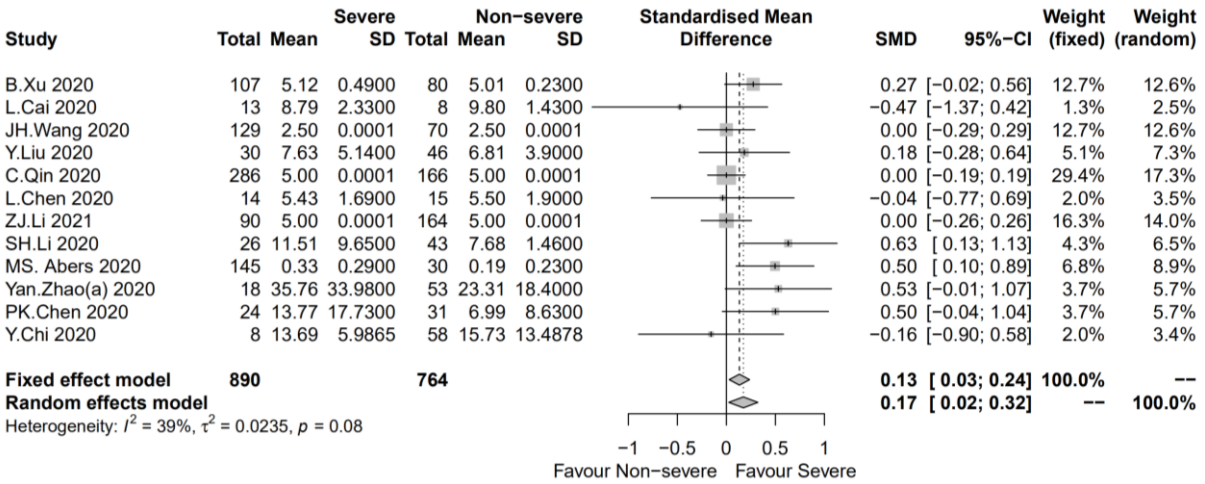
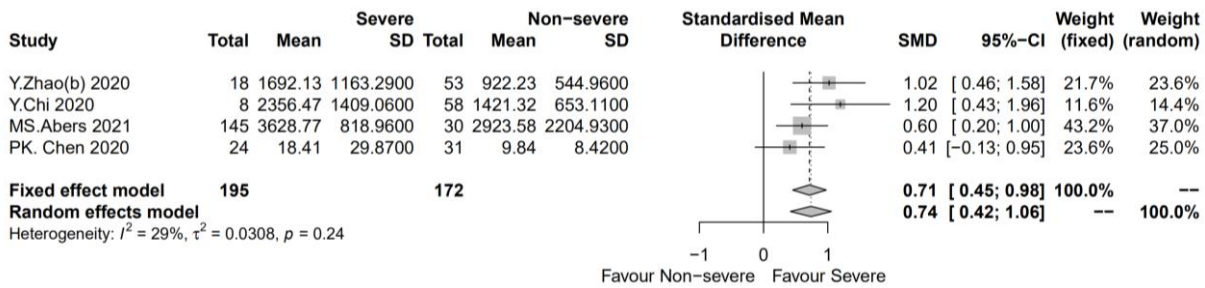
**Figure E2(A) Forest plots of immunological parameters in severe and non-severe patients of COVID-19**

