## Forest plot comparison graphics: Risk of severe Covid-19 disease

## Glossary

$\mathrm{ADJ}=0$ : crude estimate
$\mathrm{ADJ}=1$ : adjust estimate
LRB $=0$ : moderate and high risk of bias
LRB=1: low risk of bias
MRB=0: High risk of bias
$\mathrm{MRB}=1$ : moderate and low risk of bias
ALT: Alanine aminotransferase
APTT: activated partial thromboplastin time
APACHE: Acute Physiology and Chronic Health Evaluation II
AST: Aspartate aminotransferase
BUN: Blood urea nitrogen
PT: prothrombin time
SOFA: The sequential organ failure assessment score

Candidate variable: Age (older than 50-65 years), outcome: severe
Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Age increase (per 1 year), outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)

| Study |  | seTE | Odds | Ratio | OR | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| MRB $=1$ |  |  |  |  |  |  |  |  |
| Chen J_SP | 0.06 | 0.0289 |  |  | 1.06 | [1.00; 1.12] | 1.5\% | 2.6\% |
| Liang $\bar{W}_{\text {_ }}$ MC | 0.04 | 0.0073 |  | $+$ |  | [1.03; 1.06] | 23.0\% | 11.7\% |
| Mo P_ZH | 0.02 | 0.0140 |  | i |  | [1.00; 1.05] | 6.3\% | 7.2\% |
| Duan Q_WPH | 0.04 | 0.0120 |  | - | 1.04 | [1.02; 1.07] | 8.5\% | 8.3\% |
| Luo X_ECRH | 0.05 | 0.0112 |  | + | 1.05 | [1.02; 1.07] | 9.8\% | 8.9\% |
| Feng $\mathbf{Z}_{\text {_ }}$ TXH | 0.12 | 0.0407 |  |  |  | [1.04; 1.22] | 0.7\% | 1.4\% |
| Wang Y_ZH(Multicéntrico) | 0.07 | 0.0166 |  |  |  | [1.04; 1.11] | 4.5\% | 5.9\% |
| Rentsch_CT | 0.06 | 0.0241 |  |  | 1.06 | [1.01; 1.11] | 2.1\% | 3.5\% |
| Kalligeros M_MC | 0.03 | 0.0173 |  | - |  | [1.00; 1.07] | 4.1\% | 5.6\% |
| Fixed effect model |  |  |  | \% |  | [1.03; 1.05] | 60.6\% | -- |
| Random effects model |  |  |  | $\rangle$ | 1.04 | [1.03; 1.06] | -- | 55.0\% |
| Heterogeneity: $I^{2}=18 \%, \tau^{2}=<0.0001, p=0.29$ |  |  |  |  |  |  |  |  |
| MRB $=0$ |  |  |  |  |  |  |  |  |
| Shi Yu_ZPV | 0.06 | 0.0121 |  |  |  | [1.04; 1.09] | 8.4\% | 8.3\% |
| Zhou Y_CHW | 0.06 | 0.0111 |  | + | 1.06 | [1.04; 1.08] | 10.0\% | 8.9\% |
| Ma K_YCH | 0.09 | 0.0328 |  |  |  | [1.02; 1.16] | 1.1\% | 2.1\% |
| CaiQ_TPHS | 0.08 | 0.0189 |  |  |  | [1.04; 1.12] | 3.5\% | 5.0\% |
| Chao C_NFHJCH | -0.04 | 0.0344 |  |  |  | [0.90; 1.03] | 1.0\% | 1.9\% |
| FL_GHC̄TCPLA | 0.04 | 0.0147 |  | $\stackrel{-}{5}$ | 1.04 | [1.01; 1.07] | 5.7\% | 6.8\% |
| Hongying S_FAHWMU/SAHWMU | 0.09 | 0.0469 |  |  | 1.09 | [0.99; 1.20] | 0.6\% | 1.1\% |
| Zhang R_RH | 0.10 | 0.0243 |  |  |  | [1.05; 1.15] | 2.1\% | 3.4\% |
| Yu T_DPHNH | 0.03 | 0.0134 |  | $\pm$ |  | [1.00; 1.06] | 6.9\% | 7.5\% |
| Fixed effect model |  |  |  |  | 1.05 | [1.04; 1.07] | 39.4\% | -- |
| Random effects model |  |  |  |  | 1.06 | [1.04; 1.07] | -- | 45.0\% |
| Heterogeneity: $I^{2}=55 \%, \tau^{2}=0.0004, p=0.02$ |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  | $\stackrel{ }{*}$ |  | [1.04; 1.05] | 100.0\% | -- |
| Random effects model |  |  |  | $\stackrel{\rightharpoonup}{ }$ | 1.05 | [1.04; 1.06] | -- | 100.0\% |
| Heterogeneity: $I^{2}=42 \%, \tau^{2}=0.0002, p=0.03$ |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=41 \%, p=0.04$ |  |  |  | 1 |  |  |  |  |

Candidate variable: Male gender, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Smoking (Active, present smoker), outcome: severe
Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)

| Study |  | seTE | Odds | Ratio | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| MRB $=0$ |  |  |  |  |  |  |  |  |  |
| Huang C_JYH | -2.71 | 3.2344 |  |  | 0.07 | [0.00; | 37.56] | 0.1\% | 0.2\% |
| Liu F_XH | -2.42 | 3.4001 |  |  | 0.09 | [0.00; | 69.67] | 0.1\% | 0.2\% |
| Mo P_ZH | 0.52 | 0.8815 |  | ! | 1.68 | [0.30; | $9.45]$ | 0.8\% | 1.7\% |
| Shi Yu_ZPV | 0.47 | 0.4710 |  |  | 1.60 | [0.64; | 4.04] | 3.0\% | 3.3\% |
| Jin-Jin Z_MC | 1.11 | 0.7293 |  | ; | 3.04 | [0.73; | 12.69] | 1.2\% | 2.2\% |
| Wei-jie G_NHC | 1.18 | 0.2769 |  | \# | 3.25 | [1.89; | 5.59] | 8.6\% | 4.4\% |
| Chen Y_ multicentrico- FCMCH | 1.17 | 1.2746 |  |  | 3.23 | [0.27; | 39.28] | 0.4\% | 1.0\% |
| Duan Q_WPH | 0.20 | 0.4670 |  | T | 1.22 | [0.49; | 3.04] | 3.0\% | 3.4\% |
| Han Y_RHWU | 0.29 | 0.8266 |  |  | 1.33 | [0.26; | $6.74]$ | 1.0\% | 1.9\% |
| Liu T_UH | 2.67 | 3.1987 |  |  | 14.43 | [0.03; 7 | 7619.45] | 0.1\% | 0.2\% |
| Qi D_multicentrico | 2.67 | 0.3681 |  | \# | 14.46 | [7.03; | 29.75] | 4.8\% | 3.9\% |
| Shi W_SPHCC | 0.38 | 0.7120 |  |  | 1.47 | [0.36; | 5.93] | 1.3\% | 2.3\% |
| Feng $\bar{Z}_{\text {_ }}$ TXH | -2.16 | 3.1968 |  |  | 0.11 | [0.00; | 60.50] | 0.1\% | 0.2\% |
| Hu L_TH | 0.75 | 0.3817 |  | + | 2.12 | [1.00; | 4.48 ] | 4.5\% | 3.8\% |
| Li J_CHW | -0.15 | 0.4735 |  |  | 0.86 | [0.34; | $2.17]$ | 2.9\% | 3.3\% |
| Liu J_BDH | 1.03 | 1.0442 |  |  | 2.80 | [0.36; | 21.68] | 0.6\% | 1.4\% |
| Ma K_YCH | 0.97 | 0.8117 |  |  | 2.65 | [0.54; | 12.99] | 1.0\% | 1.9\% |
| Qin X_SPH | -0.07 | 0.5132 |  |  | 0.93 | [0.34; | $2.55]$ | 2.5\% | 3.1\% |
| Tabata S_SDFCH | 0.68 | 0.5448 |  |  | 1.97 | [0.68; | 5.73] | 2.2\% | 3.0\% |
| Wang G_PHTCC | -0.46 | 0.7699 |  |  | 0.63 | [0.14; | 2.86] | 1.1\% | 2.1\% |
| Wang Y_ZH(Multicéntrico) | -3.19 | 3.1718 |  |  | 0.04 | [0.00; | 20.58] | 0.1\% | 0.2\% |
| Xu Y_FAHG | -0.35 | 0.8013 |  |  | 0.71 | [0.15; | $3.39]$ | 1.0\% | 2.0\% |
| Yang L_YCPH | -0.32 | 1.0802 |  |  | 0.73 | [0.09; | $6.05]$ | 0.6\% | 1.3\% |
| Zhang H_ZH | 0.36 | 0.7206 |  | , | 1.44 | [0.35; | $5.89]$ | 1.3\% | 2.2\% |
| Jiancheng L_JH | -0.21 | 0.9332 |  |  | 0.81 | [0.13; | $5.04]$ | 0.8\% | 1.6\% |
| Kuang Y_MC | -0.32 | 0.6281 |  |  | 0.72 | [0.21; | 2.48 ] | 1.7\% | 2.6\% |
| Cao M_SPHCC | -0.06 | 1.0777 |  |  | 0.94 | [0.11; | $7.76]$ | 0.6\% | 1.3\% |
| Wang Y_CHW | 0.00 | 0.4718 |  |  | 1.00 | [0.40; | 2.53] | 3.0\% | 3.3\% |
| Liao Xuelian_MC | 1.34 | 1.2750 |  |  | 3.83 | [0.32; | 46.65] | 0.4\% | 1.0\% |
| FY_JH, SPHCC, TPH | 0.60 | 0.3857 |  |  | 1.82 | [0.86; | 3.88 ] | 4.4\% | 3.8\% |
| CM_FAHSYU | 1.08 | 0.8514 |  | - | 2.96 | [0.56; | 15.68] | 0.9\% | 1.8\% |
| WR_PHFC | 1.37 | 0.5661 |  | +- | 3.93 | [1.30; | 11.93] | 2.0\% | 2.9\% |
| Argenziano M_NYP/CUIMC | 0.10 | 0.1762 |  |  | 1.11 | [0.79; | 1.57] | 21.1\% | 5.0\% |
| Hongying S_FAHWMU/SAHWMU | 1.53 | 1.1517 |  |  | 4.61 | [0.48; | 44.06] | 0.5\% | 1.2\% |
| Jun R_TH | 0.86 | 0.5612 |  |  | 2.35 | [0.78; | $7.07]$ | 2.1\% | 2.9\% |
| Dreher M_UHA | -1.19 | 0.8730 |  |  | 0.30 | [0.05; | 1.68] | 0.9\% | 1.7\% |
| Xudan C_GEPH | -0.03 | 0.4772 |  |  | 0.97 | [0.38; | $2.46]$ | 2.9\% | 3.3\% |
| Zhang R_RH | 5.40 | 3.1972 |  |  | 221.25 | 0.42; 116 | 6498.14] | 0.1\% | 0.2\% |
| Dong J_FMC | 0.74 | 0.5286 |  | F | 2.10 | [0.75; | 5.93] | 2.4\% | 3.0\% |
| Yan X_HNU | 0.22 | 0.6608 |  |  | 1.24 | [0.34; | 4.54] | 1.5\% | 2.5\% |
| Yu T_DPHNH | -0.92 | 1.0963 |  |  | 0.40 | [0.05; | 3.41] | 0.5\% | 1.3\% |
| Kalligeros M_MC | -0.08 | 0.3995 |  |  | 0.92 | [0.42; | 2.02 ] | 4.1\% | 3.7\% |
| LiX_TH | -0.21 | 0.3271 |  |  | 0.81 | [0.43; | 1.54] | 6.1\% | 4.2\% |
| Li Y_TH | 2.17 | 1.0106 |  | , | 8.75 | [1.21; | 63.43] | 0.6\% | 1.4\% |
| Fixed effect model |  |  |  | 9 | 1.57 | [1.34; | 1.84] | 98.7\% | -- |
| Random effects model |  |  |  | Q | 1.57 | [1.21; | 2.05] | -- | 97.7\% |
| Heterogeneity: $I^{2}=50 \%, \tau^{2}=0.3087, p<0.01$ |  |  |  |  |  |  |  |  |  |
| $M R B=1$ |  |  |  |  |  |  |  |  |  |
| Liu W_MC | 2.66 | 0.7045 |  | $\leftarrow$ | 14.28 | [3.59; | 56.80] | 1.3\% | 2.3\% |
| Fixed effect model |  |  |  | $\infty$ | 14.28 | [3.59; | 56.80] | 1.3\% | -- |
| Random effects model |  |  |  | $\infty$ | 14.28 | [3.59; | 56.80] | -- | 2.3\% |
| Heterogeneity: not applicable |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  | ! | 1.62 | [1.38; | 1.89] | 100.0\% | -* |
| Random effects model |  |  |  | 0 | 1.65 | [1.25; | 2.17] | -- | 100.0\% |
| Heterogeneity: $I^{2}=54 \%, \tau^{2}=0.3656, p<0.01$ |  |  | 1 |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=50 \%, p<0.01$ |  |  | $0.001 \quad 0.11101000$ |  |  |  |  |  |  |

Candidate variable: Cardiovascular disease (coronary heart disease or congestive heart failure), outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Cardiac arrhythmia (as previous condition or new clinical finding), outcome: severe Covid-19 disease


Candidate variable: Cerebrovascular disease (History of stroke or CNS disease), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Diabetes, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)

