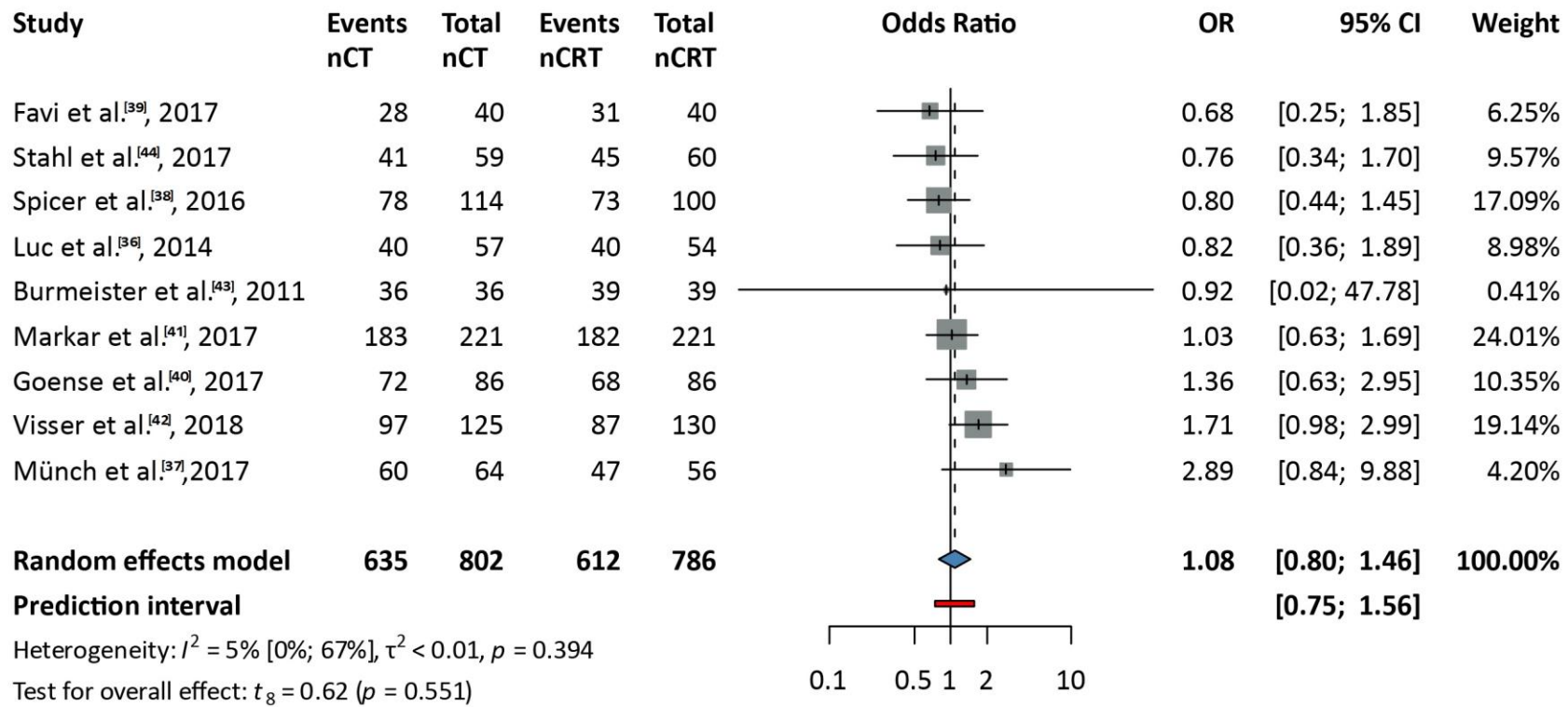
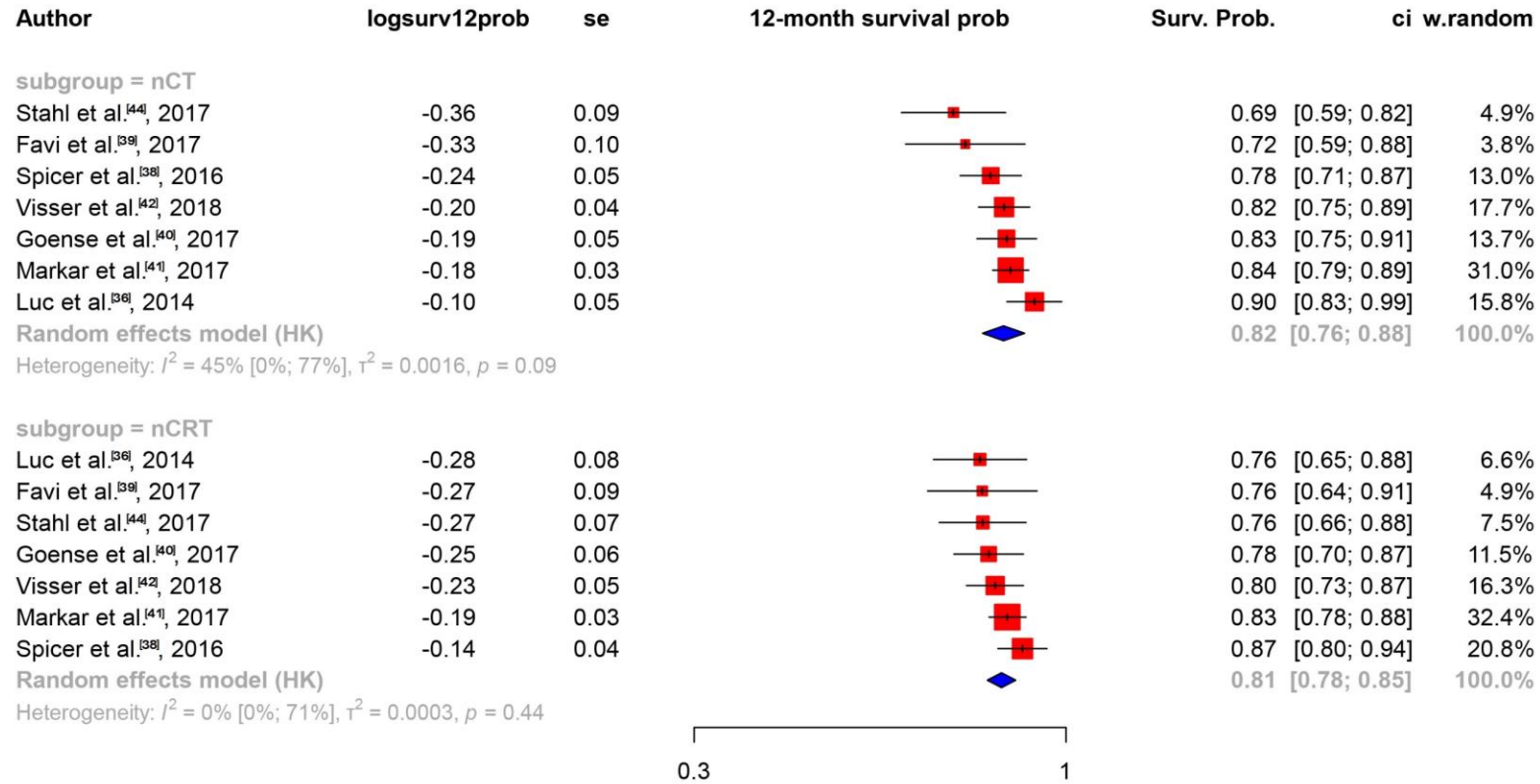


