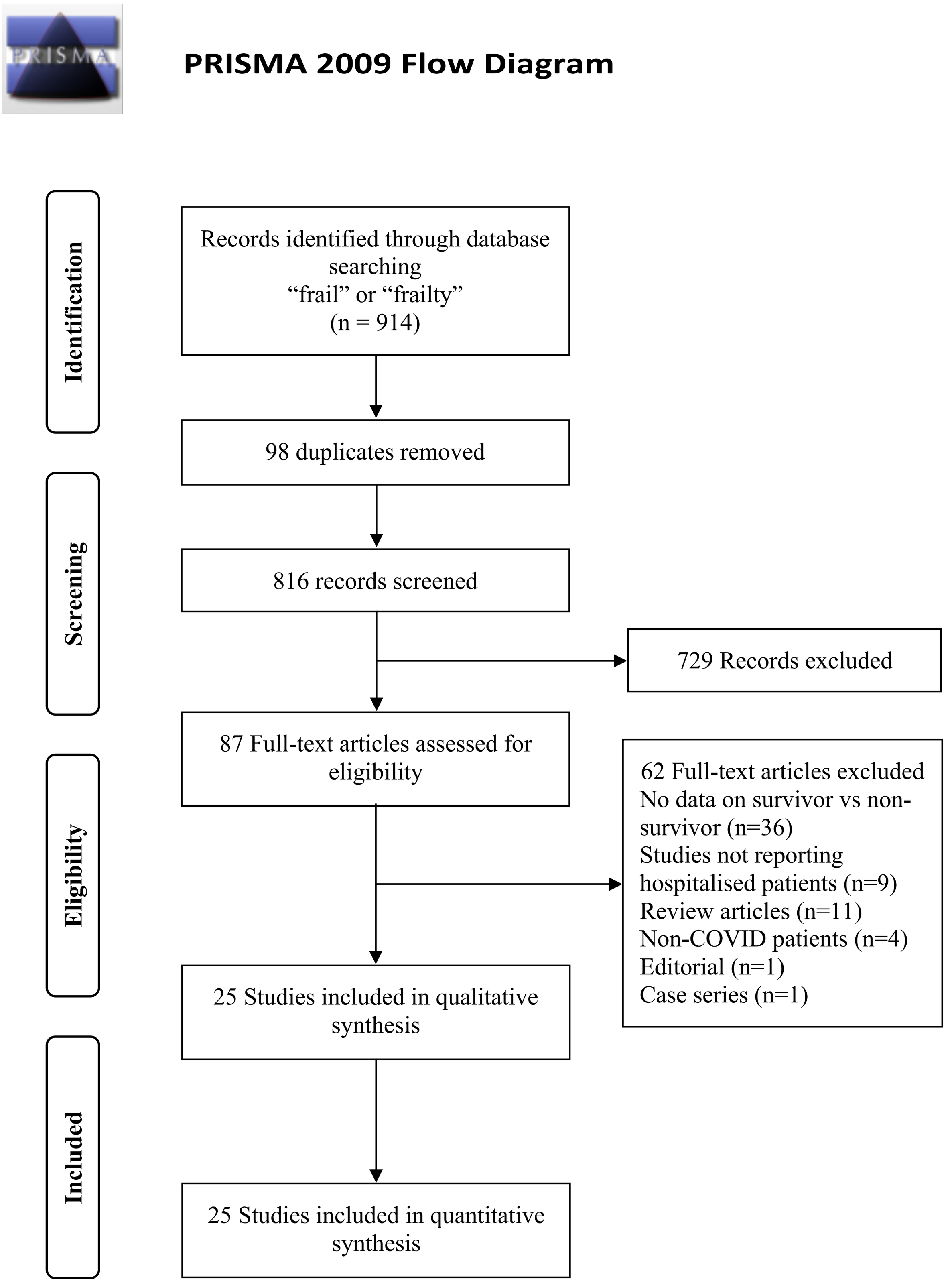
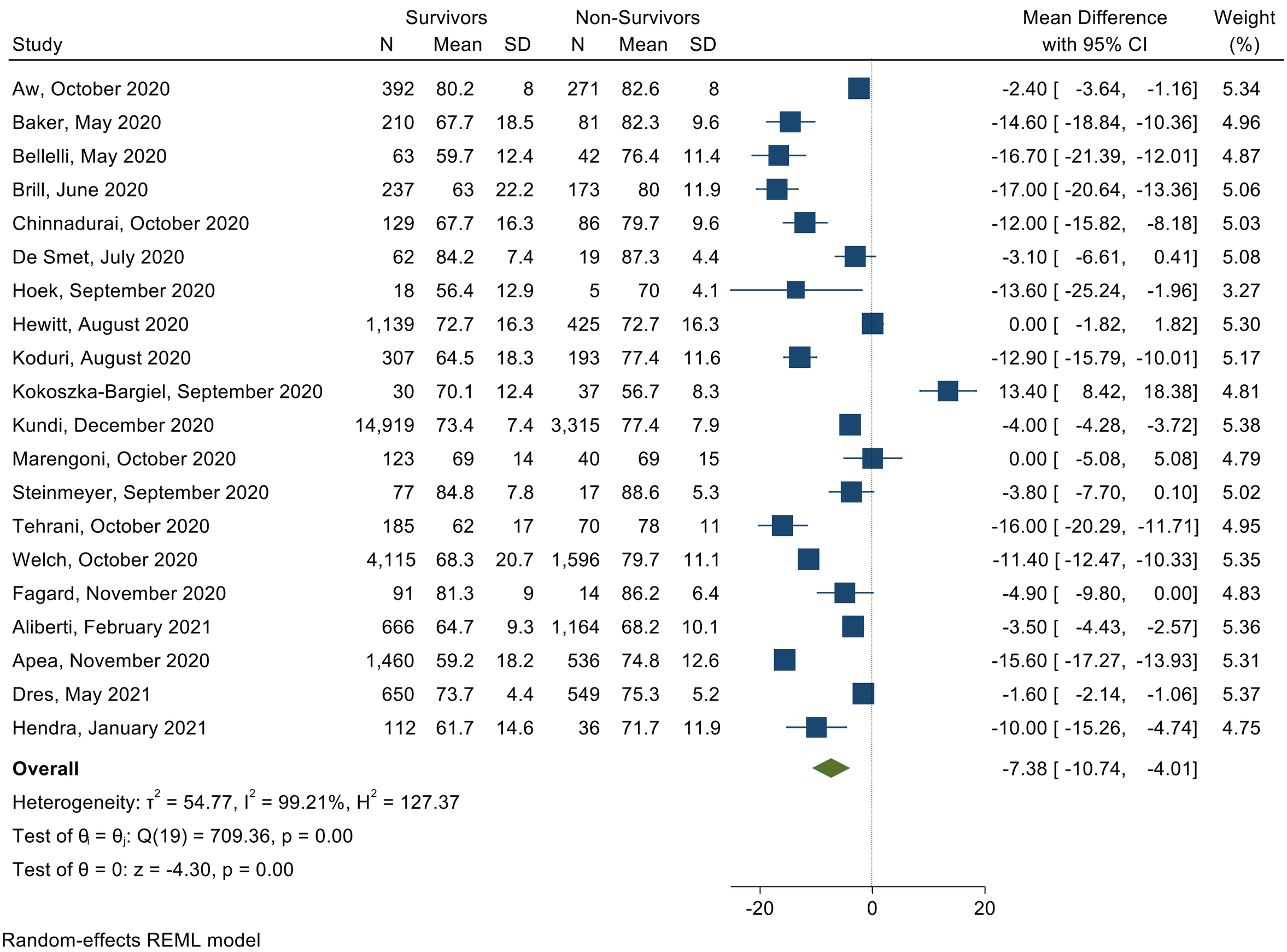
Supplementary Figure 1: PRISMA flowchart of study inclusions and exclusions.

