

# Meta-Analysis of Vitamin D Receptor Gene Polymorphisms in Childhood Asthma

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We conducted the systematic review to investigate the potential relationship between the vitamin polymorphisms of D receptor (VDR) gene and childhood asthma. Relevant studies researching on VDR polymorphisms and asthma susceptibility were searched throughout Embase, PubMed, China Science and technology journal database (CQVIP), etc. till 12 April, 2021. We calculated the pooled odds ratios (OR) and its 95% confidence interval (CI) using RevMan 5.3 software and Stata 11.0. FokI (rs2228570) could significantly affect childhood asthma risk across co dominant model (Ff vs. FF: OR (95%Cl) = 0.82 (0.65, 1.02), P = 0.071) and dominant model (ff+Ff vs. FF: OR (95%Cl) = 0.77 (0.63, 0.95), P = 0.016), especially among Caucasians in additive model (f vs. F: OR (95%Cl) = 0.63 (0.43, 0.92), P = 0.015) and dominant model (ff+Ff vs. FF: OR (95%Cl) = 0.67 (0.51, 0.88), P = 0.004). Taql (rs731236) was significantly related with childhood asthma in additive model (t vs. T: OR (95%Cl) = 0.45 (0.23, 0.89), P = 0.022), co dominant model (Tt vs. TT: OR (95%CI) = 0.36 (0.17, 0.77), P = 0.009), and dominant model (tt+Tt vs. TT: OR (95%Cl) = 0.36 (0.15, 0.87), P = 0.024) among Asian, as well as population-based subgroup in co dominant model (Tt vs. TT: OR (95%Cl) = 0.53 (0.31, 0.94), P = 0.029). However, no evidence supported the role of Apal (rs7975232) and Bsml (rs1544410) polymorphisms in childhood asthma. Fokl and Taql polymorphisms were found to be related with the susceptibility of childhood asthma. However, it seems that Apal and Bsml polymorphisms are not related with childhood asthma susceptibility.

Keywords: vitamin D receptor, polymorphisms, childhood asthma, systematic review, susceptibility

# INTRODUCTION

Asthma is recognized as a chronic heterogeneous respiratory disease, which has characterized by airway inflammation and hyper-responsiveness, and the disease affects more than 300 million people worldwide, especially among children (1). The incidence, morbidity, and mortality related with asthma was influenced by several potential risk factors such as environmental factors (2), infancy microbial, biome influences, and genetic background, including vitamin D receptor (VDR) gene (3).

Vitamin D has been shown to have potent immunomodulatory properties, and Vitamin D correlated with the regulation of adaptive and innate immune function through VDR (4). Recently, increasing evidence researched on the effect of vitamin D in asthma and demonstrated that the severity of symptoms was related with vitamin D deficiency (5, 6). Among VDR polymorphisms, four SNPs, including BsmI (rs1544410), ApaI (rs7975232), FokI (rs228570), and TaqI (rs731236) have been widely researched (7), but the relationship remains inconsistent. For example, the

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meta-analysis by Makoui et al. showed a statistical significant association between asthma risk and TaqI SNP (7). However, the systematically review by Zhen et al. showed no association between TaqI SNP and asthma risk (8). Additionally, thereafter, some new studies have been published (9–13).

Thus, it is necessary to update the report based on the previous results of researches to further explore the potential role of VDR genes polymorphism in childhood asthma susceptibility. Then, we designed the metaanalysis and explored this relationship in different races and source of controls. Finally, our data demonstrated that FokI and TaqI polymorphisms might be associated with childhood asthma susceptibility. However, ApaI and BsmI polymorphisms are not related with childhood asthma susceptibility.



### MATERIALS AND METHODS

### **Selection Strategy**

The published studies were searched from numerous databases including Embase, PubMed, WANFANG data, China National Knowledge Infrastructure (CNKI), China Science and technology journal database (CQVIP), etc. The comprehensive systematic search process was exploited till 12 April, 2021 using the following key words: ("Vitamin D receptor" OR "VDR") AND ("polymorphisms" OR "polymorphism" OR "variant" OR "mutant") AND ("children" OR "child" OR "teenager" OR "pediatric"). The selection strategies in Pubmed and Embase were shown in **Supplementary Tables 1, 2**. Moreover, in order to enroll more researches, print-out literatures, reviews, and the references of included articles were also retrieved.

### **Study Selection**

The following inclusion criteria were designed: (1) the study was designed as a case-control study or cohort study; (2) the subjects in the experiment group were children and/or adolescents with asthma, and subjects in the control group were healthy children and/or adolescents; (3) The study explored the association of VDR ApaI (rs7975232), TaqI (rs731236), BsmI (rs1544410), FokI (rs2228570) gene polymorphisms and asthma susceptibility; (4) genotype data were reported or could be calculated based on information provided in the study.

When the control group and the case group were family members or close family members, the study would be excluded. The non-research articles, such as reviews, comments, and conference summaries, would be excluded. When duplicated studies were found or same data were showed in more than one study, the study with the most specific information would be included in the present study, and other duplicated articles would be excluded.

### **Data Extraction and Quality Assessment**

Based on the designed criteria, studies were screened by two investigators independently. According to the standardized form, the information including year of publication, the name of the first author, research regions, the demographic information (age, sample size, source of the control group), polymorphism detection methods, the ethnicity of the included population, and genotype data, etc.

Newcastle-Ottawa Scale (NOS) criteria was used to assess the methodological quality of included studies, and the scale was assessed according to three aspects including subjects selection, comparability, and exposure (14). The study with a score of five or more would be considered as moderate quality, and the study with a score of four or less would be considered as poor quality.

When data extraction was finished, the extraction form would be exchanged, and the disagreements were solved by discussing.

### **Statistic Analysis**

Firstly, the Hardy-Weinberg equilibrium test (HWE) of the frequency distribution of genotypes among controls was performed. We defined the population were not in the HWE if P < 0.05. For each single nucleotide polymorphisms (SNP), we examined four models, including computational additive

model [m (mutation) vs. W (Wild)], co dominant model (mm vs. WW, Wm vs. WW), dominant model (mm+ Wm vs. WW), and recessive model (mm vs. WW + Wm). The effect of VDR polymorphisms in the childhood asthma susceptibility was assessed based on the pooled odds ratio (OR) and its 95% confidence interval (95%CI). Heterogeneity among individual studies was assessed using Cochran's Q test and I<sup>2</sup> test (15). If P < 0.05, and/or I<sup>2</sup> >50%, suggesting obvious heterogeneity between the studies, the random effects model would be selected to calculate the pooled data; If  $P \ge 0.05$  and/or I<sup>2</sup>  $\le 50\%$ , the fixed effect model would be used. RevMan 5.3 software and Stata 11.0 were enrolled to perform all statistical analyses.

# RESULTS

### **Studies Inclusion**

The detailed information associated with search process was shown in **Figure 1**. In this study, a total of 197 studies were firstly searched, including 54 articles in PubMed, 104 articles in Embase, 16 articles in Wanfang data, 18 articles in CNKI, and 5 articles in CQVIP. After removing 55 duplicated documents, there were 142 articles remaining. After that, we excluded 117 articles after browsing the titles and reading the abstract. Then, total 25 articles were fully reviewed, and seven articles were excluded, including five articles with adults as study subjects and two reviews. Finally, 18 articles were included in this meta-analysis (8–13, 16–27).

### The Baseline Characteristics and Quality Assessment of Included Studies

As shown in **Table 1**, total 3,495 subjects including 1,392 cases in asthma group and 2,103 cases in control group were enrolled in the present study. The studies included in the meta-analysis were all published from 2010 to 2020. Among these articles, the subjects in eight studies were Asians, eight articles were Caucasians, one study were Americans, and one study were African-Americans. For subjects in the control group, there were two studies with population-based controls and 16 studies with hospital-based controls.

The genotype data and HWE test results of the case group and the control group were shown in **Table 2**. NOS scores of all included studies ranged from 5 to 8, suggesting an overall moderate methodological quality (**Table 3**).

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#### Apal (rs7975232)

As shown in **Figure 2**, total 16 articles reported the association between ApaI (rs7975232) and asthma risk (8–12, 16–18, 20–27). Obvious heterogeneity across studies was observed in additive model (a vs. A:  $I^2 = 89\%$ , P < 0.00001), co dominant model (aa vs. AA:  $I^2 = 84\%$ , P < 0.00001; Aa vs. AA:  $I^2 = 63\%$ , P < 0.0006), dominant model (aa+Aa vs. AA:  $I^2 = 77\%$ , P < 0.00001), and recessive model (aa vs. AA+Aa:  $I^2 = 86\%$ , P < 0.00001). No significant association between ApaI (rs7975232) and asthma risk was calculated across additive model (a vs. A: OR (95%CI) = 0.82 (0.56, 1.21), P = 0.317), co dominant model (aa vs. AA: OR (95%CI) = 0.65 (0.31, 1.38), P = 0.263; Aa vs.

| TABLE 1 Characteristics of the included studies |
|---|
|---|

| Study                       | Area    | Ethnicity         | Source of control | Diagnostic of asthma | Polymorphisms          | Group   | n, M/F       | Age, years              |
|-----------------------------|---------|-------------------|-------------------|----------------------|------------------------|---------|--------------|-------------------------|
| Ahmed et al. (9)            | Egypt   | European          | HB                | GINA guidelines      | Apal, Taql, Bsml       | Asthma  | 50, 28/22    | 12.66±3.34              |
|                             |         |                   |                   |                      |                        | Control | 50, 29/21    | 12.08±3.53              |
| Batmaz et al. (16)          | Turkey  | European          | HB                | GINA guidelines      | Apal, Taql, Fokl, Bsml | Asthma  | 30, 20/10    | 11.74±2.4               |
|                             |         |                   |                   |                      |                        | Control | 30, 13/17    | 11.31±2.27              |
| Einisman et al. (17)        | Chile   | American          | HB                | GINA guidelines      | Apal, Taql, Fokl       | Asthma  | 75, 43/32    | 9.1 (3.5) \$            |
|                             |         |                   |                   |                      |                        | Control | 227, 114/113 | 10.3 (7.9)              |
| Hou et al. (10)             | China   | Asia              | HB                | DPGPBA (2008)        | Apal, Bsml             | Asthma  | 70, 43/27    | 8.84±3.21               |
|                             |         |                   |                   |                      |                        | Control | 70, 37/33    | 8.04±3.01               |
| Hutchinson et al. (11)      | Ireland | European          | HB                | GINA guidelines      | Apal, Taql             | Asthma  | 44, 23/21    | 8.7 (6–13, 15–1         |
|                             |         |                   |                   |                      |                        | Control | 57, NR       | NR                      |
| lordanidou et al. (18)      | Greece  | European          | HB                | GINA guidelines      | Apal, Taql, Fokl, Bsml | Asthma  | 127, 82/45   | 8.4±2.3                 |
|                             |         |                   |                   |                      |                        | Control | 91, 41/50    | 9.5±3.8                 |
| Ismail et al. (12)          | Egypt   | European          | HB                | GINA guidelines      | Fokl                   | Asthma  | 51, 28/23    | 8.6±2.7                 |
|                             |         |                   |                   |                      |                        | Control | 33, 18/15    | 7.8±2.6                 |
| Kilic et al. (12)           | Turkey  | European          | HB                | GINA guidelines      | Apal, Taql, Fokl       | Asthma  | 100, 52/48   | 9.5±2.8                 |
|                             |         |                   |                   |                      |                        | Control | 80, 42/38    | 9.5±2.5                 |
| Liu et al. (20)             | China   | Asia              | HB                | DPGPBA (2008)        | Apal, Taql, Fokl, Bsml | Asthma  | 41, 24/17    | 3.9±1.2                 |
|                             |         |                   |                   |                      |                        | Control | 41, 23/18    | 3.7±1.3                 |
| Ma et al. (21)              | China   | Asia              | PB                | DPGPBA (2008)        | Apal, Taql, Fokl, Bsml | Asthma  | 60, 32/28    | 10.2                    |
|                             |         |                   |                   |                      |                        | Control | 60, 30/30    | 10.6                    |
| Maalmi et al. (22)          | Tunisia | European          | HB                | DPGPBA (2008)        | Apal, Taql, Fokl, Bsml | Asthma  | 155, 59/96   | <b>9.1 (</b> 4–13, 15–1 |
|                             |         |                   |                   |                      |                        | Control | 225, 99/126  | 9.5 (2-13, 15-1         |
| Mo et al. (23)              | China   | Asia              | HB                | DPGPBA (2008)        | Apal, Bsml             | Asthma  | 71, NR       | NR                      |
|                             |         |                   |                   |                      |                        | Control | 71, NR       | NR                      |
| Papadopoulou et al.<br>(24) | Cyprus  | European          | PB                | NR                   | Apal, Taql, Bsml       | Asthma  | 69, 30/39    | 16.9 (15.9-18.1         |
|                             |         |                   |                   |                      |                        | Control | 671, 282/389 | 17.0 (15.9-18.0         |
| Pillai et al. (25)          | USA     | African- American | HB                | NAEPP (2007)         | Apal, Taql, Fokl       | Asthma  | 139, 81/58   | 11.2±3.5                |
|                             |         |                   |                   |                      |                        | Control | 74, 26/48    | 11.8±4.3                |
| Zhang et al. (26)           | China   | Asia              | HB                | NR                   | Apal, Fokl, Bsml       | Asthma  | 143, 86/57   | 7.56±2.39               |
|                             |         |                   |                   |                      |                        | Control | 143, 87/56   | 7.28±2.54               |
| Zhao et al. (27)            | China   | Asia              | HB                | DPGPBA (2008)        | Apal, Taql, Fokl, Bsml | Asthma  | 40, 22/18    | 3.41±1.07               |
|                             |         |                   |                   |                      |                        | Control | 40, 21/19    | 3.37±1.04               |
| Zhen and Wang (8)           | China   | Asia              | HB                | NR                   | Apal                   | Asthma  | 30, 17/13    | 5.70±2.84               |
|                             |         |                   |                   |                      |                        | Control | 40, 22/18    | 5.53±2.93               |
| Zhu et al. (13)             | China   | Asia              | HB                | DPGPBA (2008)        | Fokl, Bsml             | Asthma  | 97, 50/47    | 8.76±1.22               |
|                             |         |                   |                   |                      |                        | Control | 100, 55/45   | 8.60±1.16               |

\$, median (IQR); HB, hospital-based; PB, population-based; PCR, Polymerase chain reaction; RT-PCR, Realtime polymerase chain reaction; RFLP, restriction fragment lengths polymorphism; NR, not reported; BMI, body mass index; GINA, the Global Initiative for Asthma; NAEPP, National Asthma Education and Prevention Program (2007) (28).

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TABLE 2 | Frequency distribution of gene polymorphisms in the experimental group and the control group.

| References                  | Country |     | Case | group |    |     | Contro | l group |     | P <sub>value</sub> for<br>HWE |
|-----------------------------|---------|-----|------|-------|----|-----|--------|---------|-----|-------------------------------|
|                             |         | N   | ww   | WM    | ММ | N   | ww     | WM      | ММ  |                               |
| Apal (rs7975232)            |         |     |      |       |    |     |        |         |     |                               |
| Ahmed et al. (9)            | Egypt   | 50  | 25   | 15    | 10 | 50  | 20     | 20      | 10  | 0.2386                        |
| Batmaz et al. (16)          | Turkey  | 30  | 5    | 25    | 0  | 30  | 7      | 23      | 0   | 0.0070                        |
| Einisman et al. (17)        | Chile   | 70  | 21   | 35    | 14 | 50  | 10     | 28      | 12  | 0.3891                        |
| Hou et al. (10)             | China   | 70  | 4    | 30    | 36 | 70  | 0      | 5       | 65  | 0.7567                        |
| Hutchinson et al. (11)      | Ireland | 44  | 11   | 23    | 10 | 57  | 5      | 20      | 32  | 0.4721                        |
| lordanidou et al. (18)      | Greece  | 127 | 41   | 63    | 23 | 91  | 35     | 41      | 15  | 0.6120                        |
| Kilic et al. (12)           | Turkey  | 100 | 18   | 60    | 22 | 80  | 26     | 42      | 12  | 0.4569                        |
| Liu et al. (20)             | China   | 41  | 7    | 15    | 19 | 41  | 1      | 4       | 36  | 0.1599                        |
| Ma et al. (21)              | China   | 60  | 46   | 7     | 7  | 60  | 48     | 4       | 8   | <0.0001                       |
| Maalmi et al. (22)          | Tunisia | 155 | 92   | 57    | 6  | 225 | 142    | 70      | 13  | 0.2729                        |
| Mo et al. (23)              | China   | 71  | 4    | 31    | 36 | 71  | 14     | 28      | 29  | 0.1416                        |
| Papadopoulou et al.<br>(24) | Cyprus  | 61  | 19   | 34    | 8  | 633 | 232    | 312     | 89  | 0.3290                        |
| Pillai et al. (25)          | USA     | 125 | 55   | 59    | 11 | 72  | 35     | 33      | 4   | 0.2762                        |
| Zhang et al. (26)           | China   | 143 | 54   | 75    | 14 | 143 | 8      | 69      | 66  | 0.0637                        |
| Zhao et al. (27)            | China   | 40  | 0    | 15    | 25 | 40  | 0      | 27      | 13  | 0.0013                        |
| Zhen and Wang (8)           | China   | 30  | 3    | 2     | 25 | 40  | 6      | 14      | 20  | 0.2061                        |
| Taql (rs731236)             |         |     |      |       |    |     |        |         |     |                               |
| Ahmed et al. (9)            | Egypt   | 50  | 5    | 30    | 15 | 50  | 10     | 40      | 0   | <0.0001                       |
| Batmaz et al. (16)          | Turkey  | 30  | 18   | 9     | 3  | 30  | 15     | 10      | 5   | 0.1709                        |
| Einisman et al. (17)        | Chile   | 72  | 35   | 34    | 3  | 50  | 24     | 24      | 2   | 0.1780                        |
| Hutchinson et al. (11)      | Ireland | 44  | 17   | 21    | 6  | 57  | 34     | 23      | 0   | 0.0564                        |
| lordanidou et al. (18)      | Greece  | 127 | 43   | 68    | 16 | 91  | 35     | 38      | 18  | 0.1990                        |
| Kilic et al. (12)           | Turkey  | 100 | 31   | 61    | 8  | 80  | 28     | 32      | 20  | 0.0861                        |
| Liu et al. (20)             | China   | 41  | 6    | 11    | 24 | 41  | 1      | 5       | 35  | 0.1607                        |
| Ma et al. (21)              | China   | 60  | 6    | 7     | 47 | 60  | 5      | 6       | 49  | <0.0001                       |
| Maalmi et al. (22)          | Tunisia | 155 | 59   | 81    | 15 | 225 | 79     | 101     | 45  | 0.2230                        |
| Papadopoulou et al.<br>(24) | Cyprus  | 61  | 28   | 20    | 13 | 630 | 224    | 325     | 81  | 0.0276                        |
| Pillai et al. (25)          | USA     | 118 | 52   | 55    | 11 | 74  | 40     | 31      | 3   | 0.3137                        |
| Zhao et al. (27)            | China   | 40  | 26   | 14    | 0  | 40  | 13     | 27      | 0   | 0.0013                        |
| Bsml (rs1544410)            |         |     |      |       |    |     |        |         |     |                               |
| Ahmed et al. (9)            | Egypt   | 50  | 10   | 25    | 15 | 50  | 20     | 20      | 10  | 0.2386                        |
| Batmaz et al. (16)          | Turkey  | 30  | 2    | 12    | 16 | 30  | 5      | 13      | 12  | 0.6477                        |
| Hou et al. (10)             | China   | 70  | 0    | 4     | 66 | 70  | 0      | 5       | 65  | 0.7567                        |
| lordanidou et al. (18)      | Greece  | 127 | 20   | 67    | 40 | 91  | 19     | 39      | 33  | 0.2442                        |
| Liu et al. (20)             | China   | 41  | 9    | 11    | 21 | 41  | 1      | 4       | 36  | 0.0723                        |
| Ma et al. (21)              | China   | 60  | 5    | 10    | 45 | 60  | 6      | 6       | 48  | <0.0001                       |
| Maalmi et al. (22)          | Tunisia | 155 | 34   | 72    | 49 | 225 | 26     | 119     | 80  | 0.0663                        |
| Mo et al. (23)              | China   | 71  | 0    | 5     | 66 | 71  | 0      | 4       | 67  | 0.8070                        |
| Papadopoulou et al.<br>(24) | Cyprus  | 63  | 11   | 32    | 20 | 631 | 127    | 327     | 177 | 0.2801                        |
| Zhang et al. (26)           | China   | 143 | 56   | 74    | 13 | 143 | 72     | 65      | 6   | 0.0635                        |
| Zhao et al. (27)            | China   | 40  | 0    | 23    | 17 | 40  | 0      | 11      | 29  | 0.3133                        |
| Zhu et al. (13)             | China   | 97  | 0    | 10    | 87 | 100 | 0      | 2       | 98  | 0.9195                        |
| Fokl (rs2228570)            |         |     |      |       |    |     |        |         |     |                               |
| Batmaz et al. (16)          | Turkey  | 30  | 19   | 11    | 0  | 30  | 12     | 12      | 6   | 0.3613                        |
| Einisman et al. (17)        | Chile   | 73  | 11   | 62    | 0  | 50  | 5      | 45      | 0   | < 0.0001                      |
| lordanidou et al. (18)      | Greece  | 127 | 67   | 54    | 6  | 91  | 38     | 45      | 8   | 0.2958                        |

| References         | Country |     | Case | group |    |     | Contro | l group |    | P <sub>value</sub> for<br>HWE |
|--------------------|---------|-----|------|-------|----|-----|--------|---------|----|-------------------------------|
|                    |         | N   | ww   | WM    | MM | N   | ww     | WM      | ММ |                               |
| Ismail et al. (19) | Egypt   | 51  | 29   | 22    | 0  | 33  | 12     | 14      | 7  | 0.4497                        |
| Kilic et al. (12)  | Turkey  | 100 | 58   | 33    | 9  | 80  | 48     | 28      | 4  | 0.9744                        |
| Liu et al. (20)    | China   | 41  | 8    | 13    | 20 | 41  | 1      | 5       | 35 | 0.1607                        |
| Ma et al. (21)     | China   | 60  | 12   | 24    | 24 | 60  | 18     | 31      | 11 | 0.7124                        |
| Maalmi et al. (22) | Tunisia | 155 | 88   | 56    | 11 | 152 | 70     | 59      | 23 | 0.0808                        |
| Pillai et al. (25) | USA     | 122 | 76   | 41    | 5  | 74  | 42     | 29      | 3  | 0.4636                        |
| Zhang et al. (26)  | China   | 143 | 2    | 49    | 92 | 143 | 6      | 63      | 74 | 0.0975                        |
| Zhao et al. (27)   | China   | 40  | 19   | 14    | 7  | 40  | 15     | 16      | 9  | 0.2508                        |
| Zhu et al. (13)    | China   | 97  | 27   | 48    | 22 | 100 | 30     | 45      | 25 | 0.3283                        |

#### TABLE 3 | Quality assessment of the included studies.

| References                  | Representativen<br>of the cases | essCase<br>definition<br>adequate | Ascertainment<br>of exposure | method of<br>ascertainment<br>for cases | Control for<br>important<br>factor or<br>additional<br>factor | Selection<br>of controls   | Definition<br>of controls   | Non-<br>response<br>rate | Total<br>quality<br>scores |
|-----------------------------|---------------------------------|-----------------------------------|------------------------------|---|---|----------------------------|-----------------------------|--------------------------|----------------------------|
| Ahmed et al. (9)            | ☆                               | ${\simeq}$                        | \$                           | ☆                                       | ☆   | -                          | \$                          | ☆                        | 7                          |
| Batmaz et al. (16)          | ${\simeq}$                      | ${\simeq}$                        | $\Leftrightarrow$            | ${\simeq}$                              | $\Rightarrow$   | -                          | $\overleftrightarrow$       | $\Rightarrow$            | 7                          |
| Einisman et al. (17)        | $\overleftrightarrow$           | $\Rightarrow$                     | $\Rightarrow$                | $\Rightarrow$                           | $\Diamond$  | -                          | $\overleftrightarrow$       | -                        | 6                          |
| Hou et al. (10)             | ${\simeq}$                      | ${\leftrightarrow}$               | $\Delta$                     | $\Rightarrow$                           | -   | _                          | $\stackrel{\wedge}{\simeq}$ | ${\simeq}$               | 6                          |
| Hutchinson et al. (11)      | ${\simeq}$                      | ${\swarrow}$                      | ${\leftrightarrow}$          | ${\leftrightarrow}$                     | -   | _                          | _                           | ☆                        | 5                          |
| lordanidou et al. (18)      | $\stackrel{\frown}{\simeq}$     | $\stackrel{\frown}{\simeq}$       | ${\leftrightarrow}$          | ${\leftrightarrow}$                     | $\stackrel{\frown}{\simeq}$                                   | _                          | $\stackrel{\frown}{\simeq}$ | ${\simeq}$               | 7                          |
| Ismail et al. (19)          | $\stackrel{\frown}{\simeq}$     | $\stackrel{\sim}{\sim}$           | $\stackrel{\sim}{\sim}$      | $\stackrel{\wedge}{\simeq}$             | -   | -                          | $\stackrel{\circ}{\simeq}$  | ${\simeq}$               | 6                          |
| Kilic et al. (12)           | ${\simeq}$                      | ${\leftrightarrow}$               | $\Delta$                     | $\Rightarrow$                           | $\Rightarrow$   | _                          | $\stackrel{\wedge}{\simeq}$ | ${\simeq}$               | 7                          |
| Liu et al. (20)             | $\stackrel{\frown}{\simeq}$     | $\stackrel{\sim}{\sim}$           | $\stackrel{\sim}{\sim}$      | $\stackrel{\wedge}{\simeq}$             | ${\leftrightarrow}$   | _                          | $\stackrel{\circ}{\simeq}$  | ${\simeq}$               | 7                          |
| Ma et al. (21)              | $\stackrel{\frown}{\simeq}$     | $\stackrel{\sim}{\sim}$           | $\stackrel{\sim}{\sim}$      | $\stackrel{\wedge}{\simeq}$             | -   | $\stackrel{\circ}{\simeq}$ | $\stackrel{\circ}{\simeq}$  | ${\simeq}$               | 6                          |
| Maalmi et al. (22)          | $\stackrel{\frown}{\simeq}$     | $\stackrel{\sim}{\sim}$           | $\stackrel{\sim}{\sim}$      | $\stackrel{\wedge}{\simeq}$             | ${\leftrightarrow}$   | -                          | $\stackrel{\circ}{\simeq}$  | -                        | 6                          |
| Mo et al. (23)              | -                               | $\stackrel{\sim}{\sim}$           | $\stackrel{\sim}{\sim}$      | $\stackrel{\wedge}{\simeq}$             | -   | _                          | $\stackrel{\circ}{\simeq}$  | ${\simeq}$               | 5                          |
| Papadopoulou et al.<br>(24) | $\overleftrightarrow$           | -                                 | ${\simeq}$                   | ☆                                       | ☆   | ☆                          | ☆                           | ☆                        | 7                          |
| Pillai et al. (25)          | ${\simeq}$                      | ${\swarrow}$                      | ${\leftrightarrow}$          | ${\leftrightarrow}$                     | ${\leftrightarrow}$   | _                          | $\overleftrightarrow$       | ☆                        | 7                          |
| Zhang et al. (26)           | $\stackrel{\frown}{\simeq}$     | _                                 | ${\leftrightarrow}$          | ${\leftrightarrow}$                     | $\stackrel{\sim}{\simeq}$                                     | $\stackrel{\circ}{\simeq}$ | $\stackrel{\frown}{\simeq}$ | ${\simeq}$               | 7                          |
| Zhao et al. (27)            | $\stackrel{\frown}{\simeq}$     | $\stackrel{\frown}{\simeq}$       | ${\leftrightarrow}$          | ${\leftrightarrow}$                     | $\stackrel{\sim}{\simeq}$                                     | _                          | $\stackrel{\frown}{\simeq}$ | ${\simeq}$               | 7                          |
| Zhen and Wang (8)           | $\stackrel{\frown}{\simeq}$     | _                                 | ${\leftrightarrow}$          | ${\leftrightarrow}$                     | $\stackrel{\sim}{\simeq}$                                     | _                          | $\stackrel{\frown}{\simeq}$ | ${\simeq}$               | 6                          |
| Zhu et al. (13)             | $\Diamond$                      | $\Leftrightarrow$                 | $\Leftrightarrow$            | ☆                                       | $\Rightarrow$   | _                          | $\Rightarrow$               | ☆                        | 7                          |

AA: OR (95%CI) = 0.97 (0.66, 1.42), P = 0.866), dominant model (aa+Aa vs. AA: OR (95%CI) = 0.86 (0.55, 1.35), P = 0.520), and recessive model (aa vs. AA+Aa: OR (95%CI) = 0.73 (0.40, 1.32), P = 0.295).