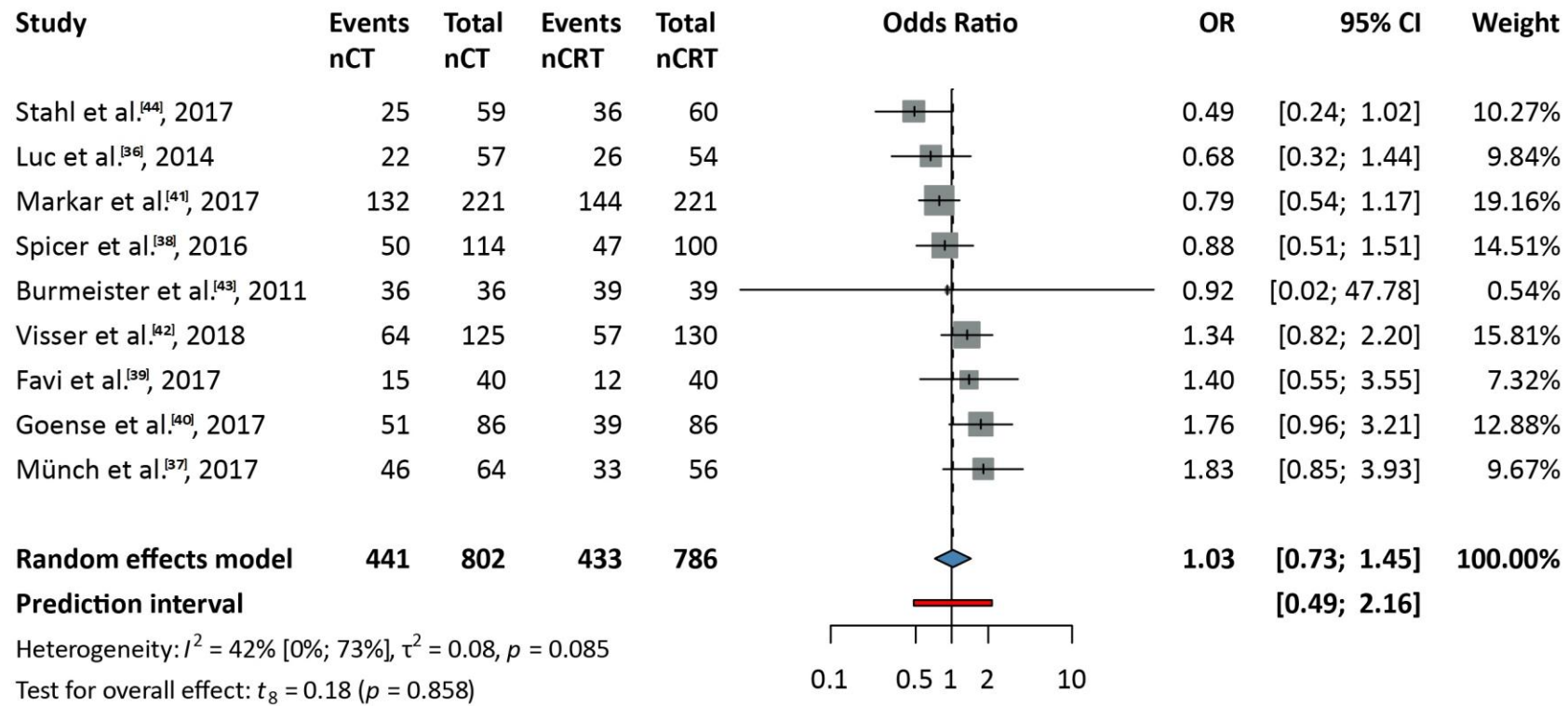
Supplementary Figure 1



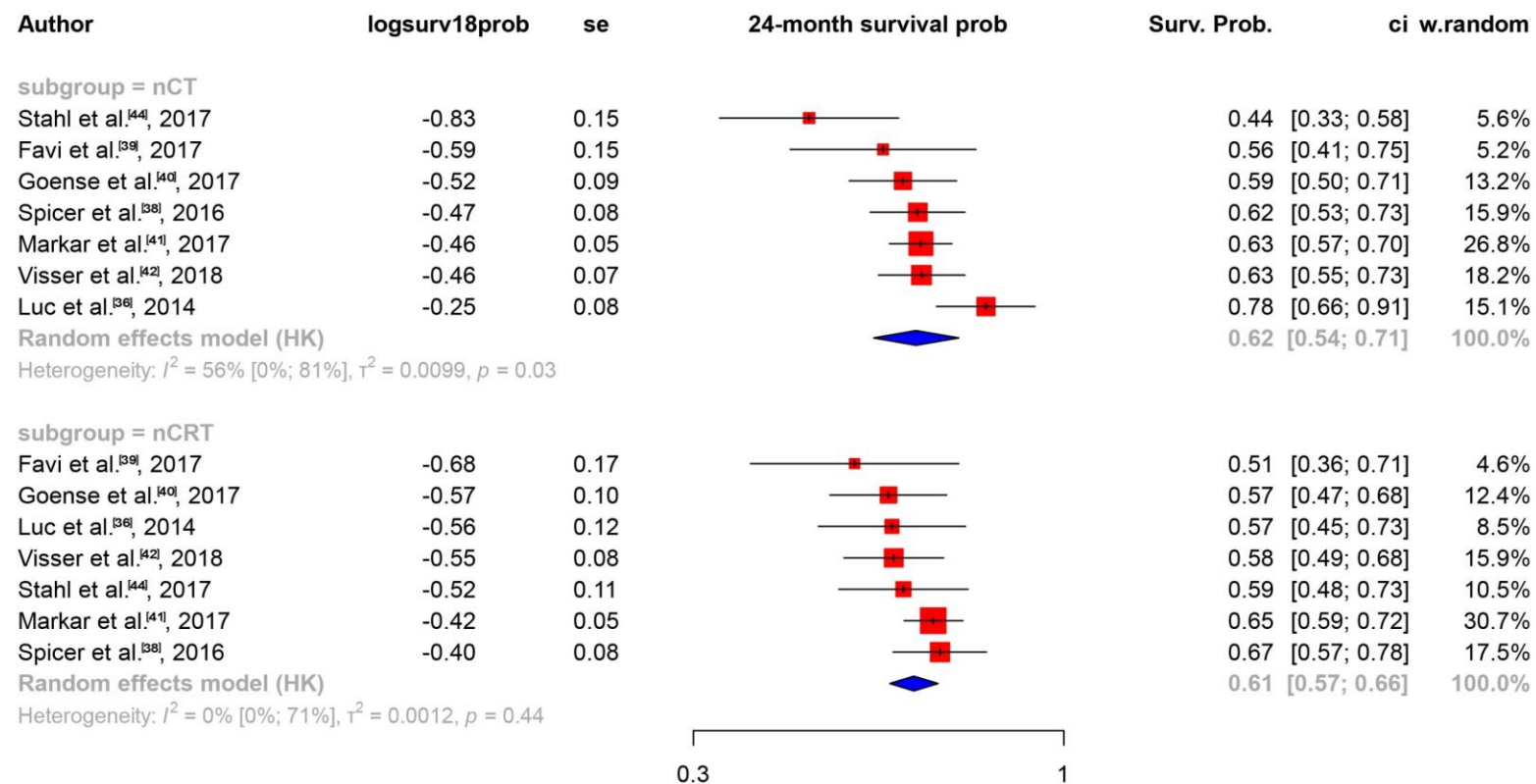
Supplementary Figure 2



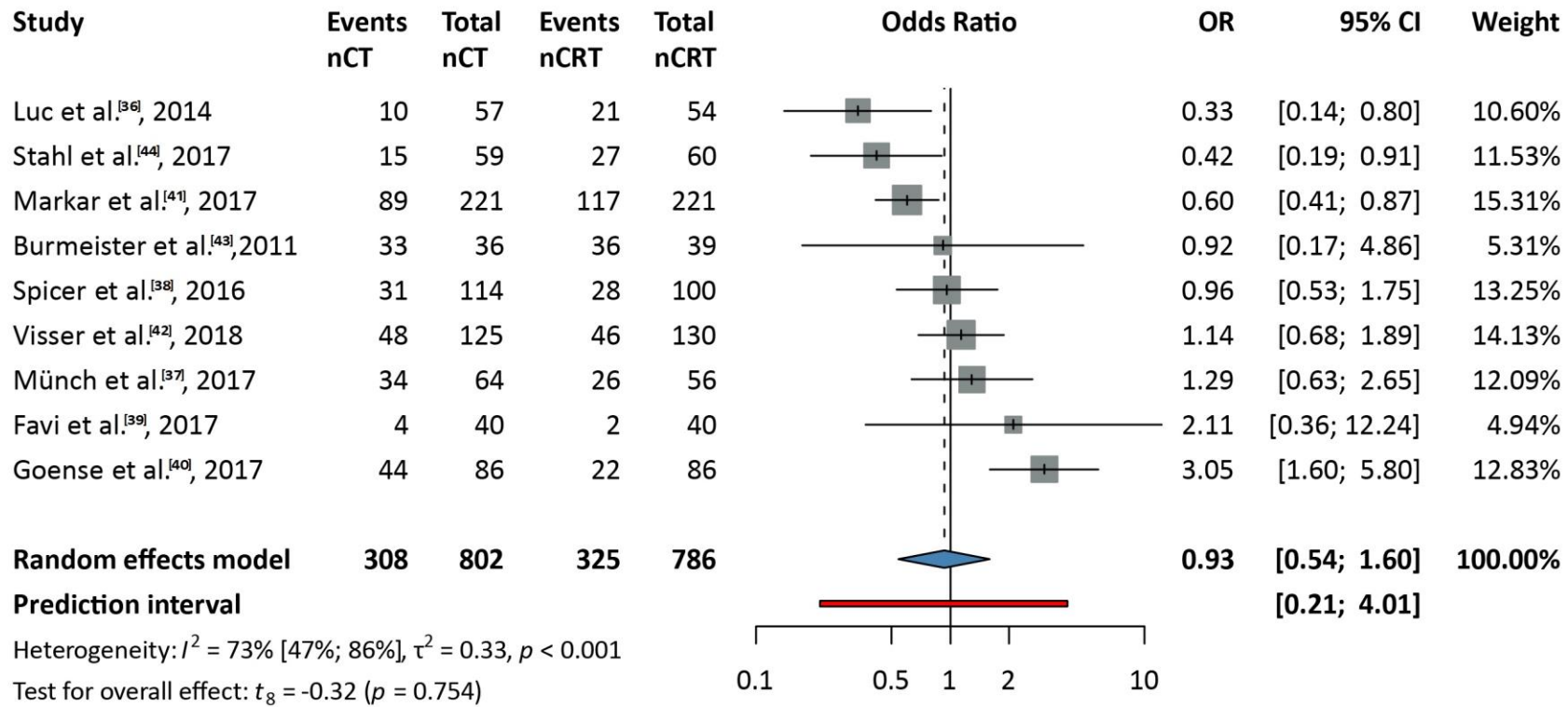
Supplementary Figure 3



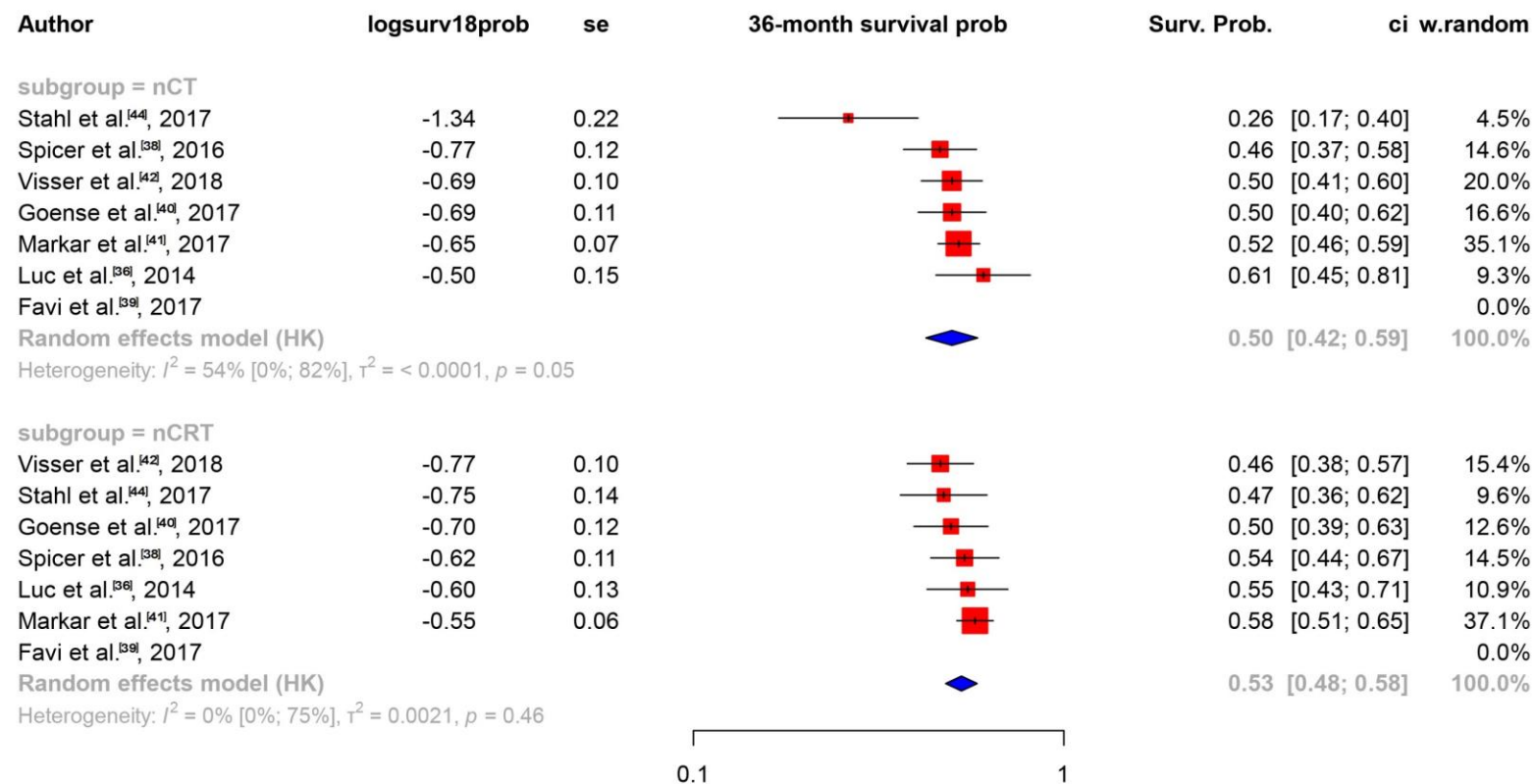
Supplementary Figure 4



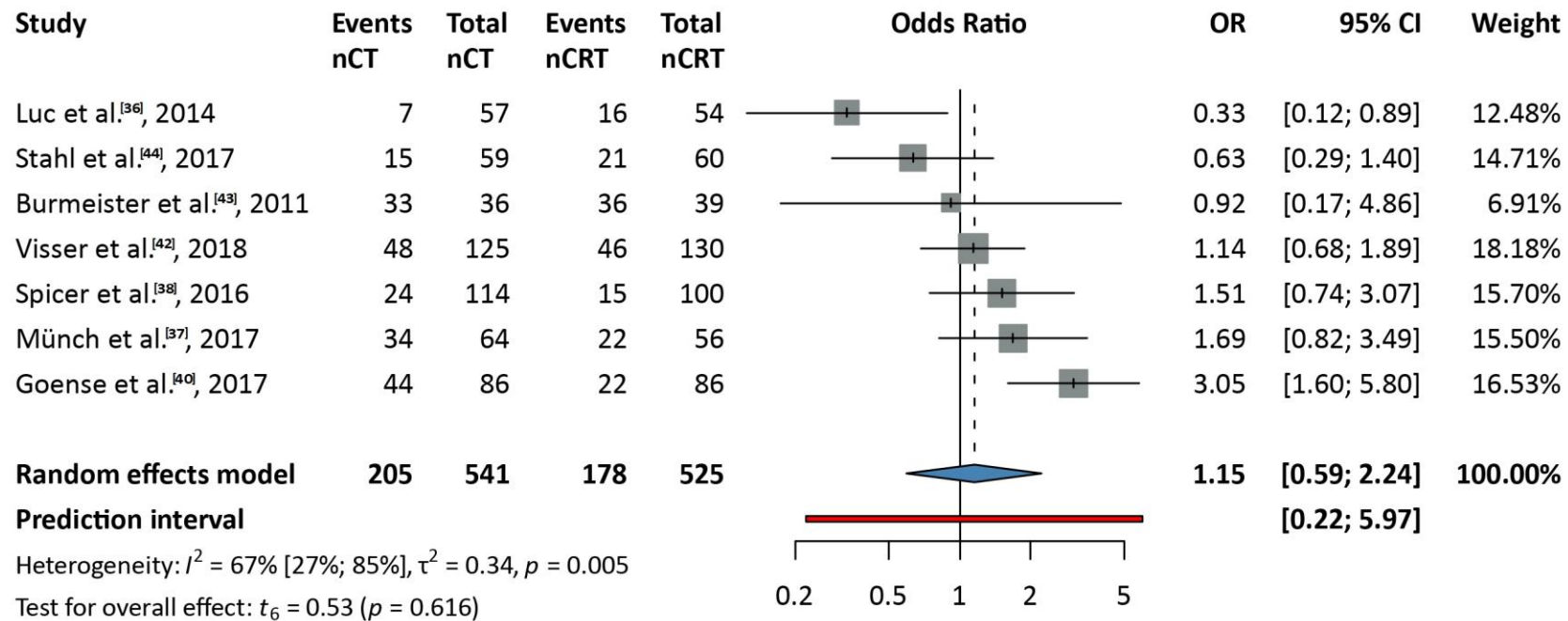
Supplementary Figure 5



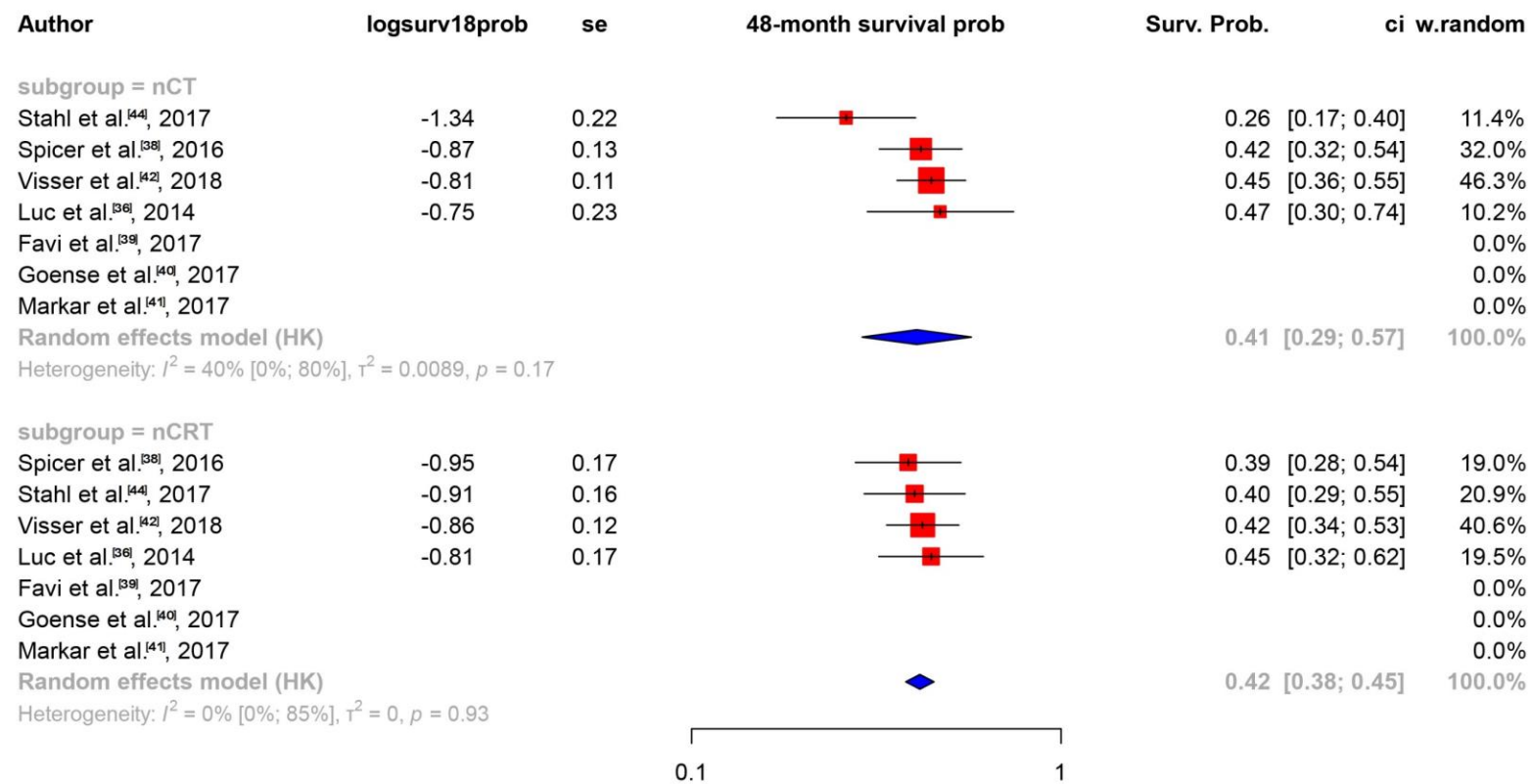
Supplementary Figure 6



