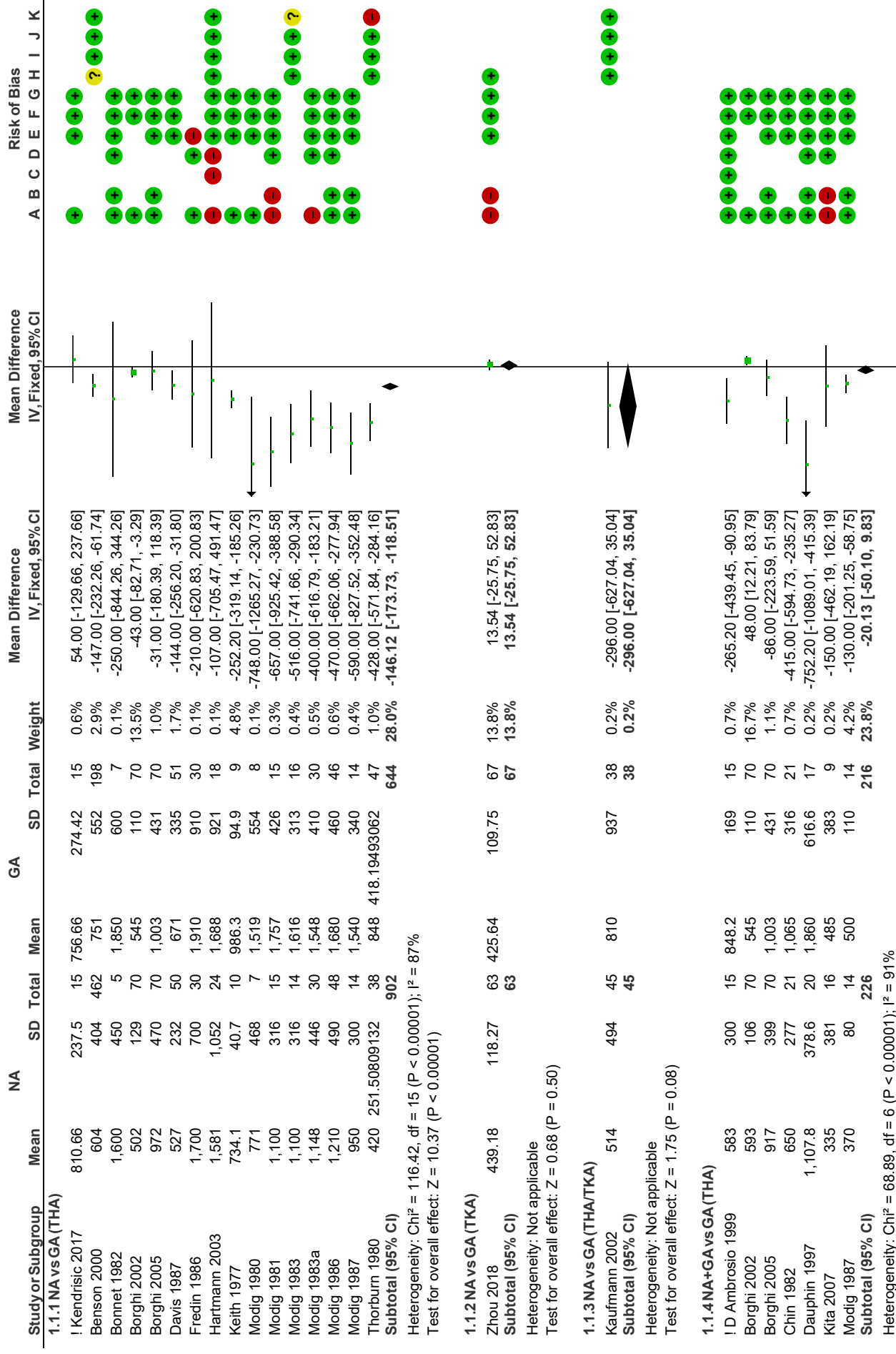
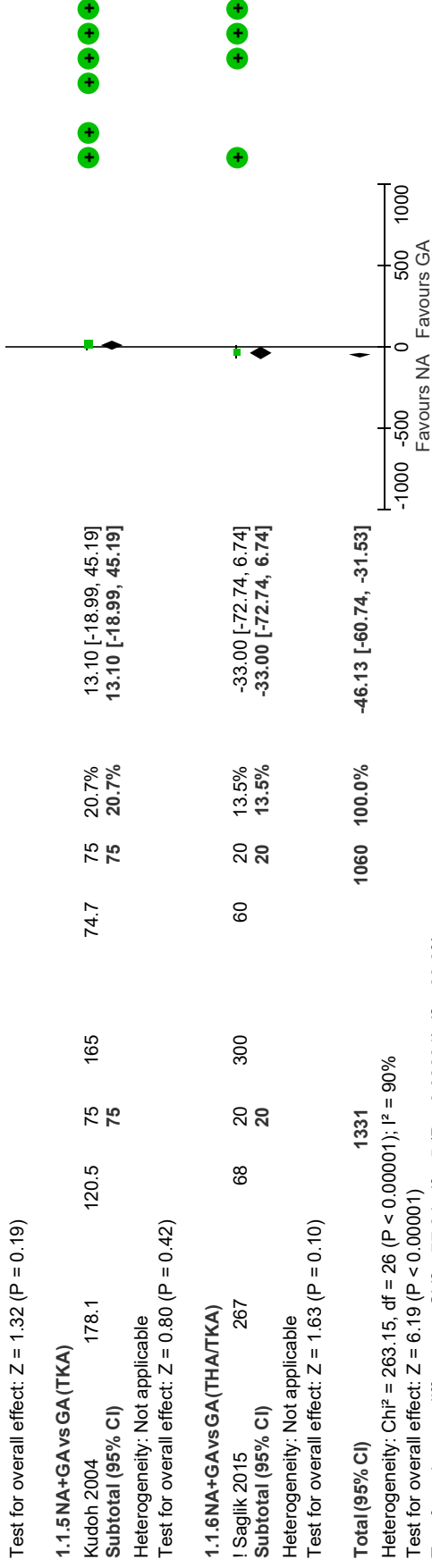


1 NA vs GA

1.1 Blood loss





Test for overall effect: Z = 1.32 (P = 0.19)

Heterogeneity: Chi² = 263.15, df = 26 (P < 0.00001); I² = 90%

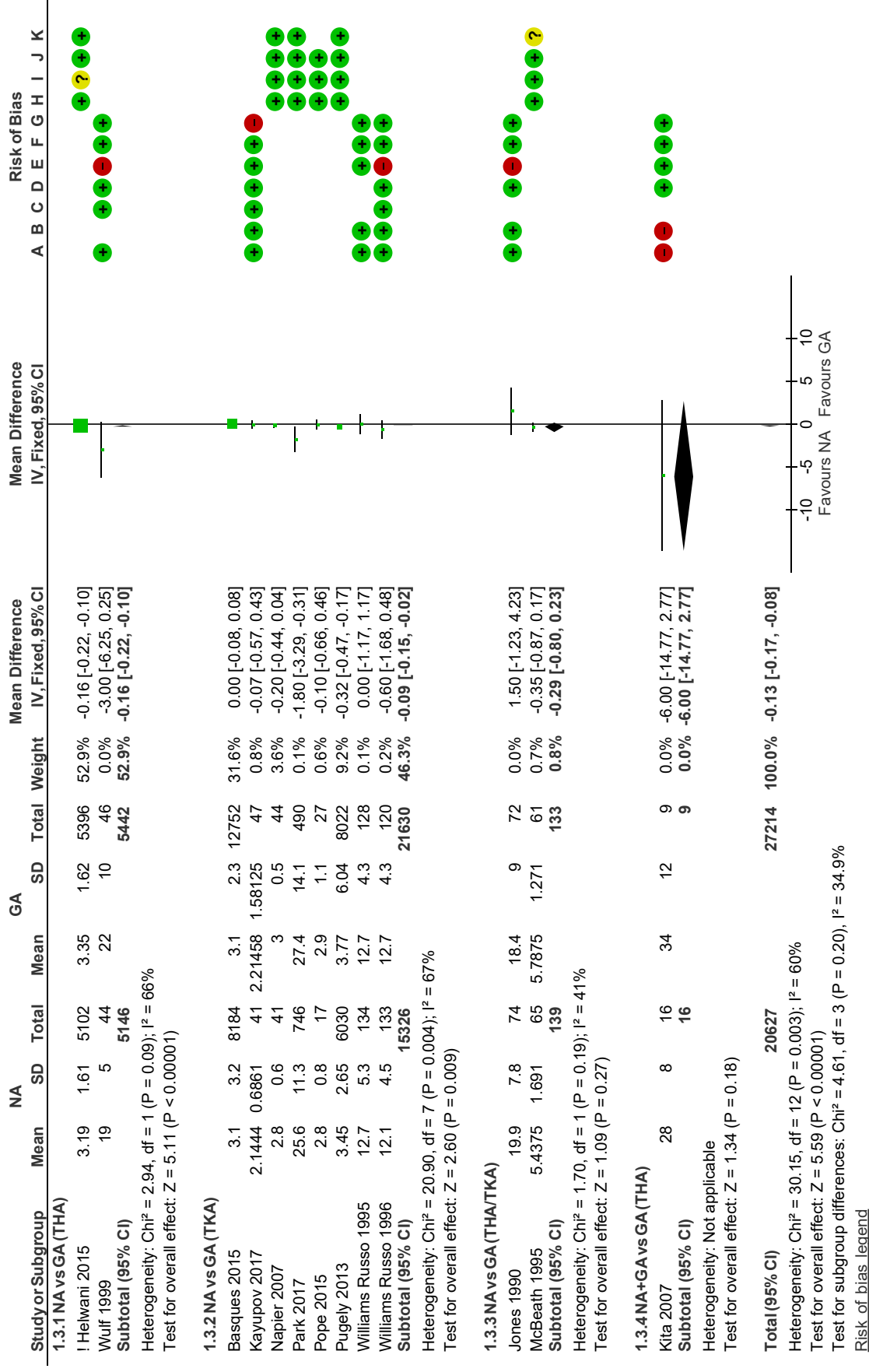
Test for overall effect: Z = 6.19 (P < 0.00001)