The subgroup analysis was performed stratified by ethnicity, HWE, and source of controls (**Table 4**). No significant association was observed in all subgroup analysis (P > 0.05). Meanwhile, the results of heterogeneity analysis showed that ethnicity, HWE, and source of subjects were not the source of heterogeneity.

#### Taql (rs731236)

As shown in **Figure 3**, total 12 articles researched on the role of TaqI (rs731236) in asthma risk (9, 11, 12, 16–18, 20–25, 27). Obvious heterogeneity across studies was observed in additive model (t vs. T:  $I^2 = 71\%$ , P < 0.0001), co dominant model (tt vs. TT:  $I^2 = 63\%$ , P = 0.002; Tt vs. TT:  $I^2 = 50\%$ , P = 0.02), dominant model (tt+Tt vs. TT:  $I^2 = 53\%$ , P = 0.82), and recessive model (tt vs. TT+Tt:  $I^2 = 73\%$ , P < 0.0001). Thus, the randomed effects model was used to calculated the pooled data, and the results showed that no significant association between TaqI (rs731236)

|    |  | Experim  |  | Contro  |  |  | Odds Ratio   | Odds                                | Ratio                      |          |
|----|--|--|--|---|--|--|--|-------------------------------------|----------------------------|----------|
|    | Study or Subgroup<br>Ahmed, AE 2020  | Events<br>35   | Total<br>100   | Events<br>40  |  | Weight<br>6.3%   | V. Random. 95% Cl<br>0.81 [0.46, 1.43]   | IV. Rando                           | om, 95% Cl                 |          |
|    | Batmaz, SB 2017  | 25   | 60   | 23  | 60   | 5.8%   | 1.15 [0.55, 2.39]  |                                     | -                          |          |
|    | Einisman, H 2015<br>Hou, C 2018  | 63<br>102  | 140<br>140   | 52<br>135   | 100<br>140   | 6.5%<br>5.0%   | 0.76 [0.45, 1.26]<br>0.10 [0.04, 0.26]   |                                     | _                          |          |
|    | Hutchinson, K 2018   | 43   | 88   | 84  | 114  | 6.3%   | 0.34 [0.19, 0.62]  | _ <b>.</b>                          |                            |          |
|    | lordanidou, M 2014<br>Kilic. M 2019  | 109<br>104   | 254<br>200   | 71<br>66  | 182<br>160   | 6.9%<br>6.8%   | 1.18 [0.80, 1.73]<br>1.54 [1.01, 2.35]   | _                                   |                            |          |
|    | Liu, Y 2016  | 53   | 82   | 76  | 82   | 5.1%   | 0.14 [0.06, 0.37]  |                                     |                            |          |
|    | Ma, JH 2014<br>Maalmi, H 2013  | 21<br>69   | 120<br>310   | 20<br>96  | 120<br>450   | 6.0%<br>7.0%   | 1.06 [0.54, 2.08]<br>1.06 [0.74, 1.50]   | _                                   | _                          |          |
|    | Mo, LY 2015  | 103  | 142  | 86  | 142  | 6.6%   | 1.72 [1.04, 2.83]  | _                                   |                            |          |
|    | Papadopoulou, A 2015<br>Pillai, DK 2011  | 50<br>81   | 122<br>250   | 490<br>41   | 1266<br>144  | 6.9%<br>6.7%   | 1.10 [0.75, 1.61]<br>1.20 [0.77, 1.89]   | _                                   | -                          |          |
|    | Zhang, Y 2017  | 103  | 286  | 201   | 286  | 7.0%   | 0.24 [0.17, 0.34]  | -                                   |                            |          |
|    | Zhao, HX 2015<br>Zhen, YF 2010   | 65<br>52   | 80<br>60   | 53<br>54  | 80<br>80   | 5.8%<br>5.3%   | 2.21 [1.07, 4.57]<br>3.13 [1.30, 7.54]   |                                     | <u> </u>                   |          |
|    | Total (95% CI)   |  | 2434   |   | 3506   | 100.0%   | 0.82 [0.56, 1.21]  | •                                   |                            |          |
|    | Total events   | 1078   |  | 1588  |  |  |  |                                     |                            |          |
|    | Heterogeneity: Tau <sup>2</sup> = 0.5<br>Test for overall effect: Z =  | 52; Chi <sup>2</sup> = 1<br>= 1 00 (P =  | 132.36, c<br>0.32)   | if = 15 (P  | < 0.000  | 001); I <sup>2</sup> = 89  | %  | 0.05 0.2                            | 1 5                        | 20       |
| в  |  | ,  |  |   |  |  |  | Favours [experimental]              |                            |          |
| Ξ. | Study or Subgroup  | Experim<br>Events  | Total  | Contro<br>Events  |  | Weight   | Odds Ratio<br>V. Random, 95% Cl  | IV, Rando                           | Ratio<br>m. 95% Cl         |          |
|    | Ahmed, AE 2020<br>Batmaz, SB 2017  | 10<br>0  | 35<br>5  | 10<br>0   | 30<br>7  | 7.7%   | 0.80 [0.28, 2.30]<br>Not estimable   |                                     | _                          |          |
|    | Einisman, H 2015   | 14   | 35   | 12  | 22   | 7.6%   | 0.56 [0.19, 1.63]  |                                     | -                          |          |
|    | Hou, C 2018<br>Hutchinson, K 2018  | 36<br>10   | 40<br>21   | 65<br>32  | 65<br>37   | 3.8%<br>7.2%   | 0.06 [0.00, 1.18]<br>0.14 [0.04, 0.51]   | · · · ·                             | -                          |          |
|    | lordanidou, M 2014   | 23   | 64   | 15  | 50   | 8.2%   | 1.31 [0.59, 2.89]  | -                                   | -                          |          |
|    | Kilic, M 2019<br>Liu, Y 2016   | 22<br>19   | 40<br>26   | 12<br>36  | 38<br>37   | 7.9%<br>5.2%   | 2.65 [1.05, 6.68]<br>0.08 [0.01, 0.66]   |                                     |                            |          |
|    | Ma, JH 2014  | 7  | 53   | 8   | 56   | 7.6%   | 0.91 [0.31, 2.72]  |                                     |                            |          |
|    | Maalmi, H 2013<br>Mo, LY 2015  | 6<br>36  | 98<br>40   | 13<br>29  | 155<br>43  | 7.8%<br>7.3%   | 0.71 [0.26, 1.94]<br>4.34 [1.29, 14.63]  |                                     |                            |          |
|    | Papadopoulou, A 2015   | 8  | 27   | 89  | 321  | 8.1%   | 1.10 [0.46, 2.60]  |                                     | <u> </u>                   |          |
|    | Pillai, DK 2011<br>Zhang, Y 2017   | 11<br>14   | 66<br>68   | 4<br>66   | 39<br>74   | 7.3%<br>7.9%   | 1.75 [0.52, 5.93]<br>0.03 [0.01, 0.08]   |                                     |                            |          |
|    | Zhao, HX 2015  | 25   | 25   | 13  | 13   |  | Not estimable  |                                     |                            |          |
|    | Zhen, YF 2010  | 25   | 28   | 20  | 26   | 6.6%   | 2.50 [0.55, 11.27]   | _                                   |                            |          |
|    | Total (95% CI)   |  | 671  |   | 1013   | 100.0%   | 0.65 [0.31, 1.38]  | -                                   | •                          |          |
|    | Total events<br>Heterogeneity: Tau <sup>2</sup> = 1.6  | 266<br>35: Chi <sup>2</sup> = 7  | 79.92. df  | 424<br>= 13 (P <  | 0.000  | 01); l² = 849  | 6  |                                     |                            |          |
|    | Test for overall effect: Z =   | = 1.12 (P =  | 0.26)  |   |  | - ,,   |  | 0.005 0.1<br>Favours [experimental] | 1 10<br>Favours [control]  | 200      |
|    |  | Experim  | nental   | Contro  | d  |  | Odds Ratio   | Odds                                | Ratio                      |          |
| C  | Study or Subgroup  | Events   | Total<br>40  |   |  |  | V. Random, 95% CI  | IV, Rando                           | om, 95% Cl                 |          |
| -  | Ahmed, AE 2020<br>Batmaz, SB 2017  | 15<br>25   | 30   | 20<br>23  | 40<br>30   | 7.5%<br>5.3%   | 0.60 [0.25, 1.46]<br>1.52 [0.42, 5.47]   |                                     |                            |          |
|    | Einisman, H 2015<br>Hou, C 2018  | 35<br>30   | 56<br>34   | 28<br>5   | 38<br>5  |  | 0.60 [0.24, 1.47]<br>0.62 [0.03, 13.14]  |                                     | _                          |          |
|    | Hutchinson, K 2018   | 23   | 34   | 20  | 25   | 5.6%   | 0.52 [0.16, 1.76]  |                                     | -                          |          |
|    | lordanidou, M 2014<br>Kilic, M 2019  | 63<br>60   | 104<br>78  | 41<br>42  | 76<br>68   | 9.7%<br>8.8%   | 1.31 [0.72, 2.39]<br>2.06 [1.01, 4.23]   | -                                   |                            |          |
|    | Liu, Y 2016  | 15   | 22   | 4   | 5  | 2.2%   | 0.54 [0.05, 5.72]  |                                     |                            |          |
|    | Ma, JH 2014<br>Maalmi, H 2013  | 7<br>57  | 53<br>149  | 4<br>70   | 52<br>212  | 5.2%<br>10.9%  | 1.83 [0.50, 6.66]<br>1.26 [0.81, 1.95]   |                                     | -                          |          |
|    | Mo, LY 2015  | 31   | 35   | 28  | 42   | 5.6%   | 3.88 [1.14, 13.17]   |                                     |                            |          |
|    | Papadopoulou, A 2015<br>Pillai, DK 2011  | 34<br>59   | 53<br>114  | 312<br>33   | 544<br>68  | 9.8%<br>9.7%   | 1.33 [0.74, 2.39]<br>1.14 [0.62, 2.08]   | _                                   | -                          |          |
|    | Zhang, Y 2017  | 75   | 129  | 69  | 77   | 8.1%   | 0.16 [0.07, 0.36]  |                                     |                            |          |
|    | Zhao, HX 2015<br>Zhen, YF 2010   | 15<br>2  | 15<br>5  | 27<br>14  | 27<br>20   | 2.8%   | Not estimable<br>0.29 [0.04, 2.17]   |                                     |                            |          |
|    | Total (95% CI)   |  | 951  |   |  | 100.0%   | 0.97 [0.66, 1.42]  | -                                   |                            |          |
|    | Total events   | 546  | 991  | 740   | 1329   | 100.0%   | 0.97 [0.06, 1.42]  |                                     |                            |          |
|    | Heterogeneity: Tau <sup>2</sup> = 0.3<br>Test for overall effect: Z =  | 31; Chi <sup>2</sup> = 3   | 37.50, df  | = 14 (P =   | 0.000  | 6); I² = 63%   |  | 0.05 0.2                            | 1 5                        | 20       |
|    | Test for overall effect. 2 -   |  |  |   |  |  |  | Favours [experimental]              |                            |          |
| D  | Study or Subgroup  | Experim<br>Events  | nental<br>Total  | Contro  |  | Weight   | Odds Ratio<br>V. Random, 95% Cl  | Odds<br>IV. Rando                   | Ratio<br>m. 95% Cl         |          |
|    | Ahmed, AE 2020   | 25   | 50   | 30  | 50   | 7.6%   | 0.67 [0.30, 1.47]  |                                     | -                          |          |
|    | Batmaz, SB 2017<br>Einisman, H 2015  | 25<br>49   | 30<br>70   | 23<br>40  | 30<br>50   | 5.5%<br>7.3%   | 1.52 [0.42, 5.47]<br>0.58 [0.25, 1.38]   |                                     | _                          |          |
|    | Hou, C 2018  | 66   | 70   | 70  | 70   | 1.9%   | 0.10 [0.01, 1.98]  | ·                                   | -                          |          |
|    | Hutchinson, K 2018   | 33   | 44<br>127  | 52  | 57<br>91   | 6.1%<br>8.6%   | 0.29 [0.09, 0.91]<br>1.31 [0.75, 2.30]   |                                     | <b>.</b>                   |          |
|    |  |  |  |   |  | 8.6%   |  | -                                   |                            |          |
|    | lordanidou, M 2014<br>Kilic, M 2019  | 86<br>82   | 100  | 56<br>54  | 80   |  | 2.19 [1.10, 4.38]  | -                                   |                            |          |
|    | lordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016   | 86<br>82<br>34   | 100<br>41  | 54<br>40  | 41   | 3.1%   | 0.12 [0.01, 1.04]  |                                     | <br>                       |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013  | 86<br>82<br>34<br>14<br>63   | 100<br>41<br>60<br>155   | 54<br>40<br>12<br>83  | 41<br>60<br>225  | 3.1%<br>7.2%<br>9.2%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]  |                                     | <br>                       |          |
|    | lordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015   | 86<br>82<br>34<br>14<br>63<br>67   | 100<br>41<br>60<br>155<br>71   | 54<br>40<br>12<br>83<br>57  | 41<br>60<br>225<br>71  | 3.1%<br>7.2%<br>9.2%<br>6.0%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]<br>4.11 [1.28, 13.20]  |                                     |                            |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013  | 86<br>82<br>34<br>14<br>63   | 100<br>41<br>60<br>155   | 54<br>40<br>12<br>83  | 41<br>60<br>225  | 3.1%<br>7.2%<br>9.2%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]  |                                     |                            |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Pilial, DK 2011<br>Zhang, Y 2017   | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70<br>89   | 100<br>41<br>60<br>155<br>71<br>61<br>125<br>143   | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135  | 41<br>60<br>225<br>71<br>633<br>72<br>143  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]<br>4.11 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>0.10 [0.04, 0.22]   |                                     |                            |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Pillai, DK 2011  | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70   | 100<br>41<br>60<br>155<br>71<br>61<br>125  | 54<br>40<br>12<br>83<br>57<br>401<br>37   | 41<br>60<br>225<br>71<br>633<br>72   | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]<br>4.11 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]  |                                     |                            |          |
|    | Iordanidou, M 2014<br>Kilic, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2017<br>Zhao, HX 2015<br>Zhen, YF 2010   | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70<br>89<br>40   | 100<br>41<br>60<br>155<br>71<br>61<br>125<br>143<br>40<br>30   | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]<br>4.11 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>0.10 [0.04, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]   |                                     |                            |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhang, Y 2017<br>Zhang, Y 2017<br>Zhang, Y 2017<br>Total (95% CI)<br>Total events   | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70<br>89<br>40<br>27<br>812  | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br><b>1217</b>  | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]<br>4.11 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>0.10 [0.04, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]  |                                     |                            |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Pilkal, DK 2011<br>Zhang, Y 2017<br>Zhao, HX 2015<br>Zhen, YF 2010<br>Total (95% CI)<br>Total (95% CI)   | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70<br>89<br>40<br>27<br>812<br>53; Chi <sup>2</sup> = 6  | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br><b>1217</b><br>60.52, df   | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]<br>4.11 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>0.10 [0.04, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]  |                                     |                            | 200      |
| _  | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhang, Y 2017<br>Zhang, Y 2017<br>Zhang, Y 2017<br>Total (95% CI)<br>Total events   | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70<br>89<br>40<br>27<br>812<br>53; Chi <sup>2</sup> = 6  | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br><b>1217</b><br>60.52, df   | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]<br>4.11 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>0.10 [0.04, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]  | 0.005 0.1<br>Favours (experimental) |                            | 200      |
| E  | lordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>s</sup> = 0.5<br>Test for overall effect: Z =   | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70<br>89<br>40<br>27<br>812<br>53; Chi <sup>2</sup> = 6<br>= 0.64 (P =<br>Experim  | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br><b>1217</b><br>60.52, df<br>60.52, df<br>60.52, df   | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34<br>1164<br>= 14 (P <   | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%<br>01);   <sup>2</sup> = 779  | 0.12 [0.01, 1.04]<br>1.72 [0.51, 2.91]<br>1.77 [0.77, 1.78]<br>4.11 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>0.10 [0.40, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]  | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Pilkal, DK 2011<br>Zhang, Y 2017<br>Zhao, HX 2015<br>Zhen, YF 2010<br>Total (95% CI)<br>Total (95% CI)   | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70<br>89<br>40<br>27<br>812<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6  | 100<br>41<br>60<br>155<br>71<br>61<br>125<br>143<br>40<br>30<br>1217<br>60.52, df  | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34<br>1164<br>= 14 (P <   | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%<br>01); l <sup>2</sup> = 77?  | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]<br>4.11 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>0.10 [0.04, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]  | Favours [experimental]<br>Odds      | Favours [control]          |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhen, HY 2017<br>Zhen, HY 2016<br>Zhen, YF 2010<br>Total (9% CI)<br>Total (9% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.5<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017   | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70<br>89<br>40<br>0<br>27<br>812<br>53; Chi <sup>2</sup> = 6<br>= 0.64 (P =<br>Experim<br>Events<br>10<br>0  | 100<br>41<br>60<br>155<br>71<br>61<br>125<br>143<br>40<br>30<br><b>1217</b><br>60.52, df<br>60.52, df<br>60.52, df<br>70.52)<br>mental<br>50<br>30   | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34<br>1164<br>= 14 (P <<br><b>Contrr</b><br><b>Events</b><br>10<br>0  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>1753  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%<br>01); l <sup>2</sup> = 77?<br>Weight<br>6.5%  | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.17 [0.77, 1.78]<br>4.11 [1.28, 1.3.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>0.10 [0.04, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]<br>5<br>Odds Ratio<br>V. Random, 95% CI<br>1.00 [0.38, 2.66]<br>Not estimable   | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio | 200      |
|    | lordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>s</sup> = 0.5<br>Total events<br>Heterogeneity: Tau <sup>s</sup> = 0.5<br>Study or Subaroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015   | 86<br>82<br>34<br>14<br>63<br>67<br>70<br>89<br>90<br>40<br>27<br>812<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6<br>10<br>84<br>27<br>812<br>812<br>10<br>10<br>10<br>10<br>11<br>10<br>10<br>11<br>10<br>10<br>10<br>10<br>10  | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br><b>1217</b><br>60.52, df<br>0.52)<br>mental<br>Total<br>50   | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34<br>1164<br>= 14 (P <<br><b>Contro</b><br><b>Events</b><br>10<br>0<br>12  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>40<br>1753<br>0.0000<br>1753  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%<br>01); l <sup>2</sup> = 779<br>Weight  | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.77 [0.77, 1.78]<br>4.11 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>1.20 [0.67, 2.15]<br>0.10 [0.04, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.36 [0.55, 1.35]<br>6<br>Odds Ratio<br>V. Random, 95% CC<br>Not estimable<br>0.79 [0.33, 1.90]   | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio | 200      |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.5<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Enisman, H 2015<br>Hou, C 2018<br>Hou, C 2018   | 86<br>82<br>34<br>14<br>63<br>67<br>74<br>22<br>70<br>89<br>40<br>27<br>53; Chi <sup>2</sup> = 6<br>= 0.64 (P =<br>Experim<br>Events<br>10<br>0<br>14<br>36<br>10  | 100<br>41<br>60<br>155<br>71<br>61<br>125<br>143<br>40<br>30<br><b>1217</b><br>60.52) df<br>60.52) df<br>60.52) df<br>60.52) df<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>44  | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34<br>1164<br>= 14 (P <<br><b>Contro</b><br><b>Events</b><br>10<br>0<br>0<br>12<br>6<br>55<br>32  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>1753<br>0.0000  | 3.1%<br>7.2%<br>6.0%<br>8.6%<br>8.5%<br>4.8%<br>100.0%<br>01); l <sup>2</sup> = 779<br>6.5%<br>6.8%<br>6.4%<br>6.8%  | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.20 [0.67, 2.15]<br>1.20 [0.67, 2.15]<br>0.10 [0.40, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]<br>0.01 [0.40, 0.22]<br>0.04 [0.55, 1.35]<br>0.04 [0.55, 1.35]<br>0.04 [0.30, 2.66]<br>Not estimable<br>0.79 [0.33, 1.90]<br>0.23 [0.10, 0.55]   | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio | 200      |
|    | lordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhen, Y 2017<br>Zhen, Y 2017<br>Total (9% CI)<br>Total (9% CI)<br>Total svents<br>Heterogeneity: Tau <sup>2</sup> = 0.5<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hou, C 2018   | 86<br>82<br>34<br>14<br>63<br>67<br>70<br>89<br>40<br>27<br>812<br>27<br>812<br>27<br>812<br>53; Chi <sup>p</sup> = €<br>= 0.64 (P =<br>Experim<br>Events<br>10<br>0<br>14<br>36   | 100<br>41<br>60<br>1555<br>71<br>61<br>125<br>143<br>40<br>30<br><b>1217</b><br>60.52, df<br>50.52, df<br>50<br>30<br>700<br>70  | 54<br>40<br>12<br>83<br>57<br>401<br>35<br>40<br>34<br>1164<br>= 14 (P <<br>Contro<br>Events<br>10<br>0<br>12<br>65   | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>40<br>1753<br>0.0000<br>1753<br>0.0000<br>0<br>1753<br>50<br>30<br>50<br>70   | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>4.8%<br>100.0%<br>01);  ² = 779<br>Weight<br>6.5%<br>6.8%<br>6.4%  | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.20 [0.57, 2.15]<br>1.20 [0.67, 2.15]<br>0.10 [0.40, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]<br>0.06 [0.55, 1.35]<br>0.06 [0.55, 1.35]<br>0.00 [0.38, 2.66]<br>Not estimable<br>0.79 [0.33, 1.90]<br>0.23 [0.10, 0.55]<br>1.20 [0.57, 2.37]   | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio | 200      |
|    | lordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, Y 2017<br>Total events<br>Total events<br>Total events<br>Total events<br>Study or Subaroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutchinson, K 2018   | 86<br>82<br>34<br>14<br>63<br>36<br>70<br>89<br>40<br>27<br>812<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6<br>9<br>40<br>27<br>10<br>20<br>14<br>36<br>10<br>0<br>14<br>36<br>10<br>23<br>22<br>19  | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br><b>1217</b><br>50.52, df<br>0.52)<br>50<br>30<br>70<br>70<br>44<br>4127<br>100<br>41   | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34<br>1164<br>= 14 (P <<br>Contro<br>Events<br>10<br>0<br>12<br>65<br>322<br>15<br>12<br>36   | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>1753<br>0.0000<br>1753<br>50<br>50<br>50<br>70<br>57<br>91<br>80<br>41  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.5%<br>8.5%<br>4.8%<br>100.0%<br>01); l <sup>2</sup> = 779<br><u>Weight</u><br>6.5%<br>6.8%<br>6.8%<br>6.8%<br>6.8%<br>6.8%<br>6.8%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.28 [0.73, 2.25]<br>1.20 [0.67, 2.15]<br>1.20 [0.67, 2.15]<br>1.20 [0.67, 2.15]<br>0.06 [0.36, 6.94]<br>0.86 [0.55, 1.35]<br>5<br>Odds Ratio<br>V, Random, 95% CI<br>1.00 [0.38, 2.68]<br>Not estimable<br>0.78 [0.33, 1.90]<br>0.06 [0.03, 0.23]<br>0.23 [0.10, 0.55]<br>1.12 [0.55, 2.29]<br>1.60 [0.74, 3.37]<br>0.21 [0.04, 0.37]  | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio | 200      |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.5<br><u>Study or Subaroup</u><br><u>Ahmed, AE 2020</u><br>Batmaz, SB 2017<br>Enisman, H 2015<br>Hou, C 2018<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019  | 86<br>82<br>34<br>14<br>63<br>67<br>70<br>89<br>40<br>27<br>812<br>53; Chi <sup>p</sup> = 6<br>= 0.64 (P =<br>Experim<br>Events<br>0<br>10<br>0<br>14<br>366<br>10<br>23<br>22   | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br><b>1217</b><br>60.52, df<br>50<br>50<br>30<br>700<br>70<br>44<br>127<br>100  | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34<br>1164<br>= 14 (P <<br><b>Controt</b><br><b>Events</b><br>10<br>0<br>12<br>65<br>32<br>15   | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>1753<br>0.0000<br>0<br>1753<br>50<br>30<br>50<br>50<br>30<br>57<br>91<br>80   | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%<br>01);   <sup>2</sup> = 779<br><u>Weight</u><br>6.5%<br>6.8%<br>6.4%<br>6.8%<br>6.4%<br>7.1%<br>7.0%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.20 [0.57, 2.15]<br>1.20 [0.67, 2.15]<br>0.10 [0.40, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]<br>6<br>Odds Ratio<br>V, Random, 95% CI<br>Not estimable<br>0.79 [0.33, 1.90]<br>0.23 [0.10, 0.55]<br>1.20 [0.57, 2.45]<br>1.60 [0.74, 3.47]<br>0.26 [0.29, 2.54]  | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio |          |
|    | lordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maaimi, H 2013<br>Ma, JH 2014<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhen, Y 2017<br>Zhao, LY 2016<br>Zhen, YF 2010<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.6<br>Study or Subbroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchineson, M 2014<br>Ma, JH 2014<br>Maalmi, H 2013<br>Maalmi, H 2013  | 86<br>82<br>34<br>14<br>63<br>367<br>42<br>70<br>89<br>40<br>27<br>812<br>53; Chi <sup>2</sup> = 6<br>= 0.64 (P =<br>Experim<br>Events<br>10<br>0<br>14<br>4<br>36<br>10<br>23<br>3<br>22<br>10<br>9<br>9<br>9<br>7<br>6<br>36   | 100<br>41<br>40<br>55<br>71<br>125<br>143<br>40<br>325<br>50<br>50<br>50<br>50<br>30<br>70<br>70<br>70<br>44<br>41<br>27<br>100<br>41<br>60<br>55<br>71  | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>1355<br>40<br>34<br>1164<br>= 14 (P <<br><b>Contru</b><br><b>Events</b><br>10<br>0<br>12<br>65<br>322<br>15<br>12<br>36<br>8<br>8<br>13<br>29  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>1753<br>0.0000<br>1753<br>50<br>30<br>50<br>50<br>50<br>50<br>57<br>91<br>80<br>41<br>60<br>225<br>71   | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%<br>01); l <sup>2</sup> = 779<br>01); l <sup>2</sup> = 779<br>0.6,5%<br>6.8%<br>6.8%<br>6.8%<br>6.8%<br>6.3%<br>6.3%<br>6.3%<br>6.3%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.20 [0.57, 2.15]<br>1.20 [0.67, 2.15]<br>0.10 [0.40, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]<br>0.06 [0.55, 1.35]<br>0.06 [0.55, 1.35]<br>0.06 [0.30, 2.26]<br>Not estimable<br>0.79 [0.33, 1.90]<br>0.23 [0.10, 0.55]<br>1.20 [0.57, 2.47]<br>0.26 [0.20, 2.24]<br>0.66 [0.24, 3.47]<br>0.26 [0.24, 3.47]<br>0.26 [0.24, 3.47]<br>0.26 [0.24, 3.47]  | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio | +<br>200 |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, Y 2017<br>Total events<br>Total events<br>Total events<br>Total events<br>Study or Subaroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Hutchinson, H 2015<br>Hordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014  | 86<br>82<br>34<br>14<br>63<br>36<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>42<br>70<br>40<br>42<br>70<br>40<br>42<br>70<br>40<br>42<br>70<br>40<br>40<br>70<br>40<br>70<br>40<br>70<br>40<br>70<br>80<br>80<br>80<br>80<br>80<br>80<br>80<br>80<br>80<br>80<br>80<br>80<br>80 | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>0.52<br>50<br>50.52, df<br>50<br>30<br>70<br>70<br>44<br>42<br>120<br>70<br>41<br>25<br>50<br>30<br>70<br>70<br>44<br>42<br>120<br>70<br>10<br>50<br>50<br>30<br>70<br>70<br>10<br>55<br>50<br>50<br>50<br>50<br>71<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50  | 54<br>40<br>12<br>83<br>57<br>401<br>37<br>135<br>40<br>34<br>1164<br>= 14 (P <<br>Contro<br>Events<br>10<br>0<br>12<br>65<br>5<br>32<br>15<br>12<br>36<br>8<br>8<br>13   | 41<br>60<br>2255<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>50<br>50<br>50<br>50<br>50<br>50<br>57<br>91<br>80<br>0<br>225   | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>100.0%<br>001); I <sup>2</sup> = 779<br>Weight<br>6.5%<br>6.8%<br>6.8%<br>6.8%<br>6.8%<br>7.1%<br>7.0%<br>6.2%<br>6.5%   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.41 [1.28, 13.20]<br>1.28 [0.73, 2.25]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]<br>5<br>Odds Ratio<br>V, Random, 95% CI<br>1.00 [0.38, 2.66]<br>Not estimable<br>0.79 [0.33, 1.90]<br>Not estimable<br>0.79 [0.34, 1.90]<br>Not estimable<br>0.79 [0.74, 1.74]<br>Not estimable<br>0.75 [0.75, 1.75]<br>Not estimable<br>0.75 [0.75, 1.75]<br>Not estimable<br>0.75 [0.75, 1.75]<br>Not estimable<br>0.75 [0.75, 1.75] | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Plilai, DK 2011<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Total (95% CI)<br>Total (95% CI)<br>To     | 866<br>822<br>34<br>414<br>463<br>367<br>70<br>89<br>40<br>27<br>812<br>812<br>812<br>812<br>812<br>812<br>812<br>812<br>812<br>812  | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>30<br><b>1217</b><br>50.52, df<br>0.52)<br><b>tental</b><br>50<br>30<br>30<br>30<br>70<br>70<br>30<br>30<br>70<br>44<br>127<br>100<br>155<br>51<br>43<br>143   | $\begin{matrix} 54\\ 40\\ 12\\ 12\\ 83\\ 57\\ 401\\ 135\\ 57\\ 401\\ 135\\ 40\\ 34\\ 1164\\ 40\\ 34\\ 1164\\ 10\\ 0\\ 12\\ 15\\ 32\\ 23\\ 6\\ 32\\ 15\\ 12\\ 13\\ 29\\ 9\\ 88\\ 81\\ 3\\ 29\\ 88\\ 84\\ 46\\ 6\end{matrix}$   | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>0<br>1753<br>0.0000<br>0<br>1753<br>30<br>50<br>30<br>50<br>70<br>91<br>80<br>40<br>225<br>71<br>633<br>72<br>143<br>30<br>20<br>20<br>20<br>20<br>20<br>20<br>20<br>20<br>20<br>2  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>4.8%<br>100.0%<br>01);   <sup>2</sup> = 779<br>Weight<br>6.5%<br>6.8%<br>6.8%<br>6.8%<br>6.8%<br>6.2%<br>6.5%<br>6.5%<br>6.5%<br>7.2%<br>7.2%<br>7.3%  | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.28 [0.57, 2.91]<br>1.28 [0.67, 2.25]<br>1.20 [0.67, 2.15]<br>1.20 [0.67, 2.15]<br>1.20 [0.67, 2.15]<br>1.20 [0.67, 2.15]<br>1.00 [0.40, 0.22]<br>Not estimable<br>0.46 [0.55, 1.35]<br>5<br>Odds Ratio<br>V. Random, 95% Cf<br>1.00 [0.38, 2.66]<br>Not estimable<br>0.79 [0.33, 1.90]<br>Not estimable<br>0.79 [0.33, 1.90]<br>1.12 [0.56, 2.29]<br>1.60 [0.74, 3.47]<br>0.26 [0.24, 1.77]<br>1.49 [0.77, 2.89]<br>0.29 [0.70, 0.24]<br>0.42 [0.70, 0.24]  | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio | 200      |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maaimi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhen, YK 2015<br>Zhen, YK 2015<br>Total (9% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.6<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutchinson, H 2014<br>Maaimi, H 2013<br>Maaimi, H 2014<br>Maaimi, H 2015<br>Papadopoulou, A 2015   | 86<br>82<br>34<br>14<br>63<br>67<br>42<br>70<br>89<br>9<br>40<br>27<br>812<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6<br>53; Chi <sup>2</sup> = 6<br>7<br>6<br>6<br>8<br>9<br>9<br>9<br>9<br>9<br>7<br>6<br>6<br>36<br>8<br>8<br>11   | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br><b>1217</b><br>50.52, df<br>50<br>50<br>50<br>50<br>50<br>70<br>70<br>70<br>70<br>44<br>127<br>16<br>50<br>50<br>50<br>50<br>50<br>50<br>70<br>17<br>51<br>50<br>50<br>71<br>17<br>55<br>50<br>71<br>125<br>5<br>50<br>71<br>125<br>5<br>50<br>71<br>125<br>5<br>5<br>71<br>125<br>5<br>5<br>71<br>125<br>5<br>5<br>71<br>125<br>5<br>5<br>71<br>125<br>5<br>5<br>71<br>125<br>5<br>5<br>71<br>125<br>5<br>5<br>71<br>125<br>5<br>71<br>125<br>5<br>71<br>125<br>5<br>71<br>125<br>5<br>71<br>71<br>72<br>71<br>72<br>71<br>72<br>71<br>72<br>71<br>72<br>71<br>72<br>71<br>72<br>71<br>72<br>72<br>71<br>72<br>72<br>72<br>72<br>72<br>72<br>72<br>72<br>72<br>72<br>72<br>72<br>72 | $\begin{matrix} 54\\ 400\\ 12\\ 137\\ 401\\ 337\\ 401\\ 34\\ 1164\\ 40\\ 34\\ 1164\\ 40\\ 34\\ 10\\ 10\\ 10\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 15\\ 12\\ 12\\ 15\\ 12\\ 12\\ 12\\ 12\\ 12\\ 12\\ 12\\ 12\\ 12\\ 12$ | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>1753<br>0.0000<br>1753<br>0.0000<br>1753<br>0.0000<br>16<br>1753<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>4.8%<br>100.0%<br>01); l <sup>2</sup> = 779<br>6.5%<br>6.8%<br>6.4%<br>6.8%<br>7.1%<br>6.6%<br>6.4%<br>6.8%<br>7.1%<br>7.0%<br>6.5%<br>6.5%<br>6.5%<br>6.5%<br>6.5%<br>6.5%<br>6.5%<br>6.5   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.28 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.20 [0.67, 2.15]<br>0.10 [0.47, 2.15]<br>0.10 [0.40, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.36 [0.55, 1.35]<br>5<br>Odds Ratio<br>V.Random. 95% CI<br>1.00 [0.38, 2.66]<br>Not estimable<br>0.79 [0.33, 1.90]<br>0.36 [0.03, 0.23]<br>0.23 [0.10, 0.55]<br>1.21 [0.55, 2.29]<br>1.60 [0.77, 2.89]<br>0.66 [0.24, 1.77]<br>1.49 [0.77, 2.89]<br>0.92 [0.24, 2.61]<br>0.49 [0.24, 0.55, 3.63]<br>0.33 [0.07, 0.24]<br>0.49 [0.24, 0.55, 3.63]<br>0.33 [0.07, 0.24]   | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio | 200      |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhen, HY 2017<br>Total (9% CI)<br>Total (9% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.5<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutching, Y 2017<br>Zhao, HX 2015<br>Zhen, YF 2010   | 866<br>822<br>34<br>41<br>41<br>41<br>463<br>367<br>70<br>89<br>9<br>40<br>27<br>812<br>27<br>812<br>27<br>812<br>20<br>819<br>40<br>27<br>812<br>20<br>819<br>40<br>27<br>812<br>27<br>812<br>812<br>812<br>812<br>812<br>812<br>812<br>812<br>812<br>812   | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br><b>1217</b><br><b>50</b> .52, df<br>0.52)<br><b>total</b><br><b>50</b> .52, df<br>0.52)<br><b>total</b><br>100<br>44<br>41<br>27<br>100<br>41<br>125<br>57<br>11<br>00<br>55<br>51<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50   | $\begin{matrix} 54\\ 40\\ 0\\ 12\\ 83\\ 37\\ 135\\ 40\\ 137\\ 135\\ 40\\ 34\\ 1164\\ (P < \begin{matrix} \\ \\ \\ \hline \\ \\ \hline \\ \\ \hline \\ \\ \hline \\ \\ \\ \\ \\ \\$  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>1753<br>0.0000<br>1753<br>0.0000<br>16<br>16<br>16<br>16<br>16<br>16<br>16<br>16<br>16<br>16  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>7.6%<br>4.8%<br>4.8%<br>100.0%<br>01); l <sup>2</sup> = 779<br>01); l <sup>2</sup> = 779<br>0.5%<br>6.8%<br>6.8%<br>6.8%<br>6.3%<br>6.3%<br>6.2%<br>7.2%<br>6.3%<br>6.3%<br>6.1% | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.28 [0.57, 2.91]<br>1.20 [0.67, 2.15]<br>0.10 [0.47, 2.15]<br>0.10 [0.46, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]<br>6<br>Odds Ratio<br>V. Random. 95% CI<br>1.00 [0.38, 2.68]<br>Not estimable<br>0.79 [0.33, 1.90]<br>0.06 [0.03, 0.23]<br>0.23 [0.10, 0.55]<br>1.12 [0.55, 2.29]<br>1.60 [0.74, 3.47]<br>0.26 [0.24, 1.77]<br>1.28 [0.56, 3.28]<br>0.46 [0.24, 1.77]<br>1.26 [0.26, 3.28]<br>0.46 [0.24, 1.77]<br>1.26 [0.26, 3.28]<br>0.46 [0.24, 1.77]<br>1.48 [0.57, 6.38]<br>0.34 [0.17, 0.34]<br>0.46 [0.24, 1.77]<br>1.48 [0.57, 6.38]<br>0.31 [0.77, 2.34]<br>0.46 [0.24, 1.77]<br>1.48 [0.57, 6.38]<br>0.31 [0.77, 2.34]<br>0.46 [0.24, 1.77]  | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maaimi, H 2013<br>Mo, LY 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Total (9% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.6<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutchinson, K 2018<br>Hutchinson, H 2014<br>Maaimi, H 2013<br>Maaimi, H 2014<br>Maaimi, H 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015   | 866<br>822<br>34<br>41<br>41<br>41<br>463<br>367<br>70<br>89<br>9<br>40<br>27<br>812<br>27<br>812<br>27<br>812<br>20<br>819<br>40<br>27<br>812<br>20<br>819<br>40<br>27<br>812<br>27<br>812<br>812<br>812<br>812<br>812<br>812<br>812<br>812<br>812<br>812   | 100<br>41<br>60<br>155<br>71<br>125<br>143<br>40<br>30<br>1217<br>50.52, df<br>0.52)<br>50<br>30<br>70<br>70<br>44<br>4127<br>70<br>00<br>100<br>100<br>100<br>100<br>101<br>100<br>100<br>100   | $\begin{matrix} 54\\ 40\\ 0\\ 12\\ 83\\ 37\\ 135\\ 40\\ 137\\ 135\\ 40\\ 34\\ 1164\\ (P < \begin{matrix} \\ \\ \\ \hline \\ \\ \hline \\ \\ \hline \\ \\ \hline \\ \\ \\ \\ \\ \\$  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>1753<br>0.0000<br>1753<br>0.0000<br>16<br>16<br>16<br>16<br>16<br>16<br>16<br>16<br>16<br>16  | 3.1%<br>7.2%<br>9.2%<br>6.0%<br>8.6%<br>8.5%<br>7.6%<br>4.8%<br>4.8%<br>100.0%<br>01); l <sup>2</sup> = 779<br>6.5%<br>6.8%<br>6.4%<br>6.8%<br>7.1%<br>6.4%<br>6.8%<br>7.1%<br>6.3%<br>6.3%<br>6.5%<br>6.3%<br>6.5%<br>6.5%<br>6.5%<br>6.5%<br>6.5%<br>6.5%<br>6.5%<br>6.5   | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.28 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.20 [0.67, 2.15]<br>0.10 [0.47, 2.15]<br>0.10 [0.40, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.36 [0.55, 1.35]<br>5<br>Odds Ratio<br>V.Random. 95% CI<br>1.00 [0.38, 2.66]<br>Not estimable<br>0.79 [0.33, 1.90]<br>0.36 [0.03, 0.23]<br>0.23 [0.10, 0.55]<br>1.21 [0.55, 2.29]<br>1.60 [0.77, 2.89]<br>0.66 [0.24, 1.77]<br>1.49 [0.77, 2.89]<br>0.92 [0.24, 2.61]<br>0.49 [0.24, 0.55, 3.63]<br>0.33 [0.07, 0.24]<br>0.49 [0.24, 0.55, 3.63]<br>0.33 [0.07, 0.24]   | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio |          |
|    | Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Plilai, DK 2011<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Study or Subaroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Batmaz, SB 2017<br>Sathagenergy SB 2017<br>Sathagenergy SB 2017<br>Sathagenergy SB 2017<br>Zhao, HX 2015<br>Plilai, DK 2011<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Plilai, DK 2011<br>Zhao, HX 2015<br>Plilai, DK 2011<br>Zhao, HX 2015<br>Plilai, DK 2011<br>Zhao, YZ 2015<br>Plilai, DK 2011<br>Zhao, HX 2015<br>Zhao, | 866<br>822<br>344<br>463<br>474<br>472<br>742<br>742<br>742<br>742<br>742<br>742<br>742<br>742   | 1000<br>411<br>600<br>1555<br>711<br>1255<br>80.522, df<br>80.522<br>500<br>300<br>700<br>700<br>700<br>700<br>700<br>700<br>41<br>1255<br>711<br>600<br>701<br>701<br>1255<br>711<br>1255<br>712<br>712<br>712<br>712<br>712<br>712<br>712<br>712<br>712<br>712   | 54<br>400<br>12<br>83<br>57<br>70<br>135<br>401<br>37<br>135<br>40<br>40<br>40<br>40<br>40<br>0<br>2<br>50<br>2<br>50<br>2<br>50<br>2<br>50<br>2  | 41<br>60<br>225<br>71<br>633<br>72<br>143<br>40<br>40<br>1753<br>0.0000<br>1753<br>0.0000<br>1753<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.00000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.0000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000<br>0.00000000 | 3.1% (%) (%) (%) (%) (%) (%) (%) (%) (%) (%  | 0.12 [0.01, 1.04]<br>1.22 [0.51, 2.91]<br>1.71 [0.77, 1.78]<br>1.28 [0.57, 2.91]<br>1.71 [0.77, 1.78]<br>1.20 [0.67, 2.15]<br>0.10 [0.40, 0.22]<br>Not estimable<br>1.59 [0.36, 6.94]<br>0.86 [0.55, 1.35]<br>6<br>Odds Ratio<br>V. Random. 95% CI<br>1.00 [0.38, 2.66]<br>Not estimable<br>0.79 [0.33, 1.90]<br>0.06 [0.03, 0.23]<br>0.23 [0.10, 0.55]<br>1.12 [0.55, 2.29]<br>1.60 [0.74, 3.47]<br>0.26 [0.24, 1.77]<br>1.92 [0.40, 0.37]<br>0.26 [0.24, 1.77]<br>1.92 [0.40, 0.37]<br>0.26 [0.24, 1.77]<br>1.92 [0.40, 0.37]<br>0.26 [0.24, 1.77]<br>1.92 [0.40, 0.37]<br>0.26 [0.24, 1.77]<br>1.92 [0.40, 0.37]<br>0.46 [0.24, 1.77]<br>1.92 [0.40, 0.37]<br>0.46 [0.24, 1.77]<br>1.93 [0.40, 0.38]<br>0.73 [0.40, 1.32]   | Favours [experimental]<br>Odds      | Favours [control]<br>Ratio |          |

