Sunnlamontary Figure 1. PRISMA flowchart of study inclusions and evolusions

PRISMA

TRANSPARENT REPORTING of SYSTEMATIC REVIEWS



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews* and *Meta-Analyses: The PRISMA Statement. PLoS Med* 6(7): e1000097. doi:10.1371/journal.pmed1000097 **For more information, visit www.prisma-statement.org.**

Supplementary Figure 2: Standardised mean difference in age and agestratified raw outcomes between survivors and non-survivors

| | Sı | Survivors Non-Survivors | | Non-Survivors | | | Mean Difference | Weight | |
|---|--------------|-------------------------|------|---------------|------|------|-----------------|--------------------------|------|
| Study | N | Mean | SD | Ν | Mean | SD | : | with 95% CI | (%) |
| Aw, October 2020 | 392 | 80.2 | 8 | 271 | 82.6 | 8 | | -2.40 [-3.64, -1.16] | 5.34 |
| Baker, May 2020 | 210 | 67.7 | 18.5 | 81 | 82.3 | 9.6 | | -14.60 [-18.84, -10.36] | 4.96 |
| Bellelli, May 2020 | 63 | 59.7 | 12.4 | 42 | 76.4 | 11.4 | | -16.70 [-21.39, -12.01] | 4.87 |
| Brill, June 2020 | 237 | 63 | 22.2 | 173 | 80 | 11.9 | | -17.00 [-20.64, -13.36] | 5.06 |
| Chinnadurai, October 2020 | 129 | 67.7 | 16.3 | 86 | 79.7 | 9.6 | | -12.00 [-15.82, -8.18] | 5.03 |
| De Smet, July 2020 | 62 | 84.2 | 7.4 | 19 | 87.3 | 4.4 | | -3.10 [-6.61, 0.41] | 5.08 |
| Hoek, September 2020 | 18 | 56.4 | 12.9 | 5 | 70 | 4.1 | | -13.60 [-25.24, -1.96] | 3.27 |
| Hewitt, August 2020 | 1,139 | 72.7 | 16.3 | 425 | 72.7 | 16.3 | | 0.00 [-1.82, 1.82] | 5.30 |
| Koduri, August 2020 | 307 | 64.5 | 18.3 | 193 | 77.4 | 11.6 | | -12.90 [-15.79, -10.01] | 5.17 |
| Kokoszka-Bargiel, September 2020 | 30 | 70.1 | 12.4 | 37 | 56.7 | 8.3 | | - 13.40 [8.42, 18.38] | 4.81 |
| Kundi, December 2020 | 14,919 | 73.4 | 7.4 | 3,315 | 77.4 | 7.9 | | -4.00 [-4.28, -3.72] | 5.38 |
| Marengoni, October 2020 | 123 | 69 | 14 | 40 | 69 | 15 | | 0.00 [-5.08, 5.08] | 4.79 |
| Steinmeyer, September 2020 | 77 | 84.8 | 7.8 | 17 | 88.6 | 5.3 | | -3.80 [-7.70, 0.10] | 5.02 |
| Tehrani, October 2020 | 185 | 62 | 17 | 70 | 78 | 11 | | -16.00 [-20.29, -11.71] | 4.95 |
| Welch, October 2020 | 4,115 | 68.3 | 20.7 | 1,596 | 79.7 | 11.1 | | -11.40 [-12.47, -10.33] | 5.35 |
| Fagard, November 2020 | 91 | 81.3 | 9 | 14 | 86.2 | 6.4 | | -4.90 [-9.80, 0.00] | 4.83 |
| Aliberti, February 2021 | 666 | 64.7 | 9.3 | 1,164 | 68.2 | 10.1 | | -3.50 [-4.43, -2.57] | 5.36 |
| Apea, November 2020 | 1,460 | 59.2 | 18.2 | 536 | 74.8 | 12.6 | | -15.60 [-17.27, -13.93] | 5.31 |
| Dres, May 2021 | 650 | 73.7 | 4.4 | 549 | 75.3 | 5.2 | | -1.60 [-2.14, -1.06] | 5.37 |
| Hendra, January 2021 | 112 | 61.7 | 14.6 | 36 | 71.7 | 11.9 | | -10.00 [-15.26, -4.74] | 4.75 |
| Overall | | | | | | | • | -7.38 [-10.74, -4.01] | |
| Heterogeneity: $\tau^2 = 54.77$, $I^2 = 99.21\%$ | $H^2 = 12^2$ | 7.37 | | | | | | | |
| Test of $\theta_i = \theta_j$: Q(19) = 709.36, p = 0.0 | 0 | | | | | | | | |
| Test of θ = 0: z = -4.30, p = 0.00 | | | | | | | | | |
| | | | | | | | -20 0 | 20 | |



Supplementary Figure 3: Age-stratified ge and non-survivors.

(3a) Funnel plot





Effect size: _meta_es Std. Err.: _meta_se

Regression-based Egger test for small-study effects Random-effects model Method: REML

H0: beta1 = 0; no small-study effects beta1 = 0.53 SE of beta1 = 0.273 z = 1.93Prob > |z| = 0.0539

(3c) Forest plots based on quality of studies (NOS)

| | Ν | Лаle | Fe | emale | | Log Risk Ratio | Weight |
|---|-------------------------|---------|--------|----------|---|-----------------------|--------|
| Study | Died | Survive | d Died | Survived | | with 95% CI | (%) |
| Good | | | | | | | |
| Welch, October 2020 | 2,177 | 972 | 1,938 | 624 | | -0.09 [-0.12, -0.06] | 18.49 |
| Apea, November 2020 | 859 | 351 | 601 | 185 | | -0.07 [-0.13, -0.02] | 11.09 |
| Dres, May 2021 | 473 | 400 | 177 | 149 | | -0.00 [-0.12, 0.11] | 3.22 |
| Hendra, January 2021 | 60 | 24 | 52 | 12 | | -0.13 [-0.31, 0.05] | 1.46 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 =$ | = 0.02%, H ² | = 1.00 | | | • | -0.08 [-0.11, -0.06] | |
| Test of $\theta = \theta$: Q(3) = 2.38 r | y = 0.50 | | | | | | |

