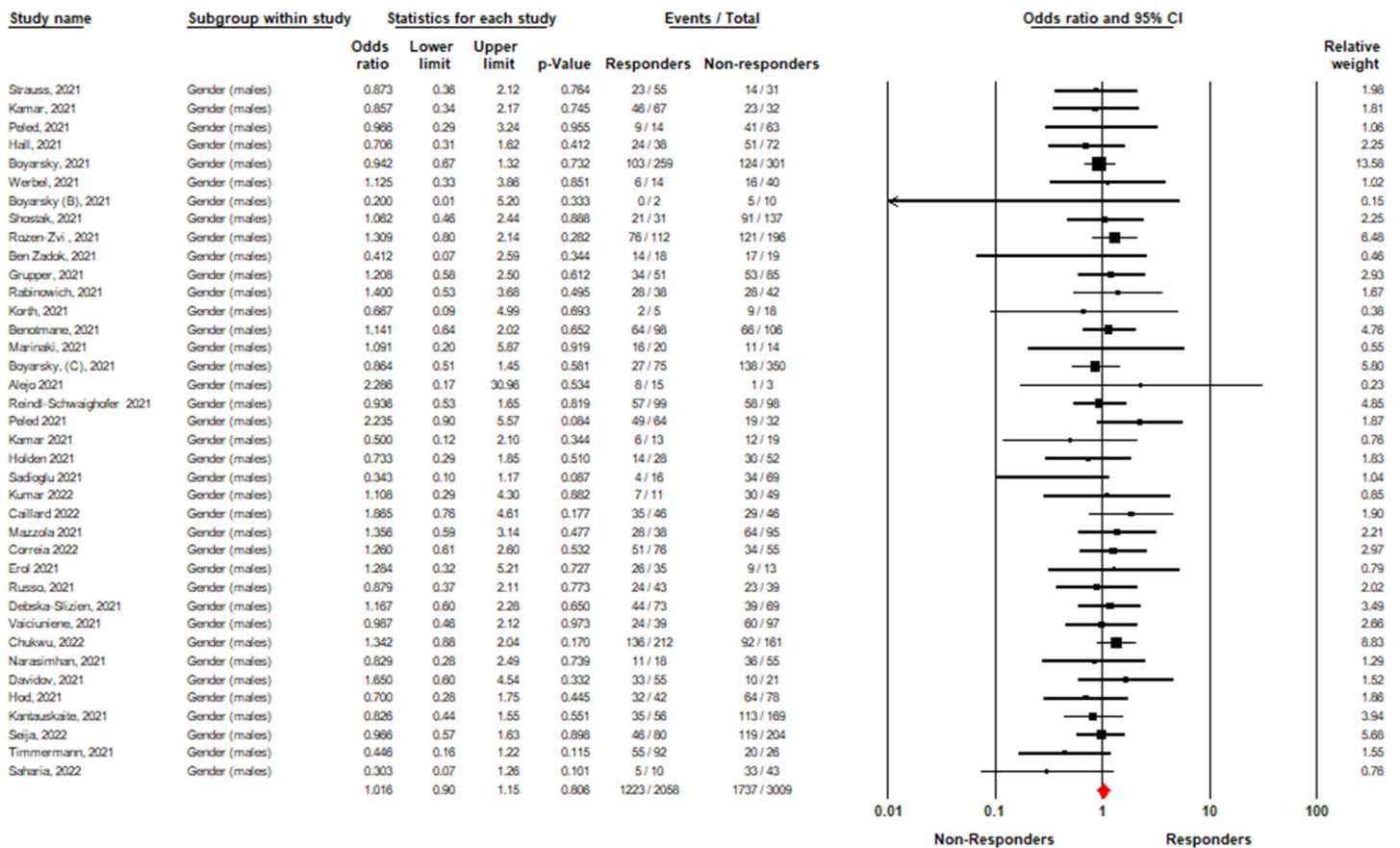
#OR (95%CI): 1.005 (0.65 to 1.55) $P = 0.98$

The weighted odds ratio of all 9 studies taking deceased donor status into consideration is 1.005

Decreased donor status has no significant effect on the pooled odds of vaccine response (pooled p-value=0.98)

The estimated heterogeneity of the model (τ^2) is 0.212 and the percentage of variation across the effect sizes that is due to heterogeneity rather than chance (I^2) is 54% (p-value=0.027)

Gender (Males)



Heterogeneity: $\tau^2=0.0$; $Q=25.28$, $df=37$, $P=0.928$; $I^2=0\%$

#Studies: 38 #Patients: 5067

#Responders: 1223/2058 #Non-responders: 1737/3009

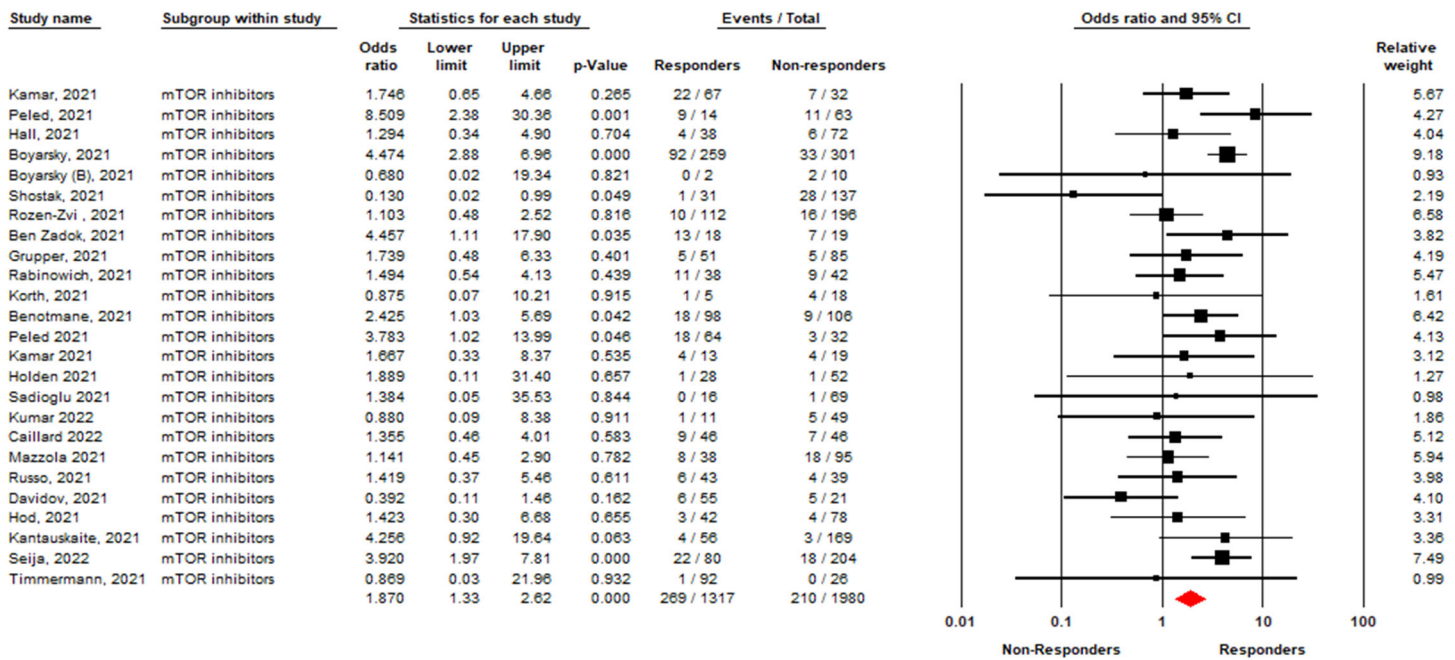
#OR (95%CI): 1.016 (0.9 to 1.15) $P = 0.806$