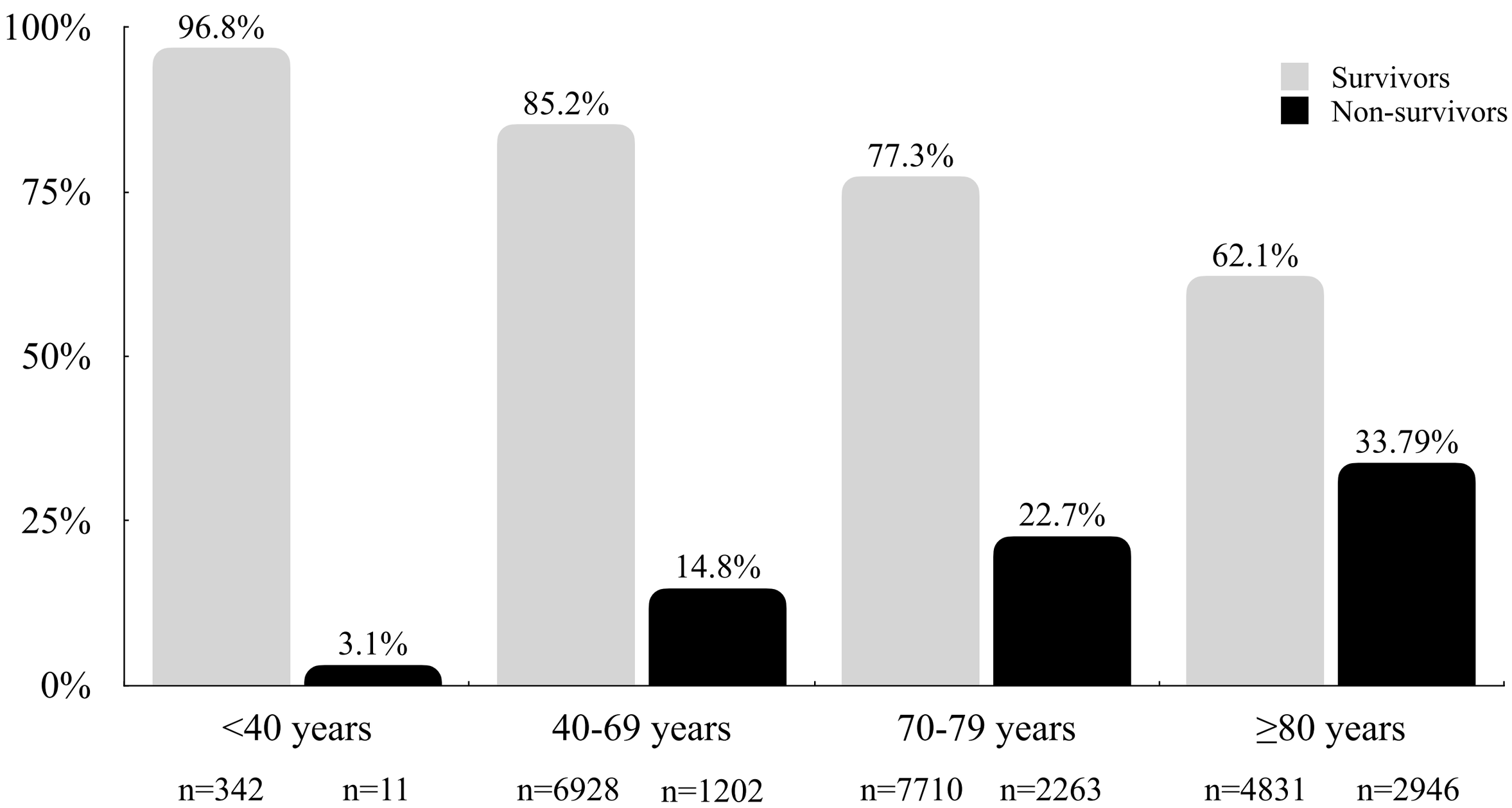


From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

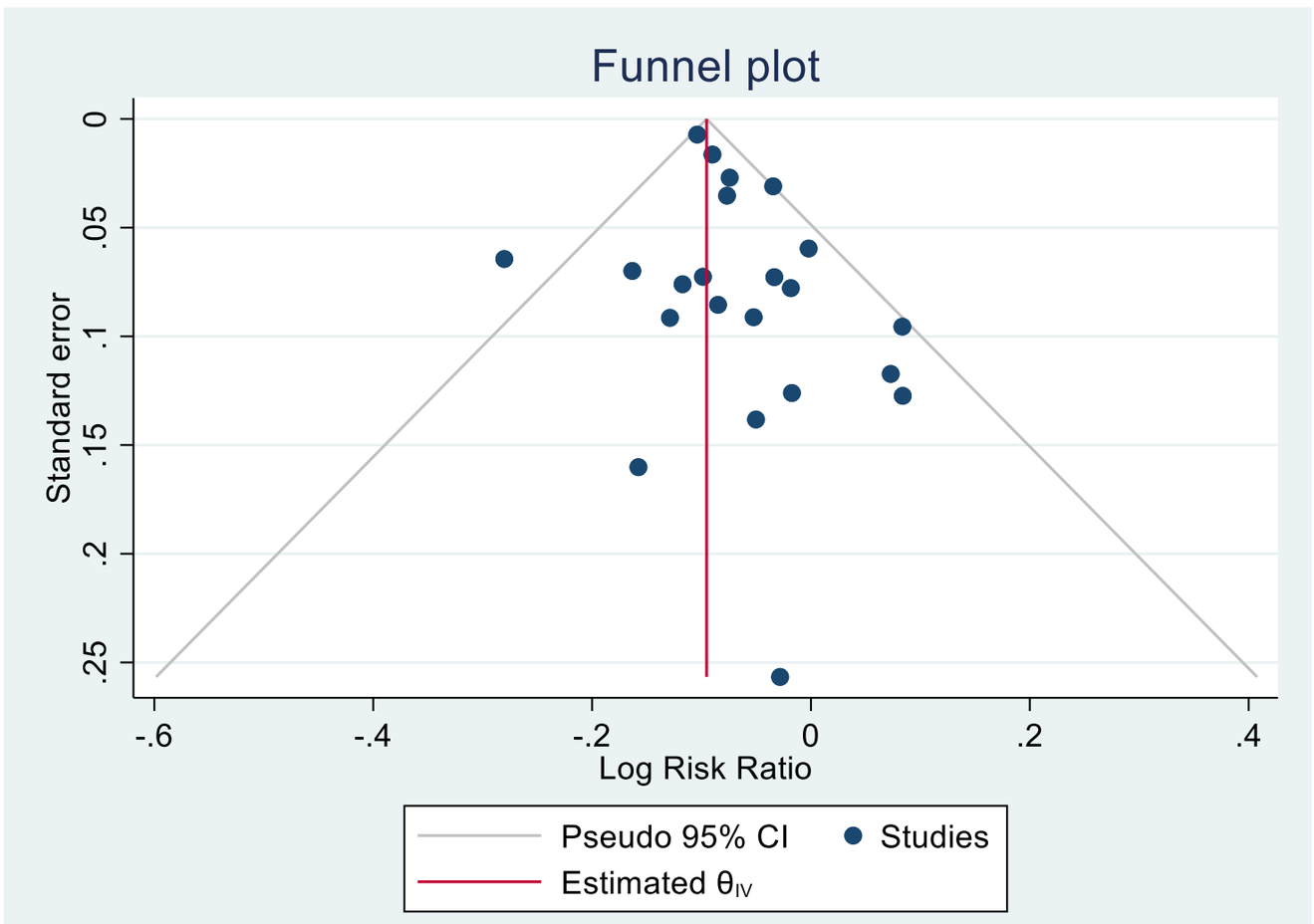
Supplementary Figure 2: Standardised mean difference in age and age-stratified raw outcomes between survivors and non-survivors





Supplementary Figure 3: Age-stratified gender difference amongst survivors and non-survivors.