FIGURE 2 | Forest plot for meta-analyzing the association between Vitamin D receptor Apal (rs7975232) polymorphisms and childhood asthma. (A) additive model: a vs. A; (B) co dominant model: aa vs. AA; (C) co dominant model: Aa vs. AA; (D) dominant model: aa+Aa vs. AA; (E) recessive model: aa vs. AA+Aa.

#### TABLE 4 | Outcomes of the subgroup analysis.

| Model            | No. of studies | Heterog | eneity test    | Effect            | size    |
|------------------|----------------|---------|----------------|-------------------|---------|
|                  |                | l² (%)  | P <sub>H</sub> | OR (95% CI)       | P value |
| Apal (rs7975232) |                |         |                |                   |         |
| a vs. A          | 16             | 88.7    | <0.001         | 0.82 (0.56, 1.21) | 0.317   |
| Ethnicity        |                |         |                | <b>x</b>          |         |
| American         | 1              | NA      | NA             | 0.76 (0.45, 1.26) | 0.285   |
| Asian            | 7              | 93.6    | <0.001         | 0.65 (0.25, 1.70) | 0.378   |
| Caucasians       | 7              | 67.3    | 0.005          | 0.98 (0.72, 1.33) | 0.876   |
| African-American | 1              | NA      | NA             | 1.20 (0.77, 1.89) | 0.417   |
| HWE              |                |         |                |                   |         |
| Yes              | 13             | 90.3    | <0.001         | 0.73 (0.47, 1.13) | 0.163   |
| No               | 3              | 17.7    | 0.297          | 1.37 (0.88, 2.16) | 0.167   |
| Source           |                |         |                |                   |         |
| HB               | 14             | 90.0    | <0.001         | 0.79 (0.50, 1.22) | 0.287   |
| PB               | 2              | 0       | 0.927          | 1.09 (0.78, 1.52) | 0.607   |
| aa vs. AA        | 16             | 83.7    | < 0.001        | 0.65 (0.31, 1.38) | 0.263   |
| Ethnicity        | -              |         |                |                   |         |
| American         | 1              | NA      | NA             | 0.56 (0.19, 1.63) | 0.285   |
| Asian            | 7              | 90.8    | <0.001         | 0.37 (0.06, 2.48) | 0.305   |
| Caucasians       | 7              | 65.2    | 0.013          | 0.89 (0.46, 1.74) | 0.737   |
| African-American | 1              | NA      | NA             | 1.75 (0.52, 5.93) | 0.369   |
| HWE              |                |         |                |                   |         |
| Yes              | 13             | 85.0    | <0.001         | 0.63 (0.28, 1.42) | 0.264   |
| No               | 3              | NA      | NA             | 0.91 (0.31, 2.72) | 0.280   |
| Source           | -              |         |                |                   |         |
| HB               | 14             | 86.0    | <0.001         | 0.59 (0.24, 1.46) | 0.254   |
| PB               | 2              | 0       | 0.795          | 1.02 (0.52, 2.01) | 0.948   |
| Aa vs. AA        | 16             | 62.7    | < 0.001        | 0.97 (0.66, 1.42) | 0.866   |
| Ethnicity        |                |         |                | (,)               |         |
| American         | 1              | NA      | NA             | 0.60 (0.24, 1.47) | 0.260   |
| Asian            | 7              | 72.9    | <0.001         | 0.71 (0.19, 2.67) | 0.615   |
| Caucasians       | 7              | 9.2     | 0.358          | 1.24 (0.94, 1.63) | 0.128   |
| African-American | 1              | NA      | NA             | 1.14 (0.62, 2.08) | 0.674   |
| HWE              | ·              |         |                |                   | 0.07.1  |
| Yes              | 13             | 67.0    | <0.001         | 0.90 (0.59, 1.38) | 0.637   |
| No               | 3              | 0       | 0.844          | 1.67 (0.67, 4.14) | 0.272   |
| Source           | -              | -       |                |                   |         |
| HB               | 14             | 66.6    | <0.001         | 0.89 (0.57, 1.39) | 0.612   |
| PB               | 2              | 0.0     | 0.662          | 1.40 (0.82, 2.40) | 0.213   |
| aa+Aa vs. AA     | 16             | 76.9    | <0.001         | 0.86 (0.55, 1.35) | 0.520   |
| Ethnicity        |                |         |                | (,)               |         |
| American         | 1              | NA      | NA             | 0.58 (0.25, 1.38) | 0.220   |
| Asian            | 7              | 86.9    | <0.001         | 0.53 (0.12, 2.25) | 0.391   |
| Caucasians       | 7              | 46.8    | 0.080          | 1.14 (0.79, 1.62) | 0.488   |
| African-American | 1              | NA      | NA             | 1.20 (0.67, 2.15) | 0.532   |
| HWE              |                |         | 1.47.4         |                   | 0.002   |
| Yes              | 13             | 79.9    | <0.001         | 0.80 (0.48, 1.33) | 0.393   |
| No               | 3              | 0       | 0.778          | 1.31 (0.64, 2.68) | 0.467   |
| Source           | -              | -       |                |                   | 0.107   |
| HB               | 14             | 79.8    | <0.001         | 0.79 (0.47, 1.36) | 0.400   |
| PB               | 2              | 0       | 0.926          | 1.26 (0.78, 2.03) | 0.339   |
| aa vs. AA+Aa     | 16             | 85.6    | <0.001         | 0.73 (0.40, 1.32) | 0.295   |