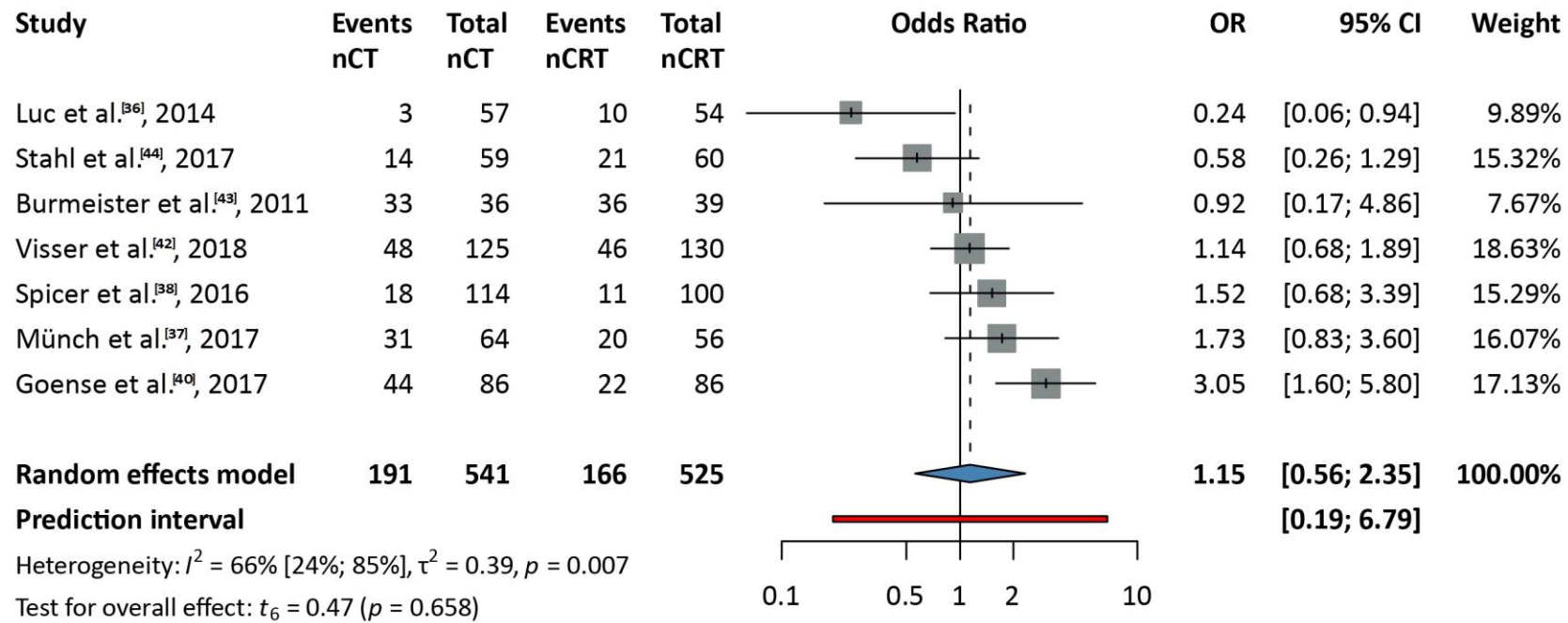
Supplementary Figure 7



Supplementary Figure 8

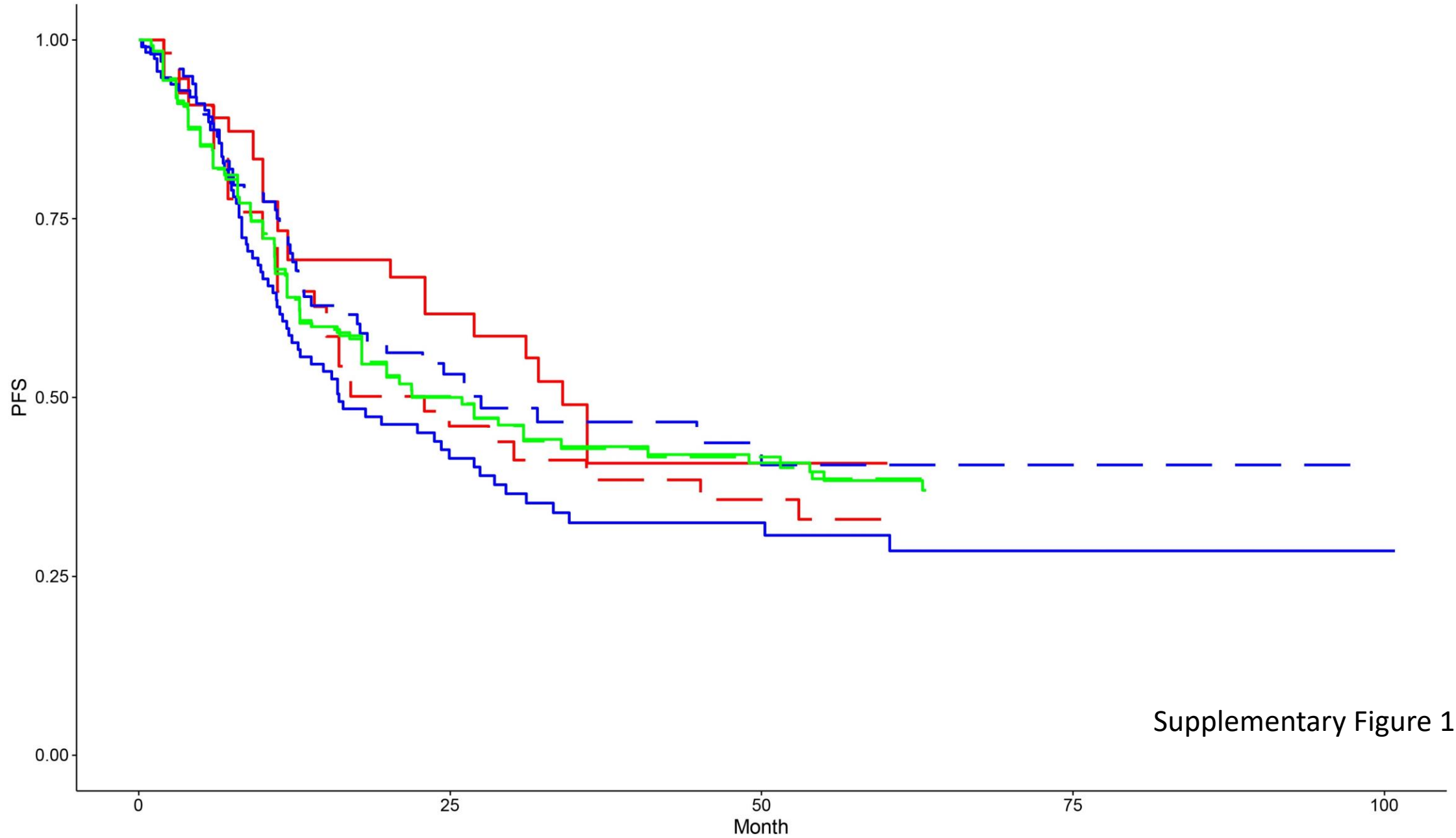


Supplementary Figure 9

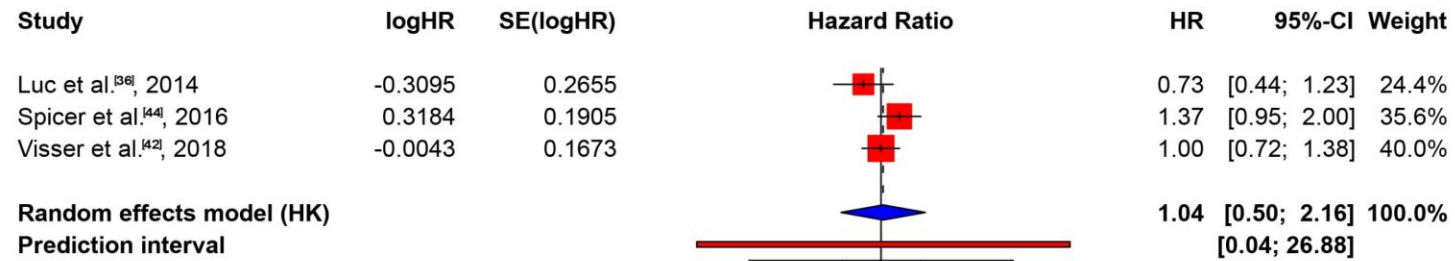


Supplementary Figure 10

Strata Luc et al.^[36], 2014 - nCRT Spicer et al.^[38], 2016 - nCRT Visser et al.^[42], 2018 - nCRT
Luc et al.^[36], 2014 - nCT Spicer et al.^[38], 2016 - nCT Visser et al.^[42], 2018 - nCT