The weighted odds ratio of all studies taking gender into consideration is 1.016

Gender has no significant effect on the pooled odds of vaccine response (pooled p-value=0.8)

The estimated heterogeneity of the model (τ^2) is 0.000 and the percentage of variation across the effect sizes that is due to heterogeneity rather than chance (I^2) is 0% (p-value=0.928)

mTOR inhibitors



Heterogeneity: $\tau^2=0.27$; $Q=43.04$, $df=24$, $P=0.010$; $I^2=44.2\%$

#Studies: 25 #Patients: 3297

#Responders: 269/1317 #Non-responders: 210/1980

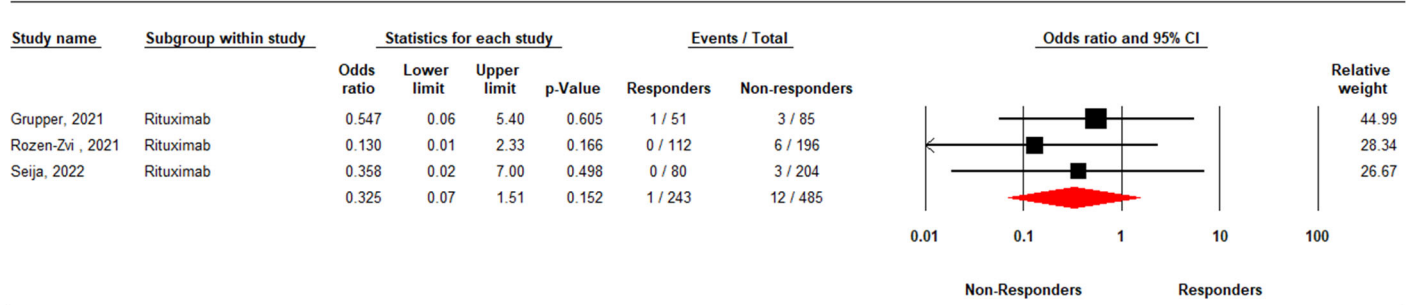
#OR (95%CI): 1.87 (1.33 to 2.62) $P < 0.001$

The weighted odds ratio of all studies taking mTOR inhibitors into consideration is 1.87

mTOR inhibitors significantly increase the pooled odds of vaccine response by 87% (pooled p -value<0.001) Higher mTOR inhibitors is associated with higher vaccine response

The estimated heterogeneity of the model (τ^2) is 0.27 and the percentage of variation across the effect sizes that is due to heterogeneity rather than chance (I^2) is 44% (p -value=0.01)

Rituximab



Heterogeneity: $\tau^2=0$; $Q=0.588$, $df=2$, $P=0.745$; $I^2=0\%$

#Studies: 3 #Patients: 728

#Responders: 1/243 #Non-responders: 12/485

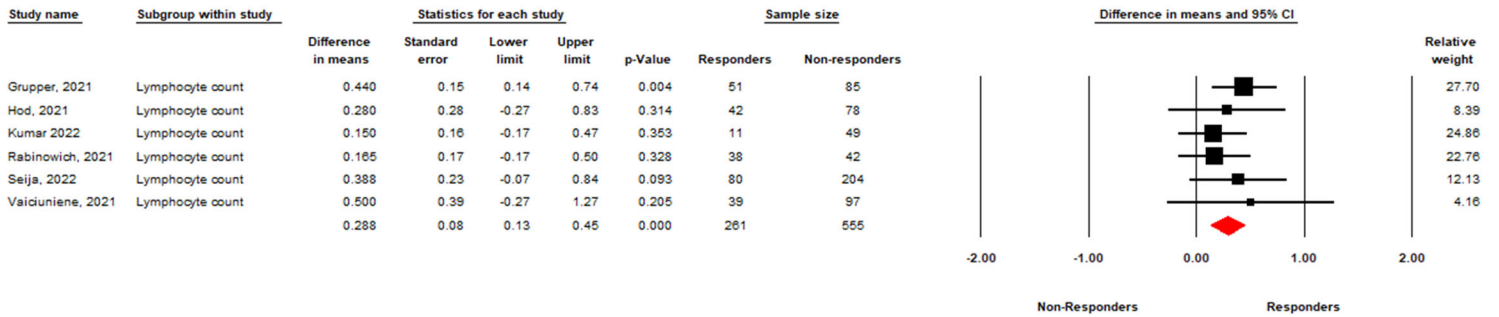
#OR (95%CI): 0.325 (0.07 to 1.51) P = 0.152

The weighted odds ratio of all 3 studies taking Rituximab exposure into consideration is 0.325

Rituximab exposure has on significant effect on the pooled odds of vaccine response (pooled p-value=0.152)

The estimated heterogeneity of the model (τ^2) is 0 and the percentage of variation across the effect sizes that is due to heterogeneity rather than chance (I^2) is 0% (p-value=0.745)

Lymphocyte count



Heterogeneity: $\tau^2=0$; $Q=2.72$, $df=5$, $P=0.743$; $I^2=0\%$

#Studies: 6 #Patients: 816 #Responers: 261
 #Diff mean (95%CI): 0.288 (0.13 to 0.45) $P < 0.001$