| Model            | No. of studies | Heterog | eneity test    | Effect             | size    |
|------------------|----------------|---------|----------------|--------------------|---------|
|                  |                | l² (%)  | P <sub>H</sub> | OR (95% CI)        | P value |
| Ethnicity        |                |         |                |                    |         |
| American         | 1              | NA      | NA             | 0.79 (0.33, 1.90)  | 0.600   |
| Asian            | 7              | 92.5    | <0.001         | 0.60 (0.17, 2.04)  | 0.409   |
| Caucasians       | 7              | 58.5    | 0.034          | 0.81 (0.48, 1.39)  | 0.446   |
| African-American | 1              | NA      | NA             | 1.64 (0.50, 5.36)  | 0.412   |
| HWE              |                |         |                |                    |         |
| Yes              | 13             | 85.8    | <0.001         | 0.64 (0.34, 1.20)  | 0.165   |
| No               | 3              | 72.9    | 0.055          | 1.78 (0.45, 6.96)  | 0.409   |
| Source           |                |         |                | - (                |         |
| HB               | 14             | 87.6    | <0.001         | 0.70 (0.35, 1.40)  | 0.319   |
| PB               | 2              | 0.0     | 0.916          | 0.90 (0.48, 1.69)  | 0.745   |
| Taql (rs731236)  | -              | 0.0     | 010110         |                    | 01110   |
| t vs. T          | 12             | 71.1    | <0.001         | 0.93 (0.70, 1.23)  | 0.608   |
| Ethnicity        | 14             | 11.1    | ~0.001         | 0.00 (0.70, 1.20)  | 0.000   |
| American         | 1              | NA      | NA             | 0.99 (0.56, 1.75)  | 0.970   |
| Asian            | 3              | 55.4    | 0.106          | 0.45 (0.23, 0.89)  | 0.022   |
| Caucasians       | 7              | 71.5    | 0.002          | 1.06 (0.77, 1.47)  | 0.711   |
| African-American | ,<br>1         | NA      | NA             | 1.45 (0.92, 2.30)  | 0.112   |
| HWE              | I              | INA     | IN/A           | 1.40 (0.92, 2.30)  | 0.112   |
|                  | 0              | 70.0    | 0.001          | 0.01 (0.66, 1.07)  | 0.500   |
| Yes<br>No        | 8              | 70.8    | 0.001          | 0.91 (0.66, 1.27)  | 0.582   |
|                  | 4              | 77.9    | 0.004          | 0.96 (0.52, 1.78)  | 0.888   |
| Source           | 10             | 70.0    | 0.001          |                    | 0.070   |
| HB               | 10             | 76.3    | < 0.001        | 0.93 (0.66, 1.30)  | 0.670   |
| PB               | 2              | 0       | 0.699          | 0.93 (0.66, 1.30)  | 0.661   |
| tt vs. ∏         | 12             | 63.5    | 0.002          | 0.92 (0.49, 1.70)  | 0.783   |
| Ethnicity        |                |         |                |                    |         |
| American         | 1              | NA      | NA             | 1.03 (0.16, 6.63)  | 0.976   |
| Asian            | 3              | 56.5    | 0.129          | 0.37 (0.06, 2.40)  | 0.300   |
| Caucasians       | 7              | 71.0    | 0.002          | 0.96 (0.44, 2.09)  | 0.912   |
| African-American | 1              | NA      | NA             | 2.82 (0.74, 10.79) | 0.130   |
| HWE              |                |         |                |                    |         |
| Yes              | 8              | 56.2    | 0.025          | 0.71 (0.36, 1.40)  | 0.320   |
| No               | 4              | 70.6    | 0.033          | 2.01 (0.46, 8.77)  | 0.351   |
| Source           |                |         |                |                    |         |
| HB               | 10             | 67.7    | 0.002          | 0.93 (0.42, 2.07)  | 0.857   |
| PB               | 2              | 3.5     | 0.407          | 1.15 (0.62, 2.12)  | 0.665   |
| Tt vs. TT        | 12             | 50.2    | 0.024          | 1.00 (0.72, 1.38)  | 0.996   |
| Ethnicity        |                |         |                |                    |         |
| American         | 1              | NA      | NA             | 0.97 (0.46, 2.03)  | 0.939   |
| Asian            | 3              | 0       | 0.379          | 0.36 (0.17, 0.77)  | 0.009   |
| Caucasians       | 7              | 48.6    | 0.070          | 1.13 (0.78, 1.65)  | 0.513   |
| African-American | 1              | NA      | NA             | 1.36 (0.75, 2.49)  | 0.312   |
| HWE              |                |         |                |                    |         |
| Yes              | 8              | 0       | 0.693          | 1.26 (0.99, 1.60)  | 0.064   |
| No               | 4              | 49.2    | 0.116          | 0.57 (0.29, 1.15)  | 0.120   |
| Source           |                |         |                |                    |         |
| HB               | 10             | 41.4    | 0.082          | 1.11 (0.81, 1.53)  | 0.521   |
| PB               | 2              | 0.0     | 0.438          | 0.53 (0.31, 0.94)  | 0.029   |
| tt+Tt vs. TT     | 12             | 53.3    | 0.015          | 0.96 (0.70, 1.32)  | 0.817   |

| Model            | No. of studies | Heterog          | eneity test    | Effect            | size    |
|------------------|----------------|------------------|----------------|-------------------|---------|
|                  |                | l² (%)           | P <sub>H</sub> | OR (95% CI)       | P value |
| Ethnicity        |                |                  |                |                   |         |
| American         | 1              | NA               | NA             | 0.98 (0.47, 2.01) | 0.947   |
| Asian            | 3              | 29.0             | 0.244          | 0.36 (0.15, 0.87) | 0.024   |
| Caucasians       | 7              | 42.7             | 0.106          | 1.08 (0.77, 1.50) | 0.663   |
| African-American | 1              | NA               | NA             | 1.49 (0.83, 2.68) | 0.178   |
| HWE              |                |                  |                |                   |         |
| Yes              | 8              | 30.6             | 0.184          | 1.12 (0.84, 1.50) | 0.437   |
| No               | 4              | 64.1             | 0.039          | 0.70 (0.32, 1.51) | 0.362   |
| Source           |                |                  |                |                   |         |
| HB               | 10             | 56.6             | 0.014          | 1.02 (0.71, 1.47) | 0.901   |
| PB               | 2              | 0                | 0.739          | 0.67 (0.41, 1.10) | 0.112   |
| tt vs. TT+Tt     | 12             | 72.6             | <0.001         | 0.87 (0.47, 1.62) | 0.658   |
| Ethnicity        |                |                  |                |                   |         |
| American         | 1              | NA               | NA             | 1.04 (0.17, 6.48) | 0.964   |
| Asian            | 3              | 65.5             | 0.089          | 0.46 (0.14, 1.50) | 0.304   |
| Caucasians       | 7              | 79.3             | <0.009         | 0.97 (0.41, 2.28) | 0.198   |
| African-American | 1              | NA               | <0.001<br>NA   | 2.43 (0.66, 9.03) | 0.941   |
| HWE              | I              | INA              | INA            | 2.43 (0.00, 9.03) | 0.164   |
|                  | 0              | E7 0             | 0.000          | 0.60.(0.20.1.00)  | 0.005   |
| Yes              | 8              | 57.8             | 0.020          | 0.60 (0.32, 1.09) | 0.095   |
| No               | 4              | 73.5             | 0.023          | 2.06 (0.59, 7.27) | 0.259   |
| Source           | 10             |                  | 0.004          |                   | 0.500   |
| HB               | 10             | 69.2             | 0.001          | 0.78 (0.38, 1.61) | 0.503   |
| PB               | 2              | 51.7             | 0.150          | 1.30 (0.59, 2.86) | 0.521   |
| Bsml (rs1544410) |                |                  |                |                   |         |
| o vs. B          | 12             | 73.2             | <0.001         | 0.87 (0.62, 1.21) | 0.408   |
| Ethnicity        |                |                  |                |                   |         |
| Asian            | 7              | 79.9             | <0.001         | 0.57 (0.28, 1.17) | 0.128   |
| Caucasians       | 5              | 62.5             | 0.031          | 1.12 (0.82, 1.54) | 0.481   |
| HWE              |                |                  |                |                   |         |
| Yes              | 11             | 75.6             | <0.001         | 0.86 (0.60, 1.23) | 0.419   |
| No               | 1              | NA               | NA             | 0.88 (0.44, 1.77) | 0.724   |
| Source           |                |                  |                |                   |         |
| HB               | 10             | 77.6             | <0.001         | 0.81 (0.54, 1.24) | 0.336   |
| PB               | 2              | 0                | 0.527          | 1.08 (0.78, 1.49) | 0.662   |
| bb vs. BB        | 12             | 68.0             | 0.003          | 1.16 (0.61, 2.21) | 0.665   |
| Ethnicity        |                |                  |                |                   |         |
| Asian            | 7              | 79.5             | 0.008          | 0.74 (0.12, 4.40) | 0.741   |
| Caucasians       | 5              | 66.2             | 0.019          | 1.24 (0.62, 2.50) | 0.539   |
| HWE              |                |                  |                |                   |         |
| Yes              | 11             | 72.6             | 0.001          | 1.16 (0.56, 2.40) | 0.690   |
| No               | 1              | NA               | NA             | 1.13 (0.32, 3.94) | 0.854   |
| Source           |                |                  |                | . ,               |         |
| HB               | 10             | 76.7             | 0.001          | 1.12 (0.45, 2.76) | 0.805   |
| PB               | 2              | 0                | 0.844          | 1.25 (0.65, 2.42) | 0.501   |
| Bb vs. BB        | 12             | 55.6             | 0.027          | 1.22 (0.76, 1.96) | 0.409   |
| Ethnicity        |                |                  |                | (                 | 000     |
| Asian            | 7              | 0                | 0.401          | 1.42 (0.90, 2.23) | 0.130   |
| Caucasians       | 5              | 68.4             | 0.013          | 1.22 (0.62, 2.40) | 0.130   |
| HWE              | 0              | JU. <del>T</del> | 0.010          | 1.22 (0.02, 2.40) | 0.001   |
| Yes              | 11             | 60.8             | 0.018          | 1.18 (0.71, 1.96) | 0.524   |

| Model            | No. of studies | Heterog | eneity test    | Effect              | size    |
|------------------|----------------|---------|----------------|---------------------|---------|
|                  |                | l² (%)  | P <sub>H</sub> | OR (95% CI)         | P value |
| No               | 1              | NA      | NA             | 2.00 (0.42, 9.52)   | 0.384   |
| Source           |                |         |                | <b>x</b> . <b>y</b> |         |
| HB               | 10             | 67.3    | 0.009          | 1.20 (0.64, 2.24)   | 0.576   |
| PB               | 2              | 0.0     | 0.514          | 1.25 (0.65, 2.39)   | 0.505   |
| bb+Bb vs. BB     | 12             | 68.5    | 0.002          | 1.14 (0.67, 1.93)   | 0.627   |
| Ethnicity        | 12             | 00.0    | 0.002          | 1.14 (0.07, 1.30)   | 0.021   |
| Asian            | 7              | 70.5    | 0.034          | 0.80 (0.23, 2.81)   | 0.732   |
|                  | 5              | 70.5    |                | 1.25 (0.64, 2.47)   |         |
| Caucasians       | 5              | 12.2    | 0.006          | 1.25 (0.64, 2.47)   | 0.515   |
| HWE              |                | 70.0    | 0.004          |                     |         |
| Yes              | 11             | 73.0    | 0.001          | 1.13 (0.63, 2.01)   | 0.686   |
| No               | 1              | NA      | NA             | 1.22 (0.35, 4.24)   | 0.752   |
| Source           |                |         |                |                     |         |
| HB               | 10             | 77.4    | <0.001         | 1.10 (0.54, 2.25)   | 0.788   |
| PB               | 2              | 0       | 0.972          | 1.20 (0.66, 2.17)   | 0.552   |
| bb vs. BB+Bb     | 12             | 61.5    | 0.003          | 0.80 (0.54, 1.20)   | 0.278   |
| Ethnicity        |                |         |                |                     |         |
| Asian            | 7              | 69.2    | 0.003          | 0.55 (0.25, 1.18)   | 0.124   |
| Caucasians       | 5              | 0       | 0.414          | 1.01 (0.77, 1.32)   | 0.948   |
| HWE              |                |         |                |                     |         |
| Yes              | 11             | 64.9    | 0.001          | 0.80 (0.52, 1.24)   | 0.326   |
| No               | 1              | NA      | NA             | 0.75 (0.32, 1.77)   | 0.513   |
| Source           |                |         |                | <b>x</b> . <b>y</b> |         |
| HB               | 10             | 66.5    | 0.001          | 0.75 (0.46, 1.24)   | 0.267   |
| PB               | 2              | 0.0     | 0.375          | 1.04 (0.65, 1.66)   | 0.870   |
| Fokl (rs2228570) | -              | 0.0     | 01010          |                     | 0.07.0  |
| f vs. F          | 12             | 76.7    | <0.001         | 0.78 (0.57, 1.05)   | 0.102   |
| Ethnicity        | 12             | 10.1    | <0.001         | 0.10 (0.01, 1.00)   | 0.102   |
| American         | 1              | NA      | NA             | 0.90 (0.54, 1.51)   | 0.694   |
| Asian            | 5              | 84.4    | < 0.001        | 0.90 (0.50, 1.63)   | 0.721   |
| Caucasians       |                |         |                |                     |         |
|                  | 5              | 62.7    | 0.030          | 0.63 (0.43, 0.92)   | 0.015   |
| African-American | 1              | NA      | NA             | 0.85 (0.52, 1.39)   | 0.524   |
| HWE              |                |         |                |                     |         |
| Yes              | 11             | 78.8    | <0.001         | 0.76 (0.55, 1.06)   | 0.107   |
| No               | 1              | NA      | NA             | 0.90 (0.54, 1.51)   | 0.694   |
| Source           |                |         |                |                     |         |
| HB               | 11             | 73.2    | <0.001         | 0.72 (0.54, 0.97)   | 0.030   |
| PB               | 1              | NA      | NA             | 1.90 (1.14, 3.17)   | 0.015   |
| ff vs. FF        | 12             | 67.6    | 0.001          | 0.67 (0.34, 1.34)   | 0.260   |
| Ethnicity        |                |         |                |                     |         |
| American         | 1              | NA      | NA             | NA                  | NA      |
| Asian            | 5              | 70.7    | 0.008          | 1.05 (0.38, 2.91)   | 0.925   |
| Caucasians       | 5              | 62.9    | 0.029          | 0.37 (0.13, 1.07)   | 0.067   |
| African-American | 1              | NA      | NA             | 0.92 (0.21, 4.05)   | 0.913   |
| HWE              |                |         |                |                     |         |
| Yes              | 11             | 67.6    | 0.001          | 0.67 (0.34, 1.34)   | 0.260   |
| No               | 1              | NA      | NA             | NA                  | NA      |
| Source           |                |         |                |                     |         |
| HB               | 11             | 59.3    | 0.008          | 0.57 (0.29, 1.11)   | 0.095   |
| PB               | 1              | NA      | NA             | 3.27 (1.18, 9.09)   | 0.023   |
| Ff vs. FF        | 12             | 0       | 0.890          | 0.82 (0.65, 1.02)   | 0.020   |

| Model            | No. of studies | Heterog | eneity test    | Effect            | size    |
|------------------|----------------|---------|----------------|-------------------|---------|
|                  |                | l² (%)  | P <sub>H</sub> | OR (95% CI)       | P value |
| Ethnicity        |                |         |                |                   |         |
| American         | 1              | NA      | NA             | 0.63 (0.20, 1.93) | 0.415   |
| Asian            | 5              | 72.9    | <0.001         | 1.06 (0.68, 1.65) | 0.796   |
| Caucasians       | 5              | 32.1    | 0.172          | 0.75 (0.56, 1.00) | 0.052   |
| African-American | 1              | NA      | NA             | 0.78 (0.43, 1.43) | 0.425   |
| HWE              |                |         |                |                   |         |
| Yes              | 11             | 0       | 0.854          | 0.82 (0.66, 1.03) | 0.093   |
| No               | 1              | NA      | NA             | 0.63 (0.20, 1.93) | 0.415   |
| Source           |                |         |                |                   |         |
| HB               | 11             | 0       | 0.883          | 0.80 (0.64, 1.00) | 0.052   |
| PB               | 1              | NA      | NA             | 1.16 (0.47, 2.87) | 0.746   |
| ff+Ff vs. FF     | 12             | 34.7    | 0.112          | 0.77 (0.63, 0.95) | 0.016   |
| Ethnicity        |                |         |                |                   |         |
| American         | 1              | NA      | NA             | 0.63 (0.20, 1.93) | 0.415   |
| Asian            | 5              | 53.6    | 0.071          | 1.08 (0.72, 1.63) | 0.714   |
| Caucasians       | 5              | 11.6    | 0.340          | 0.67 (0.51, 0.88) | 0.004   |
| African-American | 1              | NA      | NA             | 0.79 (0.44, 1.43) | 0.443   |
| HWE              |                |         |                |                   |         |
| Yes              | 11             | 40.2    | 0.081          | 0.78 (0.63, 0.96) | 0.021   |
| No               | 1              | NA      | NA             | 0.63 (0.20, 1.93) | 0.415   |
| Source           |                |         |                |                   |         |
| HB               | 11             | 24.1    | 0.214          | 0.73 (0.59, 0.91) | 0.005   |
| PB               | 1              | NA      | NA             | 1.71 (0.74, 3.97) | 0.208   |
| ff vs. FF+Ff     | 12             | 74.2    | <0.001         | 0.71 (0.39, 1.29) | 0.266   |
| Ethnicity        |                |         |                |                   |         |
| American         | 1              | NA      | NA             | NA                | NA      |
| Asian            | 5              | 81.6    | <0.001         | 0.94 (0.42, 2.10) | 0.880   |
| Caucasians       | 5              | 59.8    | 0.041          | 0.43 (0.16, 1.17) | 0.099   |
| African-American | 1              | NA      | NA             | 1.01 (0.23, 4.36) | 0.988   |
| HWE              |                |         |                |                   |         |
| Yes              | 11             | 74.2    | <0.001         | 0.71 (0.39, 1.29) | 0.266   |
| No               | 1              | NA      | NA             | NA                | NA      |
| Source           |                |         |                |                   |         |
| HB               | 11             | 70.7    | <0.001         | 0.60 (0.33, 1.11) | 0.103   |
| PB               | 1              | NA      | NA             | 2.97 (1.29, 6.83) | 0.010   |

and asthma risk was observed across additive model (t vs. T: OR (95%CI) = 0.93 (0.70, 1.23), P = 0.608), co dominant model [tt vs. TT: OR (95%CI) = 0.92 (0.49, 1.70), P = 0.783; Tt vs. TT: OR (95%CI) = 1.00 (0.72, 1.38), P = 0.996], dominant model [tt+Tt vs. TT: OR (95%CI) = 0.96 (0.70, 1.32), P = 0.817], and recessive model [tt vs. TT+Tt: OR (95%CI) = 0.87 (0.47, 1.62), P = 0.658].

Further subgroup analysis showed that HWE and source of control were two sources for the obvious heterogeneity across co dominant model (Tt vs. TT). Notably, significant association was found in additive model [t vs. T: OR (95%CI) = 0.45 (0.23, 0.89), P = 0.022], co dominant model [Tt vs. TT: OR (95%CI) = 0.36 (0.17, 0.77), P = 0.009], and dominant model [tt+Tt vs. TT: OR (95%CI) = 0.36 (0.15, 0.87), P = 0.024] among Asians. Moreover, significant association was also found in the population-based

subgroup in co dominant model [Tt vs. TT: OR (95%CI) = 0.53 (0.31, 0.94), P = 0.029].

#### Bsml (rs1544410)

As shown in **Figure 4**, total 12 articles researched on the role of BsmI (rs1544410) in asthma risk (9, 10, 13, 16, 18, 20–24, 26, 27). Obvious heterogeneity across studies was observed in additive model (b vs. B:  $I^2 = 73\%$ , P < 0.0001), co dominant model (bb vs. BB:  $I^2 = 68\%$ , P = 0.003; Bb vs. BB:  $I^2 = 56\%$ , P = 0.03), dominant model (bb+Bb vs. BB:  $I^2 = 68\%$ , P = 0.002), and recessive model (bb vs. BB+Bb:  $I^2 = 62\%$ , P = 0.003). Thus, the randomed effects model was used to calculated the pooled data, and the results showed that no significant association between BsmI (rs1544410) and asthma risk was observed across additive model (b vs. B: OR (95%CI) = 0.87 (0.62, 1.21), P = 0.408), co

dominant model (bb vs. BB: OR (95%CI) = 1.16 (0.61, 2.21), *P* = 0.665; Bb vs. BB: OR (95%CI) = 1.22 (0.76, 1.96), *P* = 0.409), dominant model (bb+Bb vs. BB: OR (95%CI) = 1.14 (0.67, 1.93), *P* = 0.627), and recessive model (bb vs. BB+Bb: OR (95%CI) = 0.80 (0.54, 1.20), *P* = 0.278).

Further subgroup analysis showed that no significant association was observed in all subgroup analysis (P > 0.05). Meanwhile, the results of heterogeneity analysis showed that ethnicity, HWE, and source of subjects were not the source of heterogeneity.

#### Fokl (rs2228570)

As shown in **Figure 5**, total 12 articles researched on the role of FokI (rs2228570) in asthma risk (12, 13, 16–22, 25–27). Obvious heterogeneity across studies was observed in additive model (f vs. F:  $I^2 = 77\%$ , P < 0.00001), co dominant model (ff vs. FF:  $I^2 = 68\%$ , P = 0.0006), and recessive model (ff vs. FF+Ff:  $I^2 = 74\%$ , P < 0.0001). Thus, the randomed effects model was used to calculated the pooled data, and the results showed that no significant association between FokI (rs2228570) and asthma risk was observed across additive model (f vs. F: OR (95%CI) = 0.78 (0.57, 1.05), P = 0.102), co dominant model (ff vs. FF: OR (95%CI) = 0.67 (0.34, 1.34), P = 0.260), and recessive model (ff vs. FF+Ff: OR (95%CI) = 0.71 (0.39, 1.29), P = 0.266).

No significant obvious heterogeneity across studies was observed in co dominant model (Ff vs. FF:  $I^2 = 0\%$ , P = 0.89) and dominant model (ff+Ff vs. FF:  $I^2 = 35\%$ , P = 0.02), thus, the fixed effect model was used to calculate the pooled data, and the results showed that FokI (rs2228570) could significantly affect the risk of asthma across co dominant model (Ff vs. FF: OR (95%CI) = 0.82 (0.65, 1.02), P = 0.071) and dominant model (ff+Ff vs. FF: OR (95%CI) = 0.77 (0.63, 0.95), P = 0.016).

As for FokI (rs2228570), race, source of controls, HWE were not the source for the obvious heterogeneity. Subgroup analysis showed that FokI (rs2228570) SNP was significantly related with the risk of asthma in additive model (f vs. F: OR (95%CI) = 0.63 (0.43, 0.92), P = 0.015) and dominant model (ff+Ff vs. FF: OR (95%CI) = 0.67 (0.51, 0.88), P = 0.004) among Caucasians. Meanwhile, significant association was found in additive model (f vs. F: OR (95%CI) = 0.72 (0.54, 0.97), P = 0.03) and dominant model (ff+Ff vs. FF: OR (95%CI) = 0.67 (0.51, 0.88), P = 0.004) in the hospital-based subgroup. Significant association was found in additive model (f vs. F: OR (95%CI) = 1.90 (1.14, 3.17), P =0.015), co dominant model (ff vs. FF: OR (95%CI) = 3.27 (1.18, 9.09), P = 0.023), and recessive model (ff vs. FF+Ff: OR (95%CI) = 2.97 (1.29, 6.83), P = 0.01) in population-based subgroup.

#### **Publication Bias**

No significant publication bias was observed for ApaI (rs7975232), TaqI (rs731236), BsmI (rs1544410), FokI (rs2228570) across the genotype models (P>0.05).

### DISCUSSION

Among childhood, asthma is accepted as the most common chronic disease. Recently, accumulating evidence researched the function role of VDR gene polymorphism in childhood asthma, and four SNPs, including BsmI (rs1544410), ApaI (rs7975232), FokI (rs2228570), and TaqI (rs731236), were the main gene locuses (3, 29). Based on the meta-analysis, our data showed that FokI (rs2228570) could significantly affect the risk of childhood asthma across co dominant model and dominant model, especially among Caucasians. Notably, among Asians, significant correction between TaqI (rs731236) and childhood asthma was also found in additive model (t vs. T), co dominant model (Tt vs. TT), and dominant model (tt+Tt vs. TT), as well as population-based subgroup in co dominant model (Tt vs. TT). No relationship was found between childhood asthma and the polymorphisms of ApaI (rs7975232) and BsmI (rs1544410).

Previous evidence showed that the level of Vitamin D was closely related with airway remodeling, the number of T regulatory cells, and expression level of pro-inflammatory cytokines and NF- $\kappa$ B (30). The connection between the deficiency of Vitamin D and poor asthma outcomes has been previously reported, such as worse symptomatology and poor lung function, and these defects could be reversed for offspring if Vitamin D was supplemented in deficient pregnant rodents (31). Zhen et al. demonstrated that, two out of four VDR polymorphisms could significantly affect the susceptibility of childhood asthma, including FokI and TaqI (8). Similarly, our study supported FokI and TaqI polymorphisms were associated with childhood asthma. Interestingly, it was different from the finding of a previous study (32), which gave support for that VDR gene ApaI (rs7975232) could contribute to asthma susceptibility.

The conflicting results might be explained by the following aspects. Firstly, it is well known that asthma is a clinical syndrome, and no gold standard test have been reported for making the diagnosis. Thus, physicians used multiple algorithms to make the final diagnosis, such as breath shortness, cough history, or wheezing history (33). Meanwhile, other baseline characteristics, such as smoking status, stress, gender, and age, were all related with the diagnosis of asthma (1). Secondly, based on genome-wide analysis studies, the researchers found that over 100 candidate genes were associated with the risk and development of asthma (34). Thirdly, the study designs and different genotyping methods might also account for the conflicting results. The obvious heterogeneity across included studies might also be attributed to these reasons.

There are some limitations should be noted. Firstly, the number of studies included in some subgroups was small, and more high-quality studies would be needed to verify the stability of the results. Secondly, since most of the included studies did not report the family history, living habits and other information of the study subjects, the quantitatively analyze based on these factors could not be performed to determine whether they affect the relationship between VDR gene polymorphisms and the childhood asthma susceptibility. Thirdly, the obvious heterogeneity across included studies could not be ignored. However, the moderate quality suggested that the analysis results had good credibility.