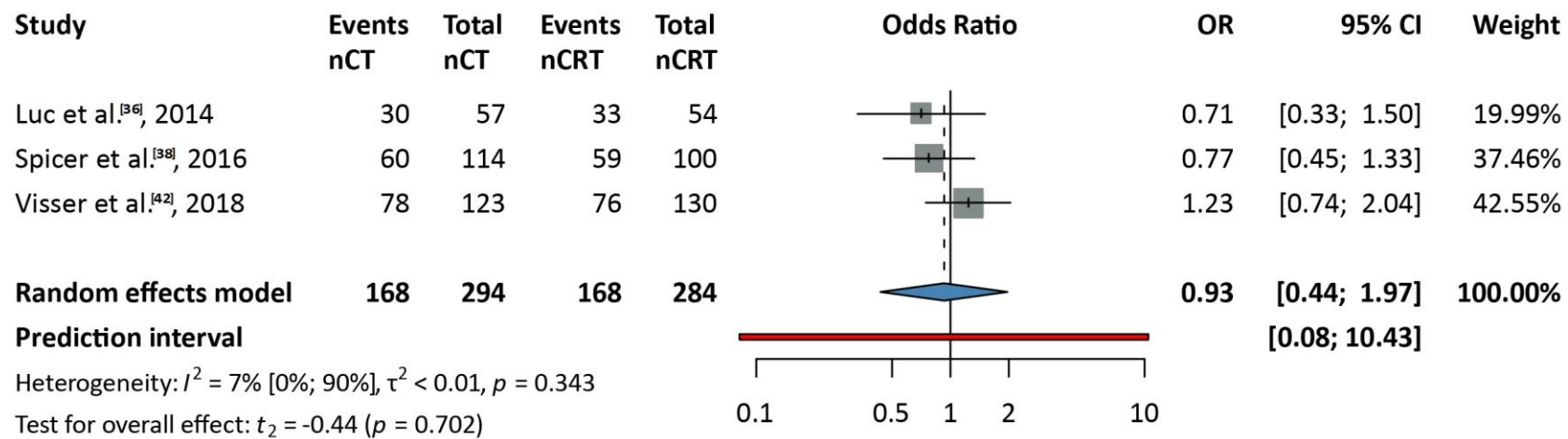


Supplementary Figure 11

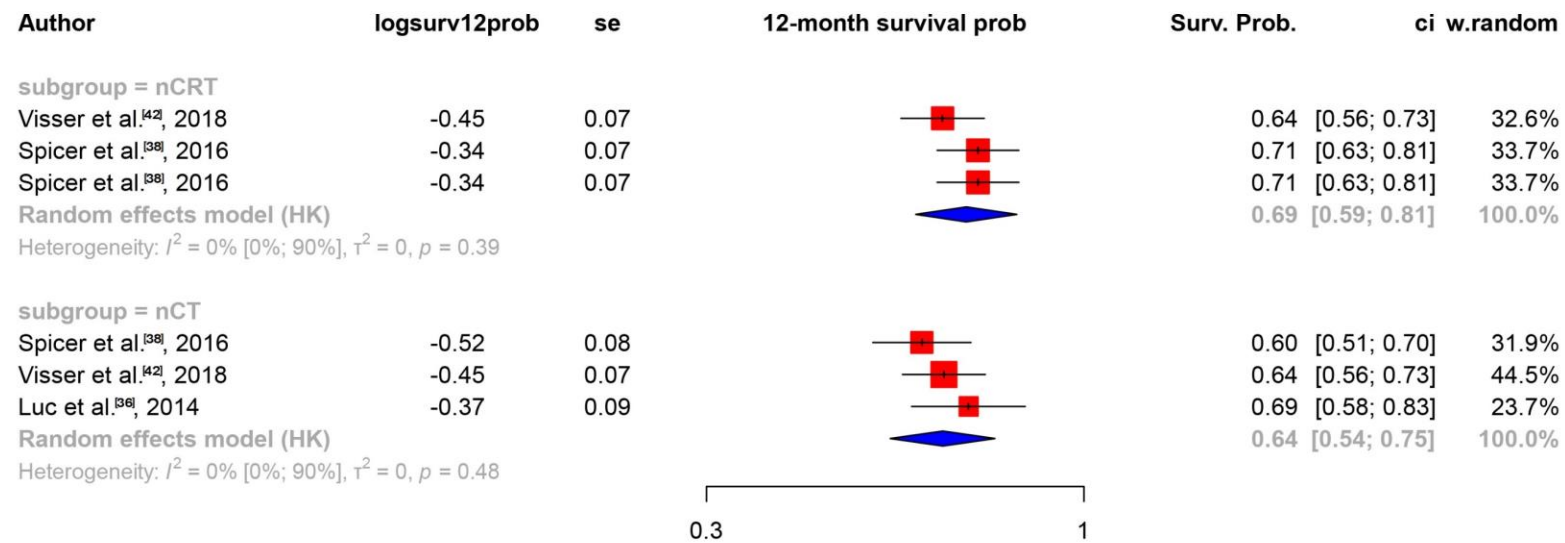


Heterogeneity: $I^2 = 49\%$ [0%; 85%], $\tau^2 = 0.0389$, $p = 0.14$

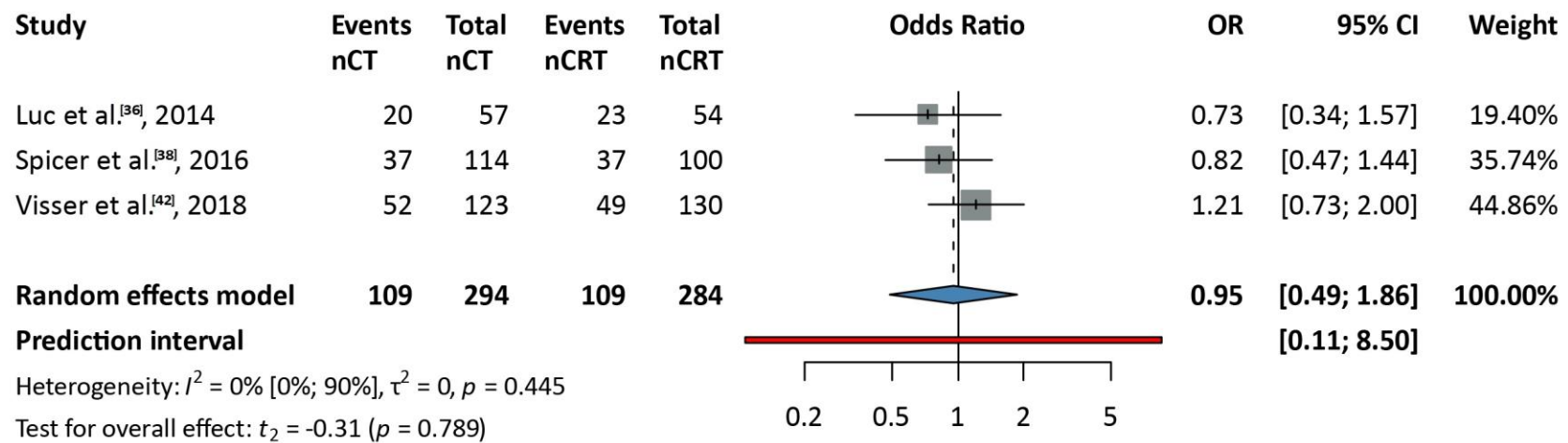
Supplementary Figure 12



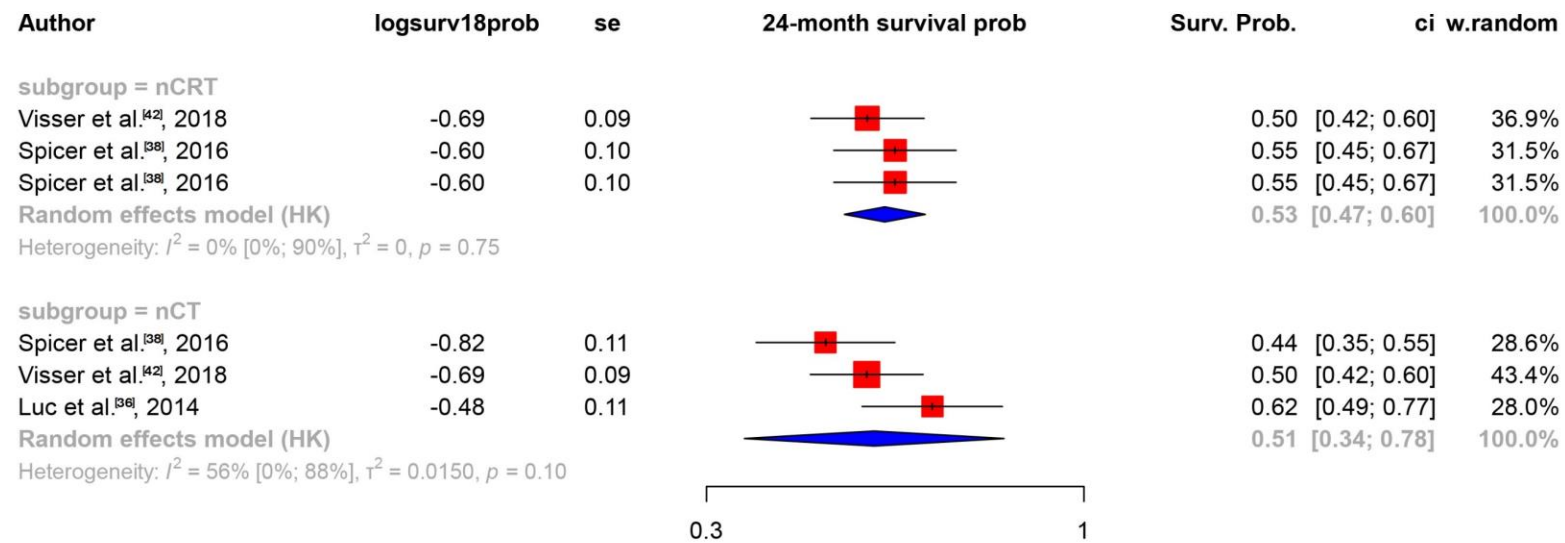
Supplementary Figure 13



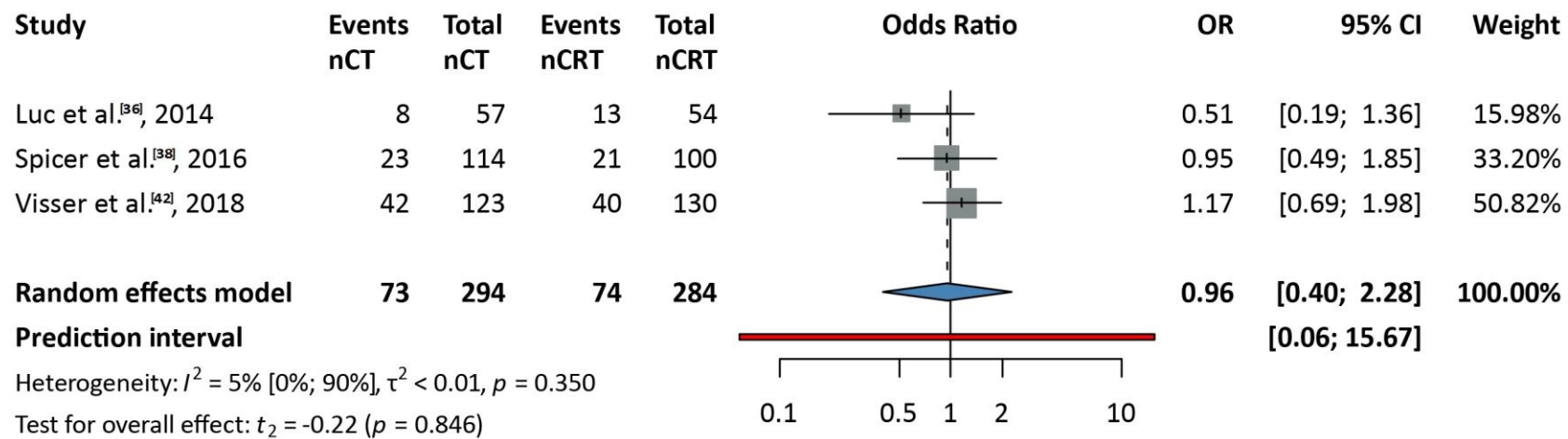
Supplementary Figure 14



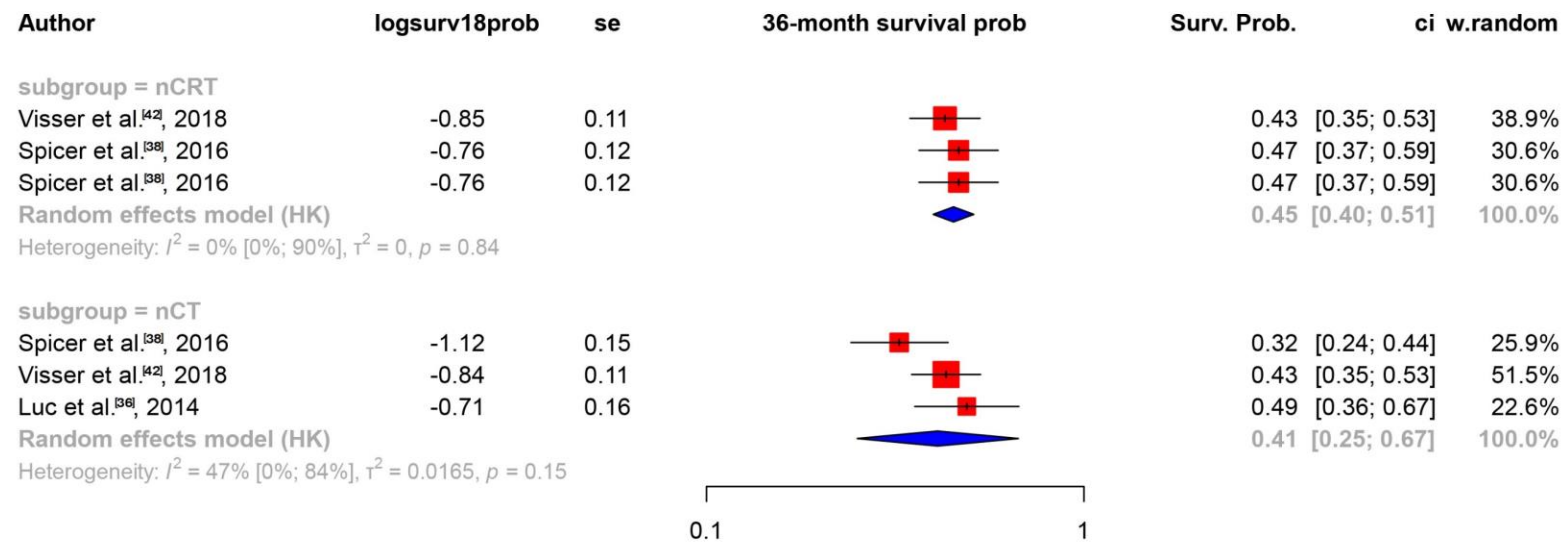