(3a) Funnel plot

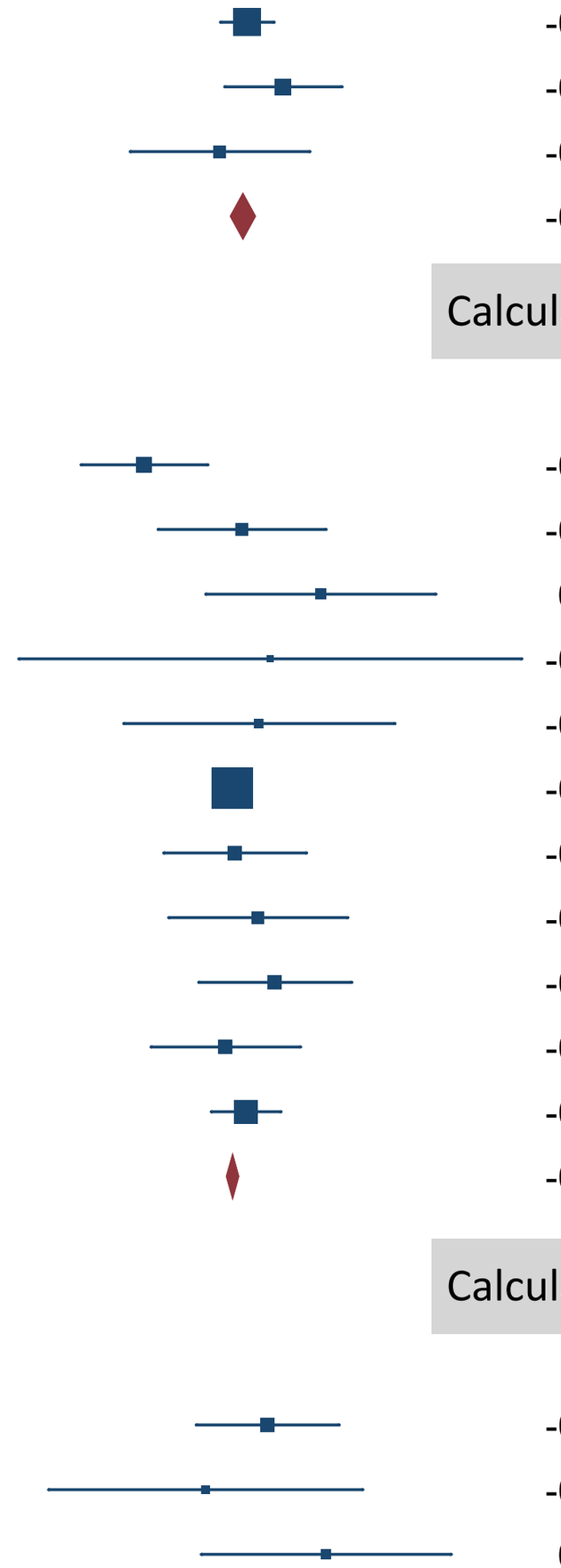


(3b) Egger's Test

```
. . 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 =      0.53
       SE of beta1 =     0.273
                 z =      1.93
          Prob > |z| =    0.0539
```

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

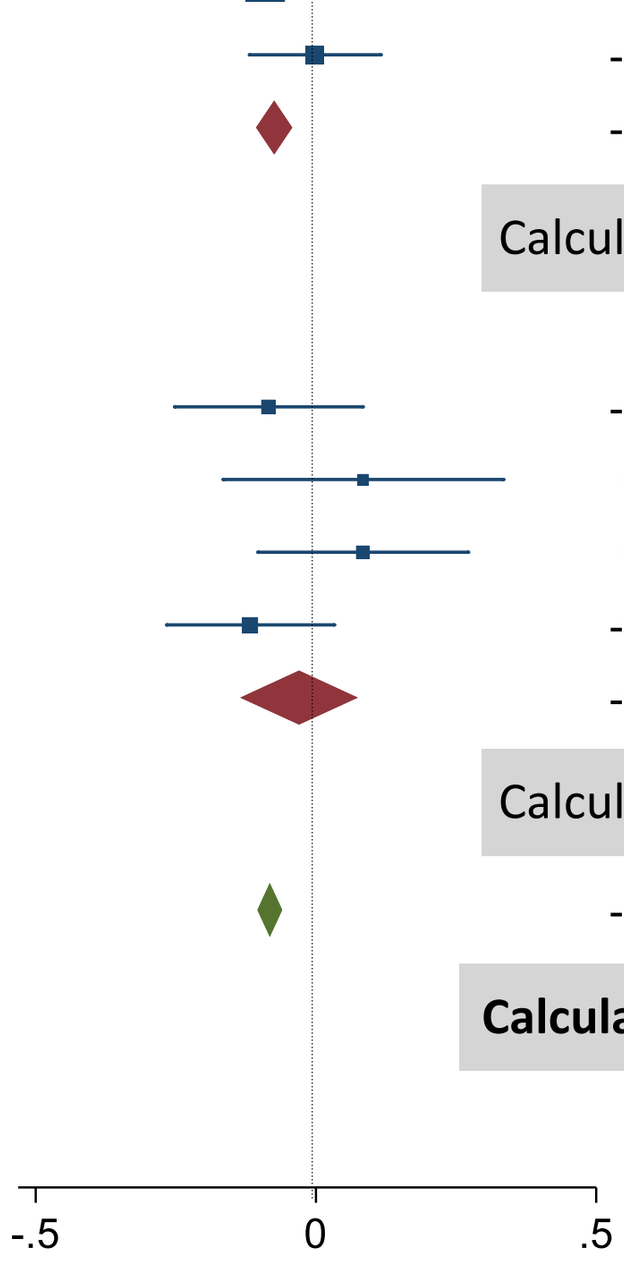
Study	Male Died	Male Survived	Female Died	Female Survived	Log Risk Ratio with 95% CI	Weight (%)
Good						
Welch, October 2020	2,177	972	1,938	624	-0.09 [-0.12, -0.06]	18.49
Apea, November 2020	859	351	601	185	-0.07 [-0.13, -0.02]	11.09
Dres, May 2021	473	400	177	149	-0.00 [-0.12, 0.11]	3.22
Hendra, January 2021	60	24	52	12	-0.13 [-0.31, 0.05]	1.46
Heterogeneity: τ^2 = 0.00, I^2 = 0.02%, H^2 = 1.00					-0.08 [-0.11, -0.06]	
Test of $\theta_i = \theta_j$: Q(3) = 2.38, p = 0.50					Calculated RR = 1.08 [1.06-1.11]	
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: τ^2 = 0.00, I^2 = 0.00%, H^2 = 1.00					-0.10 [-0.12, -0.09]	
Test of $\theta_i = \theta_j$: Q(10) = 12.20, p = 0.27					Calculated RR = 1.08 [1.06-1.11]	
Poor						
Baker, May 2020	113	46	97	35	-0.03 [-0.18, 0.11]	2.24
Bellelli, May 2020	41	31	22	11	-0.16 [-0.47, 0.16]	0.49
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
Hewitt, August 2020	648	255	491	170	-0.03 [-0.10, 0.03]	9.24
Koduri, August 2020	172	128	135	65	-0.16 [-0.30, -0.03]	2.41
Steinmeyer, September 2020	36	6	41	11	0.08 [-0.10, 0.27]	1.34
Heterogeneity: τ^2 = 0.00, I^2 = 0.00%, H^2 = 1.00					-0.04 [-0.09, 0.01]	
Test of $\theta_i = \theta_j$: Q(6) = 6.34, p = 0.39					Calculated RR = 1.08 [1.06-1.11]	
Overall					-0.08 [-0.10, -0.06]	
Heterogeneity: τ^2 = 0.00, I^2 = 23.02%, H^2 = 1.30					**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						