Fair

| Aw, October 2020 | 185 | 174 | 208 | 97 | | -0.28 [-0.41, -0.15] 2.80 |
|--|--|--|--|---|----------|---|
| Brill, June 2020 | 134 | 111 | 103 | 70 | | -0.08 [-0.25, 0.08] 1.65 |
| Chinnadurai, October 2020 | 82 | 51 | 47 | 35 | | - 0.07 [-0.16, 0.30] 0.90 |
| Hoek, September 2020 | 14 | 4 | 4 | 1 | | -0.03 [-0.53, 0.47] 0.19 |
| Knights, September 2020 | 38 | 20 | 31 | 14 | | -0.05 [-0.32, 0.22] 0.65 |
| Kundi, December 2020 | 6,569 | 1,929 | 8,350 | 1,386 | | -0.10 [-0.12, -0.09] 26.87 |
| Maguire, September 2020 | 91 | 33 | 81 | 19 | | -0.10 [-0.24, 0.04] 2.25 |
| Marengoni, October 2020 | 73 | 27 | 50 | 15 | | -0.05 [-0.23, 0.13] 1.46 |
| Tehrani, October 2020 | 108 | 42 | 77 | 28 | | -0.02 [-0.17, 0.13] 1.97 |
| Fagard, November 2020 | 45 | 10 | 46 | 4 | | -0.12 [-0.27, 0.03] 2.06 |
| Aliberti, February 2021 | 653 | 408 | 511 | 258 | | -0.08 [-0.15, -0.01] 7.66 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0$ | 0.00%, H ² | = 1.00 | | | • | -0.10 [-0.12, -0.09] |
| Test of $\theta_i = \theta_j$: Q(10) = 12.20, p | o = 0.27 | | | | | |
| | | | | | | Calculated RR = $1.08 [1.06 - 1.11]$ |
| | | | | | | |
| Poor | | | | | | |
| Poor Baker, May 2020 | 113 | 46 | 97 | 35 | | -0.03 [-0.18, 0.11] 2.24 |
| Poor Baker, May 2020 Bellelli, May 2020 | 113 41 | 46 31 | 97 22 | 35 11 | | -0.03 [-0.18, 0.11] 2.24 -0.16 [-0.47, 0.16] 0.49 |
| Poor Baker, May 2020 Bellelli, May 2020 Davis, October 2020 | 113 41 87 | 46 31 61 | 97 22 40 | 35 11 34 | _ | -0.03 [-0.18, 0.11] 2.24 -0.16 [-0.47, 0.16] 0.49 0.08 [-0.17, 0.33] 0.77 |
| Poor Baker, May 2020 Bellelli, May 2020 Davis, October 2020 De Smet, July 2020 | 113 41 87 25 | 46 31 61 8 | 97 22 40 37 | 35 11 34 11 | | -0.03 [-0.18, 0.11] 2.24 -0.16 [-0.47, 0.16] 0.49 0.08 [-0.17, 0.33] 0.77 -0.02 [-0.26, 0.23] 0.78 |
| Poor Baker, May 2020 Bellelli, May 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 | 113 41 87 25 648 | 46 31 61 8 255 | 97 22 40 37 491 | 35 11 34 11 170 | | -0.03 [-0.18, 0.11] 2.24 -0.16 [-0.47, 0.16] 0.49 0.08 [-0.17, 0.33] 0.77 -0.02 [-0.26, 0.23] 0.78 -0.03 [-0.10, 0.03] 9.24 |
| Poor Baker, May 2020 Bellelli, May 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 | 113 41 87 25 648 172 | 46 31 61 8 255 128 | 97 22 40 37 491 135 | 35 11 34 11 170 65 | | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| Poor Baker, May 2020 Bellelli, May 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 | 113 41 87 25 648 172 36 | 46 31 61 8 255 128 6 | 97 22 40 37 491 135 41 | 35 11 34 11 170 65 11 | | $\begin{array}{c} -0.03 \left[-0.18, \ 0.11 \right] & 2.24 \\ -0.16 \left[-0.47, \ 0.16 \right] & 0.49 \\ 0.08 \left[-0.17, \ 0.33 \right] & 0.77 \\ -0.02 \left[-0.26, \ 0.23 \right] & 0.78 \\ -0.03 \left[-0.10, \ 0.03 \right] & 9.24 \\ -0.16 \left[-0.30, \ -0.03 \right] & 2.41 \\ 0.08 \left[-0.10, \ 0.27 \right] & 1.34 \end{array}$ |
| Poor Baker, May 2020 Bellelli, May 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 Steinmeyer, September 2020 Heterogeneity: $r^2 = 0.00$, $l^2 = 0$ | 113 41 87 25 648 172 36 0.00%, H ² | 46 31 61 8 255 128 6 = 1.00 | 97 22 40 37 491 135 41 | 35 11 34 11 170 65 11 | | $\begin{array}{c} -0.03 \left[-0.18, \ 0.11 \right] & 2.24 \\ -0.16 \left[-0.47, \ 0.16 \right] & 0.49 \\ 0.08 \left[-0.17, \ 0.33 \right] & 0.77 \\ -0.02 \left[-0.26, \ 0.23 \right] & 0.78 \\ -0.03 \left[-0.10, \ 0.03 \right] & 9.24 \\ -0.16 \left[-0.30, \ -0.03 \right] & 2.41 \\ 0.08 \left[-0.10, \ 0.27 \right] & 1.34 \\ -0.04 \left[-0.09, \ 0.01 \right] \end{array}$ |
| Poor Baker, May 2020 Bellelli, May 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 Steinmeyer, September 2020 Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0$ Test of $\theta_i = \theta_j$: Q(6) = 6.34, p = | 113 41 87 25 648 172 36 0.00%, H ² = 0.39 | 46 31 61 8 255 128 6 = 1.00 | 97 22 40 37 491 135 41 | 35 11 34 11 170 65 11 | | $\begin{array}{c} -0.03 \left[-0.18, \ 0.11 \right] & 2.24 \\ -0.16 \left[-0.47, \ 0.16 \right] & 0.49 \\ 0.08 \left[-0.17, \ 0.33 \right] & 0.77 \\ -0.02 \left[-0.26, \ 0.23 \right] & 0.78 \\ -0.03 \left[-0.10, \ 0.03 \right] & 9.24 \\ -0.16 \left[-0.30, \ -0.03 \right] & 2.41 \\ 0.08 \left[-0.10, \ 0.27 \right] & 1.34 \\ -0.04 \left[-0.09, \ 0.01 \right] \end{array}$ $\begin{array}{c} \mbox{Calculated RR} = 1.08 \left[1.06 - 1.11 \right] \end{array}$ |
| Poor Baker, May 2020 Bellelli, May 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 Steinmeyer, September 2020 Heterogeneity: $\tau^2 = 0.00$, $l^2 = 0$ Test of $\theta_l = \theta_j$: Q(6) = 6.34, p = | 113 41 87 25 648 172 36 0.00%, H ² 0.39 | 46 31 61 8 255 128 6 = 1.00 | 97 22 40 37 491 135 41 | 35 11 34 11 170 65 11 | | $\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$ |

Calculated RR = 1.08 [1.06-1.11]