Supplementary Figure 15



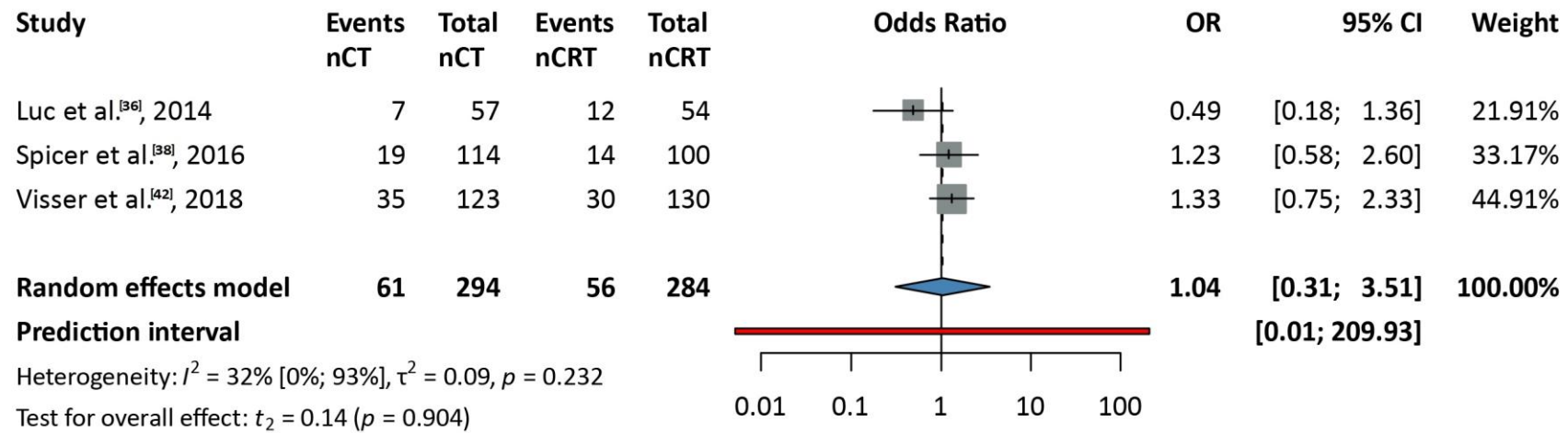
Supplementary Figure 16



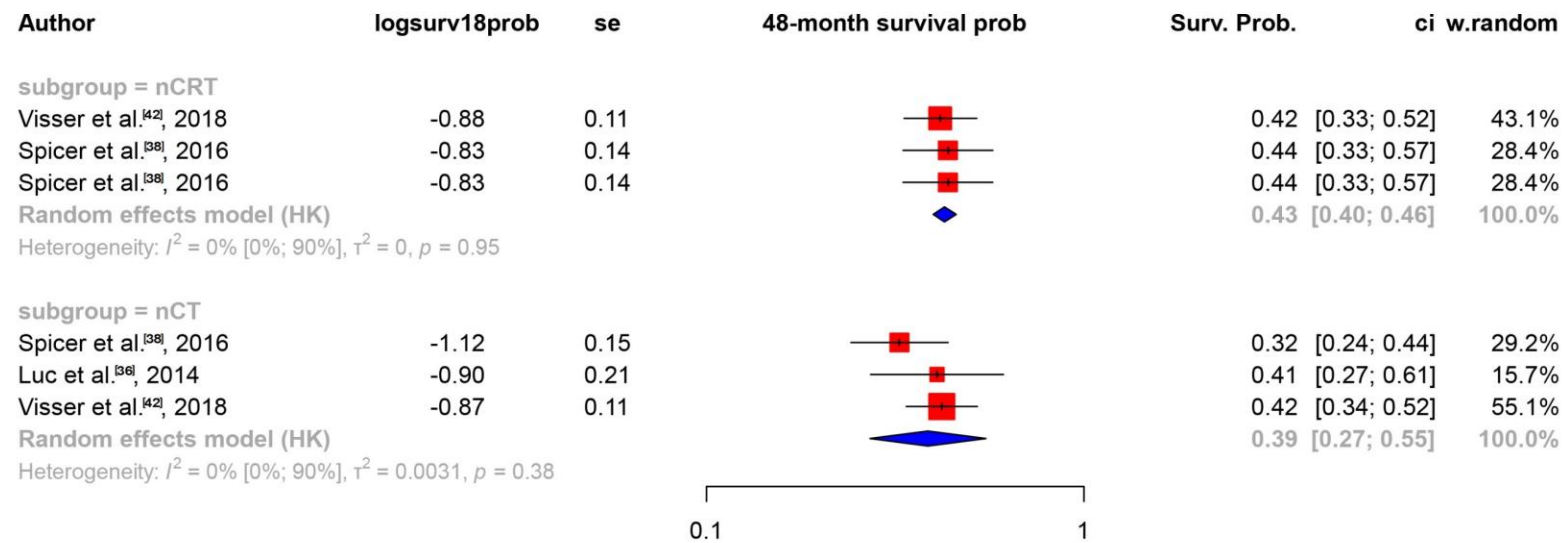
Supplementary Figure 17



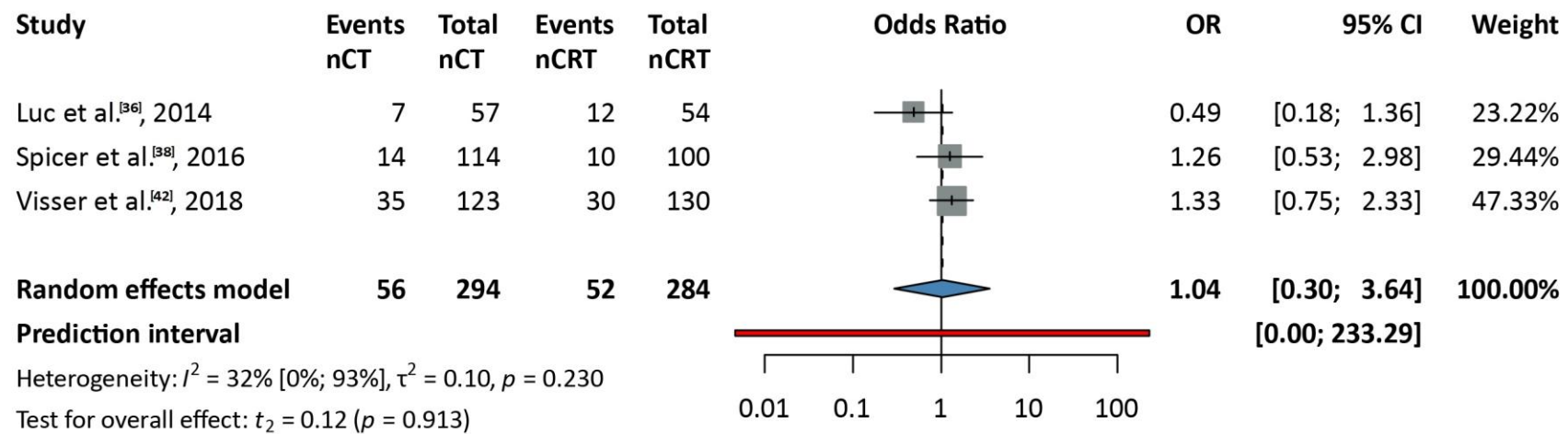
Supplementary Figure 18



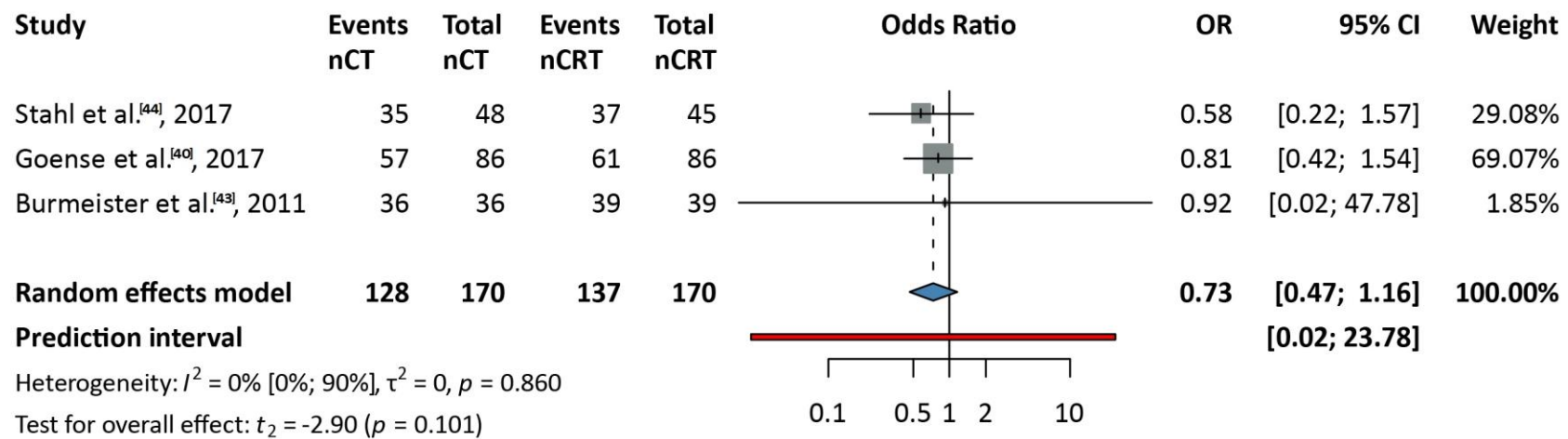
Supplementary Figure 19



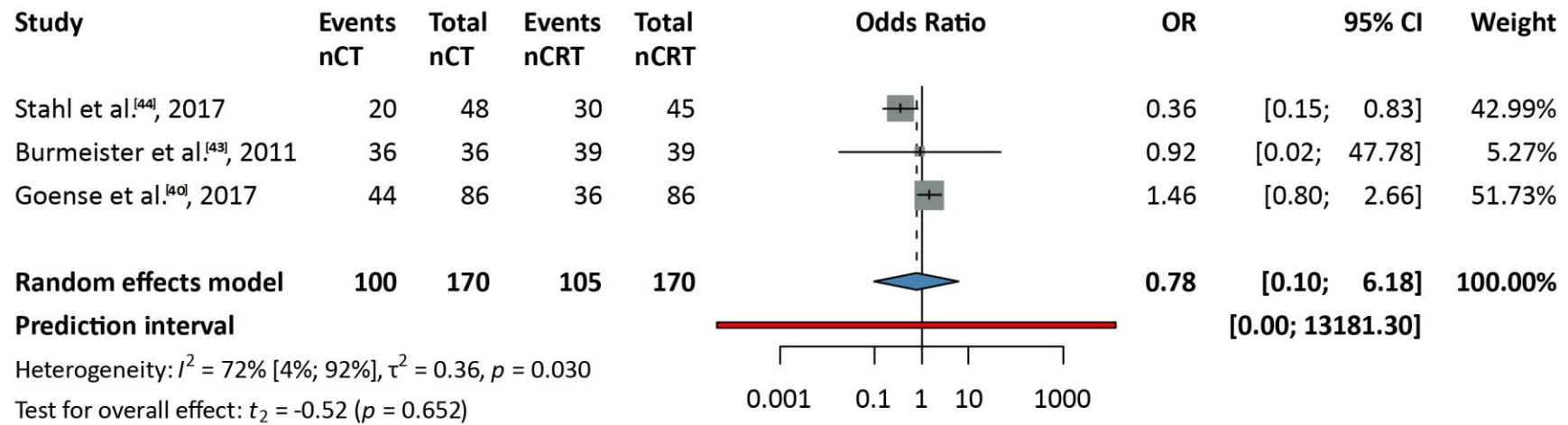
Supplementary Figure 20



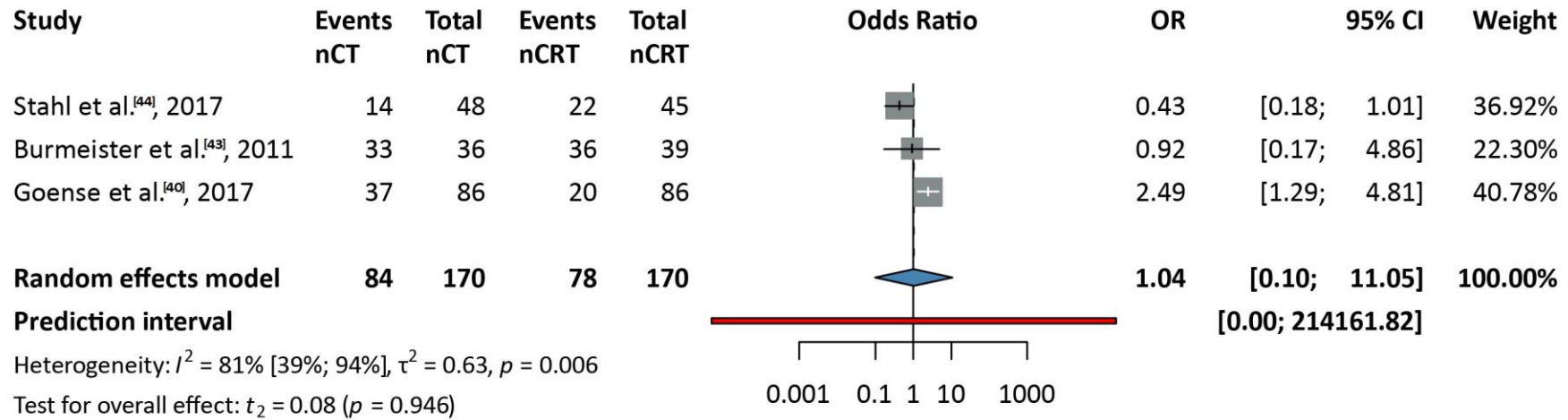
Supplementary Figure 21