Test for subgroup differences: Chi² = 77.84, df = 5 (P < 0.00001), I² = 93.6%

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding

1.3 Length of hospital stay (LOS)

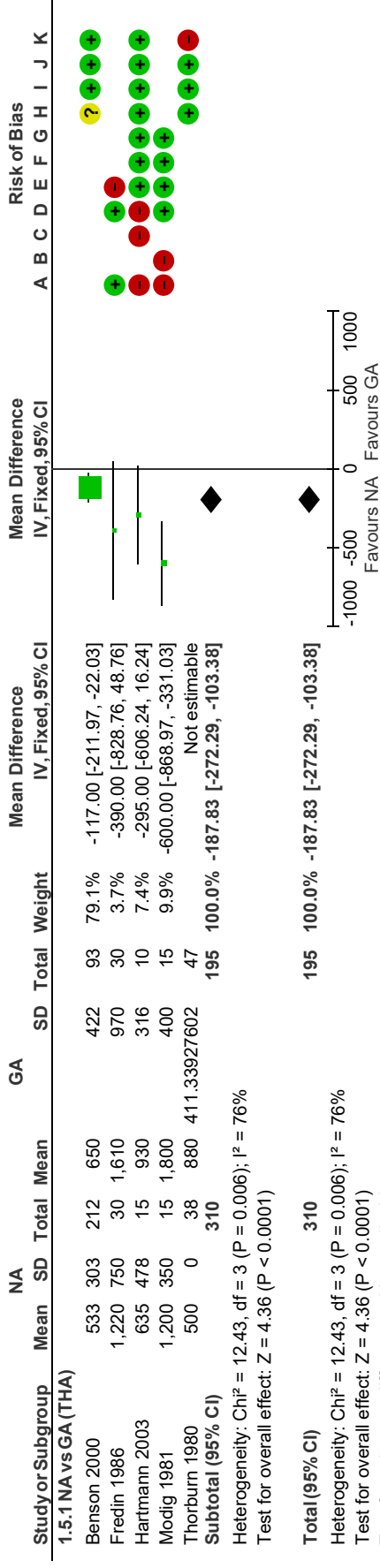


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)

- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding

1.5 Blood transfusion, ml



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding

1.10 Total Cost/case (Anesthesia+recovery: drugs and supplies; personal costs not included)

Study or Subgroup	NA		GA		Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias										
	Mean	SD	Mean	SD				A	B	C	D	E	F	G	H	I	J	K

1.10.1 NA vs GA (THA/TKA)															
Gonano 2006	46.3	11	20	89.6	13	20	100.0%	-43.30 [-50.76, -35.84]	+	+	+	+	+	+	+
Subtotal (95% CI)		20				20	100.0%	-43.30 [-50.76, -35.84]							

Heterogeneity: Not applicable
 Test for overall effect: Z = 11.37 (P < 0.00001)

Total (95% CI)		20				20	100.0%	-43.30 [-50.76, -35.84]							
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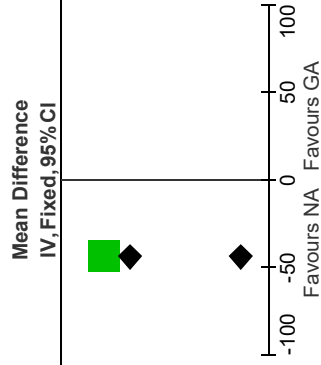
Heterogeneity: Not applicable

Test for overall effect: Z = 11.37 (P < 0.00001)

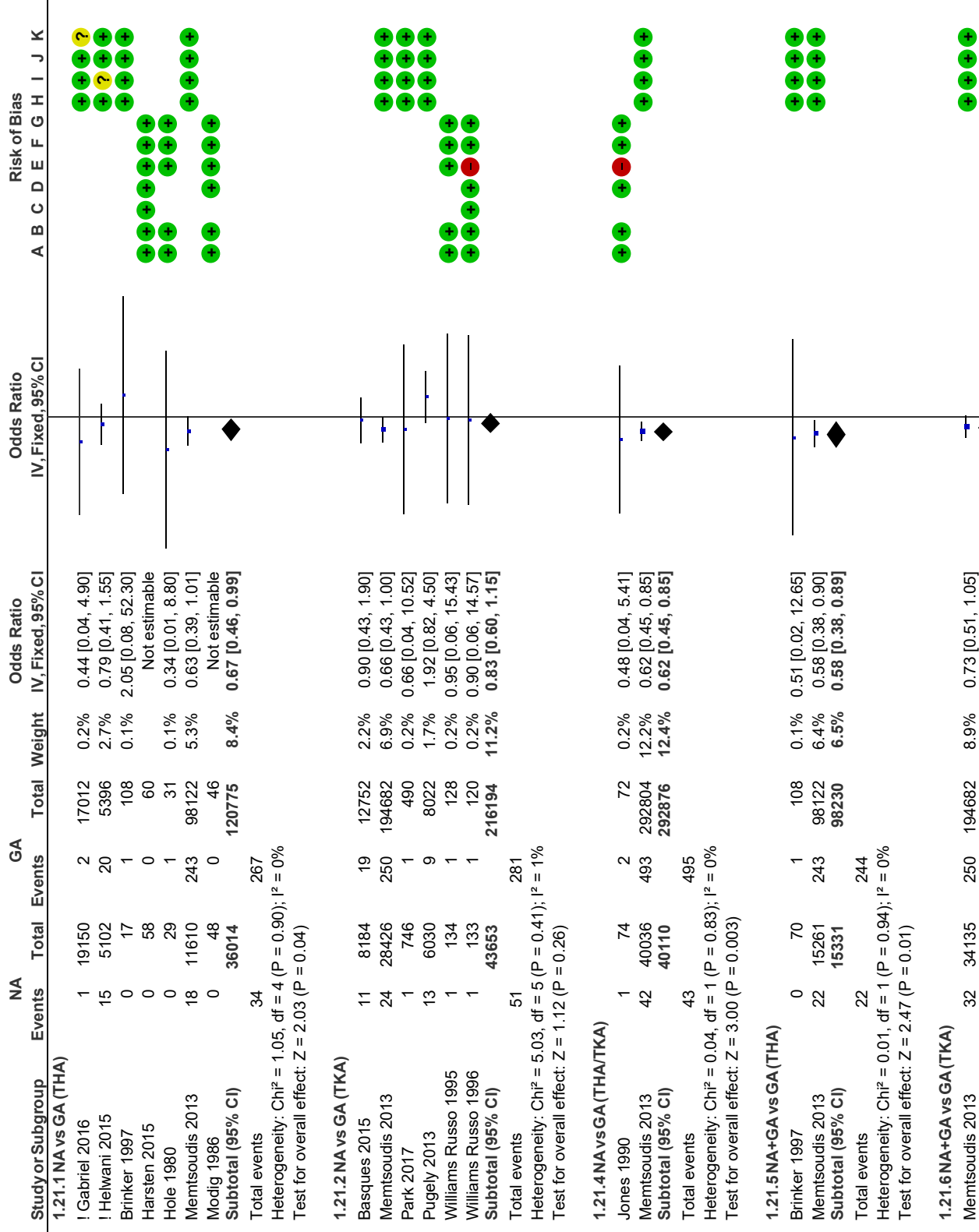
Test for subgroup differences: Not applicable