Test of $\theta_i = \theta_j$: Q(21) = 28.31, p = 0.13

Test of group differences: $Q_b(2) = 7.39$, p = 0.02





(3d) Age-stratification

| Study Died Survived Died Survived | With 95% CI | (%) |
|---|----------------------------|----------|
| 60-60 voars | | |
| 00-09 years | | |
| Aw, October 202018517420897- | -0.28 [-0.41, -0.15] | 2.80 |
| Hoek, September 2020 14 4 1 | -0.03 [-0.53, 0.47] | 0.19 |
| Knights, September 2020 38 20 31 14 | -0.05 [-0.32, 0.22] | 0.65 |
| Koduri, August 202017212813565 | -0.16 [-0.30, -0.03] | 2.41 |
| Marengoni, October 2020 73 27 50 15 | -0.05 [-0.23, 0.13] | 1.46 |
| Tehrani, October 2020108427728 | -0.02 [-0.17, 0.13] | 1.97 |
| Aliberti, February 2021 653 408 511 258 | -0.08 [-0.15, -0.01] | 7.66 |
| Apea, November 2020859351601185 | -0.07 [-0.13, -0.02] | 11.09 |
| Hendra, January 2021 60 24 52 12 | -0.13 [-0.31, 0.05] | 1.46 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 42.10\%$, $H^2 = 1.73$ | -0.11 [-0.16, -0.05] | |
| Test of $\theta_i = \theta_j$: Q(8) = 11.58, p = 0.17 | | |
| | Calculated RR = 1.12 [1. | 05-1.17] |
| 70-79 years | | |
| Baker, May 2020113469735 | -0.03 [-0.18, 0.11] | 2.24 |
| Bellelli, May 2020 41 31 22 11 - | -0.16 [-0.47, 0.16] | 0.49 |
| Chinnadurai, October 2020 82 51 47 35 | 0.07 [-0.16, 0.30] | 0.90 |
| De Smet, July 2020 25 8 37 11 | -0.02 [-0.26, 0.23] | 0.78 |
| Hewitt, August 2020 648 255 491 170 | -0.03 [-0.10, 0.03] | 9.24 |
| Kundi, December 2020 6,569 1,929 8,350 1,386 | -0.10 [-0.12, -0.09] | 26.87 |
| Maguire, September 2020 91 33 81 19 | -0.10 [-0.24, 0.04] | 2.25 |
| Welch, October 2020 2,177 972 1,938 624 | -0.09 [-0.12, -0.06] | 18.49 |
| Dres, May 2021 473 400 177 149 | -0.00 [-0.12, 0.11] | 3.22 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 45.39\%$, $H^2 = 1.83$ | -0.07 [-0.11, -0.04] | |
| Test of $\theta_i = \theta_j$: Q(8) = 11.11, p = 0.20 | Calculated RR = 1.07 [1 | 04-1 12] |





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(5c) Forest plots based on quality of studies (NOS)

| Study | Fi Died S | Frail Non-Frail Survived Died Survived | | | Log Risk Ratio with 95% CI | Weight (%) |
|--|-----------------|---|-------|-----|-------------------------------|---------------|
| Good | | | | | | |
| Welch, October 2020 | 863 | 1,578 | 2,215 | 425 | -0.86 [-0.92, -0.81] | 5.74 |
| Osuafor, February 2021 | 83 | 59 | 57 | 15 | -0.30 [-0.49, -0.12] | 5.48 |
| Apea, November 2020 | 800 | 445 | 660 | 91 | -0.31 [-0.36, -0.26] | 5.75 |
| Dres, May 2021 | 29 | 70 | 560 | 426 | -0.66 [-0.97, -0.35] | 5.01 |
| Heterogeneity: $\tau^2 = 0.08 I^2 = 0.7$ | $60\% H^2 = 11$ | 73 | | | 0 53 [0 82 0 25] | |

Test of $\theta_i = \theta_i$: Q(3) = 216.59, p = 0.00

Fair

| Aw, October 2020 | 256 | 214 | 136 | 57 | | |
|--|-------|-------|-------|-----|--|--|
| Chinnadurai, October 2020 | 88 | 17 | 41 | 69 | | |
| Hoek, September 2020 | 0 | 1 | 18 | 4 | | |
| Kundi, December 2020 | 9,697 | 2,598 | 5,222 | 717 | | |
| Maguire, September 2020 | 105 | 14 | 65 | 38 | | |
| Marengoni, October 2020 | 117 | 25 | 5 | 15 | | |
| Tehrani, October 2020 | 28 | 43 | 52 | 20 | | |
| Fagard, November 2020 | 48 | 14 | 43 | 0 | | |
| Aliberti, February 2021 | 239 | 255 | 925 | 411 | | |
| Heterogeneity: $\tau^2 = 0.28$, $I^2 = 98.71\%$, $H^2 = 77.25$ | | | | | | |
| Test of $\theta = \theta$: $\Omega(8) = 133.80$, $p = 0.00$ | 0 | | | | | |

Poor

| Davis, October 2020 | 37 | 18 | 90 | 77 |
|--|-------------|-----|-----|-----|
| De Smet, July 2020 | 46 | 18 | 16 | 1 |
| Hewitt, August 2020 | 543 | 256 | 624 | 136 |
| Koduri, August 2020 | 89 | 116 | 208 | 72 |
| Kokoszka-Bargiel, September 2020 | 9 | 10 | 21 | 27 |
| Owen, July 2020 | 51 | 45 | 63 | 47 |
| Steinmeyer, September 2020 | 9 | 3 | 68 | 14 |
| Heterogeneity: $\tau^2 = 0.05$, $I^2 = 85.10\%$, | $H^2 = 6.7$ | 1 | | |
| Test of $\theta_i = \theta_i$: Q(6) = 30.53, p = 0.00 | | | | |

Overall

Heterogeneity: $\tau^2 = 0.17$, $I^2 = 98.86\%$, $H^2 = 87.93$ Test of $\theta_i = \theta_i$: Q(19) = 875.07, p = 0.00

Test of group differences: $Q_b(2) = 6.71$, p = 0.03

Calculated RR = 1.70 [0.78-2.27]







Supplementary Figure 5: ICU Admission: survivor vs. non-survivor analysis.

(5a) Funnel plot



(5b) Egger's Test

. . meta bias, egger

Effect-size label: Log Risk Ratio Effect size: _meta_es Std. Err.: _meta_se

Regression-based Egger test for small-study effects Random-effects model Method: REML

H0: beta1 = 0; no small-study effects beta1 = 0.05 SE of beta1 = 0.669 z = 0.07Prob > |z| = 0.9450

| | ICU Admission No ICU Admis | | | | |
|--|----------------------------|-----|-------|-------|--|
| Study | Yes | No | Yes | No | |
| Good | | | | | |
| Welch, October 2020 | 421 | 226 | 3,694 | 1,370 | |
| Apea, November 2020 | 210 | 151 | 1,250 | 38 | |
| Dres, May 2021 | 650 | 549 | 0 | (| |
| Hendra, January 2021 | 5 | 5 | 31 | 107 | |
| Heterogeneity: $\tau^2 = 0.16$, $I^2 = 97.33\%$, | $H^2 = 37.4$ | 1 | | | |
| Test of $\theta_i = \theta_j$: Q(3) = 15.61, p = 0.00 | | | | | |

(5c) Forest plots based on quality of studies

| Study | ICU Ad Died | mission I Survived | No ICU . d Died | Admissior Survived |
|--|----------------|-----------------------|--------------------|-----------------------|
| Good | | | | |
| Welch, October 2020 | 421 | 226 | 3,694 | 1,370 |
| Apea, November 2020 | 210 | 151 | 1,250 |) 385 |
| Dres, May 2021 | 650 | 549 | С |) 0 |
| Hendra, January 2021 | 5 | 5 | 31 | 107 |
| Heterogeneity: $\tau^2 = 0.16$, $I^2 = 97.33\%$, | $H^2 = 37.4$ | 41 | | |
| Test of $\theta_i = \theta_j$: Q(3) = 15.61, p = 0.00 | | | | |