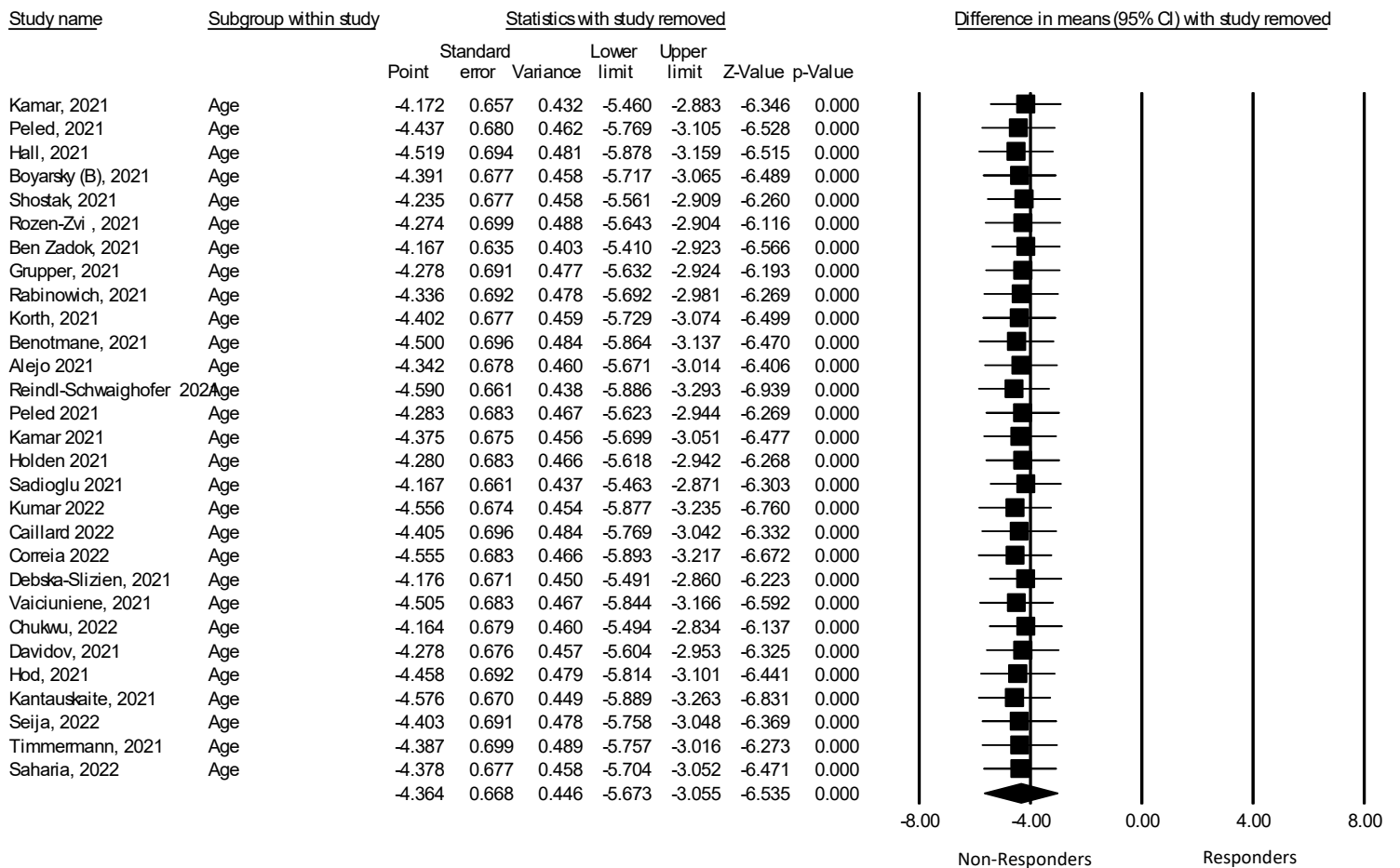
The weighted mean difference of all 6 studies taking lymphocyte count into consideration is 0.288 with a pooled standard error of 0.081, the pooled mean difference in lymphocyte count shows that responders have increased lymphocyte count by 0.288 units compared to non-responders(pooled p-value<0.001). Higher lymphocyte count is associated with higher vaccine response.

The estimated heterogeneity of the model (τ^2) is 0.00 and the percentage of variation across the effect sizes that is due to heterogeneity rather than chance (I^2) is 0% (p-value=0.743)

Figure S2: Sensitivity Analysis

Age

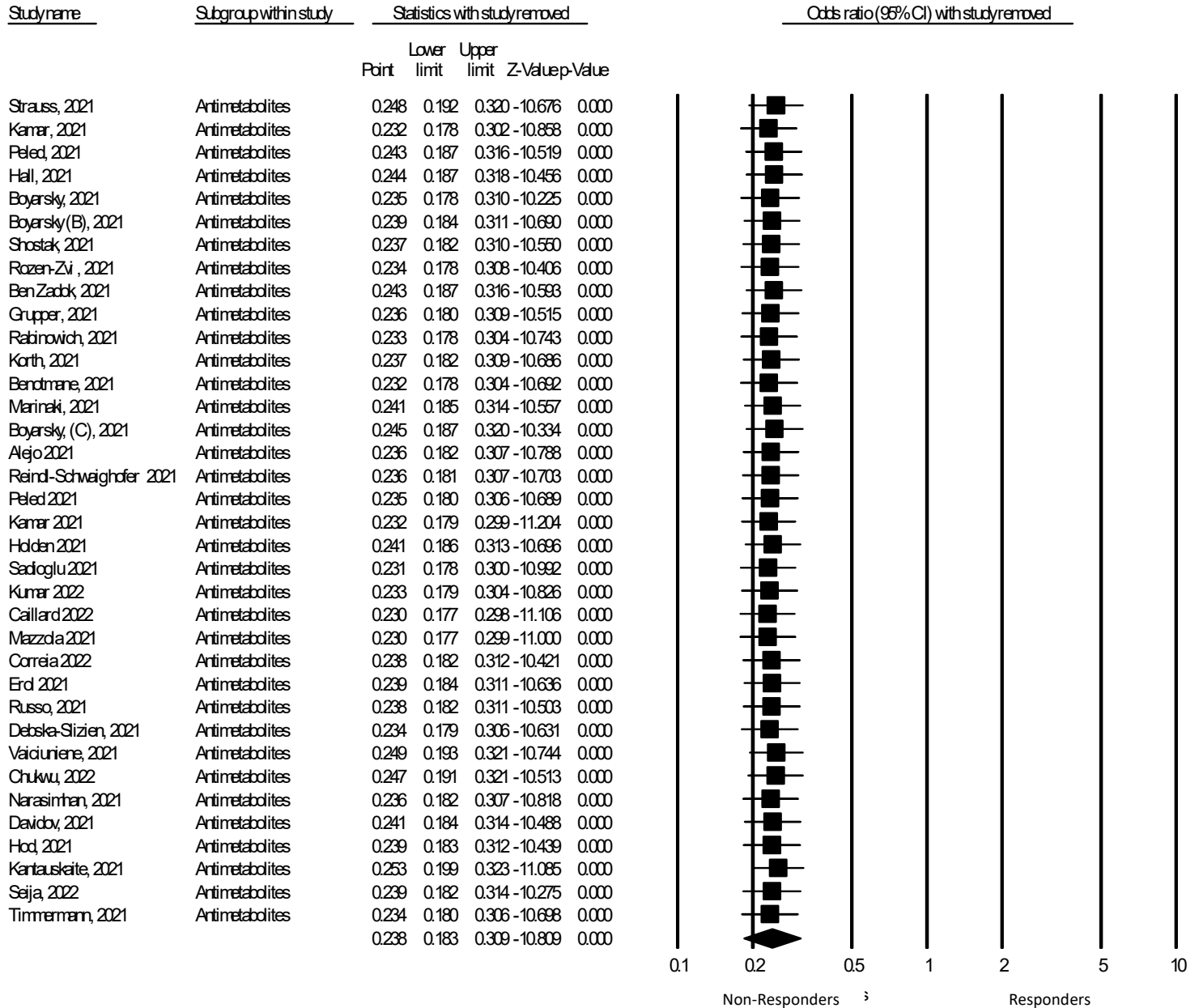
Age sensitivity analysis



After removing one study, the p- value did not lose the significance of the point estimates and this means that there is a high heterogeneity among the studies, and this may lead to a decreased certainty of the results due to wide variability between studies.