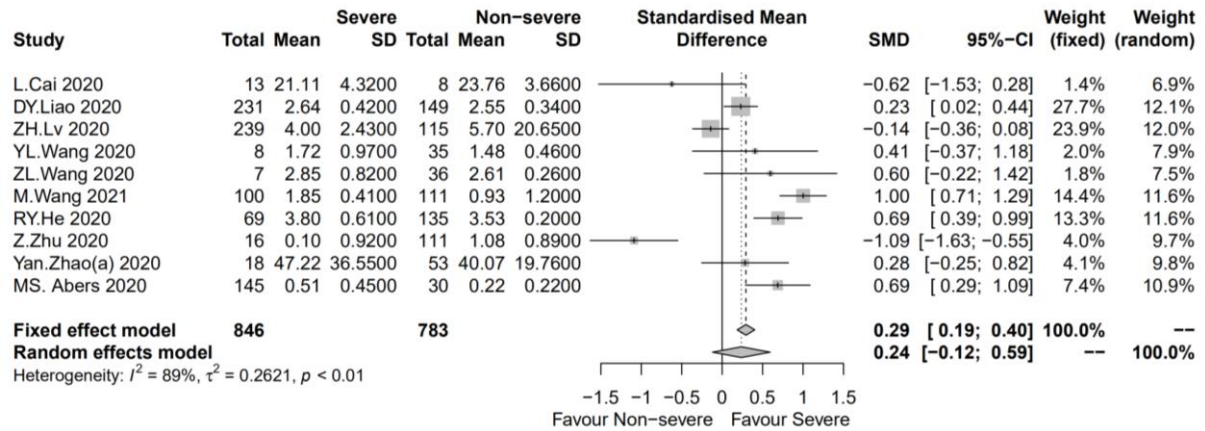
**(1) IL-1β**



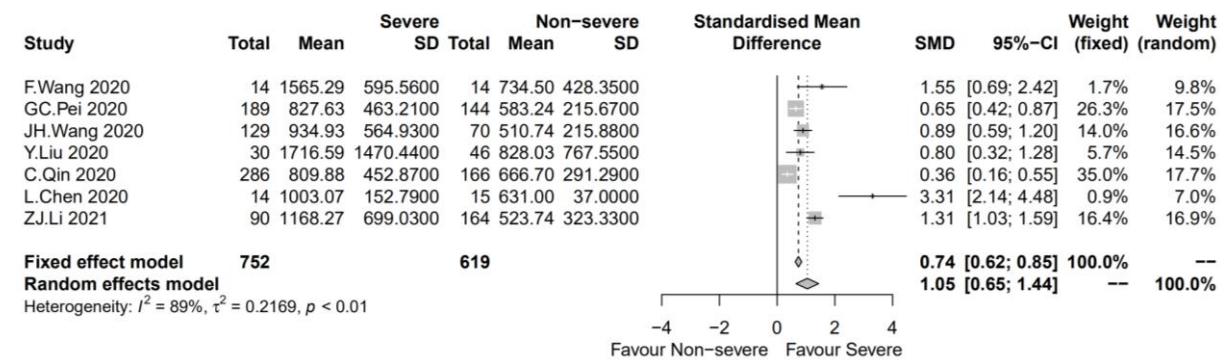

**(2) IL-1Ra**



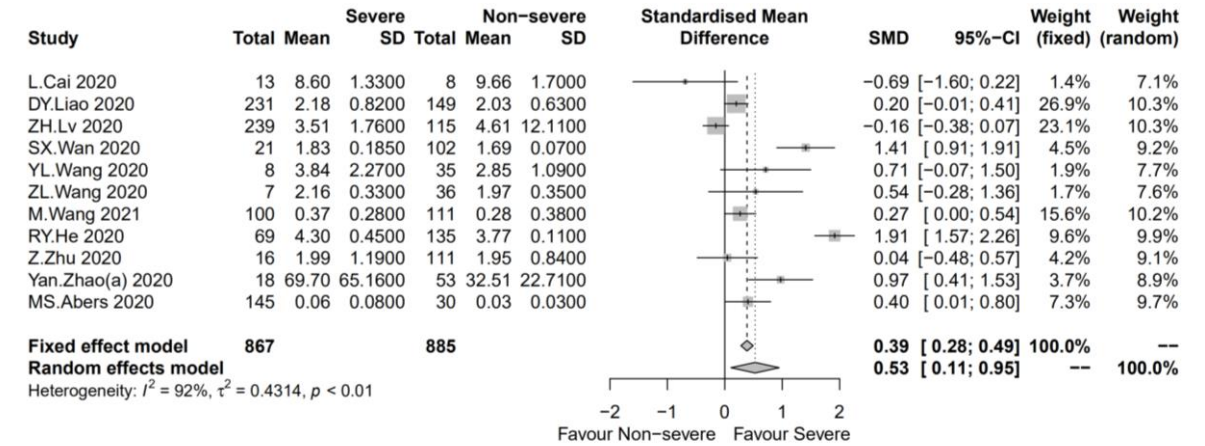

**(3) IL-2**




**(4) IL-2R**

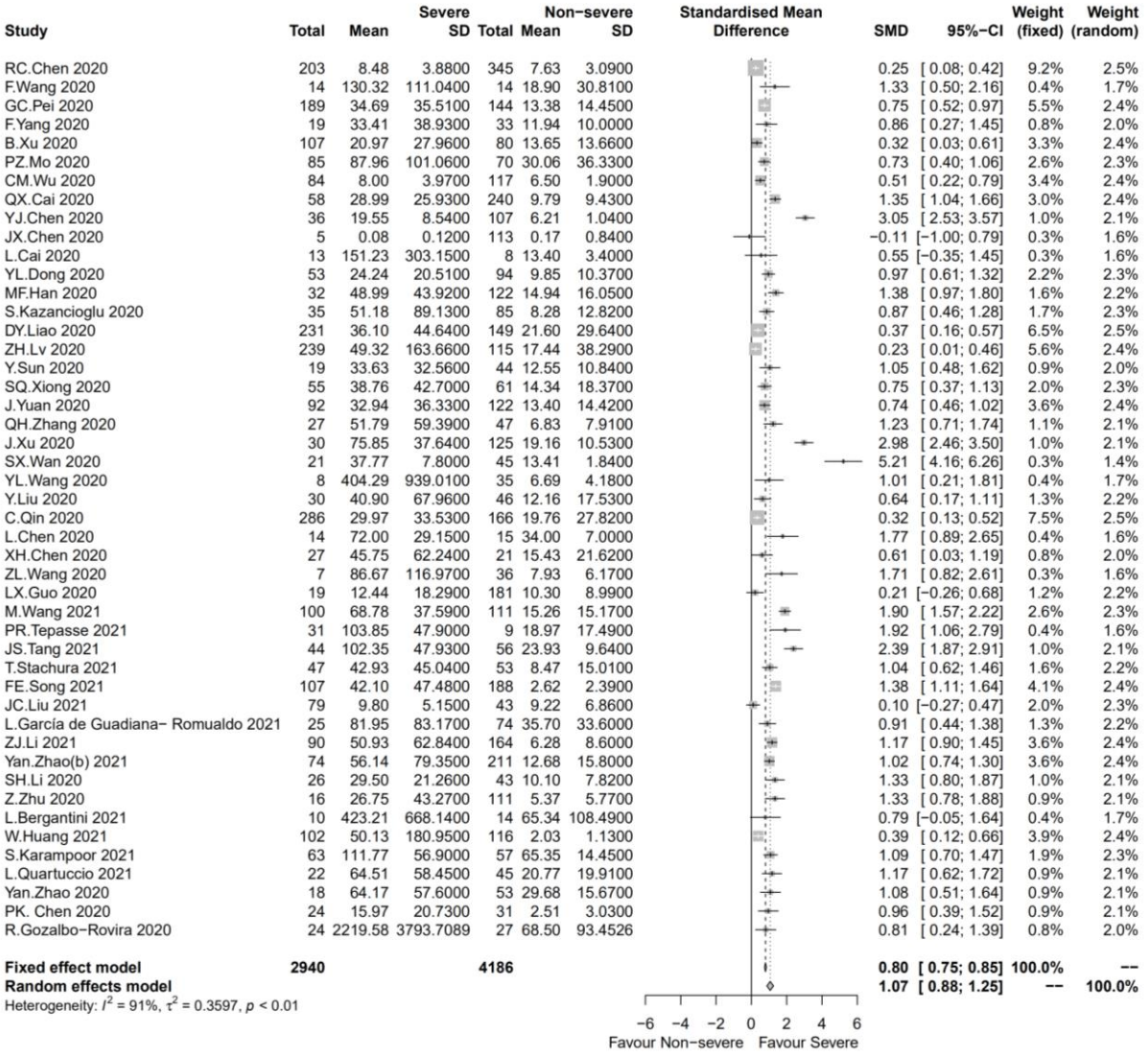



**(5) IL-4**

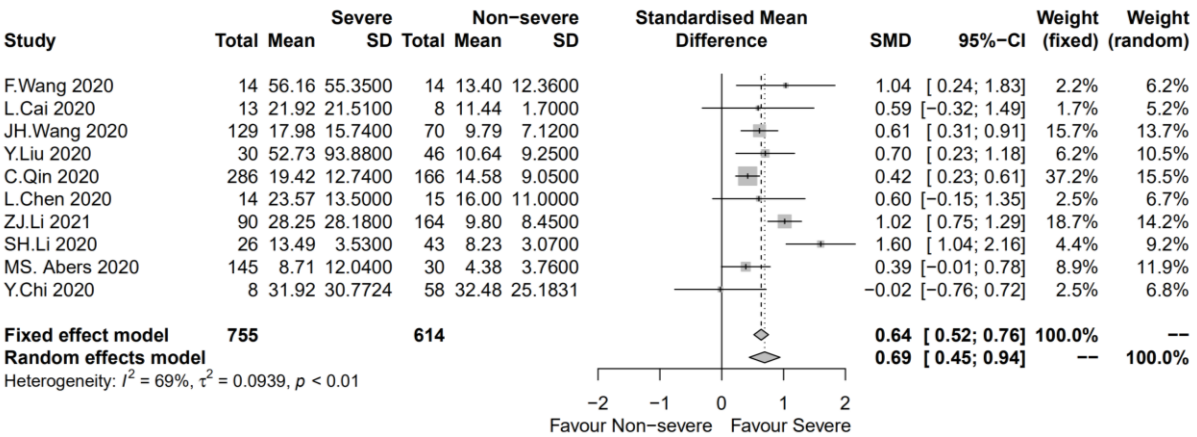


## Figure E2(A) (Continued)

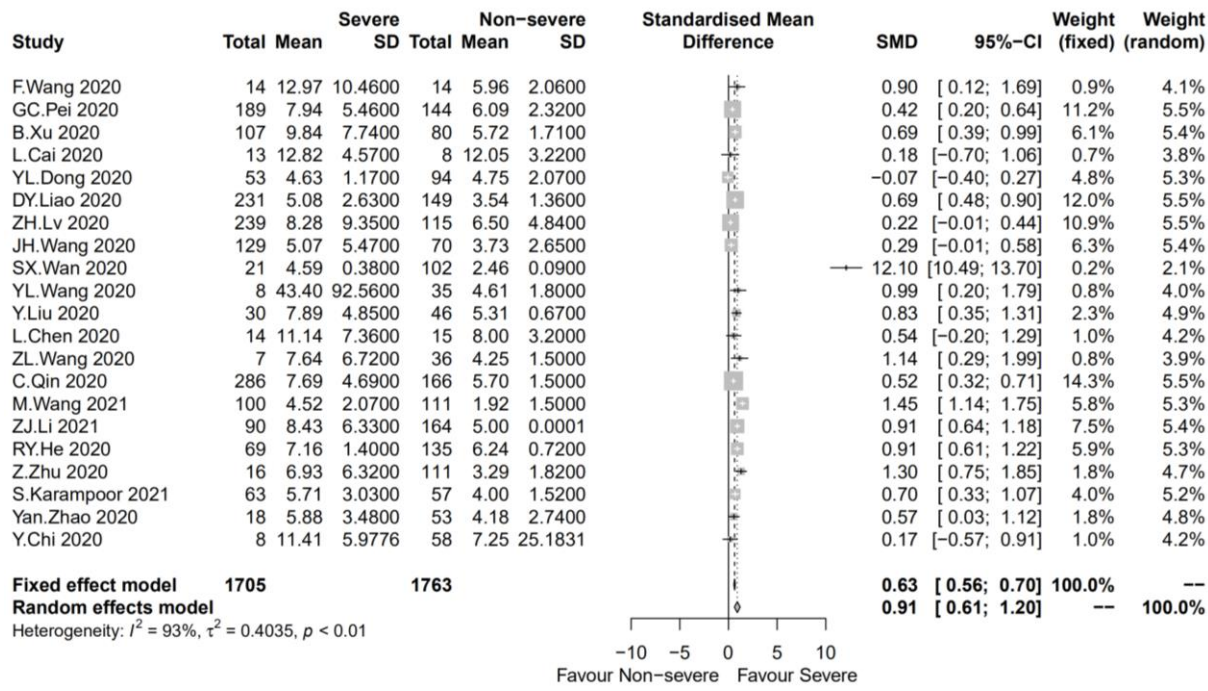
### (6) IL-6




### (7) IL-8

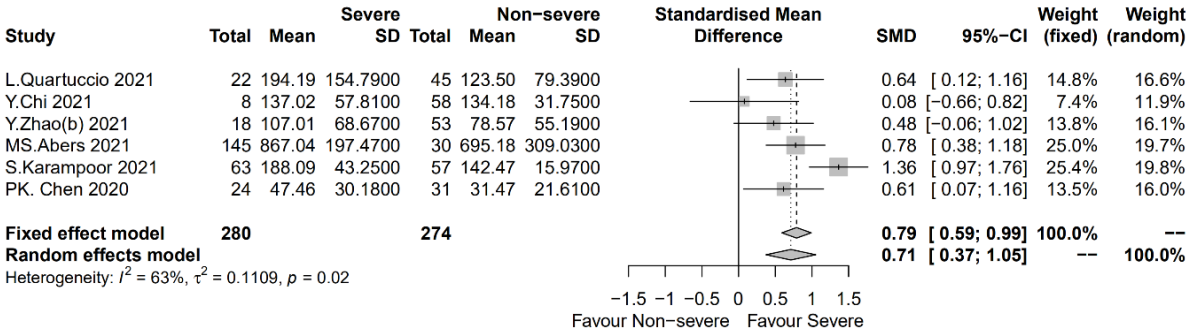



### (8) IL-10

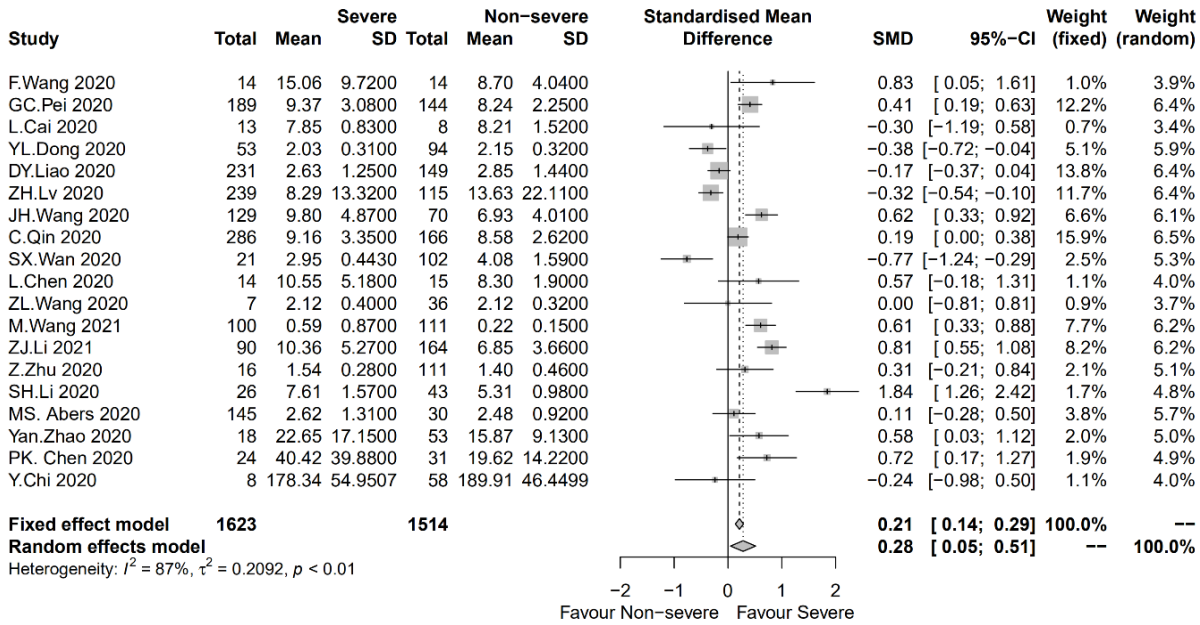


## Figure E2(A) (Continued)

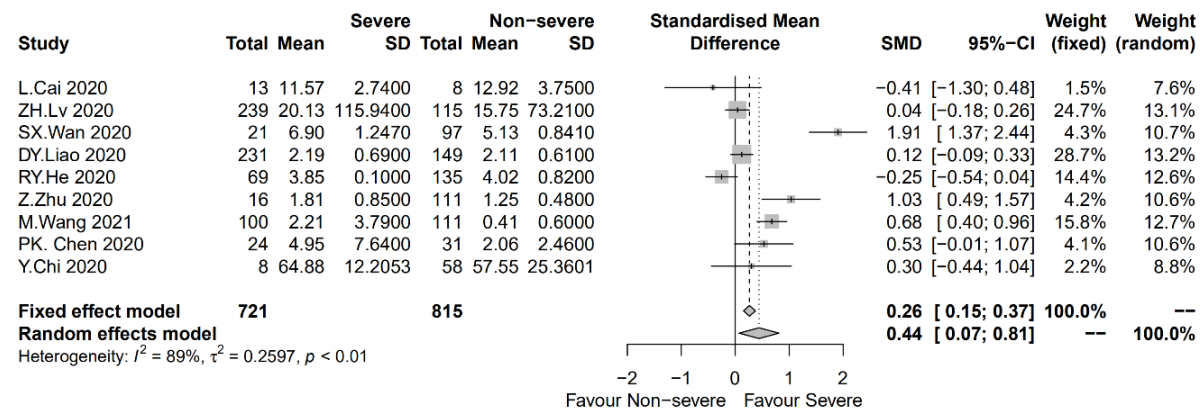
### (9) IL-18



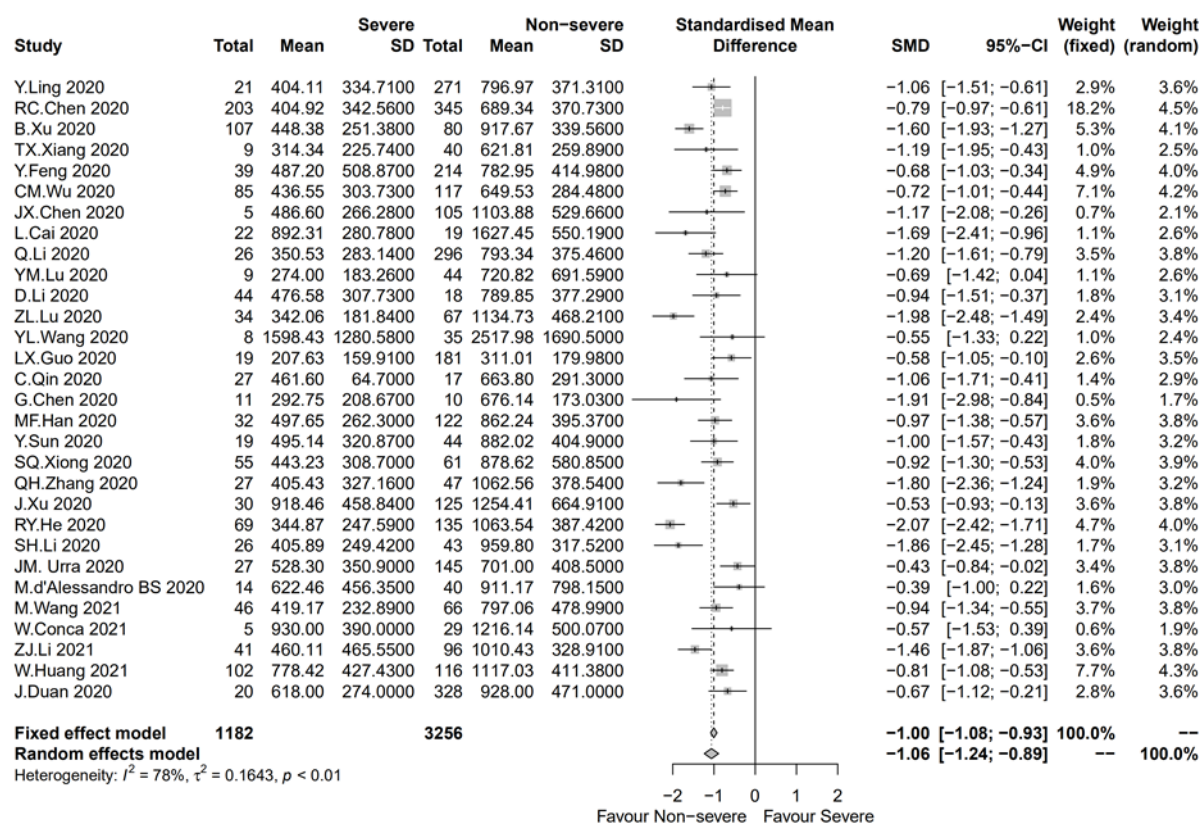

### (10) TNF-α




### (11) IFN-γ




### (12) CD3+T(ab)

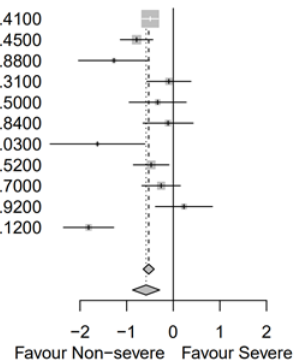


## Figure E2(A) (Continued)

### (13) CD3+T(%)

| Study | Severe Total | Mean | SD | Non−severe Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| RC.Chen 2020 | 203 | 60.81 | 16.1900 | 345 | 66.93 | 9.4100 | −0.49 | [−0.67; −0.32] | 44.4% | 12.4% |
| Y.Feng 2020 | 39 | 56.41 | 32.7000 | 214 | 69.00 | 10.4500 | −0.79 | [−1.13; −0.44] | 11.3% | 10.9% |
| YM.Lu 2020 | 9 | 48.20 | 6.6800 | 44 | 65.02 | 13.8800 | −1.27 | [−2.03; −0.51] | 2.4% | 6.8% |
| LX.Guo 2020 | 19 | 26.55 | 14.5100 | 181 | 29.32 | 30.3100 | −0.09 | [−0.57; 0.38] | 6.1% | 9.6% |
| C.Qin 2020 | 27 | 60.00 | 10.8000 | 17 | 63.40 | 8.5000 | −0.33 | [−0.95; 0.28] | 3.7% | 8.2% |
| JJ.Xie 2020 | 34 | 74.81 | 6.2800 | 22 | 75.75 | 10.8400 | −0.11 | [−0.65; 0.43] | 4.8% | 9.0% |
| G.Chen 2020 | 11 | 56.02 | 7.0400 | 10 | 69.65 | 9.0300 | −1.63 | [−2.64; −0.61] | 1.3% | 5.0% |
| M.Wang 2021 | 46 | 62.53 | 14.6300 | 66 | 68.68 | 11.5200 | −0.47 | [−0.86; −0.09] | 9.4% | 10.6% |
| JM. Urra 2020 | 27 | 69.30 | 13.2000 | 145 | 72.00 | 9.7000 | −0.26 | [−0.67; 0.15] | 8.1% | 10.3% |
| M.d'Alessandro BS 2020 | 14 | 73.46 | 18.1200 | 40 | 70.94 | 6.9200 | 0.23 | [−0.38; 0.84] | 3.7% | 8.2% |
| K.Deng 2021 | 17 | 26.37 | 26.8400 | 149 | 56.71 | 15.1200 | −1.82 | [−2.36; −1.28] | 4.7% | 8.9% |
| **Fixed effect model** | **446** | | | **1233** | | | **−0.53** | **[−0.64; −0.41]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **−0.58** | **[−0.87; −0.29]** | **−−** | **100.0%** |

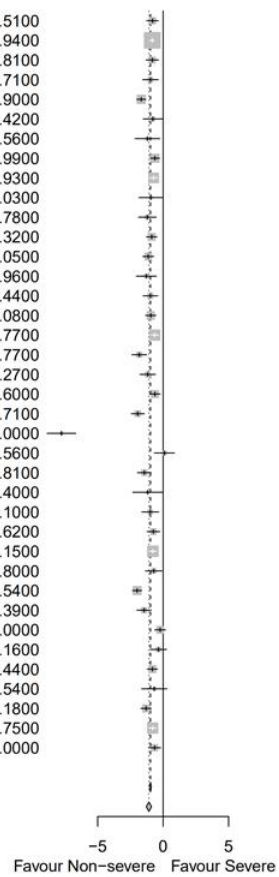
Heterogeneity: $I^2$ = 78%, $\tau^2$ = 0.1683, $p$ < 0.01