Fair

| Aw, October 2020 | 22 | 15 | 371 | | | | |
|--|-------|-------|--------|--|--|--|--|
| Brill, June 2020 | 30 | 26 | 207 | | | | |
| Chinnadurai, October 2020 | 12 | 12 | 117 | | | | |
| Hoek, September 2020 | 1 | 1 | 17 | | | | |
| Knights, September 2020 | 27 | 8 | 47 | | | | |
| Kundi, December 2020 | 1,843 | 2,667 | 13,076 | | | | |
| Marengoni, October 2020 | 8 | 3 | 115 | | | | |
| Tehrani, October 2020 | 25 | 16 | 160 | | | | |
| Aliberti, February 2021 | 531 | 611 | 135 | | | | |
| Heterogeneity: $\tau^2 = 0.22$, $I^2 = 95.67\%$, $H^2 = 23.09$ | | | | | | | |
| Test of $\theta_i = \theta_j$: Q(8) = 543.67, p = 0.00 | | | | | | | |

Poor

| Baker, May 2020 | 45 | 14 | 177 | | |
|--|----|----|-----|--|--|
| De Smet, July 2020 | 4 | 3 | 58 | | |
| Koduri, August 2020 | 72 | 48 | 230 | | |
| Kokoszka-Bargiel, September 2020 | 14 | 18 | 16 | | |
| Owen, July 2020 | 9 | 8 | 9 | | |
| Steinmeyer, September 2020 | 3 | 4 | 74 | | |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$ | | | | | |
| Test of $\theta_i = \theta_i$: Q(5) = 3.89, p = 0.57 | | | | | |

Overall

Heterogeneity: $\tau^2 = 0.14$, $I^2 = 96.30\%$, $H^2 = 27.00$ Test of $\theta_i = \theta_j$: Q(18) = 984.51, p = 0.00

Test of group differences: $Q_b(2) = 0.11$, p = 0.95

| 0 | Fair | | | | |
|-----|---|--------------|---------|---------|-----|
| 107 | Aw, October 2020 | 22 | 15 | 371 | 256 |
| | Brill, June 2020 | 30 | 26 | 207 | 147 |
| | Chinnadurai, October 2020 | 12 | 12 | 117 | 74 |
| | Hoek, September 2020 | 1 | 1 | 17 | Z |
| | Knights, September 2020 | 27 | 8 | 47 | 26 |
| 256 | Kundi, December 2020 | 1,843 | 2,667 | 13,076 | 648 |
| 147 | Marengoni, October 2020 | 8 | 3 | 115 | 37 |
| 74 | Tehrani, October 2020 | 25 | 16 | 160 | 54 |
| 4 | Aliberti, February 2021 | 531 | 611 | 135 | 553 |
| 26 | Heterogeneity: $\tau^2 = 0.22$, $I^2 = 95.67\%$, | $H^2 = 23.$ | 09 | | |
| 648 | Test of $\theta_i = \theta_j$: Q(8) = 543.67, p = 0.00 |) | | | |
| 37 | | | | | |
| 54 | Poor | | | | |
| 553 | Baker, May 2020 | 45 | 14 | 177 | 68 |
| | De Smet, July 2020 | 4 | 3 | 58 | 16 |
| | Koduri, August 2020 | 72 | 48 | 230 | 142 |
| | Kokoszka-Bargiel, September 2020 | 14 | 18 | 16 | 19 |
| | Owen, July 2020 | 9 | 8 | 9 | ε |
| ~~~ | Steinmeyer, September 2020 | 3 | 4 | 74 | 13 |
| 68 | Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, H | $H^2 = 1.00$ | | | |
| 16 | Test of $\theta_i = \theta_j$: Q(5) = 3.89, p = 0.57 | | | | |
| 142 | | | | | |
| 19 | Overall | | | | |
| 8 | Heterogeneity: $\tau^2 = 0.14$, $I^2 = 96.30\%$, | $H^2 = 27.$ | 00 | | |
| 13 | Test of $\theta_i = \theta_j$: Q(18) = 984.51, p = 0.0 | 00 | | | |
| | Test of group differences: $Q_{o}(2) = 0.1^{\circ}$ | 1, p = 0.9 | 5 | | |
| | Random-effects REML model | | | | |
| | -0.06 | [-0.25, | 0.14] | | |
| | Calculated R | R = 0.9 | 94 [0.7 | 8-1.15] | |

-2

-1

0

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Supplementary Figure 6: Invasive Mechanical Ventilation (IMV):

(6a) Funnel plot



(6b) Egger's Test

. . meta bias, egger

Effect-size label: Log Risk Ratio Effect size: _meta_es Std. Err.: _meta_se

Regression-based Egger test for small-study effects Random-effects model Method: REML

| 0: | beta1 | = | 0; | no | sm | all-study | effects |
|----|-------|----|-----|-----|----|-----------|---------|
| | | | bet | ta1 | = | 0.24 | |
| | SE c | of | bet | ta1 | = | 0.853 | |
| | | | | Z | = | 0.29 | |
| | Pro | ob | > | z | = | 0.7756 | |

| | IN | 1V | Non | -IMV |
|--|-----------|-------|-----|------|
| Study | Yes | No | Yes | No |
| Good | | | | |
| Apea, November 2020 | 146 | 135 | 64 | 16 |
| Dres, May 2021 | 350 | 390 | 300 | 159 |
| Hendra, January 2021 | 5 | 5 | 31 | 107 |
| Heterogeneity: $\tau^2 = 0.33$, $I^2 = 97.48\%$, | $H^2 = 3$ | 89.61 | | |
| Test of $\theta_i = \theta_j$: Q(2) = 11.81, p = 0.00 | | | | |

(6c) Forest plots based on quality of studies

| | IN | ΛV | Non | -IMV | |
|--|--------------|--------|------|---------|---|
| Study | Died Su | rvived | Died | Survive | d |
| Good | | | | | |
| Apea, November 2020 | 146 | 135 | 64 | 16 | |
| Dres, May 2021 | 350 | 390 | 300 | 159 | |
| Hendra, January 2021 | 5 | 5 | 31 | 107 | |
| Heterogeneity: $\tau^2 = 0.33$, $I^2 = 97.48$ % | $%, H^2 = 3$ | 39.61 | | | |
| Test of $\theta_i = \theta_j$: Q(2) = 11.81, p = 0.00 |) | | | | |

Fair

| Brill, June 2020 | 10 | 26 | 227 | 147 |
|---|-----------|-------|-----|-----|
| Chinnadurai, October 2020 | 3 | 5 | 126 | 81 |
| Hoek, September 2020 | 1 | 1 | 17 | 4 |
| Knights, September 2020 | 8 | 1 | 66 | 33 |
| Marengoni, October 2020 | 32 | 0 | 124 | 7 |
| Tehrani, October 2020 | 20 | 10 | 180 | 60 |
| Aliberti, February 2021 | 299 | 554 | 232 | 57 |
| Heterogeneity: $\tau^2 = 0.19$, $I^2 = 95.67\%$, | $H^2 = 2$ | 23.07 | | |
| Test of $\theta_i = \theta_j$: Q(6) = 209.16, p = 0.00 | | | | |