| Study | TE | seTE | Odds Ratio | OR |  | 95\%-CI | Weight (fixed) | $\begin{array}{r} \text { Weight } \\ \text { (random) } \end{array}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| MRB $=0$ |  |  |  |  |  |  |  |  |
| Wuc_WJH | 1.47 | 0.5029 |  | 4.35 | [1.62; | 11.66] | 0.9\% | 1.3\% |
| Gao $\mathrm{Y}_{\text {- }} \mathrm{FSH}$ | 2.89 | 1.1466 |  | 18.00 | [1.90; | 170.33] | 0.2\% | 0.3\% |
| Huang C_JYH | -1.39 | 1.1286 | + | 0.25 | [0.03; | 2.28] | 0.2\% | 0.3\% |
| $\mathrm{LiK}_{\mathrm{K}} \mathrm{CMU}$ | 5.40 | 3.1965 |  | 222.33 |  |  | 0.0\% | 0.0\% |
| LiuF XH | 2.20 | 10.5597 |  |  | [0.42; 116905.58] [0.00; 8763252695.66] |  | 0.0\% | 0.0\% |
| Liu W_MC | 1.56 | 0.9816 | : | 4.74 | [0.69; | 32.45] | 0.2\% | 0.4\% |
| Liu $Y_{\text {_St }}^{\text {STP }}$ | 1.10 | 1.6330 | ; | 3.00 | [0.12; | 73.64] | 0.1\% | 0.2\% |
| Peng YD_WU | 0.30 | 0.6316 | + | 1.35 | [0.39; | $4.66]$ | 0.6\% | 0.9\% |
| Shi Yu_ZPV | 1.15 | 0.4632 | + | 3.15 | [1.27; | ${ }^{7.81]}$ | 1.1\% | 1.4\% |
| Jin-Jin Z_MC | 0.26 | 0.5194 | , | 1.30 | [0.47; | 3.59] | 0.9\% | 1.2\% |
| Wei-jie $\overline{\text { G }}$ NHC | 1.73 | 0.3047 | \% | 5.65 | [3.11; | 10.27] | 2.5\% | 2.3\% |
| Lu Jiatao WHH | 0.05 | 0.3998 | t | 1.05 | [0.48; | $2.31]$ | 1.5\% | 1.7\% |
| Chen X_GHCTC | 1.29 | 0.6938 | + | 3.64 | [0.93; | 14.18] | 0.5\% | 0.8\% |
| Chen $\mathrm{Y}_{-}^{-m}$ ulticentr ico- FCMCH | 0.21 | 0.7744 | , | 1.24 | [0.27; | 5.64] | 0.4\% | 0.7\% |
| Duan Q-WPH | 1.15 | 0.4533 | + | 3.17 | [1.30; | $7.71]$ | 1.1\% | 1.5\% |
| Han Y_RHWU | 0.29 | 0.8266 | $\cdots$ | 1.33 | [0.26; | 6.74] | 0.3\% | 0.6\% |
| Liu T UH | 3.04 | 3.1935 |  | 20.86 | [0.04; | 10906.91] | 0.0\% | 0.0\% |
| Liu Y_CHW | 2.67 | 1.0644 | $-$ | 14.40 | [1.79; | 116.01] | 0.2\% | 0.4\% |
| Liu Yo- ${ }^{-}$SCH | -0.20 | 0.9142 | t | 0.82 | [0.14; | ${ }^{4.90]}$ | 0.3\% | 0.5\% |
| Qi D D multicentr ico | 1.52 | ${ }^{0.4313}$ | * | 4.58 | [1.97; | ${ }^{10.66]}$ | 1.3\% | 1.6\% |
| Shi W_SPHCC | -0.18 0.42 | 0.8095 0.904 | + | 0.83 1.53 | ${ }^{[0.17 ;}$ | 4.06] | 0.4\% | 0.6\% |
| Song CYF F AHZU Sun F ZHWU | 0.42 1.09 | 0.9004 0.6543 | + | 1.53 2.98 | ${ }^{[0.26 \% ;}$ | $\left.{ }^{8.91]} 10.73\right]$ | ${ }_{\text {e }}^{0.5 \%}$ | 0.9.9\% |
| Shijiao Y_HHMU | 1.81 | 0.6206 | - | 6.13 | [1.82; | $20.69]$ | 0.6\% | 0.9\% |
| Zhang G_ZHWU | 0.38 | 0.4868 | + | 1.47 | [0.57; | 3.81] | 1.0\% | 1.3\% |
| Zhang H_CPHMC | 0.86 | 0.8922 | + | 2.36 | [0.41; | 13.58] | 0.3\% | 0.5\% |
| Zhang Y_WCUH | 0.86 | ${ }^{0.3272}$ |  | 2.37 | [1.25; | 4.50] | 2.2\% | 2.2\% |
| Zhou Y_CHW | 1.07 | 0.2560 | 1 | 2.91 | [1.76; | 4.80] | 3.6\% | 2.7\% |
| Lei L_CUTGH | 6.35 | 3.2576 |  | 572.00 | [0.96; | 339067.57] | 0.0\% | 0.0\% |
| Jing L_wUH | 1.71 | 0.9493 | + | 5.56 | ${ }^{\text {[0.86; }}$ | 35.71] | 0.3\% | 0.5\% |
| Chen G_TH | 0.69 | 1.3123 | : | 2.00 | ${ }^{[0.15 ;}$ | 26.19] | 0.1\% | 0.3\% |
| Bai X_WPH | 0.70 | 0.5117 | + | 2.02 | [0.74; | $5.50]$ | 0.9\% | 1.3\% |
| Chen X . $\mathrm{FHC/LCH}$ | 0.90 | ${ }^{0.4870}$ | + | 2.45 3 3 | [0.94; | ${ }^{6.37]}$ | 1.0\% | 1.3\% |
| ${ }_{\text {Feng Z TXH }}^{\text {Hu LT }}$ | 1.12 1.27 | 0.8671 0.3396 | + | 3.08 3.58 |  | $16.83]$ $6.96]$ | - ${ }_{\text {2.3\% }}$ | ${ }^{0.1 \%}$ |
| Li J_Chw | 0.48 | 0.3992 | + | 1.62 | [0.74; | 3.54] | 1.5\% | 1.7\% |
| Liu J_BD | 1.50 | 0.9636 | + | 4.50 | [0.68; | 29.75] | 0.3\% | 0.4\% |
| $\mathrm{MaK} \mathrm{K}^{\text {YCH }}$ | 2.39 | 0.7546 | + | 10.95 | [2.49; | ${ }^{48.05]}$ | 0.4\% | 0.7\% |
| Lei P- BH (Multicéntr ico) | 0.95 | 0.6948 | $+$ | 2.60 | [0.67; | 10.14] | 0.5\% | 0.8\% |
| Qin X _SPH | 2.04 | ${ }^{0.8254}$ | - | 7.70 | [1.53; | ${ }^{38.84]}$ | 0.3\% | 0.6\% |
| Wang G PHTCC | 0.76 | 0.6135 | + | 2.14 | [0.64; | ${ }^{7.11]}$ | 0.6\% | 1.0\% |
| Wang $\mathrm{Y}^{-} \mathrm{ZH}$ (Multicéntr ico) | 1.09 | 0.4247 | + | 2.97 | [1.29; | ${ }^{6.83]}$ | 1.3\% | 1.6\% |
| Wang Z CH | 3.70 0.10 | ${ }^{1.1446}$ | - | 40.50 | [4.30; | ${ }^{381.73]}$ | 0.2\% | 0.3\% |
| ${ }_{\text {Xu Y }}$ Yang L_ YCPH | 0.10 0.37 | 0.6607 0.5961 | * | 1.10 1.45 | ${ }_{\text {[0.45; }}$ | $4.02]$ $4.66]$ | 0.7\% | - ${ }^{0.9 \%}$ |
| Zhang $\overline{\text { _ }}$ ZH | 1.11 | 0.6609 | + | 3.03 | [0.83; | 11.08] | 0.5\% | 0.9\% |
| Zhao W_BYH | 0.39 | 0.9080 | \% | 1.47 | [0.25; | 8.73] | 0.3\% | 0.5\% |
| Huang H_GEPH | 2.35 | 0.8462 | + | 10.50 | [2.00; | 55.14] | 0.3\% | 0.6\% |
| Jiancheng L_JH | 1.40 | 0.7851 |  | 4.04 | [0.87; | 18.81] | 0.4\% | 0.6\% |
| Mingfeng H_SPH | 2.58 | 0.7130 | $\pm$ | 13.22 | [3.27; | 53.48 | 0.5\% | 0.8\% |
| Wentao X_IDH | 3.99 | 3.2020 |  | 54.03 | [0.10; | 28715.76] | 0.0\% | 0.0\% |
| Kuang Y_MC | 0.97 | 0.6231 | + | 2.63 | [0.77; | 8.91] | 0.6\% | 0.9\% |
| Zeng G_TPHS | 1.46 | 0.4244 | * | 4.30 | [1.87; | ${ }^{9.88]}$ | 1.3\% | 1.6\% |
| Caio_TPHS | 1.30 | 0.4993 | 4 | 3.68 | [1.38; | 9.79] | 0.9\% | 1.3\% |
| Cao M_ SPHCC | 0.41 | 0.8011 | * | 1.50 | [0.31; | $7.22]$ | 0.4\% | 0.6\% |
| Wang Y_CHW | 0.91 | ${ }^{0.5626}$ | * | 2.48 | [0.82; | $7.46]$ | 0.7\% | 1.1\% |
| Liao Xuelian MC | 0.47 | 0.7488 | + | 1.60 | [0.37; | 6.94] | 0.4\% | 0.7\% |
| Chao C _ NFHICH | 2.77 | 3.3277 |  | 15.91 | ${ }^{[0.02 ; ~}$ | 10819.14] | 0.0\% | 0.0\% |
| Leis RHZHTHC ${ }_{\text {FY }}^{\text {LH, SPHCC }}$, TPH | 1.73 -0.23 | 0.9146 0.4564 | + | 5.67 0.79 | ${ }^{[0.94 ;}$ [0.32; | $34.03]$ $1.94]$ | - ${ }_{\text {0, }}$ | 0.5\% |
| CM_FAHSYU | 1.84 | 0.9000 | + | 6.27 | [1.08; | 36.60] | 0.3\% | 0.5\% |
| FL_GHCTCPLA | 0.66 | 0.4651 | - | 1.94 | [0.78; | 4.83] | 1.1\% | 1.4\% |
| JX WFPH | 2.13 | 0.8508 | + | 8.40 | [1.59; | 44.51] | 0.3\% | 0.6\% |
| MY_multicenter 43 hosp | 0.68 | 0.4696 | * | 1.97 | [0.79; | ${ }^{4.95]}$ | 1.1\% | 1.4\% |
| Colombi D Gdsh | ${ }_{0}^{0.66}$ | ${ }^{0.3641}$ |  | 1.93 630 | ${ }^{\text {[0.94; }}$ | $3.93]$ $5628]$ | 1.8\% | 1.9\% |
| Chen J.F AH ${ }_{\text {Argeniano M }}$ | 1.84 0.33 | 1.1173 0.1527 | : | 6.30 1.39 | ${ }_{\text {[1.03; }}{ }^{[0.71 ;}$ | $56.28]$ $1.88]$ | $0.2 \%$ $10.0 \%$ | $0.3 \%$ $3.5 \%$ |
| Colaner i M_PSM | -1.52 | 1.1299 | + | 0.22 | [0.02; | $2.00]$ | 0.2\% | 0.3\% |
| Hongying S_F AHWMU/SAHWMU | -0.06 | 0.6769 | , | 0.94 | [0.25; | ${ }^{3.55]}$ | 0.5\% | 0.8\% |
| Xin L_CHWChospitales en Hunan | 1.27 | 0.5806 | + | 3.57 | [1.14; | 11.15] | 0.7\% | 1.0\% |
| Ying S _hospitales en Beijing | 1.37 | 0.9590 | + | 3.94 | [0.60; | 25.79] | 0.3\% | 0.5\% |
| Chen W_YH | 2.91 | 1.2878 | : | 18.29 | [1.47; | 228.187 | 0.1\% | 0.3\% |
| ${ }_{\text {Jun R_TH }}^{\text {Wang } \mathrm{X}}$ DFH | 0.59 1.21 | ${ }_{0}^{0.4641}$ | * | 1.80 3.36 | ${ }^{[0.72 ;}$; | $4.47]$ $8.15]$ | 1.1\% | 1.4\% ${ }^{1.5 \%}$ |
| Herold $\mathrm{T}_{\text {U }} \mathrm{UH}$ | 1.57 | 1.2813 | : | 4.80 | [0.39; | 59.14] | 0.1\% | 0.3\% |
| Dreher M_UHA | 0.36 | 0.5767 | $\stackrel{1}{1}$ | 1.43 | [0.46; | ${ }^{4.42]}$ | 0.7\% | 1.1\% |
| Minhua Y ZHWU | 1.10 | 0.6992 | + | 3.00 | [0.76; | ${ }^{11.81]}$ | 0.5\% | 0.8\% |
| Li J_CHW | 0.75 | 0.2243 | , | 2.12 | [1.37; | ${ }^{3.29]}$ | 4.6\% | 2.9\% |
| Zhou M MC | 0.55 | 0.3160 |  | 1.73 | [0.93; | ${ }^{3.21]}$ | 2.3\% | 2.2\% |
| Yuc_TH | 0.65 | 0.1443 | \% | 1.91 | [1.44; | ${ }^{2.53]}$ | 11.2\% | 3.6\% |
| Wangl_RH | 1.31 | 0.6894 | + | 3.71 | ${ }^{[0.96 ;}$ | 14.34] | 0.5\% | 0.8\% |
| Wang L LSPH Wan S TGCH | -0.43 2.33 | 3.3468 0.7784 | :- | 0.65 10.31 | ${ }^{[0.00 ;}$ [2.24; | 458.56] 47.42$]$ | 0.0\% | 0.0\% |
| Zhang $\mathrm{R}_{\text {- }} \mathrm{RH}$ | 5.60 | 3.1936 |  | 270.00 | [0.52; | $141178.69]$ | 0.0\% | 0.0\% |
| Yan X_HNU | 2.01 | 0.4857 | - | 7.44 | [2.87; | 19.27] | 1.0\% | 1.3\% |
| Zhang L_WUH | 0.49 | 0.2314 |  | 1.63 | [1.03; | ${ }^{2.56]}$ | 4.4\% | 2.9\% |
| Hu D_UH | 0.89 | 0.4929 | * | 2.43 | [0.92; | ${ }^{6.38]}$ | 1.0\% | 1.3\% |
| Xie J_Uhw | $\stackrel{0.18}{0}$ | ${ }^{0.4945}$ |  | 1.19 9 | [0.45; | $3.15]$ 26801 | 1.0\% | ${ }_{1}^{1.3 \%}$ |
|  | 2.20 0.59 | 0.5561 0.8623 | + | 9.01 1.80 | ${ }^{[3.03 ;}$ [0.33; | 26.80] $9.76]$ | 0.8\% | 1.1\% |
| $\mathrm{LiX}_{\text {- }}{ }^{\text {P }}$ | 0.65 | 0.2452 |  | 1.92 | [1.19; | 3.10] | 3.9\% | 2.7\% |
| Li Y_TH | 2.89 | 3.3613 | ; | 18.00 | [0.02; | 13073.69] | 0.0\% | 0.0\% |
| Fixed eff ect model |  |  |  | 2.29 | [2.07; | $2.53 \mid$ | 91.2\% |  |
| Random eff ects model Heterogeneity: $T^{2}=34 \%,{ }^{2}=0.1268$ | $p<0.01$ |  |  | 2.56 | [2.21; | $2.95]$ | - | 91.5\% |
| MRB $=1$ |  |  |  |  |  |  |  |  |
| Liang W_MC | 0.79 | 0.2582 |  | 2.21 | [1.33; | ${ }^{3.67]}$ | 3.5\% | 2.6\% |
| Mo P Z ZH | ${ }_{0}^{0.76}$ | ${ }_{0}^{0.7607}$ |  | 2.14 1 1.69 | ${ }^{[0.48 ;}$ | ${ }^{9.51]}$ | 0.4\% | 0.7\% |
| Rentsch_CT Bi Q_STPH $^{\text {a }}$ ( | 0.52 1.36 | 0.2890 0.4447 | + | 1.69 3.90 | ${ }_{[1.63 ;}{ }^{0.96}$ | ${ }^{2.938]}$ | 2.8\% $1.2 \%$ | 2.4\% |
| Kalligeros M_MC | 0.65 | 0.5075 | + | 1.91 | [0.71; | $5.16]$ | 0.9\% | 1.3\% |
| Fixed eff ect model |  |  | 6 | 2.15 | [1.57; | 2.971 | 8.8\% |  |
| Random eff ects model <br> Heterogencity: $l^{2}=0 \%,{ }^{2}=0, p=0.6$ |  |  |  | 2.15 | [1.57; | 2.971 |  | 8.5\% |
| Fixed eff ect model |  |  | i | 2.28 | [2.07; | $2.50 \mid$ | 100.0\% | - |
| Random eff ects model |  |  |  | 2.51 | [2.20; | 2.871 | - | 100.0\% |
| Heterogeneity: $I^{2}=32 \%,{ }^{2}=0.1094$, | $p<0.01$ |  | $\boxed{11}$ |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=33 \%, p<$ | 0.01 |  | 0.00111000 |  |  |  |  |  |

Candidate variable: Arterial hypertension, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)

| Study | TE seTE | Odds Ratio | OR |  | $95 \%-\mathrm{Cl}$ | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| MRB $=0$ 边 |  |  |  |  |  |  |  |
| Wu C WJu | 0.870 .3637 | $+$ | 2.38 | [1.17; | 4.85] | 1.3\% | 1.5\% |
| Gao Y_FSH | 0.690 .6843 |  | 2.00 | [0.52; | 7.65] | 0.4\% | 0.8\% |
| Huang C_JYH | 0.090 .9394 | - | 1.09 | [0.17; | 6.88] | 0.2\% | 0.5\% |
| Li K_CMU | 0.470 .9460 | i | 1.59 | [0.25; | 10.18] | 0.2\% | 0.5\% |
| Liu $\bar{W}$ _MC | 0.820 .8937 | - | 2.26 | [0.39; | 13.03] | 0.2\% | 0.5\% |
| Liu Y_STP | 0.561 .4638 |  | 1.75 | [0.10; | 30.84] | 0.1\% | 0.2\% |
| Mo P-Z ${ }^{\text {ZH }}$ | 0.250 .3823 | + | 1.28 | [0.61; | 2.71 ] | 1.2\% | 1.4\% |
| Wang D_ZH | 1.630 .4150 |  | 5.09 | [2.26; | 11.48] | 1.0\% | 1.3\% |
| Shi Yu_ŻPV | 1.000 .3682 | $\div$ | 2.71 | [1.32; | 5.58] | 1.3\% | 1.5\% |
| Jin-Jin Z_MC | 0.640 .3733 |  | 1.89 | [0.91; | 3.94] | 1.2\% | 1.5\% |
| Wei-jie G_NHC | 1.260 .2704 | * | 3.53 | [2.08; | 5.99] | 2.4\% | 1.8\% |
| Lu Jiatao_WH | 0.460 .2718 | \% | 1.58 | [0.93; | 2.69] | 2.3\% | 1.8\% |
| Qi Xiaolong_MC | -1.15 1.4793 | $!$ | 0.32 | [0.02; | 5.78] | 0.1\% | 0.2\% |
| Chen X_GHCTC | 1.470 .6513 | :- | 4.36 | [1.22; | 15.64] | 0.4\% | 0.8\% |
| Chen $Y_{\text {- multicentrico- } \mathrm{FCMCH}}$ | 1.460 .7138 |  | 4.29 | [1.06; | 17.36] | 0.3\% | 0.7\% |
| Fan T_RHWU | 0.600 .3919 | \% | 1.83 | [0.85; | 3.94] | 1.1\% | 1.4\% |
| Han Y_RHWU | 0.290 .6026 |  | 1.34 | [0.41; | 4.36] | 0.5\% | 0.9\% |
| Liu T_UH | 3.333 .1906 |  | 28.00 | [0.05; 145 | 4555.62] | 0.0\% | 0.0\% |
| Liu Y_CHW | 0.500 .4079 | - | 1.64 | [0.74; | 3.65] | 1.0\% | 1.3\% |
| Liu Yo_Sch | -0.90 1.1557 |  | 0.41 | [0.04; | 3.93] | 0.1\% | 0.3\% |
| Qi D_multicentrico | 2.360 .5016 | $\stackrel{+}{\square}$ | 10.54 | [3.94; | $28.17]$ | 0.7\% | 1.1\% |
| Shi W_SPHCC | 0.660 .3749 |  | 1.94 | [0.93; | 4.04] | 1.2\% | 1.4\% |
| Song $\bar{C} Y$ _FAHZU | 2.000 .6184 | $\stackrel{ }{\square}$ | 7.43 | [2.21; | 24.95] | 0.5\% | 0.9\% |
| Sun F_ZHWU | 1.380 .4456 | \% | 3.96 | [1.66; | 9.49] | 0.9\% | 1.2\% |
| Shijiao Y_HHMU | 1.390 .4650 | + | 4.03 | [1.62; | 10.02] | 0.8\% | 1.2\% |
| Zhang G_ZHWU | 1.490 .3404 | - | 4.42 | [2.27; | $8.61]$ | 1.5\% | 1.6\% |
| Zhang H-CPHMC | -0.41 1.2036 |  | 0.67 | [0.06; | 7.05] | 0.1\% | 0.3\% |
| Zhou Y_CHW | 1.540 .2377 |  | 4.66 | [2.92; | 7.42] | 3.1\% | 1.9\% |
| Lei L_CUTGH | 0.821 .2346 | - | 2.28 | [0.20; | 25.61] | 0.1\% | 0.3\% |
| Jing L_WUH | 2.791 .1677 | $\stackrel{1}{4}$ | 16.25 | [1.65; | $160.24]$ | 0.1\% | 0.3\% |
| Chen G_TH | 1.641 .2263 | i, | 5.14 | [0.46; | 56.89] | 0.1\% | 0.3\% |
| Bai X_WPH | 1.440 .4545 | $\square$ | 4.22 | [1.73; | 10.29] | 0.8\% | 1.2\% |
| Chen X _FHC/LCH | 1.910 .3734 | - | 6.77 | [3.26; | 14.08] | 1.2\% | 1.5\% |
| Feng Z_TXH | 1.600 .5945 | ! | 4.93 | [1.54; | 15.82] | 0.5\% | 0.9\% |
| Hu L_TH | 0.280 .4219 | + | 1.33 | [0.58; | 3.04] | 1.0\% | 1.3\% |
| Li J_C̄HW | 0.500 .3707 | \% | 1.64 | [0.79; | $3.40]$ | 1.3\% | 1.5\% |
| Liu J_BDH | 1.240 .6712 | : | 3.45 | [0.93; | 12.87] | 0.4\% | 0.8\% |
| Ma K_YCH | 0.560 .6748 |  | 1.75 | [0.47; | 6.57] | 0.4\% | 0.8\% |
| Qin X_SPH | 2.180 .6926 | $\stackrel{\square}{\square}$ | 8.87 | [2.28; | 34.47] | 0.4\% | 0.7\% |
| Wang G_PHTCC | 1.620 .4072 | - | 5.06 | [2.28; | 11.25] | 1.0\% | 1.4\% |
| Wang Z_UH | 1.960 .7620 | $\div$ | 7.08 | [1.59; | 31.54] | 0.3\% | 0.6\% |
| XuY_FĀHG | 0.610 .6072 | + | 1.83 | [0.56; | 6.03] | 0.5\% | 0.9\% |
| Yang L_YCPH | 0.520 .4430 | $t$ | 1.69 | [0.71; | 4.02] | 0.9\% | 1.3\% |
| Zhang $\mathrm{H}-\mathrm{ZH}$ | 1.460 .5263 | + | 4.32 | [1.54; | 12.13] | 0.6\% | 1.0\% |
| Zhao W_BYH | 1.410 .5948 | + | 4.08 | [1.27; | ${ }^{13.10]}$ | 0.5\% | 0.9\% |
| Huang H_GEPH | 2.130 .5329 | $\stackrel{-}{\sim}$ | 8.41 | [2.96; | 23.89] | 0.6\% | 1.0\% |
| Jiancheng L_JH | 0.710 .4014 | $+$ | 2.03 | [0.93; | 4.46] | 1.1\% | 1.4\% |
| Mingfeng H_SPH | 1.340 .4812 | ! | 3.81 | [1.48; | 9.79] | 0.7\% | 1.2\% |
| Wentao X_IDH | 4.203 .1967 |  | 66.76 | [0.13; 351 | 5119.29] | 0.0\% | 0.0\% |
| Kuang Y M MC | 0.120 .5594 | + | 1.13 | [0.38; | 3.39] | 0.6\% | 1.0\% |
| Zeng G_TPHS | 1.080 .3216 | + | 2.95 | [1.57; | 5.55] | 1.7\% | 1.6\% |
| CaiQ_TPHS | 0.380 .5354 | + | 1.46 | [0.51; | $4.17]$ | 0.6\% | 1.0\% |
| Cao $\bar{M}_{1}$ SPHCC | 0.610 .5276 |  | 1.83 | [0.65; | 5.16] | 0.6\% | 1.0\% |
| Wang $\bar{Y}^{\prime} \mathrm{CHW}$ | 1.650 .5008 | $\square$ | 5.22 | [1.96; | ${ }^{13.92]}$ | 0.7\% | 1.1\% |
| Liao Xuelian_MC | 1.290 .7240 | " | 3.64 | [0.88; | 15.03] | 0.3\% | 0.7\% |
| Chao C_NFHJJCH | 0.770 .7333 | : | 2.15 | [0.51; | 9.06] | 0.3\% | 0.7\% |
| Lei S_RHZHTHC | 1.730 .7710 |  |  | [1.24; | 25.49] | 0.3\% | 0.6\% |
| FY_JH, SPHCC, TPH | -0.14 0.2694 |  | 0.87 | [0.51; | 1.48] | 2.4\% | 1.8\% |
| CM_FAHSYU | 0.600 .5771 |  | 1.83 | [0.59; | 5.67] | 0.5\% | 0.9\% |
| FL_GHCTCPLA | 0.990 .5088 |  | 2.68 | [0.99; | 7.26] | 0.7\% | 1.1\% |
| JX_WFPH | 0.350 .7969 |  | 1.41 | [0.30; | 6.74] | 0.3\% | 0.6\% |
| MY_multicenter 43 hosp | 0.510 .3173 | $\stackrel{4}{3}$ |  | [0.90; | 3.12] | 1.7\% | 1.6\% |
| Chen J_FAH | 0.810 .6492 | 1 | 2.24 | [0.63; | 7.99] | 0.4\% | 0.8\% |
| Argenziano M_NYP/CUIMC | 0.460 .1587 | 1 |  | [1.16; | 2.15] | 6.9\% | 2.1\% |
| Colaneri M_PSM | -0.34 0.6649 | + |  | [0.19; | 2.61] | 0.4\% | 0.8\% |
| Hongying S_FAHWMU/SAHWMU | 0.310 .4710 | + |  | [0.54; | 3.43] | 0.8\% | 1.2\% |
| Xin L_CHWC/hospitales en Hunan | 2.810 .5847 |  |  | [5.30; | 52.42] | 0.5\% | 0.9\% |
| Ying S_hospitales en Beijing | 0.180 .6851 | $\frac{i}{i}$ |  | [0.31; | 4.60] | 0.4\% | 0.8\% |
| Chen W_YH | 3.230 .9828 |  |  | [3.67; 1 | 172.96] | 0.2\% | 0.4\% |
| Jun R_TH | 1.100 .4154 |  | 3.00 | [1.33; | 6.771 | 1.0\% | 1.3\% |
| Yang G_HPHTCM | 0.490 .2686 |  |  | [0.96; | 2.75] | 2.4\% | 1.8\% |
| Wang X DFH | 0.330 .4510 | - | 1.39 | [0.57; | 3.37] | 0.9\% | 1.2\% |
| Herold TTUH | 1.910 .8819 | $\stackrel{!}{1}$ | 6.75 | [1.20; | 38.02] | 0.2\% | 0.5\% |
| Dreher M_UHA | -0.31 0.6188 | $\stackrel{+}{*}$ |  | [0.22; | 2.48] | 0.5\% | 0.9\% |
| Zhou M M M ${ }^{\text {C }}$ | 0.540 .2906 | $*$ | 1.71 | [0.97; | ${ }^{3.02]}$ | 2.1\% | 1.7\% |
| Yuc_TH | 0.360 .1223 | * | 1.44 | [1.13; | 1.83] | 11.6\% | 2.2\% |
| WangL_RH | 0.380 .6387 | $+$ | 1.47 | [0.42; | $5.14]$ | 0.4\% | 0.8\% |
| ZengZ_HH | -0.15 0.2756 |  | 0.86 | [0.50; | $1.47]$ | 2.3\% | 1.8\% |
| Wang L_SPH | 0.950 .7568 | $\square$ | 2.592.67 | [0.59; | 11.41] | 0.3\% | 0.7\% |
| Wan S_TGCH | 0.980 .7523 | $\stackrel{\square}{i}$ |  | [0.61; | 11.65] | 0.3\% | 0.7\% |
| Zhang R_RH | 2.370 .5606 |  |  | [3.57; | 32.12] | 0.6\% | 1.0\% |
| Zheng X_FAH | 1.830 .7473 |  | 6.23 | [1.44; | 26.95] | 0.3\% | 0.7\% |
| Zhang L_WUH | 1.040 .1956 | $\frac{i}{+}$ |  | [1.92; | 4.13] | 4.5\% | 2.0\% |
| Hu D_UH | 1.100 .4180 | ! |  | [1.33; | 6.83] | 1.0\% | 1.3\% |
| Xie J_UHW | 1.100 .3867 |  |  | [1.40; | 6.39] | 1.2\% | 1.4\% |
| Yang A | 2.480 .5951 | $\stackrel{\square}{\square}$ |  | [3.74; | 38.52] | 0.5\% | 0.9\% |
| Zheng F_NHCFH | 2.090 .4971 |  |  | [3.04; | $21.37]$ | 0.7\% | 1.1\% |
| LiX_TH | 0.790 .1908 |  |  | [1.52; | 3.21] | 4.8\% | 2.1\% |
| LiY_TH | 0.631 .4804 |  |  | [0.10; | 34.13] | 0.1\% | 0.2\% |
| Fixed effect model |  |  | 2.27 | [2.09; | $2.47]$ | 92.3\% |  |
| Random effects modelHeterogeneity: $P^{2}=56 \%, \tau^{2}=0.2211, p<0.01$ |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| MRB $=1$ |  |  |  |  |  |  |  |
| Liang W_MC | 0.630 .2209 | : | 1.88 | [1.22; | $2.90]$ | 3.6\% | 2.0\% |
| Wang Y_ZH(Multicéntrico) | 0.260 .4403 | + | 1.30 | [0.55; | 3.08] | 0.9\% | 1.3\% |
| Rentsch_CT | 0.410 .3940 |  | 1.51 | [0.70; | 3.27] | 1.1\% | 1.4\% |
| Bi Q_STPH | 1.450 .3327 | - | 4.28 | [2.23; | $8.21]$ | 1.6\% | 1.6\% |
| Kalligeros M_MC | -0.24 0.5443 |  | 0.79 | [0.27; | 2.30] | 0.6\% | 1.0\% |
| Fixed effect model |  | \% | 1.93 | [1.44; | $2.59]$ | 7.7\% |  |
| Random effects model |  | \% | 1.81 | [1.10; | 2.96] | -- | 7.2\% |
| Heterogeneity: $I^{2}=58 \%, \tau^{2}=0.1787, p$ | 0 $=0.05$ |  |  |  |  |  |  |
| Fixed effect model |  | $!$ | 2.24 | [2.07; | 2.44] | 100.0\% | - |
| Random effects model |  | - | 2.54 | [2.21; | 2.92] |  | 100.0\% |
| Heterogeneity: $I^{2}=56 \%, \tau^{2}=0.2135, p$ | , < 0.01 |  |  |  |  |  |  |
| Residual heterogeneity: $1^{2}=56 \%, p<0$ | 0.01 | 0.11101000 | 1000 |  |  |  |  |