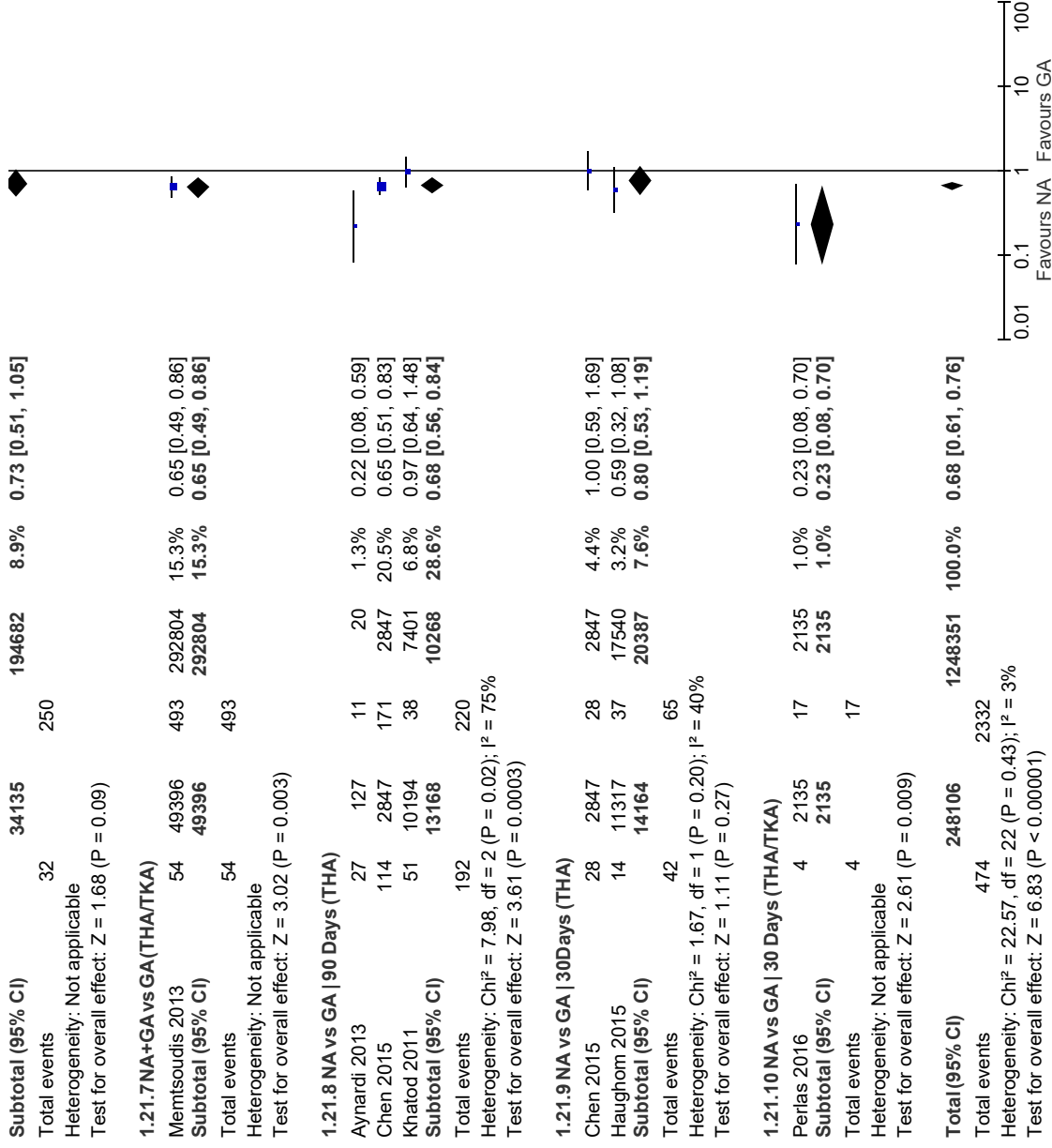
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding



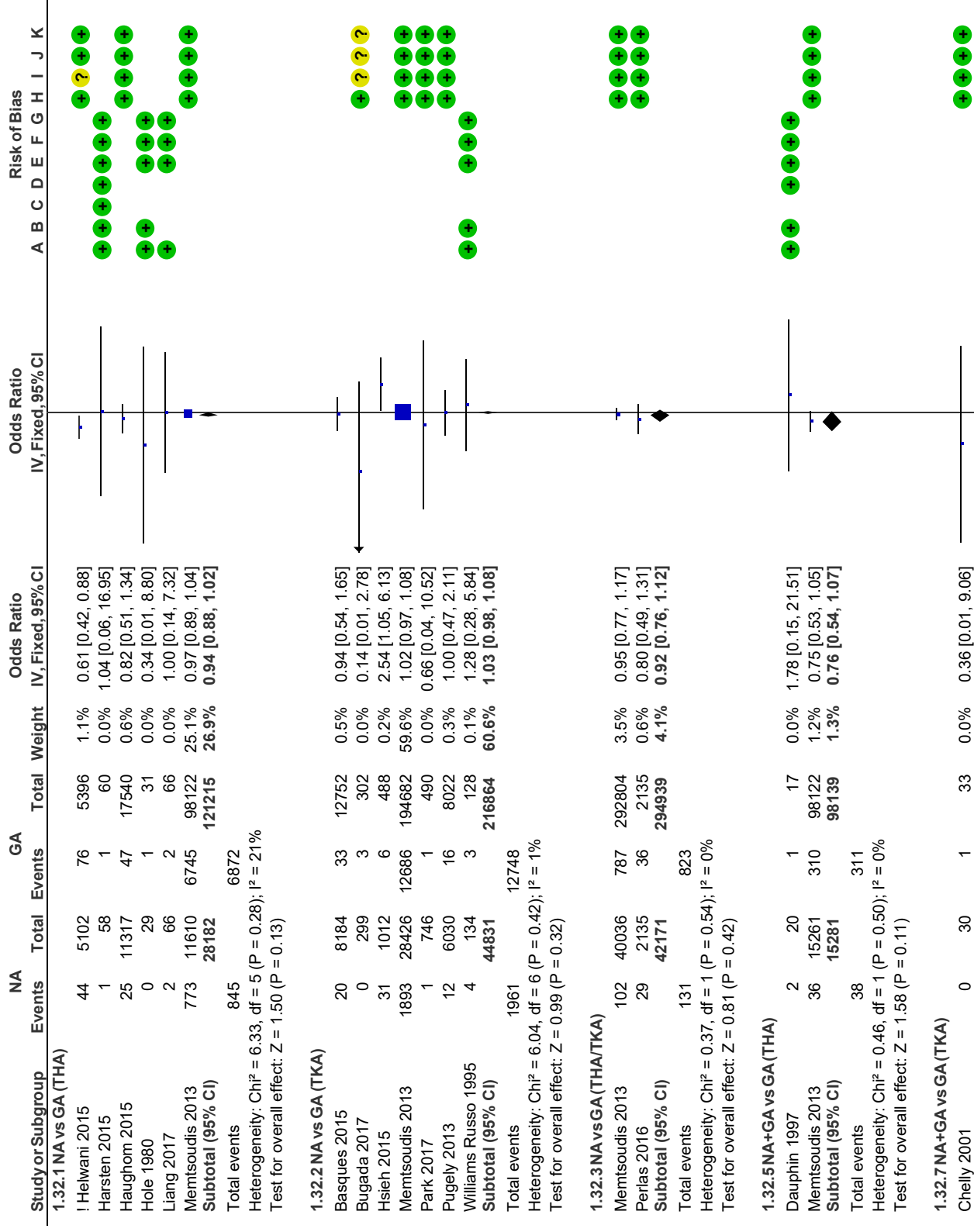
1.21 Mortality

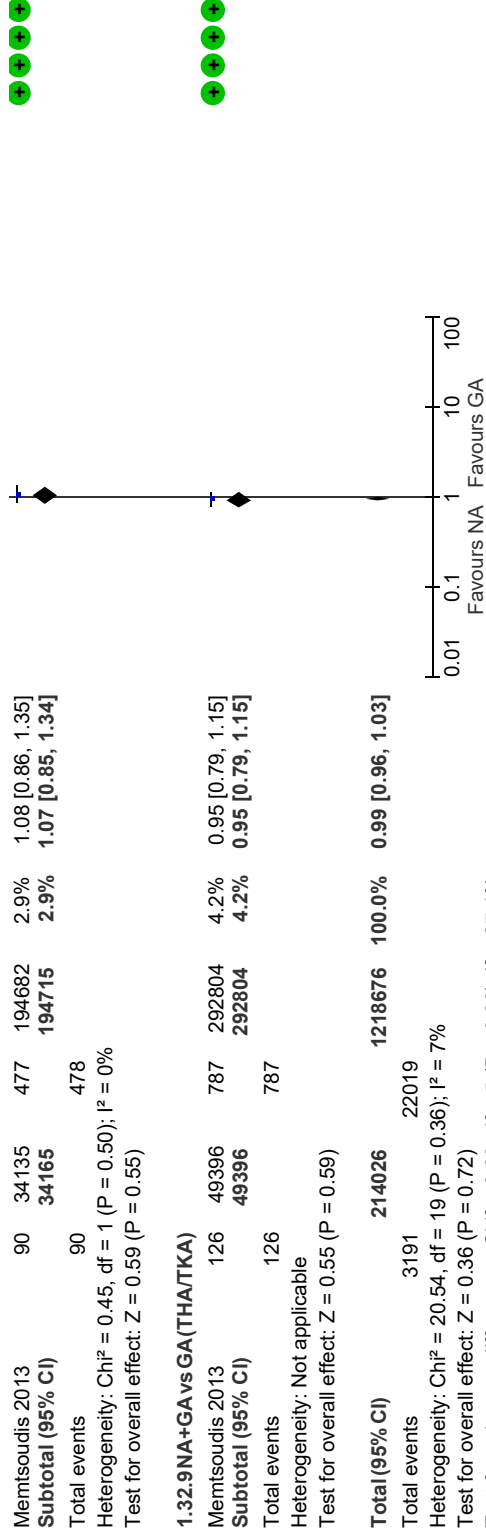




- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding

1.32 Cardiac incl. MI





- Risk of bias legend**
- (A) Random sequence generation (selection bias)
 - (B) Allocation concealment (selection bias)
 - (C) Blinding of participants and personnel (performance bias)
 - (D) Blinding of outcome assessment (detection bias)
 - (E) Incomplete outcome data (attrition bias)
 - (F) Selective reporting (reporting bias)
 - (G) Other bias
 - (H) Observational Study: Incomplete follow-up
 - (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
 - (J) Observational Study: Flawed measurement of exposure or outcome
 - (K) Observational Study: Failure to adequately control for confounding

1.33 Cardiac excl. MI

Study or Subgroup	NA		GA		Total Weight	Odds Ratio IV, Fixed, 95% CI	Odds Ratio IV, Fixed, 95% CI	Risk of Bias																								
	Events	Total	Events	Total				A	B	C	D	E	F	G	H	I	J	K														
1.33.1 NA vs GA (THA)																																
Gabriel 2016	3	9625	15	18079	0.0%	0.38 [0.11, 1.30]	0.38 [0.11, 1.30]										+	+	+													
Harsten 2015	1	58	1	60	0.0%	1.04 [0.06, 16.95]	1.04 [0.06, 16.95]										+	+	+													
Haughom 2015	6	11317	19	17540	0.0%	0.49 [0.20, 1.23]	0.49 [0.20, 1.23]										+	+	+													
Hole 1980	0	29	1	31	0.0%	0.34 [0.01, 8.80]	0.34 [0.01, 8.80]										+	+	+													
Memtsoudis 2013	736	11610	6435	98122	6.5%	0.96 [0.89, 1.04]	0.96 [0.89, 1.04]										+	+	+													
Subtotal (95% CI)	32639		133832		6.6%	0.96 [0.88, 1.03]											+	+	+													
Total events: 6471																																
Heterogeneity: Chi² = 4.66, df = 4 (P = 0.32); I² = 14%																																
Test for overall effect: Z = 1.14 (P = 0.25)																																
1.33.2 NA vs GA (TKA)																																
Basques 2015	2	8184	15	12752	0.0%	0.21 [0.05, 0.91]	0.21 [0.05, 0.91]										+	+	+													
Memtsoudis 2013	1828	28426	12209	194682	15.8%	1.03 [0.98, 1.08]	1.03 [0.98, 1.08]										+	+	+													
Park 2017	1	746	1	490	0.0%	0.66 [0.04, 10.52]	0.66 [0.04, 10.52]										+	+	+													
Pugely 2013	4	6030	7	8022	0.0%	0.76 [0.22, 2.60]	0.76 [0.22, 2.60]										+	+	+													
Subtotal (95% CI)	43386		215946		15.8%	1.02 [0.97, 1.08]											+	+	+													
Total events: 12232																																
Heterogeneity: Chi² = 4.83, df = 3 (P = 0.18); I² = 38%																																
Test for overall effect: Z = 0.94 (P = 0.35)																																
1.33.3 NA vs GA (THA/TKA)																																
Memtsoudis 2013	2564	40036	18644	292804	22.3%	1.01 [0.96, 1.05]	1.01 [0.96, 1.05]										+	+	+													
Subtotal (95% CI)	40036		292804		22.3%	1.01 [0.96, 1.05]											+	+	+													
Total events: 18644																																
Heterogeneity: Not applicable																																
Test for overall effect: Z = 0.28 (P = 0.78)																																
1.33.4 NA+GA vs GA (THA)																																
Memtsoudis 2013	1014	15261	6435	98122	8.7%	1.01 [0.95, 1.09]	1.01 [0.95, 1.09]										+	+	+													
Subtotal (95% CI)	15261		98122		8.7%	1.01 [0.95, 1.09]											+	+	+													
Total events: 6435																																
Heterogeneity: Not applicable																																
Test for overall effect: Z = 0.40 (P = 0.69)																																
1.33.5 NA+GA vs GA (TKA)																																
Memtsoudis 2013	2273	34135	12209	194682	18.9%	1.07 [1.02, 1.12]	1.07 [1.02, 1.12]										+	+	+													
Subtotal (95% CI)	34135		194682		18.9%	1.07 [1.02, 1.12]											+	+	+													
Total events: 12209																																
Heterogeneity: Not applicable																																
Test for overall effect: Z = 2.71 (P = 0.007)																																
1.33.6 NA+GA vs GA (THA/TKA)																																



Memisoudis 2013 3287 49396 18644 282804 27.6% 1.01 [0.97, 1.05]
 Subtotal (95% CI) 49396 282804 27.6% 1.01 [0.97, 1.05]

Total events 3287 18644

Heterogeneity: Not applicable

Test for overall effect: Z = 0.51 (P = 0.61)

Total (95% CI) 214853 1218190 100.0% 1.02 [1.00, 1.04]

Total events 11719 74635

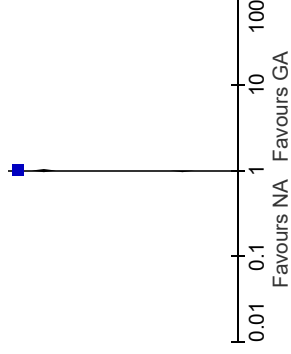
Heterogeneity: Chi² = 16.36, df = 12 (P = 0.18); I² = 27%

Test for overall effect: Z = 1.78 (P = 0.08)