Poor

| Baker, May 2020 | 11 | 11 | 199 | 70 |
|---|-------|----|-----|-----|
| Koduri, August 2020 | 36 | 28 | 266 | 162 |
| Kokoszka-Bargiel, September 2020 | 14 | 18 | 16 | 19 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, H^2 | = 1.0 | 0 | | |
| Test of $\theta_i = \theta_j$: Q(2) = 1.59, p = 0.45 | | | | |

Overall

Heterogeneity: $\tau^2 = 0.13$, $I^2 = 94.17\%$, $H^2 = 17.15$ Test of $\theta_i = \theta_j$: Q(12) = 236.85, p = 0.00

Test of group differences: $Q_b(2) = 0.56$, p = 0.76

Random-effects REML model

| | Fair | | | | |
|---|---|-----------|-------|-------|-----|
| | Brill, June 2020 | 10 | 26 | 227 | 147 |
| | Chinnadurai, Octobe | - 1 0 | | | 10] |
| | Hoek, September 20 | = 1.0 | 0 [U. | 53-Z. | IZJ |
| | Knights, September 2020 | 8 | 1 | 66 | 33 |
| | Marengoni, October 2020 | 32 | 0 | 124 | 7 |
| | Tehrani, October 2020 | 20 | 10 | 180 | 60 |
| - | Aliberti, February 2021 | 299 | 554 | 232 | 57 |
| | Heterogeneity: $\tau^2 = 0.19$, $I^2 = 95.67\%$, | $H^2 = 2$ | 23.07 | | |
| | Test of $\theta_i = \theta_j$: Q(6) = 209.16, p = 0.00 |) | | | |

Poor

| Baker, May 2020 | | 11 | 11 | 199 | 70 |
|--|-----------------------------|--------|------|-------|-----|
| Koduri, August 2020 | | 36 | 28 | 266 | 162 |
| Kokoszka-Bargiel, S | Calculated RR = | 1.34 | [0.9 | 92-1. | 93] |
| Heterogeneity: $\tau^2 = 0$ | .00, $I^2 = 0.00\%$, H^2 | = 1.00 |) | | |
| Test of $\theta_i = \theta_j$: Q(2) = | 1.59, p = 0.45 | | | | |

Overall

Heterogeneity: $\tau^2 = 0.13$, $I^2 = 94.17\%$, $H^2 = 17.15$ Test of $\theta_i = \theta_j$: Q(12) = 236.85, p = 0.00 Test of group differe Calculated RR = 1.16 [0.96-1.40]



(7a) Frail vs. non-frail

| | F | rail | Non- | Frail | | Log Risk Ratio | Weight |
|--|-----------------------|---------|----------|-------|------|-----------------------|----------|
| Study | Died Su | urvived | Died Sur | vived | | with 95% CI | (%) |
| CFS | | | | | | | |
| Aw, October 2020 | 256 | 214 | 136 | 57 | | -0.26 [-0.38, -0.13] | 5.64 |
| Chinnadurai, October 2020 | 88 | 17 | 41 | 69 | | 0.81 [0.55, 1.07] | 5.23 |
| Davis, October 2020 | 37 | 18 | 90 | 77 | | 0.22 [-0.01, 0.45] | 5.32 |
| De Smet, July 2020 | 46 | 18 | 16 | 1 | | -0.27 [-0.46, -0.08] | 5.45 |
| Hoek, September 2020 | 0 | 1 | 18 | 4 | | -1.17 [-3.58, 1.24] | 0.57 |
| Hewitt, August 2020 | 543 | 256 | 624 | 136 | | -0.19 [-0.25, -0.13] | 5.74 |
| Koduri, August 2020 | 89 | 116 | 208 | 72 | | -0.54 [-0.71, -0.37] | 5.52 |
| Kokoszka-Bargiel, September 2020 | 9 | 10 | 21 | 27 | | 0.08 [-0.49, 0.65] | 3.82 |
| Maguire, September 2020 | 105 | 14 | 65 | 38 | | 0.34 [0.17, 0.50] | 5.54 |
| Marengoni, October 2020 | 117 | 25 | 5 | 15 | | — 1.19 [0.43, 1.96] | 3.02 |
| Owen, July 2020 | 51 | 45 | 63 | 47 | | -0.08 [-0.32, 0.17] | 5.26 |
| Tehrani, October 2020 | 28 | 43 | 52 | 20 | | -0.61 [-0.93, -0.28] | 4.97 |
| Welch, October 2020 | 863 | 1,578 | 2,215 | 425 | | -0.86 [-0.92, -0.81] | 5.74 |
| Fagard, November 2020 | 48 | 14 | 43 | 0 | | -0.25 [-0.39, -0.11] | 5.60 |
| Osuafor, February 2021 | 83 | 59 | 57 | 15 | | -0.30 [-0.49, -0.12] | 5.48 |
| Aliberti, February 2021 | 239 | 255 | 925 | 411 | | -0.36 [-0.46, -0.26] | 5.68 |
| Dres, May 2021 | 29 | 70 | 560 | 426 | | -0.66 [-0.97, -0.35] | 5.01 |
| Heterogeneity: $\tau^2 = 0.21$, $I^2 = 97.68\%$ | , H ² = 43 | .04 | | | • | -0.15 [-0.39, 0.08] | |
| Test of $\theta_i = \theta_j$: Q(16) = 551.97, p = 0. | 00 | | | | Cale | culated RR = 1.16 [0. | 92-1.48] |
| Others | | | | | | | |
| Kundi, December 2020 | 9,697 | 2,598 | 5,222 | 717 | | -0.11 [-0.12, -0.10] | 5.77 |
| Steinmeyer, September 2020 | 9 | 3 | 68 | 14 | | -0.10 [-0.44, 0.24] | 4.88 |
| Apea, November 2020 | 800 | 445 | 660 | 91 | | -0.31 [-0.36, -0.26] | 5.75 |

Apea, November 20208002Heterogeneity: $\tau^2 = 0.02$, $I^2 = 95.82\%$, $H^2 = 23.91$ Test of $\theta_i = \theta_j$: Q(2) = 61.88, p = 0.00

Overall

Heterogeneity: $\tau^2 = 0.17$, $I^2 = 98.86\%$, $H^2 = 87.93$ Test of $\theta_i = \theta_j$: Q(19) = 875.07, p = 0.00