Random-effects REML model

(3d) Age-stratification

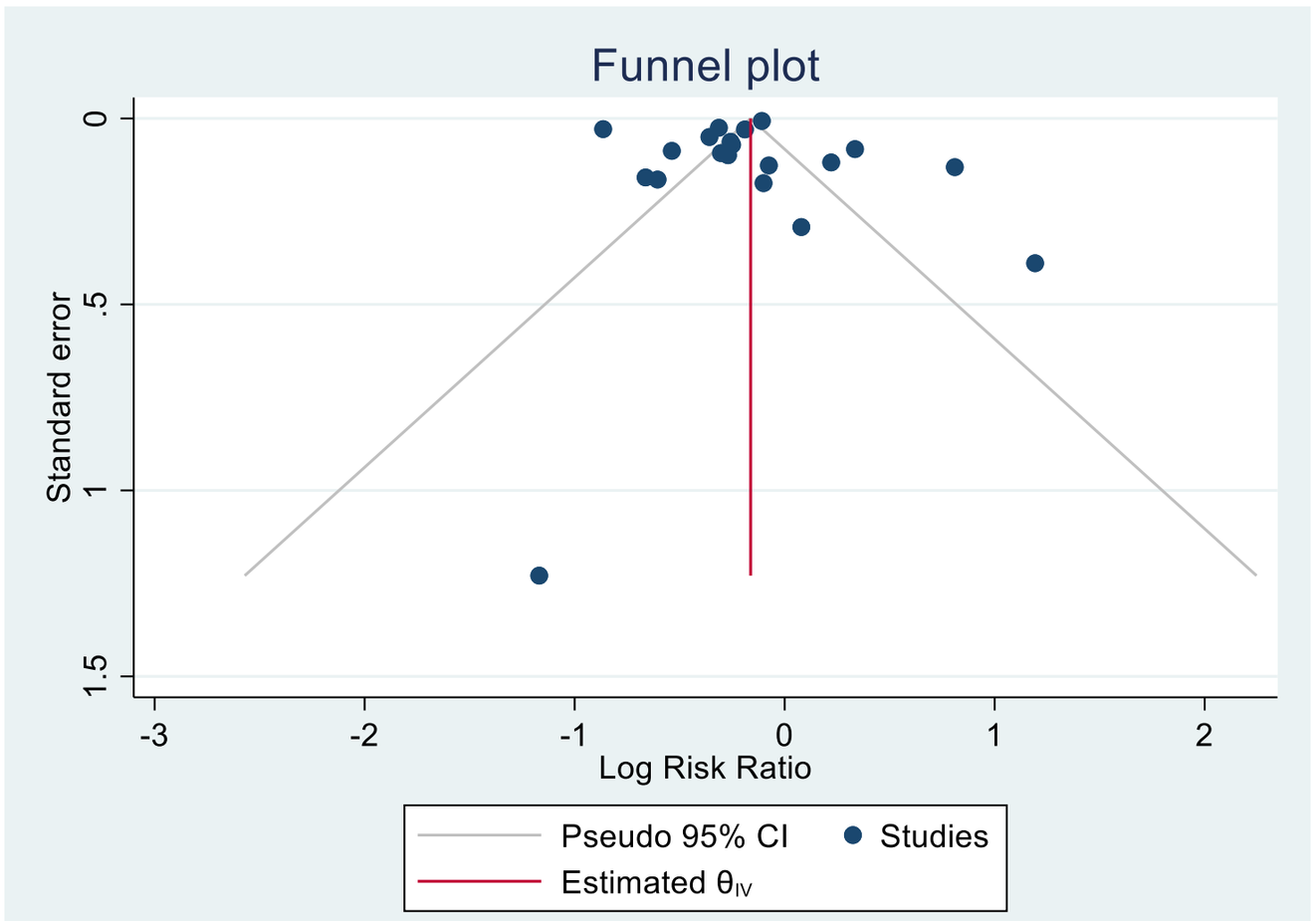
Study	Male Died	Male Survived	Female Died	Female Survived	Log Risk Ratio with 95% CI	Weight (%)
60-69 years						
Aw, October 2020	185	174	208	97	-0.28 [-0.41, -0.15]	2.80
Hoek, September 2020	14	4	4	1	-0.03 [-0.53, 0.47]	0.19
Knights, September 2020	38	20	31	14	-0.05 [-0.32, 0.22]	0.65
Koduri, August 2020	172	128	135	65	-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 2020	108	42	77	28	-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 2020	859	351	601	185	-0.07 [-0.13, -0.02]	11.09
Hendra, January 2021	60	24	52	12	-0.13 [-0.31, 0.05]	1.46
Heterogeneity: τ^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 2020	113	46	97	35	-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: τ^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]	
≥80 years						
Brill, June 2020	134	111	103	70	-0.08 [-0.25, 0.08]	1.65
Davis, October 2020	87	61	40	34	0.08 [-0.17, 0.33]	0.77
Steinmeyer, September 2020	36	6	41	11	0.08 [-0.10, 0.27]	1.34
Fagard, November 2020	45	10	46	4	-0.12 [-0.27, 0.03]	2.06
Heterogeneity: τ^2 = 0.00, I^2 = 24.86%, H^2 = 1.33					-0.03 [-0.13, 0.07]	
Test of $\theta_i = \theta_j$: Q(3) = 3.92, p = 0.27						
					Calculated RR = 1.03 [0.93-1.14]	
Overall					-0.08 [-0.10, -0.06]	
Heterogeneity: τ^2 = 0.00, I^2 = 23.02%, H^2 = 1.30						
Test of $\theta_i = \theta_j$: Q(21) = 28.31, p = 0.13						
					Calculated RR = 1.08 [1.06-1.11]	
Test of group differences: $Q_b(2)$ = 1.76, p = 0.41						



Random-effects REML model

Supplementary Figure 4: Frail vs. non-frail patients

(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 =      0.82
      SE of beta1 =     0.828
                z =      0.98
      Prob > |z| =    0.3247