Antimetabolites

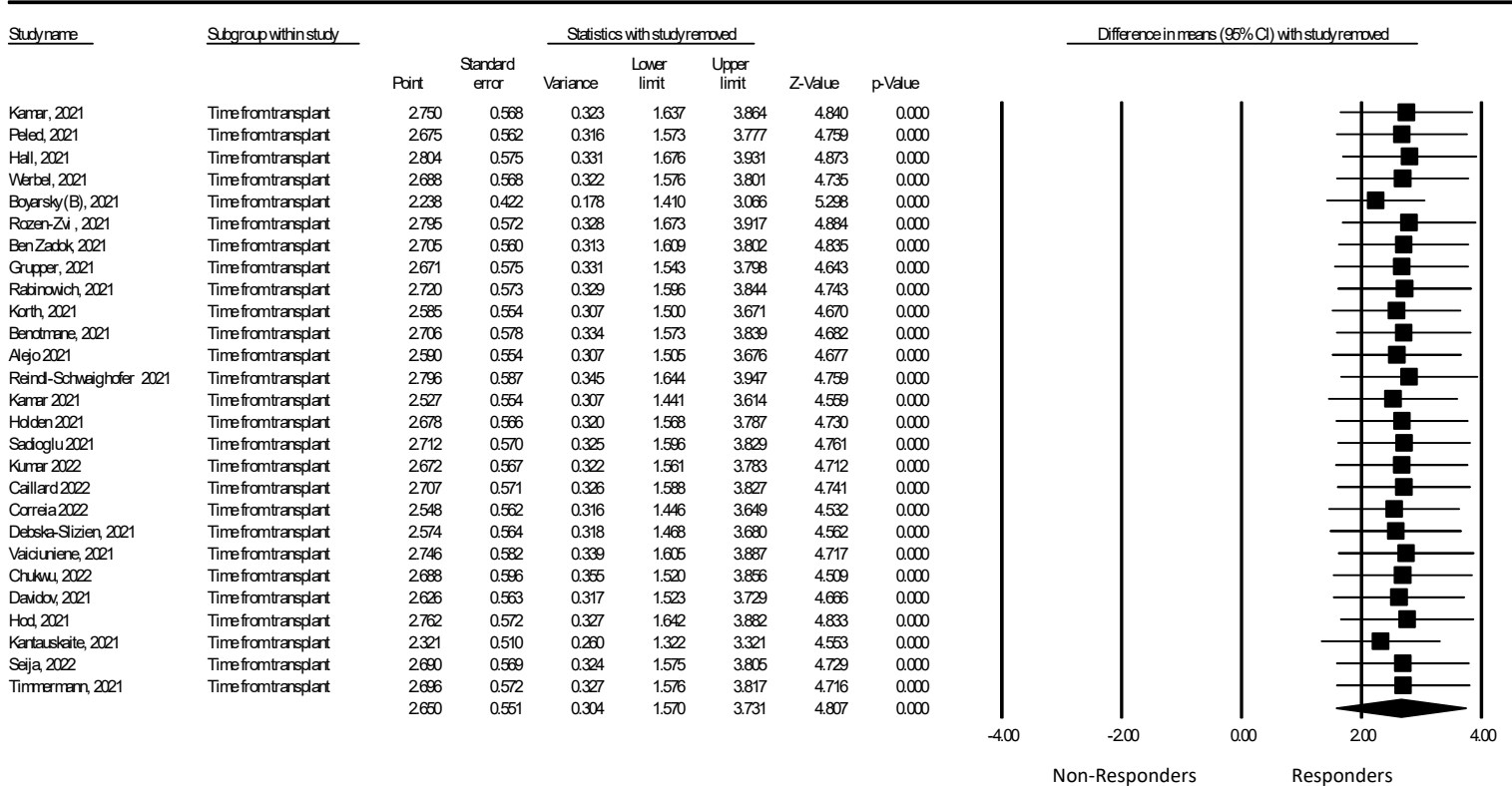
Antimetabolites sensitivity



After removing one study, the p-value did not lose the significance of the point estimates and this means that there is a high heterogeneity among the studies and this may lead to a decreased certainty of the results due to wide variability between studies.