### (14) CD4+T(ab)

| Study | Severe Total | Mean | SD | Non−severe Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| Y.Ling 2020 | 21 | 265.44 | 243.2800 | 271 | 471.73 | 252.5100 | −0.82 | [−1.27; −0.37] | 2.3% | 2.8% |
| RC.Chen 2020 | 203 | 247.65 | 183.3600 | 345 | 423.34 | 225.9400 | −0.83 | [−1.01; −0.65] | 14.4% | 3.2% |
| YL.Zheng 2020 | 26 | 273.92 | 185.2100 | 63 | 553.25 | 377.8100 | −0.83 | [−1.30; −0.36] | 2.1% | 2.8% |
| F.Yang 2020 | 19 | 137.50 | 173.0000 | 33 | 391.15 | 293.7100 | −0.97 | [−1.57; −0.38] | 1.3% | 2.5% |
| B.Xu 2020 | 107 | 248.77 | 149.3100 | 80 | 591.39 | 259.9000 | −1.67 | [−2.01; −1.34] | 4.1% | 3.0% |
| TX.Xiang 2020 | 9 | 221.32 | 181.6500 | 40 | 352.75 | 160.4200 | −0.79 | [−1.53; −0.05] | 0.9% | 2.3% |
| G.Chen 2020 | 11 | 177.06 | 123.6700 | 10 | 360.45 | 168.5600 | −1.20 | [−2.15; −0.25] | 0.5% | 1.9% |
| Y.Feng 2020 | 39 | 305.35 | 311.8100 | 214 | 474.62 | 258.9900 | −0.63 | [−0.98; −0.28] | 3.9% | 3.0% |
| CM.Wu 2020 | 84 | 257.52 | 197.0600 | 117 | 410.74 | 216.9300 | −0.73 | [−1.02; −0.44] | 5.6% | 3.1% |
| JX.Chen 2020 | 5 | 307.80 | 164.6700 | 105 | 597.87 | 311.0300 | −0.94 | [−1.84; −0.03] | 0.6% | 2.0% |
| L.Cai 2020 | 22 | 594.69 | 205.9700 | 19 | 937.24 | 343.7800 | −1.21 | [−1.88; −0.53] | 1.0% | 2.4% |
| MF.Han 2020 | 32 | 273.59 | 165.3200 | 122 | 465.87 | 230.3200 | −0.88 | [−1.28; −0.47] | 2.9% | 2.9% |
| Q.Li 2020 | 26 | 193.32 | 152.1600 | 296 | 472.69 | 251.0500 | −1.14 | [−1.55; −0.73] | 2.8% | 2.9% |
| YM.Lu 2020 | 9 | 163.11 | 147.0200 | 44 | 384.48 | 173.9600 | −1.28 | [−2.04; −0.52] | 0.8% | 2.2% |
| Y.Sun 2020 | 19 | 263.66 | 142.1100 | 44 | 482.72 | 247.4400 | −0.98 | [−1.54; −0.41] | 1.5% | 2.6% |
| SQ.Xiong 2020 | 55 | 250.51 | 135.9000 | 61 | 446.00 | 252.0800 | −0.95 | [−1.33; −0.56] | 3.2% | 2.9% |
| J.Yuan 2020 | 92 | 418.45 | 265.2100 | 122 | 598.17 | 286.7700 | −0.64 | [−0.92; −0.37] | 6.1% | 3.1% |
| QH.Zhang 2020 | 27 | 207.21 | 191.7600 | 47 | 663.87 | 273.7700 | −1.83 | [−2.39; −1.27] | 1.5% | 2.6% |
| D.Li 2020 | 44 | 282.52 | 166.8000 | 18 | 490.41 | 192.2700 | −1.18 | [−1.77; −0.59] | 1.4% | 2.6% |
| J.Xu 2020 | 30 | 330.43 | 211.0000 | 125 | 481.25 | 243.6000 | −0.63 | [−1.04; −0.23] | 2.9% | 2.9% |
| ZL.Lu 2020 | 34 | 213.26 | 118.8900 | 67 | 663.57 | 269.7100 | −1.94 | [−2.43; −1.44] | 1.9% | 2.7% |
| SX.Wan 2020 | 21 | 263.20 | 28.8300 | 102 | 451.30 | 23.0000 | −7.77 | [−8.86; −6.68] | 0.4% | 1.7% |
| YL.Wang 2020 | 8 | 1377.25 | 622.2500 | 35 | 1256.81 | 1288.5600 | 0.10 | [−0.67; 0.87] | 0.8% | 2.2% |
| Y.Liu 2020 | 30 | 96.66 | 50.6000 | 46 | 444.64 | 303.8100 | −1.44 | [−1.96; −0.92] | 1.8% | 2.7% |
| YL.Zhou 2020 | 5 | 377.20 | 229.6000 | 12 | 698.20 | 267.4000 | −1.18 | [−2.32; −0.04] | 0.4% | 1.6% |
| Y.Yang 2020 | 36 | 321.82 | 206.6000 | 14 | 586.84 | 378.1000 | −0.99 | [−1.64; −0.34] | 1.1% | 2.4% |
| LX.Guo 2020 | 19 | 522.84 | 349.0400 | 181 | 839.30 | 429.6200 | −0.75 | [−1.22; −0.27] | 2.0% | 2.8% |
| JT.Cao 2020 | 153 | 335.95 | 204.6300 | 91 | 514.93 | 262.1500 | −0.78 | [−1.05; −0.51] | 6.5% | 3.1% |
| C.Qin 2020 | 27 | 285.10 | 168.0000 | 17 | 420.50 | 207.8000 | −0.72 | [−1.35; −0.09] | 1.2% | 2.5% |
| RY.He 2020 | 69 | 193.88 | 143.8600 | 135 | 632.70 | 249.5400 | −1.99 | [−2.34; −1.64] | 3.8% | 3.0% |
| SH.Li 2020 | 26 | 218.66 | 154.5100 | 43 | 523.79 | 232.3900 | −1.46 | [−2.01; −0.91] | 1.6% | 2.6% |
| JM. Urra 2020 | 27 | 340.30 | 251.9000 | 145 | 395.90 | 241.0000 | −0.23 | [−0.64; 0.18] | 2.8% | 2.9% |
| M.d'Alessandro BS 2020 | 14 | 379.30 | 266.8900 | 40 | 505.49 | 372.1600 | −0.36 | [−0.97; 0.26] | 1.2% | 2.5% |
| M.Wang 2021 | 46 | 239.15 | 164.3600 | 66 | 467.06 | 330.4400 | −0.82 | [−1.22; −0.43] | 3.0% | 2.9% |
| W.Conca 2021 | 5 | 539.00 | 219.0000 | 29 | 725.79 | 275.5400 | −0.68 | [−1.64; 0.29] | 0.5% | 1.9% |
| ZJ.Li 2021 | 41 | 302.08 | 345.7100 | 96 | 651.19 | 226.1800 | −1.30 | [−1.70; −0.90] | 3.0% | 2.9% |
| W.Huang 2021 | 102 | 467.12 | 274.5400 | 116 | 687.79 | 274.7500 | −0.80 | [−1.08; −0.52] | 6.1% | 3.1% |
| J.Duan 2020 | 20 | 320.00 | 153.0000 | 328 | 484.00 | 257.0000 | −0.65 | [−1.10; −0.19] | 2.3% | 2.8% |
| **Fixed effect model** | **1563** | | | **3739** | | | **−0.97** | **[−1.04; −0.90]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **−1.09** | **[−1.29; −0.89]** | **−−** | **100.0%** |

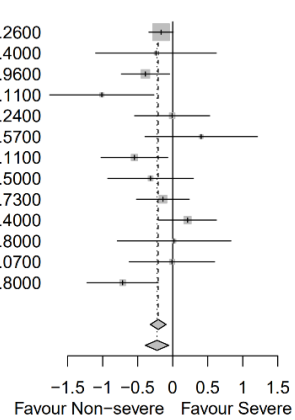
Heterogeneity: $I^2$ = 87%, $\tau^2$ = 0.3152, $p$ < 0.01




### (15) CD4+T(%)

| Study | Severe Total | Mean | SD | Non−severe Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| RC.Chen 2020 | 203 | 37.79 | 11.3600 | 345 | 39.38 | 8.2600 | −0.17 | [−0.34; 0.01] | 42.5% | 18.8% |
| G.Chen 2020 | 11 | 34.71 | 5.6000 | 10 | 36.33 | 7.4000 | −0.24 | [−1.10; 0.62] | 1.7% | 3.3% |
| Y.Feng 2020 | 39 | 35.92 | 25.7700 | 214 | 41.00 | 8.9600 | −0.39 | [−0.73; −0.05] | 10.9% | 11.9% |
| YM.Lu 2020 | 9 | 27.72 | 8.3000 | 44 | 38.73 | 11.1100 | −1.01 | [−1.76; −0.27] | 2.3% | 4.2% |
| JJ.Xie 2020 | 34 | 46.38 | 10.0800 | 22 | 46.46 | 9.2400 | −0.01 | [−0.54; 0.53] | 4.5% | 6.9% |
| ZL.Wang 2020 | 7 | 42.14 | 19.6500 | 43 | 37.76 | 8.5700 | 0.41 | [−0.40; 1.21] | 2.0% | 3.7% |
| LX.Guo 2020 | 19 | 60.25 | 12.4400 | 181 | 67.42 | 13.1100 | −0.55 | [−1.02; −0.07] | 5.7% | 8.1% |
| C.Qin 2020 | 27 | 37.20 | 8.4000 | 17 | 39.80 | 7.5000 | −0.32 | [−0.93; 0.29] | 3.4% | 5.7% |
| M.Wang 2021 | 46 | 37.16 | 9.3800 | 66 | 38.78 | 12.7300 | −0.14 | [−0.52; 0.24] | 9.0% | 10.8% |
| JM.Urra 2020 | 27 | 44.10 | 10.9000 | 145 | 41.50 | 12.4000 | 0.21 | [−0.20; 0.62] | 7.6% | 9.8% |
| L.Bergantini 2021 | 10 | 44.60 | 13.0000 | 14 | 44.40 | 7.8000 | 0.02 | [−0.79; 0.83] | 1.9% | 3.6% |
| M.d'Alessandro BS 2020 | 14 | 44.64 | 12.3600 | 40 | 44.77 | 13.0700 | −0.01 | [−0.62; 0.60] | 3.5% | 5.8% |
| K.Deng 2021 | 17 | 43.79 | 22.5500 | 149 | 55.70 | 15.8000 | −0.72 | [−1.22; −0.21] | 5.0% | 7.5% |
| **Fixed effect model** | **463** | | | **1290** | | | **−0.21** | **[−0.32; −0.09]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **−0.22** | **[−0.39; −0.06]** | **−−** | **100.0%** |

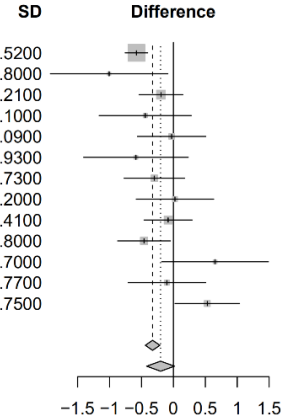
Heterogeneity: $I^2$ = 38%, $\tau^2$ = 0.0312, $p$ = 0.08




### (16) CD8+T(%)

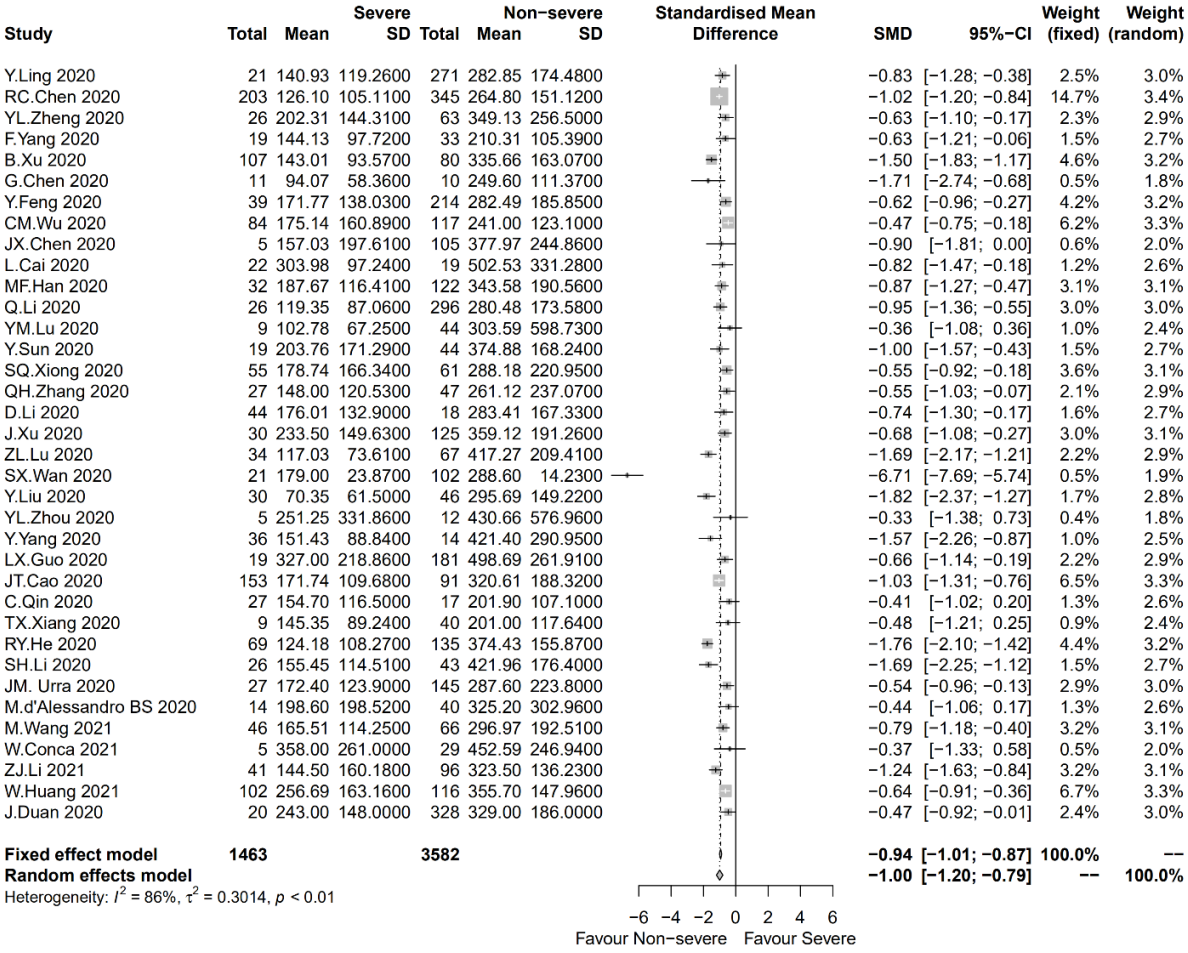
| Study | Severe Total | Mean | SD | Non−severe Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| RC.Chen 2020 | 203 | 19.66 | 7.8900 | 345 | 24.47 | 8.5200 | −0.58 | [−0.76; −0.40] | 41.7% | 13.0% |
| G.Chen 2020 | 11 | 18.61 | 7.3800 | 10 | 27.64 | 9.8000 | −1.01 | [−1.93; −0.09] | 1.5% | 4.0% |
| Y.Feng 2020 | 39 | 22.86 | 13.1900 | 214 | 24.65 | 8.2100 | −0.20 | [−0.54; 0.15] | 11.2% | 10.6% |
| YM.Lu 2020 | 9 | 18.63 | 6.7800 | 44 | 23.35 | 11.1000 | −0.44 | [−1.16; 0.28] | 2.5% | 5.6% |
| JJ.Xie 2020 | 34 | 23.87 | 9.6200 | 22 | 24.17 | 12.0900 | −0.03 | [−0.56; 0.51] | 4.5% | 7.7% |
| ZL.Wang 2020 | 7 | 22.10 | 5.9100 | 36 | 26.16 | 6.9300 | −0.59 | [−1.41; 0.23] | 1.9% | 4.8% |
| LX.Guo 2020 | 19 | 36.43 | 10.8300 | 181 | 42.44 | 20.7300 | −0.30 | [−0.77; 0.17] | 5.8% | 8.5% |
| C.Qin 2020 | 27 | 19.70 | 9.2000 | 17 | 19.50 | 6.2000 | 0.02 | [−0.58; 0.63] | 3.5% | 6.8% |
| M.Wang 2021 | 46 | 24.79 | 7.1500 | 66 | 25.45 | 8.4100 | −0.08 | [−0.46; 0.29] | 9.2% | 10.0% |
| JM. Urra 2020 | 27 | 23.10 | 9.4000 | 145 | 28.40 | 11.8000 | −0.46 | [−0.87; −0.05] | 7.6% | 9.4% |
| L. Bergantini 2021 | 10 | 31.00 | 18.0000 | 14 | 22.00 | 8.7000 | 0.65 | [−0.18; 1.49] | 1.9% | 4.6% |
| M.d'Alessandro BS 2020 | 14 | 23.18 | 14.8300 | 40 | 24.42 | 10.7700 | −0.10 | [−0.71; 0.51] | 3.5% | 6.8% |
| K.Deng 2021 | 17 | 45.84 | 15.1200 | 149 | 37.96 | 14.7500 | 0.53 | [ 0.03; 1.04] | 5.1% | 8.1% |
| **Fixed effect model** | **463** | | | **1283** | | | **−0.33** | **[−0.44; −0.21]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **−0.20** | **[−0.42; 0.02]** | **−−** | **100.0%** |