```

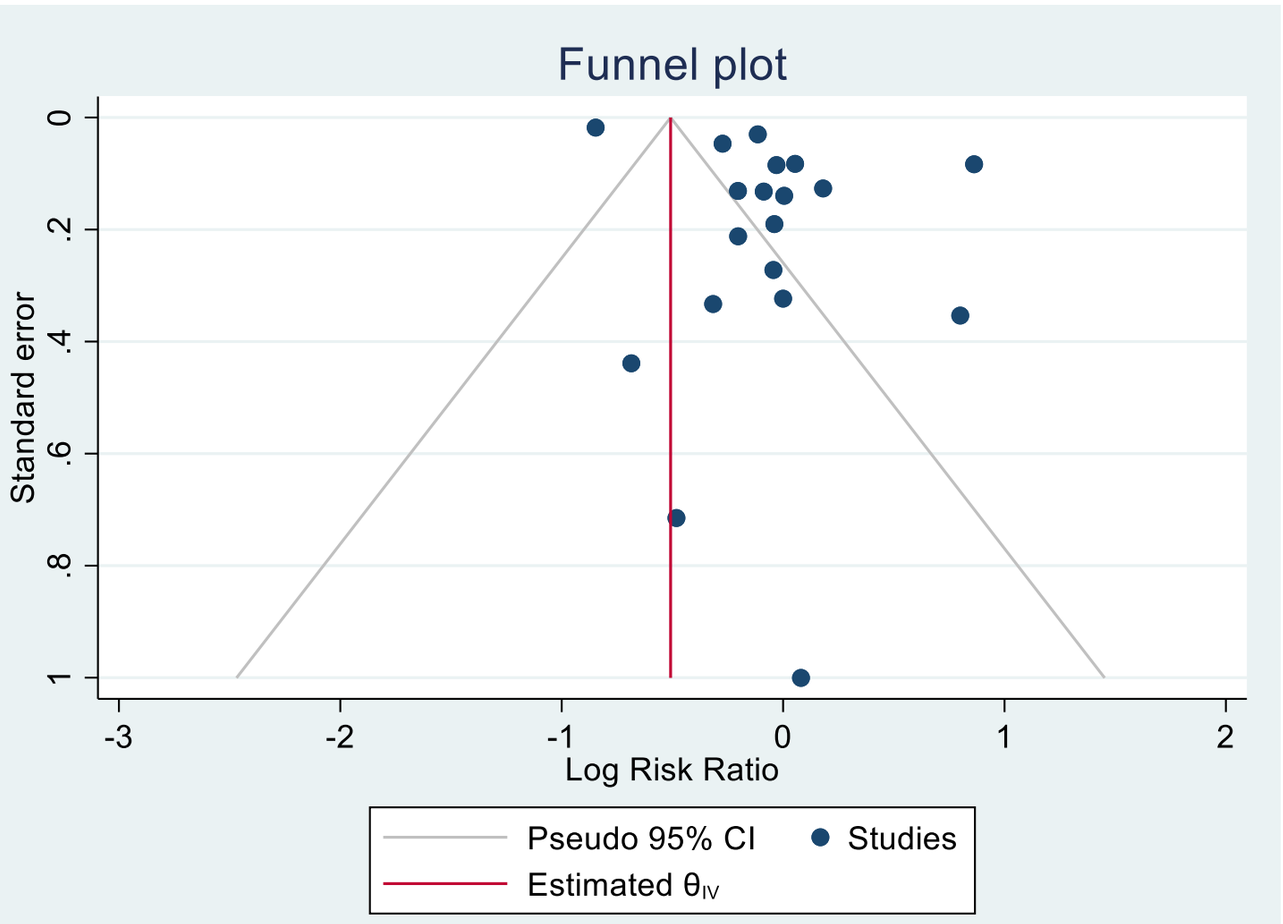
(5c) Forest plots based on quality of studies (NOS)

Study	Frail Died	Frail Survived	Non-Frail Died	Non-Frail 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: τ^2 = 0.08, I^2 = 97.60%, H^2 = 41.73					-0.53 [-0.82, -0.25]	
Test of $\theta_i = \theta_j$: Q(3) = 216.59, p = 0.00					Calculated RR = 1.70 [0.78-2.27]	
Fair						
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
Hoek, September 2020	0	1	18	4	-1.17 [-3.58, 1.24]	0.57
Kundi, December 2020	9,697	2,598	5,222	717	-0.11 [-0.12, -0.10]	5.77
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
Tehrani, October 2020	28	43	52	20	-0.61 [-0.93, -0.28]	4.97
Fagard, November 2020	48	14	43	0	-0.25 [-0.39, -0.11]	5.60
Aliberti, February 2021	239	255	925	411	-0.36 [-0.46, -0.26]	5.68
Heterogeneity: τ^2 = 0.28, I^2 = 98.71%, H^2 = 77.25					Calculated RR = 1.43 [1.30-1.58]	
Test of $\theta_i = \theta_j$: Q(8) = 133.80, p = 0.00						
Poor						
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
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
Owen, July 2020	51	45	63	47	-0.08 [-0.32, 0.17]	5.26
Steinmeyer, September 2020	9	3	68	14	-0.10 [-0.44, 0.24]	4.88
Heterogeneity: τ^2 = 0.05, I^2 = 85.10%, H^2 = 6.71					-0.15 [-0.34, 0.04]	
Test of $\theta_i = \theta_j$: Q(6) = 30.53, p = 0.00					Calculated RR = 1.04 [0.96-1.40]	
Overall					-0.16 [-0.35, 0.03]	
Heterogeneity: τ^2 = 0.17, I^2 = 98.86%, H^2 = 87.93					**Calculated RR = 1.17 [0.97-1.42]**	
Test of $\theta_i = \theta_j$: Q(19) = 875.07, p = 0.00						
Test of group differences: $Q_b(2)$ = 6.71, p = 0.03						

Random-effects REML model

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

(5a) Funnel plot

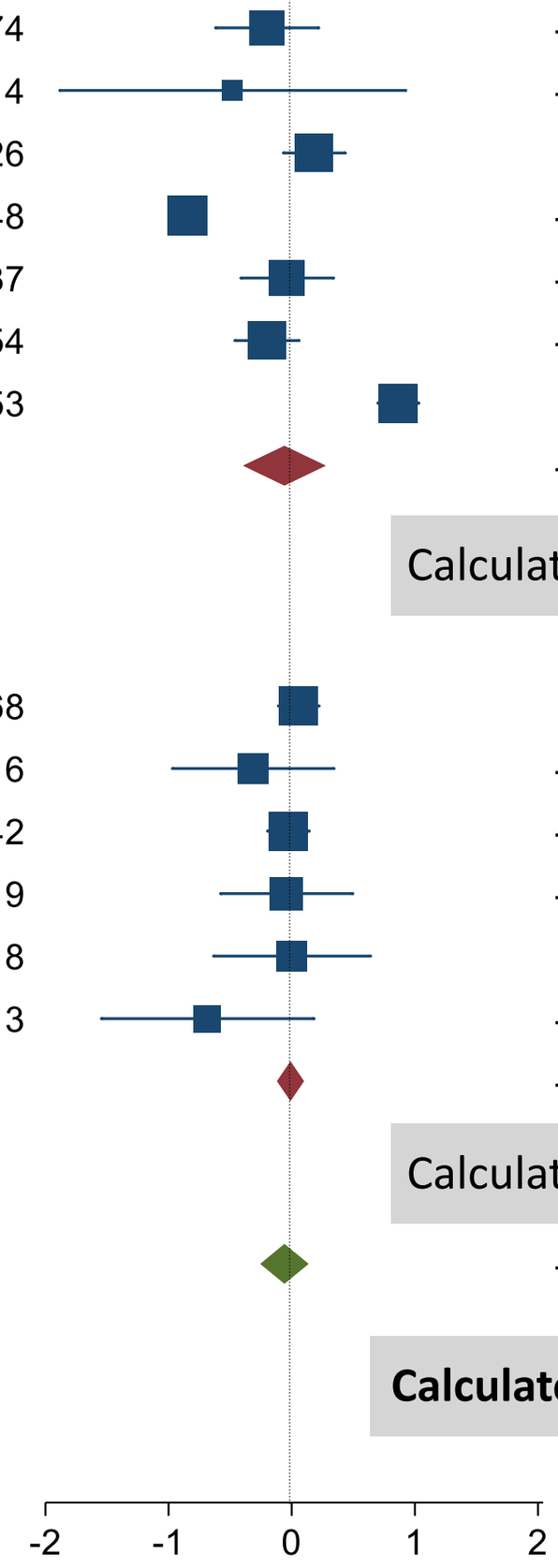


(5b) Egger's Test