Candidate variable: Obesity, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Chronic kidney disease, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Asthma, outcome: severe Covid-19 disease

| Study |  | seTE | Odds | Ratio | OR |  | 5\%-CI | Weight (fixed) | Weight random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |
| Wang Z_UH | -1.61 | 3.2583 |  |  | 0.20 | [0.00; 1 | 18.26] | 0.4\% | 0.4\% |
| Argenziano M_NYP/CUIMC | 0.16 | 0.2298 |  |  | 1.17 | [0.75; | 1.84] | 80.7\% | 80.7\% |
| Ying S_hospitales en Beijing | 0.87 | 1.4418 |  |  | 2.39 | [0.14; | 40.31] | 2.0\% | 2.0\% |
| Dreher M_UHA | 0.88 | 0.9174 |  | + | 2.40 | [0.40; | 14.49] | 5.1\% | 5.1\% |
| Zhang L_WUH | -0.62 | 0.7963 | , |  | 0.5 | [0.11; | 2.57] | 6.7\% | 6.7\% |
| LiX_TH | 0.45 | 0.9169 |  |  | 1.56 | [0.26; | 9.42] | 5.1\% | 5.1\% |
| Fixed effect model |  |  |  |  | 1.18 | [0.79; | 1.77] | 100.0\% | -- |
| Random effects model |  |  |  |  | 1.18 | [0.79; | 1.77] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.82$ |  |  |  |  |  |  |  |  |  |
| Fixed effect modelRandom effects model |  |  |  |  | 1.18 | [0.79; | 1.77] | 100.0\% | -- |
|  |  |  |  |  | 1.18 | [0.79; | 1.77] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.82$Residual heterogeneity: $I^{2}=0 \%, p=0.82$ |  |  |  |  |  |  |  |  |  |
|  |  |  | 0.11 | 110 |  |  |  |  |  |

Candidate variable: COPD, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)

| Study | TE | seTE | Odds Ratio | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| URB $=0$ |  |  |  |  |  |  |  |  |
| Sao Y_FSH | 0.14 | 0.8125 | i | 1.15 | [0.23; | 5.65] | 1.3\% | 1.7\% |
| łuang C_JYH | 5.44 | 10.0561 |  | 231.00 | [0.00; 83828 | 36391.12] | 0.0\% | 0.0\% |
| _i K_CMU | 2.38 | 1.1468 | $\because$ | 10.86 | [1.15; | 102.77] | 0.6\% | 0.9\% |
| Иo P_ZH | 1.23 | 1.1300 | $\div$ | 3.41 | [0.37; | 31.21] | 0.7\% | 1.0\% |
| Nang D_ZH | 2.22 | 1.1720 | - | 9.18 | [0.92; | 91.31] | 0.6\% | 0.9\% |
| Jin-Jin Z_MC | 3.33 | 3.2490 |  | 27.82 | [0.05; | 16215.51] | 0.1\% | 0.1\% |
| Nei-jie G_NHC | 3.18 | 0.6004 | * | 23.96 | [7.39; | 77.73] | 2.3\% | 2.7\% |
| _u Jiatao_WHH | 1.23 | 1.0066 | $\div$ | 3.43 | [0.48; | 24.65] | 0.8\% | 1.2\% |
| Zhen Y_ multicentrico- FCMCH | 0.83 | 0.8526 | t | 2.30 | [0.43; | 12.25] | 1.1\% | 1.6\% |
| Juan Q-WPH | 0.17 | 0.6196 | * | 1.19 | [0.35; | 4.01] | 2.2\% | 2.5\% |
| -iu Y_CHW | 0.06 | 1.0189 | - | 1.06 | [0.14; | 7.80] | 0.8\% | 1.2\% |
| -iu Yo_SCH | 4.29 | 3.2720 |  | 73.29 | [0.12; | 44681.63] | 0.1\% | 0.1\% |
| Song CY_FAHZU | 0.41 | 1.2483 | 1 | 1.50 | [0.13; | 17.32] | 0.5\% | 0.8\% |
| Sun F_ZHWU | 0.81 | 1.2445 | $t$ | 2.24 | [0.20; | 25.68] | 0.5\% | 0.8\% |
| Shijiao Y_HHMU | -1.66 | 3.2498 | i | 0.19 | [0.00; | 110.96] | 0.1\% | 0.1\% |
| Zhang G_ZHWU | 1.86 | 0.8807 | ; | 6.43 | [1.14; | 36.14] | 1.1\% | 1.5\% |
| Zhao W_SXH | 1.64 | 1.1709 | $\therefore$ | 5.14 | [0.52; | 51.03] | 0.6\% | 0.9\% |
| Zhou Y_CHW | 2.45 | 1.1012 | $\cdots$ | 11.56 | [1.34; | 100.10] | 0.7\% | 1.0\% |
| Zhen L_MC | 1.43 | 0.4337 | 鱼 | 4.18 | [1.79; | 9.78] | 4.4\% | 4.0\% |
| 3ai X_WPH | 1.83 | 1.1326 | is | 6.24 | [0.68; | 57.44] | 0.7\% | 1.0\% |
| Shen X_FHC/LCH | 1.66 | 0.6530 | + | 5.24 | [1.46; | 18.86] | 2.0\% | 2.4\% |
| =eng Z_TXH | 2.26 | 1.0416 | i- | 9.54 | [1.24; | 73.47] | 0.8\% | 1.1\% |
| łu L_TH | 0.85 | 1.1151 | - | 2.34 | [0.26; | 20.78] | 0.7\% | 1.0\% |
| -i J_CHW | 1.33 | 0.7013 | + | 3.76 | [0.95; | 14.88] | 1.7\% | 2.1\% |
| _iu J_BDH | 1.50 | 0.9636 | i | 4.50 | [0.68; | 29.75] | 0.9\% | 1.3\% |
| Иa K_YCH | 0.82 | 0.9514 | - | 2.26 | [0.35; | 14.58] | 0.9\% | 1.3\% |
| -ei P_BH (Multicéntrico) | 1.05 | 0.8040 | + | 2.85 | [0.59; | 13.78] | 1.3\% | 1.7\% |
| 2in X_SPH | 4.48 | 3.2024 |  | 88.20 | [0.17; | 46922.57] | 0.1\% | 0.1\% |
| Nang G_PHTCC | 3.94 | 3.3382 | ! | 51.25 | [0.07; | 35575.14] | 0.1\% | 0.1\% |
| Nang Z_UH | 1.49 | 1.0498 | i | 4.42 | [0.56; | 34.57] | 0.8\% | 1.1\% |
| Xu Y_FĀHG | 1.44 | 1.1974 | : | 4.24 | [0.41; | 44.27] | 0.6\% | 0.9\% |
| Yang L_YCPH | 2.19 | 0.7933 | - | 8.96 | [1.89; | 42.42] | 1.3\% | 1.8\% |
| Zhang H_ZH | 3.56 | 3.2261 | + | 35.00 | [0.06; | 19502.94] | 0.1\% | 0.1\% |
| Zhao W_BYH | 1.16 | 0.8625 | - | 3.18 | [0.59; | 17.22] | 1.1\% | 1.5\% |
| Jiancheng L_JH | 2.36 | 3.2499 | i, | 10.61 | [0.02; | 6195.74] | 0.1\% | 0.1\% |
| Uingfeng H_SPH | 4.35 | 3.2508 |  | 77.27 | [0.13; | 45190.41] | 0.1\% | 0.1\% |
| Nentao X IDH | -1.48 | 1.1397 | + | 0.23 | [0.02; | 2.12] | 0.6\% | 1.0\% |
| <uang Y_MC | 0.52 | 1.2411 | $\square$ | 1.69 | [0.15; | 19.22] | 0.5\% | 0.8\% |
| Nang Y_CHW | 1.42 | 0.8909 | + | 4.12 | [0.72; | 23.60] | 1.1\% | 1.5\% |
| _iao Xuelian_MC | 1.22 | 0.7855 | + | 3.38 | [0.72; | 15.74] | 1.4\% | 1.8\% |
| -ei S_RHZHTHC | 2.61 | 3.3352 |  | 13.57 | [0.02; | 9366.23] | 0.1\% | 0.1\% |
| =Y_JH, SPHCC, TPH | 1.90 | 0.4487 | \# | 6.69 | [2.78; | 16.13] | 4.1\% | 3.8\% |
| Solombi D_GdSH | 0.45 | 0.3489 | + | 1.56 | [0.79; | 3.10] | 6.9\% | 4.9\% |
| Argenziano M_NYP/CUIMC | -0.12 | 0.3109 | + | 0.89 | [0.48; | 1.64] | 8.6\% | 5.3\% |
| Solaneri M_PSM | -2.56 | 3.2596 | ; | 0.08 | [0.00; | 46.06] | 0.1\% | 0.1\% |
| fongying S_FAHWMU/SAHWMU | 4.43 | 3.2514 |  | 83.74 | [0.14; | 49034.62] | 0.1\% | 0.1\% |
| こhen W_YH | -0.24 | 3.3522 | ; | 0.79 | [0.00; | 563.79] | 0.1\% | 0.1\% |
| łerold T_UH | 0.10 | 1.2827 | $!$ | 1.10 | [0.09; | 13.59] | 0.5\% | 0.8\% |
| Jreher M | 0.34 | 0.6854 | $\dagger$ | 1.40 | [0.37; | $5.37]$ | 1.8\% | 2.2\% |
| _i J_CHW | -0.14 | 0.4865 | * | 0.87 | [0.33; | $2.25]$ | 3.5\% | 3.5\% |
| Zhou M_MC | 0.42 | 0.7763 | \% | 1.52 | [0.33; | $6.96]$ | 1.4\% | 1.8\% |
| YuC_TH | 0.33 | 0.2637 | + | 1.39 | [0.83; | 2.32] | 12.0\% | 6.0\% |
| Nang L_SPH | -1.63 | 3.2303 | T | 0.20 | [0.00; | 110.29] | 0.1\% | 0.1\% |
| Nan S_TGCH | 0.92 | 1.2490 | ! | 2.50 | [0.22; | 28.91] | 0.5\% | 0.8\% |
| Zhang R_RH | 2.29 | 1.1754 | i- | 9.89 | [0.99; | $99.00]$ | 0.6\% | 0.9\% |
| Zhang L_WUH | 0.91 | 0.4477 | \% | 2.49 | [1.04; | 5.99] | 4.2\% | 3.8\% |
| Xie J_UHW | 0.57 | 1.4252 | - | 1.76 | [0.11; | 28.75] | 0.4\% | 0.6\% |
| Nu J_TFAH | 3.07 | 3.3359 | ! | 21.62 | [0.03; | 14941.20] | 0.1\% | 0.1\% |
| Theng F_NHCFH | 0.82 | 0.8908 | $t$ | 2.27 | [0.40; | 13.00] | 1.1\% | 1.5\% |
| _iX_TH | 1.25 | 0.5783 | + | 3.49 | [1.12; | 10.85] | 2.5\% | 2.8\% |
| $\mathrm{I}^{-} \mathrm{Y}_{-} \mathrm{TH}$ | 2.77 | 1.2500 | - | 16.00 | [1.38; | 185.40] | 0.5\% | 0.8\% |
| Fixed effect model |  |  | ; | 2.43 | [2.00; | 2.95] | 84.3\% | - |
| -eterogeneity: $I^{2}=26 \%, \tau^{2}=0.2185, p=0.04$ |  |  |  |  |  |  |  |  |
| VRB $=1$ |  |  |  |  |  |  |  |  |
| _iang W_MC | 1.22 | 0.4629 | \# | 3.40 | [1.37; | 8.42] | 3.9\% | 3.7\% |
| 2entsch_CT | 0.59 | 0.3466 | + | 1.81 | [0.92; | 3.57] | 7.0\% | 4.9\% |
| 3 Q Q STPH | 0.82 | 0.5860 | + | 2.27 | [0.72; | 7.17] | 2.4\% | 2.7\% |
| <alligeros M_MC | 0.41 | 0.5938 | $+$ | 1.50 | [0.47; | 4.80] | 2.4\% | 2.7\% |
| Fixed effect model |  |  | 8 | 2.13 | [1.36; | $3.35]$ | 15.7\% | - |
| Random effects model |  |  | 0 | 2.13 | [1.36; | 3.35] | -- | 14.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.66$ |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  | - | 2.38 | [1.99; | 2.84] | 100.0\% | - |
| Random effects model |  |  |  | 2.70 | [2.14; | 3.40] | -- | 100.0\% |
| łeterogeneity: $I^{2}=23 \%, \tau^{2}=0.1641, p=0.06$ |  |  | ¢11 |  |  |  |  |  |
|  |  |  |  |  |  |  |  |

Candidate variable: Tuberculosis, outcome: severe Covid-19 disease

| Study |  | seTE |  | Odds | Ratio |  | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |  |  |
| Mo P_ZH | 3.21 | 3.2204 |  |  |  |  | 24.76 | [0.04; 136 | 3642.22] | 1.8\% | 1.8\% |
| Jin-Jin Z_MC | 3.33 | 3.2490 |  |  |  |  | 27.82 | [0.05; 16 | 6215.51] | 1.7\% | 1.7\% |
| Zhang H_CPHMC | -1.50 | 3.3493 |  |  |  |  | 0.22 | [0.00; | 157.66] | 1.6\% | 1.6\% |
| Bai X_WPH | 0.41 | 0.7303 |  |  | - |  | 1.50 | [0.36; | $6.28]$ | 34.1\% | 34.1\% |
| Zhang H_ZH | -3.37 | 3.2260 |  |  |  |  | 0.03 | [0.00; | 19.21] | 1.7\% | 1.7\% |
| CM_FAHSYU | 4.03 | 3.2529 |  |  |  |  | 56.21 | [0.10; 330 | 23015.36] | 1.7\% | 1.7\% |
| Ying S_hospitales en Beijing | -1.38 | 3.3446 |  |  |  |  | 0.25 | [0.00; | 176.78] | 1.6\% | 1.6\% |
| Bi Q_STPH | -0.85 | 1.0672 |  | 4 |  |  | 0.43 | [0.05; | 3.46] | 16.0\% | 16.0\% |
| LiX_TH | -0.19 | 0.6763 |  |  |  |  | 0.83 | [0.22; | 3.11] | 39.8\% | 39.8\% |
| Fixed effect model |  |  |  |  |  |  | 1.00 | [0.44; | 2.32] | 100.0\% | -- |
| Random effects model |  |  |  |  |  |  | 1.00 | [0.44; | $2.32]$ | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.64$ |  |  |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  |  | 1.00 | [0.44; | 2.32] | 100.0\% | -- |
| Random effects model |  |  |  |  |  |  | 1.00 | [0.44; | 2.32] | - | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.64$ |  |  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=0 \%, p=0.64$ |  |  | 0.001 | 0.1 | 110 | 1000 |  |  |  |  |  |

Candidate variable: Cancer (solid or active haematologic cancer), outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: HIV infection, outcome: severe Covid-19 disease

| Study |  | seTE | Odds | Ratio |  | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |  |
| Mo P_ZH | 2.77 | 3.2484 |  |  |  | 16.02 | [0.03; | 9329.05] | 25.4\% | 25.4\% |
| Wang D_ZH | -1.92 | 3.2502 | + |  |  | 0.15 | [0.00; | 85.41] | 25.3\% | 25.3\% |
| Sun F_ZHWU | -1.28 | 3.2514 | + |  |  | 0.28 | [0.00; | 162.41] | 25.3\% | 25.3\% |
| Mingfeng H_SPH | -0.87 | 3.3392 |  |  |  | 0.42 | [0.00; | 292.23] | 24.0\% | 24.0\% |
| Fixed effect model |  |  |  |  |  | 0.73 | [0.03; | 17.99] | 100.0\% | -- |
| Random effects model <br> Heterogeneity: $1^{2}=0 \%, \tau^{2}=0, p=0.74$ |  |  |  |  |  | 0.73 | [0.03; | 17.99] | -- | 100.0\% |
|  |  |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  | 0.73 | [0.03; | 17.99] | 100.0\% | -- |
| Random effects model |  |  |  |  |  | 0.73 | [0.03; | 17.99] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.74$ |  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=0 \%, p=0.74$ |  |  | 0.11 | 110 | 1000 |  |  |  |  |  |

Candidate variable: Immunocompromised, outcome: severe Covid-19 disease


Candidate variable: Autoimmune disease, outcome: severe Covid-19 disease

| Study TE seTE |  | Odds | Ratio |  | OR | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |
| Zhang H_CPHMC -1.50 3.3493 |  |  |  |  | 0.22 | [0.00; 157.66] | 1.3\% | 1.3\% |
| Wang Y_ZH(Multicéntrico) -0.58 3.2475 |  |  |  |  | 0.56 | [0.00; 326.09] | 1.4\% | 1.4\% |
| Argenziano M_NYP/CUIMC 0.150 .3942 |  |  |  |  | 1.16 | [0.53; 2.51] | 97.2\% | 97.2\% |
| Fixed effect model |  |  |  |  | 1.12 | [0.52; 2.40] | 100.0\% | -- |
| Random effects model |  |  |  |  | 1.12 | [0.52; 2.40] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.87$ |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  | 1.12 | $[0.52 ; 2.40]$ | 100.0\% | -- |
| Random effects model |  |  |  |  | 1.12 | [0.52; 2.40] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.87$ | $\bigcirc$ | , |  | $\checkmark$ |  |  |  |  |
| Residual heterogeneity: $I^{2}=0 \%, p=0.87$ | 0.001 | 0.1 | 110 | 1000 |  |  |  |  |

Candidate variable: Chronic liver disease, outcome: severe Covid-19
disease


Candidate variable: Thyroid disease, outcome: severe Covid-19 disease

| Study |  | seTE |  | Odds | Ratio |  | OR | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |  |
| Jin-Jin Z_MC | 1.79 | 1.1317 |  |  |  |  | 6.00 | [0.65; 55.14] | 25.5\% | 25.5\% |
| Chen X_GHCTC | 0.66 | 1.0493 |  |  |  |  |  | [0.25; 15.12] | 29.6\% | 29.6\% |
| Shijiao Y_HHMU | 1.32 | 1.4269 |  |  |  |  |  | [0.23; 61.35] | 16.0\% | 16.0\% |
| Jing L_WUH | -2.29 | 3.2623 |  |  |  |  |  | [0.00; 60.55] | 3.1\% | 3.1\% |
| Cao M_SPHCC | 0.66 | 1.1231 |  |  |  |  |  | [0.21; 17.47] | 25.9\% | 25.9\% |
| Fixed effect model |  |  |  |  |  |  | 2.62 | [0.86; 8.02] | 100.0\% | -- |
| Random effects modelHeterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.78$ |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  |  |  | [0.86; 8.02] | 100.0\% | -- |
| Random effects model |  |  |  |  |  |  | 2.62 | [0.86; 8.02] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.78$ |  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=0 \%, p=0.780 .001$ |  |  |  | 0.1 | 110 | 1000 |  |  |  |  |

Candidate variable: Chronic gastric disease: History of peptic ulcer or gastritis, outcome: severe Covid-19 disease

| Study | TE seTE |  | Odds | Ratio |  | OR | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |
| Jin-Jin Z_MC | -0.60 0.8549 |  |  |  |  | 0.55 | [0.10; 2.94] | 4.2\% | 4.2\% |
| Zhao W_SXH | 1.641 .1709 |  |  |  |  | 5.14 | [0.52; 51.03] | 2.2\% | 2.2\% |
| Zhen L_MC | 0.880 .4875 |  |  | I- |  | 2.40 | [0.92; 6.25] | 12.8\% | 12.8\% |
| Bai X_WPH | 0.210 .4888 |  |  |  |  | 1.24 | [0.47; 3.22] | 12.7\% | 12.7\% |
| Hu L_TH | 1.040 .5955 |  |  | ; |  | 2.82 | [0.88; 9.05] | 8.6\% | 8.6\% |
| Li J_CHW | 0.760 .4945 |  |  |  |  | 2.14 | [0.81; 5.64] | 12.5\% | 12.5\% |
| Lei $\bar{P}$ _BH (Multicéntrico) | -2.47 3.2113 |  |  |  |  | 0.08 | [0.00; 45.87] | 0.3\% | 0.3\% |
| Chen W_YH | -0.24 3.3522 |  |  | 1 |  | 0.79 | [0.00; 563.79] | 0.3\% | 0.3\% |
| Li J_CHW | 0.240 .2561 |  |  |  |  | 1.28 | [0.77; 2.11] | 46.4\% | 46.4\% |
| Fixed effect model |  |  |  | Q |  | 1.55 | [1.10; 2.19] | 100.0\% | -- |
| Random effects model |  |  |  | ¢ |  | 1.55 | [1.10; 2.19] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.60$ |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  | 1.55 | [1.10; 2.19] | 100.0\% | -- |
| Random effects model |  |  |  |  |  | 1.55 | [1.10; 2.19] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.60$ |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=0 \%, p=0.60$ |  | 0.001 | 0.1 | 110 | 1000 |  |  |  |  |