Time from transplant

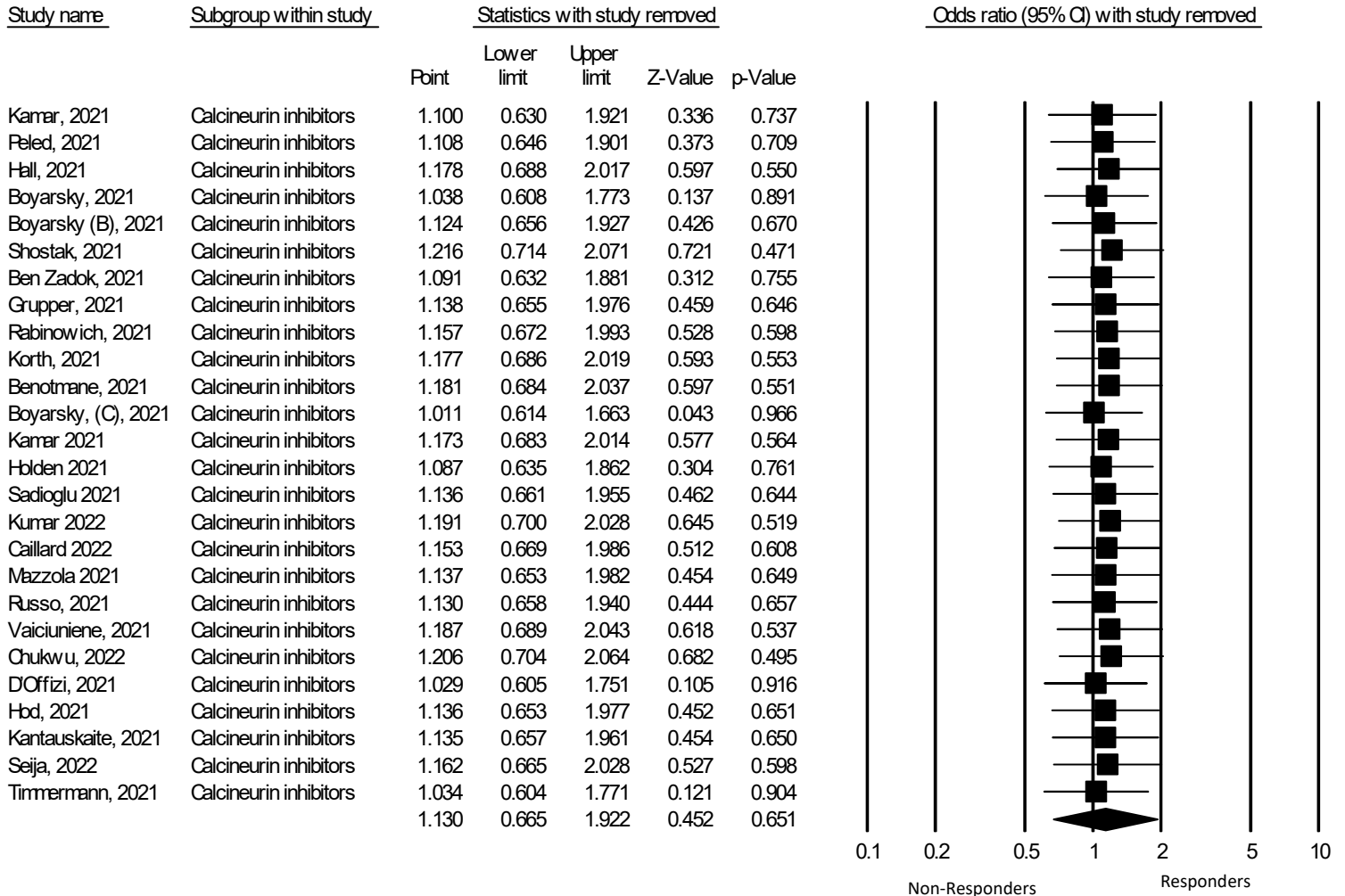
Time from transplant sensitivity



After removing one study, the p- value did not lose the significance of the point estimates and this means that there is a high heterogeneity among the studies and this may lead to a decreased certainty of the results due to wide variability between studies.

Calcineurin

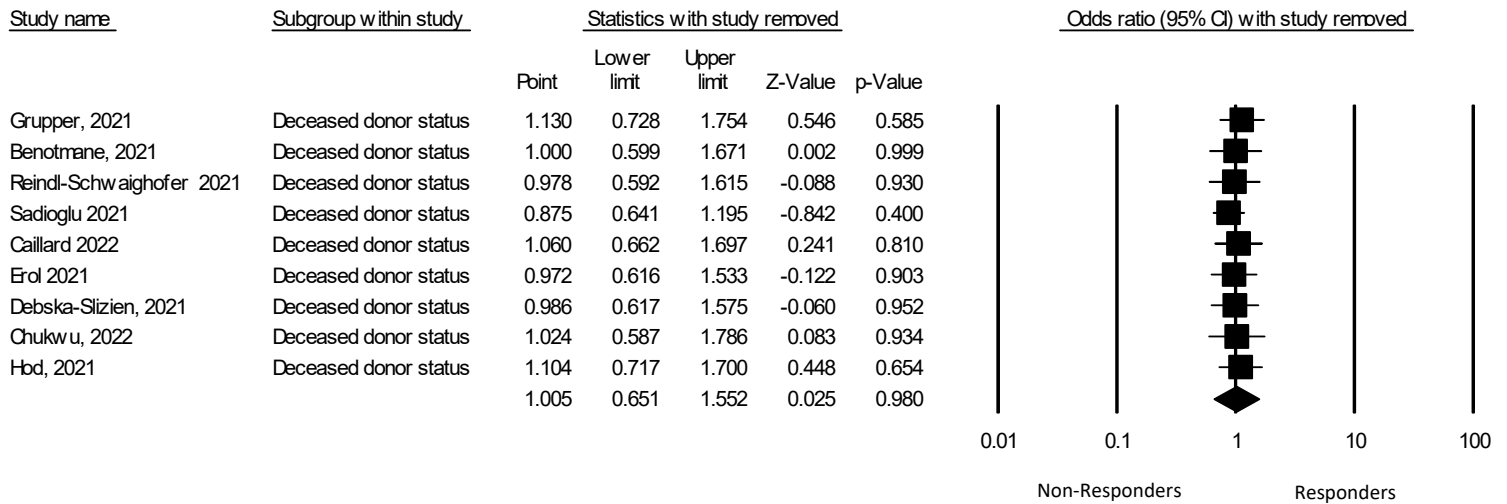
Calcineurin inhibitors sensitivity



After the removal of one study, the significance of the point estimates is lost and this means that the heterogeneity is low and the removed study was causing the increased variability, the results are certain and robust.