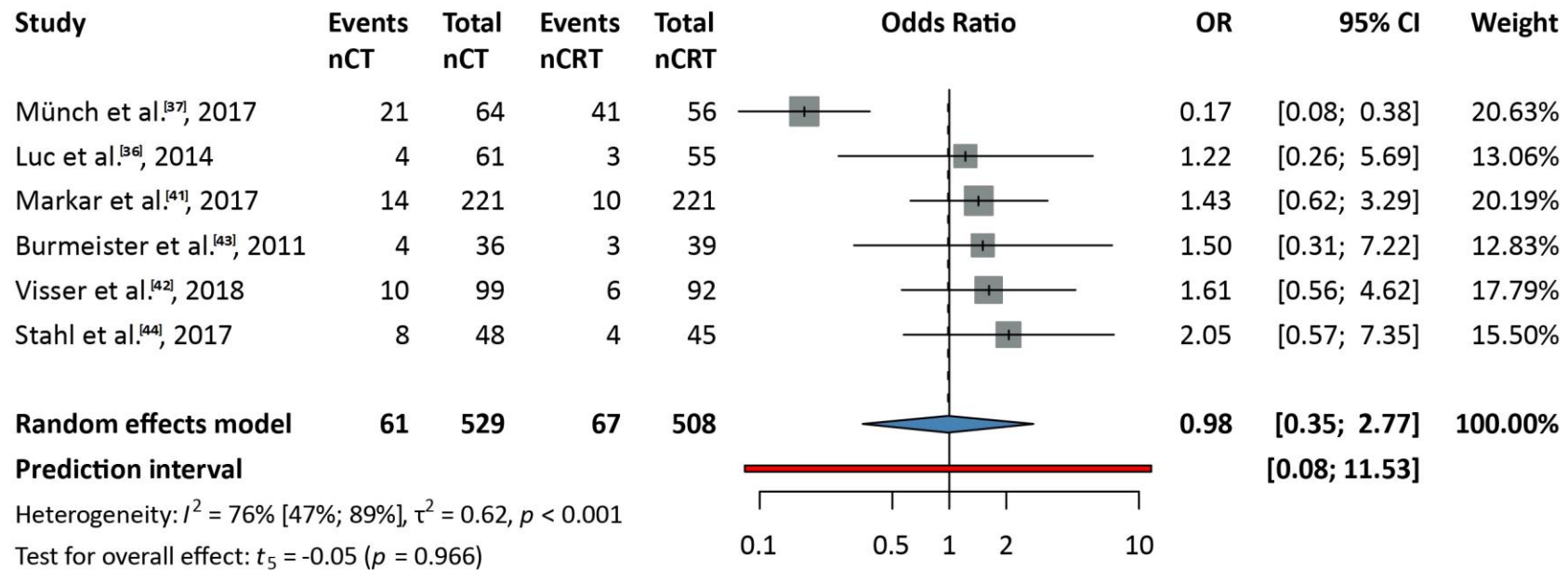
Supplementary Figure 22



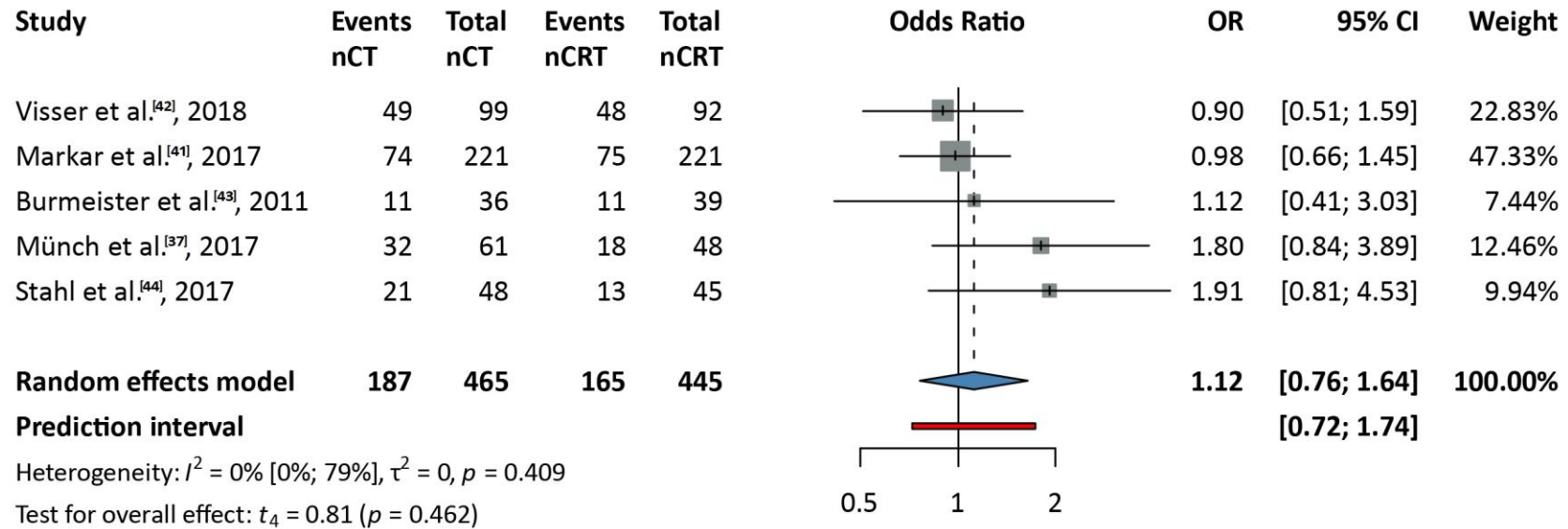
Supplementary Figure 23



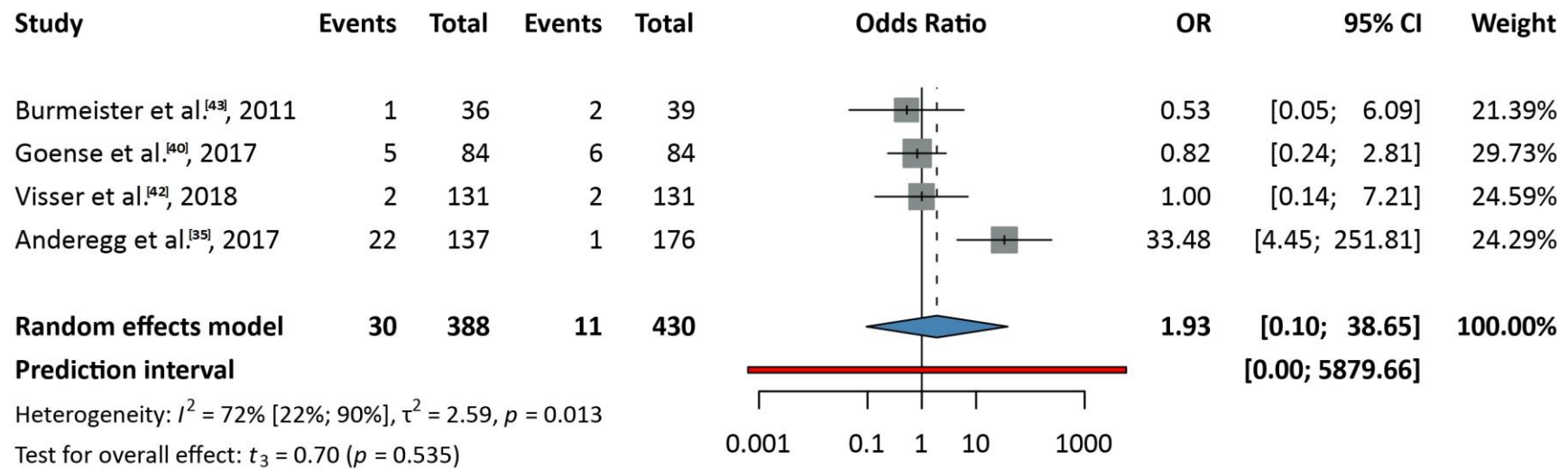
Supplementary Figure 24



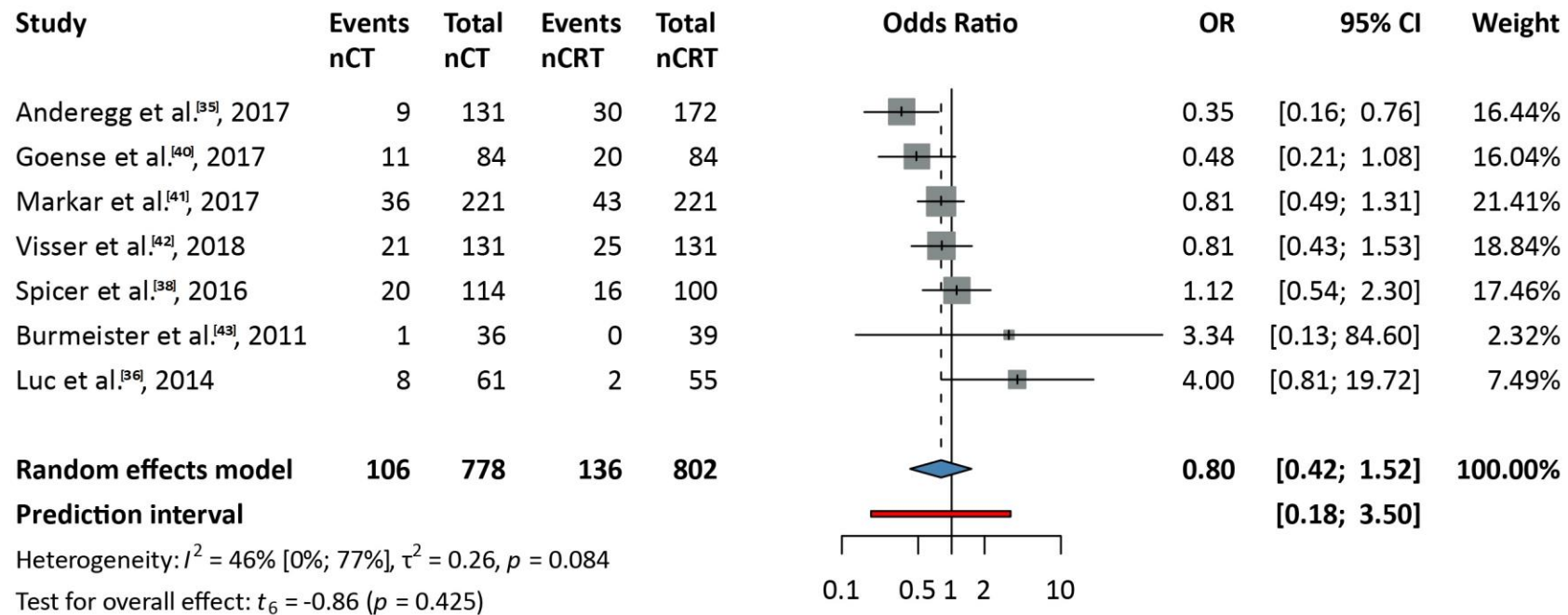
Supplementary Figure 25



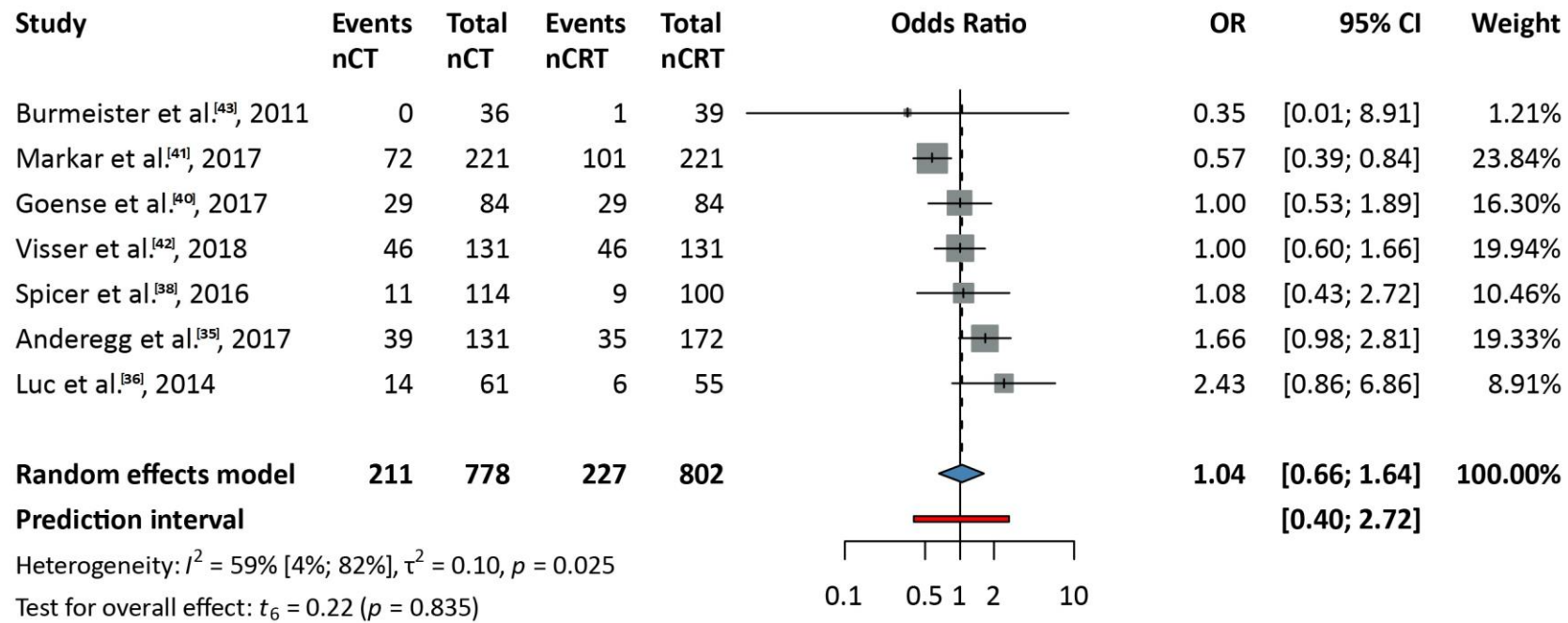
Supplementary Figure 26



Supplementary Figure 27



Supplementary Figure 28



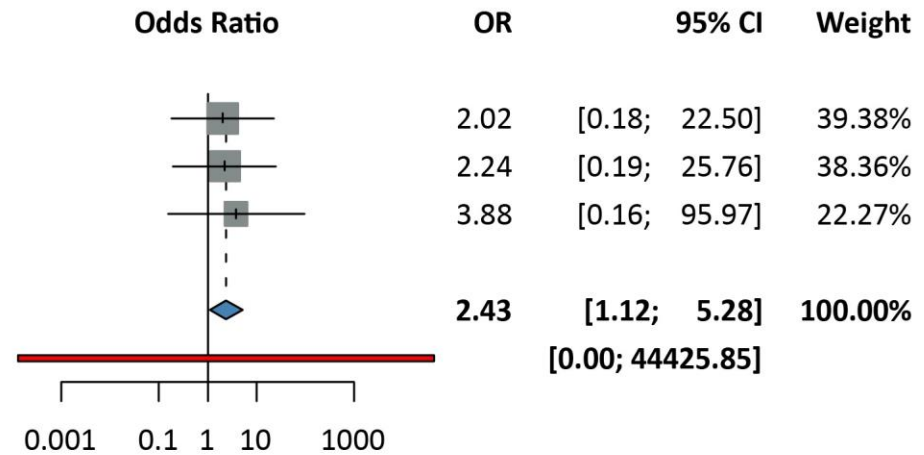
Supplementary Figure 29