Heterogeneity: $I^2$ = 63%, $\tau^2$ = 0.0877, $p$ < 0.01

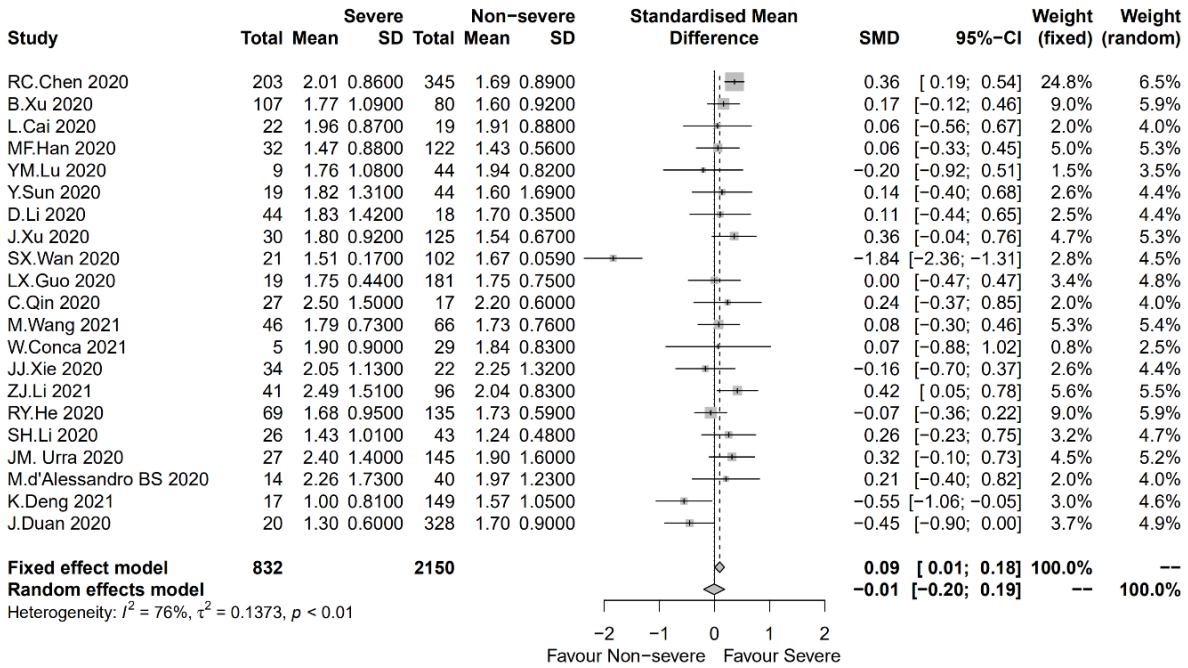


## Figure E2(A) (Continued)

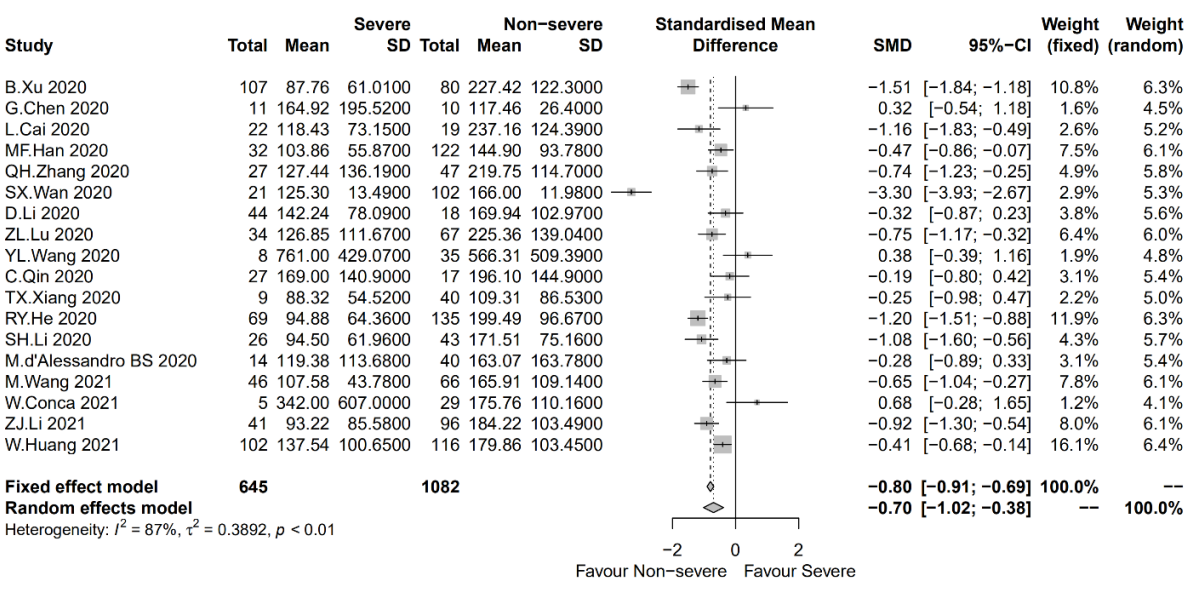
### (17) CD8+T(ab)




### (18) CD4+T/CD8+T ratio




### (19) B cell(ab)

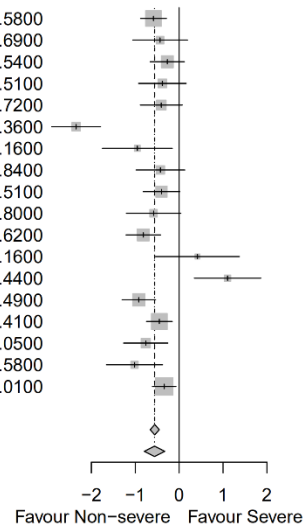


## Figure E2(A) (Continued)

### (20) NK cell (ab)

| Study | Severe Total | Mean | SD | Non−severe Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| B.Xu 2020 | 107 | 78.99 | 64.4800 | 80 | 113.67 | 50.5800 | −0.59 | [−0.88; −0.29] | 12.3% | 6.8% |
| L.Cai 2020 | 22 | 177.75 | 129.0200 | 19 | 244.50 | 172.6900 | −0.43 | [−1.06; 0.19] | 2.8% | 5.0% |
| MF.Han 2020 | 32 | 137.83 | 77.6000 | 122 | 169.36 | 124.5400 | −0.27 | [−0.66; 0.12] | 7.1% | 6.3% |
| Y.Sun 2020 | 19 | 146.10 | 142.5400 | 44 | 218.97 | 204.5100 | −0.38 | [−0.92; 0.16] | 3.7% | 5.4% |
| QH.Zhang 2020 | 27 | 161.94 | 213.6700 | 47 | 273.08 | 296.7200 | −0.41 | [−0.89; 0.07] | 4.7% | 5.8% |
| SX.Wan 2020 | 21 | 119.60 | 16.5000 | 102 | 147.00 | 10.3600 | −2.35 | [−2.90; −1.79] | 3.5% | 5.4% |
| YL.Wang 2020 | 8 | 134.26 | 216.2300 | 35 | 350.42 | 224.1600 | −0.95 | [−1.75; −0.16] | 1.7% | 4.1% |
| D.Li 2020 | 44 | 116.81 | 85.4200 | 18 | 152.90 | 78.8400 | −0.43 | [−0.98; 0.13] | 3.5% | 5.4% |
| ZL.Lu 2020 | 34 | 126.85 | 111.6700 | 67 | 197.33 | 197.5100 | −0.40 | [−0.82; 0.01] | 6.2% | 6.2% |
| C.Qin 2020 | 27 | 113.00 | 71.8000 | 17 | 160.20 | 90.8000 | −0.58 | [−1.20; 0.04] | 2.8% | 5.0% |
| M.Wang 2021 | 46 | 95.41 | 56.6100 | 66 | 169.65 | 107.6200 | −0.82 | [−1.21; −0.42] | 7.0% | 6.3% |
| W.Conca 2021 | 5 | 197.00 | 139.0000 | 29 | 148.14 | 110.1600 | 0.42 | [−0.54; 1.37] | 1.2% | 3.4% |
| TX.Xiang 2020 | 9 | 110.60 | 79.4300 | 40 | 69.79 | 17.4400 | 1.10 | [ 0.34; 1.86] | 1.9% | 4.3% |
| ZJ.Li 2021 | 41 | 93.22 | 85.5800 | 96 | 184.22 | 103.4900 | −0.92 | [−1.30; −0.54] | 7.4% | 6.4% |
| RY.He 2020 | 69 | 113.47 | 77.2300 | 135 | 156.65 | 103.4100 | −0.45 | [−0.74; −0.16] | 12.5% | 6.9% |
| SH.Li 2020 | 26 | 110.92 | 87.0600 | 43 | 204.44 | 138.0500 | −0.76 | [−1.26; −0.26] | 4.2% | 5.7% |
| M.d'Alessandro BS 2020 | 14 | 67.54 | 69.1900 | 40 | 151.07 | 84.5800 | −1.02 | [−1.66; −0.38] | 2.6% | 4.9% |
| W.Huang 2021 | 102 | 154.97 | 113.1800 | 116 | 195.10 | 121.0100 | −0.34 | [−0.61; −0.07] | 15.0% | 7.0% |
| **Fixed effect model** | **653** | | | **1116** | | | **−0.56** | **[−0.66; −0.45]** | **100.0%** | **--** |
| **Random effects model** | | | | | | | **−0.56** | **[−0.79; −0.33]** | **--** | **100.0%** |

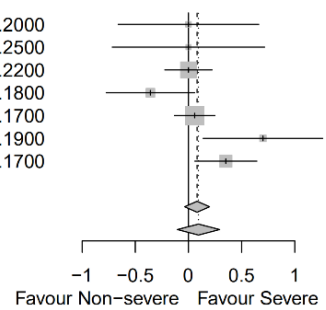
Heterogeneity: $I^2$ = 78%, $\tau^2$ = 0.1855, $p$ < 0.01




### (21) C3

| Study | Severe Total | Mean | SD | Non−severe Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| J.Liu 2020 | 13 | 0.80 | 0.1000 | 27 | 0.80 | 0.2000 | 0.00 | [−0.66; 0.66] | 3.2% | 7.0% |
| YM.Lu 2020 | 9 | 1.13 | 0.2700 | 44 | 1.13 | 0.2500 | 0.00 | [−0.72; 0.72] | 2.7% | 6.2% |
| ZH.Lv 2020 | 239 | 1.04 | 0.2200 | 115 | 1.04 | 0.2200 | 0.00 | [−0.22; 0.22] | 27.9% | 22.3% |
| ZL.Lu 2020 | 34 | 0.80 | 0.2200 | 67 | 0.87 | 0.1800 | −0.36 | [−0.77; 0.06] | 8.0% | 13.1% |
| C.Qin 2020 | 286 | 0.89 | 0.1700 | 166 | 0.88 | 0.1700 | 0.06 | [−0.13; 0.25] | 37.7% | 24.0% |
| D.Li 2020 | 44 | 1.03 | 0.1600 | 18 | 0.91 | 0.1900 | 0.70 | [ 0.14; 1.26] | 4.4% | 8.9% |
| RY.He 2020 | 69 | 0.90 | 0.1700 | 135 | 0.84 | 0.1700 | 0.35 | [ 0.06; 0.64] | 16.2% | 18.5% |
| **Fixed effect model** | **694** | | | **572** | | | **0.08** | **[−0.04; 0.20]** | **100.0%** | **--** |
| **Random effects model** | | | | | | | **0.09** | **[−0.10; 0.29]** | **--** | **100.0%** |

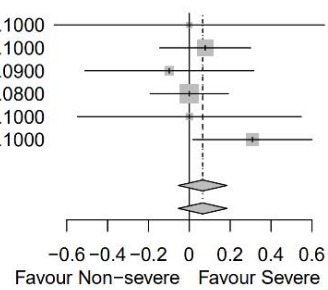
Heterogeneity: $I^2$ = 53%, $\tau^2$ = 0.0333, $p$ = 0.04