Candidate variable: Dyslipidemia, outcome: severe Covid-19 disease

| Study |  | seTE |  | Odds | Ratio |  | OR | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  | + |  |  |  |  |  |  |
| Jin-Jin Z_MC | -0.60 | 0.8549 |  | $\stackrel{1}{1}$ |  |  | 0.55 | [0.10; 2.94] | 39.9\% | 39.9\% |
| Chen X_FHC/LCH | -0.52 | 1.0722 |  | $\stackrel{1}{+}$ |  |  | 0.59 | [0.07; 4.86] | 25.3\% | 25.3\% |
| Liu J_BDH | 0.99 | 1.4442 |  | , | $\mp$ |  | 2.69 | [0.16; 45.57] | 14.0\% | 14.0\% |
| Zhang H_ZH | -1.07 | 1.1819 |  | i |  |  | 0.34 | [0.03; 3.49] | 20.9\% | 20.9\% |
| Fixed effect model |  |  |  |  |  |  | 0.63 | [0.22; 1.83] | 100.0\% | - |
| Random effects mod |  |  |  |  |  |  | 0.63 | [0.22; 1.83] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.73$ |  |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  |  | 0.63 | [0.22; 1.83] | 100.0\% | -- |
| Random effects model |  |  |  |  |  |  | 0.63 | [0.22; 1.83] | - | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.73$ |  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity | $=0 \%, p$ | $=0.73$ | 0.1 | 0.5 | 12 | 10 |  |  |  |  |

Candidate variable: Any chronic condition or comorbidities, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Respiratory failure, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Tachypnea, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Hypoxemia, outcome: severe Covid-19 disease

| Study |  | seTE |  | Odds | Ratio |  | OR | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |  |
| Hu L_TH | 2.42 | 0.6352 |  |  |  |  | 11.28 | [ 3.25; 39.18] | 6.8\% | 18.0\% |
| Kuang Y_MC |  | 0.4483 |  |  |  |  | 2.71 | [ 1.13; 6.53] | 13.6\% | 20.4\% |
| Liao Xuelian_MC | -0.33 | 0.6935 |  |  |  |  | 0.72 | [0.18; 2.80] | 5.7\% | 17.3\% |
| Colombi D_GdSH | 1.28 | 0.2762 |  |  | $+$ |  | 3.60 | [2.10; 6.19] | 35.9\% | 22.2\% |
| LiX_TH | 3.05 | 0.2686 |  |  |  |  | 21.16 | [12.50; 35.82] | 38.0\% | 22.2\% |
| Fixed effect model |  |  |  |  |  |  | 6.69 | [ 4.84; 9.25] | 100.0\% | -- |
| Random effects model |  |  |  |  |  |  | 4.69 | [ 1.56; 14.10] | -- | 100.0\% |
| Heterogeneity: $I^{2}=90 \%, \tau^{2}=1.3490, p<0.01$ |  |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  |  |  | [ 4.84; 9.25] | 100.0\% | -- |
| Random effects model |  |  |  |  |  |  | 4.69 | [ 1.56; 14.10] | - | 100.0\% |
| Heterogeneity: $I^{2}=90 \%, \tau^{2}=1.3490, p<0.01$ |  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=90 \%, p<0.01$ |  |  | 0.1 | 0.51 | 2 | 10 |  |  |  |  |

Candidate variable: Dyspnea, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Chest pain, outcome: severe Covid-19 disease


Candidate variable: Low blood pressure, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: High fever (more than $39^{\circ} \mathrm{C}$ ), outcome: severe Covid-19 disease


Candidate variable: Fever, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Rhinorrhea, outcome: severe Covid-19 disease


Candidate variable: Odynophagia, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Conjunctivitis, outcome: severe Covid-19 disease

| Study |  | seTE | Odds | Ratio | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |
| Wei-jie G_NHC | 4.81 | 4.4847 |  | + | 122.46 | [0.02; 80 | 2230.56] | 6.8\% | 6.8\% |
| Liu T_UH | 0.48 | 3.3324 |  | i | 1.62 | [0.00; | 1110.37] | 12.3\% | 12.3\% |
| Liu Yo_SCH | 2.01 | 1.2966 |  |  | 7.43 | [0.59; | 94.32] | 81.0\% | 81.0\% |
| Fixed effect model |  |  |  |  | 7.45 | [0.76; | 73.33] | 100.0\% | -- |
| Random effects mo |  |  |  |  | 7.45 | [0.76; | 73.33] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.74$ |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  | 7.45 | [0.76; | 73.33] | 100.0\% | - |
| Random effects model |  |  |  | - | 7.45 | [0.76; | 73.33] | - | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.74$ |  |  | $\bigcirc$ | 1 |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=0 \%, p=0.74$ |  |  | 0.0010 .11 | 11010 |  |  |  |  |  |

Candidate variable: Cough, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Productive Cough, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Hemoptysis, outcome: severe Covid-19 disease


Candidate variable: Fatigue, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Myalgia/arthralgia, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Headache, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study | TE | seTE | Odds Ratio | OR |  | 95\%-CI | Weight (fixed) | $\begin{aligned} & \text { Weight } \\ & \text { (random) } \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |
| Huang C_JYH | -2.84 | 3.2352 |  | 0.06 | [0.00; | 33.11] | 0.1\% | 0.1\% |
| Li K_CMU | 0.17 | 0.7514 | T | 1.18 | [0.27; | 5.15] | 1.2\% | 1.7\% |
| Mo P_ZH | 0.33 | 0.7488 |  | 1.40 | [0.32; | 6.06] | 1.2\% | 1.7\% |
| Wang D_ZH | 0.37 | 0.7353 |  | 1.45 | [0.34; | 6.15] | 1.2\% | 1.7\% |
| Wei-jie G_NHC | -0.16 | 0.3874 | + | 0.85 | [0.40; | 1.82] | 4.4\% | 3.5\% |
| Lu Jiatao_WHH | 0.44 | 0.4411 | + | 1.55 | [0.65; | 3.67] | 3.4\% | 3.1\% |
| Qi Xiaolong_MC | -0.12 | 0.8515 | 1 | 0.89 | [0.17; | 4.72] | 0.9\% | 1.4\% |
| Chen Y_m ulticentr ico- FCMCH | -0.34 | 1.2733 |  | 0.71 | [0.06; | 8.66] | 0.4\% | 0.7\% |
| Duan Q_WPH | -1.79 | 0.7773 | 7 | 0.17 | [0.04; | $0.76]$ | 1.1\% | 1.6\% |
| Fan T_RHWU | -0.74 | 0.4723 | H | 0.48 | [0.19; | 1.20] | 3.0\% | 2.9\% |
| Liu T_UH | 2.67 | 3.1987 |  | 14.43 | [0.03; 7 | 7619.45] | 0.1\% | 0.1\% |
| Liu Yo_SCH | -1.92 | 3.2676 |  | 0.15 | [0.00; | 88.37] | 0.1\% | 0.1\% |
| Shijiao Y_HHMU | 0.79 | 0.5929 |  | 2.20 | [0.69; | 7.05] | 1.9\% | 2.3\% |
| Zhang G_ZHWU | -0.08 | 0.5942 | $+$ | 0.92 | [0.29; | $2.96]$ | 1.9\% | 2.3\% |
| Zhang H_CPHMC | -0.45 | 0.8908 |  | 0.64 | [0.11; | 3.66] | 0.8\% | 1.3\% |
| Zhao W_SXH | 0.50 | 1.0185 |  | 1.65 | [0.22; | 12.15] | 0.6\% | 1.1\% |
| Zhen L_MC | -0.78 | 0.5812 | 4 | 0.46 | [0.15; | 1.43] | 2.0\% | 2.4\% |
| Tian S_57 hospitales | 0.01 | 0.6580 |  | 1.01 | [0.28; | $3.66]$ | 1.5\% | 2.0\% |
| Lei L_CUTGH | -2.17 | 3.2206 |  | 0.11 | [0.00; | 62.68] | 0.1\% | 0.1\% |
| Jing L_WUH | -0.45 | 0.8973 |  | 0.64 | [0.11; | 3.69] | 0.8\% | 1.3\% |
| Chen G_TH | 0.00 | 1.4907 |  | 1.00 | [0.05; | 18.57] | 0.3\% | 0.5\% |
| Bai X_WPH | 0.18 | 0.5111 |  | 1.20 | [0.44; | 3.27] | 2.5\% | 2.7\% |
| Chen X_FHC/LCH | 0.52 | 0.5416 |  | 1.67 | [0.58; | 4.84] | 2.3\% | 2.6\% |
| Feng Z_TXH | 0.78 | 1.1531 |  | 2.18 | [0.23; | 20.88] | 0.5\% | 0.9\% |
| Hu L_TH | -0.94 | 3.2228 |  | 0.39 | [0.00; | 215.88] | 0.1\% | 0.1\% |
| Li J_CHW | 0.26 | 0.7296 |  | 1.29 | [0.31; | 5.39] | 1.2\% | 1.8\% |
| Liu J_BDH | -1.17 | 0.7062 | $\pm$ | 0.31 | [0.08; | 1.24] | 1.3\% | 1.8\% |
| Ma K_YCH | -2.56 | 3.2129 |  | 0.08 | [0.00; | 41.77] | 0.1\% | 0.1\% |
| Qin X_SPH | 0.36 | 0.5703 |  | 1.44 | [0.47; | 4.40] | 2.0\% | 2.4\% |
| Wang G_PHTCC | 1.22 | 0.5894 | $\pm$ | 3.40 | [1.07; | 10.80] | 1.9\% | 2.3\% |
| Wang Z_UH | -3.43 | 3.1928 |  | 0.03 | [0.00; | 16.95] | 0.1\% | 0.1\% |
| Xu Y_GH | 1.68 | 1.3316 |  | 5.38 | [0.40; | 73.09] | 0.4\% | 0.7\% |
| Yang L_YCPH | -0.84 | 0.7641 | $\cdots$ | 0.43 | [0.10; | 1.93] | 1.1\% | 1.6\% |
| Zhao W_BYH | -3.74 | 3.1893 |  | 0.02 | [0.00; | 12.31] | 0.1\% | 0.1\% |
| Huang H_GEPH | 0.47 | 0.4921 | \# | 1.60 | [0.61; | 4.21] | 2.7\% | 2.8\% |
| Jiancheng L_JH | -0.62 | 1.4271 |  | 0.54 | [0.03; | 8.83] | 0.3\% | 0.6\% |
| Wentao X_IDH | -0.74 | 1.2440 |  | 0.48 | [0.04; | 5.46] | 0.4\% | 0.8\% |
| Zeng G_TPHS | -0.34 | 0.5662 | - | 0.71 | [0.23; | 2.16] | 2.1\% | 2.4\% |
| CaiQ_TPHS | -2.49 | 3.1977 |  | 0.08 | [0.00; | 43.58] | 0.1\% | 0.1\% |
| Cao M_SPHCC | -3.38 | 3.1781 |  | 0.03 | [0.00; | 17.31] | 0.1\% | 0.1\% |
| Lei S_RHZHTHC | 0.98 | 0.8342 | - | 2.67 | [0.52; | 13.68] | 0.9\% | 1.4\% |
| JX_WFPH | 0.49 | 0.9040 |  | 1.62 | [0.28; | 9.56] | 0.8\% | 1.3\% |
| Argenziano M_NYP/CUIMC | -0.58 | 0.2907 |  | 0.56 | [0.32; | $0.99]$ | 7.8\% | 4.2\% |
| Xin L_CHWC/hospitales en Hunan | -0.08 | 0.6000 |  | 0.92 | [0.28; | 2.99] | 1.8\% | 2.3\% |
| Ying S_hospitales en Beijing | -1.23 | 1.1070 | + | 0.29 | [0.03; | 2.57] | 0.5\% | 0.9\% |
| Chen W_YH | 0.95 | 1.2143 |  | 2.58 | [0.24; | 27.91] | 0.4\% | 0.8\% |
| Jun R_TH | -2.03 | 0.4424 | $\pm$ | 0.13 | [0.06; | $0.31]$ | 3.4\% | 3.1\% |
| Wang X_DFH | 0.32 | 0.2716 |  | 1.37 | [0.81; | $2.34]$ | 9.0\% | 4.4\% |
| Dreher M_UHA | -2.16 | 3.3455 |  | 0.12 | [0.00; | 81.50] | 0.1\% | 0.1\% |
| Zhou M_MC | -0.14 | 0.4678 | $\frac{1}{1}$ | 0.87 | [0.35; | 2.18] | 3.0\% | 3.0\% |
| YuC_TH | 0.27 | 0.3803 | $\stackrel{+}{+}$ | 1.32 | [0.62; | 2.77] | 4.6\% | 3.6\% |
| Wang L_SPH | -2.38 | 3.2031 |  | 0.09 | [0.00; | 49.32] | 0.1\% | 0.1\% |
| Zheng X_F AH | -2.48 | 0.6669 | $\rightarrow$ | 0.08 | [0.02; | $0.31]$ | 1.5\% | 2.0\% |
| Yan X_HNU | 0.35 | 0.5895 | 1 | 1.42 | [0.45; | 4.50] | 1.9\% | 2.3\% |
| Bi Q_STPH | 0.28 | 0.3597 | $+$ | 1.32 | [0.65; | $2.67]$ | 5.1\% | 3.7\% |
| Jia M_RHWU | -0.93 | 1.2725 | , | 0.39 | [0.03; | 4.78] | 0.4\% | 0.7\% |
| Wu J_TF AH | 7.27 | 3.1674 |  | 1437.56 | [2.89; 714 | 102.39] | 0.1\% | 0.1\% |
| Zheng F_NHCFH | 0.86 | 0.6493 | F | 2.37 | [0.66; | 8.44] | 1.6\% | 2.1\% |
| LiX_TH | -0.40 | 0.2743 |  | 0.67 | [0.39; | 1.15] | 8.8\% | 4.4\% |
| Fixed eff ect model |  |  |  | 0.89 | [0.76; | 1.04] | 97.8\% |  |
| Random eff ects model |  |  |  | 0.89 | [0.71; | 1.11] | -- | 96.8\% |
| Heterogeneity: $I^{2}=35 \%,{ }^{2}=0.2169, p<0.01$ |  |  |  |  |  |  |  |  |
| ADJ $=1$ |  |  |  |  |  |  |  |  |
| Ying W_MC | -1.11 | 0.7426 | $\cdots$ | 0.33 | [0.08; | 1.41] | 1.2\% | 1.7\% |
| Zhang R_RH | 1.36 | 0.8160 | $\square$ | 3.90 | [0.79; | 19.30] | 1.0\% | 1.5\% |
| Fixed eff ect model |  |  |  | 1.01 | [0.34; | $2.96]$ | 2.2\% |  |
| Random eff ects model |  |  |  | 1.11 | [0.10; | 12.46] | - | 3.2\% |
| Heterogeneity: $I^{2}=80 \%,{ }^{2}=2.4409, p=0.03$ |  |  |  |  |  |  |  |  |
| Fixed eff ect model |  |  |  | 0.89 | [0.76; | 1.04] | 100.0\% | -- |
| Random eff ects model |  |  | , | 0.89 | [0.71; | 1.12] | -- | 100.0\% |
| Heterogeneity: $I^{2}=36 \%,{ }^{2}=0.2329, p<0.01$Residual heterogeneity: $I^{2}=37 \%, p<0.01$ |  |  | 111 |  |  |  |  |  |
|  |  |  | $0.001 \quad 0.11101000$ |  |  |  |  |  |

Candidate variable: Vomits, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study | TE | seTE | Odds Ratio | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\mathrm{ADJ}=0$ |  |  |  |  |  |  |  |  |
| Mo P_ZH | 0.51 | 1.2355 | T | 1.66 | [0.15; | 18.73] | 0.6\% | 1.4\% |
| Wang D_ZH | 1.51 | 0.9347 |  | 4.55 | [0.73; | 28.39] | 1.1\% | 2.2\% |
| Jin-Jin Z_MC | -0.58 | 0.8551 | T | 0.56 | [0.10; | 2.99] | 1.3\% | 2.5\% |
| Lu Jiatao_WHH | -0.17 | 0.7989 | $+$ | 0.84 | [0.18; | 4.03] | 1.5\% | 2.7\% |
| Duan Q_WPH | 0.21 | 0.5100 | + | 1.23 | [0.45; | $3.35]$ | 3.6\% | 4.4\% |
| Liu T_UH | -1.05 | 0.9092 | 4 | 0.35 | [0.06; | 2.09] | 1.1\% | 2.3\% |
| Liu Yo_SCH | 0.83 | 1.0089 | 4 | 2.29 | [0.32; | 16.51] | 0.9\% | 1.9\% |
| Qi D_m ulticentr ico | -0.14 | 1.1068 | T | 0.87 | [0.10; | 7.57] | 0.8\% | 1.7\% |
| Shijiao Y_HHMU | 1.68 | 0.7889 | + | 5.38 | [1.15; | 25.23] | 1.5\% | 2.7\% |
| Zhang H_CPHMC | -1.50 | 3.3493 |  | 0.22 | [0.00; | 157.66] | 0.1\% | 0.2\% |
| Zhao W_SXH | 1.21 | 1.2398 |  | 3.35 | [0.29; | 38.04] | 0.6\% | 1.4\% |
| Zhen L_MC | -0.72 | 1.1286 | + | 0.48 | [0.05; | 4.42] | 0.7\% | 1.6\% |
| Lei L_CUTGH | -1.60 | 3.2422 | - | 0.20 | [0.00; | 116.15] | 0.1\% | 0.2\% |
| Jing L_WUH | 3.01 | 3.3513 |  | 20.25 | [0.03; | 14422.44] | 0.1\% | 0.2\% |
| Chen X_FHC/LCH | -0.47 | 0.7694 | T | 0.63 | [0.14; | $2.84]$ | 1.6\% | 2.8\% |
| Hu L_TH | 4.67 | 3.3398 |  | 106.92 | [0.15; | 74452.09] | 0.1\% | 0.2\% |
| Li J_CHW | -0.51 | 0.5778 | + | 0.60 | [0.19; | 1.87] | 2.8\% | 3.9\% |
| Liu J_BDH | 0.60 | 0.9614 |  | 1.82 | [0.28; | 11.99] | 1.0\% | 2.1\% |
| Ma K_YCH | 1.20 | 1.4382 | T | 3.32 | [0.20; | 55.56] | 0.5\% | 1.1\% |
| Lei P_BH (Multicéntr ico) | 0.15 | 1.1797 | + | 1.17 | [0.12; | 11.78] | 0.7\% | 1.5\% |
| Wang G_PHTCC | 1.05 | 0.8852 |  | 2.87 | [0.51; | 16.28] | 1.2\% | 2.3\% |
| Wang Z_UH | 0.71 | 1.2632 | i | 2.04 | [0.17; | 24.24] | 0.6\% | 1.4\% |
| Yang L_YCPH | 1.83 | 1.0212 | - | 6.26 | [0.85; | 46.32] | 0.9\% | 1.9\% |
| Zhang H_ZH | 0.58 | 0.6981 | + | 1.79 | [0.46; | 7.03] | 1.9\% | 3.2\% |
| Zhao W_BYH | 1.16 | 0.8625 | + | 3.18 | [0.59; | 17.22] | 1.3\% | 2.4\% |
| Zeng G_TPHS | -0.02 | 0.5825 | + | 0.98 | [0.31; | 3.08] | 2.8\% | 3.9\% |
| Lei S_RHZHTHC | -0.50 | 1.2768 | ? | 0.61 | [0.05; | 7.41] | 0.6\% | 1.3\% |
| JX_WFPH | -1.98 | 3.2256 | - | 0.14 | [0.00; | 76.72] | 0.1\% | 0.2\% |
| Argenziano M_NYP/CUIMC | -0.80 | 0.2377 |  | 0.45 | [0.28; | 0.72 ] | 16.7\% | 6.7\% |
| Jun R_TH | 2.20 | 0.4851 | * | 9.00 | [3.48; | 23.29] | 4.0\% | 4.6\% |
| Wang X_DFH | 0.63 | 0.4602 | ${ }_{4}^{+}$ | 1.88 | [0.76; | 4.62] | 4.5\% | 4.8\% |
| Dreher M_UHA | 0.08 | 1.4434 | + | 1.09 | [0.06; | 18.40] | 0.5\% | 1.1\% |
| Zhou M_MC | 0.01 | 0.5269 | - | 1.01 | [0.36; | $2.84]$ | 3.4\% | 4.3\% |
| YuC_TH | -0.54 | 0.4860 | $+$ | 0.59 | [0.23; | 1.52] | 4.0\% | 4.6\% |
| Zheng X_F AH | -1.23 | 3.2557 | 1 | 0.29 | [0.00; | 172.90] | 0.1\% | 0.2\% |
| Zhang L_WUH | 0.19 | 0.2082 |  | 1.21 | [0.80; | 1.82] | 21.8\% | 6.9\% |
| Bi Q_STPH | 0.53 | 0.4737 | 4 | 1.69 | [0.67; | 4.28] | 4.2\% | 4.7\% |
| Wu J_TF AH | 6.60 | 10.0174 |  | 736.29 | [0.00; 2476710 | 24477.10] | 0.0\% | 0.0\% |
| LiX_TH | -0.20 | 0.3130 | + | 0.82 | [0.44; | 1.51] | 9.6\% | 6.0\% |
| Fixed eff ect model |  |  |  | 1.10 | [0.91; | 1.33] | 98.7\% | - |
| Random eff ects model |  |  | 1 | 1.29 | [0.95; | 1.74] | - | 97.6\% |
| Heterogeneity: $I^{2}=39 \%,{ }^{2}=0.2539, p<0.01$ |  |  |  |  |  |  |  |  |
| $\mathrm{ADJ}=1$ |  |  |  |  |  |  |  |  |
| ZhangX_MC | 2.74 | 0.8638 | - | 15.55 | [2.86; | 84.52] | 1.3\% | 2.4\% |
| Fixed eff ect model |  |  | $\diamond$ | 15.55 | [2.86; | 84.52] | 1.3\% | - |
| Random eff ects model |  |  | $\diamond$ | 15.55 | [2.86; | 84.52] | - | 2.4\% |
| Heterogeneity: not applicab le |  |  |  |  |  |  |  |  |
| Fixed eff ect model |  |  |  | 1.14 | [0.94; | 1.37] | 100.0\% | - |
| Random eff ects model |  |  | 1 | 1.38 | [1.01; | 1.90] | -- | 100.0\% |
| Heterogeneity: $I^{2}=45 \%,{ }^{2}=0.3367, p<0.01$ |  |  | $\checkmark$ |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=39 \%, p<0.01$ |  |  | 0.00111000 |  |  |  |  |  |