### CONCLUSION

In summary, we concluded that FokI and TaqI polymorphisms were associated with childhood asthma susceptibility. However,

|   |   | Experim  |   | Cont   |   |   | Odds Ratio   |   | Ratio  |
|---|---|--|---|--|---|---|--|---|--|
|   | Study or Subgroup   | Events   |   |  |   |   | IV, Random, 95% C  | I IV, Rando                                       | m, 95% Cl  |
|   | Ahmed, AE 2020<br>Batmaz, SB 2017   | 60<br>15   | 100<br>60   | 40<br>20   | 100<br>60   | 8.3%<br>6.2%  | 2.25 [1.28, 3.96]<br>0.67 [0.30, 1.47]   |   |  |
|   | Einisman, H 2015  | 40   | 144   | 28   | 100   | 8.3%  | 0.99 [0.56, 1.75]  |   |  |
|   | Hutchinson, K 2018  | 33   | 88  | 23   | 114   | 7.7%  | 2.37 [1.27, 4.45]  |   |  |
|   | Iordanidou, M 2014  | 100  | 254   | 74   | 182   | 10.2%   | 0.95 [0.64, 1.40]<br>0.77 [0.50, 1.17]   |   | _  |
|   | Kilic, M 2019<br>Liu, Y 2016  | 77<br>59   | 200<br>82   | 72<br>75   | 160<br>82   | 9.8%<br>5.4%  | 0.24 [0.10, 0.60]  | · · · · · · · · · · · · · · · · · · ·             |  |
|   | Ma, JH 2014   | 101  | 120   | 104  | 120   | 6.9%  | 0.82 [0.40, 1.68]  |   |  |
|   | Maalmi, H 2013  | 111  | 310   | 191  | 450   | 11.0%   | 0.76 [0.56, 1.02]  | -   |  |
|   | Papadopoulou, A 2015<br>Pillai, DK 2011   | 46<br>77   | 122<br>236  | 487<br>37  | 1260<br>148   | 10.2%<br>9.4%   | 0.96 [0.65, 1.41]<br>1.45 [0.92, 2.30]   |   |  |
|   | Zhao, HX 2015   | 14   | 230   | 27   | 80  | 6.7%  | 0.42 [0.20, 0.87]  |   |  |
|   |   |  |   |  |   |   |  |   |  |
|   | Total (95% CI)<br>Total events  | 733  | 1796  | 1178   | 2856  | 100.0%  | 0.93 [0.70, 1.23]  |   |  |
|   | Heterogeneity: Tau <sup>2</sup> = 0.1   |  | 38.06, df   |  | < 0.000   | 1); l <sup>2</sup> = 71   | %  |   |  |
|   | Test for overall effect: Z =  | = 0.51 (P =  | 0.61)   |  |   |   |  | 0.1 0.2 0.5 Favours [experimental]                | 2 5 10<br>Favours [control]  |
| в |   | E  |   | 0  |   |   |  |   |  |
|   | Study or Subgroup   | Experime<br>Events   |   | Contr<br>Events  |   | Weight  | Odds Ratio<br>IV, Random, 95% CI   | Odds<br>IV. Rando                                 |  |
|   | Ahmed, AE 2020  | 15   | 20  | 0  | 10  |   | 59.18 [2.95, 1187.72]  |   | · · · ·  |
|   | Batmaz, SB 2017   | 3  | 21  | 5  | 20  | 8.0%  | 0.50 [0.10, 2.44]  |   |  |
|   | Einisman, H 2015<br>Hutchinson, K 2018  | 3<br>6   | 38<br>23  | 2<br>0   | 26<br>34  | 6.7%<br>3.5%  | 1.03 [0.16, 6.63]<br>25.63 [1.36, 481.59]  |   |  |
|   | lordanidou, M 2014  | 16   | 23<br>59  | 18   | 53  | 13.2%   | 0.72 [0.32, 1.62]  |   | _  |
|   | Kilic, M 2019   | 8  | 39  | 20   | 48  | 12.0%   | 0.36 [0.14, 0.95]  |   |  |
|   | Liu, Y 2016   | 24   | 30  | 35   | 36  | 5.5%  | 0.11 [0.01, 1.01]  |   |  |
|   | Ma, JH 2014<br>Maalmi, H 2013   | 47<br>15   | 53<br>74  | 49<br>45   | 54<br>124   | 10.0%<br>14.1%  | 0.80 [0.23, 2.80]<br>0.45 [0.23, 0.88]   |   |  |
|   | Papadopoulou, A 2015  | 13   | 41  | 81   | 305   | 13.9%   | 1.28 [0.63, 2.60]  | +   | -  |
|   | Pillai, DK 2011   | 11   | 63  | 3  | 43  | 9.5%  | 2.82 [0.74, 10.79]   | +   |  |
|   | Zhao, HX 2015   | 0  | 26  | 0  | 13  |   | Not estimable  |   |  |
|   | Total (95% CI)  |  | 487   |  | 766   | 100.0%  | 0.92 [0.49, 1.70]  |   | •  |
|   | Total events  | 161  |   | 258  |   |   |  |   |  |
|   | Heterogeneity: Tau <sup>2</sup> = 0.5<br>Test for overall effect: Z =   |  |   | = 10 (P =  | 0.002)  | ; l² = 63%  |  | 0.001 0.1 1                                       | 10 1000  |
| С | rescior overall effect. Z =   | - 0.20 (F =  | 0.70)   |  |   |   |  | Favours [experimental]                            |  |
| 0 |   | Experime   |   | Contr  |   |   | Odds Ratio   | Odds  |  |
|   | Study or Subgroup<br>Ahmed, AE 2020   | Events<br>30   | Total<br>35   | Events<br>40   | 50  | Weight<br>5.4%  | IV, Random, 95% CI<br>1.50 [0.46, 4.85]  | IV, Rando   | 1,95% CI   |
|   | Batmaz, SB 2017   | 9  | 27  | 10   | 25  | 5.7%  | 0.75 [0.24, 2.33]  |   |  |
|   | Einisman, H 2015  | 34   | 69  | 24   | 48  | 9.5%  | 0.97 [0.46, 2.03]  |   |  |
|   | Hutchinson, K 2018<br>Iordanidou, M 2014  | 21<br>68   | 38<br>111   | 23<br>38   | 57<br>73  | 8.4%<br>11.4%   | 1.83 [0.80, 4.19]<br>1.46 [0.80, 2.65]   | 1   | ÷  |
|   | Kilic, M 2019   | 61   | 92  | 30   | 60  | 10.4%   | 1.72 [0.88, 3.35]  | +   | -  |
|   | Liu, Y 2016   | 11   | 17  | 5  | 6   | 1.7%  | 0.37 [0.03, 3.91]  | · · · ·   |  |
|   | Ma, JH 2014   | 7  | 13  | 6  | 11  | 3.3%  | 0.97 [0.19, 4.87]  |   |  |
|   | Maalmi, H 2013<br>Papadopoulou, A 2015  | 81<br>20   | 140<br>48   | 101<br>325   | 180<br>549  | 13.8%<br>11.4%  | 1.07 [0.69, 1.68]<br>0.49 [0.27, 0.90]   |   | _  |
|   | Pillai, DK 2011   | 55   | 107   | 31   | 71  | 11.3%   | 1.36 [0.75, 2.49]  | -   | -  |
|   | Zhao, HX 2015   | 14   | 40  | 27   | 40  | 7.4%  | 0.26 [0.10, 0.66]  |   |  |
|   | Total (95% CI)  |  | 737   |  | 1170  | 100.0%  | 1.00 [0.72, 1.38]  |   | •  |
|   | Total events  | 411  |   | 662  |   |   |  |   |  |
|   | Heterogeneity: Tau <sup>2</sup> = 0.1   |  |   | = 11 (P =  | 0.02);  | l² = 50%  |  | 0.02 0.1 1  | 10 50  |
|   | Test for overall effect: Z =  | = 0.00 (P =  | 1.00)   |  |   |   |  | Favours [experimental]                            |  |
| D |   | Experime   | ental   | Contr  | ol  |   | Odds Ratio   | Odds  | Ratio  |
|   | Study or Subgroup   | Events   |   |  | Total   |   | IV, Random, 95% CI   |   | n. 95% Cl  |
|   |   |  |   |  |   |   |  | IV, Rando   |  |
|   | Ahmed, AE 2020<br>Batmaz, SB 2017   | 45<br>12   | 50  | 40   | 50  | 5.3%  | 2.25 [0.71, 7.14]  | IV. Rando   | _  |
|   | Batmaz, SB 2017   | 12   | 50<br>30  | 40<br>15   |   | 5.3%<br>6.2%<br>9.1%  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]   |   | _  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018   | 12<br>37<br>27   | 50<br>30<br>72<br>44  | 40<br>15<br>26<br>23   | 50<br>30<br>50<br>57  | 6.2%<br>9.1%<br>8.2%  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]   |   |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014   | 12<br>37<br>27<br>84   | 50<br>30<br>72<br>44<br>127   | 40<br>15<br>26<br>23<br>56   | 50<br>30<br>50<br>57<br>91  | 6.2%<br>9.1%<br>8.2%<br>11.3%   | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]  | IV. Rando   |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019  | 12<br>37<br>27   | 50<br>30<br>72<br>44  | 40<br>15<br>26<br>23<br>56<br>52   | 50<br>30<br>50<br>57<br>91<br>80  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]   |   |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014   | 12<br>37<br>27<br>84<br>69   | 50<br>30<br>72<br>44<br>127<br>100  | 40<br>15<br>26<br>23<br>56   | 50<br>30<br>50<br>57<br>91  | 6.2%<br>9.1%<br>8.2%<br>11.3%   | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]  |   |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013  | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155   | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146  | 50<br>30<br>50<br>57<br>91<br>80<br>41<br>60<br>225   | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%   | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.35]  | IV. Rando<br>                                     |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015  | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61   | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406   | 50<br>30<br>57<br>91<br>80<br>41<br>60<br>225<br>630  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%  | $\begin{array}{c} 2.25 \ [0.71, \ 7.14] \\ 0.67 \ [0.24, \ 1.85] \\ 0.98 \ [0.47, \ 2.01] \\ 2.35 \ [1.05, \ 5.25] \\ 1.22 \ [0.70, \ 2.14] \\ 1.20 \ [0.64, \ 2.24] \\ 0.15 \ [0.02, \ 1.27] \\ 0.82 \ [0.24, \ 2.84] \\ 0.88 \ [0.58, \ 1.35] \\ 0.65 \ [0.38, \ 1.10] \end{array}$  | IV. Rando   |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pilai, JK 2011   | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118  | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34   | 50<br>30<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%   | $\begin{array}{c} 2.25 \left[ 0.71, 7.14 \right] \\ 0.67 \left[ 0.24, 1.85 \right] \\ 0.98 \left[ 0.47, 2.01 \right] \\ 2.35 \left[ 1.05, 5.25 \right] \\ 1.22 \left[ 0.70, 2.14 \right] \\ 1.20 \left[ 0.64, 2.24 \right] \\ 0.15 \left[ 0.02, 1.27 \right] \\ 0.82 \left[ 0.24, 2.84 \right] \\ 0.88 \left[ 0.58, 1.36 \right] \\ 0.65 \left[ 0.38, 1.10 \right] \\ 1.49 \left[ 0.83, 2.68 \right] \end{array}$  | N. Rando  |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pilai, JK 2011<br>Zhao, HX 2015   | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118<br>40  | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406   | 50<br>30<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%<br>7.0%   | $\begin{array}{c} 2.25 \left[ 0.71, 7.14 \right] \\ 0.67 \left[ 0.24, 1.85 \right] \\ 0.98 \left[ 0.47, 2.01 \right] \\ 2.35 \left[ 1.05, 5.25 \right] \\ 1.22 \left[ 0.70, 2.14 \right] \\ 1.20 \left[ 0.64, 2.24 \right] \\ 0.15 \left[ 0.02, 1.27 \right] \\ 0.82 \left[ 0.24, 2.84 \right] \\ 0.88 \left[ 0.58, 1.35 \right] \\ 0.65 \left[ 0.38, 1.10 \right] \\ 1.49 \left[ 0.83, 2.68 \right] \\ 0.26 \left[ 0.10, 0.66 \right] \end{array}$  |   |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Piliai, DK 2011<br>Zhao, HX 2015<br>Total (95% CI)  | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118  | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27   | 50<br>30<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%   | $\begin{array}{c} 2.25 \left[ 0.71, 7.14 \right] \\ 0.67 \left[ 0.24, 1.85 \right] \\ 0.98 \left[ 0.47, 2.01 \right] \\ 2.35 \left[ 1.05, 5.25 \right] \\ 1.22 \left[ 0.70, 2.14 \right] \\ 1.20 \left[ 0.64, 2.24 \right] \\ 0.15 \left[ 0.02, 1.27 \right] \\ 0.82 \left[ 0.24, 2.84 \right] \\ 0.88 \left[ 0.58, 1.36 \right] \\ 0.65 \left[ 0.38, 1.10 \right] \\ 1.49 \left[ 0.83, 2.68 \right] \end{array}$  |   |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2014<br>Papadopoulou, A 2015<br>Pillal, DK 2011<br>Zhao, HX 2015<br>Total (95% CI)<br>Total events  | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118<br>40<br><b>898</b>  | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27<br>920  | 50<br>30<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40<br>1428  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%<br>7.0%   | $\begin{array}{c} 2.25 \left[ 0.71, 7.14 \right] \\ 0.67 \left[ 0.24, 1.85 \right] \\ 0.98 \left[ 0.47, 2.01 \right] \\ 2.35 \left[ 1.05, 5.25 \right] \\ 1.22 \left[ 0.70, 2.14 \right] \\ 1.20 \left[ 0.64, 2.24 \right] \\ 0.15 \left[ 0.02, 1.27 \right] \\ 0.82 \left[ 0.24, 2.84 \right] \\ 0.88 \left[ 0.58, 1.35 \right] \\ 0.65 \left[ 0.38, 1.10 \right] \\ 1.49 \left[ 0.83, 2.68 \right] \\ 0.26 \left[ 0.10, 0.66 \right] \end{array}$  |   |  |
|   | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Piliai, DK 2011<br>Zhao, HX 2015<br>Total (95% CI)  | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14<br>5; Chi <sup>2</sup> = 2  | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118<br>40<br>898<br>3.55, df =   | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27<br>920  | 50<br>30<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40<br>1428  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%<br>7.0%   | $\begin{array}{c} 2.25 \left[ 0.71, 7.14 \right] \\ 0.67 \left[ 0.24, 1.85 \right] \\ 0.98 \left[ 0.47, 2.01 \right] \\ 2.35 \left[ 1.05, 5.25 \right] \\ 1.22 \left[ 0.70, 2.14 \right] \\ 1.20 \left[ 0.64, 2.24 \right] \\ 0.15 \left[ 0.02, 1.27 \right] \\ 0.82 \left[ 0.24, 2.84 \right] \\ 0.88 \left[ 0.58, 1.35 \right] \\ 0.65 \left[ 0.38, 1.10 \right] \\ 1.49 \left[ 0.83, 2.68 \right] \\ 0.26 \left[ 0.10, 0.66 \right] \end{array}$  |   |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1   | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14<br>572<br>15; Chi <sup>2</sup> = 2<br>0.23 (P =   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118<br>40<br>898<br>3.55, df =<br>0.82)  | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27<br>920<br>= 11 (P =   | 50<br>30<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%<br>7.0%   | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.36]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]  | 0.01 0.1 1<br>Favours [experimental]              |  |
| E | Batmaz, SB 2017<br>Elnisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Piliai, DK 2011<br>Zhao, HX 2015<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =   | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14<br>5; Chi <sup>2</sup> = 2<br>: 0.23 (P =<br>Experim  | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118<br>40<br>898<br>(3.55, df =<br>0.82)<br>mental   | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27<br>920<br>= 11 (P =   | 50<br>30<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%<br>7.0%   | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.38 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.35]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]  | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u>   | 12<br>37<br>27<br>84<br>69<br>35<br>55<br>44<br>96<br>33<br>66<br>14<br>572<br>55; Chi <sup>2</sup> = 2<br>5; Chi <sup>2</sup> = 2<br>5; Chi <sup>2</sup> = 2<br>2<br>2.0.23 (P =  | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118<br>40<br>898<br>3.555, df =<br>0.82)<br>mental<br>Total  | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27<br>920<br>= 11 (P =<br><b>Cont</b> u<br><b>Events</b>   | 50<br>30<br>50<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40<br><b>1428</b><br>0.01);<br><b>rol</b><br><b>Total</b>   | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%<br>7.0%<br>100.0%<br>I <sup>2</sup> = 53%<br>Weight   | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.36]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>Odds Ratio<br>IV, Random, 95% C   | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017  | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>66<br>14<br>572<br>572<br>572<br>14<br>572<br>572<br>572<br>9<br>572<br>14<br>572<br>572<br>572<br>14<br>572<br>572<br>572<br>572<br>572<br>572<br>572<br>572<br>572<br>572  | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>155<br>61<br>118<br>40<br>898<br>3.555, df =<br>0.82)<br>mental<br>Total<br>50<br>30<br>30<br>30<br>30<br>30<br>30<br>30<br>30<br>30<br>3   | 40<br>15<br>26<br>33<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27<br>920<br>= 11 (P =<br><b>Contri<br/>Events</b><br>0<br>5<br>5  | 50<br>30<br>50<br>57<br>91<br>80<br>141<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>30   | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%<br>7.0%<br>100.0%<br>I <sup>2</sup> = 53%<br>Weight<br>3.6%<br>7.7%   | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.36]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>Odds Ratio<br>IV, Random, 95% C<br>44, 10 [2.55, 761.37]<br>0.56 [0.12, 2.57]   | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Piliai, DK 2011<br>Zhao, HX 2015<br>Total (95% Cl)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015  | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14<br>572<br>5; Chi <sup>2</sup> = 2<br>0.23 (P =<br>Experim<br>Events<br>15<br>3<br>3   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118<br>40<br>898<br>3.55, df =<br>0.82)<br>mental<br>Total<br>50<br>30<br>72   | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27<br>920<br>= 11 (P =<br><b>Contr</b><br><b>Events</b><br>0<br>5<br>2   | 50<br>30<br>50<br>57<br>91<br>60<br>41<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>30<br>57<br>57<br>74<br>40<br>57<br>74<br>50<br>57<br>74<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>7.0%<br>10.9%<br>7.0%<br>100.0%<br>I <sup>2</sup> = 53%<br>Weight<br>3.6%<br>7.7%<br>6.4%  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.38 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.68 [0.58, 1.35]<br>0.66 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.26 [0.70, 1.32]<br>0.066 [0.70, 1.32]<br>0.066 [0.70, 1.32]<br>0.066 [0.70, 1.32]  | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018   | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14<br>572<br>5; Chi <sup>2</sup> = 2<br>:0.23 (P =<br>Events<br>15<br>3<br>3<br>6<br>15<br>3<br>3<br>6<br>15<br>15<br>15<br>15<br>15<br>15<br>15<br>15<br>15<br>15   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118<br>40<br>898<br>3.555, df =<br>898<br>3.555, df =<br>0.82)<br>mental<br>50<br>30<br>72<br>44   | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27<br>920<br>= 11 (P =<br>920<br>= 11 (P =<br>0<br>5<br>2<br>0<br>0<br>5<br>2<br>0<br>0  | 50<br>30<br>50<br>57<br>91<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>30<br>50<br>57<br>74<br>40<br>1428<br>50<br>50<br>57<br>57<br>74<br>50<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%<br>7.0%<br>100.0%<br>I <sup>2</sup> = 53%<br>I <sup>2</sup> = 53%<br>I <sup>2</sup> = 53%<br>I <sup>2</sup> = 53% | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.38 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.35]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>Odds Ratio<br>[V. Random. 55% C<br>44.10 [2.55, 761.37]<br>0.56 [0.12, 2.57]<br>1.04 [0.17, 6.43]   | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014  | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14<br>572<br>5; Chi <sup>2</sup> = 2<br>2: 0.23 (P =<br>Experim<br>Events<br>15<br>3<br>3<br>6<br>6<br>16  | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>100<br>41<br>118<br>40<br>898<br>3.55, df =<br>0.82)<br>tental<br>Total<br>50<br>30<br>72<br>44<br>127  | 40<br>15<br>26<br>52<br>33<br>56<br>52<br>40<br>55<br>55<br>146<br>406<br>406<br>34<br>27<br>920<br>920<br>920<br>920<br>920<br>920<br>920<br>920<br>920<br>920  | 50<br>30<br>50<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>30<br>57<br>91<br>91<br>80<br>41<br>60<br>0<br>74<br>40<br>1428<br>0.01);<br>75<br>74<br>74<br>75<br>75<br>75<br>75<br>75<br>75<br>75<br>75<br>75<br>75   | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>13.3%<br>11.7%<br>10.9%<br>100.0%<br>I2 = 53%<br>Weight<br>3.6%<br>7.7%<br>6.4%<br>3.5%<br>12.1%  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.68 [0.58, 1.35]<br>0.66 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.96 [0.70, 1.32]<br>0.96 [0.70, 1.32]<br>0.96 [0.70, 1.32]<br>0.96 [0.71, 6.48]<br>19.42 [1.06, 354, 72]<br>0.58 [0.28, 1.22]<br>0.58 [0.28, 1.22]   | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016  | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14<br>572<br>5; Chi <sup>2</sup> = 2<br>:0.23 (P =<br>Events<br>15<br>3<br>3<br>6<br>15<br>3<br>3<br>6<br>15<br>15<br>15<br>15<br>15<br>15<br>15<br>15<br>15<br>15   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>60<br>155<br>61<br>118<br>40<br>898<br>3.555, df =<br>898<br>3.555, df =<br>0.82)<br>mental<br>50<br>30<br>72<br>44   | 40<br>15<br>26<br>23<br>56<br>52<br>40<br>55<br>146<br>406<br>34<br>27<br>920<br>= 11 (P =<br>920<br>= 11 (P =<br>0<br>5<br>2<br>0<br>0<br>5<br>2<br>0<br>0  | 50<br>30<br>50<br>57<br>91<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>30<br>50<br>57<br>74<br>40<br>1428<br>50<br>50<br>57<br>57<br>74<br>50<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>1.9%<br>4.7%<br>13.3%<br>11.7%<br>10.9%<br>7.0%<br>100.0%<br>I <sup>2</sup> = 53%<br>I <sup>2</sup> = 53%<br>I <sup>2</sup> = 53%<br>I <sup>2</sup> = 53% | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.30]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.96 [0.70, 1.32]<br>0.96 [0.70, 1.32]<br>0.56 [0.12, 2.57]<br>1.04 [0.17, 6.48]<br>19.42 [1.06, 354.72]<br>0.58 [0.28, 1.22]<br>0.58 [0.28, 1.22]<br>0.26 [0.11, 0.63, 0.70]  | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014  | 12<br>37<br>27<br>84<br>96<br>35<br>54<br>96<br>33<br>66<br>14<br>572<br>5; Chi <sup>2</sup> = 2<br>0.23 (P =<br>Experim<br>Events<br>15<br>3<br>3<br>6<br>16<br>8<br>8<br>24<br>47  | 50<br>30<br>72<br>44<br>127<br>100<br>0<br>155<br>61<br>118<br>40<br>898<br>33.55, df =<br>33.55, df =<br><b>Total</b><br>50<br>0.82)<br><b>total</b><br>50<br>0.082)<br><b>total</b><br>100<br>100<br>100<br>100<br>100<br>100<br>100<br>10  | 40<br>15<br>26<br>52<br>33<br>56<br>52<br>40<br>40<br>55<br>51<br>40<br>6<br>34<br>40<br>6<br>55<br>52<br>920<br>920<br>920<br>920<br>920<br>920<br>920<br>92  | 50<br>30<br>50<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>30<br>57<br>91<br>80<br>0.01);<br>79<br>1428<br>0.01);<br>70<br>1428<br>0.01);<br>70<br>1428<br>0.01);<br>70<br>1428<br>0.01);<br>70<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>1 | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>4.7%<br>13.3%<br>10.9%<br>7.0%<br>10.9%<br>7.0%<br>10.0%<br>12 53%<br>6.4%<br>3.6%<br>7.7%<br>6.4%<br>3.5%<br>12.1%<br>11.3%<br>11.3%                     | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.38 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>0.45 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.35]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.96 [0.70, 1.32]<br>0.96 [0.70, 1.32]<br>0.96 [0.71, 6.48]<br>19.42 [1.06, 354.72]<br>0.58 [0.28, 1.22]<br>0.58 [0.28, 1.22]<br>0.28 [1.10, 6.33]<br>0.24 [10.08, 0.70]<br>0.81 [0.33, 1.99]  | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillal, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014   | 12<br>377<br>27<br>84<br>69<br>35<br>54<br>96<br>61<br>14<br>572<br>55; Chi <sup>2</sup> = 2<br>55; Chi <sup>2</sup> = 2<br>53<br>53<br>54<br>14<br>572<br>55; Chi <sup>2</sup> = 2<br>53<br>53<br>54<br>54<br>14<br>572<br>55; Chi <sup>2</sup> = 2<br>53<br>54<br>54<br>54<br>54<br>54<br>54<br>54<br>55<br>54<br>54<br>56<br>14<br>57<br>55<br>54<br>56<br>56<br>56<br>56<br>56<br>56<br>56<br>56<br>56<br>56<br>56<br>56<br>56   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>100<br>41<br>155<br>61<br>118<br>40<br>898<br>838<br>3.55, df =<br>50<br>300<br>72<br>44<br>127<br>75<br>61<br>118<br>40<br>898<br>81<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>55<br>61<br>118<br>50<br>50<br>100<br>100<br>100<br>108<br>100<br>100<br>100<br>10   | 40<br>15<br>26<br>23<br>356<br>52<br>24<br>40<br>65<br>52<br>40<br>406<br>34<br>27<br>920<br>920<br>920<br>920<br>920<br>920<br>920<br>920<br>920<br>920   | 50<br>30<br>50<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>70<br>Total<br>50<br>30<br>50<br>74<br>40<br>1428<br>0.01);<br>91<br>80<br>40<br>225<br>57<br>79<br>18<br>80<br>225<br>57<br>79<br>18<br>80<br>225<br>57<br>74<br>40<br>1428<br>80<br>1428<br>57<br>74<br>40<br>1428<br>57<br>74<br>40<br>1428<br>57<br>74<br>40<br>1428<br>57<br>74<br>40<br>1428<br>57<br>74<br>40<br>1428<br>57<br>74<br>40<br>1428<br>50<br>57<br>74<br>40<br>1428<br>50<br>50<br>74<br>40<br>1428<br>50<br>50<br>50<br>74<br>40<br>50<br>50<br>50<br>74<br>40<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>50<br>5   | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>4.7%<br>13.3%<br>4.7%<br>13.3%<br>10.9%<br>7.0%<br>100.0%<br>100.0%<br>100.0%<br>10.2%<br>11.3%<br>10.2%<br>11.3%   | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.36]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.41 [0.25, 761, 37]<br>1.04 [0.17, 6.48]<br>19.42 [1.06, 354.72]<br>0.56 [0.28, 1.22]<br>0.26 [0.11, 0.63]<br>0.24 [0.08, 0.70]<br>0.81 [0.33, 1.99]<br>0.43 [0.33, 0.80]   | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Piliai, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015   | 12<br>37<br>27<br>84<br>99<br>55<br>54<br>96<br>33<br>66<br>14<br>572<br>5; Chi <sup>2</sup> = 2<br>5; Chi <sup></sup> | 50<br>30<br>72<br>44<br>127<br>100<br>0<br>155<br>61<br>118<br>40<br>898<br>33.55, df =<br>33.55, df =<br><b>Total</b><br>50<br>0.82)<br><b>total</b><br>50<br>0.082)<br><b>total</b><br>100<br>100<br>100<br>100<br>100<br>100<br>100<br>10  | 40<br>15<br>26<br>52<br>33<br>56<br>52<br>40<br>40<br>55<br>51<br>40<br>6<br>34<br>40<br>6<br>55<br>52<br>920<br>920<br>920<br>920<br>920<br>920<br>920<br>92  | 50<br>30<br>50<br>57<br>91<br>80<br>41<br>60<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>30<br>57<br>91<br>80<br>0.01);<br>79<br>1428<br>0.01);<br>70<br>1428<br>0.01);<br>70<br>1428<br>0.01);<br>70<br>1428<br>0.01);<br>70<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>1428<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>14<br>1 | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>4.7%<br>13.3%<br>4.7%<br>10.9%<br>7.0%<br>100.0%<br>100.0%<br>100.0%<br>100.0%<br>10.2%<br>10.2%<br>11.2%<br>11.2%  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.38 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>0.45 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.35]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.96 [0.71, 6.48]<br>19.42 [1.06, 354, 72]<br>0.58 [0.28, 1.22]<br>0.58 [0.28, 1.22]<br>0.58 [0.28, 1.22]<br>0.58 [0.28, 1.22]<br>0.58 [0.35, 1.39]<br>0.43 [0.33, 1.99]<br>0.43 [0.35, 3.54]                   | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillal, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014   | 12<br>377<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>66<br>14<br>55 Chi <sup>2</sup> = 2<br>0.23 (P =<br>Exertis<br>15<br>3<br>3<br>6<br>16<br>8<br>8<br>24<br>47<br>15<br>13  | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>100<br>155<br>61<br>118<br>40<br>898<br>83<br>50<br>0.82)<br>************************************   | 40<br>15<br>26<br>23<br>35<br>6<br>52<br>24<br>40<br>406<br>406<br>406<br>406<br>406<br>406<br>407<br>920<br>920<br>920<br>0<br>5<br>2<br>2<br>0<br>0<br>146<br>6<br>2<br>34<br>427<br>920<br>0<br>0<br>5<br>2<br>2<br>2<br>3<br>40<br>0<br>34<br>427<br>34<br>427<br>920<br>0<br>0<br>146<br>6<br>2<br>34<br>40<br>6<br>2<br>34<br>40<br>6<br>2<br>34<br>40<br>6<br>2<br>34<br>40<br>6<br>2<br>34<br>40<br>6<br>2<br>34<br>40<br>6<br>2<br>7<br>7<br>7<br>7<br>8<br>8<br>9<br>20<br>0<br>0<br>0<br>0<br>146<br>6<br>2<br>146<br>6<br>2<br>146<br>6<br>2<br>146<br>6<br>2<br>146<br>6<br>2<br>146<br>6<br>146<br>6<br>146<br>6<br>146<br>146<br>146  | 50<br>300<br>507<br>91<br>800<br>225<br>6300<br>1428<br>0.01);<br>rol<br>Total<br>500<br>50<br>0.01);<br>rol<br>1428<br>0.01);<br>800<br>0.01);<br>1428<br>0.01);<br>74<br>40<br>1428<br>0.01);<br>757<br>140<br>140<br>140<br>140<br>140<br>140<br>140<br>140  | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>4.7%<br>13.3%<br>4.7%<br>13.3%<br>10.9%<br>7.0%<br>100.0%<br>100.0%<br>100.0%<br>10.2%<br>11.3%<br>10.2%<br>11.3%   | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.35 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.15 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.36]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.41 [0.25, 761, 37]<br>1.04 [0.17, 6.48]<br>19.42 [1.06, 354.72]<br>0.56 [0.28, 1.22]<br>0.26 [0.11, 0.63]<br>0.24 [0.08, 0.70]<br>0.81 [0.33, 1.99]<br>0.43 [0.33, 0.80]   | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Liu, Y 2016<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015 | 12<br>377<br>27<br>84<br>69<br>35<br>54<br>96<br>14<br>572<br>5572<br>572<br>572<br>2023 (P =<br>Experim<br>Events<br>16<br>8<br>24<br>47<br>15<br>11<br>11  | 50<br>30<br>72<br>44<br>127<br>100<br>155<br>56<br>30<br>0.62)<br><b>898</b><br><b>898</b><br><b>898</b><br><b>898</b><br><b>118</b><br>40<br><b>118</b><br>50<br>30<br>72<br>44<br><b>127</b><br><b>100</b><br><b>155</b><br>55<br>61<br>100<br><b>155</b><br>61<br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>100</b><br><b>101</b><br><b>100</b><br><b>101</b><br><b>100</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>101</b><br><b>1</b> | 40<br>15<br>26<br>23<br>35<br>6<br>52<br>24<br>40<br>55<br>27<br>920<br>920<br>920<br>920<br>920<br>920<br>920<br>920  | 50<br>30<br>50<br>57<br>91<br>80<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>50<br>57<br>74<br>40<br>0.01);<br>rol<br>10<br>50<br>57<br>74<br>40<br>0.01);<br>75<br>630<br>57<br>74<br>40<br>0.01);<br>75<br>75<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>74<br>40<br>74<br>74<br>40<br>74<br>74<br>74<br>74<br>74<br>74<br>74<br>74<br>74<br>75<br>75<br>75<br>75<br>75<br>75<br>75<br>75<br>75<br>75   | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>10.3%<br>11.7%<br>10.9%<br>10.0%<br>100.0%<br>100.0%<br>Weight<br>3.6%<br>6.4%<br>3.5%<br>6.4%<br>11.3%<br>10.2%<br>8.8%                                  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.38 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>0.88 [0.58, 1.35]<br>0.65 [0.38, 1.10]<br>1.48 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.96 [0.12, 2.57]<br>1.04 [0.17, 6.48]<br>9.42 [1.06, 354.72]<br>0.28 [0.23, 1.99]<br>0.43 [0.23, 0.80]<br>1.84 [0.95, 3.54]<br>2.43 [0.66, 9.03]<br>Not estimable                         | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015   | 12<br>37<br>27<br>84<br>69<br>35<br>54<br>96<br>33<br>36<br>66<br>14<br>55; Chi <sup>2</sup> = 2<br>5; Chi <sup>2</sup> = 2<br>5; Chi <sup>2</sup> = 2<br>5; Chi <sup>2</sup> = 2<br>5; Chi <sup>2</sup> = 2<br>5<br>5<br>5<br>5<br>4<br>5<br>5<br>4<br>5<br>5<br>4<br>6<br>14<br>5<br>5<br>5<br>4<br>5<br>5<br>4<br>5<br>6<br>14<br>5<br>5<br>5<br>4<br>5<br>6<br>6<br>14<br>5<br>5<br>5<br>4<br>5<br>6<br>6<br>14<br>5<br>5<br>5<br>4<br>5<br>6<br>6<br>14<br>5<br>5<br>5<br>4<br>5<br>6<br>6<br>7<br>2<br>7<br>7<br>8<br>8<br>7<br>7<br>8<br>9<br>6<br>9<br>6<br>3<br>3<br>3<br>6<br>6<br>7<br>14<br>5<br>5<br>5<br>4<br>6<br>7<br>7<br>2<br>5<br>5<br>7<br>2<br>7<br>7<br>8<br>7<br>8<br>9<br>6<br>3<br>3<br>3<br>6<br>6<br>7<br>14<br>7<br>7<br>7<br>7<br>7<br>7<br>7<br>8<br>7<br>7<br>7<br>8<br>7<br>7<br>7<br>7<br>7<br>7<br>7   | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>100<br>41<br>155<br>61<br>118<br>898<br>3.55, df =<br>3.55, df =<br>100<br>898<br>100<br>898<br>100<br>105<br>61<br>118<br>808<br>100<br>100<br>100<br>105<br>100<br>100<br>105<br>100<br>105<br>105  | 40<br>15<br>26<br>23<br>356<br>52<br>23<br>40<br>05<br>55<br>146<br>406<br>34<br>407<br>920<br>0<br>920<br>0<br>0<br>5<br>2<br>2<br>0<br>0<br>0<br>5<br>2<br>2<br>40<br>0<br>5<br>5<br>2<br>2<br>2<br>40<br>0<br>5<br>5<br>2<br>2<br>2<br>40<br>0<br>5<br>5<br>2<br>2<br>2<br>40<br>0<br>5<br>5<br>2<br>2<br>2<br>40<br>0<br>5<br>5<br>2<br>2<br>2<br>2<br>40<br>0<br>5<br>5<br>2<br>2<br>2<br>2<br>2<br>2<br>2<br>2<br>2<br>2<br>2<br>2<br>2  | 50<br>30<br>50<br>57<br>91<br>80<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>50<br>57<br>74<br>40<br>0.01);<br>rol<br>10<br>50<br>57<br>74<br>40<br>0.01);<br>75<br>630<br>57<br>74<br>40<br>0.01);<br>75<br>75<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>40<br>74<br>74<br>40<br>74<br>74<br>40<br>74<br>74<br>74<br>74<br>74<br>74<br>74<br>74<br>74<br>75<br>75<br>75<br>75<br>75<br>75<br>75<br>75<br>75<br>75   | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>10.4%<br>4.7%<br>13.3%<br>4.7%<br>10.9%<br>7.0%<br>100.0%<br>100.0%<br>100.0%<br>100.0%<br>10.2%<br>10.2%<br>11.2%<br>11.2%  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.38 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.64, 2.24]<br>0.88 [0.58, 1.35]<br>0.65 [0.38, 1.10]<br>1.49 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.96 [0.12, 2.57]<br>1.04 [0.17, 6.48]<br>0.42 [0.68, 54.72]<br>0.28 [0.28, 1.22]<br>0.28 [0.11, 0.63]<br>0.24 [0.08, 3.74]<br>0.43 [0.23, 0.80]<br>1.84 [0.95, 3.54]<br>2.43 [0.66, 9.03] | 0.01 0.1 1<br>Favours [experimental]<br>Odds      |  |
| E | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total events   | $\begin{array}{c} 12\\ 37\\ 27\\ 84\\ 69\\ 35\\ 54\\ 96\\ 33\\ 66\\ 14\\ 572\\ 5:\ Chi^2=2\\ 0.23\ (P=\\ \hline \\ 5:\ Chi^2=2\\ 0.23\ (P=\\ \hline \\ 5:\ Chi^2=2\\ 16\\ 14\\ 14\\ 14\\ 16\\ 15\\ 15\\ 11\\ 0\\ 161\\ \end{array}$  | 50<br>30<br>72<br>44<br>127<br>100<br>155<br>56<br>118<br>40<br>898<br>898<br>898<br>80.82)<br>rental<br>Total<br>127<br>100<br>0.82)<br>rental<br>127<br>100<br>155<br>51<br>118<br>40<br>898<br>80<br>80<br>80<br>80<br>80<br>80<br>80<br>80<br>80<br>8   | 40<br>40<br>15<br>26<br>23<br>35<br>66<br>23<br>35<br>67<br>40<br>65<br>57<br>146<br>406<br>34<br>406<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>5 | 50<br>30<br>57<br>91<br>80<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>0<br>0<br>0<br>1<br>80<br>0.01);<br>rol<br>1<br>80<br>0.01);<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1   | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>11.3%<br>11.3%<br>11.7%<br>7.0%<br>110.9%<br>7.0%<br>110.9%<br>7.0%<br>110.9%<br>7.7%<br>8.8%<br>11.3%<br>11.2%<br>8.8%  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.38 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>0.45 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.36]<br>0.65 [0.38, 1.10]<br>1.44 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.96 [0.71, 1.63]<br>1.94 [0.85, 3.54]<br>2.43 [0.66, 9.03]<br>Not estimable<br>0.87 [0.47, 1.62]  | 0.01 0.1 1<br>Favours [experimenta]<br>U.V. Rando | 10 100<br>Favours [control]<br>Ratio<br>m. 95% Cl  |
| Ξ | Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Einisman, H 2015<br>Hutchinson, K 2018<br>Iordanidou, M 2014<br>Kilic, M 2019<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Pillai, DK 2011<br>Zhao, HX 2015   | $12 \\ 37 \\ 27 \\ 84 \\ 69 \\ 35 \\ 54 \\ 96 \\ 33 \\ 66 \\ 14 \\ 572 \\ 5. Chi^2 = 2 \\ 6. 23 (P = 10) \\ 15 \\ 15 \\ 15 \\ 33 \\ 6 \\ 16 \\ 8 \\ 24 \\ 47 \\ 15 \\ 13 \\ 11 \\ 11 \\ 10 \\ 0 \\ 161 \\ 69; Chi^2 = 3 \\ 21 \\ 20 \\ 100 \\$  | 50<br>30<br>72<br>44<br>127<br>100<br>41<br>55<br>61<br>118<br>43<br>898<br>838<br>50<br>62<br>72<br>44<br>118<br>40<br>898<br>838<br>50<br>72<br>44<br>127<br>700<br>72<br>44<br>18<br>50<br>72<br>41<br>18<br>50<br>72<br>127<br>70<br>100<br>898<br>838<br>836<br>50, 60, 61<br>118<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>127<br>70<br>100<br>0<br>155<br>56<br>11<br>70<br>100<br>155<br>56<br>11<br>70<br>100<br>105<br>56<br>11<br>70<br>100<br>105<br>56<br>11<br>70<br>100<br>105<br>56<br>11<br>70<br>100<br>105<br>56<br>11<br>70<br>100<br>105<br>56<br>10<br>10<br>10<br>105<br>56<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10   | 40<br>40<br>15<br>26<br>23<br>35<br>66<br>23<br>35<br>67<br>40<br>65<br>57<br>146<br>406<br>34<br>406<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>57<br>146<br>65<br>57<br>146<br>65<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>57<br>5 | 50<br>30<br>57<br>91<br>80<br>225<br>630<br>74<br>40<br>1428<br>0.01);<br>rol<br>Total<br>50<br>0<br>0<br>0<br>1<br>80<br>0.01);<br>rol<br>1<br>80<br>0.01);<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1<br>1   | 6.2%<br>9.1%<br>8.2%<br>11.3%<br>11.3%<br>11.3%<br>11.7%<br>7.0%<br>110.9%<br>7.0%<br>110.9%<br>7.0%<br>110.9%<br>7.7%<br>8.8%<br>11.3%<br>11.2%<br>8.8%  | 2.25 [0.71, 7.14]<br>0.67 [0.24, 1.85]<br>0.98 [0.47, 2.01]<br>2.38 [1.05, 5.25]<br>1.22 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>1.20 [0.70, 2.14]<br>0.45 [0.02, 1.27]<br>0.82 [0.24, 2.84]<br>0.88 [0.58, 1.36]<br>0.65 [0.38, 1.10]<br>1.44 [0.83, 2.68]<br>0.26 [0.10, 0.66]<br>0.96 [0.70, 1.32]<br>0.96 [0.71, 1.63]<br>1.94 [0.85, 3.54]<br>2.43 [0.66, 9.03]<br>Not estimable<br>0.87 [0.47, 1.62]  | 0.01 0.1 1<br>Favours [experimental]<br>Odds      | To the second se |