### (22) C4

| Study | Severe Total | Mean | SD | Non−severe Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| J.Liu 2020 | 13 | 0.30 | 0.1000 | 27 | 0.30 | 0.1000 | 0.00 | [−0.66; 0.66] | 3.2% | 3.2% |
| ZH.Lv 2020 | 239 | 0.26 | 0.1400 | 115 | 0.25 | 0.1000 | 0.08 | [−0.14; 0.30] | 28.5% | 28.5% |
| ZL.Lu 2020 | 34 | 0.23 | 0.1200 | 67 | 0.24 | 0.0900 | −0.10 | [−0.51; 0.31] | 8.3% | 8.3% |
| C.Qin 2020 | 286 | 0.26 | 0.0800 | 166 | 0.26 | 0.0800 | 0.00 | [−0.19; 0.19] | 38.6% | 38.6% |
| D.Li 2020 | 44 | 0.25 | 0.0800 | 18 | 0.25 | 0.1000 | 0.00 | [−0.55; 0.55] | 4.7% | 4.7% |
| RY.He 2020 | 69 | 0.26 | 0.0900 | 135 | 0.23 | 0.1000 | 0.31 | [ 0.02; 0.60] | 16.6% | 16.6% |
| **Fixed effect model** | **685** | | | **528** | | | **0.07** | **[−0.05; 0.18]** | **100.0%** | **--** |
| **Random effects model** | | | | | | | **0.07** | **[−0.05; 0.18]** | **--** | **100.0%** |

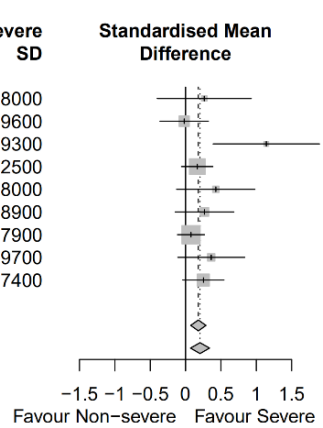
Heterogeneity: $I^2$ = 0%, $\tau^2$ = 0, $p$ = 0.57




### (23) IgA

| Study | Severe Total | Mean | SD | Non−severe Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| J.Liu 2020 | 13 | 2.40 | 0.6000 | 27 | 2.20 | 0.8000 | 0.26 | [−0.40; 0.93] | 2.7% | 3.8% |
| Y.Feng 2020 | 39 | 2.44 | 1.3200 | 214 | 2.46 | 0.9600 | −0.02 | [−0.36; 0.32] | 10.1% | 11.8% |
| YM.Lu 2020 | 9 | 3.57 | 1.7700 | 44 | 2.29 | 0.9300 | 1.14 | [ 0.39; 1.89] | 2.1% | 3.0% |
| ZH.Lv 2020 | 239 | 2.68 | 1.1000 | 115 | 2.49 | 1.2500 | 0.16 | [−0.06; 0.39] | 23.6% | 20.9% |
| D.Li 2020 | 44 | 2.49 | 1.1200 | 18 | 2.04 | 0.8000 | 0.43 | [−0.13; 0.98] | 3.8% | 5.3% |
| ZL.Lu 2020 | 34 | 2.32 | 0.6400 | 67 | 2.10 | 0.8900 | 0.27 | [−0.15; 0.68] | 6.8% | 8.7% |
| C.Qin 2020 | 286 | 2.24 | 0.9800 | 166 | 2.17 | 0.7900 | 0.08 | [−0.11; 0.27] | 32.0% | 24.6% |
| LX.Guo 2020 | 19 | 2.86 | 1.1600 | 181 | 2.50 | 0.9700 | 0.36 | [−0.11; 0.84] | 5.2% | 6.9% |
| RY.He 2020 | 69 | 2.13 | 1.0800 | 135 | 1.91 | 0.7400 | 0.25 | [−0.04; 0.54] | 13.8% | 14.9% |
| **Fixed effect model** | **752** | | | **967** | | | **0.18** | **[ 0.07; 0.29]** | **100.0%** | **--** |
| **Random effects model** | | | | | | | **0.20** | **[ 0.07; 0.34]** | **--** | **100.0%** |

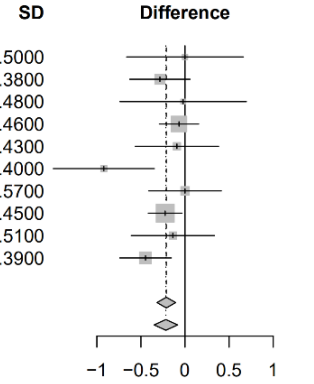
Heterogeneity: $I^2$ = 24%, $\tau^2$ = 0.0097, $p$ = 0.23




### (24) IgM

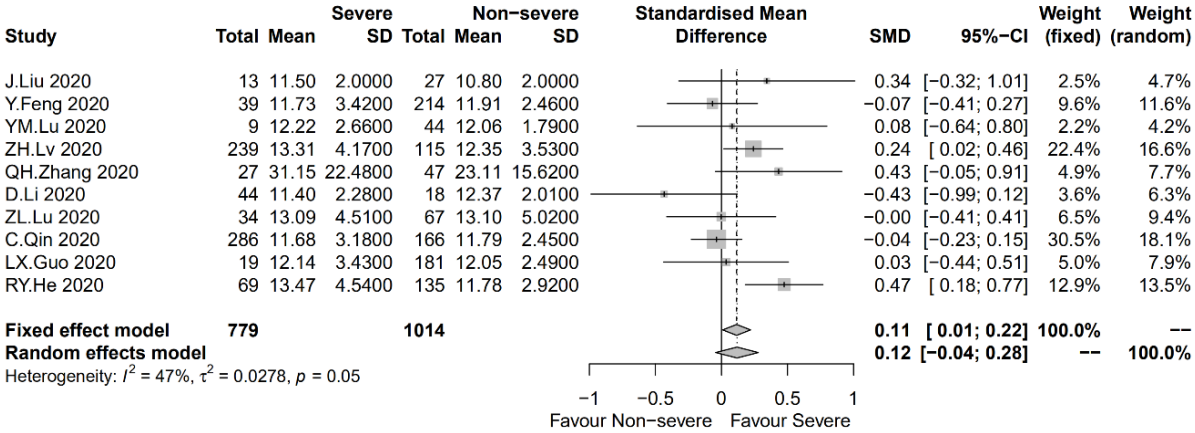
| Study | Severe Total | Mean | SD | Non−severe Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| J.Liu 2020 | 13 | 1.10 | 0.3000 | 27 | 1.10 | 0.5000 | 0.00 | [−0.66; 0.66] | 2.5% | 3.7% |
| Y.Feng 2020 | 39 | 0.84 | 0.4100 | 214 | 0.95 | 0.3800 | −0.29 | [−0.63; 0.06] | 9.5% | 11.1% |
| YM.Lu 2020 | 9 | 1.05 | 0.4400 | 44 | 1.06 | 0.4800 | −0.02 | [−0.74; 0.70] | 2.2% | 3.2% |
| ZH.Lv 2020 | 239 | 0.98 | 0.4300 | 115 | 1.01 | 0.4600 | −0.07 | [−0.29; 0.15] | 22.5% | 19.3% |
| QH.Zhang 2020 | 27 | 1.63 | 1.6500 | 47 | 1.77 | 1.4300 | −0.09 | [−0.57; 0.38] | 5.0% | 6.7% |
| D.Li 2020 | 44 | 0.85 | 0.3500 | 18 | 1.19 | 0.4000 | −0.92 | [−1.49; −0.35] | 3.4% | 4.8% |
| ZL.Lu 2020 | 34 | 1.17 | 0.5300 | 67 | 1.17 | 0.5700 | 0.00 | [−0.41; 0.41] | 6.6% | 8.4% |
| C.Qin 2020 | 286 | 0.96 | 0.4400 | 166 | 1.06 | 0.4500 | −0.23 | [−0.42; −0.03] | 30.3% | 22.3% |
| LX.Guo 2020 | 19 | 0.95 | 0.4800 | 181 | 1.02 | 0.5100 | −0.14 | [−0.61; 0.34] | 5.0% | 6.7% |
| RY.He 2020 | 69 | 0.94 | 0.4200 | 135 | 1.12 | 0.3900 | −0.45 | [−0.74; −0.15] | 13.0% | 13.8% |
| **Fixed effect model** | **779** | | | **1014** | | | **−0.21** | **[−0.32; −0.11]** | **100.0%** | **--** |
| **Random effects model** | | | | | | | **−0.22** | **[−0.35; −0.08]** | **--** | **100.0%** |

Heterogeneity: $I^2$ = 26%, $\tau^2$ = 0.0112, $p$ = 0.20



## Figure E2(A) (Continued)

### (25) IgG




### (26) IgE

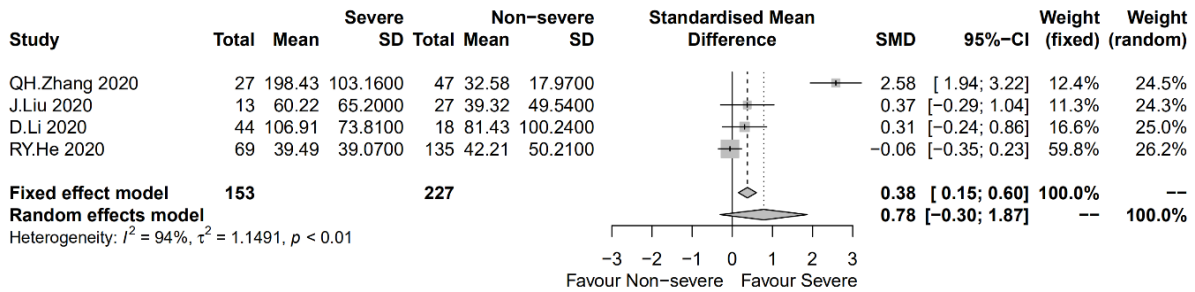
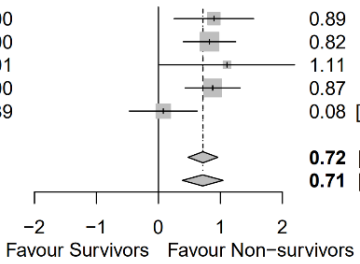


**Figure E2(B) Forest plot of immunological parameters in non-survivors and survivors of COVID-19**

**(1) IL-1β**

| Study | Non-survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%-CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| FF.Sai 2021 | 15 | 12.31 | 17.7500 | 32 | 3.18 | 1.9400 | 0.89 | [ 0.25; 1.54] | 14.1% | 17.3% |
| B.Xu 2020 | 28 | 6.67 | 3.8700 | 117 | 5.20 | 0.6300 | 0.82 | [ 0.40; 1.25] | 32.3% | 27.6% |
| H.Huang 2020 | 4 | 13.33 | 22.8000 | 27 | 5.00 | 0.0001 | 1.11 | [ 0.02; 2.20] | 4.9% | 7.7% |
| E.Sozio 2021 | 28 | 0.54 | 0.4800 | 83 | 0.28 | 0.2000 | 0.87 | [ 0.43; 1.32] | 29.4% | 26.4% |
| KY.Li 2020 | 15 | 4.46 | 0.7361 | 87 | 4.34 | 1.7339 | 0.08 | [−0.47; 0.63] | 19.3% | 21.1% |
| **Fixed effect model** | **90** | | | **346** | | | **0.72** | **[ 0.48; 0.96]** | **100.0%** | -- |
| **Random effects model** | | | | | | | **0.71** | **[ 0.39; 1.04]** | -- | **100.0%** |

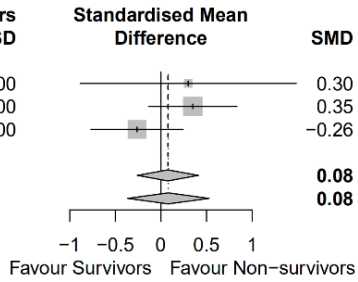
Heterogeneity: $I^2$ = 41%, $\tau^2$ = 0.0550, $p$ = 0.15




**(2) IL-2**

| Study | Non-survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%-CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| L.Cai 2020 | 4 | 22.52 | 7.3200 | 9 | 20.70 | 4.9000 | 0.30 | [−0.89; 1.48] | 8.0% | 12.4% |
| XB.Feng 2020 | 20 | 2.92 | 0.9500 | 94 | 2.73 | 0.4100 | 0.35 | [−0.14; 0.83] | 47.9% | 44.8% |
| Jun. Zhang 2020 | 18 | 2.47 | 0.3200 | 93 | 2.55 | 0.3000 | −0.26 | [−0.77; 0.24] | 44.0% | 42.8% |
| **Fixed effect model** | **42** | | | **196** | | | **0.08** | **[−0.26; 0.41]** | **100.0%** | -- |
| **Random effects model** | | | | | | | **0.08** | **[−0.37; 0.53]** | -- | **100.0%** |

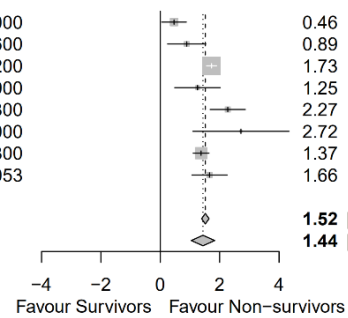
Heterogeneity: $I^2$ = 35%, $\tau^2$ = 0.0550, $p$ = 0.22




**(3) IL-2R**

| Study | Non-survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%-CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| J.Zhang 2021 | 26 | 1028.64 | 851.5500 | 182 | 773.81 | 493.2000 | 0.46 | [0.05; 0.88] | 9.1% | 14.7% |
| FF.Sai 2021 | 15 | 2428.15 | 3045.8400 | 32 | 783.07 | 775.2600 | 0.89 | [0.25; 1.53] | 3.8% | 12.0% |
| M.Luo 2021 | 201 | 1092.35 | 564.7900 | 817 | 478.17 | 280.8200 | 1.73 | [1.56; 1.90] | 53.0% | 17.0% |
| YL.Yan 2020 | 39 | 1259.88 | 556.4600 | 9 | 572.96 | 442.5900 | 1.25 | [0.48; 2.03] | 2.6% | 10.5% |
| Y.Huang 2020 | 15 | 1244.32 | 571.7100 | 136 | 504.56 | 286.2300 | 2.27 | [1.68; 2.87] | 4.4% | 12.6% |
| H.Huang 2020 | 2 | 1729.50 | 1602.5000 | 27 | 558.11 | 289.2000 | 2.72 | [1.10; 4.34] | 0.6% | 4.4% |
| T.Chen 2020 | 113 | 1295.92 | 660.8300 | 161 | 627.36 | 306.9300 | 1.37 | [1.11; 1.64] | 21.9% | 16.2% |
| KY.Li 2020 | 15 | 1295.11 | 727.6802 | 87 | 582.70 | 353.4053 | 1.66 | [1.06; 2.25] | 4.4% | 12.6% |
| **Fixed effect model** | **426** | | | **1451** | | | **1.52** | **[1.39; 1.64]** | **100.0%** | -- |
| **Random effects model** | | | | | | | **1.44** | **[1.04; 1.83]** | -- | **100.0%** |

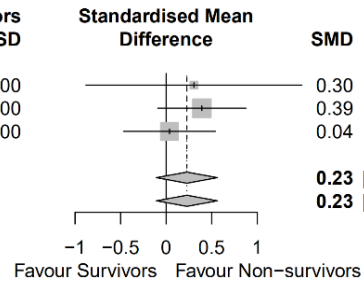
Heterogeneity: $I^2$ = 84%, $\tau^2$ = 0.2330, $p$ < 0.01