Type of donor

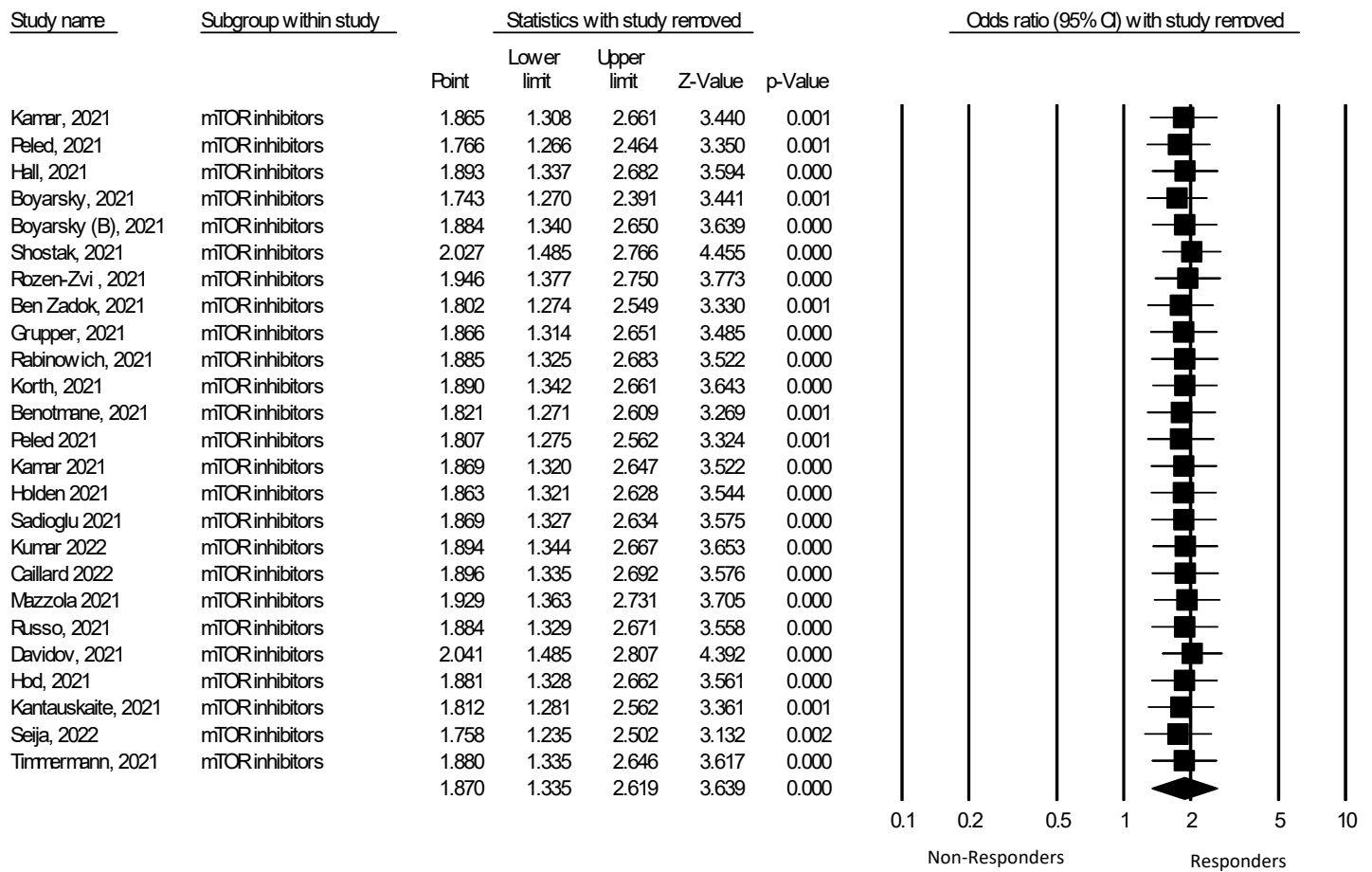
Deceased donor status sensitivity



After the removal of one study, the significance of the point estimates is lost and this means that the heterogeneity is low and the removed study was causing the increased variability, the results are certain and robust.

mTor

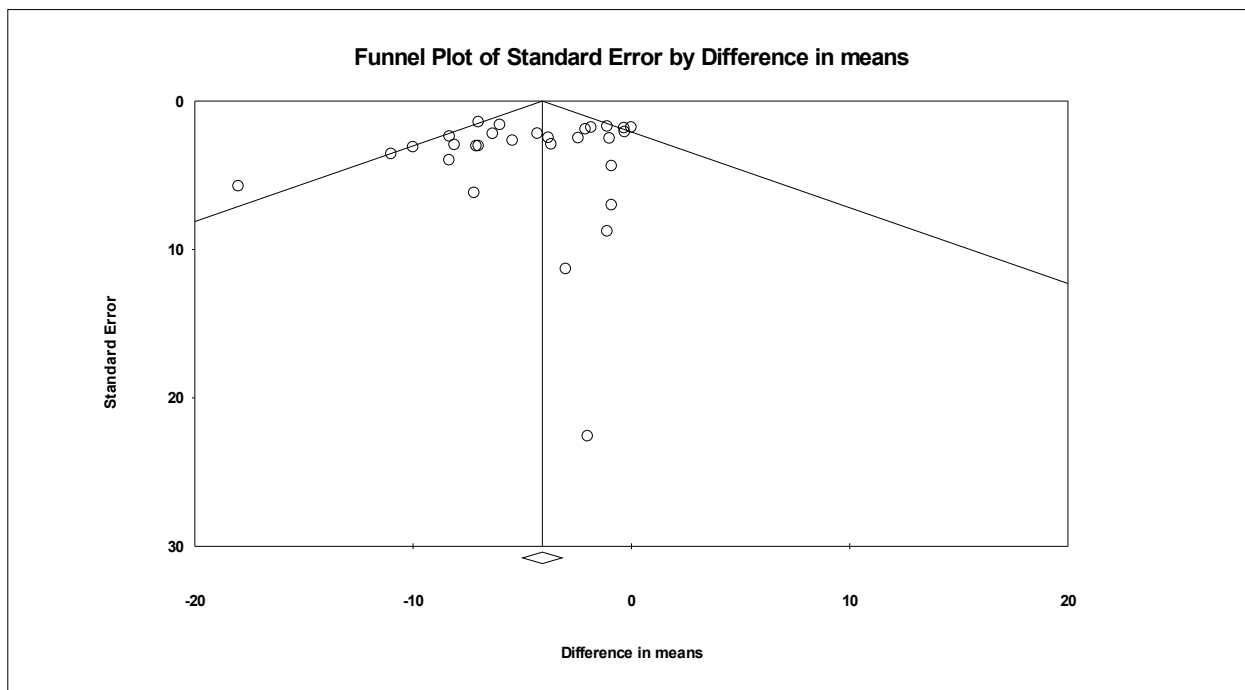
mTOR inhibitors sensitivity



After removing one study, the p- value did not lose the significance of the point estimates and this means that there is a high heterogeneity among the studies, and this may lead to a decreased certainty of the results due to wide variability between studies.