Test of group differences: $Q_b(1) = 0.07$, p = 0.79



(7b) Male vs. female

| | M | ale | Fer | nale | | Log Risk Ratio | Weight |
|--|-----------|-----------------------|-------|----------|----------|-----------------------|--------|
| Study | Died | Survived | Died | Survived | | with 95% CI | (%) |
| CFS | | | | | | | |
| Aw, October 2020 | 185 | 174 | 208 | 97 | B | -0.28 [-0.41, -0.15] | 2.80 |
| Baker, May 2020 | 113 | 46 | 97 | 35 | | -0.03 [-0.18, 0.11] | 2.24 |
| Brill, June 2020 | 134 | 111 | 103 | 70 | | -0.08 [-0.25, 0.08] | 1.65 |
| Chinnadurai, October 2020 | 82 | 51 | 47 | 35 | | 0.07 [-0.16, 0.30] | 0.90 |
| Davis, October 2020 | 87 | 61 | 40 | 34 | | 0.08 [-0.17, 0.33] | 0.77 |
| De Smet, July 2020 | 25 | 8 | 37 | 11 | | -0.02 [-0.26, 0.23] | 0.78 |
| Hoek, September 2020 | 14 | 4 | 4 | 1 — | | -0.03 [-0.53, 0.47] | 0.19 |
| Hewitt, August 2020 | 648 | 255 | 491 | 170 | | -0.03 [-0.10, 0.03] | 9.24 |
| Knights, September 2020 | 38 | 20 | 31 | 14 | | -0.05 [-0.32, 0.22] | 0.65 |
| Koduri, August 2020 | 172 | 128 | 135 | 65 | | -0.16 [-0.30, -0.03] | 2.41 |
| Maguire, September 2020 | 91 | 33 | 81 | 19 | | -0.10 [-0.24, 0.04] | 2.25 |
| Marengoni, October 2020 | 73 | 27 | 50 | 15 | | -0.05 [-0.23, 0.13] | 1.46 |
| Tehrani, October 2020 | 108 | 42 | 77 | 28 | | -0.02 [-0.17, 0.13] | 1.97 |
| Welch, October 2020 | 2,177 | 972 | 1,938 | 624 | | -0.09 [-0.12, -0.06] | 18.49 |
| Fagard, November 2020 | 45 | 10 | 46 | 4 | | -0.12 [-0.27, 0.03] | 2.06 |
| Aliberti, February 2021 | 653 | 408 | 511 | 258 | | -0.08 [-0.15, -0.01] | 7.66 |
| Dres, May 2021 | 473 | 400 | 177 | 149 | | -0.00 [-0.12, 0.11] | 3.22 |
| Hendra, January 2021 | 60 | 24 | 52 | 12 | | -0.13 [-0.31, 0.05] | 1.46 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 2$ | 20.61%, ⊦ | l ² = 1.26 | | | • | -0.08 [-0.11, -0.05] | |
| Test of $A = A \cdot O(17) = 20.74$ r | n = 0.24 | | | | | | |

Calculated RR = 1.08 [1.05-1.12]

Others



(7c) ICU Admission

| | ICU Adı | mission No | DICU A | dmission | | Log Risk Ratio | Weight |
|---|--------------|------------|--------|----------|-----|---------------------------------------|----------|
| Study | Died | Survived | Died | Survived | | with 95% CI | (%) |
| CFS | | | | | | | |
| Aw, October 2020 | 22 | 15 | 371 | 256 | | 0.00 [-0.27, 0.28] | 6.27 |
| Baker, May 2020 | 45 | 14 | 177 | 68 | | 0.05 [-0.11, 0.22] | 6.81 |
| Brill, June 2020 | 30 | 26 | 207 | 147 | - | -0.09 [-0.35, 0.17] | 6.35 |
| Chinnadurai, October 2020 | 12 | 12 | 117 | 74 | | -0.20 [-0.62, 0.21] | 5.40 |
| De Smet, July 2020 | 4 | 3 | 58 | 16 | | -0.32 [-0.97, 0.34] | 3.98 |
| Hoek, September 2020 | 1 | 1 | 17 | 4 – | | -0.48 [-1.88, 0.92] | 1.53 |
| Knights, September 2020 | 27 | 8 | 47 | 26 | - | 0.18 [-0.07, 0.43] | 6.41 |
| Koduri, August 2020 | 72 | 48 | 230 | 142 | | -0.03 [-0.20, 0.14] | 6.79 |
| Kokoszka-Bargiel, September 2020 | 14 | 18 | 16 | 19 | | -0.04 [-0.58, 0.49] | 4.66 |
| Marengoni, October 2020 | 8 | 3 | 115 | 37 | | -0.04 [-0.41, 0.33] | 5.67 |
| Owen, July 2020 | 9 | 8 | 9 | 8 | | 0.00 [-0.63, 0.63] | 4.08 |
| Tehrani, October 2020 | 25 | 16 | 160 | 54 | | -0.20 [-0.46, 0.05] | 6.36 |
| Welch, October 2020 | 421 | 226 | 3,694 | 1,370 | | -0.11 [-0.17, -0.06] | 7.10 |
| Aliberti, February 2021 | 531 | 611 | 135 | 553 | | 0.86 [0.70, 1.03] | 6.81 |
| Dres, May 2021 | 650 | 549 | 0 | 0 — | | 0.08 [-1.88, 2.04] | 0.87 |
| Hendra, January 2021 | 5 | 5 | 31 | 107 | | - 0.80 [0.11, 1.49] | 3.76 |
| Heterogeneity: $\tau^2 = 0.08$, $I^2 = 86.75\%$, | $H^2 = 7.55$ | 5 | | | • | 0.05 [-0.12, 0.23] | |
| Test of $\theta_i = \theta_j$: Q(15) = 134.27, p = 0.0 | 0 | | | | | · · · · · · · · · · · · · · · · · · · | · · - • |
| | | | | | Cal | culated RR = 1.05 [0.8 | 89-1.26] |
| Others | | | | | | | |
| Kundi, December 2020 | 1,843 | 2,667 | 13,076 | 648 | | -0.85 [-0.88, -0.81] | 7.13 |
| Steinmeyer, September 2020 | 3 | 4 | 74 | 13 | | -0.69 [-1.55, 0.17] | 3.00 |
| Apea, November 2020 | 210 | 151 | 1,250 | 385 | | -0.27 [-0.36, -0.18] | 7.04 |
| Heterogeneity: $\tau^2 = 0.11$, $I^2 = 97.84\%$, | $H^2 = 46.1$ | 9 | | | | -0.58 [-1.01, -0.15] | |



Overall

Heterogeneity: $\tau^2 = 0.14$, $I^2 = 96.30\%$, $H^2 = 27.00$ Test of $\theta_i = \theta_j$: Q(18) = 984.51, p = 0.00