FIGURE 3 | Forest plot for meta-analyzing the association between Vitamin D receptor Taql (rs731236) polymorphisms and childhood asthma. (A) additive model: t vs. T; (B) co dominant model: tt vs. TT; (C) co dominant model: Tt vs. TT; (D) dominant model: tt+Tt vs. TT; (E) recessive model: tt vs. TT+Tt.

|   | Study or Subgroup  | Experim<br>Events  | ental<br>Total   | Contr  |  | Weight  | Odds Ratio<br>IV, Random, 95% C   | Odds Ratio<br>IV. Random, 95% Cl   |
|---|--|--|--|--|--|---|---|--|
|   | Ahmed, AE 2020   | 55   | 100  | 40   | 100  | 9.9%  | 1.83 [1.05, 3.21]   |  |
|   | Batmaz, SB 2017  | 44   | 60   | 37   | 60   | 7.9%  | 1.71 [0.79, 3.70]   | +  |
|   | Hou, C 2018  | 136  | 140  | 135  | 140  | 4.3%  | 1.26 [0.33, 4.79]   |  |
|   | lordanidou, M 2014<br>Liu, Y 2016  | 147<br>53  | 254<br>82  | 105<br>76  | 182<br>82  | 11.6%<br>6.5%   | 1.01 [0.69, 1.48]<br>0.14 [0.06, 0.37]  | [  |
|   | Ma, JH 2014  | 100  | 120  | 102  | 120  | 8.6%  | 0.88 [0.44, 1.77]   |  |
|   | Maalmi, H 2013   | 170  | 310  | 279  | 450  | 12.4%   | 0.74 [0.55, 1.00]   |  |
|   | Mo, LY 2015<br>Papadopoulou, A 2015  | 137<br>72  | 142<br>126   | 138<br>681   | 142<br>1262  | 4.3%<br>11.7%   | 0.79 [0.21, 3.02]<br>1.14 [0.79, 1.65]  |  |
|   | Zhang, Y 2017  | 100  | 286  | 77   | 286  | 11.8%   | 1.46 [1.02, 2.09]   |  |
|   | Zhao, HX 2015  | 57   | 80   | 69   | 80   | 7.6%  | 0.40 [0.18, 0.88]   |  |
|   | Zhu, L 2019  | 184  | 194  | 198  | 200  | 3.5%  | 0.19 [0.04, 0.86]   |  |
|   | Total (95% CI)   |  | 1894   |  | 3104   | 100.0%  | 0.87 [0.62, 1.21]   | •  |
|   | Total events   | 1255   |  | 1937   |  |   |   |  |
|   | Heterogeneity: Tau <sup>2</sup> = 0.2  |  |  | = 11 (P <  | 0.000  | 1); I² = 739  | 6   | 0.05 0.2 1 5 20  |
| - | Test for overall effect: Z =   | = 0.83 (P =  | 0.41)  |  |  |   |   | Favours [experimental] Favours [control]   |
| В |  | Experim  |  | Contr  |  |   | Odds Ratio  | Odds Ratio   |
|   | Study or Subgroup  | Events   |  |  |  | Weight  | IV, Random, 95% C   | IV, Random, 95% Cl   |
|   | Ahmed, AE 2020<br>Batmaz, SB 2017  | 15<br>16   | 25<br>18   | 10<br>12   | 30<br>17   | 12.7%<br>7.8%   | 3.00 [1.00, 9.04]<br>3.33 [0.55, 20.22]   |  |
|   | Hou, C 2018  | 66   | 66   | 65   | 65   | 1.070   | Not estimable   |  |
|   | lordanidou, M 2014   | 40   | 60   | 33   | 52   | 15.6%   | 1.15 [0.53, 2.51]   |  |
|   | Liu, Y 2016  | 21   | 30   | 36   | 37   | 6.3%  | 0.06 [0.01, 0.55]   |  |
|   | Ma, JH 2014<br>Maalmi, H 2013  | 45<br>49   | 50<br>83   | 48<br>80   | 54<br>106  | 11.5%<br>17.0%  | 1.13 [0.32, 3.94]<br>0.47 [0.25, 0.87]  |  |
|   | Mo, LY 2015  | 66   | 66   | 67   | 67   |   | Not estimable   |  |
|   | Papadopoulou, A 2015<br>Zhang, Y 2017  | 20<br>13   | 31<br>69   | 177<br>6   | 304<br>78  | 15.7%<br>13.4%  | 1.30 [0.60, 2.82]<br>2.79 [1.00, 7.79]  |  |
|   | Zhang, Y 2017<br>Zhao, HX 2015   | 13<br>17   | 69<br>17   | 6<br>29  | 78<br>29   | 13.4%   | 2.79 [1.00, 7.79]<br>Not estimable  | -  |
|   | Zhu, L 2019  | 87   | 87   | 98   | 98   |   | Not estimable   |  |
|   | Total (05% CI)   |  | 602  |  | 027  | 100 0%  | 1 16 10 64 0 043  | <b>_</b>   |
|   | Total (95% CI)<br>Total events   | 455  | 602  | 661  | 931  | 100.0%  | 1.16 [0.61, 2.21]   | T  |
|   | Heterogeneity: Tau <sup>2</sup> = 0.5  | 54; Chi <sup>2</sup> = 2   |  |  | 0.003);  | l² = 68%  |   | 0.005 0.1 1 10 20  |
| _ | Test for overall effect: Z =   | = 0.45 (P =  | 0.66)  |  |  |   |   | Favours [experimental] Favours [control]   |
| С |  | Experim  | ental  | Contr  | ol   |   | Odds Ratio  | Odds Ratio   |
|   | Study or Subgroup  | Events   | Total  |  |  | Weight  | IV. Random, 95% C   |  |
|   | Ahmed, AE 2020   | 25   | 35   | 20   | 40   | 12.6%   | 2.50 [0.96, 6.53]   |  |
|   | Batmaz, SB 2017<br>Hou, C 2018   | 12<br>4  | 14<br>4  | 13<br>5  | 18<br>5  | 5.4%  | 2.31 [0.37, 14.21]<br>Not estimable   |  |
|   | lordanidou, M 2014   | 67   | 87   | 39   | 58   | 16.0%   | 1.63 [0.78, 3.43]   | +  |
|   | Liu, Y 2016  | 11   | 20   | 4  | 5  | 3.5%  | 0.31 [0.03, 3.24]   | · · · · · · · · · · · · · · · · · · ·  |
|   | Ma, JH 2014<br>Maalmi, H 2013  | 10<br>72   | 15<br>106  | 6<br>119   | 12<br>145  | 6.8%<br>18.7%   | 2.00 [0.42, 9.52]<br>0.46 [0.26, 0.83]  |  |
|   | Mo, LY 2015  | 5  | 5  | 4  | 145  | 10.776  | Not estimable   |  |
|   | Papadopoulou, A 2015   | 32   | 43   | 327  | 454  | 16.4%   | 1.13 [0.55, 2.31]   |  |
|   | Zhang, Y 2017<br>Zhao, HX 2015   | 74<br>23   | 130  | 65   | 137  | 20.6%   | 1.46 [0.90, 2.37]<br>Not estimable  | T•   |
|   | Zhao, HX 2015<br>Zhu, L 2019   | 10   | 23<br>10   | 11<br>2  | 11<br>2  |   | Not estimable   |  |
|   |  |  |  |  |  |   |   |  |
|   |  |  |  |  |  |   |   |  |
|   | Total (95% CI)   | 345  | 492  | 615  | 891  | 100.0%  | 1.22 [0.76, 1.96]   | +  |
|   | Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2  | 345<br>22; Chi² =  |  | 615<br>= 7 (P =  |  |   | 1.22 [0.76, 1.96]   | <b>+</b>   |
|   | Total events   | 22; Chi² =   | 15.78, df  |  |  |   | 1.22 [0.76, 1.96]   | 0.02 0.1 1 10 5<br>Favours [experimental] Favours [control]  |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2  | 22; Chi <sup>2</sup> =<br>= 0.83 (P =  | 15.78, df<br>0.41)   | = 7 (P =   | 0.03); I   |   |   | Favours [experimental] Favours [control]   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2  | 22; Chi² =   | 15.78, df<br>0.41)<br>ental  | = 7 (P = )<br>Contr  | 0.03); I<br>ol   |   | 1.22 [0.76, 1.96]<br>Odds Ratio<br>IV, Random, 95% C  | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.:<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020  | 22; Chi <sup>2</sup> = -<br>= 0.83 (P =<br>Experim<br>Events<br>40   | 15.78, df<br>0.41)<br>ental<br><u>Total</u><br>50  | = 7 (P =<br>Contr<br>Events<br>30  | 0.03); I<br>ol<br><u>Total</u><br>50   | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%  | Odds Ratio<br>IV. Random, 95% C<br>2.67 [1.09, 6.52]  | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017   | 22; Chi <sup>2</sup> = -<br>= 0.83 (P =<br>Experim<br>Events<br>40<br>28   | 15.78, df<br>0.41)<br>eental<br><u>Total</u><br>50<br>30   | = 7 (P =<br>Contr<br><u>Events</u><br>30<br>25   | 0.03); I<br>ol<br><u>Total</u><br>50<br>30   | ² = 56%<br>Weight   | Odds Ratio<br>IV, Random, 95% C<br>2.67 [1.09, 6.52]<br>2.80 [0.50, 15.73]  | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014  | 22; Chi <sup>2</sup> =<br>= 0.83 (P =<br>Experim<br>Events<br>40<br>28<br>70<br>107  | 15.78, df<br>0.41)<br>Total<br>50<br>30<br>70<br>127   | Events<br>30<br>25<br>70<br>72   | 0.03); I<br>ol<br><u>Total</u><br>50<br>30<br>70<br>91   | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%   | Odds Ratio<br><u>IV. Random. 95% C</u><br>2.67 [1.09, 6.52]<br>2.80 [0.50, 15.73]<br>Not estimable<br>1.41 [0.70, 2.83]   | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.:<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016  | 22; Chi <sup>2</sup> =<br>= 0.83 (P =<br>Experim<br>Events<br>40<br>28<br>70<br>107<br>32  | 15.78, df<br>0.41)<br>Total<br>50<br>30<br>70<br>127<br>41   | = 7 (P =<br>Contr<br><u>Events</u><br>30<br>25<br>70<br>72<br>40   | 0.03); I<br>ol<br><u>Total</u><br>50<br>30<br>70<br>91<br>41   | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%   | Odds Ratio<br>IV. Random, 95% C<br>2.67 [1.09, 6.52]<br>2.80 [0.50, 15.73]<br>Not estimable<br>1.41 [0.70, 2.83]<br>0.09 [0.01, 0.74]   | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.:<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014   | 22; Chi <sup>2</sup> =<br>= 0.83 (P =<br>Experim<br>Events<br>40<br>28<br>70<br>107<br>32<br>55  | 15.78, df<br>0.41)<br>eental<br><u>Total</u><br>50<br>30<br>70<br>127<br>41<br>60  | = 7 (P =<br><u>Contr</u><br><u>Events</u><br>30<br>25<br>70<br>72<br>40<br>54  | 0.03); I<br>ol<br><u>Total</u><br>50<br>30<br>70<br>91<br>41<br>60   | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%   | Odds Ratio<br>IV, Random, 95% C<br>2.60 [1.09, 6.52]<br>2.80 [0.50, 15.73]<br>Not estimable<br>1.41 [0.70, 2.83]<br>0.09 [0.01, 0.74]<br>1.22 [0.35, 4.24]  | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE: 2020<br>Batmaz, SB: 2017<br>Hou, C; 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015   | 22; Chi <sup>2</sup> = -<br>= 0.83 (P =<br>Experim<br>Events<br>40<br>28<br>70<br>107<br>32<br>55<br>121<br>71   | 15.78, df<br>0.41)<br>ental<br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>71  | = 7 (P =<br>Contr<br><u>Events</u><br>30<br>25<br>70<br>72<br>40<br>54<br>199<br>71  | 0.03); I<br>ol<br><u>Total</u><br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71  | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%  | Odds Ratio<br>IV. Random. 95% C<br>2.80 [0.50, 15.73]<br>Not estimable<br>1.41 [0.70, 2.83]<br>0.09 [0.01, 0.74]<br>1.22 [0.35, 4.24]<br>0.46 [0.27, 0.81]<br>Not estimable   | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau* = 0;<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, BS 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015   | 22; Chi <sup>2</sup> = -<br>= 0.83 (P =<br><u>Experim</u><br><u>Events</u><br>40<br>28<br>70<br>107<br>32<br>55<br>121<br>71<br>52   | 15.78, df<br>0.41)<br>eental<br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>71<br>63   | = 7 (P =<br>Contr<br><u>Events</u><br>30<br>25<br>70<br>72<br>40<br>54<br>199<br>71<br>504   | 0.03); I<br>ol<br><u>Total</u><br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>631   | <sup>2</sup> = 56%<br>Weight<br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%  | Odds Ratio<br><u>IV, Random, 95% C</u><br>2.67 [10.9, 6.52]<br>2.80 [0.50, 15.73]<br>Not estimable<br>1.41 [0.70, 2.83]<br>0.09 [0.01, 0.74]<br>1.22 [0.35, 4.24]<br>0.46 [0.27, 0.81]<br>Not estimable<br>1.19 [0.60, 2.35]  | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.;<br>Test for overall effect: Z :<br>Study or Subgroup<br>Batmaz, SB 2017<br>Hou, C 2018<br>Jordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Zhang, Y 2017   | 22; Chi <sup>2</sup> =<br>= 0.83 (P =<br>Experim<br>Events<br>40<br>28<br>70<br>107<br>32<br>55<br>121<br>71<br>1<br>52<br>87  | 15.78, df<br>0.41)<br>eental<br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>71<br>63<br>143  | = 7 (P =<br><u>Contr</u><br><u>Events</u><br>30<br>25<br>70<br>25<br>70<br>54<br>199<br>71<br>504<br>71  | 0.03); I<br>ol<br><u>Total</u><br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>631<br>143  | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%  | Odds Ratio<br><u>1V. Random. 95% C</u><br>2.67 (1.09, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>0.46 (0.27, 0.81)<br>Not estimable<br>1.19 (0.60, 2.35)<br>1.58 (0.99, 2.52)   | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau* = 0;<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, BS 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015   | 22; Chi <sup>2</sup> = -<br>= 0.83 (P =<br><u>Experim</u><br><u>Events</u><br>40<br>28<br>70<br>107<br>32<br>55<br>121<br>71<br>52   | 15.78, df<br>0.41)<br>eental<br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>71<br>63   | = 7 (P =<br>Contr<br><u>Events</u><br>30<br>25<br>70<br>72<br>40<br>54<br>199<br>71<br>504   | 0.03); I<br>ol<br><u>Total</u><br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>631   | <sup>2</sup> = 56%<br>Weight<br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%  | Odds Ratio<br><u>IV, Random, 95% C</u><br>2.67 [10.9, 6.52]<br>2.80 [0.50, 15.73]<br>Not estimable<br>1.41 [0.70, 2.83]<br>0.09 [0.01, 0.74]<br>1.22 [0.35, 4.24]<br>0.46 [0.27, 0.81]<br>Not estimable<br>1.19 [0.60, 2.35]  | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhu, L 2019   | 22; Chi <sup>2</sup> =<br>= 0.83 (P =<br>Experim<br>Events<br>40<br>28<br>70<br>107<br>32<br>55<br>121<br>71<br>52<br>87<br>40   | 15.78, df<br>0.41)<br>eental<br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>71<br>63<br>143<br>40<br>97  | = 7 (P =<br>Contr<br><u>Events</u><br>30<br>25<br>70<br>72<br>40<br>54<br>199<br>71<br>504<br>71<br>40   | 0.03); I<br><b>Total</b><br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>143<br>40<br>100  | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%  | Odds Ratio<br>(V. Random, 95% CZ<br>267 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>1.26 (0.27, 0.81)<br>Not estimable<br>Not estimable<br>Not estimable  | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau* = 0;<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Zhang, Y 2017<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhu, L 2019<br>Total (95% CI)   | 22; Chi <sup>2</sup> =<br>= 0.83 (P =<br>Experim<br>40<br>288<br>70<br>107<br>32<br>55<br>121<br>71<br>52<br>87<br>40<br>97  | 15.78, df<br>0.41)<br>eental<br>Total<br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>71<br>63<br>143<br>40   | = 7 (P =<br>Contr<br><u>Events</u><br>30<br>25<br>70<br>72<br>40<br>54<br>199<br>71<br>504<br>71<br>40<br>100  | 0.03); I<br><b>Total</b><br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>143<br>40<br>100  | <sup>2</sup> = 56%<br>Weight<br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%  | Odds Ratio<br>(V. Random, 95% C. 2<br>2.67 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>Not estimable<br>1.19 (0.60, 2.35)<br>1.58 (0.99, 2.52)<br>Not estimable   | Favours [experimental] Favours [control]<br>Odds Ratio   |
| D | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Study or Subgroup<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Zhang, Y 2015<br>Zhang, Y 2015<br>Zhu, L 2019<br>Total (95% CI)<br>Total events  | 22; Chi <sup>2</sup> =<br>= 0.83 (P =<br>Experim<br>Events<br>40<br>28<br>70<br>107<br>32<br>55<br>121<br>71<br>52<br>87<br>40<br>97<br>800  | 15.78, df<br>0.41)<br>eental<br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>711<br>63<br>143<br>40<br>97<br><b>947</b>   | = 7 (P =<br>Contr<br>Events<br>30<br>25<br>70<br>72<br>40<br>54<br>199<br>71<br>504<br>71<br>40<br>100<br>1276   | 0.03); I<br><b>ol</b><br><b>Total</b><br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>631<br>143<br>40<br>100<br>1552  | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%  | Odds Ratio<br>(V. Random, 95% CZ<br>267 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>1.26 (0.27, 0.81)<br>Not estimable<br>Not estimable<br>Not estimable  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI   |
| D | Total events<br>Heterogeneity: Tau* = 0;<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Zhang, Y 2017<br>Zhao, HX 2015<br>Zhao, HX 2015<br>Zhu, L 2019<br>Total (95% CI)   | 22; Chi <sup>2</sup> =<br>= 0.83 (P =<br>Experim<br>Events<br>40<br>288<br>70<br>107<br>322<br>55<br>121<br>71<br>522<br>87<br>40<br>97<br>800<br>34; Chi <sup>2</sup> =<br>2  | 15.78, df<br>0.41)<br>ental<br><u>Total</u><br>50<br>30<br>70<br>127<br>41<br>63<br>143<br>40<br>97<br>947<br>22.21, df  | = 7 (P =<br>Contr<br>Events<br>30<br>25<br>70<br>72<br>40<br>54<br>199<br>71<br>504<br>71<br>40<br>100<br>1276   | 0.03); I<br><b>ol</b><br><b>Total</b><br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>631<br>143<br>40<br>100<br>1552  | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%  | Odds Ratio<br>(V. Random, 95% CZ<br>267 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>1.26 (0.27, 0.81)<br>Not estimable<br>Not estimable<br>Not estimable  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random. 95% Cl   |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.;<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maaimi, H 2013<br>Mo, LY 2015<br>Zhaa, HX 2015<br>Zhao, HX 2015<br>Zhu, L 2019<br>Total (95% CI)<br>Total events   | 22; Chi <sup>2</sup> = -<br>= 0.83 (P =<br>Experim<br>Events<br>400<br>288<br>70<br>107<br>322<br>555<br>121<br>711<br>522<br>87<br>400<br>97<br>8000<br>34; Chi <sup>2</sup> = =<br>0.49 (P =   | 15.78, df<br>0.41)<br>ental<br>Total<br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>71<br>63<br>143<br>40<br>97<br>947<br>22.21, df<br>0.63)   | = 7 (P =<br><u>Contr</u><br><u>Events</u><br>30<br>255<br>70<br>72<br>40<br>54<br>199<br>71<br>504<br>71<br>40<br>100<br>1276<br>= 7 (P =  | 0.03);  <br>ol<br>Total<br>50<br>30<br>70<br>91<br>141<br>631<br>143<br>40<br>100<br>1552<br>0.002);   | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%  | Odds Ratio<br>(V. Random. 95% C. 2<br>2.67 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>Not estimable<br>1.19 (0.60, 2.35)<br>1.56 (0.99, 2.52)<br>Not estimable<br>Not estimable<br>1.14 (0.67, 1.93)   | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI   |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maailmi, H 2013<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhang, Y 2017<br>Zhao, HX 2015<br>Zhu, L 2019<br>Total (9%% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.<br>Test for overall effect: Z :  | 22; Chi <sup>2</sup> = = 0.83 (P = 0.33 (P = 0 | 15.78, df<br>0.41)<br>ental<br>Total<br>500<br>30<br>70<br>127<br>41<br>60<br>155<br>71<br>63<br>143<br>40<br>97<br>947<br>22.21, df<br>0.63)<br>ental   | = 7 (P =<br><u>Contr</u><br><u>Events</u><br>30<br>25<br>70<br>72<br>40<br>54<br>199<br>71<br>504<br>71<br>504<br>71<br>00<br>1276<br>= 7 (P =   | 0.03);  <br>ol<br><u>Total</u><br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>631<br>143<br>40<br>100<br>1552<br>0.002);<br>ol  | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%<br>  <sup>2</sup> = 68%  | Odds Ratio<br><u>IV. Random, 35% C7</u><br>2.67 [10.9, 6.52]<br>2.80 [0.50, 15.73]<br>Not estimable<br>1.41 [0.70, 2.83]<br>0.06 [[0.01, 0.74]<br>1.22 [0.35, 4.24]<br>0.46 [0.27, 0.41]<br>Not estimable<br>Not estimable<br>Not estimable<br>1.14 [0.67, 1.93]<br>Odds Ratio  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.;<br>Test for overall effect: Z :<br><u>Study or Subgroup</u><br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Zhao, HX 2015<br>Zhu, L 2019<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.:<br>Test for overall effect: Z :<br><u>Study or Subgroup</u><br>Ahmed, AE 2020  | 22; Chi <sup>2</sup> = -<br>= 0.83 (P =<br>Experim<br>Events<br>400<br>288<br>70<br>107<br>322<br>555<br>121<br>711<br>522<br>87<br>400<br>97<br>8000<br>34; Chi <sup>2</sup> = =<br>0.49 (P =   | 15.78, df<br>0.41)<br><b>Total</b><br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>71<br>63<br>143<br>40<br>97<br>947<br>947<br>22.21, df<br>0.63)<br><b>ental</b><br>50  | = 7 (P =<br>Contr<br>Events<br>30<br>25<br>70<br>72<br>40<br>504<br>199<br>71<br>504<br>40<br>100<br>1276<br>= 7 (P =<br>Contr<br>Events<br>10<br>10<br>1276<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10   | ol<br>Total<br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>143<br>40<br>100<br>1552<br>0.002);<br>ol<br>Total<br>50   | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%<br>  <sup>2</sup> = 68%<br><u>Weight</u><br>8.4%   | Odds Ratio<br><u>IV. Random. 95% C</u><br>2.67 (10, 9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>0.46 (0.27, 0.81)<br>Not estimable<br>Not estimable<br>1.14 (0.67, 1.93)<br>Odds Ratio<br><u>IV. Random. 95% C</u><br>1.71 (0.68, 4.30)   | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Study or Subgroup<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Zhu, L 2019<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017   | 22; Chi <sup>2</sup> = = 0.83 (P =<br>Experim<br>Events<br>40<br>28<br>70<br>107<br>32<br>55<br>121<br>71<br>52<br>87<br>40<br>97<br>800<br>34; Chi <sup>2</sup> = ;<br>0.49 (P =<br>Experim<br>Events<br>15<br>16   | 15.78, df<br>0.41)<br>Total<br>50<br>30<br>70<br>127<br>41<br>133<br>40<br>97<br>947<br>22.21, df<br>0.63)<br>ental<br>Total<br>50<br>0.63)  | Contr<br>Events<br>300<br>72<br>40<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>55<br>70<br>70<br>72<br>72<br>70<br>55<br>70<br>70<br>72<br>72<br>70<br>55<br>70<br>72<br>72<br>70<br>55<br>70<br>70<br>72<br>72<br>70<br>55<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>71<br>72<br>70<br>71<br>72<br>70<br>71<br>72<br>71<br>70<br>71<br>70<br>71<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>70<br>71<br>70<br>70<br>70<br>70<br>71<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70   | 0.03); I<br>Total<br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>631<br>143<br>40<br>100<br>1552<br>0.002);<br>ol<br>Total<br>50<br>30<br>30<br>0<br>1552<br>0<br>1552<br>0<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10   | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>17.0%<br>15.6%<br>18.0%<br>100.0%<br>  <sup>2</sup> = 68%<br><u>Weight</u><br>8.4%<br>7.6%   | Odds Ratio<br><u>IV. Random. 95%, C7</u><br>2.67 (10.9, 6.52)<br>2.80 (10.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>Not estimable<br>1.19 (0.60, 2.35)<br>1.58 (0.99, 2.52)<br>Not estimable<br>Not estimable<br>1.14 (0.67, 1.93)<br>Odds Ratio<br><u>IV. Random. 95%, C7</u><br>1.71 (0.68, 4.30)<br>1.71 (0.62, 4.77)  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Zhao, HX 2015<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018  | 22; Chi <sup>2</sup> = =<br>0.83 (P =<br>Experin<br>Events<br>40<br>28<br>70<br>107<br>322<br>55<br>121<br>71<br>52<br>87<br>40<br>97<br>800<br>34; Chi <sup>2</sup> = ;<br>= 0.49 (P =<br>Experin<br>Events<br>15<br>16<br>66   | 15.78, df<br>0.41)<br>ental<br><u>Total</u><br>50<br>30<br>70<br>127<br>41<br>60<br>155<br>71<br>63<br>143<br>143<br>40<br>97<br>947<br>22.21, df<br>0.63)<br>ental<br><u>Total</u><br>50<br>30<br>0<br>70<br>947<br>947<br>947<br>947<br>947<br>947<br>947<br>947   | = 7 (P =<br>Contr<br>Events<br>300<br>25<br>700<br>25<br>700<br>25<br>700<br>25<br>700<br>25<br>700<br>25<br>700<br>25<br>700<br>72<br>400<br>54<br>4199<br>711<br>504<br>701<br>100<br>100<br>100<br>100<br>100<br>100<br>100   | 0.03); i<br><b>Total</b><br>500<br>300<br>70<br>911<br>40<br>225<br>711<br>631<br>143<br>400<br>100<br>1552<br>0.002);<br>01<br><b>Total</b><br>500<br>300<br>70<br>0<br><b>Total</b><br>500<br>300<br>70<br>1552<br>500<br>500<br>500<br>500<br>500<br>500<br>500   | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%<br>  <sup>2</sup> = 68%<br><u>Weight</u><br>8.4%<br>7.6%<br>5.5%   | Odds Ratio<br><u>IV. Random. 