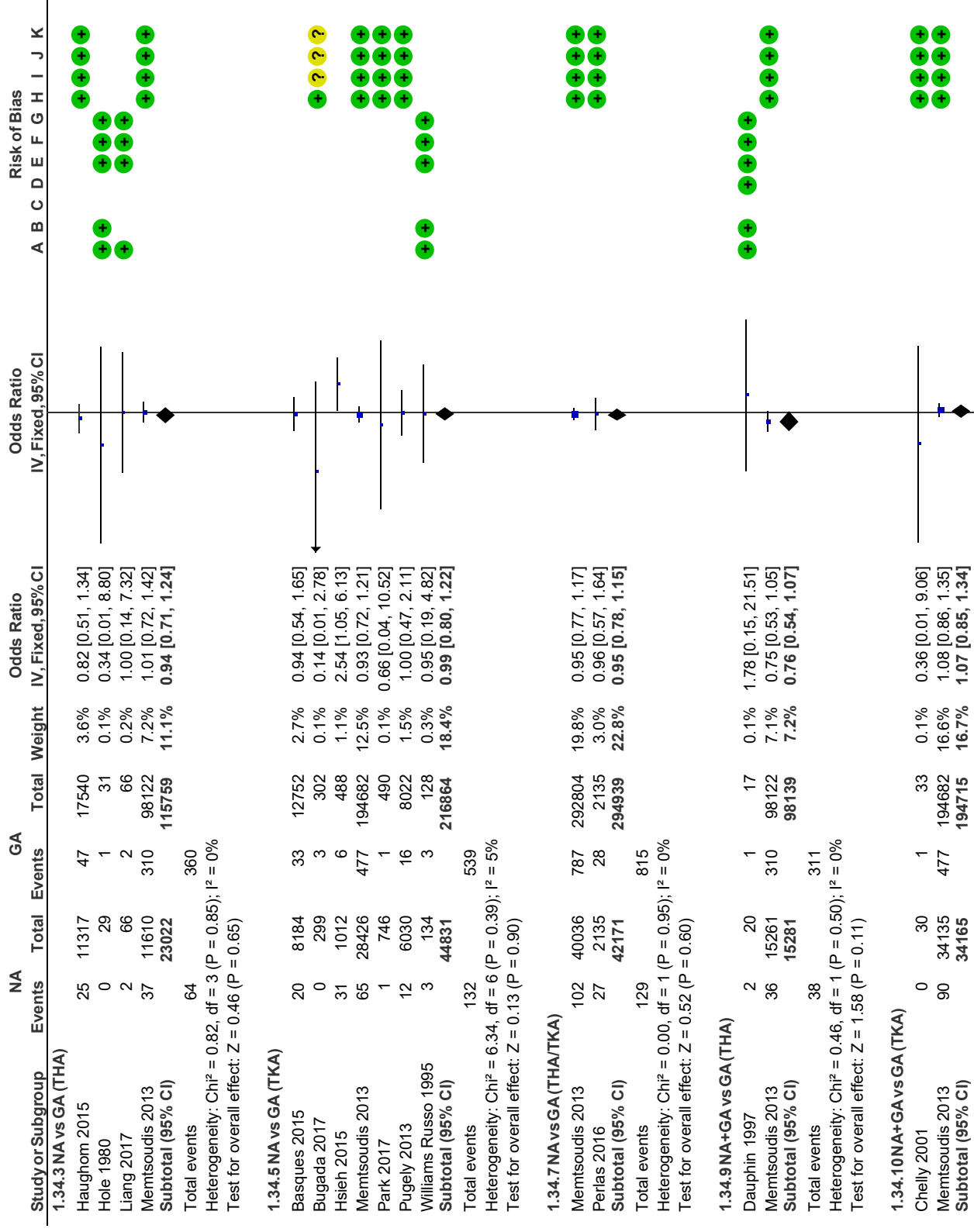
Test for subgroup differences: Chi² = 6.87, df = 5 (P = 0.23), I² = 27.2%

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
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- (K) Observational Study: Failure to adequately control for confounding



1.34 Myocardial infarction



Total events 90 478
 Heterogeneity: $\text{Chi}^2 = 0.45$, $\text{df} = 1$ ($P = 0.50$); $I^2 = 0\%$
 Test for overall effect: $Z = 0.59$ ($P = 0.55$)

1.34.11NA+GAsvsGA(THA/TKA)

Memtsoudis 2013	126	49396	787	292804	23.8%	0.95 [0.79, 1.15]
Subtotal (95% CI)	49396	292804	292804	23.8%	0.95	[0.79, 1.15]



Total events 126 787
 Heterogeneity: Not applicable
 Test for overall effect: $Z = 0.55$ ($P = 0.59$)

Total (95% CI) 208866 1213220 100.0% 0.96 [0.87, 1.05]

Total events 579 3290

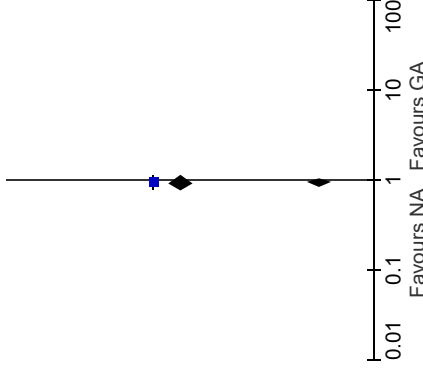
Heterogeneity: $\text{Chi}^2 = 10.90$, $\text{df} = 17$ ($P = 0.86$); $I^2 = 0\%$

Test for overall effect: $Z = 0.91$ ($P = 0.36$)

Test for subgroup differences: $\text{Chi}^2 = 2.84$, $\text{df} = 5$ ($P = 0.73$), $I^2 = 0\%$

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding



1.35 Pulmonary (excl. Pneumonia)

Study or Subgroup	Events	NA	Total	GA	Events	Total	Weight	Odds Ratio		Risk of Bias
								IV, Fixed, 95% CI	IV, Fixed, 95% CI	
1.35.1 NA vs GA (THA)										
! Helwani 2015	23	5102	47	5396	1.2%	0.52 [0.31, 0.85]				+
Haughom 2015	17	11317	51	17540	1.0%	0.52 [0.30, 0.89]				+
Memtsoudis 2013	61	11610	710	98122	4.2%	0.72 [0.56, 0.94]				+
Subtotal (95% CI)	28029		121058		6.3%	0.65 [0.52, 0.80]				+
Total events	101		808							+
Heterogeneity: Chi ² = 2.16, df = 2 (P = 0.34); I ² = 8%										
Test for overall effect: Z = 3.99 (P < 0.0001)										
1.35.2 NA vs GA (TKA)										
Basques 2015	11	8184	36	12752	0.6%	0.48 [0.24, 0.93]				+
Chu 2006	1	30	2	30	0.0%	0.48 [0.04, 5.63]				+
Memtsoudis 2013	131	28426	1312	194682	8.9%	0.68 [0.57, 0.82]				+
Park 2017	1	746	2	490	0.0%	0.33 [0.03, 3.62]				+
Pugely 2013	15	6030	16	8022	0.6%	1.25 [0.62, 2.53]				+
Subtotal (95% CI)	43416		215976		10.2%	0.69 [0.58, 0.81]				+
Total events	159		1368							+
Heterogeneity: Chi ² = 4.34, df = 4 (P = 0.36); I ² = 8%										
Test for overall effect: Z = 4.38 (P < 0.0001)										
1.35.3 NA vs GA (THA/TKA)										
! Weingarten 2015	766	5503	2070	6467	33.7%	0.34 [0.31, 0.38]				+
Memtsoudis 2013	192	40036	2022	292804	13.1%	0.69 [0.60, 0.80]				+
Subtotal (95% CI)	45539		299271		46.9%	0.42 [0.39, 0.45]				+
Total events	958		4092							+
Heterogeneity: Chi ² = 61.90, df = 1 (P < 0.00001); I ² = 98%										
Test for overall effect: Z = 21.78 (P < 0.00001)										
1.35.4 NA+GA vs GA (THA)										
Memtsoudis 2013	73	15261	710	98122	4.9%	0.66 [0.52, 0.84]				+
Subtotal (95% CI)	15261		98122		4.9%	0.66 [0.52, 0.84]				+
Total events	73		710							+
Heterogeneity: Not applicable										
Test for overall effect: Z = 3.38 (P = 0.0007)										
1.35.5 NA+GA vs GA (TKA)										
Chelly 2001	1	30	2	33	0.0%	0.53 [0.05, 6.21]				+
Memtsoudis 2013	206	34135	1312	194682	13.3%	0.89 [0.77, 1.04]				+
Subtotal (95% CI)	34165		194715		13.3%	0.89 [0.77, 1.03]				+
Total events	207		1314							+
Heterogeneity: Chi ² = 0.17, df = 1 (P = 0.68); I ² = 0%										
Test for overall effect: Z = 1.51 (P = 0.13)										