**(4) IL-4**

| Study | Non-survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%-CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| L.Cai 2020 | 4 | 9.08 | 2.5100 | 9 | 8.41 | 1.8400 | 0.30 | [−0.88; 1.49] | 8.0% | 8.0% |
| XB.Feng 2020 | 20 | 2.48 | 1.4500 | 94 | 2.19 | 0.4700 | 0.39 | [−0.09; 0.88] | 47.8% | 47.8% |
| Jun.Zhang 2020 | 18 | 1.97 | 0.5000 | 93 | 1.95 | 0.5400 | 0.04 | [−0.47; 0.54] | 44.2% | 44.2% |
| **Fixed effect model** | **42** | | | **196** | | | **0.23** | **[−0.11; 0.56]** | **100.0%** | -- |
| **Random effects model** | | | | | | | **0.23** | **[−0.11; 0.56]** | -- | **100.0%** |

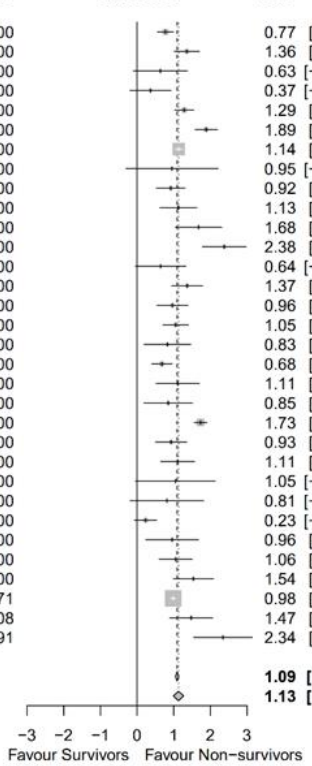
Heterogeneity: $I^2$ = 0%, $\tau^2$ = 0, $p$ = 0.61




**(5) IL-6**

| Study | Non-survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%-CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| RC.Chen 2020 | 103 | 10.19 | 4.2700 | 445 | 7.58 | 3.1200 | 0.77 | [ 0.56; 0.99] | 4.3% | 4.4% |
| F.Zhou 2020 | 54 | 10.96 | 5.2600 | 137 | 6.40 | 2.1800 | 1.36 | [ 1.01; 1.70] | 1.7% | 3.8% |
| YL.Yan 2020 | 39 | 74.70 | 85.3600 | 9 | 23.87 | 32.5000 | 0.63 | [−0.10; 1.37] | 0.4% | 2.1% |
| TL.Chen 2020 | 19 | 217.33 | 330.8100 | 36 | 119.91 | 216.9500 | 0.37 | [−0.19; 0.93] | 0.7% | 2.8% |
| T.Chen 2020 | 113 | 85.51 | 83.5000 | 161 | 14.48 | 16.6000 | 1.29 | [ 1.02; 1.55] | 2.9% | 4.2% |
| L.Wang 2020 | 65 | 104.60 | 110.9900 | 274 | 11.44 | 10.3500 | 1.89 | [ 1.58; 2.19] | 2.2% | 4.0% |
| DJ.Altschul 2020 | 621 | 103.71 | 101.8700 | 1733 | 35.03 | 35.1700 | 1.14 | [ 1.04; 1.23] | 21.7% | 4.8% |
| L.Cai 2020 | 4 | 988.14 | 1799.7100 | 9 | 25.09 | 32.5400 | 0.95 | [−0.30; 2.21] | 0.1% | 1.0% |
| F.Ciceri 2020 | 34 | 110.51 | 115.7800 | 121 | 47.76 | 46.8900 | 0.92 | [ 0.52; 1.31] | 1.3% | 3.6% |
| XB.Feng 2020 | 20 | 97.59 | 138.6900 | 94 | 25.59 | 30.4000 | 1.13 | [ 0.62; 1.63] | 0.8% | 3.1% |
| H.Yang 2020 | 13 | 96.17 | 105.5000 | 81 | 19.13 | 26.7100 | 1.68 | [ 1.04; 2.31] | 0.5% | 2.5% |
| Y.Huang 2020 | 15 | 92.10 | 119.0000 | 136 | 4.04 | 5.4000 | 2.38 | [ 1.78; 2.98] | 0.6% | 2.7% |
| S.Hue 2020 | 13 | 5.50 | 0.7000 | 25 | 4.90 | 1.0000 | 0.64 | [−0.04; 1.33] | 0.4% | 2.3% |
| Yang.Zhao 2020 | 33 | 75.66 | 100.4600 | 102 | 7.67 | 5.6300 | 1.37 | [ 0.94; 1.79] | 1.1% | 3.4% |
| Jing.Zhang 2021 | 26 | 44.39 | 39.0600 | 182 | 18.48 | 24.5900 | 0.96 | [ 0.54; 1.39] | 1.2% | 3.5% |
| ZG.Wang 2021 | 56 | 101.83 | 154.3900 | 100 | 3.99 | 4.4400 | 1.05 | [ 0.71; 1.40] | 1.7% | 3.8% |
| FF.Sai 2021 | 15 | 1391.25 | 2892.4800 | 32 | 31.62 | 38.5300 | 0.83 | [ 0.19; 1.47] | 0.5% | 2.5% |
| G.Li 2021 | 95 | 19.04 | 21.0800 | 116 | 9.06 | 5.2500 | 0.68 | [ 0.40; 0.96] | 2.6% | 4.2% |
| L.García de Guadiana− Romualdo 2021 | 14 | 101.75 | 106.8400 | 85 | 40.40 | 41.4000 | 1.11 | [ 0.52; 1.70] | 0.6% | 2.7% |
| P.Sinha 2020 | 17 | 572.67 | 687.1200 | 22 | 169.10 | 147.4000 | 0.85 | [ 0.19; 1.51] | 0.5% | 2.4% |
| M.Luo 2021 | 201 | 73.70 | 83.0500 | 817 | 7.97 | 10.0500 | 1.73 | [ 1.56; 1.90] | 7.0% | 4.6% |
| B.Xu 2020 | 28 | 36.54 | 38.5000 | 117 | 15.33 | 17.0800 | 0.93 | [ 0.50; 1.35] | 1.1% | 3.4% |
| CM.Wu 2020 | 44 | 10.79 | 5.7000 | 40 | 6.05 | 1.4400 | 1.11 | [ 0.65; 1.57] | 1.0% | 3.3% |
| H.Huang 2020 | 4 | 23.24 | 9.6800 | 27 | 9.81 | 12.7600 | 1.05 | [−0.04; 2.13] | 0.2% | 1.3% |
| R.Zayat 2021 | 8 | 625.44 | 761.8000 | 9 | 165.25 | 181.0500 | 0.81 | [−0.19; 1.82] | 0.2% | 1.4% |
| CT.Yang 2021 | 58 | 10.74 | 4.3300 | 145 | 9.57 | 5.3200 | 0.23 | [−0.07; 0.54] | 2.2% | 4.0% |
| R.Scotto 2021 | 15 | 756.09 | 1119.2900 | 19 | 30.26 | 43.5700 | 0.96 | [ 0.24; 1.68] | 0.4% | 2.2% |
| E.Sozio 2021 | 28 | 449.35 | 798.3400 | 83 | 25.92 | 35.3100 | 1.06 | [ 0.60; 1.51] | 1.0% | 3.3% |
| Jun.Zhang 2020 | 18 | 44.02 | 61.1000 | 93 | 6.04 | 4.9400 | 1.54 | [ 0.99; 2.08] | 0.7% | 2.9% |
| J.Berenguer 2020 | 1131 | 228.35 | 350.3455 | 2904 | 41.40 | 47.4671 | 0.98 | [ 0.91; 1.06] | 39.6% | 4.9% |
| KY.Li 2020 | 15 | 73.77 | 115.7320 | 87 | 7.69 | 10.9308 | 1.47 | [ 0.89; 2.06] | 0.6% | 2.7% |
| T.Li 2021 | 9 | 73.30 | 85.0976 | 63 | 4.28 | 4.9391 | 2.34 | [ 1.54; 3.14] | 0.3% | 1.9% |
| **Fixed effect model** | **2928** | | | **8304** | | | **1.09** | **[ 1.05; 1.14]** | **100.0%** | -- |
| **Random effects model** | | | | | | | **1.13** | **[ 0.99; 1.27]** | -- | **100.0%** |

Heterogeneity: $I^2$ = 84%, $\tau^2$ = 0.1074, $p$ < 0.01

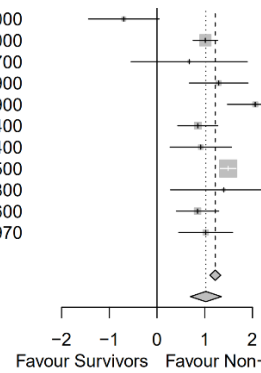


## Figure E2(B) (Continued)

### (6) IL-8

| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| YL.Yan 2020 | 39 | 32.34 | 28.5500 | 9 | 82.30 | 157.2000 | −0.70 | [−1.44; 0.04] | 2.4% | 7.8% |
| T.Chen 2020 | 113 | 40.33 | 40.1000 | 161 | 13.23 | 9.3000 | 1.01 | [ 0.76; 1.27] | 20.1% | 12.2% |
| L.Cai 2020 | 4 | 164.62 | 385.7100 | 9 | 18.29 | 18.3700 | 0.67 | [−0.54; 1.89] | 0.9% | 4.6% |
| H.Yang 2020 | 13 | 32.90 | 30.1000 | 81 | 13.60 | 10.7900 | 1.29 | [ 0.68; 1.91] | 3.5% | 8.9% |
| Y.Huang 2020 | 15 | 39.00 | 34.6800 | 136 | 11.84 | 8.0900 | 2.06 | [ 1.48; 2.64] | 3.9% | 9.2% |
| Jing.Zhang 2021 | 26 | 25.71 | 24.0000 | 182 | 14.98 | 9.9400 | 0.85 | [ 0.43; 1.27] | 7.5% | 10.8% |
| FF.Sai 2021 | 15 | 37.27 | 41.7100 | 32 | 13.78 | 11.6400 | 0.92 | [ 0.27; 1.56] | 3.2% | 8.7% |
| M.Luo 2021 | 201 | 35.39 | 29.5900 | 817 | 13.11 | 7.9500 | 1.49 | [ 1.32; 1.66] | 46.8% | 12.7% |
| H.Huang 2020 | 4 | 34.23 | 46.3000 | 27 | 10.69 | 7.2800 | 1.40 | [ 0.28; 2.51] | 1.1% | 5.2% |
| E.Sozio 2021 | 28 | 43.78 | 25.4700 | 83 | 28.16 | 15.1600 | 0.85 | [ 0.41; 1.29] | 6.7% | 10.6% |
| KY.Li 2020 | 15 | 21.42 | 11.7777 | 87 | 11.55 | 9.1970 | 1.02 | [ 0.45; 1.59] | 4.1% | 9.4% |
| **Fixed effect model** | **473** | | | **1624** | | | **1.22** | **[ 1.11; 1.34]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **1.02** | **[ 0.70; 1.35]** | **−−** | **100.0%** |

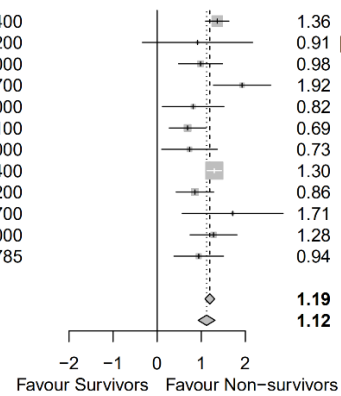
Heterogeneity: $I^2$ = 82%, $\tau^2$ = 0.2085, $p$ < 0.01




### (7) IL-10

| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| T.Chen 2020 | 113 | 13.78 | 8.1100 | 161 | 6.19 | 2.5400 | 1.36 | [ 1.10; 1.63] | 17.3% | 14.8% |
| L.Cai 2020 | 4 | 21.78 | 20.4200 | 9 | 10.93 | 3.3200 | 0.91 | [−0.34; 2.17] | 0.8% | 2.1% |
| XB.Feng 2020 | 20 | 7.73 | 5.7400 | 94 | 4.83 | 1.9000 | 0.98 | [ 0.48; 1.48] | 4.9% | 8.6% |
| H.Yang 2020 | 13 | 11.66 | 9.2100 | 81 | 5.17 | 0.3700 | 1.92 | [ 1.28; 2.57] | 2.9% | 6.1% |
| S.Hue 2020 | 13 | 503.70 | 116.5000 | 25 | 397.10 | 133.1000 | 0.82 | [ 0.12; 1.51] | 2.5% | 5.5% |
| J.Zhang 2021 | 26 | 10.28 | 10.9000 | 182 | 6.93 | 3.2100 | 0.69 | [ 0.27; 1.11] | 7.1% | 10.5% |
| FF.Sai 2021 | 15 | 10.59 | 11.4500 | 32 | 5.07 | 4.5000 | 0.73 | [ 0.10; 1.37] | 3.1% | 6.3% |
| M.Luo 2021 | 201 | 10.36 | 7.6200 | 817 | 5.71 | 1.3400 | 1.30 | [ 1.13; 1.46] | 45.5% | 18.0% |
| B.Xu 2020 | 28 | 14.16 | 13.2700 | 117 | 7.76 | 5.2200 | 0.86 | [ 0.43; 1.28] | 6.8% | 10.3% |
| H.Huang 2020 | 4 | 34.25 | 49.4400 | 27 | 6.04 | 2.2700 | 1.71 | [ 0.57; 2.86] | 0.9% | 2.5% |
| J.Zhang 2020 | 18 | 5.93 | 2.7000 | 93 | 4.04 | 1.1000 | 1.28 | [ 0.74; 1.81] | 4.3% | 7.9% |
| KY.Li 2020 | 15 | 6.42 | 4.9074 | 87 | 4.58 | 0.6785 | 0.94 | [ 0.38; 1.51] | 3.9% | 7.4% |
| **Fixed effect model** | **470** | | | **1725** | | | **1.19** | **[ 1.08; 1.30]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **1.12** | **[ 0.93; 1.31]** | **−−** | **100.0%** |

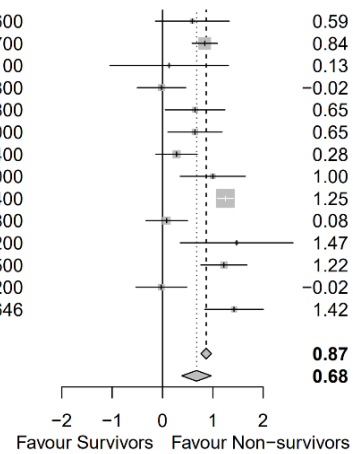
Heterogeneity: $I^2$ = 49%, $\tau^2$ = 0.0456, $p$ = 0.03