Candidate variable: Diarrhea, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study | TE seTE | Odds Ratio | OR | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $A D J=0$ |  |  |  |  |  |  |
| Huang C_JYH | -1.58 3.3510 |  | 0.21 | [0.00; 146.02] | 0.0\% | 0.0\% |
| Mo P_ZH | 0.750 .8527 |  | 2.12 | [0.40; 11.30] | 0.5\% | 0.7\% |
| Peng YD_WU | -0.09 0.8126 |  | 0.91 | [0.19; 4.48] | 0.5\% | 0.8\% |
| Wang D_ZH | 0.850 .5793 |  | 2.35 | [0.75; 7.31] | 1.0\% | 1.4\% |
| Young BE_MC | -2.96 3.2592 |  | 0.05 | [0.00; 30.75] | 0.0\% | 0.1\% |
| Jin-Jin Z_MC | 0.420 .5067 |  | 1.52 | [0.56; 4.11] | 1.4\% | 1.8\% |
| Wei-jie G_NHC | 0.510 .5415 |  | 1.66 | [0.57; 4.80] | 1.2\% | 1.6\% |
| Lu Jiatao_WHH | -1.23 0.7475 |  | 0.29 | [0.07; 1.27] | 0.6\% | 0.9\% |
| Qi Xiaolong_MC | -1.15 1.4793 |  | 0.32 | [0.02; 5.78] | 0.2\% | 0.2\% |
| Chen $\mathrm{Y}_{\text {_ }}$ multicentrico- FCMCH | -0.79 1.2072 | , | 0.45 | [0.04; 4.82] | 0.2\% | 0.4\% |
| Chu J_TH | 2.083 .2342 |  | 7.97 | [0.01; 4515.72] | 0.0\% | 0.1\% |
| Fan T_ RHWU | -0.18 0.4366 | + | 0.84 | [0.36; 1.97] | 1.8\% | 2.3\% |
| Liu T_UH | -1.10 0.7078 | + | 0.33 | [0.08; 1.33] | 0.7\% | 1.0\% |
| Liu Y_CHW | 0.060 .6120 | $+$ | 1.06 | [0.32; 3.53] | 0.9\% | 1.3\% |
| Liu Yo_SCH | 0.230 .9425 |  | 1.26 | [0.20; 7.97] | 0.4\% | 0.6\% |
| Qi D_multicentrico | 0.650 .7087 |  | 1.91 | [0.48; 7.68] | 0.7\% | 1.0\% |
| Shijiao Y_HHMU | 0.660 .6437 |  | 1.94 | [0.55; 6.84] | 0.9\% | 1.2\% |
| Zhang G_ZHWU | 0.610 .4495 |  | 1.83 | [0.76; 4.43] | 1.7\% | 2.2\% |
| Zhang H_CPHMC | 0.680 .6814 |  | 1.97 | [0.52; 7.48] | 0.8\% | 1.1\% |
| Zhao W_SXH | 0.510 .8395 |  | 1.67 | [0.32; 8.64] | 0.5\% | 0.7\% |
| Zhen L_MC | -0.84 0.4537 | - | 0.43 | [0.18; 1.05] | 1.7\% | 2.1\% |
| Lei L_CUTGH | -1.92 3.2286 |  | 0.15 | [0.00; 82.05] | 0.0\% | 0.1\% |
| Jing L_WUH | 1.551 .2764 |  | 4.73 | [0.39; 57.69] | 0.2\% | 0.3\% |
| Chen G_TH | -1.35 1.2599 |  | 0.26 | [0.02; 3.06] | 0.2\% | 0.3\% |
| Chen X_FHC/LCH | 0.210 .5261 | T | 1.23 | [0.44; 3.44] | 1.3\% | 1.7\% |
| Feng Z_TXH | 1.550 .9138 |  | 4.69 | [0.78; 28.13] | 0.4\% | 0.6\% |
| LiJ_CHW | -0.17 0.4372 | T | 0.85 | [0.36; 1.99] | 1.8\% | 2.3\% |
| Liu J_BDH | -0.72 1.1349 | $\cdots$ | 0.49 | [0.05; 4.51] | 0.3\% | 0.4\% |
| Ma K_YCH | 2.050 .9103 |  | 7.75 | [1.30; 46.15] | 0.4\% | 0.6\% |
| Lei $P^{-}$BH (Multicéntrico) | -0.21 0.5102 |  | 0.81 | [0.30; 2.21] | 1.4\% | 1.8\% |
| Qin X_SPH | -0.27 1.2444 |  | 0.76 | [0.07; 8.76] | 0.2\% | 0.3\% |
| Wang G_PHTCC | -0.97 1.0509 | , | 0.38 | [0.05; 2.97] | 0.3\% | 0.5\% |
| Wang Z_UH | -0.02 0.8542 | - | 0.98 | [0.18; 5.22] | 0.5\% | 0.7\% |
| Yang L_YCPH | 0.520 .6848 |  | 1.68 | [0.44; 6.42] | 0.8\% | 1.1\% |
| Zhang H_ZH | 0.770 .6820 |  | 2.17 | [0.57; 8.26] | 0.8\% | 1.1\% |
| Zhao W_BYH | -1.17 3.3434 |  | 0.31 | [0.00; 218.20] | 0.0\% | 0.0\% |
| Jin X_MC | 1.210 .3155 | * | 3.36 | [1.81; 6.24] | 3.5\% | 3.7\% |
| Jiancheng L_JH | 0.690 .8253 |  | 1.99 | [0.40; 10.05] | 0.5\% | 0.7\% |
| Wentao X_IDH | 0.360 .6294 | , | 1.44 | [0.42; 4.94] | 0.9\% | 1.2\% |
| Zeng G_TPHS | 0.110 .4289 | + | 1.12 | [0.48; 2.58] | 1.9\% | 2.3\% |
| CaiQ_TPHS | 1.250 .6876 | - | 3.48 | [0.90; 13.40] | 0.7\% | 1.0\% |
| Cao M_SPHCC | -2.51 3.1859 |  | 0.08 | [0.00; 41.78] | 0.0\% | 0.1\% |
| Gong Jiao_MC | 1.320 .7614 | - | 3.74 | [0.84; 16.65] | 0.6\% | 0.9\% |
| Chao C_NFHJCH | -0.72 1.1874 |  | 0.48 | [0.05; 4.97] | 0.2\% | 0.4\% |
| Lei S_RHZHTHC | 0.251 .4584 |  | 1.29 | [0.07; 22.41] | 0.2\% | 0.3\% |
| FL_GHCTCPLA | -0.22 1.1362 |  | 0.80 | [0.09; 7.46] | 0.3\% | 0.4\% |
| JX_WFPH | 0.860 .7757 |  | 2.36 | [0.52; 10.78] | 0.6\% | 0.8\% |
| MY_multicenter 43 hosp | -0.23 0.4869 | + | 0.79 | [0.31; 2.06] | 1.5\% | 1.9\% |
| Chen J_FAH | -0.37 1.4470 |  | 0.69 | [0.04; 11.80] | 0.2\% | 0.3\% |
| Argenziano M NYP/CUIMC | -0.19 0.1827 |  | 0.83 | [0.58; 1.18] | 10.6\% | 6.6\% |
| Colaneri M_PSM | 1.241 .2669 |  | 3.47 | [0.29; 41.53] | 0.2\% | 0.3\% |
| Xin L_CHWC/hospitales en Hunan | 0.230 .6226 |  | 1.25 | [0.37; 4.25] | 0.9\% | 1.3\% |
| Ying S_hospitales en Beijing | -0.59 1.1535 | - | 0.56 | [0.06; 5.33] | 0.3\% | 0.4\% |
| Chen W_YH | -0.24 3.3522 |  | 0.79 | [0.00; 563.79] | 0.0\% | 0.0\% |
| Wang X-DFH | 0.160 .2821 | 4 | 1.18 | [0.68; 2.05] | 4.4\% | 4.2\% |
| Dreher M_UHA | 1.390 .8740 |  | 4.00 | [0.72; 22.18] | 0.5\% | 0.7\% |
| Xie H_WJH | 0.980 .8036 |  | 2.67 | [0.55; 12.88] | 0.5\% | 0.8\% |
| Zhou M_MC | 0.250 .4106 |  | 1.29 | [0.58; 2.88] | 2.1\% | 2.5\% |
| YuC_TH | 0.200 .2368 | + | 1.22 | [0.76; 1.93] | 6.3\% | 5.2\% |
| Wang L_SPH | -2.18 3.2085 |  | 0.11 | [0.00; 60.85] | 0.0\% | 0.1\% |
| Zhang R_RH | 2.170 .8668 | - | 8.80 | [1.61; 48.12] | 0.5\% | 0.7\% |
| Yang J_WUH | 1.070 .8218 | $\square$ | 2.92 | [0.58; 14.60] | 0.5\% | 0.8\% |
| Zhang L_WUH | 0.080 .1880 | - | 1.09 | [0.75; 1.57] | 10.0\% | 6.4\% |
| Zheng X FAH | 0.671 .1880 |  | 1.96 | [0.19; 20.07] | 0.2\% | 0.4\% |
| Yan X_HNU | 0.690 .6807 | \% | 1.99 | [0.52; 7.55] | 0.8\% | 1.1\% |
| Zhang L_WUH | 0.490 .2113 |  | 1.63 | [1.08; 2.47] | 7.9\% | 5.8\% |
| Bi Q_STPH | 0.240 .2966 | + | 1.27 | [0.71; 2.27] | 4.0\% | 4.0\% |
| Xie J_UHW | -0.00 0.4139 |  | 1.00 | [0.44; 2.24] | 2.1\% | 2.5\% |
| Jia M_RHWU | 1.041 .2061 |  | 2.82 | [0.27; 30.02] | 0.2\% | 0.4\% |
| Wu J_TFAH | 2.731 .0884 |  | 15.27 | [1.81; 128.94] | 0.3\% | 0.4\% |
| Zheng F_NHCFH | -1.39 1.0515 | ? | 0.25 | [0.03; 1.95] | 0.3\% | 0.5\% |
| LiX_TH | -0.10 0.1823 |  | 0.91 | [0.64; 1.30] | 10.6\% | 6.6\% |
| LiY_TH | -0.98 1.2076 | 1 | 0.38 | [0.04; 4.00] | 0.2\% | 0.4\% |
| Fixed effect model |  | 1 | 1.21 | [1.08; 1.36] | 99.1\% | - |
| Random effects model |  | ¢ | 1.26 | [1.09; 1.45] | -- | 98.8\% |
| Heterogeneity: $I^{2}=14 \%, \tau^{2}=0.0432, p=0.17$ |  |  |  |  |  |  |
| $A D J=1$ |  |  |  |  |  |  |
| Ying W_MC | 1.290 .6392 | $\square$ | 3.65 | [1.04; 12.77] | 0.9\% | 1.2\% |
| Fixed effect model |  | $\infty$ | 3.65 | [1.04; 12.77] | 0.9\% | -- |
| Random effects model |  | $\infty$ | 3.65 | [1.04; 12.77] | -- | 1.2\% |
| Heterogeneity: not applicable |  |  |  |  |  |  |
| Fixed effect model |  | ? | 1.22 | [1.09; 1.37] | 100.0\% | .* |
| Random effects model |  | d | 1.28 | [1.10; 1.48] | -- | 100.0\% |
| Heterogeneity: $I^{2}=16 \%, r^{2}=0.0500, p$ | $p=0.13$ | 11 |  |  |  |  |
| Residual heterogeneity: $I^{2}=14 \%, p=0$ | 0.17 | $0.001 \quad 0.1110$ | 1000 |  |  |  |

Candidate variable: Anorexia, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Abdominal pain, outcome: severe Covid-19 disease


Candidate variable: Anemia, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: High WBC (greater than $10.0 \times 10^{9} / \mathrm{L}$ ), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: High Neutrophil count (greater than $6.3 \times 10^{9} / \mathrm{L}$ ), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Neutrophil count increase (per $1 \times 10^{9} \mathrm{U} / \mathrm{L}$ ), outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Low neutrophil count (Less than $1.8 \times 10^{9} / \mathrm{L}$ ), outcome: severe Covid-19 disease


Candidate variable: Leukopenia (Less than 3.5-4 x $10^{9} / \mathrm{L}$ ), outcome: severe Covid-19 disease

| Study |  | seTE |  | Odds | Ratio |  | OR | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |  |
| Huang C_JYH | -1.79 | 1.1180 |  |  |  |  | 0.17 | [0.02; 1.49] | 0.4\% | 1.3\% |
| Li K_CMŪ | 0.50 | 0.6953 |  |  |  |  |  | [0.42; 6.45] | 1.1\% | 2.5\% |
| Liu F_XH | -3.46 | 3.3255 |  |  |  |  |  | [0.00; 21.38] | 0.0\% | 0.2\% |
| Liu W_MC | -0.40 | 0.7177 |  |  |  |  |  | [0.16; 2.74] | 1.1\% | 2.4\% |
| Jin-Jin Z_MC | -0.38 | 0.4512 |  |  |  |  | 0.68 | [0.28; 1.65] | 2.7\% | 3.7\% |
| Wei-jie G_NHC | -1.21 | 0.3870 |  | $\pm$ |  |  | 0.30 | [0.14; 0.63] | 3.7\% | 4.1\% |
| Qi D_multicentrico | 0.89 | 0.3226 |  |  | + |  | 2.44 | [1.30; 4.59] | 5.3\% | 4.5\% |
| Shijiao Y_HHMU | -1.07 | 0.5661 |  | $\rightarrow$ |  |  | 0.34 | [0.11; 1.04] | 1.7\% | 3.1\% |
| Zhang G_ZHWU | -0.87 | 0.3733 |  | $\pm$ |  |  | 0.42 | [0.20; 0.87] | 4.0\% | 4.2\% |
| Zhen L_MC | -1.01 | 0.4789 |  | $\pm$ |  |  | 0.36 | [0.14; 0.93] | 2.4\% | 3.6\% |
| Jing L_WUH | -0.84 | 0.8766 |  |  |  |  | 0.43 | [0.08; 2.41] | 0.7\% | 1.9\% |
| Chen G_TH | -3.82 | 3.2524 |  |  |  |  | 0.02 | [0.00; 12.88] | 0.1\% | 0.2\% |
| Chen X_FHC/LCH | -0.00 | 0.3237 |  |  |  |  | 1.00 | [0.53; 1.88] | 5.3\% | 4.5\% |
| Hu L_TH | -0.41 | 0.5187 |  |  |  |  |  | [0.24; 1.83] | 2.1\% | 3.3\% |
| Tabata S_SDFCH | 0.28 | 0.5522 |  |  |  |  | 1.32 | [0.45; 3.90] | 1.8\% | 3.2\% |
| Wang Z_UH | -1.80 | 0.7103 |  | $\cdots$ |  |  |  | [0.04; 0.67] | 1.1\% | 2.4\% |
| Yang L_YCPH | -1.51 | 0.7537 |  | $\square$ |  |  | 0.22 | [0.05; 0.97] | 1.0\% | 2.3\% |
| Zhao W_BYH | -0.88 | 0.5552 |  | $\rightarrow$ |  |  |  | [0.14; 1.23] | 1.8\% | 3.2\% |
| Zhang G_WXDPH | -1.43 | 0.5183 |  | $\cdots$ |  |  |  | [0.09; 0.66] | 2.1\% | 3.3\% |
| Cao M_SPHCC | -0.49 | 0.7755 |  |  |  |  | 0.61 | [0.13; 2.80] | 0.9\% | 2.2\% |
| Liao Xuelian_MC | -0.07 | 0.8423 |  |  |  |  | 0.93 | [0.18; 4.86] | 0.8\% | 2.0\% |
| JX_WFPH | 2.17 | 0.9431 |  |  | - |  |  | [1.39; 55.87] | 0.6\% | 1.7\% |
| MY_multicenter 43 hosp | -0.31 | 0.4473 |  |  |  |  |  | [0.30; 1.76] | 2.8\% | 3.8\% |
| Colaneri M_PSM | 0.19 | 0.6200 |  |  |  |  |  | [0.36; 4.08] | 1.4\% | 2.8\% |
| Xin L_CHWC/hospitales en Hunan | -0.13 | 0.4033 |  |  |  |  |  | [0.40; 1.93] | 3.4\% | 4.0\% |
| Chen W_YH | 1.47 | 0.9535 |  |  |  |  |  | [0.67; 28.24] | 0.6\% | 1.7\% |
| Wang X_DFH | 0.02 | 0.3038 |  |  | + |  |  | [0.57; 1.86] | 6.0\% | 4.6\% |
| YuC_TH | -0.09 | 0.1735 |  |  |  |  |  | [0.65; 1.28] | 18.4\% | 5.4\% |
| Wan S_TGCH | -0.77 | 0.6628 |  | $\rightarrow$ |  |  | 0.46 | [0.13; 1.70] | 1.3\% | 2.6\% |
| Bi Q_STPH | 0.97 | 0.2416 |  |  | $\pm$ |  |  | [1.64; 4.22] | 9.5\% | 5.0\% |
| Zheng F_NHCFH | -0.59 | 0.4356 |  | + |  |  |  | [0.24; 1.31] | 2.9\% | 3.8\% |
| LiX_TH | -0.75 | 0.2083 |  | $+$ |  |  |  | [0.31; 0.71] | 12.7\% | 5.2\% |
| LiY_TH | -1.29 | 1.1899 |  |  |  |  |  | [0.03; 2.83] | 0.4\% | 1.2\% |
| Fixed effect model |  |  |  |  |  |  |  | [0.69; 0.92] | 100.0\% | -- |
| Random effects model |  |  |  |  |  |  | 0.70 | [0.53; 0.93] | -- | 100.0\% |
| Heterogeneity: $I^{2}=65 \%, \tau^{2}=0.3642, p<0.01$ |  |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  |  |  | [0.69; 0.92] | 100.0\% | -- |
| Random effects model |  |  |  |  |  |  |  | [0.53; 0.93] | -- | 100.0\% |
| Heterogeneity: $I^{2}=65 \%, \tau^{2}=0.3642, p<0.01$Residual heterogeneity: $I^{2}=65 \%, p<0.01$ |  |  |  | 1 |  |  |  |  |  |  |
|  |  |  | 0.001 | 0.1 | 110 | 1000 |  |  |  |  |