95% C</u><br>2.67 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>0.46 (0.27, 0.81)<br>Not estimable<br>1.19 (0.60, 2.35)<br>Not estimable<br>Not estimable<br>1.14 [0.67, 1.93]<br>Odds Ratio<br><u>IV. Random. 95% C</u><br>1.71 (0.68, 4.30)<br>1.71 (0.68, 4.30)<br>1.71 (0.68, 4.30)<br>1.71 (0.68, 4.30)<br>1.71 (0.68, 4.30)  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Study or Subgroup<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Zhu, L 2019<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017   | 22; Chi <sup>2</sup> = = 0.83 (P =<br>Experim<br>Events<br>40<br>28<br>70<br>107<br>32<br>55<br>121<br>71<br>52<br>87<br>40<br>97<br>800<br>34; Chi <sup>2</sup> = ;<br>0.49 (P =<br>Experim<br>Events<br>15<br>16   | 15.78, df<br>0.41)<br>Total<br>50<br>30<br>70<br>127<br>41<br>133<br>40<br>97<br>947<br>22.21, df<br>0.63)<br>ental<br>Total<br>50<br>0.63)  | Contr<br>Events<br>300<br>72<br>40<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>54<br>70<br>72<br>72<br>70<br>55<br>70<br>70<br>72<br>72<br>70<br>55<br>70<br>70<br>72<br>72<br>70<br>55<br>70<br>72<br>72<br>70<br>55<br>70<br>70<br>72<br>72<br>70<br>55<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>72<br>72<br>70<br>71<br>72<br>70<br>71<br>72<br>70<br>71<br>72<br>71<br>70<br>71<br>70<br>71<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>71<br>70<br>70<br>71<br>70<br>70<br>70<br>70<br>71<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70   | 0.03); I<br>Total<br>50<br>30<br>70<br>91<br>41<br>60<br>225<br>71<br>631<br>143<br>40<br>100<br>1552<br>0.002);<br>ol<br>Total<br>50<br>30<br>30<br>0<br>1552<br>0<br>1552<br>0<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10   | <sup>2</sup> = 56%<br><u>Weight</u><br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>17.0%<br>15.6%<br>18.0%<br>100.0%<br>  <sup>2</sup> = 68%<br><u>Weight</u><br>8.4%<br>7.6%   | Odds Ratio<br><u>IV. Random. 95%, C7</u><br>2.67 (10.9, 6.52)<br>2.80 (10.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>Not estimable<br>1.19 (0.60, 2.35)<br>1.58 (0.99, 2.52)<br>Not estimable<br>Not estimable<br>1.14 (0.67, 1.93)<br>Odds Ratio<br><u>IV. Random. 95%, C7</u><br>1.71 (0.68, 4.30)<br>1.71 (0.62, 4.77)  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br>Study or Subgroup<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2018<br>No, LY 2018<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhang, Y 2017<br>Zhao, HX 2015<br>Zhu, L 2019<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014  | 22: Chi <sup>2</sup> = =<br>0.83 (P =<br>Events<br>40<br>28<br>70<br>107<br>32<br>55<br>121<br>71<br>52<br>87<br>40<br>97<br>800<br>34: Chi <sup>2</sup> =<br>= 0.49 (P =<br>Experim<br>Events<br>16<br>66<br>40<br>21<br>45   | 15.78, df<br><b>Total</b><br><b>Total</b><br>50<br>30<br>127<br>41<br>63<br>143<br>40<br>0.63)<br>97<br>947<br>947<br>722.21, df<br>0.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10.63)<br>10. 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| <sup>2</sup> = 56% Weight<br>13.1%<br>6.5% 15.4%<br>4.8%<br>9.7%<br>9.7%<br>17.0% 15.6%<br>18.0% 100.0% <sup>2</sup> = 68% Weight<br>8.4%<br>7.6%<br>5.6% 11.6%<br>7.0% 3.16% <   | Odds Ratio<br><u>IV. Random, 95% C7</u><br>2.67 [10.9, 6.52]<br>2.80 [0.50, 15.73]<br>Not estimable<br>1.41 [0.70, 2.83]<br>0.09 [0.01, 0.74]<br>1.22 [0.35, 4.24]<br>0.46 [0.27, 0.81]<br>Not estimable<br>1.19 [0.60, 2.35]<br>Not estimable<br>Not estimable<br>1.14 [0.67, 1.93]<br>Odds Ratio<br><u>IV. Random, 95% C7</u><br><u>IV. Random, 95% C7<br/><u>IV. Random, 95% C7</u><br/><u>IV. Random, 95% C7<br/><u>IV. Random, 95% C7</u><br/><u>IV. Random, 95% C7</u><br/><u>IV. Random, 95% C7<br/><u>IV. Random, 95% C7</u><br/><u>IV. Random, 95% C7<br/><u>IV. Random, 95% C7</u><br/><u>IV. Random, 95% C7<br/><u>IV. Random, 95% C7</u><br/><u>IV. Random, 95% C7<br/><u>IV. </u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u> | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events           Heterogeneity: Tau <sup>2</sup> = 0.2           Test for overall effect: Z = 1           Test for overall effect: Z = 1           Study or Subgroup           Jahmed, AE 2020           Batmaz, SB 2017           Hou, G 2018           Iordanidou, M 2014           Liu, Y 2016           Maa, JH 2014           Maaj, H 2013           Mo, LY 2015           Zhao, HX 2015           Total (95% CI)           Total events           Heterogeneity: Tau <sup>2</sup> = 0.1           Test for overall effect: Z = 1           Study or Subgroup           Ahmed, AE 2020           Batmaz, SB 2017           Hou, C 2018           Iordanidou, M 2014           Liu, Y 2016           Ma, JH 2014           Maalmin, H 2013   | 22; Chi <sup>2</sup> = =<br>0.83 (P =<br>Experint<br>28 40<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>20<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>29<br>70<br>28<br>70<br>29<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>29<br>70<br>28<br>70<br>28<br>70<br>29<br>70<br>28<br>70<br>28<br>70<br>29<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>28<br>70<br>29<br>70<br>29<br>70<br>20<br>29<br>70<br>20<br>20<br>29<br>70<br>20<br>20<br>20<br>20<br>20<br>20<br>20<br>20<br>20<br>20<br>20<br>20<br>20   | 15.78, df<br>15.78, df<br>10.41)<br>10.41)<br>10.41)<br>10.41)<br>10.41<br>10.40<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.4 | = 7 (P =<br>Contr<br><u>Events</u><br>30<br>25<br>70<br>72<br>40<br>0<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>70<br>72<br>70<br>70<br>72<br>70<br>70<br>72<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70  | 0.03); I<br><b>Total</b><br>50<br>30<br>70<br>91<br>41<br>631<br>143<br>40<br>100<br>1552<br>0.002);<br>ol<br><b>Total</b><br>50<br>30<br>0<br>0<br><b>Total</b><br>50<br>30<br>0<br>100<br>225  | * = 56%<br>Weight<br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%<br>18.0%<br>100.0%<br>18.0%<br>18.0%<br>10.0%<br>18.0%<br>12.5%<br>11.6%<br>1.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>13.5%<br>13.5%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.2%<br>15.6%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>1  | Odds Ratio<br>(V. Random, 95% C<br>2.67 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>1.42 (0.35, 4.24)<br>1.42 (0.35, 4.24)<br>1.42 (0.63, 4.24)<br>1.42 (0.63, 4.24)<br>1.40 (0.67, 1.93)<br>1.58 (0.99, 2.52)<br>1.58 (0.59, 4.53)<br>0.58 (0.56, 4.52)<br>0.58 (0.54, 1.29)   | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maaimi, H 2013<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhang, Y 2017<br>Zhao, HX 2015<br>Zhu, L 2019<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maaimi, H 2013<br>Ma, JH 2014<br>Maaimi, H 2013  | 22: Ch <sup>2</sup> = 0.83 (P = 0.84 | 15.78, df<br>0.41)<br>ental<br>500<br>300<br>700<br>127<br>41<br>600<br>155<br>71<br>633<br>400<br>947<br>947<br>947<br>947<br>947<br>947<br>947<br>947  | = 7 (P =<br>Contr<br>Events<br>30<br>25<br>70<br>72<br>40<br>0<br>24<br>70<br>72<br>40<br>0<br>54<br>41<br>99<br>91<br>1276<br>504<br>71<br>100<br>12276<br>504<br>40<br>100<br>100<br>100<br>100<br>100<br>100<br>10  | 0.03); I<br>ol<br>Total<br>50<br>30<br>70<br>91<br>41<br>60<br>100<br>1552<br>0.002);<br>ol<br>Total<br>50<br>30<br>70<br>0<br>1552<br>0.002);<br>1552<br>0.002);<br>1552<br>0.002);<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>1552<br>15 | * = 56%           Weight           13.1%           6.5%           15.4%           9.8%           17.0%           18.0%           100.0%           12.4%           8.4%           7.6%           11.6%           8.4%           7.5%           11.6%           8.4%           7.5%           5.5%  | Odds Ratio<br><u>IV. Random, 35%, C7</u><br>2.67 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>0.06 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>0.06 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>1.06 (0.27, 0.84)<br>Not estimable<br>Not estimable<br>Not estimable<br>1.14 [0.67, 1.93]<br>Odds Ratio<br><u>IV. Random, 35%, C7</u><br><u>IV. Random, 35%, C7<br/><u>IV. Random, 35%, C7</u><br/><u>IV. Random, 35%, C7</u><br/><u>IV. Random, 35%, C7<br/><u>IV. Random, 35%, C7<br/><u>IV. Random, 35%, C7</u><br/><u>IV. Random, 35%, C7<br/><u>IV. Random, 35%, C7</u><br/><u>IV. Random, 35%, C7</u><br/><u>IV. Random, 35%, C7<br/><u>IV. Random, 45%, C7</u><br/><u>IV. Random, 45%, C7<br/><u>IV. Random, 45%, C</u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u>   | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Lu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhang, Y 2017<br>Zhao, HX 2017<br>Zhao, HX 2017<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2017   | 22; Chi <sup>2</sup> = =<br>0.83 (P =<br>Experint<br>28 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  | 15.78, df<br>15.78, df<br>10.41)<br>10.41)<br>10.41)<br>10.41)<br>10.41<br>10.40<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.41<br>10.4 | = 7 (P =<br>Contr<br><u>Events</u><br>30<br>25<br>70<br>72<br>40<br>0<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>40<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>72<br>70<br>70<br>72<br>70<br>70<br>72<br>70<br>70<br>72<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70<br>70  | 0.03); I<br><b>Total</b><br>50<br>30<br>70<br>91<br>41<br>631<br>143<br>40<br>100<br>1552<br>0.002);<br>ol<br><b>Total</b><br>50<br>30<br>0<br>0<br><b>Total</b><br>50<br>30<br>0<br>100<br>225  | * = 56%<br>Weight<br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%<br>18.0%<br>100.0%<br>18.0%<br>18.0%<br>10.0%<br>18.0%<br>12.5%<br>11.6%<br>1.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>12.5%<br>13.5%<br>13.5%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.6%<br>15.2%<br>15.6%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>15.2%<br>1  | Odds Ratio<br>(V. Random, 95% C<br>2.67 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>0.09 (0.01, 0.74)<br>1.22 (0.35, 4.24)<br>1.42 (0.35, 4.24)<br>1.42 (0.35, 4.24)<br>1.42 (0.63, 4.24)<br>1.42 (0.63, 4.24)<br>1.40 (0.67, 1.93)<br>1.58 (0.99, 2.52)<br>1.58 (0.59, 4.53)<br>0.58 (0.56, 4.52)<br>0.58 (0.54, 1.29)   | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br>Study or Subgroup<br>Test for overall effect: Z =<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Papadopoulou, A 2015<br>Zhu, L 2019<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Zhag, Y 2017<br>Zhao, HX 2015<br>Zhang, Y 2017<br>Zhao, HX 2015  | 22; Ch <sup>2</sup> = 0.83 (P) = 0.84 (P) = 0.84 (P) = 0.44 (P) = | 15.78, df<br>0.41)<br>ental<br>Total<br>500<br>300<br>700<br>127<br>41<br>40<br>0.63)<br>143<br>22.2.1, df<br>0.63)<br>ental<br>Total<br>700<br>127<br>947<br>947<br>947<br>141<br>63<br>303<br>143<br>40<br>97<br>947<br>141<br>141<br>141<br>141<br>141<br>141<br>141<br>1   | = 7 (P =<br>Contr<br>Events<br>30<br>25<br>57<br>72<br>40<br>54<br>199<br>971<br>504<br>40<br>100<br>1276<br>6<br>25<br>10<br>100<br>1276<br>100<br>1276<br>100<br>1276<br>100<br>1276<br>100<br>100<br>100<br>100<br>100<br>100<br>100<br>10  | 0.03); I<br>Total<br>Total<br>50<br>30<br>91<br>41<br>143<br>40<br>100<br>225<br>71<br>143<br>40<br>100<br>1552<br>0.002);<br>00<br>Total<br>50<br>00<br>70<br>91<br>41<br>40<br>100<br>205<br>71<br>41<br>40<br>100<br>205<br>71<br>41<br>40<br>100<br>205<br>71<br>41<br>40<br>100<br>205<br>71<br>41<br>40<br>100<br>205<br>71<br>41<br>40<br>100<br>205<br>71<br>41<br>40<br>100<br>205<br>71<br>41<br>40<br>100<br>205<br>71<br>41<br>40<br>100<br>70<br>100<br>205<br>70<br>100<br>205<br>70<br>100<br>205<br>70<br>100<br>205<br>70<br>100<br>205<br>70<br>100<br>205<br>70<br>100<br>205<br>70<br>100<br>205<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>205<br>70<br>100<br>205<br>70<br>100<br>70<br>100<br>205<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>100<br>70<br>101<br>100<br>70<br>101<br>100<br>70<br>101<br>100<br>70<br>101<br>101   | * = 56%<br>Weight<br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%<br>1*<br>18.0%<br>100.0%<br>1*<br>18.0%<br>100.0%<br>1*<br>8.4%<br>5.5%<br>11.7%<br>5.5%<br>11.7%<br>8.9%<br>8.9%<br>8.9%  | Odds Ratio<br><u>IV. Random, 95%, CZ</u><br>2.67 (1,09, 6,52)<br>2.80 (0,50, 15, 73)<br>Not estimable<br>1.41 (0,70, 2.83)<br>0.09 (0,01, 0,74)<br>1.22 (0,35, 4.24)<br>1.42 (0,35, 4.24)<br>Not estimable<br>1.19 (0,60, 2.35)<br>1.58 (0,99, 2.52)<br>Not estimable<br>Not estimable<br>1.14 (0,67, 1,93)<br>Odds Ratio<br><u>IV. Random, 95%, CZ</u><br>1.77 (10,68, 4.30)<br>0.81 (0,46, 1.43)<br>0.15 (0,50, 4.54)<br>0.81 (0,46, 1.43)<br>0.15 (0,50, 4.54)<br>0.75 (0,22, 1.77)<br>0.84 (0,54, 1.29)<br>0.41 (0,54, 1.29)<br>0.75 (0,22, 1.77)<br>0.84 (0,54, 1.29)<br>0.43 (0,24, 1.71)<br>0.84 (0,54, 1.29)<br>0.43 (0,24, 1.71)<br>0.84 (0,54, 1.29)<br>0.28 (0,11, 0,71)<br>0.28 (0,11, 0  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.<br>Test for overall effect: Z :<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Lu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhang, Y 2017<br>Zhao, HX 2017<br>Zhao, HX 2017<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2017   | 22: Ch <sup>2</sup> = 0.83 (P = 0.83) (P = 0.83) (P = 0.83) (P = 0.84) (P =  | 15.78, df<br>0.41)<br>ental<br>500<br>300<br>700<br>127<br>41<br>600<br>125<br>71<br>135<br>71<br>143<br>409<br>947<br>947<br>947<br>947<br>500<br>127<br>947<br>947<br>500<br>127<br>143<br>400<br>907<br>947<br>947<br>143<br>143<br>400<br>155<br>71<br>165<br>165<br>175<br>143<br>143<br>143<br>143<br>143<br>143<br>143<br>143   | = 7 (P =<br>Contr<br>Events<br>30<br>25<br>70<br>72<br>40<br>199<br>71<br>40<br>100<br>1276<br>= 7 (P =<br>Contr<br>Events<br>10<br>1276<br>40<br>100<br>1276<br>40<br>100<br>100<br>1276<br>40<br>100<br>100<br>100<br>100<br>100<br>100<br>100   | 0.03); I<br>ol<br>Total<br>50<br>30<br>70<br>91<br>41<br>631<br>143<br>40<br>100<br>1552<br>0.002);<br>ol<br>Total<br>50<br>30<br>0<br>70<br>0<br>1552<br>0.002);<br>16<br>16<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10<br>10  | * = 56%<br>Weight<br>13.1%<br>6.5%<br>15.4%<br>4.8%<br>15.4%<br>9.7%<br>17.0%<br>15.6%<br>18.0%<br>100.0%<br>100.0%<br>100.0%<br>100.0%<br>100.0%<br>10.0%<br>10.0%<br>11.7%<br>5.5%<br>11.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2%<br>1.2% | Odds Ratio<br><u>IV. Random. 95% C</u><br>2.67 (10.9, 6.52)<br>2.80 [0.50, 15.73]<br>Not estimable<br>1.41 [0.70, 2.83]<br>0.09 [0.01, 0.74]<br>1.22 [0.35, 4.24]<br>Not estimable<br>1.19 [0.60, 2.35]<br>1.56 [0.99, 2.52]<br>Not estimable<br>Not estimable<br>1.14 [0.67, 1.93]<br>Odds Ratio<br><u>IV. Random. 95% C</u><br>1.71 [0.68, 4.30]<br>1.71 [0.68, 4.30]<br>1.71 [0.68, 4.30]<br>1.71 [0.68, 4.30]<br>1.71 [0.68, 4.30]<br>1.71 [0.64, 4.41]<br>0.84 [0.54, 4.129]<br>0.79 [0.20, 3.06]<br>1.19 [0.68, 2.08]<br>0.28 [0.84, 6.19]<br>2.28 [0.84, 6.19]   | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
| E | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Study or Subgroup<br>Test for overall effect: Z =<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Zhu, L 2019<br>Total (95% Cl)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.2<br>Study or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Mo, LY 2015<br>Zhap, Y 2017<br>Zhao, HX 2015<br>Zhao, Y 2017<br>Zhao, HX 2015<br>Zhao, Y 2017<br>Zhao, HX 2015<br>Zhao, LY 2015  | 22; Ch <sup>2</sup> = 0.83 (P) = 0.84 (P) = 0.84 (P) = 0.44 (P) = | 15.78, df<br>0.41)<br>ental<br>Total<br>500<br>300<br>700<br>127<br>41<br>40<br>0.63)<br>143<br>22.2.1, df<br>0.63)<br>ental<br>Total<br>700<br>127<br>947<br>947<br>947<br>141<br>63<br>303<br>143<br>40<br>97<br>947<br>141<br>141<br>141<br>141<br>141<br>141<br>141<br>1   | = 7 (P =<br>Contr<br>Events<br>30<br>25<br>57<br>72<br>40<br>54<br>199<br>971<br>504<br>40<br>100<br>1276<br>6<br>25<br>10<br>100<br>1276<br>100<br>1276<br>100<br>1276<br>100<br>1276<br>100<br>100<br>100<br>100<br>100<br>100<br>100<br>10  | 0.0.3); I<br>ol<br>Total<br>50<br>30<br>070<br>91<br>41<br>143<br>40<br>100<br>1552<br>00<br>1552<br>00<br>1052<br>00<br>10552<br>00<br>10552<br>00<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10552<br>10555<br>10555<br>10555<br>105555<br>105555<br>105555<br>105555<br>105555<br>1055555   | <sup>2</sup> = 56% Weight 13,1% 6.5% 15,4% 4.8% 9,7% 17.0% 15,6% 18,0% 100.0% 12,0% 18,0% 100.0% 12,0% 5,5% 11,7% 7,8% 5,55% 11,7% 7,8% 5,55% 11,7% 7,8% 8,9% 4,7%  | Odds Ratio<br>(V. Random, 95%, C.<br>2.67 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>(0.54, 2.44)<br>1.42 (0.35, 4.24)<br>1.41 (0.60, 2.35)<br>1.58 (0.99, 2.52)<br>Not estimable<br>Not estimable<br>1.14 (0.67, 1.93)<br>Odds Ratio<br>(V. Random, 95%, C.<br>1.71 (0.68, 4.30)<br>1.71 (0.62, 4.77)<br>1.27 (0.33, 4.94)<br>0.81 (0.46, 1.43)<br>0.75 (0.32, 1.77)<br>0.84 (0.54, 1.23)<br>0.76 (0.32, 1.77)<br>0.76 (0.32, 1.77)<br>0  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Situdy or Subgroup<br>Test for overall effect: Z =<br>Situdy or Subgroup<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Na, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhang, Y 2017<br>Zhao, HX 2015<br>Total (95% CI)<br>Total events<br>Heterogeneity: Tau <sup>2</sup> = 0.1<br>Situdy or Subgroup<br>Ahmed, AE 2020<br>Batmaz, SB 2017<br>Hou, C 2018<br>Iordanidou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Papadopoulou, M 2014<br>Liu, Y 2016<br>Ma, JH 2014<br>Maalmi, H 2013<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Papadopoulou, A 2015<br>Zhang, Y 2015<br>Papadopoulou, A 2015<br>Zhang, Y 2015<br>Zhu, L 2019<br>Total (95% CI)<br>Total (95% CI)  | 22: Ch <sup>2</sup> = 0.83 (P = 0.84 (P = 0.48 | 15.78, df<br>0.41)<br>ental<br>Total<br>50<br>30<br>070<br>127<br>41<br>60<br>155<br>71<br>63<br>143<br>40<br>947<br>947<br>22.21, df<br>50<br>0.63)<br>ental<br>50<br>30<br>070<br>143<br>40<br>947<br>947<br>947   | = 7 (P = 1<br>Contr<br>Events<br>30<br>30<br>27<br>40<br>40<br>40<br>40<br>40<br>40<br>40<br>40<br>40<br>40  | 0.03); I<br>ol<br>Total<br>50<br>30<br>0<br>91<br>41<br>143<br>40<br>0<br>2255<br>71<br>1631<br>100<br>1552<br>0<br>0<br>Total<br>50<br>30<br>0<br>1552<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>100<br>100<br>100<br>100<br>100<br>100<br>100   | **************************************  | Odds Ratio<br><u>IV. Random, 95%, CZ</u><br>2.67 (1,09, 6,52)<br>2.80 (0,50, 15, 73)<br>Not estimable<br>1.41 (0,70, 2.83)<br>0.09 (0,01, 0,74)<br>1.22 (0,35, 4.24)<br>1.42 (0,35, 4.24)<br>Not estimable<br>1.19 (0,60, 2.35)<br>1.58 (0,99, 2.52)<br>Not estimable<br>Not estimable<br>1.14 (0,67, 1,93)<br>Odds Ratio<br><u>IV. Random, 95%, CZ</u><br>1.77 (10,68, 4.30)<br>0.81 (0,46, 1.43)<br>0.15 (0,50, 4.54)<br>0.81 (0,46, 1.43)<br>0.15 (0,50, 4.54)<br>0.75 (0,22, 1.77)<br>0.84 (0,54, 1.29)<br>0.41 (0,54, 1.29)<br>0.75 (0,22, 1.77)<br>0.84 (0,54, 1.29)<br>0.41 (0,54, 1.29)<br>0.41 (0,54, 1.29)<br>0.41 (0,54, 1.29)<br>0.41 (0,54, 1.29)<br>0.41 (0,54, 1.29)<br>0.42 (0,14, 0.24)<br>0.42 (0,24, 1.27)<br>0.44 (0,54, 1.29)<br>0.42 (0,14, 0.14)<br>0.42 (0,14, 0  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |
|   | Total events           Heterogeneity: Tau <sup>2</sup> = 0.2           Test for overall effect: Z = 1           Test for overall effect: Z = 1           Study or Subgroup           Jahmed, AE 2020           Batmaz, SB 2017           Hou, C 2018           Iordanidou, M 2014           Liu, Y 2016           Ma, JH 2014           Ma, JH 2014           Ma, JH 2015           Papadopoulou, A 2015           Zhao, HX 2015           Abmed, AE 1020           Batmaz, SB 2017           Hou, C 2018           Iordanidou, M 2014           Liu, Y 2016           Ma, JH 2014           Maalmin, H 2013           Mo, LY 2015           Papadopoulou, A 2015           Zhao, HX 2015           Zhao, ZhX 2015           Zhao, | 22: Ch <sup>2</sup> = 0.83 (P = 0.83) (P = 0.83) (P = 0.83) (P = 0.83) (P = 0.84) (P =  | 15.78, df<br>0.41)<br>ental<br>Total<br>50<br>300<br>700<br>127<br>41<br>63<br>143<br>143<br>40<br>97<br>947<br>22.21, df<br>60<br>0.63)<br>102<br>103<br>143<br>50<br>71<br>71<br>63<br>143<br>40<br>97<br>947<br>722<br>22.4, df<br>60<br>70<br>70<br>71<br>71<br>71<br>71<br>71<br>71<br>71<br>71<br>71<br>71   | = 7 (P = 1<br>Contr<br>Events<br>30<br>30<br>27<br>40<br>40<br>40<br>40<br>40<br>40<br>40<br>40<br>40<br>40  | 0.03); I<br>ol<br>Total<br>50<br>30<br>0<br>91<br>41<br>143<br>40<br>0<br>2255<br>71<br>1631<br>100<br>1552<br>0<br>0<br>Total<br>50<br>30<br>0<br>1552<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>143<br>40<br>0<br>20<br>255<br>71<br>100<br>100<br>100<br>100<br>100<br>100<br>100   | **************************************  | Odds Ratio<br>(V. Random, 95%, C.<br>2.67 (10.9, 6.52)<br>2.80 (0.50, 15.73)<br>Not estimable<br>1.41 (0.70, 2.83)<br>(0.54, 2.44)<br>1.42 (0.35, 4.24)<br>1.41 (0.60, 2.35)<br>1.58 (0.99, 2.52)<br>Not estimable<br>Not estimable<br>1.14 (0.67, 1.93)<br>Odds Ratio<br>(V. Random, 95%, C.<br>1.71 (0.68, 4.30)<br>1.71 (0.62, 4.77)<br>1.27 (0.33, 4.94)<br>0.81 (0.46, 1.43)<br>0.75 (0.32, 1.77)<br>0.84 (0.54, 1.23)<br>0.76 (0.32, 1.77)<br>0.76 (0.32, 1.77)<br>0  | Favours [experimental] Favours [control]<br>Odds Ratio<br>IV. Random, 95% CI<br>IV. Random, 95% CI |