### (8) TNF-α

| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| YL.Yan 2020 | 39 | 13.51 | 8.9300 | 9 | 8.45 | 5.1600 | 0.59 | [−0.14; 1.33] | 2.0% | 6.1% |
| T.Chen 2020 | 113 | 12.71 | 6.7600 | 161 | 8.80 | 2.1700 | 0.84 | [ 0.59; 1.09] | 17.1% | 9.1% |
| L.Cai 2020 | 4 | 8.06 | 0.8700 | 9 | 7.81 | 2.0100 | 0.13 | [−1.05; 1.31] | 0.8% | 3.8% |
| XB.Feng 2020 | 20 | 3.17 | 2.0700 | 94 | 3.21 | 2.0300 | −0.02 | [−0.50; 0.46] | 4.6% | 7.7% |
| H.Yang 2020 | 13 | 12.57 | 8.4700 | 81 | 8.94 | 4.9800 | 0.65 | [ 0.05; 1.24] | 3.1% | 7.0% |
| Y.Huang 2020 | 15 | 10.95 | 3.1100 | 136 | 8.64 | 3.6000 | 0.65 | [ 0.11; 1.18] | 3.7% | 7.3% |
| Jing.Zhang 2021 | 26 | 11.61 | 7.1400 | 182 | 10.34 | 4.0400 | 0.28 | [−0.13; 0.69] | 6.3% | 8.2% |
| FF.Sai 2021 | 15 | 26.56 | 28.3000 | 32 | 10.07 | 4.5000 | 1.00 | [ 0.35; 1.65] | 2.6% | 6.6% |
| M.Luo 2021 | 201 | 11.74 | 7.4700 | 817 | 7.01 | 2.0400 | 1.25 | [ 1.09; 1.41] | 40.2% | 9.5% |
| B.Xu 2020 | 28 | 12.52 | 3.5200 | 117 | 12.06 | 5.8800 | 0.08 | [−0.33; 0.50] | 6.3% | 8.2% |
| H.Huang 2020 | 4 | 26.14 | 37.7600 | 27 | 7.40 | 2.6200 | 1.47 | [ 0.35; 2.59] | 0.9% | 4.0% |
| E.Sozio 2021 | 28 | 24.27 | 10.7800 | 83 | 15.96 | 4.7500 | 1.22 | [ 0.76; 1.68] | 5.1% | 7.9% |
| Jun.Zhang 2020 | 18 | 2.07 | 0.3500 | 93 | 2.08 | 0.4200 | −0.02 | [−0.53; 0.48] | 4.2% | 7.6% |
| KY.Li 2020 | 15 | 15.03 | 12.2684 | 87 | 7.44 | 2.8646 | 1.42 | [ 0.84; 2.00] | 3.2% | 7.0% |
| **Fixed effect model** | **539** | | | **1928** | | | **0.87** | **[ 0.76; 0.97]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **0.68** | **[ 0.38; 0.97]** | **−−** | **100.0%** |

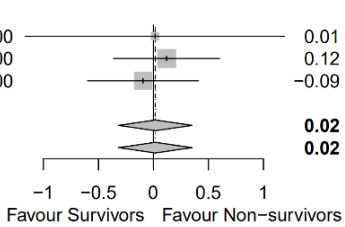
Heterogeneity: $I^2$ = 83%, $\tau^2$ = 0.2296, $p$ < 0.01




### (9) IFN-γ

| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| L.Cai 2020 | 4 | 11.80 | 4.7000 | 9 | 11.75 | 2.4500 | 0.01 | [−1.16; 1.19] | 8.1% | 8.1% |
| XB.Feng 2020 | 20 | 2.66 | 1.2800 | 94 | 2.54 | 0.9300 | 0.12 | [−0.36; 0.60] | 48.0% | 48.0% |
| Jun.Zhang 2020 | 18 | 2.09 | 0.3600 | 93 | 2.14 | 0.5500 | −0.09 | [−0.60; 0.41] | 43.9% | 43.9% |
| **Fixed effect model** | **42** | | | **196** | | | **0.02** | **[−0.32; 0.35]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **0.02** | **[−0.32; 0.35]** | **−−** | **100.0%** |

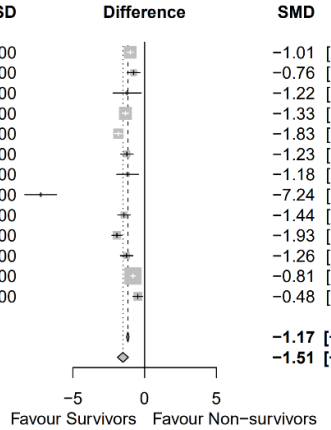
Heterogeneity: $I^2$ = 0%, $\tau^2$ = 0, $p$ = 0.84




### (10) CD3+T(ab)

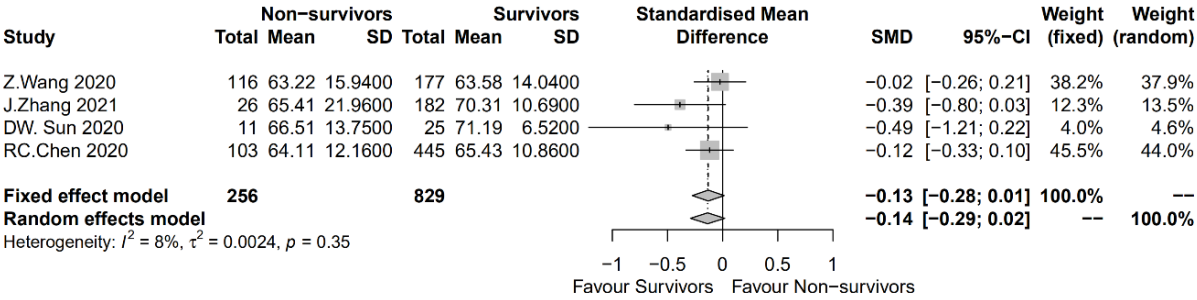
| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| RC.Chen 2020 | 103 | 298.29 | 147.7500 | 445 | 664.45 | 397.1500 | −1.01 | [−1.23; −0.78] | 14.8% | 8.6% |
| CM.Wu 2020 | 44 | 314.33 | 173.2000 | 40 | 536.21 | 375.6200 | −0.76 | [−1.21; −0.32] | 3.7% | 7.9% |
| L.Cai 2020 | 7 | 618.00 | 322.0000 | 15 | 974.40 | 261.0000 | −1.22 | [−2.20; −0.24] | 0.8% | 5.6% |
| Yang.Zhao 2020 | 125 | 290.89 | 199.8800 | 414 | 805.59 | 425.5200 | −1.33 | [−1.55; −1.12] | 15.8% | 8.6% |
| Z.Wang 2020 | 116 | 288.35 | 164.7800 | 177 | 796.48 | 329.9900 | −1.83 | [−2.11; −1.55] | 9.5% | 8.5% |
| B.Xu 2020 | 28 | 164.00 | 106.6300 | 117 | 463.29 | 262.7100 | −1.23 | [−1.67; −0.80] | 3.8% | 8.0% |
| DW.Sun 2020 | 11 | 698.46 | 393.6800 | 25 | 1089.68 | 290.1500 | −1.18 | [−1.95; −0.41] | 1.3% | 6.5% |
| J.Wang 2020 | 16 | 168.71 | 27.5300 | 93 | 369.89 | 27.6200 | −7.24 | [−8.35; −6.12] | 0.6% | 5.1% |
| Jing.Zhang 2021 | 26 | 329.49 | 212.7100 | 182 | 971.24 | 468.1600 | −1.44 | [−1.87; −1.00] | 3.9% | 8.0% |
| LK.Xiong 2021 | 85 | 302.81 | 177.6000 | 105 | 1091.50 | 522.6100 | −1.93 | [−2.28; −1.59] | 6.1% | 8.3% |
| WD.Qin 2021 | 23 | 282.30 | 212.5600 | 239 | 770.61 | 399.7700 | −1.26 | [−1.70; −0.82] | 3.8% | 7.9% |
| M.Luo 2021 | 201 | 385.94 | 180.3400 | 817 | 630.69 | 325.2600 | −0.81 | [−0.97; −0.65] | 29.3% | 8.7% |
| ZG.Wang 2021 | 56 | 64.11 | 12.7800 | 100 | 69.72 | 11.0600 | −0.48 | [−0.81; −0.15] | 6.7% | 8.3% |
| **Fixed effect model** | **841** | | | **2769** | | | **−1.17** | **[−1.25; −1.08]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **−1.51** | **[−1.89; −1.13]** | **−−** | **100.0%** |

Heterogeneity: $I^2$ = 94%, $\tau^2$ = 0.4263, $p$ < 0.01

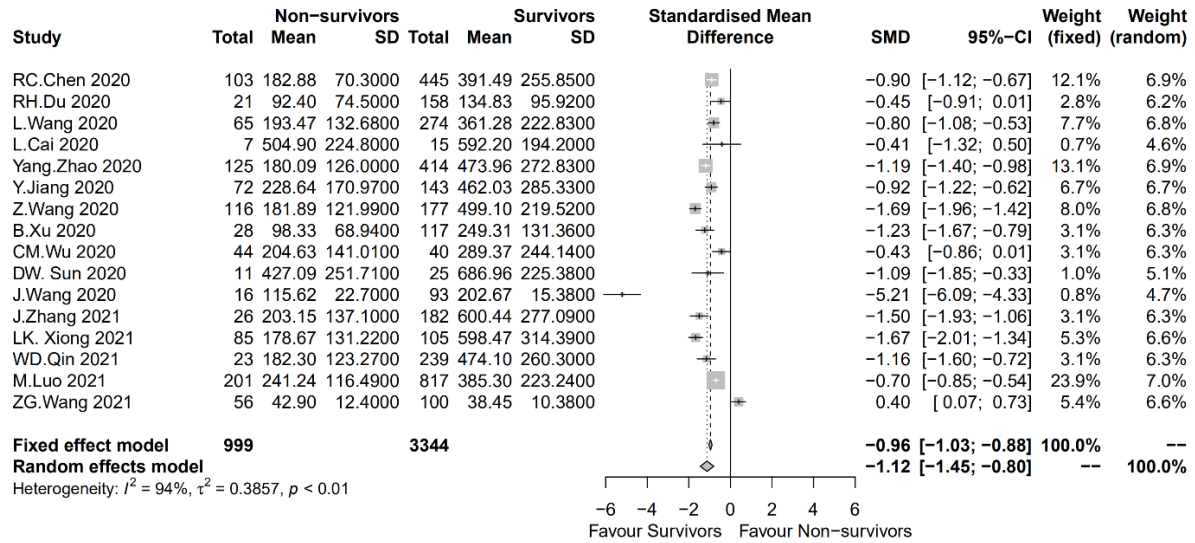


## Figure E2(B) (Continued)

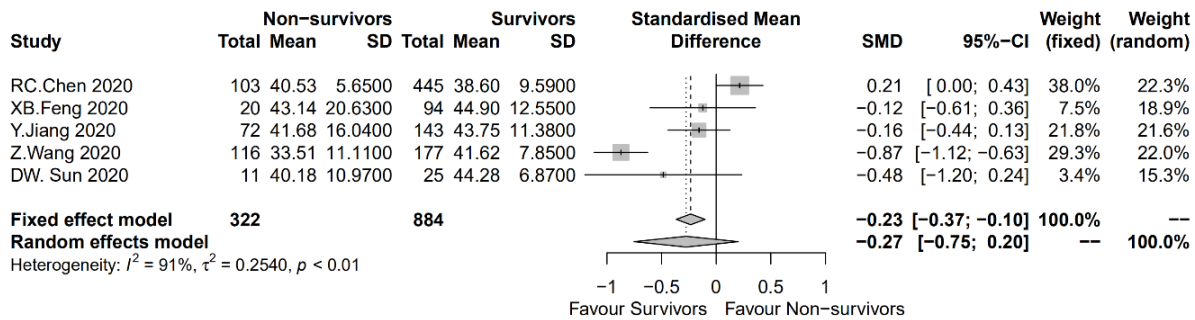
### (11) CD3(%)