Candidate variable：Low Lymphocyte count（less than 0．8－1．5x 109／L）， outcome：severe Covid－19 disease，subgroup analysis by risk of bias（high vs moderate／low）

| Study | TE | seTE | Odds | Ratio | OR |  | 95\％－Cl | （fixed） | random） |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| URB $=0$ |  |  |  |  |  |  |  |  |  |
| łuang C＿JYH |  | 0.8570 |  | $i$ | 4.77 | ［ 0．89； | 25．57］ | 0．4\％ | 0．9\％ |
| ＿i K＿CMŪ |  | 0.5712 |  | $\stackrel{+}{i}$ | 7.60 | ［ 2．48； | 23．28］ | 0．9\％ | 1．8\％ |
| ＿iu F＿XH | 0.00 | 1.5811 |  | i | 1.00 | ［ 0．05； | 22．17］ | 0．1\％ | 0．3\％ |
| ．iu W＿MC | 0.47 | 0.6689 |  | ＋ | 1.60 | ［ 0．43； | 5．94］ | 0．7\％ | 1．4\％ |
| Jin－Jin Z＿MC | 0.64 | 0.4250 |  | F | 1.90 | ［ 0．83； | 4．38］ | 1．7\％ | 2．7\％ |
| Nei－jie G＿NHC | 0.97 | 0.5276 |  | $!$ | 2.64 | ［ 0．94； | 7．43］ | 1．1\％ | 2．0\％ |
| ．iu T＿UH | 1.55 | 0.6755 |  | ； | 4.71 | ［ 1．25； | 17．72］ | 0．7\％ | 1．4\％ |
| Kiao M＿ECRH | 1.24 | 0.2092 |  | \％ | 3.45 | ［ 2．29； | 5．20］ | 6．9\％ | 4．9\％ |
| 2 D ＿multicentrico | 0.69 | 0.5553 |  | $\stackrel{+}{+}$ | 1.99 | ［ 0．67； | 5．91］ | 1．0\％ | 1．9\％ |
| Shijiao Y＿HHMU | 1.15 | 0.3994 |  | ＋ | 3.17 | ［ 1．45； | $6.93]$ | 1．9\％ | 2．9\％ |
| ？hang G＿ZHWU | 1.11 | 0.4382 |  | ＋ | 3.04 | ［ 1．29； | 7．18］ | 1．6\％ | 2．6\％ |
| Ihen L＿MC | 1.08 | 0.3778 |  | $+$ | 2.95 | ［ 1．40； | $6.18]$ | 2．1\％ | 3．1\％ |
| ling L＿WUH | 1.58 | 0.7660 |  | i | 4.85 | ［ 1．08； | 21．76］ | 0．5\％ | 1．1\％ |
| こhen G＿TH | 3.18 | 1.2528 |  |  | 24.00 | ［ 2．06； | 279．61］ | 0．2\％ | 0．5\％ |
| Chen X＿FHC／LCH | 1.43 | 0.3304 |  | $\stackrel{+}{*}$ | 4.18 | ［ 2．19； | 7．98］ | 2．8\％ | 3．5\％ |
| łu L＿TH | 2.27 | 0.7476 |  | $\frac{i}{t}$ | 9.69 | ［ 2．24； | 41．92］ | 0．5\％ | 1．2\％ |
| 「abata S＿SDFCH | 1.46 | 0.5652 |  | $i$ | 4.30 | ［ 1．42； | 13．02］ | 0．9\％ | 1．8\％ |
| Nang Z＿UH | 2.05 | 0.7147 |  | $\stackrel{i}{i}$ | 7.76 | ［ 1．91； | 31．51］ | 0．6\％ | 1．3\％ |
| ＜u Y＿FAHG | 4.53 | 3.1992 |  |  | 92.94 | ［ 0．18； 49 | 9135．11］ | 0．0\％ | 0．1\％ |
| ＜u Y＿GH | 1.76 | 1.2696 |  |  | 5.83 | ［ 0．48； | 70．24］ | 0．2\％ | 0．5\％ |
| Yang L＿YCPH | 1.19 | 0.5620 |  | ！ | 3.29 | ［ 1．09； | 9．91］ | 1．0\％ | 1．8\％ |
| Ihao W＿BYH | 1.95 | 0.5741 |  | $\frac{i}{i}$ | 7.05 | ［ 2．29； | 21．72］ | 0．9\％ | 1．8\％ |
| ＜uang Y＿MC | 1.06 | 0.4128 |  | $i$ | 2.89 | ［ 1．29； | $6.50]$ | 1．8\％ | 2．8\％ |
| ？hang G＿WXDPH | 2.48 | 0.8191 |  | ， | 11.93 | ［ 2．40； | 59．44］ | 0．5\％ | 1．0\％ |
| こao M＿SPHCC | 6.83 | 1.1839 |  |  | 922.67 | ［90．64； 9 | 9392．08］ | 0．2\％ | 0．5\％ |
| ＿iao Xuelian＿MC | 0.50 | 1.1039 |  | ！ | 1.65 | ［ 0．19； | 14．36］ | 0．2\％ | 0．6\％ |
| ＿ei S＿RHZHTHC | 1.32 | 1.1782 |  | ！ | 3.73 | ［ 0．37； | 37．58］ | 0．2\％ | 0．5\％ |
| ＝Y＿JH，SPHCC，TPH | 1.19 | 0.2829 |  | $\stackrel{4}{4}$ | 3.30 | ［ 1．90； | 5．75］ | 3．8\％ | 4．0\％ |
| IX＿WFPH | 1.96 | 0.8766 |  | it | 7.07 | ［ 1．27； | 39．41］ | 0．4\％ | 0．9\％ |
| UY＿multicenter 43 hosp | 1.11 | 0.2694 |  | $\stackrel{+}{*}$ | 3.05 | ［ 1．80； | 5．16］ | 4．2\％ | 4．1\％ |
| Jolombi D＿GdSH | 0.83 | 0.2736 |  | 4 | 2.30 | ［ 1．35； | 3．93］ | 4．1\％ | 4．1\％ |
| Solaneri M＿PSM | 3.63 | 3.2106 |  |  | 37.86 | ［ 0．07； 20 | 0468．87］ | 0．0\％ | 0．1\％ |
| tongying S＿FAHWMU／SAHWMU | 0.92 | 1.3102 |  | i | 2.50 | ［ 0．19； | 32．59］ | 0．2\％ | 0．4\％ |
| ＜in L＿CHWC／hospitales en Hunan | 1.78 | 0.3858 |  | － | 5.93 | ［ 2．78； | 12．64］ | 2．0\％ | 3．0\％ |
| こhen W＿YH | 6.68 | 3.2356 |  |  | 796.25 | ［ 1．40；452 | 2057．58］ | 0．0\％ | 0．1\％ |
| Jun R＿TH | 0.99 | 0.4683 |  | $t$ | 2.68 | ［ 1．07； | 6.71 ］ | 1．4\％ | 2．4\％ |
| Ihou M＿MC | 1.29 | 0.2811 |  | 4 | 3.65 | ［ 2．10； | $6.33]$ | 3．8\％ | 4．0\％ |
| －ei J＿UHHUST | 1.27 | 0.3092 |  | 4 | 3.57 | ［ 1．95； | $6.54]$ | 3．2\％ | 3．7\％ |
| ruc＿TH | 0.61 | 0.1040 |  |  | 1.84 | ［ 1．50； | $2.26]$ | 28．1\％ | 6．0\％ |
| Nan S＿TGCH | 2.19 | 0.6555 |  | ＋ | 8.93 | ［ 2．47； | 32．26］ | 0．7\％ | 1．5\％ |
| Jong J＿FMC | 1.50 | 0.5053 |  | $\frac{+}{+}$ | 4.50 | ［ 1．67； | 12．11］ | 1．2\％ | 2．1\％ |
| －i H＿TH | 1.04 | 0.4054 |  | $t$ | 2.82 | ［ 1．27； | $6.25]$ | 1．8\％ | 2．8\％ |
| Zheng F＿NHCFH | 0.99 | 0.4243 |  | $i$ | 2.69 | ［ 1．17； | $6.18]$ | 1．7\％ | 2．7\％ |
| ．iX＿TH | 1.34 | 0.2685 |  | ＊ | 3.81 | ［ 2．25； | $6.45]$ | 4．2\％ | 4．2\％ |
| ．i $\mathrm{Y}_{-}$TH | 0.13 | 1.3024 |  | ！ | 1.14 | ［ 0．09； | 14．68］ | 0．2\％ | 0．4\％ |
| －ixed effect model |  |  |  | 1 | 2.90 | ［ 2．59； | 3．25］ | 90．6\％ | － |
| Random effects model |  |  |  | ！ | 3.60 | ［ 2．98； | $4.37]$ | －－ | 91．4\％ |
| łeterogeneity：$I^{2}=46 \%, \tau^{2}=0.1444, p<0.01$ |  |  |  |  |  |  |  |  |  |
| URB $=1$ |  |  |  |  |  |  |  |  |  |
| 2entsch＿CT | 0.97 | 0.2325 |  | 4 | 2.65 | ［ 1．68； | 4．18］ | 5．6\％ | 4．6\％ |
| 3 Q Q＿STPH | 0.88 | 0.2837 |  | $\stackrel{4}{4}$ | 2.42 | ［ 1．39； | 4．22］ | 3．8\％ | 4．0\％ |
| －ixed effect model |  |  |  | 0 | 2.56 | ［ 1．80； | 3．63］ | 9．4\％ | － |
| Random effects model |  |  |  | \％ | 2.56 | ［ 1．80； | 3．63］ | －－ | 8．6\％ |
| Heterogeneity：$I^{2}=0 \%, \tau^{2}=0, p=0.80$ |  |  |  |  |  |  |  |  |  |
| －ixed effect model |  |  |  | ！ | 2.87 | ［ 2．58； | 3．20］ | 100．0\％ | － |
| २andom effects model |  |  |  | $i$ | 3.47 | ［ 2．91； | 4．14］ | －－ | 100．0\％ |
| teterogeneity：$I^{2}=44 \%, \tau^{2}=0.1235, p<0.01$ |  |  | $\ldots \ldots$ |  |  |  |  |  |  |

Candidate variable: Low platelet count (less than 100-150 x 109/L), outcome:severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: High creatinine (more than $1.5 \mathrm{mg} \%$ ), outcome: severe Covid19 disease, subgroup analysis by risk of bias (high vs moderate/low)

| Study | TE | seTE | Odds | Ratio | OR |  | 95\%-CI | Weight (fixed) | Weight random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| MRB $=0$ |  |  |  | i |  |  |  |  |  |
| Huang C_JYH | 0.86 | 1.0627 |  | $!$ | 2.36 | [0.29; | 18.97] | 1.0\% | 1.9\% |
| Wei-jie G_NHC |  | 0.6046 |  | $\cdots$ | 10.53 | [3.22; | 34.45] | 3.0\% | 4.8\% |
| Liu T_UH | 0.48 | 3.3324 |  |  | 1.62 | [0.00; | 1110.37] | 0.1\% | 0.2\% |
| Xiao M_ECRH | 1.83 | 0.3448 |  | + | 6.24 | [3.17; | 12.26] | 9.1\% | 9.0\% |
| Qi D_multicentrico | 2.62 | 1.1658 |  |  | 13.79 | [1.40; | 135.47] | 0.8\% | 1.7\% |
| Shi W_ SPHCC | 0.67 | 0.5388 |  | * | 1.96 | [0.68; | ; 5.63] | 3.7\% | 5.6\% |
| Shijiao Y_HHMU | 4.88 | 3.2103 |  |  | 132.00 | [0.24; 71 | 1312.19] | 0.1\% | 0.2\% |
| Zhen L_MC | 1.46 | 0.4973 |  | \% | 4.32 | [1.63; | 11.45] | 4.4\% | 6.2\% |
| Chen X_FHC/LCH | 0.76 | 0.7083 |  |  | 2.13 | [0.53; | - 8.55] | 2.2\% | 3.8\% |
| Yang L_YCPH | 1.02 | 0.4113 |  | + | 2.78 | [1.24; | ; 6.22] | 6.4\% | 7.6\% |
| Zhao W_BYH | -1.93 | 3.2549 |  |  | 0.14 | [0.00; | 85.33] | 0.1\% | 0.2\% |
| Zhang G_WXDPH | 0.15 | 0.5084 |  |  | 1.17 | [0.43; | ; 3.16] | 4.2\% | 6.0\% |
| Cao M_SPHCC | 1.48 | 0.7381 |  | $!$ | 4.39 | [1.03; | 18.66] | 2.0\% | 3.6\% |
| Liao Xuelian_MC | 2.69 | 0.9953 |  | - | 14.79 | [2.10; | 104.00] | 1.1\% | 2.2\% |
| JX_WFPH | 4.10 | 3.3578 |  |  | 60.43 | [0.08; 43 | 4592.13] | 0.1\% | 0.2\% |
| Hongying S_FAHWMU/SAHWMU | 0.60 | 0.8938 |  |  | 1.83 | [0.32; | 10.53] | 1.4\% | 2.6\% |
| Jun R_TH | 0.74 | 0.4299 |  | + | 2.09 | [0.90; | $4.85]$ | 5.8\% | 7.3\% |
| Zhou M_MC | 1.13 | 0.2746 |  | + | 3.10 | [1.81; | 5.31] | 14.3\% | 10.7\% |
| YuC_TH | 0.85 | 0.3204 |  | + | 2.33 | [1.25; | ; 4.37] | 10.5\% | 9.6\% |
| Yang J_WUH | 2.63 | 2.2726 |  |  | 13.87 | [0.16; | 1192.64] | 0.2\% | 0.5\% |
| Bi Q_STPH | 5.97 | 3.1805 |  |  | 390.04 | [0.77; 1987 | 98780.31] | 0.1\% | 0.2\% |
| Zheng F_NHCFH | 1.50 | 1.4290 |  |  | 4.48 | [0.27; | 73.78] | 0.5\% | 1.1\% |
| LiX_TH | 0.49 | 0.1960 |  |  | 1.63 | [1.11; | $2.40]$ | 28.1\% | 12.7\% |
| Fixed effect model |  |  |  | ! | 2.66 | [2.17; | $3.26]$ | 99.0\% | - |
| Random effects model |  |  |  | - | 3.03 | [2.22; | 4.14] | -- | 98.1\% |
| Heterogeneity: $I^{2}=36 \%, \tau^{2}=0.1542, p=0.05$ |  |  |  |  |  |  |  |  |  |
| $M R B=1$ |  |  |  |  |  |  |  |  |  |
| Liu W_MC | -0.34 | 1.0621 |  |  | 0.71 | [0.09; | 5.69] | 1.0\% | 1.9\% |
| Fixed effect model |  |  |  |  | 0.71 | [0.09; | 5.69] | 1.0\% | -- |
| Random effects model |  |  |  |  | 0.71 | [0.09; | 5.69] | -- | 1.9\% |
| Heterogeneity: not applicable |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  | $\bigcirc$ | 2.62 | [2.14; | 3.22] | 100.0\% | -- |
| Random effects model |  |  |  | $\stackrel{\circ}{*}$ | 2.95 | [2.16; | 4.03] | -- | 100.0\% |
| Heterogeneity: $I^{2}=36 \%, \tau^{2}=0.1588, p=0.04$Residual heterogeneity: $I^{2}=36 \%, p=0.05$ |  |  |  |  |  |  |  |  |  |
|  |  |  | 0.0010 .11101000 |  |  |  |  |  |  |

Candidate variable: Creatinine increase (per $0.1 \mathrm{mg} \%$ ), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study TE seTE | Odds Ratio | OR | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |
| Wu C_WJH 0.060 .0286 |  | 1.06 | [1.00; 1.12] | 0.0\% | 14.8\% |
| Yu T_DPHNH 0.020 .0132 |  |  | [0.99; 1.05] | 0.1\% | 33.7\% |
| Fixed effect model | $\bigcirc$ |  | [1.00; 1.05] | 0.1\% | -- |
| Random effects model |  | 1.03 | [1.00; 1.07] | -- | 48.5\% |
| Heterogeneity: $I^{2}=29 \%, \tau^{2}=0.0002, p=0.23$ |  |  |  |  |  |
| ADJ $=1$ |  |  |  |  |  |
| Fan T_RHWU 0.000 .0004 |  |  | [1.00; 1.00] | 99.9\% | 51.5\% |
| Fixed effect model |  |  | [1.00; 1.00] | 99.9\% | -- |
| Random effects model |  | 1.00 | [1.00; 1.00] | -- | 51.5\% |
| Heterogeneity: not applicable |  |  |  |  |  |
| Fixed effect model |  |  | [1.00; 1.00] | 100.0\% | -- |
| Random effects model | $\xrightarrow{\sim}$ | 1.02 | [0.99; 1.04] | - | 100.0\% |
| Heterogeneity: $I^{2}=70 \%, \tau^{2}=0.0003, p=0.04$ |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=29 \%, p=0.28 .9$ | 1 |  |  |  |  |

Candidate variable: Acute kidney injury, outcome: severe Covid-19 disease


Candidate variable: High BUN (more than 5.2-9.5 mmol/L), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: High LDH (more than 240-250 U/L), outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)

| Study | TE | seTE |  | Odds | Ratio |  | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| MRB = 0 |  |  |  |  | ' |  |  |  |  |  |  |
| Huang C_JYH | 1.95 | 1.1145 |  |  |  |  | 7.06 | [ 0.79; | 62.72] | 0.4\% | 1.7\% |
| Wei-jie G_NHC | 1.32 | 0.3404 |  |  | - |  | 3.73 | [ 1.92; | 7.27] | 4.4\% | 5.2\% |
| Duan Q_WPH | 1.00 | 0.4156 |  |  | $1:$ |  | 2.71 | [ 1.20; | 6.12] | 2.9\% | 4.7\% |
| Liu T_UH | 2.93 | 1.0788 |  |  | ! |  | 18.75 | [ 2.26; | 155.34] | 0.4\% | 1.8\% |
| Qi D_multicentrico | 0.94 | 0.3436 |  |  | 4 |  | 2.57 | [ 1.31; | 5.03] | 4.3\% | 5.2\% |
| Zhen L_MC | 1.46 | 0.5089 |  |  | $\stackrel{1}{1}$ |  | 4.30 | [ 1.59; | 11.66] | 2.0\% | 4.1\% |
| Chen X_FHC/LCH | 2.32 | 0.3669 |  |  | - |  | 10.20 | [ 4.97; | 20.94] | 3.8\% | 5.0\% |
| Hu L_TH | 1.77 | 0.8641 |  |  |  |  | 5.88 | [ 1.08; | 32.01] | 0.7\% | 2.4\% |
| Tabata S_SDFCH | 0.66 | 0.4810 |  |  | ${ }^{+1}$ |  | 1.93 | [ 0.75; | 4.95] | 2.2\% | 4.3\% |
| Wang Z_UH | 2.43 | 0.8343 |  |  | $\frac{1}{1}$, |  | 11.33 | [ 2.21; | 58.15] | 0.7\% | 2.5\% |
| Xu Y_FAHG | 1.49 | 0.7446 |  |  | ! |  | 4.45 | [ 1.03; | 19.16] | 0.9\% | 2.9\% |
| Yang L_YCPH | 2.23 | 0.5232 |  |  | - |  | 9.31 | [ 3.34; | 25.95] | 1.9\% | 4.0\% |
| Kuang $\bar{Y}$ _MC | 2.11 | 0.5116 |  |  | ! |  | 8.29 | [ 3.04; | 22.59] | 1.9\% | 4.1\% |
| CaiQ_TPHS | 2.67 | 0.5046 |  |  | :- |  | 14.51 | [ 5.40; | 39.02] | 2.0\% | 4.2\% |
| MY_multicenter 43 hosp | 0.66 | 0.2867 |  |  | - |  | 1.94 | [ 1.11; | 3.41] | 6.2\% | 5.5\% |
| Hongying S_FAHWMU/SAHWMU | 3.06 | 1.0820 |  |  |  |  | 21.38 | [ 2.56; 17 | 178.19] | 0.4\% | 1.8\% |
| Zhou M_MC | 1.19 | 0.4710 |  |  | $\because$ |  | 3.29 | [ 1.31; | 8.28] | 2.3\% | 4.4\% |
| YuC_TH | 0.35 | 0.1252 |  |  | +! |  | 1.42 | [ 1.11; | 1.81] | 32.4\% | 6.3\% |
| Zhang R_RH | 0.92 | 0.5809 |  |  | ! |  | 2.50 | [ 0.80; | 7.81] | 1.5\% | 3.7\% |
| Zhang L_WUH | 1.12 | 0.2155 |  |  | + |  | 3.05 | [ 2.00; | 4.65] | 10.9\% | 5.9\% |
| Zheng F_NHCFH | 1.55 | 0.4314 |  |  | $\stackrel{+}{\text { i }}$ |  | 4.70 | [ 2.02 ; | 10.94] | 2.7\% | 4.6\% |
| LiX_TH | 1.62 | 0.2277 |  |  | 年 |  | 5.06 | [ 3.24; | 7.91] | 9.8\% | 5.9\% |
| Li Y_TH | 0.69 | 0.8660 |  |  | +1: |  | 2.00 | [ 0.37; | 10.92] | 0.7\% | 2.4\% |
| Fixed effect model |  |  |  |  | $\bigcirc$ |  | 2.83 | [ 2.46; | 3.27] | 95.4\% | - |
| Random effects model |  |  |  |  | is |  | 4.22 | [ 3.02; | 5.90] | -- | 92.7\% |
| Heterogeneity: $I^{2}=74 \%, \tau^{2}=0.4021, p<0.01$ |  |  |  |  | ' |  |  |  |  |  |  |
| MRB $=1$ |  |  |  |  | ' |  |  |  |  |  |  |
| Huang H_GEPH | 5.39 | 1.2399 |  |  | ! |  | 219.60 | [19.33; 24 | 494.65] | 0.3\% | 1.5\% |
| Colombi D_GdSH | 1.10 | 0.3494 |  |  | $+$ |  | 3.00 | [ 1.51; | 5.95] | 4.2\% | 5.1\% |
| Dong J_FMC | 3.38 | 1.8722 |  |  |  |  | 29.35 | [ 0.75; 11 | 151.35] | 0.1\% | 0.7\% |
| Fixed effect model <br> Random effects model |  |  |  |  | $\bigcirc$ |  | 4.37 | [ 2.29; | 8.37] | 4.6\% | -- |
|  |  |  |  |  |  |  | 22.51 | [ 1.04; 4 | 487.75] | -- | 7.3\% |
| Heterogeneity: $I^{2}=84 \%, \tau^{2}=5.9142, p<0.01$ |  |  |  |  | 1 1 1 1 |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  | 0 - |  | 2.89 | [ 2.51; | 3.32] | 100.0\% | -- |
| Random effects model |  |  |  |  | $\diamond$ |  | 4.48 | [ 3.21; | 6.25] | -- | 100.0\% |
| Heterogeneity: $I^{2}=75 \%, \tau^{2}=0.4420, p<0.01$ |  |  | 1 |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=76 \%, p<0.01$ |  |  | 0.001 | 0.1 | 10 | 1000 |  |  |  |  |  |

Candidate variable: LDH increase (per 1 U/L), outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: High CK (more than 185-200 U/L), outcome: severe Covid-19 disease