Test of group differences: $Q_0(1) = 7.23$, p = 0.01



(7d) Invasive Mechanical Ventilation

| | IN | ٨V | Non | n-IMV | | | Log Risk Ratio | Weight |
|---|-----------|--------|-------|------------|----|---|---------------------------|----------|
| Study | Died | Surviv | ed Di | ied Surviv | ed | | with 95% CI | (%) |
| CFS | | | | | | | | |
| Baker, May 2020 | 11 | 11 | 199 | 70 | | | -0.39 [-0.82, 0.03] | 7.60 |
| Brill, June 2020 | 10 | 26 | 227 | 147 | | | -0.78 [-1.31, -0.25] | 6.57 |
| Chinnadurai, October 2020 | 3 | 5 | 126 | 81 | | | -0.48 [-1.39, 0.42] | 3.90 |
| Hoek, September 2020 | 1 | 1 | 17 | 4 - | | | -0.48 [-1.88, 0.92] | 2.07 |
| Knights, September 2020 | 8 | 1 | 66 | 33 | | _ | 0.29 [0.02, 0.56] | 9.04 |
| Koduri, August 2020 | 36 | 28 | 266 | 162 | | | -0.10 [-0.33, 0.13] | 9.39 |
| Kokoszka-Bargiel, September 2020 | 14 | 18 | 16 | 19 | | | -0.04 [-0.58, 0.49] | 6.56 |
| Marengoni, October 2020 | 32 | 0 | 124 | 7 | | | 0.04 [-0.02, 0.10] | 10.32 |
| Tehrani, October 2020 | 20 | 10 | 180 | 60 | | | -0.12 [-0.38, 0.15] | 9.10 |
| Aliberti, February 2021 | 299 | 554 | 232 | 57 | | | -0.83 [-0.94, -0.72] | 10.15 |
| Dres, May 2021 | 350 | 390 | 300 | 159 | | | -0.32 [-0.42, -0.22] | 10.18 |
| Hendra, January 2021 | 5 | 5 | 31 | 107 | | | - 0.80 [0.11, 1.49] | 5.24 |
| Heterogeneity: $\tau^2 = 0.14$, $I^2 = 94.42\%$, | $H^2 = T$ | 17.91 | | | • | | -0.20 [-0.44, 0.05] | |
| Test of $\theta_i = \theta_j$: Q(11) = 227.59, p = 0.0 | 0 | | | | | C | Calculated RR = 1.22 [0.9 | 95-1.55] |
| Others | | | | | | | | |
| Apea, November 2020 | 146 | 135 | 64 | 16 | | | -0.43 [-0.59, -0.27] | 9.89 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = .\%$, $H^2 =$ | | | | | • | | -0.43 [-0.59, -0.27] | |
| Test of $\theta_i = \theta_j$: Q(0) = 0.00, p = . | | | | | | C | Calculated RR = 1.54 [1.3 | 31-1.80] |
| Overall | | | | | • | | -0.22 [-0.45, 0.01] | |
| Heterogeneity: $\tau^2 = 0.13$ $I^2 = 94.17\%$ | $H^2 = -$ | 17 15 | | | | | | |

Test of $\theta_i = \theta_j$: Q(12) = 236.85, p = 0.00

Test of group differences: $Q_{o}(1) = 2.48$, p = 0.12





Supplementary Figure 8: Post hoc sensitivity analysis using only CFS: Risk associated with increased frailty: CFS 1-3 (reference) with increasing CFS scores.