1.35.6NA+GA vs GA (THA/TKA)

Memtsoudis 2013	279	49396	2022	292804	18.3%	0.82 [0.72, 0.93]
Subtotal (95% CI)	49396	292804	18.3%	0.82 [0.72, 0.93]		

Total events 279 2022

Heterogeneity: Not applicable

Test for overall effect: Z = 3.16 (P = 0.002)

Total (95% CI) 215806 1221946 100.0% 0.58 [0.55, 0.61]

Total events 1777 10314

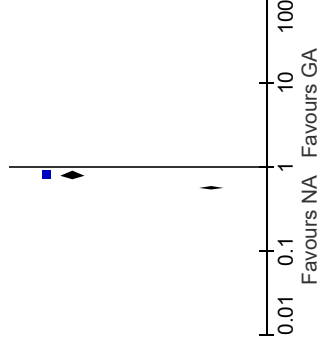
Heterogeneity: Chi² = 203.09, df = 13 (P < 0.00001); I² = 94%

Test for overall effect: Z = 19.96 (P < 0.00001)

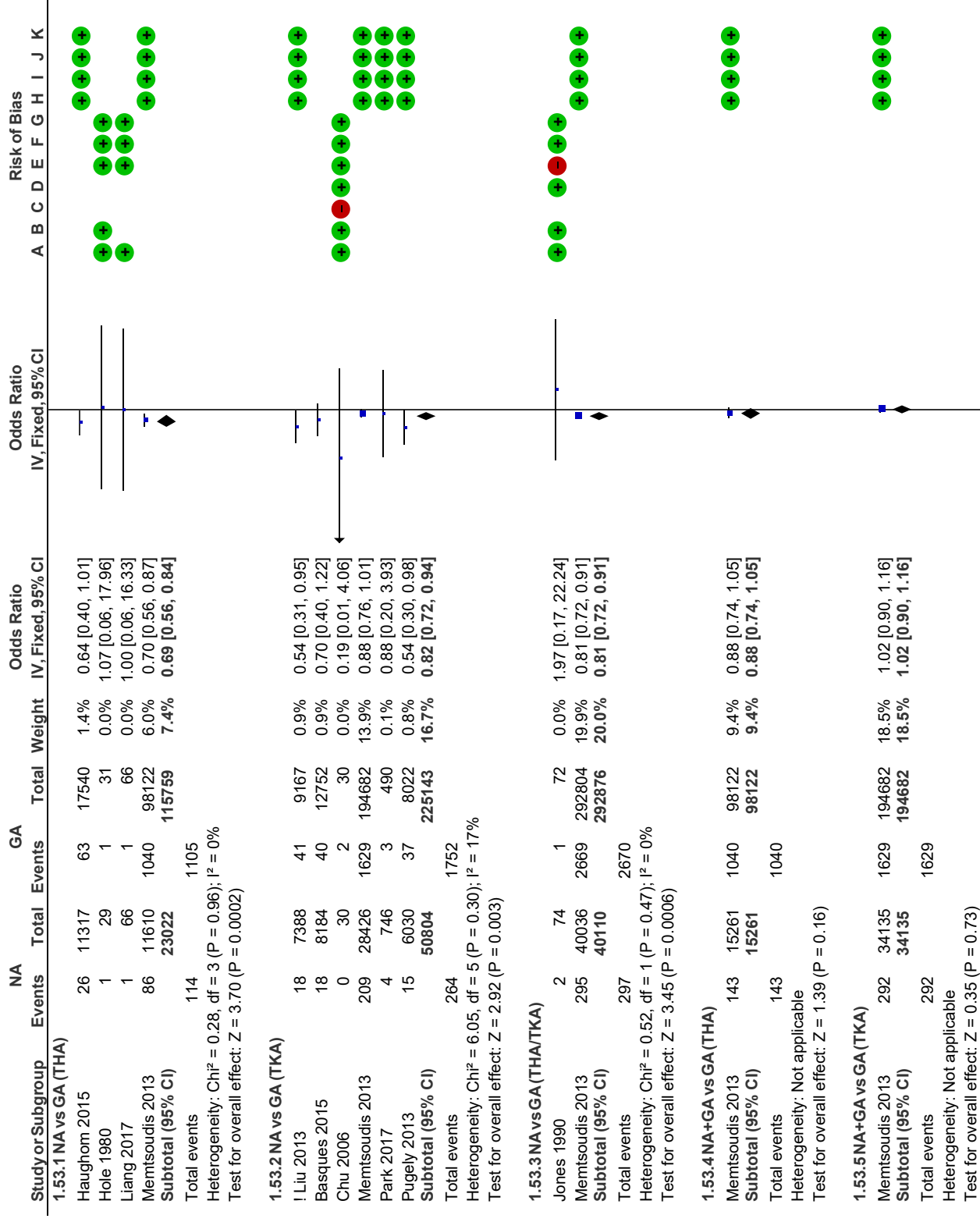
Test for subgroup differences: Chi² = 134.52, df = 5 (P < 0.00001), I² = 96.3%

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding



1.53 Pneumonia



1.53.6NA+GA vs GA(THA/TKA)
 Memtsoudis 2013 435 49396 2669 292804 28.0% 0.97 [0.87, 1.07]
 Subtotal (95% CI) 49396 292804 28.0% 0.97 [0.87, 1.07]



Total events 435 2669
 Heterogeneity: Not applicable
 Test for overall effect: Z = 0.67 (P = 0.50)

Total (95% CI) 212728 1219386 100.0% 0.89 [0.84, 0.94]

Total events 1545 10865

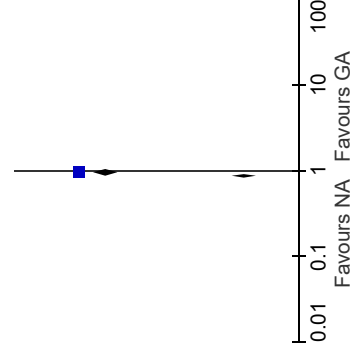
Heterogeneity: Chi² = 24.37, df = 14 (P = 0.04); I² = 43%

Test for overall effect: Z = 4.37 (P < 0.0001)