Candidate variable: Myocardial injury, outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: High CK-MB (more than 25 U/L), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study |  | seTE | Odds | Ratio |  | OR | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  | i |  |  |  |  |  |
| Wu C_WJH | 0.60 | 0.4524 |  | 1 |  | 1.82 | [0.75; 4.42] | 10.2\% | 28.1\% |
| Han Y_ RHWU | 1.28 | 0.5052 |  |  |  |  | [1.34; 9.69] | 8.2\% | 25.2\% |
| Fixed effect model |  |  |  |  |  |  | [1.27; 4.77] | 18.5\% | -- |
| Random effects mo |  |  |  |  |  | 2.47 | [1.27; 4.79] | -- | 53.3\% |
| Heterogeneity: $I^{2}=1 \%, \tau^{2}=0.0027, p=0.31$ |  |  |  |  |  |  |  |  |  |
| ADJ $=1$ |  |  |  |  |  |  |  |  |  |
| Liu R_CHW | 0.10 | 0.1604 |  |  |  |  | [0.80; 1.51] | 81.5\% | 46.7\% |
| Fixed effect model |  |  |  |  |  |  | [0.80; 1.51] | 81.5\% | -- |
| Random effects mo |  |  |  |  |  |  | [0.80; 1.51] | -- | 46.7\% |
| Heterogeneity: not applicable |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  |  | [0.96; 1.70] | 100.0\% | -- |
| Random effects model |  |  |  |  |  | 1.71 | [0.85; 3.42] | -- | 100.0\% |
| Heterogeneity: $I^{2}=65 \%, \tau^{2}=0.2432, p=0.06$ |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity | = $1 \%$, | $p=0.31$ | 0.5 | 2 | 5 |  |  |  |  |

Candidate variable: High BNP (more than $500-900 \mathrm{pg} / \mathrm{mL}$ ), outcome: severe Covid-19 disease


Candidate variable: Urea increase (per $1 \mathrm{mmol} / \mathrm{L}$ ), outcome: severe Covid-19 disease

| Study TE seTE | Odds Ratio | OR | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ | 1 |  |  |  |  |
| Wu C_WJH $\quad 0.160 .0260$ | + | 1.17 | [1.11; 1.23] | 98.4\% | 64.9\% |
| Han Y_ RHWU 0.530 .2054 | $\frac{1}{1}$ |  | [1.14; 2.54] | 1.6\% | 35.1\% |
| Fixed effect model | $\stackrel{\rightharpoonup}{*}$ | 1.18 | [1.12; 1.24] | 100.0\% | -- |
| Random effects model | + | 1.33 | [0.94; 1.89] | -- | 100.0\% |
| Heterogeneity: $I^{2}=69 \%, \tau^{2}=0.0484, p=0.07$ | $1 \vdots$ |  |  |  |  |
| Fixed effect model | $\stackrel{\prime}{\diamond}$ | 1.18 | [1.12; 1.24] | 100.0\% | - |
| Random effects model |  |  | [0.94; 1.89] | -- | 100.0\% |
| Heterogeneity: $I^{2}=69 \%, \tau^{2}=0.0484, p=0.07$ |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=69 \%, p=0.070 .5$ | 1 |  |  |  |  |

Candidate variable: High D-dimer (more than 500-1000 ng/ml), outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: Prolonged PT, outcome: severe Covid-19 disease


Candidate variable: Increase PT (per 1 second), outcome: severe Covid-19 disease


Candidate variable: Prolonged APTT time, outcome: severe Covid-19 disease


Candidate variable: Increase APTT time (per 1 second), outcome: severe Covid-19 disease

| Study TE seTE | Odds | Ratio |  | OR | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |
| Wu C_WJH -0.04 0.0238 | $+$ |  |  |  | [0.92; 1.01] | 97.1\% | 56.5\% |
| Han Y_RHWU 0.340 .1383 |  |  |  |  | [1.07; 1.84] | 2.9\% | 43.5\% |
| Fixed effect model | 4 |  |  |  | [0.93; 1.02] | 100.0\% | -- |
| Random effects model     <br> Heterogeneity: $I^{2}=86 \%, \tau^{2}=0.0613, p<0.01$  $1.13[0.78 ; 1.63]$   |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  | 0.97 | [0.93; 1.02] | 100.0\% | -- |
| Random effects model |  |  |  | 1.13 | [0.78; 1.63] | - | 100.0\% |
| Heterogeneity: $I^{2}=86 \%, \tau^{2}=0.0613, p<0.01$ | $\mid$ |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=86 \%, p<0.01$ | 0.75 | 1 | 1.5 |  |  |  |  |

Candidate variable: High ferritin (more than $300-500 \mathrm{ng} / \mathrm{mL}$ ), outcome: severe Covid-19 disease


Candidate variable: High CRP (More than 1-100 mg/l) outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: CRP increase (per $1 \mathrm{mg} / \mathrm{L}$ ), outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: High ESR (more than 10-20 mm/H), outcome: severe Covid-19 disease

| Study |  | seTE | Odds | Ratio | OR |  | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  | ! |  |  |  |  |  |
| Liu W_MC | 0.96 | 0.7784 |  | i | 2.62 | [0.57; | 12.05] | 2.4\% | 5.3\% |
| Qi D_multicentrico | 2.34 | 0.3710 |  | + | 10.42 | [5.04; | 21.56] | 10.7\% | 12.0\% |
| Zhen L_MC | 1.09 | 0.5237 |  | - | 2.98 | [1.07; | 8.33] | 5.4\% | 8.7\% |
| Chen X_FHC/LCH | 0.96 | 0.3555 |  | $\frac{4}{4}$ | 2.61 | [1.30; | 5.25] | 11.7\% | 12.4\% |
| Wang Z_UH | 2.89 | 1.0844 |  |  | 18.00 | [2.15; | 150.76] | 1.3\% | 3.1\% |
| Kuang Y_MC | 0.56 | 0.6475 |  | : | 1.76 | [0.49; | 6.26] | 3.5\% | 6.8\% |
| CaiQ_TPHS | 1.00 | 0.3017 |  | + | 2.73 | [1.51; | 4.93] | 16.2\% | 13.7\% |
| Cao M_SPHCC | 3.36 | 3.1789 |  |  | 28.80 | [0.06; 14 | 629.08] | 0.1\% | 0.4\% |
| Jun R_TH | 0.86 | 0.5284 |  | - | 2.35 | [0.84; | 6.63] | 5.3\% | 8.7\% |
| Zhou M_MC | 0.83 | 0.5332 |  | + | 2.30 | [0.81; | 6.54] | 5.2\% | 8.6\% |
| LiX_TH | 0.52 | 0.2006 |  |  | 1.68 | [1.13; | 2.49] | 36.6\% | 16.3\% |
| $\begin{array}{ll}\text { Li Y_TH } & 1.690 .9275 \\ \text { Fixed effect model } & \end{array}$ |  |  |  | i | 5.42 | [0.88; | 33.36] | 1.7\% | 4.1\% |
|  |  |  |  | 2.65 | [2.09; | 3.36] | 100.0\% |  |
| Random effects mo |  |  |  |  | $\bigcirc$ | 3.08 | [2.04; | $4.65]$ | -- | 100.0\% |
| Heterogeneity: $I^{2}=53 \%, \tau^{2}=0.2317, p=0.01$ |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  | 0 | 2.65 | [2.09; | 3.36] | 100.0\% | 100.0\% |
| Random effects model |  |  |  | $\stackrel{ }{ }$ | 3.08 | [2.04; | 4.65] | -- |  |
| Heterogeneity: $I^{2}=53$ | ${ }^{2}=0.23$ | 317, $p=0$ |  |  |  |  |  |  |  |
| Residual heterogeneity | = 53\%, | , $p=0.01$ | 0.1 | 110 |  |  |  |  |  |

Candidate variable: ESR increase (per $1 \mathrm{~mm} / \mathrm{H}$ ), outcome: severe Covid-19 disease


Candidate variable: IL-6 increase (per $1 \mathrm{pg} / \mathrm{mL}$ ), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study TE seTE | Odds | Ratio | OR 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  | ! |  |  |  |
| Wu C_WJH 0.030.0173 |  | + | 1.03 [1.00; 1.07] | 34.2\% | 34.2\% |
| Fixed effect model |  | 1 | 1.03 [1.00; 1.07] | 34.2\% | -- |
| Random effects model |  |  | 1.03 [1.00; 1.07] | -- | 34.2\% |
| Heterogeneity: not applicable |  |  |  |  |  |
| $\mathrm{ADJ}=1$ |  | + |  |  |  |
| CaiQ_TPHS $\quad 0.030 .0124$ |  | 1 | 1.03 [1.01; 1.06] | 65.8\% | 65.8\% |
| Fixed effect model |  | + | 1.03 [1.01; 1.06] | 65.8\% | -- |
| Random effects model |  | - | 1.03 [1.01; 1.06] | -- | 65.8\% |
| Heterogeneity: not applicable |  |  |  |  |  |
| Fixed effect model |  | $\longrightarrow$ | 1.03 [1.01; 1.05] | 100.0\% | -- |
| Random effects model |  | 2 | 1.03 [1.01; 1.05] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=1.00$ |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=\mathrm{NA} \%, p=\mathrm{NA}$ |  | 1 |  |  |  |

Candidate variable: High interleukin-6 (more than 5-20 pg/ml), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study | TE | seTE | Odds | Ratio | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ = 1 |  |  |  | ! |  |  |  |  |  |
| Gao Y_FSH | 2.85 | 1.0051 |  | $\frac{i}{1-}$ | 17.30 | [ 2.41; | 124.05] | 3.6\% | 11.4\% |
| FL_GHCTCPLA | 1.06 | 0.5787 |  | - | 2.89 | [ 0.93; | 8.98] | 10.9\% | 17.7\% |
| Fixed effect model |  |  |  | 8 | 4.51 | [ 1.69; | 12.06] | 14.6\% | -- |
| Random effects mod |  |  |  |  | 5.85 | [ 1.05; | 32.51] | -- | 29.0\% |
| Heterogeneity: $I^{2}=58 \%, \tau^{2}=0.9285, p=0.12$ |  |  |  |  |  |  |  |  |  |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |
| Qi D_multicentrico | 3.18 | 0.3980 |  | \# | 23.94 | [10.97; | 52.23] | 23.1\% | 20.7\% |
| Chen G_TH | 1.16 | 1.3509 |  | - | 3.20 | [ 0.23; | 45.19] | 2.0\% | 7.9\% |
| Wang Z_UH | 6.32 | 3.2286 |  | . | 558.25 | 1.00; 312 | 2617.51] | 0.4\% | 1.9\% |
| Wan S_TGCH | 1.99 | 0.5557 |  | + | 7.33 | [ 2.47; | 21.78] | 11.9\% | 18.0\% |
| LiX_TH | 1.15 | 0.2762 |  | $\pm$ | 3.15 | [ 1.83; | 5.41] | 48.0\% | 22.4\% |
| Fixed effect model |  |  |  | $\bigcirc$ | 6.27 | [ 4.18; | 9.41] | 85.4\% | -- |
| Random effects mod |  |  |  | $<$ | 8.23 | [ 2.49; | 27.19] | -- | 71.0\% |
| Heterogeneity: $I^{2}=80 \%, \tau^{2}=1.1488, p<0.01$ |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  | - | 5.98 | [ 4.11; | 8.70] | 100.0\% | -- |
| Random effects mod |  |  |  | $\rangle$ | 7.37 | [ 2.97; | 18.27] | -- | 100.0\% |
|  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=77 \%, p<0.01 \quad 0.0010 .11101000$ |  |  |  |  |  |  |  |  |  |

Candidate variable: High procalcitonin (more than 0.01-05 ng/ml), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study |  | seTE | Odds | Ratio | OR |  | 95\%-Cl | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  | ' |  |  |  |  |  |
| Huang C_JYH | 4.47 | 3.2392 |  | ! | 87.00 | [ 0.15; 49 | 9745.53] | 0.1\% | 0.5\% |
| Li K_CMU | 2.08 | 0.6080 |  | \% | 7.99 | [ 2.43; | 26.30] | 1.7\% | 4.4\% |
| Wang D_ZH | 2.39 | 0.4540 |  | -- | 10.91 | [ 4.48; | 26.56] | 3.0\% | 4.9\% |
| Jin-Jin Z_MC | 1.18 | 0.4022 |  | $\cdots$ | 3.25 | [ 1.48; | 7.15] | 3.8\% | 5.1\% |
| Wei-jie G_NHC | 2.04 | 0.3936 |  | + | 7.69 | [3.55; | 16.63] | 4.0\% | 5.1\% |
| Liu Y_CHW | 1.19 | 3.2566 |  | : | 3.28 | [ 0.01; 19 | 1942.54] | 0.1\% | 0.5\% |
| Xiao M_ECRH | 3.56 | 1.0203 |  | - | 35.22 | [ 4.77; | 260.19] | 0.6\% | 3.0\% |
| Qi D_multicentrico | 2.09 | 0.4517 |  | - | 8.05 | [ 3.32; | 19.51] | 3.0\% | 4.9\% |
| Shijiao Y_HHMU | 0.42 | 0.5275 |  | + | 1.52 | [ 0.54; | 4.28] | 2.2\% | 4.7\% |
| Zhang G_ZHWU | 2.45 | 0.3624 |  | - | 11.61 | [5.71; | 23.63] | 4.7\% | 5.2\% |
| Chen G_TH | 3.50 | 3.2577 |  | : | 33.14 | [ 0.06; 19 | 9647.54] | 0.1\% | 0.5\% |
| Hu L_TH | 0.24 | 0.3543 |  | 1 | 1.27 | [ 0.63; | 2.54] | 4.9\% | 5.3\% |
| Wang G_PHTCC | 0.81 | 0.3686 |  | + | 2.24 | [ 1.09; | 4.62] | 4.5\% | 5.2\% |
| Wang Z_UH | -2.32 | 3.2189 |  |  | 0.10 | [ 0.00 ; | 54.00] | 0.1\% | 0.5\% |
| Yang L_YCPH | 3.60 | 0.5904 |  | - | 36.69 | [11.54; | 116.70] | 1.8\% | 4.4\% |
| Zhao W_BYH | 3.30 | 3.3438 |  | : | 27.00 | [ 0.04; 189 | 8949.42] | 0.1\% | 0.5\% |
| Cao M_SPHCC | -0.11 | 0.5472 |  | ! | 0.89 | [ 0.31; | 2.61] | 2.1\% | 4.6\% |
| Lei S_RHZHTHC | 1.93 | 0.8018 |  | ! | 6.86 | [ 1.42; | 33.01] | 1.0\% | 3.7\% |
| MY_multicenter 43 hosp | -0.13 | 0.5415 |  | 1 | 0.88 | [ 0.30; | 2.54] | 2.1\% | 4.6\% |
| Hongying S_FAHWMU/SAHWMU | -1.19 | 3.2436 |  |  | 0.31 | [ 0.00; | 175.95] | 0.1\% | 0.5\% |
| Chen W_YH | 3.47 | 1.2311 |  | ' | 32.00 | [ 2.87; | 357.31] | 0.4\% | 2.4\% |
| Jun R_TH | 1.87 | 0.5670 |  | $\frac{1}{1 ;}$ | 6.52 | [ 2.15; | 19.80] | 1.9\% | 4.5\% |
| Zhou M_MC | 2.11 | 0.3473 |  | 1- | 8.28 | [ 4.19; | 16.36] | 5.1\% | 5.3\% |
| YuC_TH | 0.45 | 0.1124 |  |  | 1.57 | [ 1.26; | 1.96] | 48.8\% | 5.8\% |
| Bi Q_STPH | 3.03 | 0.6449 |  | - | 20.77 | [5.87; | 73.51] | 1.5\% | 4.2\% |
| Lix_TH | 2.90 | 0.6048 |  | - | 18.18 | [ 5.55; | 59.47] | 1.7\% | 4.4\% |
| Fixed effect model |  |  |  | ! | 2.87 | [ 2.46; | 3.35] | 99.1\% | -- |
| Random effects model |  |  |  | 18 | 5.45 | [ 3.32; | 8.95] | -- | 94.9\% |
| Heterogeneity: $I^{2}=83 \%, \tau^{2}=1.0244, p<0.01$ |  |  |  | \% |  |  |  |  |  |
|  |  |  |  | ! |  |  |  |  |  |
| Liu W_MC | -1.75 | 1.3466 |  | - | 0.17 | [ 0.01; | 2.44] | 0.3\% | 2.2\% |
| FL_GHCTCPLA | 2.18 | 1.0351 |  | , | 8.86 | [1.17; | 67.38] | 0.6\% | 2.9\% |
| Fixed effect model |  |  |  |  | 2.06 | [ 0.41; | 10.28] | 0.9\% | -- |
| Random effects model |  |  |  |  | 1.36 | [ 0.03; | 63.94] | -- | 5.1\% |
| Heterogeneity: $I^{2}=81 \%, \tau^{2}=6.2811, p=0.02$ |  |  |  | : |  |  |  |  |  |
| Fixed effect model |  |  |  | * | 2.86 | [ 2.45; | 3.33] | 100.0\% | -- |
| Random effects model |  |  |  | $\diamond$ | 5.14 | [ 3.16; | 8.35] | -- | 100.0\% |
| Heterogeneity: $I^{2}=82 \%, \tau^{2}=1.0378, p<0.01$ |  |  | 1 | 1 |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=83 \%, p<0.01$ |  |  | 0.1 | 110 |  |  |  |  |  |

Candidate variable: High total bilirubin (more than $17-21 \mathrm{pg} / \mathrm{ml}$ ), outcome: severe Covid-19 disease

| Study | TE | seTE | Odds | Ratio |  | OR | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |
| Wei-jie G_NHC | 0.89 | 0.3783 |  | - |  | 2.42 | [1.15; 5.09] | 8.9\% | 9.3\% |
| Liu T_UH | -0.05 | 1.1325 |  |  |  |  | [0.10; 8.77] | 1.0\% | 1.7\% |
| Xiao $\bar{M}$ _ECRH | 1.55 | 0.4068 |  |  | T- |  | [2.13; 10.48] | 7.7\% | 8.5\% |
| Qi D_multicentrico | 1.52 | 0.8322 |  |  |  | 4.55 | [0.89; 23.27] | 1.8\% | 2.9\% |
| Zhen L_MC | 0.75 | 0.4985 |  |  |  | 2.12 | [0.80; 5.64] | 5.1\% | 6.5\% |
| Chen X_FHC/LCH | 0.36 | 0.4915 |  |  |  |  | [0.55; 3.74] | 5.3\% | 6.7\% |
| Hu L_TH | 0.98 | 0.4781 |  |  |  |  | [1.04; 6.79] | 5.6\% | 6.9\% |
| CaiQ_TPHS | 1.99 | 0.4455 |  |  | \# | 7.32 | [3.06; 17.52] | 6.4\% | 7.6\% |
| Cao M_SPHCC |  | 1.1451 |  |  |  |  | [0.25; 22.54] | 1.0\% | 1.6\% |
| Zhou M_MC |  | 0.2995 |  |  | $\square$ |  | [3.11; 10.05] | 14.2\% | 11.8\% |
| Zhang L_WUH | 0.39 | 0.2918 |  | + |  |  | [0.83; 2.60] | 14.9\% | 12.1\% |
| Bi Q_STPH | 1.23 | 0.2526 |  |  |  |  | [2.09; 5.63] | 19.9\% | 13.6\% |
| Zheng F_NHCFH | 0.84 | 0.7383 |  |  |  |  | [0.54; 9.84] | 2.3\% | 3.6\% |
| LiX_TH | 0.96 | 0.4576 |  |  |  |  | [1.07; 6.41] | 6.1\% | 7.3\% |
| Fixed effect model |  |  |  |  |  |  | [2.40; 3.73] | 100.0\% | - |
| Random effects model |  |  |  | $i$ |  |  | [2.19; 3.97] | -- | 100.0\% |
| Heterogeneity: $I^{2}=37 \%, \tau^{2}=0.1073, p=0.08$ |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  | $\bigcirc$ |  |  | [2.40; 3.73] | 100.0\% | -- |
| Random effects model |  |  |  | $<$ | $\bigcirc$ | 2.95 | [2.19; 3.97] | -- | 100.0\% |
| Heterogeneity: $I^{2}=37 \%, \tau^{2}=0.1073, p=0.08$ |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=37 \%, p=0.08 \quad 0.1$ |  |  | 0.51 | 12 | 10 |  |  |  |  |

Candidate variable: High AST level (more than 32-40 U/l), outcome: severe Covid-19 disease


Candidate variable: AST increase (per $1 \mathrm{U} /$ ), outcome: severe Covid-19 disease, subgroup analysis by risk of bias (high vs moderate/low)


Candidate variable: High ALT level (more than 35-50 U/L), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Increase ALT level (per $1 \mathrm{U} / \mathrm{L}$ ), outcome: severe Covid-19 disease


Candidate variable: Low albumin (less than $35-40 \mathrm{~g} / \mathrm{L}$ ), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Increase albumin (per $10 \mathrm{~g} / \mathrm{L}$ ), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: High glucose (more than $6 \mathrm{mmol} / \mathrm{l}$ ), outcome: severe Covid-19 disease

| Study | TE | seTE | Odds | Ratio | OR | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |
| Zhen L_MC | 0.84 | 0.3366 |  |  | 2.31 | [1.19; 4.47] | 18.2\% | 18.2\% |
| Zhou M_MC | 1.29 | 0.2883 |  |  | 3.64 | [2.07; 6.41] | 24.8\% | 24.8\% |
| LiX_TH | 1.11 | 0.1903 |  |  | 3.03 | [2.09; 4.40] | 57.0\% | 57.0\% |
| Fixed effect model |  |  |  |  | 3.02 | [2.28; 4.00] | 100.0\% | -- |
| Random effects mod |  |  |  |  | 3.02 | [2.28; 4.00] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.59$ |  |  |  |  |  |  |  |  |
| Fixed effect modelRandom effects model |  |  |  |  | 3.02 | [2.28; 4.00] | 100.0\% | -- |
|  |  |  |  |  | 3.02 | [2.28; 4.00] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.59$Residual heterogeneity: $I^{2}=0 \%, p=0.59$ |  |  | 1 |  |  |  |  |  |
|  |  |  | 0.5 | 2 |  |  |  |  |

Candidate variable: High lactate (more than 1.5-2.2 mmol/L), outcome: severe Covid-19 disease


Candidate variable: Lactate increase (per $1 \mathrm{mmol} / \mathrm{L}$ ), outcome: severe Covid-19 disease