```
. . 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 =      0.07
      Prob > |z| =    0.9450
```

(5c) Forest plots based on quality of studies

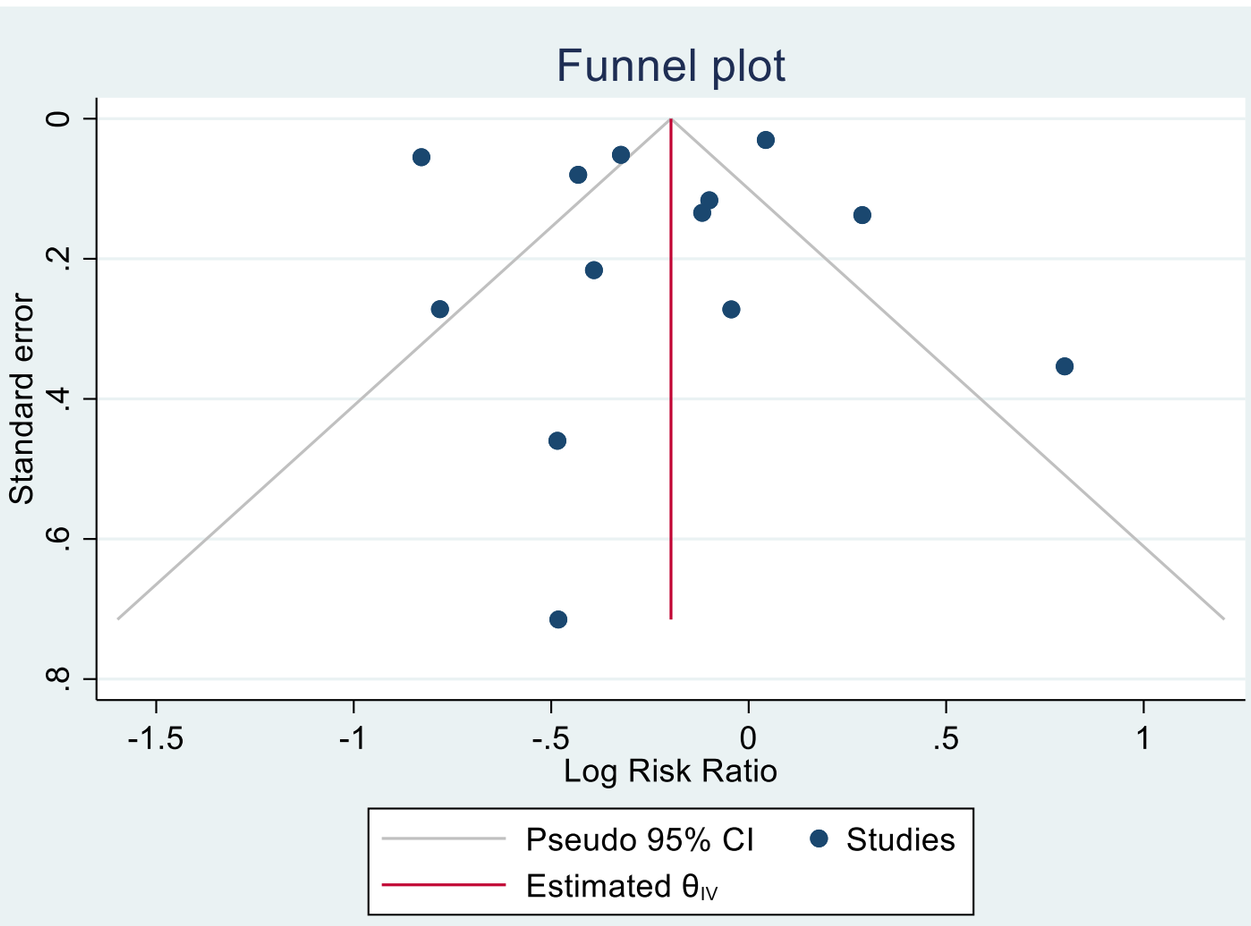
Study	ICU Admission Died	ICU Admission Survived	No ICU Admission Died	No ICU Admission Survived	Log Risk Ratio with 95% CI	Weight (%)
Good						
Welch, October 2020	421	226	3,694	1,370	-0.11 [-0.17, -0.06]	7.10
Apea, November 2020	210	151	1,250	385	-0.27 [-0.36, -0.18]	7.04
Dres, May 2021	650	549	0	0	0.08 [-1.88, 2.04]	0.87
Hendra, January 2021	5	5	31	107	0.80 [0.11, 1.49]	3.76
Heterogeneity: τ^2 = 0.16, I^2 = 97.33%, H^2 = 37.41					0.03 [-0.45, 0.52]	
Test of $\theta_i = \theta_j$: Q(3) = 15.61, p = 0.00						
					Calculated RR = 1.03 [0.64-1.68]	
Fair						
Aw, October 2020	22	15	371	256	0.00 [-0.27, 0.28]	6.27
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
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
Kundi, December 2020	1,843	2,667	13,076	648	-0.85 [-0.88, -0.81]	7.13
Marengoni, October 2020	8	3	115	37	-0.04 [-0.41, 0.33]	5.67
Tehrani, October 2020	25	16	160	54	-0.20 [-0.46, 0.05]	6.36
Aliberti, February 2021	531	611	135	553	0.86 [0.70, 1.03]	6.81
Heterogeneity: τ^2 = 0.22, I^2 = 95.67%, H^2 = 23.09					-0.06 [-0.39, 0.28]	
Test of $\theta_i = \theta_j$: Q(8) = 543.67, p = 0.00						
					Calculated RR = 0.94 [0.68-1.32]	
Poor						
Baker, May 2020	45	14	177	68	0.05 [-0.11, 0.22]	6.81
De Smet, July 2020	4	3	58	16	-0.32 [-0.97, 0.34]	3.98
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
Owen, July 2020	9	8	9	8	0.00 [-0.63, 0.63]	4.08
Steinmeyer, September 2020	3	4	74	13	-0.69 [-1.55, 0.17]	3.00
Heterogeneity: τ^2 = 0.00, I^2 = 0.00%, H^2 = 1.00					-0.01 [-0.12, 0.10]	
Test of $\theta_i = \theta_j$: Q(5) = 3.89, p = 0.57						
					Calculated RR = 0.99 [0.89-1.11]	
Overall					-0.06 [-0.25, 0.14]	
Heterogeneity: τ^2 = 0.14, I^2 = 96.30%, H^2 = 27.00						
Test of $\theta_i = \theta_j$: Q(18) = 984.51, p = 0.00						
					Calculated RR = 0.94 [0.78-1.15]	
Test of group differences: $Q_b(2)$ = 0.11, p = 0.95						



Random-effects REML model

Supplementary Figure 6: Invasive Mechanical Ventilation (IMV):

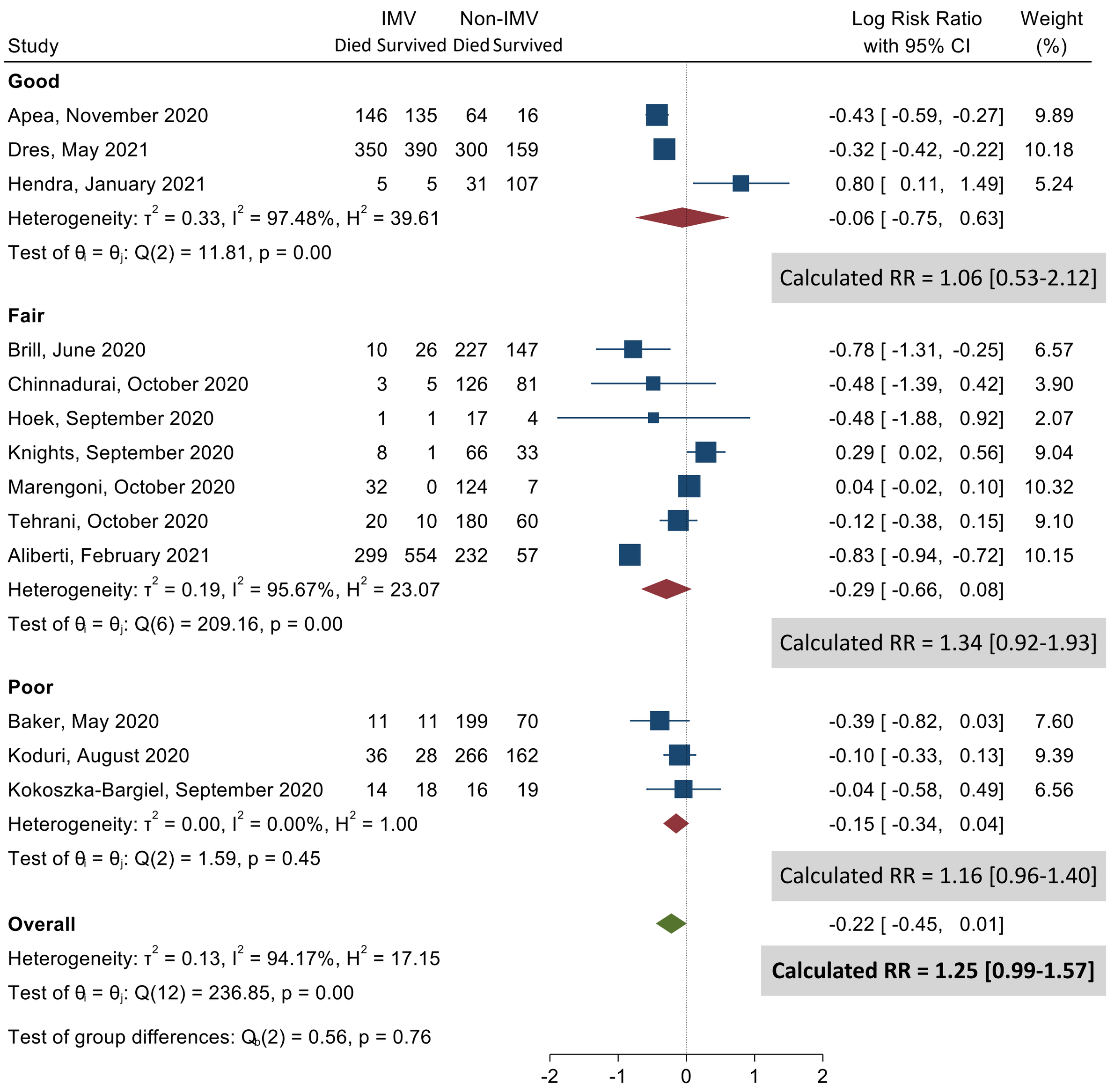
(6a) Funnel plot



(6b) Egger's Test

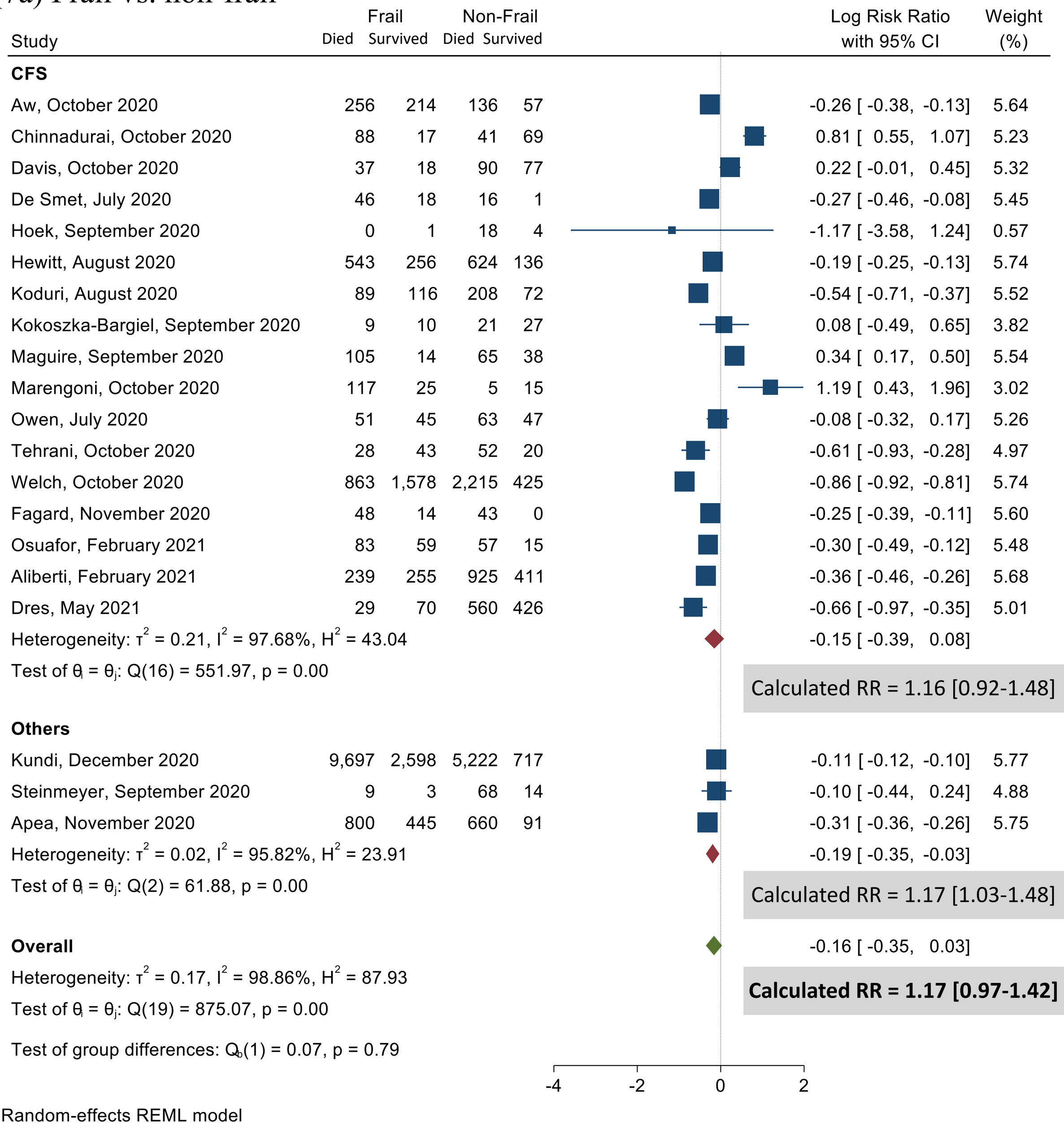
```
. . meta bias, egger