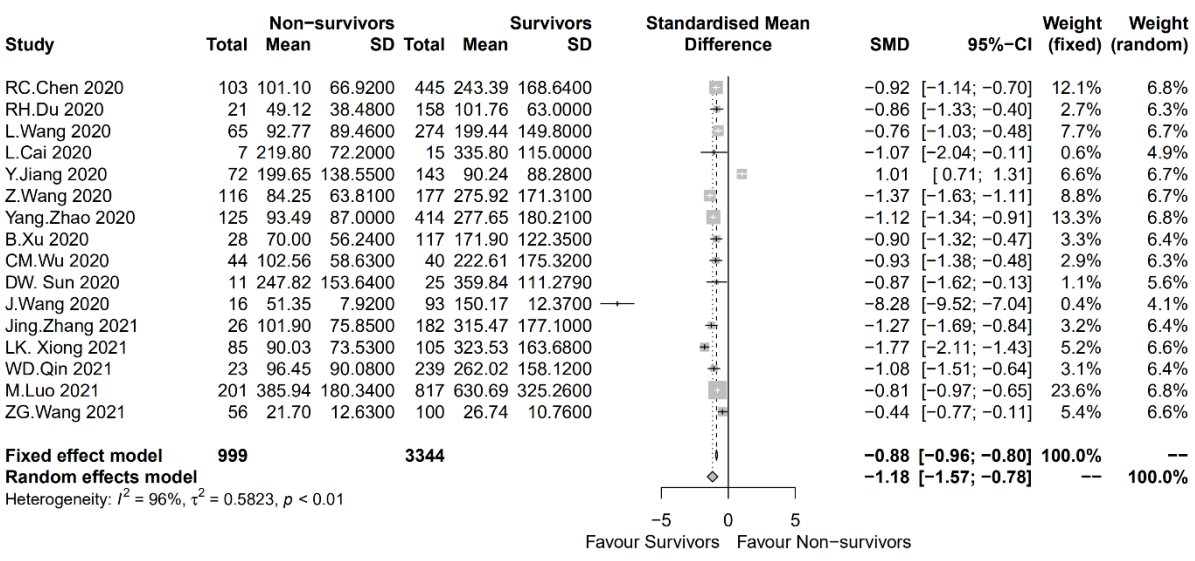

### (12) CD4+T(ab)



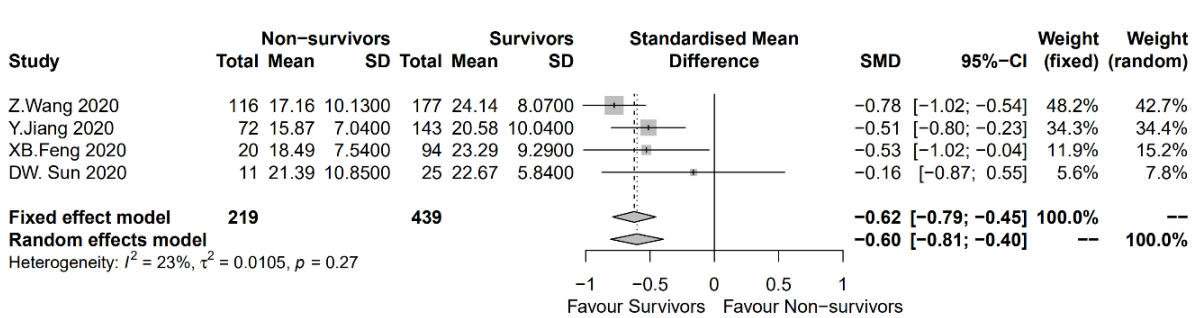

### (13) CD4+T(%)




### (14) CD8+T(ab)




### (15) CD8+T(%)

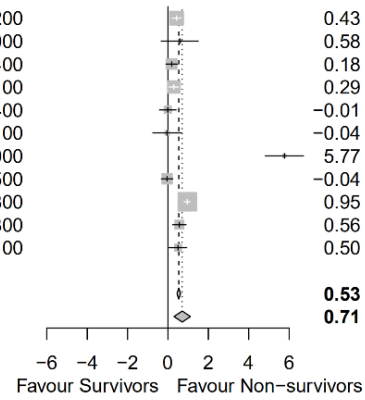


## Figure E2(B) (Continued)

### (16) CD4+T/CD8+T ratio

| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| RC.Chen 2020 | 103 | 2.10 | 0.7500 | 445 | 1.72 | 0.9200 | 0.43 | [ 0.21; 0.64] | 16.8% | 10.1% |
| L.Cai 2020 | 7 | 2.35 | 0.5500 | 15 | 1.86 | 0.9000 | 0.58 | [−0.34; 1.50] | 0.9% | 6.8% |
| Y.Jiang 2020 | 72 | 2.69 | 1.5400 | 143 | 2.41 | 1.5400 | 0.18 | [−0.10; 0.46] | 9.7% | 9.9% |
| Z.Wang 2020 | 116 | 2.09 | 1.3700 | 177 | 1.79 | 0.7100 | 0.29 | [ 0.06; 0.53] | 14.1% | 10.0% |
| B.Xu 2020 | 28 | 1.69 | 0.8000 | 117 | 1.70 | 1.1400 | −0.01 | [−0.42; 0.40] | 4.6% | 9.4% |
| DW. Sun 2020 | 11 | 1.96 | 0.9100 | 25 | 1.99 | 0.6100 | −0.04 | [−0.75; 0.67] | 1.6% | 7.9% |
| J.Wang 2020 | 16 | 2.45 | 0.3200 | 93 | 1.57 | 0.1000 | 5.77 | [ 4.82; 6.71] | 0.9% | 6.7% |
| LK. Xiong 2021 | 85 | 1.97 | 1.3500 | 105 | 2.03 | 1.4500 | −0.04 | [−0.33; 0.24] | 9.6% | 9.9% |
| M.Luo 2021 | 201 | 2.51 | 1.1900 | 817 | 1.74 | 0.6800 | 0.95 | [ 0.79; 1.11] | 30.6% | 10.2% |
| ZG.Wang 2021 | 56 | 2.33 | 2.0500 | 100 | 1.54 | 0.8300 | 0.56 | [ 0.23; 0.90] | 7.0% | 9.7% |
| E.Sozio 2021 | 28 | 2.77 | 1.8700 | 83 | 2.07 | 1.2100 | 0.50 | [ 0.06; 0.93] | 4.2% | 9.3% |
| **Fixed effect model** | **723** | | | **2120** | | | **0.53** | **[ 0.45; 0.62]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **0.71** | **[ 0.30; 1.11]** | **−−** | **100.0%** |

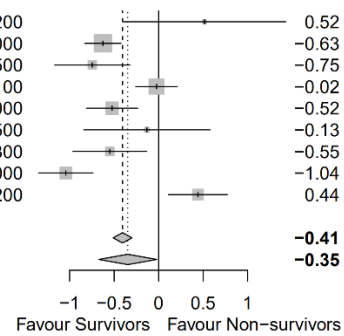
Heterogeneity: $I^2$ = 94%, $\tau^2$ = 0.4186, $p$ < 0.01




### (17) B cell(ab)

| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| L.Cai 2020 | 7 | 220.96 | 323.5100 | 15 | 119.36 | 79.4200 | 0.52 | [−0.40; 1.43] | 1.3% | 6.6% |
| Yang.Zhao 2020 | 125 | 97.49 | 74.2500 | 414 | 152.57 | 91.5000 | −0.63 | [−0.83; −0.42] | 27.1% | 13.1% |
| B.Xu 2020 | 28 | 61.32 | 50.3800 | 117 | 108.85 | 66.0500 | −0.75 | [−1.17; −0.32] | 6.3% | 11.2% |
| Z.Wang 2020 | 116 | 134.85 | 67.1900 | 177 | 136.82 | 95.1100 | −0.02 | [−0.26; 0.21] | 20.5% | 12.8% |
| Y.Jiang 2020 | 72 | 102.76 | 80.9500 | 143 | 152.51 | 101.1000 | −0.52 | [−0.81; −0.24] | 13.6% | 12.4% |
| DW. Sun 2020 | 11 | 133.68 | 120.4500 | 25 | 144.72 | 59.7500 | −0.13 | [−0.84; 0.58] | 2.2% | 8.3% |
| Jing.Zhang 2021 | 26 | 47.50 | 51.7700 | 182 | 79.56 | 59.0300 | −0.55 | [−0.96; −0.13] | 6.5% | 11.2% |
| LK. Xiong 2021 | 85 | 94.99 | 78.8000 | 105 | 238.02 | 169.5000 | −1.04 | [−1.35; −0.74] | 12.1% | 12.3% |
| ZG.Wang 2021 | 56 | 15.19 | 6.8500 | 100 | 12.30 | 6.3200 | 0.44 | [ 0.11; 0.77] | 10.3% | 12.0% |
| **Fixed effect model** | **526** | | | **1278** | | | **−0.41** | **[−0.51; −0.30]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **−0.35** | **[−0.67; −0.02]** | **−−** | **100.0%** |

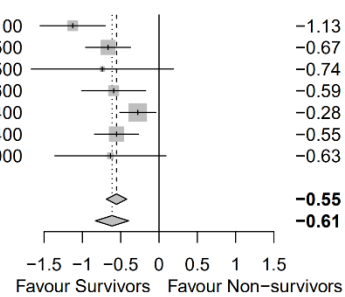
Heterogeneity: $I^2$ = 88%, $\tau^2$ = 0.1997, $p$ < 0.01




### (18) NK cell(ab)

| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| Jing.Zhang 2021 | 26 | 43.91 | 49.8100 | 182 | 195.25 | 141.6100 | −1.13 | [−1.55; −0.70] | 9.9% | 13.9% |
| LK. Xiong 2021 | 85 | 93.86 | 89.3700 | 105 | 159.53 | 105.0500 | −0.67 | [−0.96; −0.37] | 20.7% | 19.2% |
| L.Cai 2020 | 7 | 108.84 | 153.9500 | 15 | 291.59 | 265.6500 | −0.74 | [−1.67; 0.19] | 2.1% | 4.6% |
| B.Xu 2020 | 28 | 57.95 | 47.4600 | 117 | 100.03 | 75.0600 | −0.59 | [−1.01; −0.17] | 10.2% | 14.1% |
| Z.Wang 2020 | 116 | 102.63 | 95.3400 | 177 | 126.10 | 76.8400 | −0.28 | [−0.51; −0.04] | 32.3% | 21.9% |
| Y.Jiang 2020 | 72 | 88.28 | 81.4700 | 143 | 131.49 | 75.6400 | −0.55 | [−0.84; −0.27] | 21.5% | 19.4% |
| DW. Sun 2020 | 11 | 148.62 | 145.9000 | 25 | 238.82 | 136.0000 | −0.63 | [−1.36; 0.09] | 3.4% | 6.9% |
| **Fixed effect model** | **345** | | | **764** | | | **−0.55** | **[−0.69; −0.42]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **−0.61** | **[−0.83; −0.40]** | **−−** | **100.0%** |

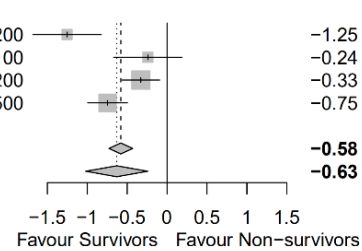
Heterogeneity: $I^2$ = 54%, $\tau^2$ = 0.0419, $p$ = 0.04




### (19) C3

| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| J.Zhang 2021 | 26 | 0.66 | 0.2400 | 182 | 0.94 | 0.2200 | −1.25 | [−1.68; −0.83] | 12.1% | 22.4% |
| WD.Qin 2021 | 23 | 0.96 | 0.1700 | 239 | 1.01 | 0.2100 | −0.24 | [−0.67; 0.19] | 12.1% | 22.4% |
| Z.Wang 2020 | 116 | 0.93 | 0.2000 | 177 | 1.00 | 0.2200 | −0.33 | [−0.56; −0.09] | 39.9% | 27.7% |
| T.Chen 2020 | 113 | 0.76 | 0.2300 | 161 | 0.90 | 0.1500 | −0.75 | [−0.99; −0.50] | 35.9% | 27.4% |
| **Fixed effect model** | **278** | | | **759** | | | **−0.58** | **[−0.73; −0.43]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **−0.63** | **[−1.02; −0.24]** | **−−** | **100.0%** |

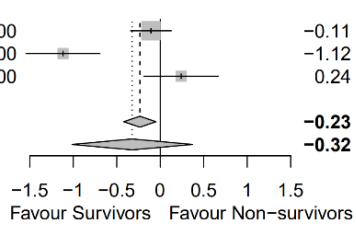
Heterogeneity: $I^2$ = 83%, $\tau^2$ = 0.1267, $p$ < 0.01




### (20) C4

| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| Z.Wang 2020 | 116 | 0.24 | 0.1100 | 177 | 0.25 | 0.0800 | −0.11 | [−0.34; 0.13] | 62.4% | 35.4% |
| J.Zhang 2021 | 26 | 0.16 | 0.0800 | 182 | 0.24 | 0.0700 | −1.12 | [−1.54; −0.69] | 19.0% | 32.4% |
| WD.Qin 2021 | 23 | 0.27 | 0.1100 | 239 | 0.25 | 0.0800 | 0.24 | [−0.19; 0.67] | 18.7% | 32.3% |
| **Fixed effect model** | **165** | | | **598** | | | **−0.23** | **[−0.42; −0.05]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **−0.32** | **[−1.01; 0.37]** | **−−** | **100.0%** |

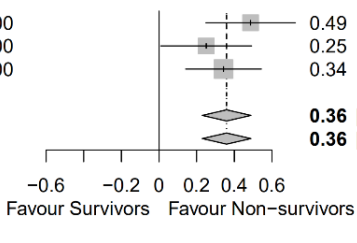
Heterogeneity: $I^2$ = 91%, $\tau^2$ = 0.3377, $p$ < 0.01




### (21) IgA

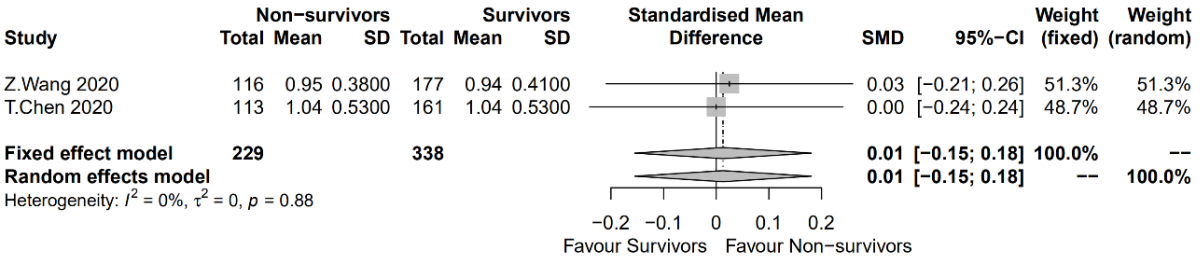
| Study | Non−survivors Total | Mean | SD | Survivors Total | Mean | SD | SMD | 95%−CI | Weight (fixed) | Weight (random) |
|---|---|---|---|---|---|---|---|---|---|---|
| Z.Wang 2020 | 116 | 2.70 | 1.3000 | 177 | 2.21 | 0.7500 | 0.49 | [0.25; 0.72] | 29.7% | 29.7% |
| T.Chen 2020 | 113 | 2.44 | 1.2800 | 161 | 2.17 | 0.9000 | 0.25 | [0.01; 0.49] | 28.8% | 28.8% |
| Yang.Zhao 2020 | 125 | 2.61 | 1.2400 | 414 | 2.28 | 0.8600 | 0.34 | [0.14; 0.54] | 41.5% | 41.5% |
| **Fixed effect model** | **354** | | | **752** | | | **0.36** | **[0.23; 0.49]** | **100.0%** | **−−** |
| **Random effects model** | | | | | | | **0.36** | **[0.23; 0.49]** | **−−** | **100.0%** |

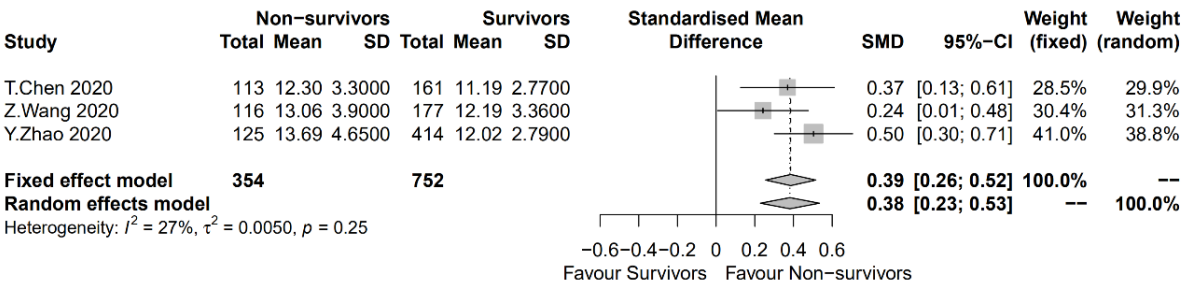
Heterogeneity: $I^2$ = 0%, $\tau^2$ = 0, $p$ = 0.39



## Figure E2(B) (Continued)

### (22) IgM




### (22) IgG