Candidate variable: Any abnormal Radiologic finding, outcome: severe Covid-19 disease

| Study | TE | seTE |  | Odds | Ratio |  | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ = 0 |  |  |  |  |  |  |  |  |  |  |  |
| Chen J_SP | 1.50 | 1.0053 |  |  |  |  | 4.46 | [0.62; | 31.99] | 4.9\% | 4.9\% |
| Young BE_MC | 1.10 | 1.0541 |  |  |  |  | 3.00 | [0.38; | 23.68] | 4.5\% | 4.5\% |
| Jin-Jin Z_MC | 1.90 | 3.3378 |  |  |  |  | 6.66 | [0.01; 4 | 4621.77] | 0.4\% | 0.4\% |
| Wei-jie G_NHC | 0.96 | 0.4021 |  |  | $+$ |  | 2.60 | [1.18; | 5.72] | 30.9\% | 30.9\% |
| Ma K_YCH | 2.37 | 1.0585 |  |  | - |  | 10.66 | [1.34; | 84.86] | 4.5\% | 4.5\% |
| Tabata S_SDFCH | 1.26 | 0.5456 |  |  | ! |  | 3.53 | [1.21; | 10.28] | 16.8\% | 16.8\% |
| Wang G_PHTCC | 3.37 | 3.1779 |  |  | ! |  | 29.02 | [0.06; 14 | 4711.80] | 0.5\% | 0.5\% |
| Wang $\mathrm{Y}_{-}^{-} \mathrm{ZH}$ (Multicéntrico) | 0.21 | 0.3653 |  |  |  |  | 1.23 | [0.60; | 2.51] | 37.5\% | 37.5\% |
| Fixed effect model |  |  |  |  | ¢ |  | 2.31 | [1.49; | 3.58] | 100.0\% | - |
| Random effects model |  |  |  |  | $\stackrel{\circ}{6}$ |  | 2.31 | [1.49; | 3.58] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.43$ |  |  |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  |  | 2.31 | [1.49; | 3.58] | 100.0\% | - |
| Random effects model $\diamond$ |  |  |  |  |  |  | 2.31 | [1.49; | 3.58] | -- | 100.0\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.43$ |  |  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=0 \%, p=0.43$ |  |  | 0.001 | 0.11 | 110 | 1000 |  |  |  |  |  |

Candidate variable: Interstitial pattern, outcome: severe Covid-19 disease


Candidate variable: Ground glass opacity, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study |  | seTE | Odds | Ratio | OR |  | 95\%-CI | (fixed) (random) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |
| Li K_CMU | 2.14 | 3.2533 |  |  | 8.48 | [0.01; | 985.36] | 0.0\% | 0.3\% |
| Liu K_MC | 0.79 | 0.5835 |  |  | 2.21 | [0.70; | 6.92] | 1.4\% | 3.7\% |
| Cao W_X-1 H | 0.73 | 0.5493 |  |  | 2.07 | [0.70; | $6.07]$ | 1.6\% | 3.9\% |
| Chu J_TH | 0.51 | 0.7176 |  |  | 1.66 | [0.41; | 6.79] | 0.9\% | 3.0\% |
| Duan Q_WPH | 0.09 | 0.5878 |  | . | 1.10 | [0.35; | 3.47] | 1.4\% | 3.7\% |
| Liu T_UH | 1.61 | 3.2309 |  |  | 5.00 | [0.01; 2 | 812.91] | 0.0\% | 0.3\% |
| Shijiao Y_HHMU | 0.87 | 0.6019 |  |  | 2.38 | [0.73; | 7.73] | 1.3\% | 3.6\% |
| Zhao W_SXH -0.7 | -0.71 | 0.5285 | $\rightarrow$ |  | 0.49 | [0.17; | 1.39] | 1.7\% | 4.0\% |
| Lei L_CUTGH | 0.43 | 1.1429 |  |  | 1.54 | [0.16; | 14.49] | 0.4\% | 1.7\% |
| Feng Z_TXH | 2.00 | 3.2006 |  |  | 7.38 | [0.01; 3 | 909.80] | 0.0\% | 0.3\% |
| Hu L_TH - | -1.37 | 0.4576 | + |  | 0.25 | [0.10; | 0.62 ] | 2.3\% | 4.4\% |
| Li J_CHW -0. | -0.68 | 0.5272 | $\cdots$ |  | 0.50 | [0.18; | 1.42] | 1.7\% | 4.0\% |
| Wang G_PHTCC | 1.54 | 0.4088 |  | - | 4.67 | [2.09; | 10.40] | 2.9\% | 4.7\% |
| Xiaofei H_MC | 1.02 | 0.5707 |  |  | 2.77 | [0.91; | 8.49] | 1.5\% | 3.8\% |
| Kuang Y_MC -0.3 | -0.33 | 0.4766 | - |  | 0.72 | [0.28; | 1.83] | 2.1\% | 4.3\% |
| FY_JH, SPHCC, TPH -0. | -0.25 | 0.3925 | $+$ |  | 0.78 | [0.36; | 1.69] | 3.1\% | 4.8\% |
| CM_FAHSYU | 1.09 | 0.5976 |  |  | 2.99 | [0.93; | 9.64] | 1.3\% | 3.6\% |
| JX_WFPH | 3.41 | 3.1987 |  |  | 30.35 | [0.06; 16 | 029.59] | 0.0\% | 0.3\% |
| MY_multicenter 43 hosp | 1.09 | 0.2959 |  | - | 2.98 | [1.67; | 5.33] | 5.5\% | 5.4\% |
| Hongying S_FAHWMU/SAHWMU -0. | -0.29 | 1.2435 |  |  | 0.75 | [0.07; | 8.58] | 0.3\% | 1.5\% |
| Xin L_CHWC/hospitales en Hunan | 2.69 | 3.1992 |  |  | 14.75 | [0.03; 7 | 797.57] | 0.0\% | 0.3\% |
| Ying S_hospitales en Beijing | 3.73 | 3.1948 |  |  | 41.69 | [0.08; 21 | 851.41] | 0.0\% | 0.3\% |
| Chen W_YH | 0.18 | 0.7170 |  |  | 1.20 | [0.29; | 4.89] | 0.9\% | 3.1\% |
| Wang X_DFH -0.5 | -0.50 | 0.2155 | + |  | 0.60 | [0.40; | 0.92] | 10.4\% | 5.8\% |
| Herold T_UH | 0.50 | 1.2142 |  |  | 1.65 | [0.15; | 17.82] | 0.3\% | 1.5\% |
| Minhua Y Z HWU -0.6 | -0.61 | 0.5929 | + |  | 0.54 | [0.17; | 1.74] | 1.4\% | 3.7\% |
| Zhou M_MC | 1.74 | 0.3689 |  | $\cdots$ | 5.67 | [2.75; | 11.69] | 3.5\% | 5.0\% |
| YuC_TH -0. | -0.17 | 0.1003 |  |  | 0.85 | [0.70; | 1.03] | 47.8\% | 6.3\% |
| Zhang R_RH | 1.50 | 1.0633 |  |  | 4.46 | [0.56; | 35.86] | 0.4\% | 1.9\% |
| Bi Q_STPH | 2.33 | 1.0220 |  |  | 10.33 | [1.39; | 76.54] | 0.5\% | 2.0\% |
| Zheng F_NHCFH | 0.80 | 0.4250 |  | $\square$ | 2.23 | [0.97; | $5.12]$ | 2.7\% | 4.6\% |
| Fixed effect model |  |  |  | : | 1.08 | [0.94; | 1.24] | 97.7\% | -- |
| Random effects model |  |  |  | \% | 1.47 | [1.04; | 2.08] | -- | 95.6\% |
| Heterogeneity: $I^{2}=70 \%, \tau^{2}=0.4636, p<0.01$ |  |  |  |  |  |  |  |  |  |
| ADJ $=1$ |  |  |  |  |  |  |  |  |  |
| Tabata S_SDFCH | 1.09 | 0.4571 |  | $\div$ | 2.97 | [1.21; | 7.27] | 2.3\% | 4.4\% |
| Fixed effect model |  |  |  | $\bigcirc$ | 2.97 | [1.21; | 7.27] | 2.3\% | -- |
| Random effects model |  |  |  | $\infty$ | 2.97 | [1.21; | 7.27] | -- | 4.4\% |
| Heterogeneity: not applicable |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  | \% | 1.11 | [0.97; | 1.27] | 100.0\% | -- |
| Random effects modelHeterogeneity: $I^{2}=70 \%, \tau^{2}=0.4703, p<0.01$ |  |  |  | $\theta$ | 1.52 | [1.08; | 2.13] | - | 100.0\% |
|  |  |  | 1 | , |  |  |  |  |  |

Candidate variable: Crazy paving pattern, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study |  | seTE |  | Odds | Ratio |  | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  | ! |  |  |  |  |  |  |
| Li K_CMU | 1.21 | 0.4999 |  |  | + |  | 3.34 | [1.25; | 8.90] | 11.9\% | 11.8\% |
| Liu K_MC | 0.99 | 0.5137 |  |  | + |  | 2.68 | [0.98; | 7.33] | 11.2\% | 11.3\% |
| Duan Q_WPH | 0.01 | 0.5516 |  |  |  |  | 1.01 | [0.34; | 2.97] | 9.8\% | 10.0\% |
| Feng Z_TXH | 1.13 | 0.5551 |  |  | + |  | 3.09 | [1.04; | 9.18] | 9.6\% | 9.9\% |
| Hu L_TH | 0.99 | 0.4264 |  |  | $\div$ |  | 2.70 | [1.17; | 6.22] | 16.3\% | 15.3\% |
| Xiaofei H_MC | 1.67 | 0.4525 |  |  | $\square$ |  | 5.34 | [2.20; | 12.96] | 14.5\% | 13.9\% |
| Kuang Y_MC | 0.34 | 0.5300 |  |  | i |  | 1.41 | [0.50; | 3.98] | 10.6\% | 10.7\% |
| Lei S_RHZHTHC | -0.24 | 4.4854 |  |  |  |  | 0.79 | [0.00; 5 | 191.50] | 0.1\% | 0.2\% |
| Hongying S_FAHWMU/SAHWMU | 0.92 | 1.2430 |  |  |  |  | 2.50 | [0.22; | 28.57] | 1.9\% | 2.2\% |
| Minhua Y_ZHWU | 0.61 | 0.5342 |  |  | + |  | 1.83 | [0.64; | 5.22] | 10.4\% | 10.6\% |
| Fixed effect model |  |  |  |  | $\hat{\beta}$ |  | 2.50 | [1.78; | 3.53] | 96.4\% | -- |
| Random effects model |  |  |  |  | ¢ |  | 2.50 | [1.78; | 3.53] | -- | 95.9\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.57$ |  |  |  |  |  |  |  |  |  |  |  |
| ADJ = 1 |  |  |  |  |  |  |  |  |  |  |  |
| Zhang R_RH | 2.73 | 0.9027 |  |  | $\square$ |  | 15.30 | [2.61; | 89.76] | 3.6\% | 4.1\% |
| Fixed effect model |  |  |  |  | $\bigcirc$ |  | 15.30 | [2.61; | 89.76] | 3.6\% | -- |
| Random effects model |  |  |  |  | $\square$ |  | 15.30 | [2.61; | 89.76] | -- | 4.1\% |
| Heterogeneity: not applicable |  |  |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  | - |  | 2.68 | [1.91; | 3.75] | 100.0\% | -- |
| Random effects model |  |  |  |  | $\diamond$ |  | 2.67 | [1.85; | 3.87] | -- | 100.0\% |
| Heterogeneity: $I^{2}=13 \%, \tau^{2}=0.0505, p=0.32$ |  |  | $\stackrel{ }{ }$ | 1 | 1 | 100 |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=0 \%, p=0.57$ |  |  | 0.001 | 0.11 | 110 | 1000 |  |  |  |  |  |

Candidate variable: Consolidation pattern, outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)

| Study |  | seTE |  | Odds | Ratio |  | OR |  | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |  |  |  |  |
| Li K_CMU | 1.85 | 0.6693 |  |  | $\leftarrow$ |  | 6.38 | [1.72; | 23.69] | 1.2\% | 3.9\% |
| Liu K_MC | 5.49 | 3.1952 |  |  |  |  | 241.94 | [0.46; 126 | 6892.91] | 0.1\% | 0.5\% |
| Jin-Jin Z_MC | 0.83 | 0.2969 |  |  | 4 |  | 2.29 | [1.28; | 4.10] | 6.3\% | 5.1\% |
| Lu Jiatao_WHH | -1.74 | 3.2466 |  |  |  |  | 0.18 | [0.00; | 102.11] | 0.1\% | 0.5\% |
| Chen Y_multicentrico- FCMCH | 0.36 | 0.6981 |  |  |  |  | 1.43 | [0.36; | 5.61] | 1.1\% | 3.8\% |
| Chu J_TH | -0.77 | 0.9417 |  | $\cdots$ |  |  | 0.46 | [0.07; | 2.92] | 0.6\% | 3.0\% |
| Qi D_multicentrico | 2.46 | 0.6246 |  |  | $\rightarrow$ |  | 11.69 | [3.44; | 39.76] | 1.4\% | 4.0\% |
| Zhao W_SXH | 0.09 | 0.3809 |  |  |  |  | 1.09 | [0.52; | 2.30] | 3.8\% | 4.8\% |
| Lei L_CUTGH | 1.90 | 0.9025 |  |  | - |  | 6.67 | [1.14; | 39.10] | 0.7\% | 3.1\% |
| Feng Z_TXH | 0.14 | 0.7993 |  |  |  |  | 1.15 | [0.24; | 5.53] | 0.9\% | 3.4\% |
| Ma K_YCH | 2.25 | 0.6774 |  |  | $\square$ |  | 9.44 | [2.50; | 35.62] | 1.2\% | 3.8\% |
| Kuang Y_MC | 1.28 | 0.4262 |  |  |  |  | 3.58 | [1.55; | 8.26] | 3.0\% | 4.7\% |
| FY_JH, SPHCC, TPH | -0.98 | 0.4446 |  | $\rightarrow$ |  |  | 0.38 | [0.16; | 0.90] | 2.8\% | 4.6\% |
| CM_FAHSYU | 2.12 | 0.5234 |  |  | - |  | 8.32 | [2.98; | 23.20] | 2.0\% | 4.4\% |
| Hongying S_FAHWMU/SAHWMU | 0.31 | 3.2973 |  |  |  |  | 1.37 | [0.00; | 876.74] | 0.1\% | 0.5\% |
| Xin L_CHWC/hospitales en Hunan | 1.31 | 0.5315 |  |  |  |  | 3.69 | [1.30; | 10.46] | 2.0\% | 4.3\% |
| Ying S_hospitales en Beijing | 0.47 | 0.6513 |  |  |  |  | 1.61 | [0.45; | 5.76] | 1.3\% | 3.9\% |
| Chen W_YH | 1.23 | 0.9271 |  |  |  |  | 3.43 | [0.56; | 21.10] | 0.6\% | 3.0\% |
| Wang X_DFH | 0.78 | 0.3674 |  |  | $\div$ |  | 2.19 | [1.07; | 4.50] | 4.1\% | 4.9\% |
| Herold T_UH | -0.44 | 0.7182 |  |  |  |  | 0.64 | [0.16; | 2.63] | 1.1\% | 3.7\% |
| Minhua Y_ZHWU | 1.06 | 0.7643 |  |  |  |  | 2.88 | [0.64; | 12.86] | 0.9\% | 3.5\% |
| Zhou M_MC | 1.88 | 0.3354 |  |  | + |  | 6.58 | [3.41; | 12.70] | 4.9\% | 5.0\% |
| YuC_TH | -0.42 | 0.1024 |  |  |  |  | 0.65 | [0.54; | 0.80] | 52.7\% | 5.5\% |
| Zhang R_RH | 1.97 | 0.5347 |  |  |  |  | 7.16 | [2.51; | 20.43] | 1.9\% | 4.3\% |
| Zheng F_NHCFH | -0.39 | 0.4257 |  |  |  |  | 0.68 | [0.30; | 1.57] | 3.0\% | 4.7\% |
| Fixed effect model |  |  |  |  |  |  | 1.20 | [1.04; | 1.40] | 97.8\% | -- |
| Random effects model |  |  |  |  | $\bigcirc$ |  | 2.35 | [1.44; | 3.83] | -- | 92.9\% |
| Heterogeneity: $I^{2}=84 \%, \tau^{2}=1.0480, p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |
| ADJ $=1$ |  |  |  |  |  |  |  |  |  |  |  |
| Tabata S_SDFCH | 1.18 | 0.5874 |  |  | $\leftarrow$ |  | 3.24 | [1.02; | 10.25] | 1.6\% | 4.1\% |
| Zhang L_TH | 1.94 | 0.9488 |  |  |  |  | 6.96 | [1.08; | 44.70] | 0.6\% | 3.0\% |
| Fixed effect model |  |  |  |  | $\rangle$ |  | 4.00 | [1.50; | 10.66] | 2.2\% | -- |
|  |  |  |  |  | $>$ |  | 4.00 | [1.50; | 10.66] | -- | 7.1\% |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.49$ |  |  |  |  |  |  |  |  |  |  |  |
| Fixed effect model |  |  |  |  |  |  | 1.24 | [1.07; | 1.43] | 100.0\% | -- |
| Random effects model |  |  |  |  | $\stackrel{\rightharpoonup}{ }$ |  | 2.46 | [1.54; | 3.93] | -- | 100.0\% |
| Heterogeneity: $I^{2}=84 \%, \tau^{2}=1.0381$, | $p<0.01$ |  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=84 \%, p<0.01$ |  |  | 0.001 | 0.11 | 10 | 1000 |  |  |  |  |  |

Candidate variable: Enlarged lymph nodes (CT assessment), outcome: severe Covid-19 disease

| Study TE | seTE |  | Odds | Ratio |  | OR | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  | i |  |  |  |  |  |
| Chu J_TH 0.31 | 0.8610 |  |  | ! |  | 1.36 | [0.25; 7.37] | 5.4\% | 6.1\% |
| Zhao W_SXH -1.73 | 3.3387 |  |  |  |  | 0.18 | [0.00; 123.53] | 0.4\% | 0.4\% |
| Feng Z_TXH 0.55 | 1.1312 |  |  |  |  | 1.73 | [0.19; 15.87] | 3.1\% | 3.6\% |
| Wang $\bar{Y} \_Z \mathrm{ZH}$ (Multicéntrico) -0.07 | 1.0569 |  |  |  |  | 0.93 | [0.12; 7.39] | 3.6\% | 4.1\% |
| Xiaofei H_MC 1.47 | 0.4321 |  |  | + |  | 4.33 | [1.86; 10.11] | 21.4\% | 21.8\% |
| Kuang Y_MC 1.16 | 1.0203 |  |  |  |  | 3.19 | [0.43; 23.55] | 3.8\% | 4.4\% |
| Colombi D_GdSH 0.65 | 0.3081 |  |  | $\pm$ |  | 1.91 | [1.04; 3.49] | 42.0\% | 37.7\% |
| Hongying S_FAHWMU/SAHWMU -0.75 | 3.2426 |  |  |  |  | 0.47 | [0.00; 273.15] | 0.4\% | 0.4\% |
| Zhou M_MC 0.03 | 0.4852 |  |  |  |  | 1.03 | [0.40; 2.67] | 16.9\% | 17.8\% |
| Zhang R_RH 2.62 | 1.1400 |  |  |  |  | 13.69 | [1.47; 127.90] | 3.1\% | 3.6\% |
| Fixed effect model |  |  |  | ¢ |  | 2.09 | [1.41; 3.09] | 100.0\% | -- |
| Random effects model |  |  |  | - |  | 2.09 | [1.37; 3.20] | -- | 100.0\% |
| Heterogeneity: $I^{2}=6 \%, \tau^{2}=0.0305, p=0.39$ |  |  |  | + |  |  |  |  |  |
| Fixed effect model |  |  |  | $\stackrel{\circ}{-}$ |  | 2.09 | [1.41; 3.09] | 100.0\% | -- |
| Random effects model |  |  |  | $\diamond$ |  | 2.09 | [1.37; 3.20] | - | 100.0\% |
| Heterogeneity: $I^{2}=6 \%, \tau^{2}=0.0305, p=0.39$ |  | , | , |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=6 \%, p=0.39$ |  | 0.001 | 0.1 | 110 | 1000 |  |  |  |  |

Candidate variable: Pleural effusion (CT assessment), outcome: severe Covid-19 disease, subgroup analysis: (crude vs adjusted)


Candidate variable: Bilateral compromise (CT assesment), outcome: severe
Covid-19 disease


Candidate variable: High APACHE score (more than 8), outcome: severe Covid-19 disease

| Study TE seTE |  | Odds Ratio |  | OR | 95\%-CI | Weight (fixed) | Weight (random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADJ $=0$ |  |  |  |  |  |  |  |
| Han Y_RHWU 0.700 .2090 | 0.700 .2090 | 1 |  | 2.02 | [1.34; 3.04] | 16.3\% | 46.2\% |
| Huang M_12 hospitales en Jiangsu 0.020 .0922 |  |  |  | 1.02 [0.85; 1.22] |  | 83.7\% | 53.8\% |
| Fixed effect model |  | I |  | 1.14 [0.97; 1.35] |  | 100.0\% | -- |
| Random effects model |  |  |  | 1.40 | [0.72; 2.73] | -- | 100.0\% |
| Heterogeneity: $I^{2}=89 \%, \tau^{2}=0.2074, p<0.01$ |  | ! |  |  |  |  |  |
| Fixed effect model |  | $\bigcirc$ |  | 1.14 | [0.97; 1.35] | 100.0\% | -- |
| Random effects model |  |  |  |  | [0.72; 2.73] | -- | 100.0\% |
| Heterogeneity: $I^{2}=89 \%, \tau^{2}=0.2074, p<0.01$ | 5 |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=89 \%, p<0.01$ | 0.5 | 1 | 2 |  |  |  |  |

Candidate variable: High SOFA score (more than 2), outcome: severe Covid-19 disease