  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

H0: beta1 = 0; no small-study effects
            beta1 =      0.24
      SE of beta1 =     0.853
                z =      0.29
      Prob > |z| =    0.7756
```

(6c) Forest plots based on quality of studies



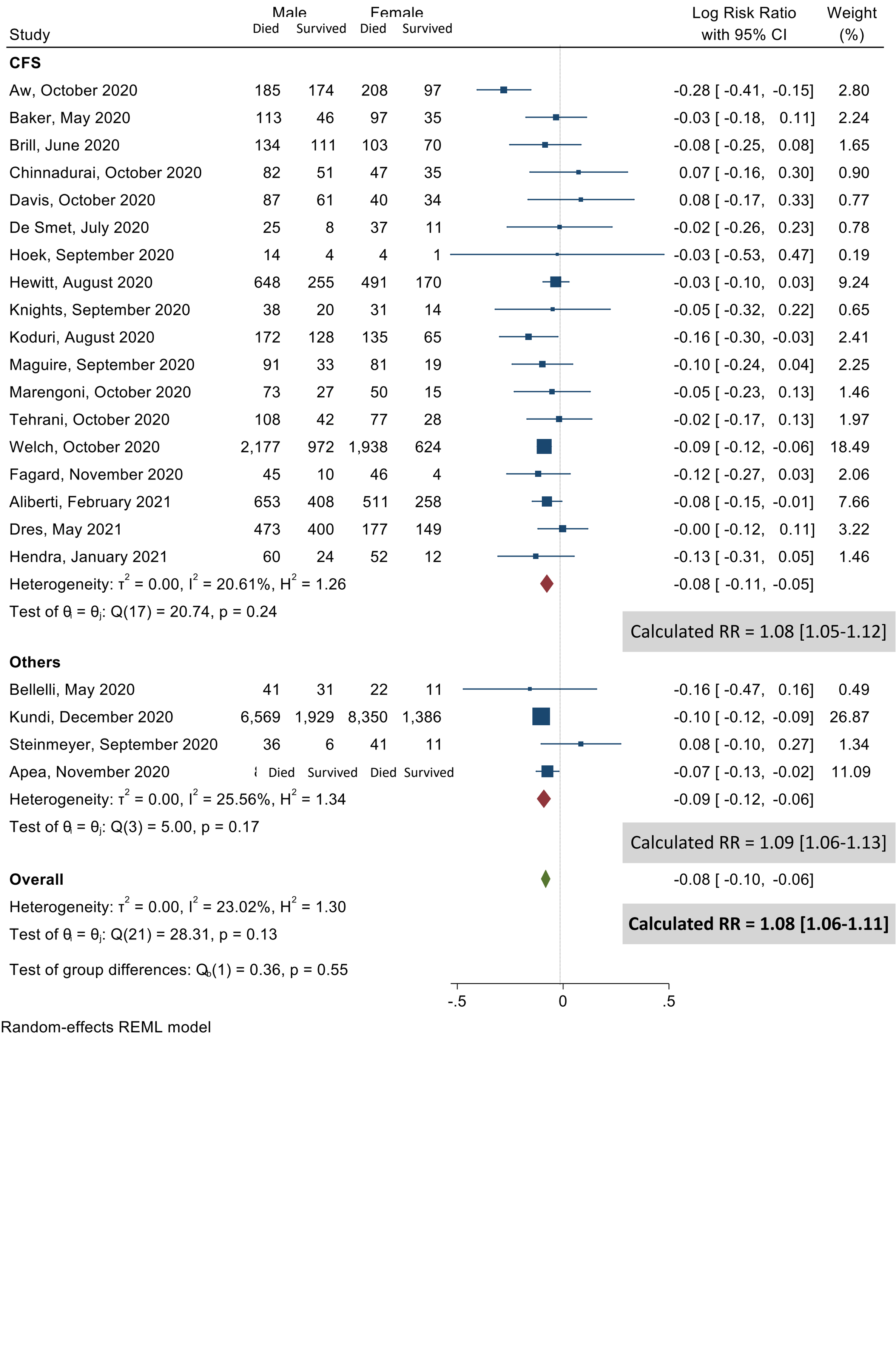
Supplementary Figure 7: Post Hoc Analysis CFS vs other frailty measures.

(7a) Frail vs. non-frail



Supplementary Figure 7: Post Hoc Analysis CFS vs other frailty measures.

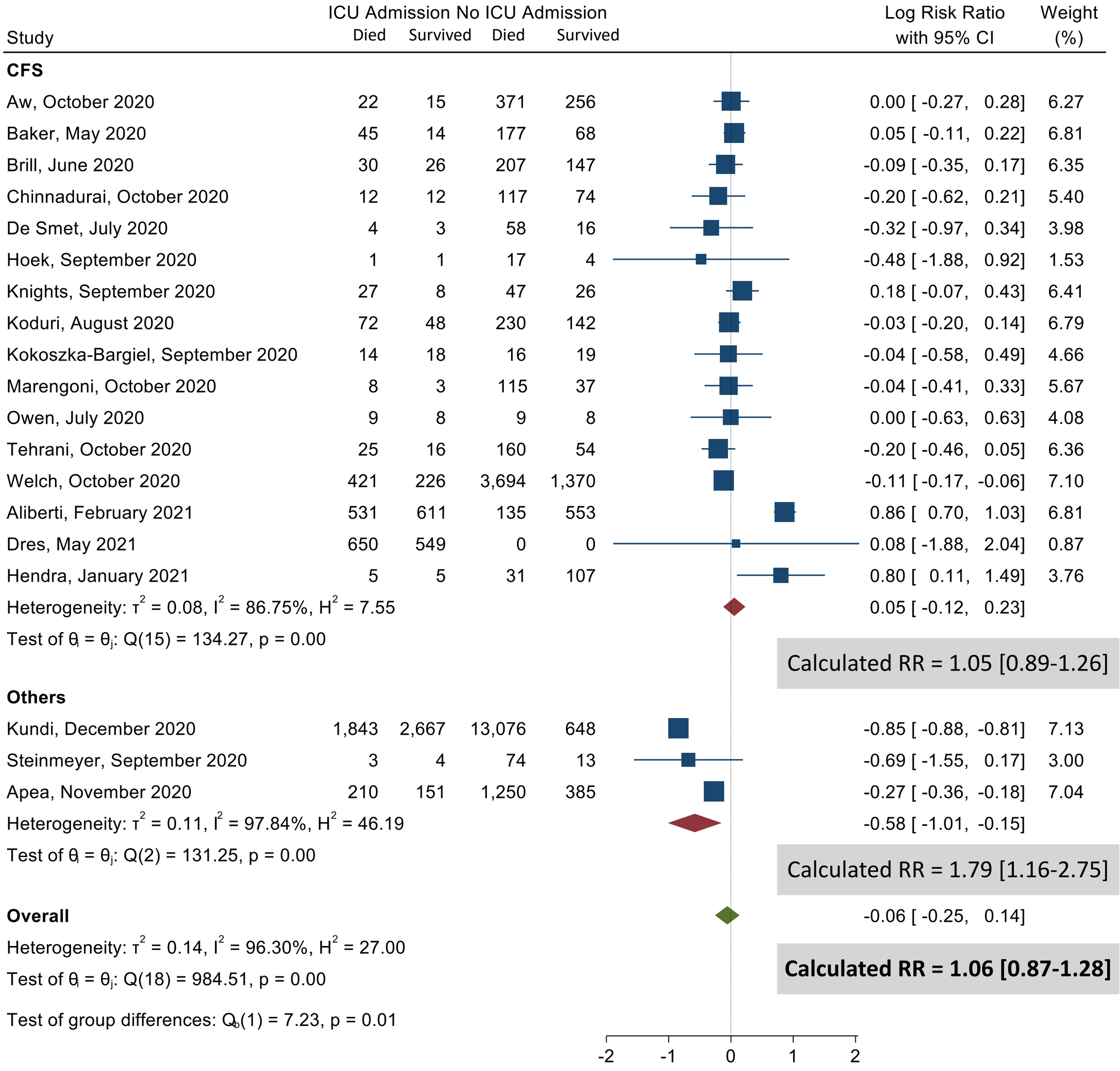
(7b) Male vs. female



Random-effects REML model

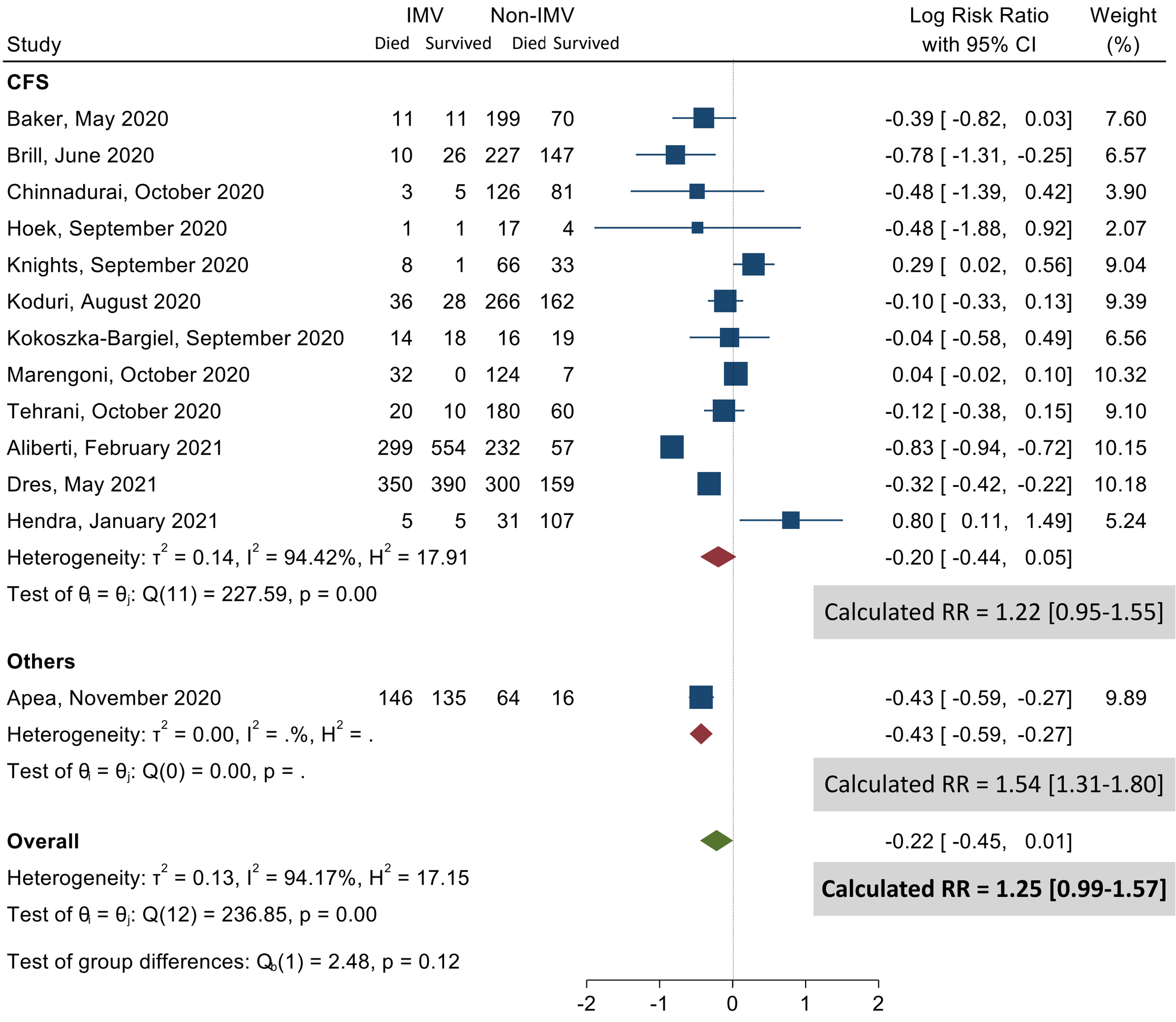
Supplementary Figure 7: Post Hoc Analysis CFS vs other frailty measures.

(7c) ICU Admission



Supplementary Figure 7: Post Hoc Analysis CFS vs other frailty measures.

(7d) Invasive Mechanical Ventilation



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

Study	CFS 1-3 Yes	CFS 1-3 No	CFS 4 Yes	CFS 4 No	Log Risk Ratio with 95% CI	Weight (%)
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	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: τ^2 = 0.03, I^2 = 78.72%, H^2 = 4.70

Test of $\theta_i = \theta_j$: Q(12) = 39.77, p = 0.00

Test of θ = 0: z = 3.66, p = 0.00

Calculated OR = 1.22 [1.09-1.36]

-.5 0 .5 1

Study	CFS 1-3 Yes	CFS 1-3 No	CFS 5 Yes	CFS 5 No	Log Risk Ratio with 95% CI	Weight (%)
Aw, October 2020	71	26	70	31	0.05 [-0.12, 0.23]	11.69
Davis, October 2020	19	5	36	21	0.23 [-0.06, 0.51]	9.96
De Smet, July 2020	12	1	5	1	0.10 [-0.29, 0.49]	8.22
Hewitt, August 2020	491	84	132	50	0.16 [0.07, 0.26]	12.67
Koduri, August 2020	170	45	26	24	0.42 [0.14, 0.69]	10.13
Marengoni, October 2020	104	17	2	3	0.76 [-0.31, 1.84]	2.38