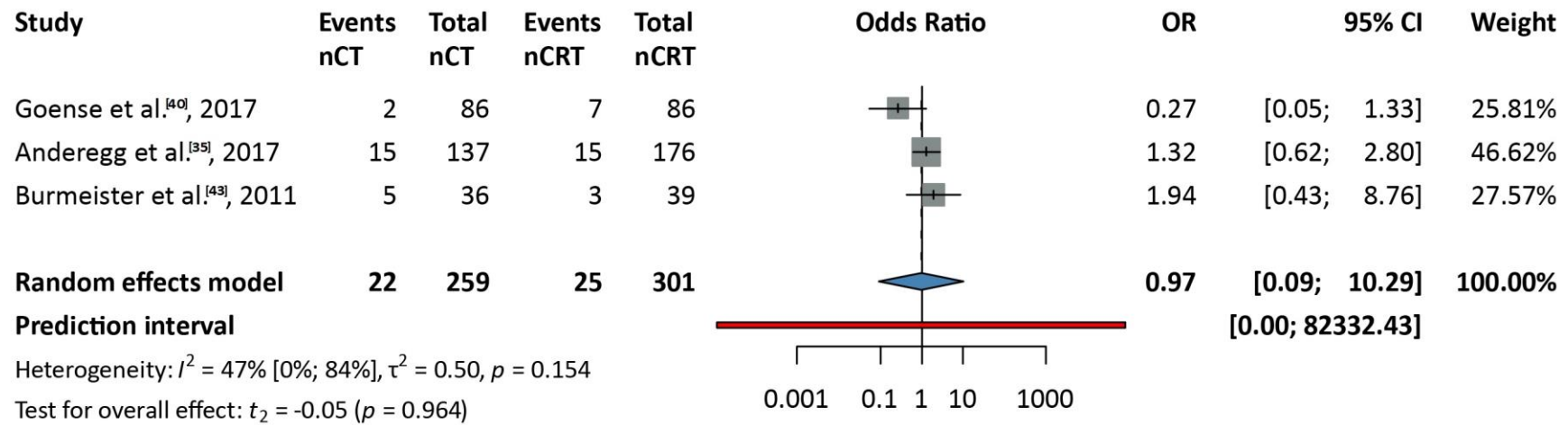
Study	Events nCT	Total nCT	Events nCRT	Total nCRT
Visser et al. ^[42] , 2018	2	131	1	131
Burmeister et al. ^[43] , 2011	2	36	1	39
Anderegg et al. ^[35] , 2017	1	137	0	176
Random effects model	5	304	2	346

Prediction interval

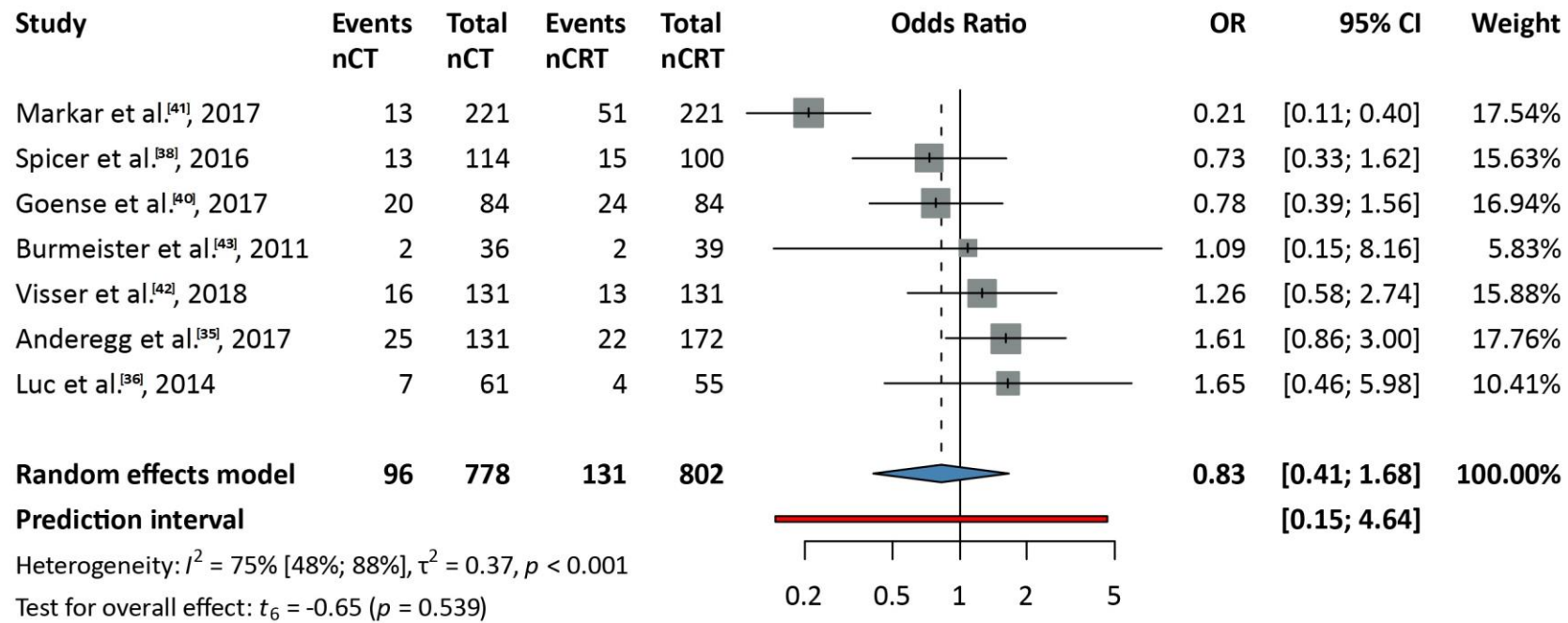
Heterogeneity: $I^2 = 0\%$ [0%; 90%], $\tau^2 = 0$, $p = 0.947$

Test for overall effect: $t_2 = 4.91$ ($p = 0.039$)