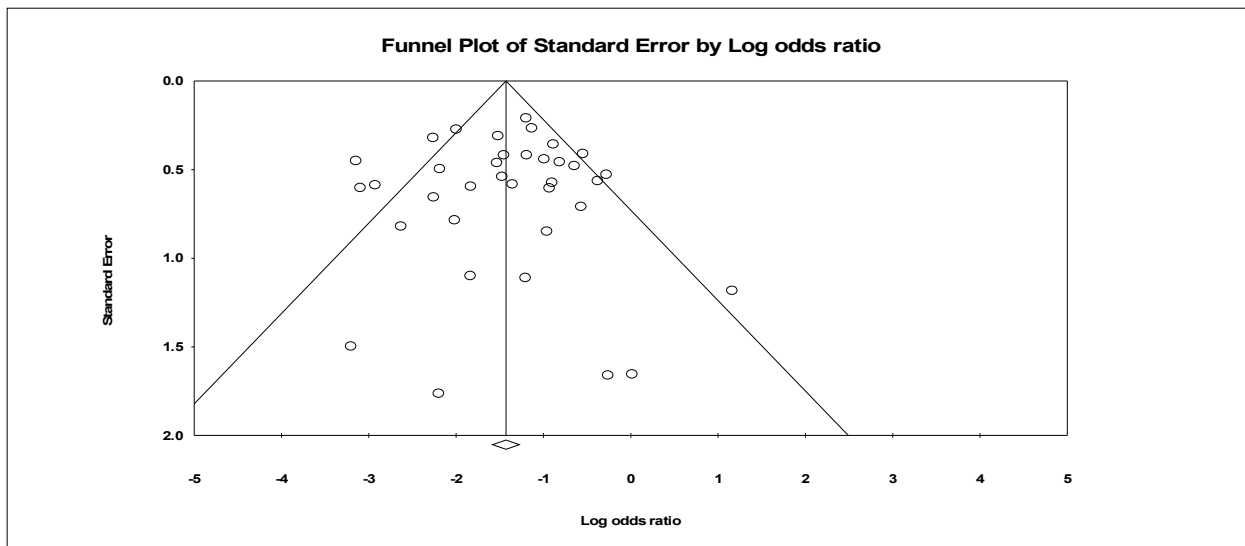
Figure S3: Funnel plots

Age



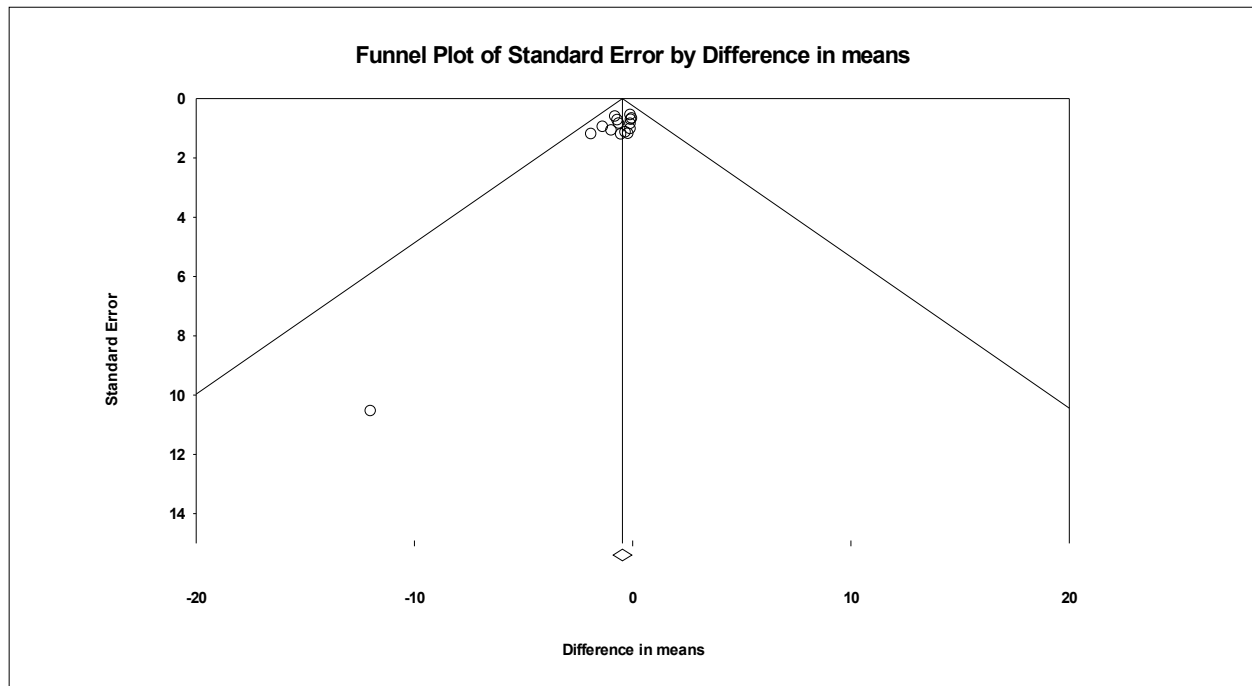
The funnel plot is approximately similar (no publication bias exists), only one study have high standard error.

Antimetabolites



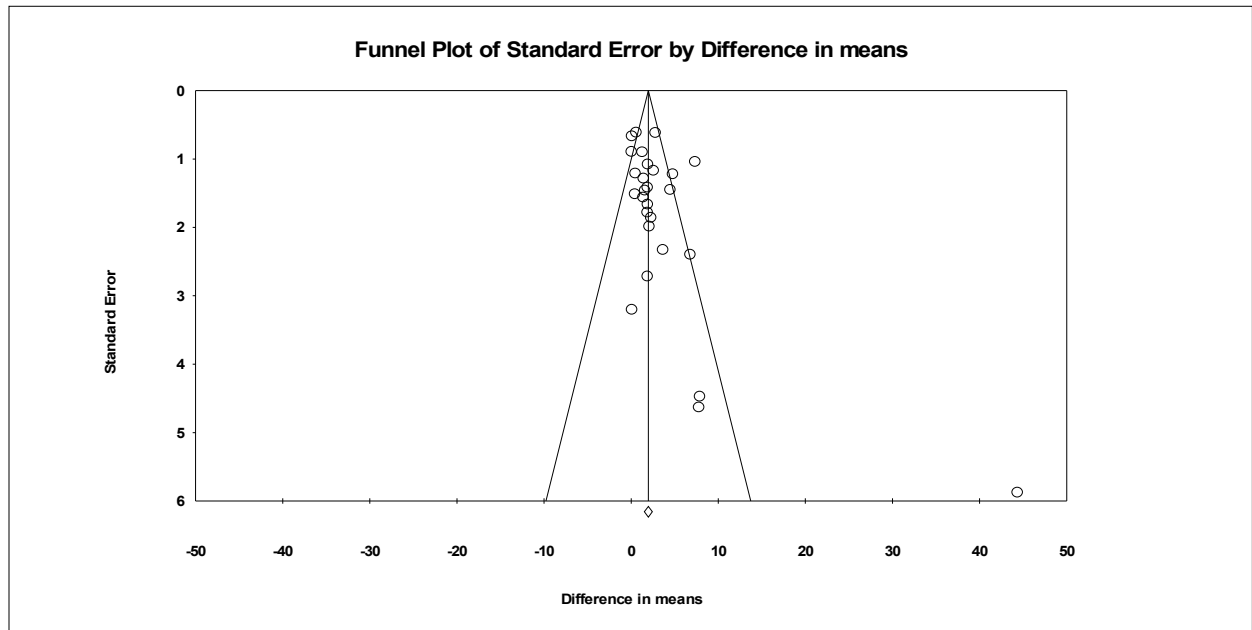
The graph is approximately similar (no publication bias exists)

BMI



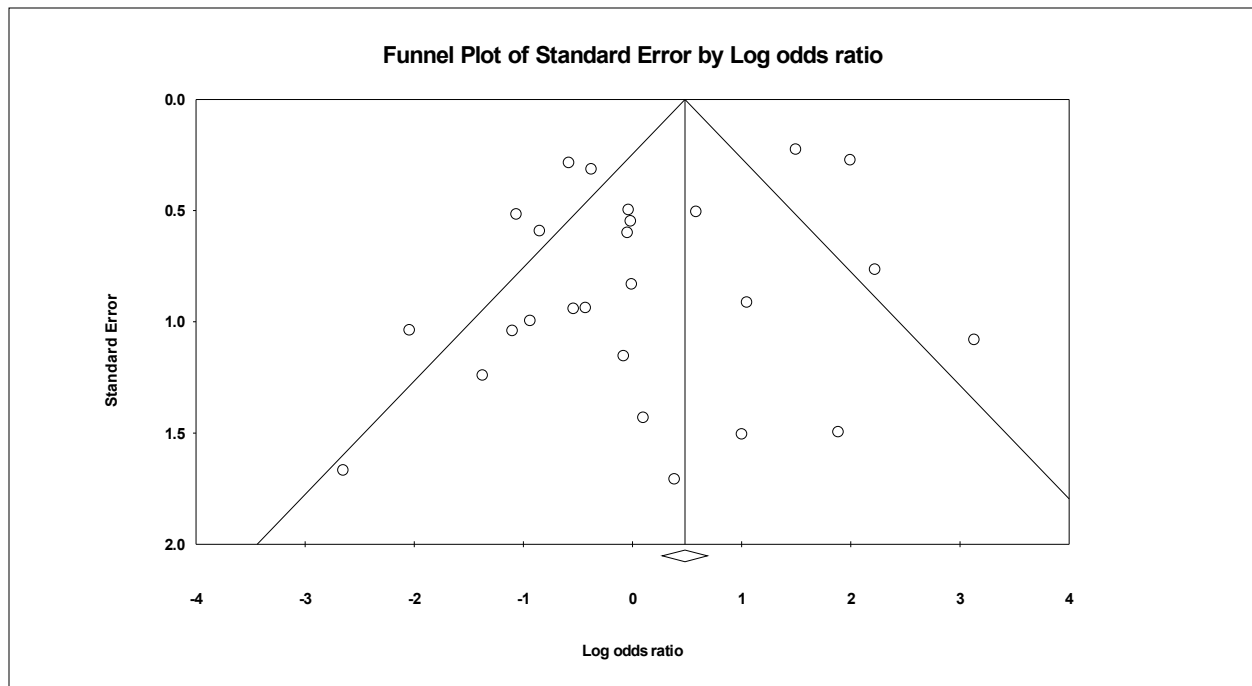
All the studies taking BMI into consideration as an important risk factor for vaccine response are precise and have low standard error, all the studies are situated on the upper part of the funnel plot except one study that has a high standard error.