| | CF | S 1-3 | CF | S 4 | | Log Risk Ratio Weight |
|---|--|---|---|--|------------|--|
| Study | Yes | No | Yes | No | | with 95% CI (%) |
| Aw, October 2020 | 71 | 26 | 66 | 31 | | 0.07 [-0.11, 0.25] 8.88 |
| Davis, October 2020 | 19 | 5 | 18 | 13 | | - 0.31 [-0.05, 0.67] 5.08 |
| De Smet, July 2020 | 12 | 1 | 4 | 0 | | -0.01 [-0.35, 0.34] 5.39 |
| Hewitt, August 2020 | 491 | 84 | 133 | 52 | | 0.17 [0.08, 0.27] 10.85 |
| Koduri, August 2020 | 170 | 45 | 39 | 27 | | 0.29 [0.08, 0.50] 8.14 |
| Maguire, September 2020 | 107 | 14 | 65 | 38 | | 0.34 [0.18, 0.50] 9.39 |
| Marengoni, October 2020 | 104 | 17 | 8 | 8 | | 0.54 [0.05, 1.04] 3.40 |
| Owen, July 2020 | 28 | 22 | 39 | 34 | | 0.05 [-0.28, 0.37] 5.71 |
| Tehrani, October 2020 | 33 | 5 | 19 | 15 | | — 0.44 [0.12, 0.76] 5.76 |
| Welch, October 2020 | 1,818 | 251 | 397 | 174 | | 0.23 [0.18, 0.29] 11.49 |
| Fagard, November 2020 | 13 | 0 | 30 | 7 | B | 0.18 [-0.00, 0.37] 8.75 |
| Aliberti, February 2021 | 297 | 1,042 | 114 | 294 | | -0.23 [-0.42, -0.05] 8.80 |
| Dres, May 2021 | 498 | 328 | 62 | 98 | | 0.44 [0.24, 0.64] 8.38 |
| Overall | | | | | • | 0.20 [0.09, 0.31] |
| | | | | | | |
| Heterogeneity: $\tau^2 = 0.03$, I^2 | = 78.72 | %, H ² = | 4.70 | | | |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 | = 78.72 7, p = 0. | %, H ² = 00 | 4.70 | | | Calculated OR = 1.22 [1.09-1.36] |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: z = 3.66, p = | = 78.72 7, p = 0. 0.00 | %, H ² = 00 | 4.70 | | | Calculated OR = 1.22 [1.09-1.36] |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: z = 3.66, p = | = 78.72 7, p = 0. 0.00 | %, H ² = 00 | 4.70 | | 5 0 .5 | Calculated OR = 1.22 [1.09-1.36] |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: z = 3.66, p = | = 78.72 7, p = 0. 0.00 CFS | %, H ² = 00 \$ 1-3 | 4.70 CF | S 5 | 5 0 .5 | Calculated OR = 1.22 [1.09-1.36] |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: z = 3.66, p = Study | = 78.72 7, p = 0. 0.00 CFS Yes | %, H ² = 00 6 1-3 No | 4.70 CF Yes | S 5 No | 5 0 .5 | Calculated OR = 1.22 [1.09-1.36] 1 Log Risk Ratio Weight with 95% CI (%) |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: z = 3.66, p = Study Aw, October 2020 | = 78.72 7, p = 0. 0.00 CFS Yes 71 | %, H ² = 00 5 1-3 No 26 | 4.70 CF Yes 70 | S 5 <u>No</u> 31 | 5 0 .5 | Calculated OR = 1.22 [1.09-1.36] 1 Log Risk Ratio with 95% CI 0.05 [-0.12, 0.23] 11.69 |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: z = 3.66, p = Study Aw, October 2020 Davis, October 2020 | = 78.72 7, p = 0. 0.00 CFS Yes 71 19 | %, H ² = 00 5 1-3 No 26 5 | 4.70 CF Yes 70 36 | S 5 <u>No</u> 31 21 | 5 0 .5 | Log Risk Ratio with 95% CI Weight (%) 0.05 [-0.12, 0.23] 11.69 0.23 [-0.06, 0.51] 9.96 |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: z = 3.66, p = Study Aw, October 2020 Davis, October 2020 De Smet, July 2020 | = 78.72 7, p = 0. 0.00 CFS Yes 71 19 12 | %, H ² = 00 5 1-3 No 26 5 1 | 4.70 CF Yes 70 36 5 | S 5 <u>No</u> 31 21 1 | 5 0 .5 | Log Risk Ratio with 95% CI Weight (%) 0.05 [-0.12, 0.23] 11.69 0.23 [-0.06, 0.51] 9.96 0.10 [-0.29, 0.49] 8.22 |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: z = 3.66, p = Study Aw, October 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 | = 78.72 7, p = 0. 0.00 CFS Yes 71 19 12 491 | %, H ² = 00 5 1-3 No 26 5 1 84 | 4.70 CF Yes 70 36 5 132 | S 5 No 31 21 1 50 | 5 0 .5 | Log Risk Ratio with 95% CI Weight (%) 0.05 [-0.12, 0.23] 11.69 0.23 [-0.06, 0.51] 9.96 0.10 [-0.29, 0.49] 8.22 0.16 [0.07, 0.26] 12.67 |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: z = 3.66, p = Study Aw, October 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 | = 78.72 7, p = 0. 0.00 CFS Yes 71 19 12 491 170 | %, $H^{2} =$ 00 5 1-3 No 26 5 1 84 45 | 4.70 CF Yes 70 36 5 132 26 | S 5 <u>No</u> 31 21 1 50 24 | 5 0 .5 | Calculated OR = 1.22 [1.09-1.36] 1 Log Risk Ratio with 95% CI Weight (%) 0.05 [-0.12, 0.23] 11.69 0.23 [-0.06, 0.51] 9.96 0.10 [-0.29, 0.49] 8.22 0.16 [0.07, 0.26] 12.67 0.42 [0.14, 0.69] 10.13 |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: $z = 3.66$, $p =$ Study Aw, October 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 Marengoni, October 2020 | = 78.72 7, p = 0. 0.00 CFS Yes 71 19 12 491 170 104 | %, $H^2 = 00$ 5 1-3 No 26 5 1 84 45 17 | 4.70 CF Yes 70 36 5 132 26 2 | S 5 No 31 21 1 50 24 3 | 5 0 .5 | 1 Log Risk Ratio with 95% CI Weight (%) $0.05 [-0.12, 0.23]$ 11.69 $0.23 [-0.06, 0.51]$ 9.96 $0.10 [-0.29, 0.49]$ 8.22 $0.16 [0.07, 0.26]$ 12.67 $0.42 [0.14, 0.69]$ 10.13 $0.76 [-0.31, 1.84]$ 2.38 |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: $z = 3.66$, $p =$ Study Aw, October 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 Marengoni, October 2020 Tehrani, October 2020 | = 78.72 7, p = 0. 0.00 CFS Yes 71 19 12 491 170 104 33 | %, $H^2 = 00$ 5 1-3 No 26 5 1 84 45 17 5 | 4.70 CF Yes 70 36 5 132 26 2 21 | S 5 No 31 21 1 50 24 3 17 | 5 0 .5 | Log Risk Ratio weight with 95% CI Weight (%) 0.05 [-0.12, 0.23] 11.69 0.23 [-0.06, 0.51] 9.96 0.10 [-0.29, 0.49] 8.22 0.16 [0.07, 0.26] 12.67 0.42 [0.14, 0.69] 10.13 0.76 [-0.31, 1.84] 2.38 0.45 [0.14, 0.76] 9.51 |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: $z = 3.66$, $p =$ Study Aw, October 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 Marengoni, October 2020 Tehrani, October 2020 Welch, October 2020 | = 78.72 7, p = 0. 0.00 CFS Yes 71 19 12 491 170 104 33 1,818 | %, $H^2 = 00$ 5 1-3 No 26 5 1 84 45 17 5 251 | 4.70 CF Yes 70 36 5 132 26 2 21 397 | S 5 No 31 21 1 50 24 3 17 207 | | Calculated OR = 1.22 [1.09-1.36] 1 Log Risk Ratio with 95% CI $0.05 [-0.12, 0.23]$ 0.05 [-0.12, 0.23] 11.69 0.23 [-0.06, 0.51] 9.96 0.10 [-0.29, 0.49] 8.22 0.16 [0.07, 0.26] 12.67 0.42 [0.14, 0.69] 0.76 [-0.31, 1.84] 2.38 0.45 [0.14, 0.76] 9.51 0.29 [0.23, 0.35] |
| Heterogeneity: $\tau^2 = 0.03$, I^2 Test of $\theta_i = \theta_j$: Q(12) = 39.7 Test of $\theta = 0$: $z = 3.66$, $p =$ Study Aw, October 2020 Davis, October 2020 De Smet, July 2020 Hewitt, August 2020 Koduri, August 2020 Marengoni, October 2020 Tehrani, October 2020 Welch, October 2020 Fagard, November 2020 | = 78.72 7, p = 0. 0.00 CFS Yes 71 19 12 491 170 104 33 1,818 13 | %, $H^2 = 00$ 5 1-3 No 26 5 1 84 45 17 5 251 0 | 4.70 CF Yes 70 36 5 132 26 2 21 397 45 | S 5 No 31 21 1 50 24 3 17 207 38 | | Log Risk Ratio with 95% CI Weight (%) 0.05 [-0.12, 0.23] 11.69 0.23 [-0.06, 0.51] 9.96 0.10 [-0.29, 0.49] 8.22 0.16 [0.07, 0.26] 12.67 0.42 [0.14, 0.69] 10.13 0.76 [-0.31, 1.84] 2.38 0.45 [0.14, 0.76] 9.51 0.29 [0.23, 0.35] 12.94 0.58 [0.36, 0.80] 11.02 |



Test of θ = 0: z = 2.35, p = 0.02

0.22 [0.04, 0.40]

Calculated OR = 1.25 [1.04-1.49]



| | CFS 1-3 | | CFS 7-9 | | | Log Risk Ratio | Weight |
|-------------------------|---------|-------|---------|-----|---|-----------------------|--------|
| Study | Yes | No | Yes | No | | with 95% CI | (%) |
| Aw, October 2020 | 71 | 26 | 85 | 81 | | 0.36 [0.17, 0.55] | 10.35 |
| Davis, October 2020 | 19 | 5 | 14 | 24 | | 0.76 [0.30, 1.23] | 7.77 |
| De Smet, July 2020 | 12 | 1 | 28 | 14 | | 0.33 [0.06, 0.59] | 9.74 |
| Hewitt, August 2020 | 491 | 84 | 214 | 152 | | 0.38 [0.29, 0.47] | 10.91 |
| Koduri, August 2020 | 170 | 45 | 35 | 58 | | 0.74 [0.47, 1.01] | 9.69 |
| Marengoni, October 2020 | 104 | 17 | 2 | 7 | | 1.35 [0.13, 2.58] | 2.79 |
| Owen, July 2020 | 28 | 22 | 24 | 20 | | 0.03 [-0.34, 0.39] | 8.78 |
| Welch, October 2020 | 1,818 | 251 | 539 | 418 | | 0.44 [0.39, 0.50] | 11.03 |
| Fagard, November 2020 | 13 | 0 | 17 | 10 | | 0.43 [0.13, 0.74] | 9.38 |
| Aliberti, February 2021 | 297 | 1,042 | 80 | 139 | | -0.50 [-0.70, -0.30] | 10.27 |
| Dres, May 2021 | 498 | 328 | 29 | 70 | | 0.72 [0.41, 1.03] | 9.31 |
| Overall | | | | | • | 0.39 [0.15, 0.62] | |

Heterogeneity: $\tau^2 = 0.13$, $I^2 = 94.32\%$, $H^2 = 17.61$



Test of $\theta_i = \theta_j$: Q(10) = 98.35, p = 0.00

Test of θ = 0: z = 3.21, p = 0.00