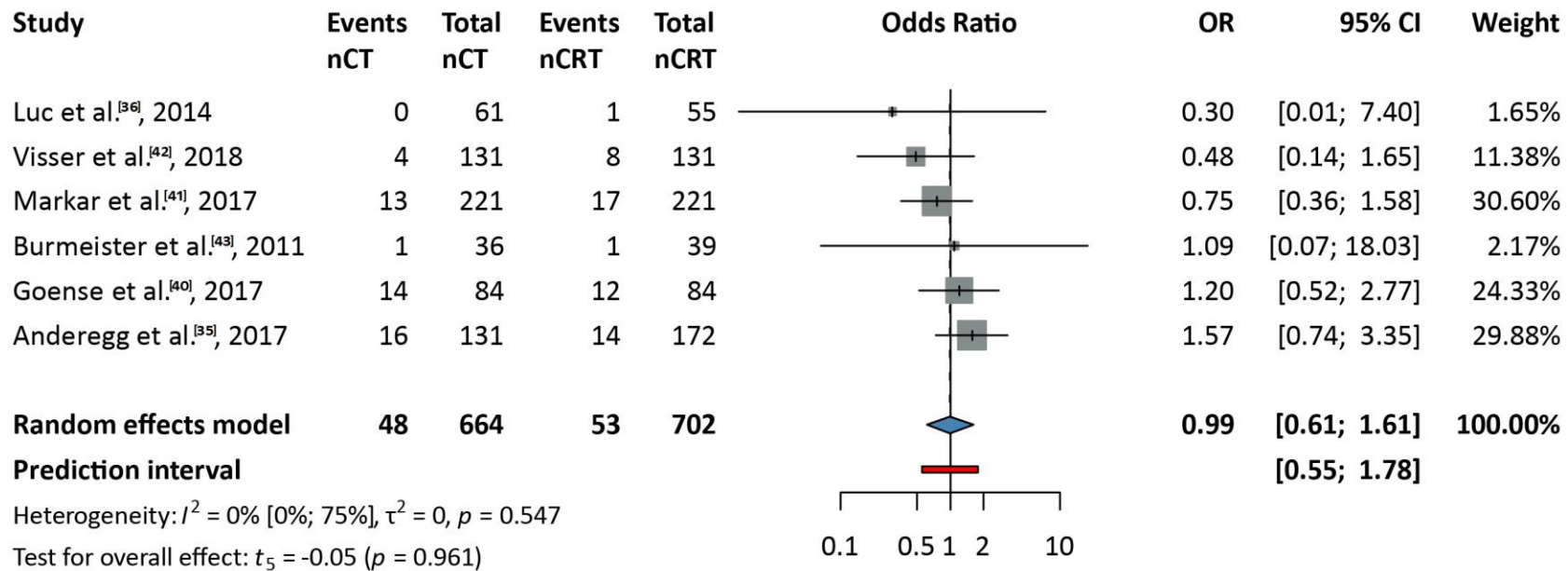




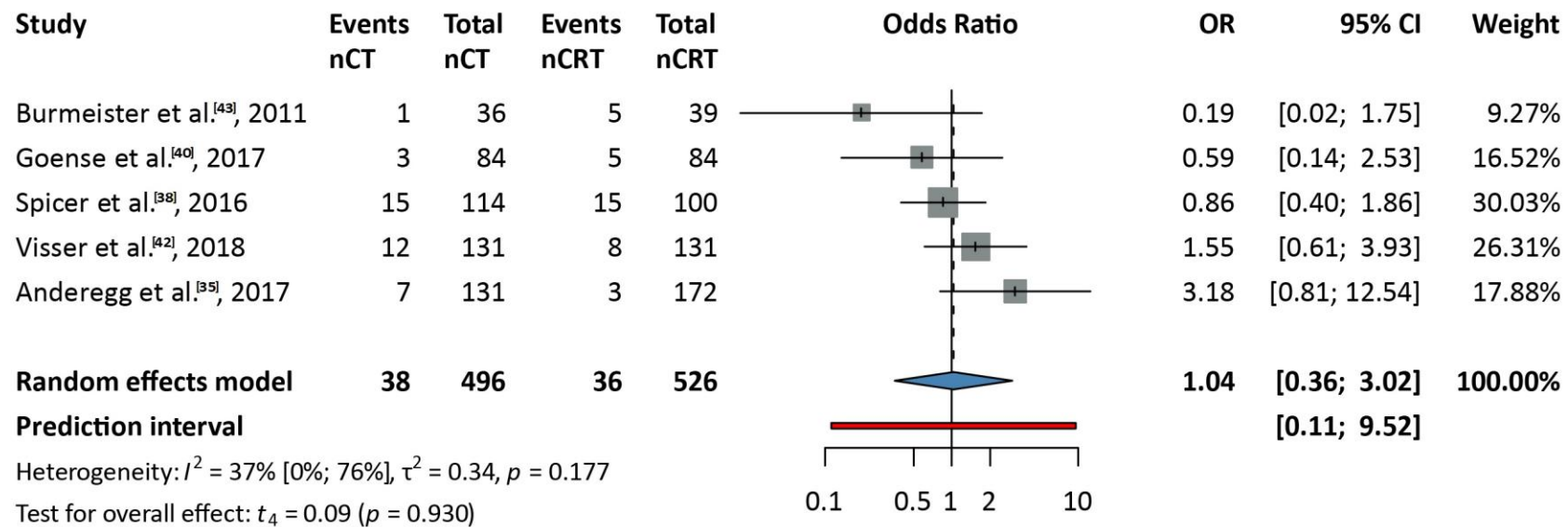
Supplementary Figure 31



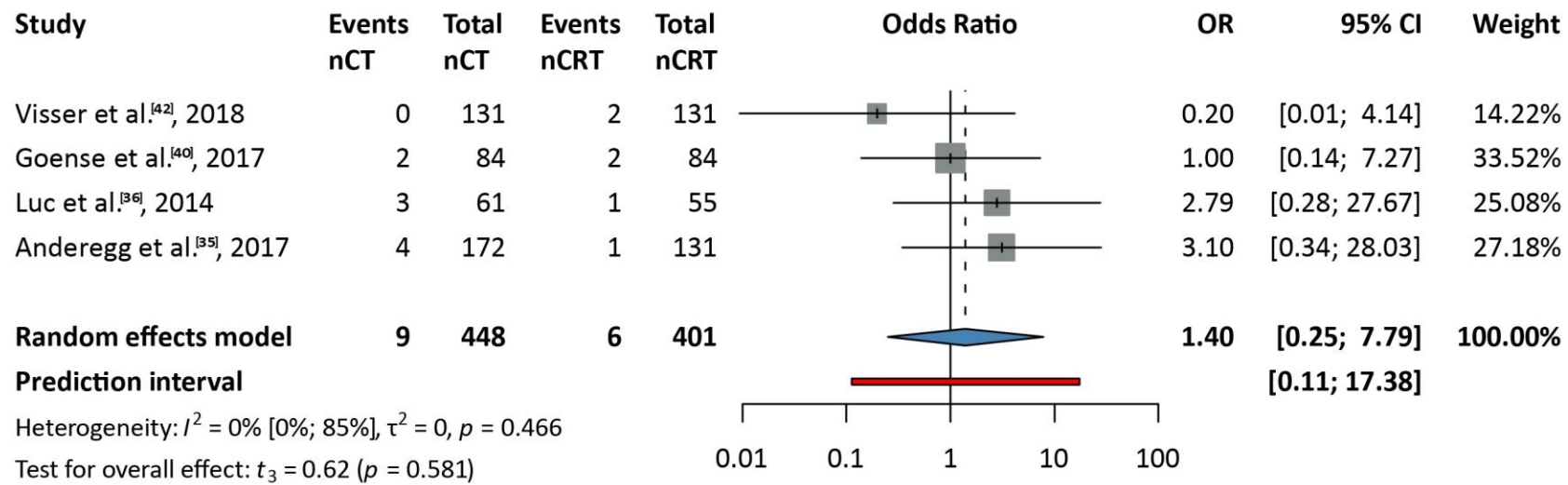
Supplementary Figure 32



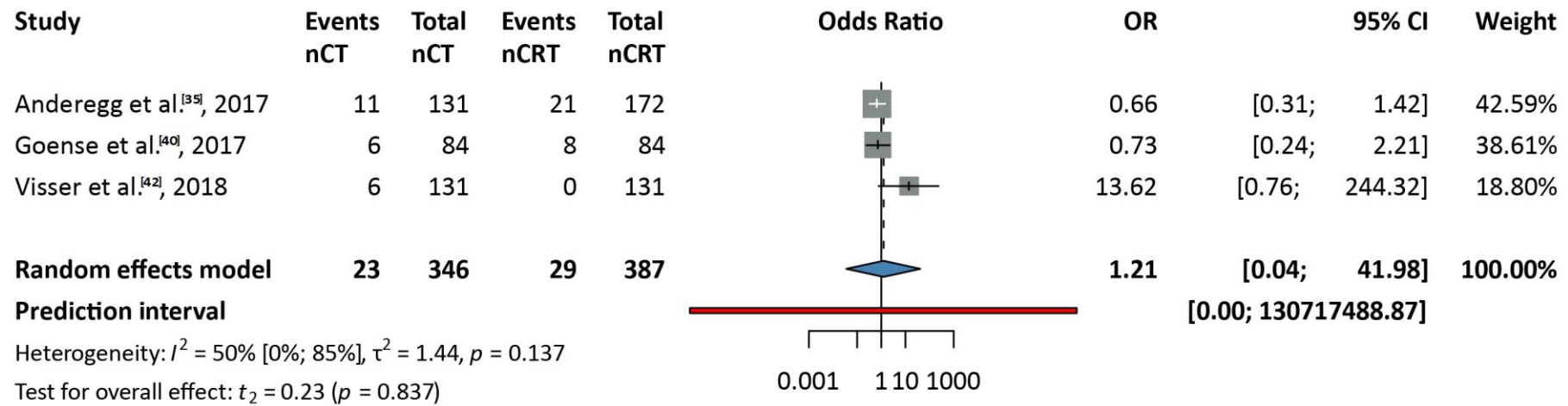
Supplementary Figure 33



Supplementary Figure 34



Supplementary Figure 35



Supplementary Figure 36

Supplementary Table 3 - Characteristic of the surgical procedure

Author	Ivor-Lewis		McKeown	
	nCT	nCRT	nCT	nCRT
Stahl et al. [44], 2017	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Burmeister et al. [43], 2011	5 (14%)	8 (20%)	28 (74%)	25 (64%)
Visser et al. [42], 2018	131 (50%)	131 (50%)	0 (0%)	0 (0%)
Markar et al. [41], 2017	209 (95%)	81 (37%)	11 (5%)	4 (2%)
Goense et al. [40], 2017	74 (86%)	77 (90%)	0 (0%)	0 (0%)
Favi et al. [39], 2017	n/a	n/a	n/a	n/a
Anderegg et al. [35], 2017	78 (57%)	115 (65%)	0 (0%)	0 (0%)
Spicer et al. [38], 2016	n/a	n/a	n/a	n/a
Luc et al. [36], 2014		100 (86%)	0 (0%)	0 (0%)
Münch et al. [37], 2017	n/a	n/a	n/a	n/a

Supplementary Table 4 - GRADE

Outcomes	No of Participants (studies)	OR (95% CI)	I ² (95% CI)	Risk of Bias	Indirectnes	Imprecision	Large effect size	Effect of plausible residual confounding	Quality of the evidence
pCR	1547	0.27 (0.16-0.46)	0.29 (0 - 0.68)	↓	-	↓	↑	↓	⊕⊕⊕ ⊕ LOW
30-day mortality	899	0.4 (0.22 - 0.71)	0 (0 - 0.85)	↓	-	-	↑	↓	⊕⊕⊕⊕ Moderate
90-day mortality	1086	0.71 (0.28 - 1.84)	0 (0 - 0.85)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
OS logHR	1540	0.98 (0.77 - 1.23)	0.35 (0 - 0.71)	↓	↓	-	↑	↓	⊕⊕⊕ ⊕ LOW
OS 12-month	1588	1.08 (0.8 - 1.46)	0.05 (0 - 0.67)	↓	-	↓	-	↓	⊕⊕ ⊕ ⊕ VERY LOW
OS 24-month	1588	1.03 (0.73 - 1.45)	0.42 (0 - 0.73)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
OS 36-month	1588	0.93 (0.54 - 1.6)	0.73 (0.47 - 0.86)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
OS 48-month	1066	0.67 (0.27 - 0.85)	0.67 (0.27 - 0.85)	↓	↓	-	-	↓	⊕⊕ ⊕ ⊕ VERY LOW
OS 60-month	1066	1.15 (0.56 - 2.35)	0.67 (0.27 - 0.85)	↓	↓	-	-	↓	⊕⊕ ⊕ ⊕ VERY LOW
DFS logHR	578	1.04 (0.5 - 2.16)	0.49 (0 - 0.85)	↓	↓	-	-	↓	⊕⊕ ⊕ ⊕ VERY LOW
DFS 12-month	578	0.93 (0.44 - 1.97)	0.07 (0 - 0.9)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
DFS 24-month	578	0.95 (0.49 - 1.86)	0 (0 - 0.9)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
DFS 36-month	578	0.96 (0.4 - 2.28)	0.05 (0 - 0.9)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
DFS 48-month	578	1.04 (0.31 - 3.51)	0.32 (0 - 0.93)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
DFS 60-month	578	1.04 (0.3 - 3.64)	0.32 (0 - 0.93)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
PFS 12-month	340	0.73 (0.47 - 1.16)	0 (0 - 0.9)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
PFS 24-month	340	0.78 (0.1 - 6.18)	0.72 (0.04 - 0.92)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
PFS 36-month	340	1.04 (0.1 - 11.05)	0.81 (0.39 - 0.94)	↓	↓	-	-	↓	⊕⊕ ⊕ ⊕ VERY LOW
Locoregional recurrence	1037	0.98 (0.35 - 2.77)	0.76 (0.47 - 0.89)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
Distal metastasis recurrence	910	1.12 (0.76 - 1.64)	0 (0 - 0.79)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
Thromboembolism	818	1.93 (0.1 - 38.65)	0.72 (0.22 - 0.90)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
Cardiac complications	1580	0.8 (0.42 - 1.52)	0.46 (0 - 0.77)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
Respiratory complication	1580	1.04 (0.66 - 1.64)	0.59 (0.04 - 0.82)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
Renal failure	650	2.43 (1.12-5.28)	0 (0 - 0.9)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
Neutropenia	560	0.97 (0.09 - 10.29)	0.47 (0 - 0.84)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
Anastomotic leakage	1580	0.83 (0.41 - 0.68)	0.75 (0.48 - 0.88)	↓	↓	-	-	↓	⊕⊕ ⊕ ⊕ VERY LOW
Chylie leakage	1366	0.99 (0.61 - 1.61)	0 (0.48 - 0.75)	↓	-	↓	-	↓	⊕⊕ ⊕ ⊕ VERY LOW
Wound infection	1022	1.04 (0.36 - 3.02)	0.37 (0 - 0.76)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
Bleeding	849	1.4 (0.425 - 7.79)	0 (0 - 0.85)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW
Vocal cord paresis	733	1.21 (0.04 - 41.98)	0.5 (0 - 0.85)	↓	-	-	-	↓	⊕⊕⊕ ⊕ LOW