Time from transplant



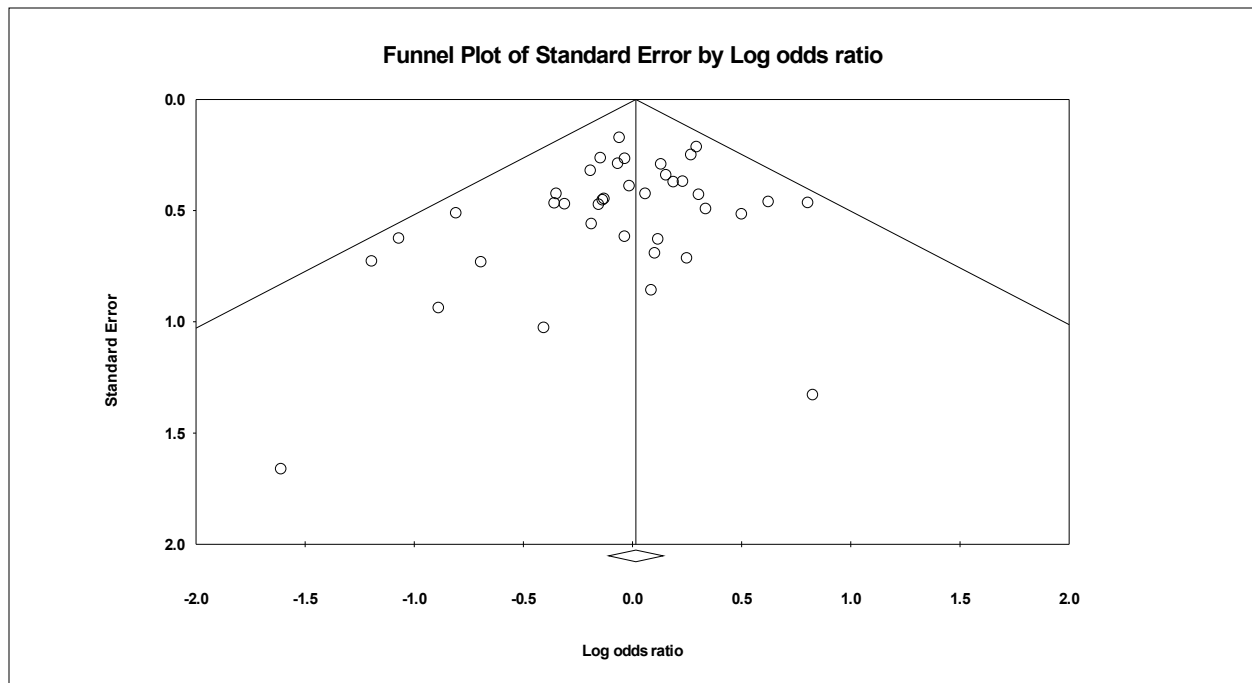
The funnel plot is approximately similar (no publication bias exists)

Calcineurin inhibitors



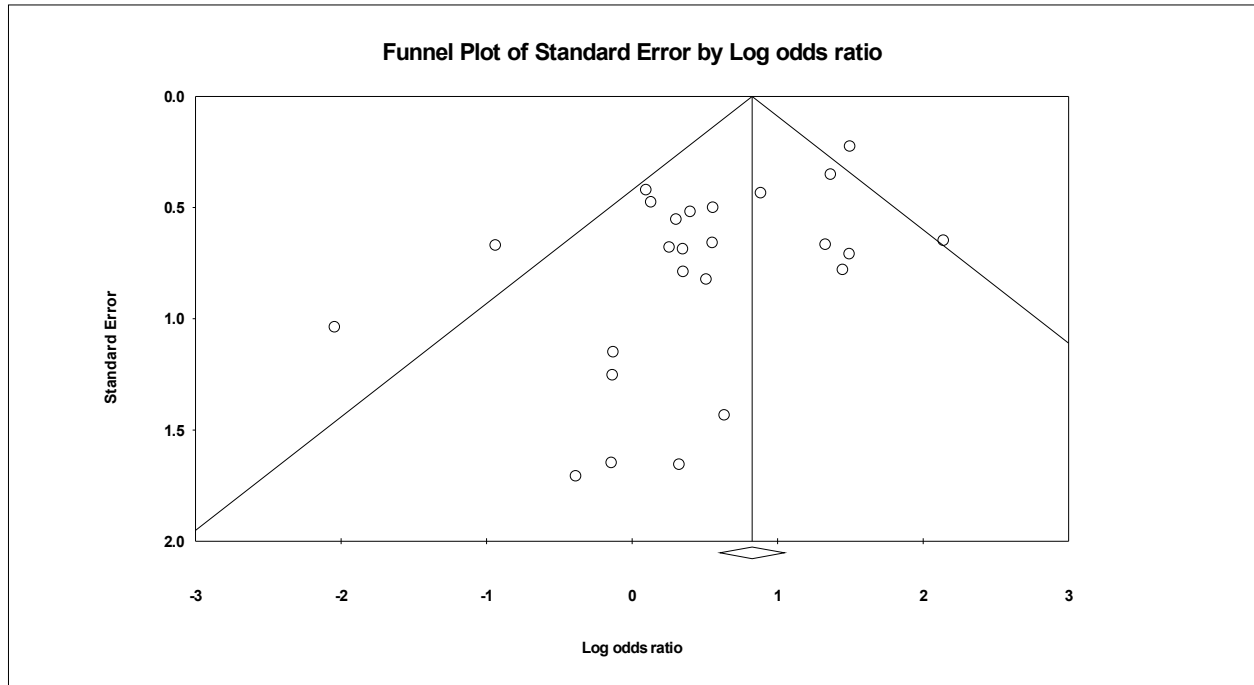
The funnel plot is approximately similar (no publication bias exists)

Gender (males)



The funnel plot is approximately similar (no publication bias exists)

mTOR inhibitors



The funnel plot is not quite similar and this may be due to the presence of a publication bias or a difference in methodological quality between studies used in this plot, these studies may differ in the sample size and this leads to higher heterogeneity between the studies.