Tehrani, October 2020	33	5	21	17	0.45 [0.14, 0.76]	9.51
Welch, October 2020	1,818	251	397	207	0.29 [0.23, 0.35]	12.94
Fagard, November 2020	13	0	45	38	0.58 [0.36, 0.80]	11.02
Aliberti, February 2021	297	1,042	98	207	-0.37 [-0.56, -0.18]	11.48
Overall					0.22 [0.04, 0.40]	

Heterogeneity: τ^2 = 0.07, I^2 = 90.40%, H^2 = 10.42

Test of $\theta_i = \theta_j$: Q(9) = 61.91, p = 0.00

Test of θ = 0: z = 2.35, p = 0.02

Calculated OR = 1.25 [1.04-1.49]

-1 0 1 2

Study	CFS 1-3 Yes	CFS 1-3 No	CFS 6 Yes	CFS 6 No	Log Risk Ratio with 95% CI	Weight (%)
Aw, October 2020	71	26	101	102	0.39 [0.20, 0.57]	11.39
Davis, October 2020	19	5	40	32	0.35 [0.06, 0.65]	10.55
De Smet, July 2020	12	1	12	6	0.33 [-0.04, 0.69]	9.89
Hewitt, August 2020	491	84	167	84	0.25 [0.16, 0.34]	11.84
Koduri, August 2020	170	45	28	34	0.56 [0.28, 0.84]	10.63
Marengoni, October 2020	104	17	4	10	1.10 [0.27, 1.93]	5.65
Owen, July 2020	28	22	23	16	-0.05 [-0.41, 0.31]	9.93
Tehrani, October 2020	33	5	7	26	1.41 [0.74, 2.08]	6.94
Welch, October 2020	1,818	251	562	318	0.32 [0.27, 0.37]	11.96
Aliberti, February 2021	297	1,042	77	148	-0.43 [-0.64, -0.23]	11.23
Overall					0.35 [0.08, 0.62]	

Heterogeneity: τ^2 = 0.16, I^2 = 95.58%, H^2 = 22.64

Test of $\theta_i = \theta_j$: Q(9) = 71.45, p = 0.00

Test of θ = 0: z = 2.51, p = 0.01

Calculated OR = 1.42 [1.08-1.86]

-1 0 1 2

Study	CFS 1-3 Yes	CFS 1-3 No	CFS 7-9 Yes	CFS 7-9 No	Log Risk Ratio with 95% CI	Weight (%)
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: τ^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

Calculated OR = 1.48 [1.16-1.86]

-1 0 1 2 3

Random-effects REML model