FIGURE 4 | Forest plot for meta-analyzing the association between Vitamin D receptor Bsml (rs1544410) polymorphisms and childhood asthma. (A) additive model: b vs. B; (B) co dominant model: bb vs. BB; (C) co dominant model: Bb vs. BB; (D) dominant model: bb+Bb vs. BB; (E): recessive model: bb vs. BB+Bb.

|                                       | Experir                             |                    | Contro  |             |                | Odds Ratio                             | Odds                                 |                         |     |
|---------------------------------------|-------------------------------------|--------------------|---|-------------|----------------|--|--------------------------------------|-------------------------|-----|
| Study or Subg<br>Batmaz, SB 20        |                                     | Total<br>60        | Events<br>24  | Total<br>60 | Weight<br>6.1% | IV, Random, 95% C<br>0.34 [0.15, 0.77] | I IV. Rando                          | om. 95% Cl              |     |
| Einisman, H 20                        |                                     | 146                | 24<br>45  | 100         | 8.6%           | 0.34 [0.15, 0.77]                      |                                      | <u> </u>                |     |
| lordanidou, M 2                       |                                     | 254                | 61  | 182         | 9.4%           | 0.70 [0.46, 1.06]                      |                                      | 1                       |     |
| Ismail, MF 2013<br>Kilic, M 2019      | 3 22<br>51                          | 102<br>200         | 28<br>36  | 66<br>160   | 7.3%<br>8.8%   | 0.37 [0.19, 0.74]<br>1.18 [0.72, 1.92] |                                      | -                       |     |
| Liu, Y 2016                           | 53                                  | 82                 | 75  | 82          | 5.7%           | 0.17 [0.07, 0.42]                      |                                      |                         |     |
| Ma, JH 2014<br>Maalmi, H 2013         | 72<br>3 78                          | 120<br>310         | 53<br>105   | 120<br>304  | 8.6%<br>9.9%   | 1.90 [1.14, 3.17]<br>0.64 [0.45, 0.90] |                                      |                         |     |
| Pillai, DK 2011                       | 51                                  | 244                | 35  | 148         | 8.8%           | 0.85 [0.52, 1.39]                      |                                      |                         |     |
| Zhang, Y 2017<br>Zhao, HX 2015        | 233                                 |                    | 211   | 286         | 9.5%           |  |                                      | _                       |     |
| Zhao, HX 2015<br>Zhu, L 2019          | 28<br>92                            | 80<br>194          | 34<br>95  | 200         | 9.6%           |  |                                      |                         |     |
| Total (95% CI)                        |                                     | 2079               |   | 1700        | 100.0%         | 0 79 10 57 4 051                       | •                                    |                         |     |
| Total events                          | 819                                 | 2070               | 802   | 1700        | 100.0%         | 0.78 [0.57, 1.05]                      | •                                    |                         |     |
| Heterogeneity:                        | Tau² = 0.21; Chi                    |                    | df = 11 (F  | < 0.00      | 1001); I² =    | 77%                                    | 01 02 05                             |                         | 10  |
| B Test for overall                    | effect: Z = 1.63 (                  | P = 0.10)          | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ |             |                |  |                                      |                         |     |
|                                       | Experir                             |                    |   |             |                |  |                                      |                         |     |
| <u>Study or Subg</u><br>Batmaz, SB 20 |                                     |                    |   |             |                |  | I IV. Rando                          | om. 95% Cl              |     |
| Einisman, H 20                        |                                     |                    |   |             | 4.078          |  |                                      |                         |     |
| lordanidou, M 2                       |                                     |                    |   |             |                |  |                                      | -                       |     |
| Ismail, MF 2013<br>Kilic, M 2019      | 5 U<br>9                            |                    |   |             |                |  | _                                    | _ <b>_</b>              |     |
| Liu, Y 2016                           | 20                                  | 28                 | 35  | 36          | 6.2%           | 0.07 [0.01, 0.61]                      |                                      |                         |     |
| Ma, JH 2014<br>Maalmi, H 2013         | 24<br>8 11                          |                    |   |             |                | 3.27 [1.18, 9.09]                      |                                      |                         |     |
| Pillai, DK 2011                       | 5                                   | 81                 | 3   | 45          | 9.0%           | 0.92 [0.21, 4.05]                      |                                      |                         |     |
| Zhang, Y 2017<br>Zhao, HX 2015        | 92<br>7                             |                    |   |             |                |  |                                      | _                       |     |
| Zhao, 11X 2013<br>Zhu, L 2019         | 22                                  |                    |   |             |                |  | _                                    | _                       |     |
| Total (95% CI)                        |                                     | 642                |   | 502         | 100.0%         | 0 67 10 24 4 241                       | -                                    |                         |     |
| Total events                          | 196                                 | 012                | 205   | 502         | 100.0%         | 0.07 [0.34, 1.34]                      | •                                    |                         |     |
|                                       |                                     |                    |   | = 0.00      | 106); l² = 6   | 8%                                     | 0.002 0.1                            | 1 10                    | 500 |
| Test for overall                      | effect: Z = 1.13 (                  | P = 0.26)          |   |             |                |  |                                      |                         |     |
|                                       |                                     | mental             |   |             |                |  |                                      |                         |     |
| <u>Study or Subc</u><br>Batmaz, SB 20 |                                     |                    |   |             |                |  | IV, Fixed                            | . 95% Cl                |     |
| Einisman, H 20                        |                                     |                    |   |             |                |  |                                      |                         |     |
| lordanidou, M                         |                                     |                    |   |             |                |  |                                      | -                       |     |
| Ismail, MF 201<br>Kilic, M 2019       | 3 22<br>33                          |                    |   |             |                |  | -                                    |                         |     |
| Liu, Y 2016                           | 13                                  | 21                 | 5   | 6           | 0.9%           | 0.33 [0.03, 3.31]                      |                                      |                         |     |
| Ma, JH 2014<br>Maalmi, H 2013         | 24<br>3 56                          |                    |   |             |                |  | _                                    |                         |     |
| Pillai, DK 2011                       | 41                                  |                    |   |             |                |  |                                      | _                       |     |
| Zhang, Y 2017                         | 49                                  |                    |   |             | 1.8%           | 2.33 [0.45, 12.07]                     |                                      |                         |     |
| Zhao, HX 2015<br>Zhu, L 2019          | i 14<br>48                          |                    |   |             |                |  | -                                    | -                       |     |
|                                       |                                     |                    |   |             |                |  |                                      |                         |     |
| Total (95% CI)<br>Total events        | 427                                 |                    | 392   | 689         | 100.0%         | 0.82 [0.65, 1.02]                      | •                                    |                         |     |
|                                       | Chi <sup>2</sup> = 5.74, df =       | 11 (P = 0          | 0.89); I <sup>2</sup> =                               | 0%          |                |  | 0.02 0.1 1                           | 10                      | 50  |
|                                       | effect: Z = 1.80                    | (P = 0.07          | )   |             |                |  | Favours [experimental]               | Favours [control]       |     |
| D                                     | Experi                              |                    | Contr   |             |                | Odds Ratio                             | Odds                                 |                         |     |
| Study or Subg<br>Batmaz, SB 20        |                                     | <u>Total</u><br>30 | Events<br>18  | Total<br>30 | Weight<br>4.0% | IV, Fixed, 95% CI<br>0.39 [0.14, 1.09] | IV. Fixed                            | , 90% CI                |     |
| Einisman, H 20                        | 15 62                               | 73                 | 45  | 50          | 3.5%           | 0.63 [0.20, 1.93]                      |                                      |                         |     |
| lordanidou, M 2                       |                                     |                    | 53<br>21  | 91<br>33    | 14.8%          | 0.64 [0.37, 1.11]                      |                                      |                         |     |
| Ismail, MF 201<br>Kilic, M 2019       | 3 22<br>42                          |                    | 21<br>32  | 33<br>80    | 5.4%<br>12.2%  | 0.43 [0.18, 1.07]<br>1.09 [0.60, 1.98] | _                                    | -                       |     |
| Liu, Y 2016                           | 33                                  | 41                 | 40  | 41          | 1.0%           | 0.10 [0.01, 0.87]                      |                                      |                         |     |
| Ma, JH 2014<br>Maalmi, H 2013         | 48<br>3 67                          | 60<br>155          | 42<br>82  | 60<br>152   | 6.2%<br>21.6%  | 1.71 [0.74, 3.97]<br>0.65 [0.41, 1.02] |                                      |                         |     |
| Pillai, DK 2011                       | 46                                  |                    | 32  | 74          | 12.7%          | 0.79 [0.44, 1.43]                      |                                      | _                       |     |
| Zhang, Y 2017                         | 141                                 |                    | 137   | 143         |                | 3.09 [0.61, 15.56]                     |                                      | _                       |     |
| Zhao, HX 2015<br>Zhu, L 2019          | 21<br>70                            | 40<br>97           | 25<br>70  | 40<br>100   | 5.5%<br>11.5%  | 0.66 [0.27, 1.62]<br>1.11 [0.60, 2.06] |                                      | <b>—</b>                |     |
|                                       | 70                                  |                    | , ,   |             |                |  |                                      |                         |     |
| Total (95% CI)                        |                                     | 1039               | E07   | 894         | 100.0%         | 0.77 [0.63, 0.95]                      | •                                    |                         |     |
| Total events<br>Heterogeneity:        | 623<br>Chi <sup>2</sup> = 16.85, df |                    | 597<br>0.11); l <sup>2</sup> =                        | 35%         |                |  |                                      | 1                       | 400 |
| Test for overall                      | effect: Z = 2.41                    |                    |   | - /0        |                |  | 0.01 0.1 1<br>Favours [experimental] | 10<br>Favours [control] | 100 |
| E                                     | Experi                              | nental             | Contro  | si.         |                | Odds Ratio                             |                                      | Ratio                   |     |
| Study or Subg                         |                                     |                    | Events  |             | Weight         | IV. Random, 95% C                      |                                      | om, 95% Cl              |     |
| Batmaz, SB 20                         |                                     | 30                 | 6   | 30          | 3.2%           | 0.06 [0.00, 1.15]                      |                                      | Ť                       |     |
| Einisman, H 20<br>Iordanidou, M 2     |                                     | 73<br>127          | 0<br>8  | 50<br>91    | 9.6%           | Not estimable<br>0.51 [0.17, 1.54]     |                                      | +                       |     |
| Ismail, MF 2013                       | 3 0                                 | 51                 | 7   | 33          | 3.3%           | 0.03 [0.00, 0.62]                      |                                      |                         |     |
| Kilic, M 2019<br>Liu, Y 2016          | 9<br>20                             | 100<br>41          | 4<br>35   | 80<br>41    | 8.9%<br>9.8%   | 1.88 [0.56, 6.34]<br>0.16 [0.06, 0.47] |                                      |                         |     |
| Ma, JH 2014                           | 24                                  | 60                 | 11  | 60          | 11.1%          | 2.97 [1.29, 6.83]                      |                                      | - <b>-</b> -            |     |
| Maalmi, H 2013<br>Billoi, DK 2011     |                                     | 155                | 23  | 152         | 11.6%          | 0.43 [0.20, 0.91]                      | -                                    | <b></b>                 |     |
| Pillai, DK 2011<br>Zhang, Y 2017      | 5<br>92                             | 122<br>143         | 3<br>74   | 74<br>143   | 7.7%<br>13.1%  | 1.01 [0.23, 4.36]<br>1.68 [1.05, 2.70] |                                      |                         |     |
| Zhao, HX 2015                         | 7                                   | 40                 | 9   | 40          | 9.6%           | 0.73 [0.24, 2.20]                      |                                      |                         |     |
| Zhu, L 2019                           | 22                                  | 97                 | 25  | 100         | 12.1%          | 0.88 [0.46, 1.70]                      | _                                    | -                       |     |
|                                       |                                     |                    |   | 004         | 400.00/        | 0.71 [0.39, 1.29]                      | -                                    | L .                     |     |
| Total (95% CI)                        |                                     | 1039               |   | 894         | 100.0%         | 0.71[0.39, 1.29]                       | •                                    |                         |     |
| Total events                          | 196<br>Tau² = 0.65; Chi             |                    | 205   |             |                |  | · · · ·                              | ,                       |     |

FIGURE 5 | Forest plot for meta-analyzing the association between Vitamin D receptor Fokl (rs2228570) polymorphisms and childhood asthma. (A) additive model: f vs. F; (B) co dominant model: ff vs. FF; (C) co dominant model: ff vs. FF; (D) dominant model: ff+Ff vs. FF; (E): recessive model: ff vs. FF+Ff.

it seems that ApaI and BsmI polymorphisms are not related with childhood asthma susceptibility. Due to these limitations, further multi-center study with high quality should be designed to verify the present conclusion.

### DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

# **AUTHOR CONTRIBUTIONS**

YZ: conception and design of the research, acquisition of data, analysis and interpretation of data, and drafting the

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manuscript. SL: statistical analysis and revision of manuscript for important intellectual content. All authors read and approved the final manuscript.

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### SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fped. 2022.843691/full#supplementary-material

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