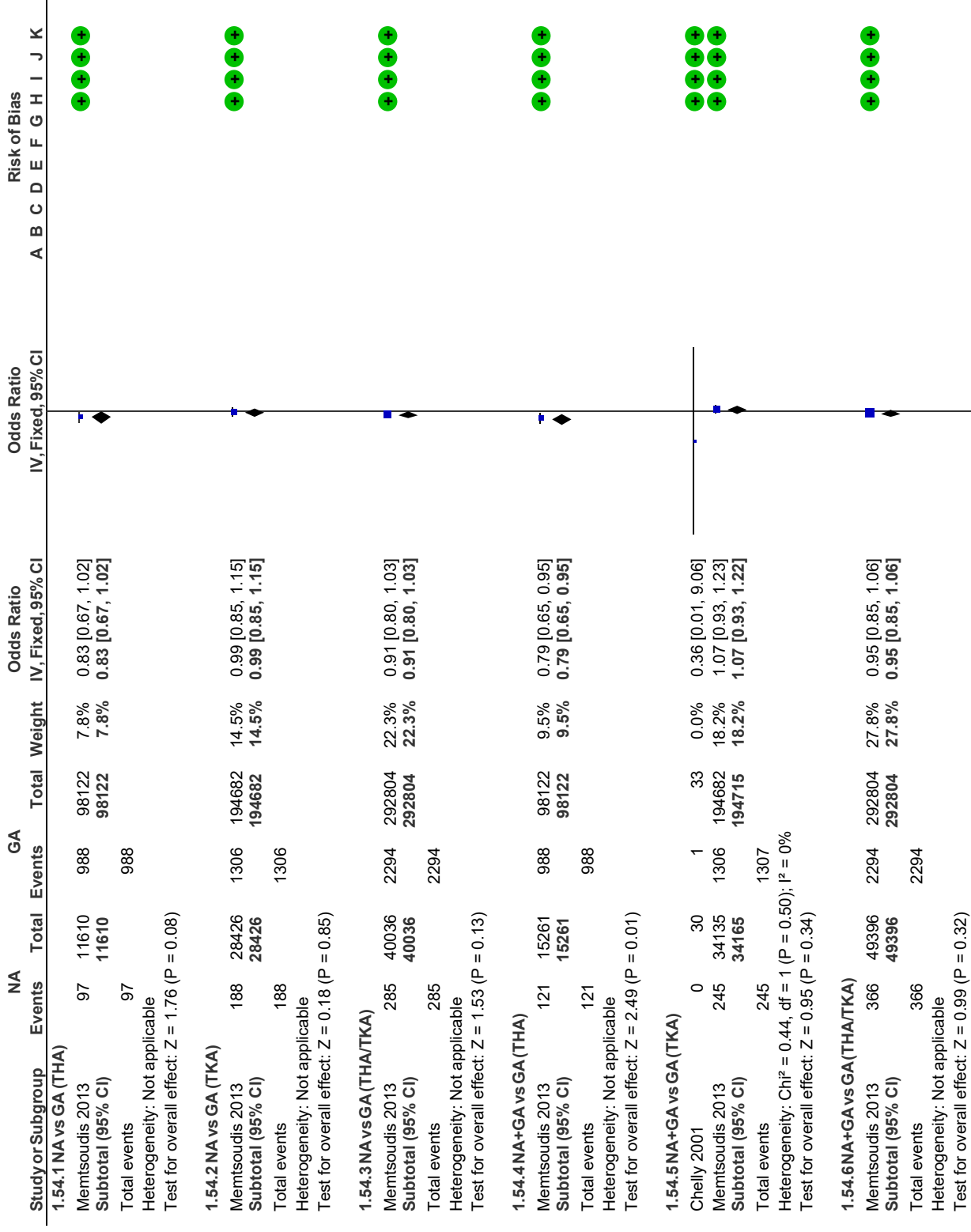
Test for subgroup differences: Chi² = 17.53, df = 5 (P = 0.004), I² = 71.5%

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding



1.54 Gastrointestinal



Total (95% CI) 178894 1171249 100.0% 0.94 [0.88, 0.99]

Total events 1302 9177

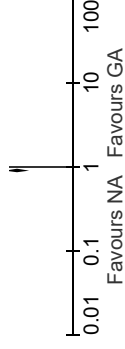
Heterogeneity: $\text{Chi}^2 = 9.31$, $\text{df} = 6$ ($P = 0.16$); $I^2 = 36\%$

Test for overall effect: $Z = 2.17$ ($P = 0.03$)

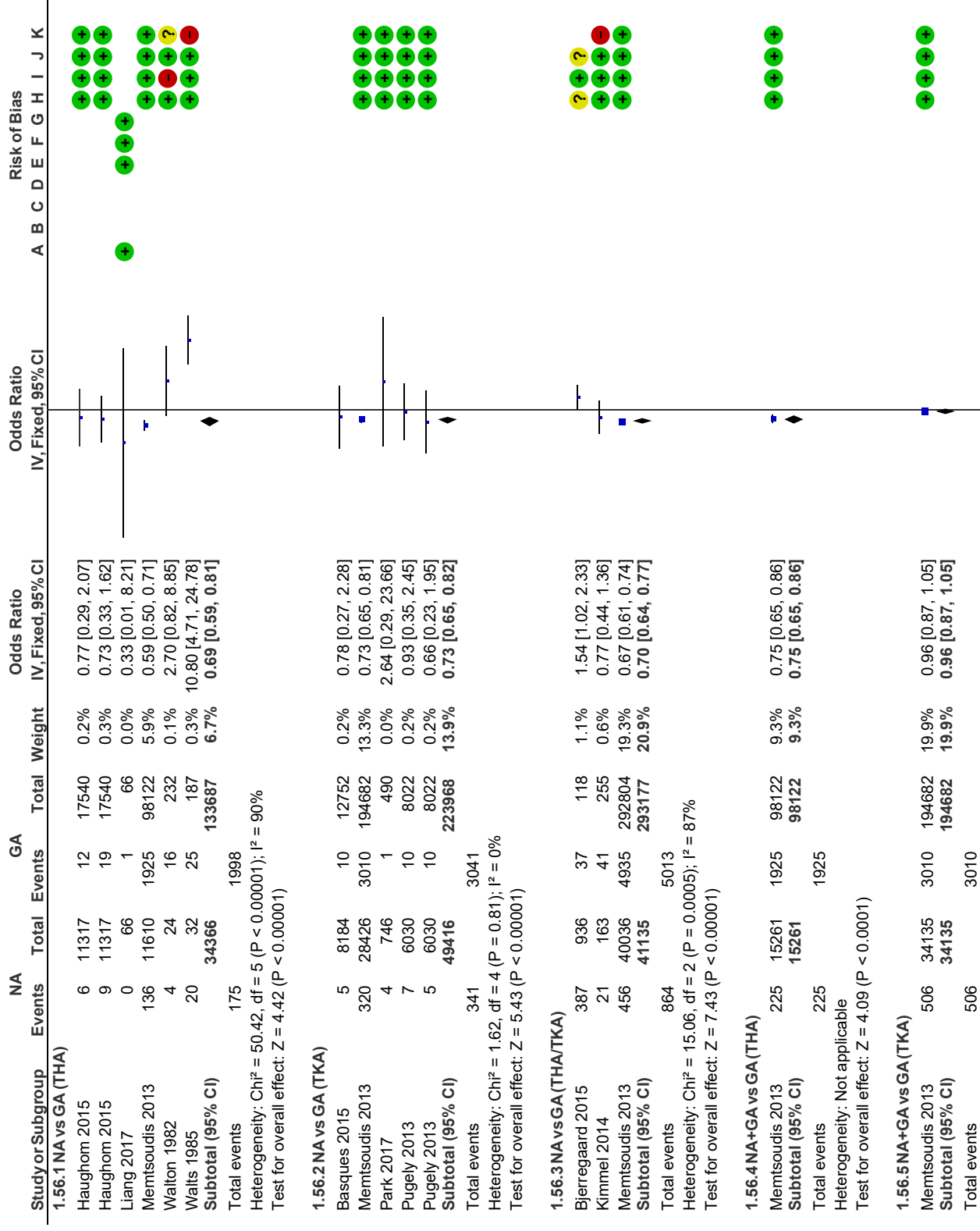
Test for subgroup differences: $\text{Chi}^2 = 8.87$, $\text{df} = 5$ ($P = 0.11$), $I^2 = 43.6\%$

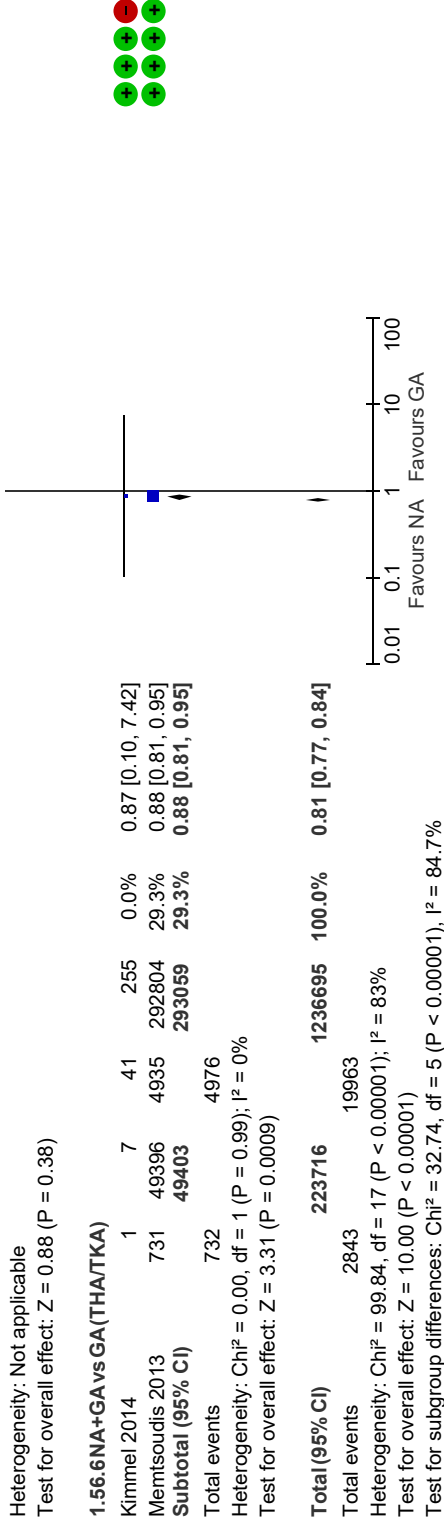
Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding



1.56 Acute renal failure

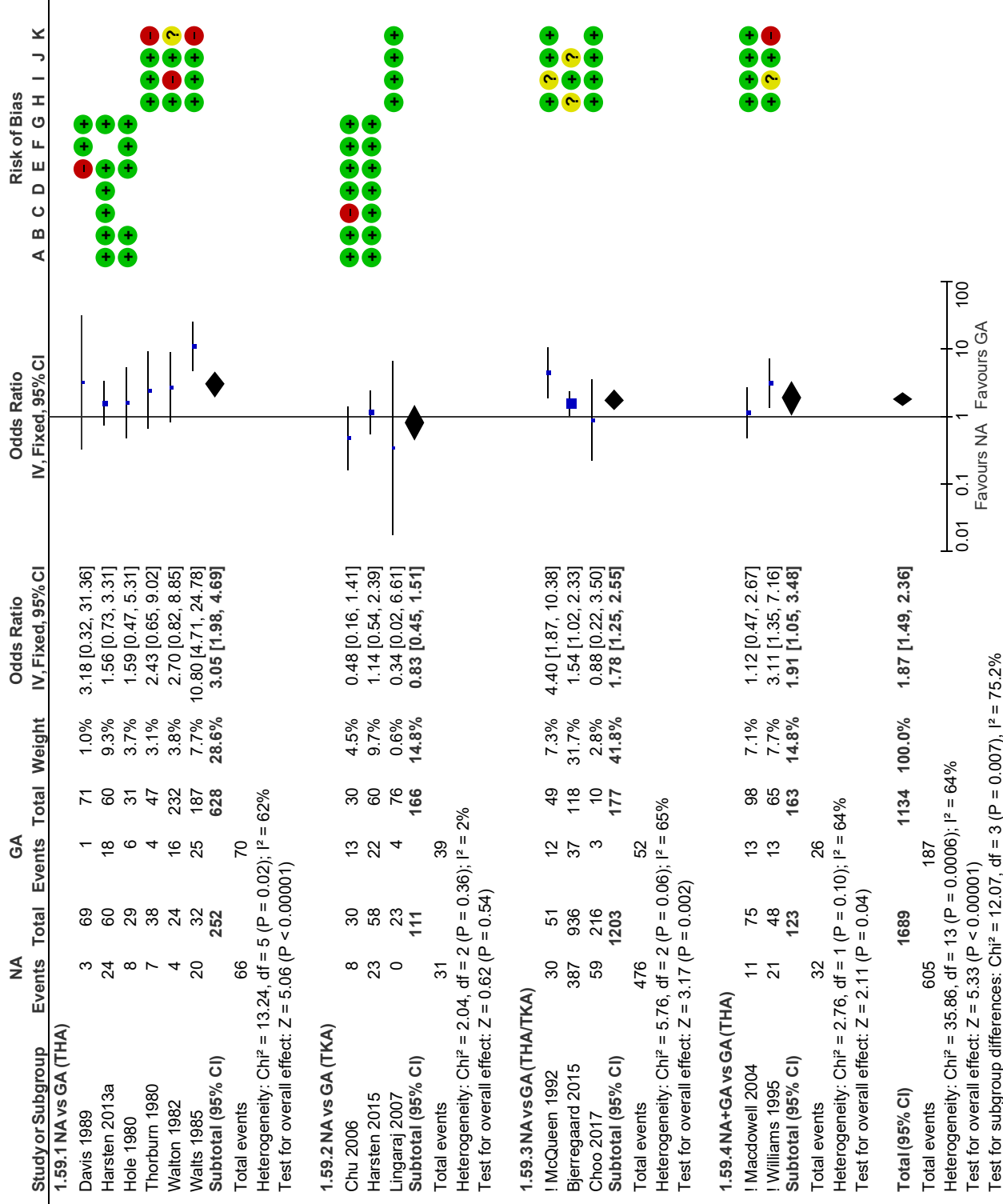




Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding

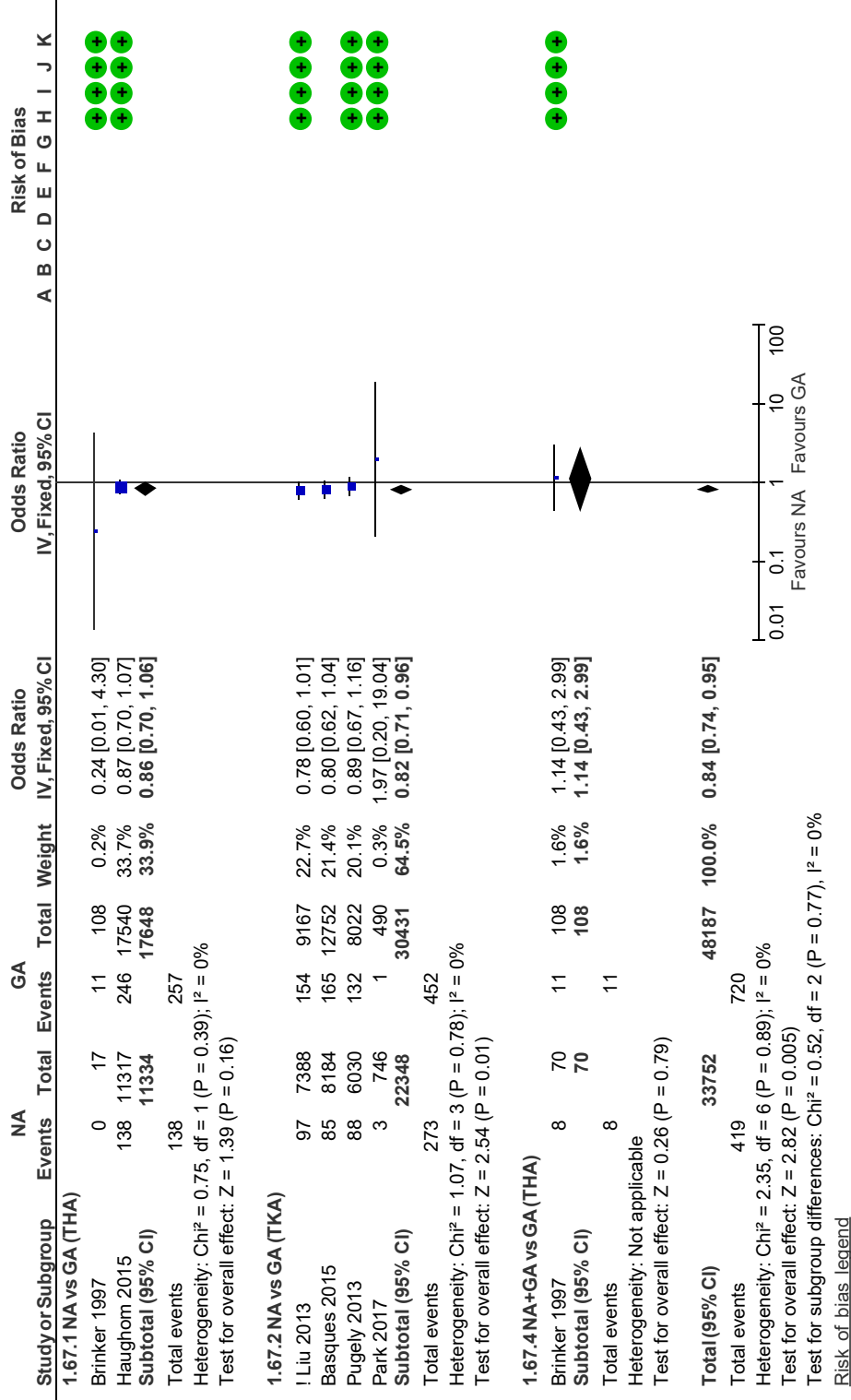
1.59 Urinary retention



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding

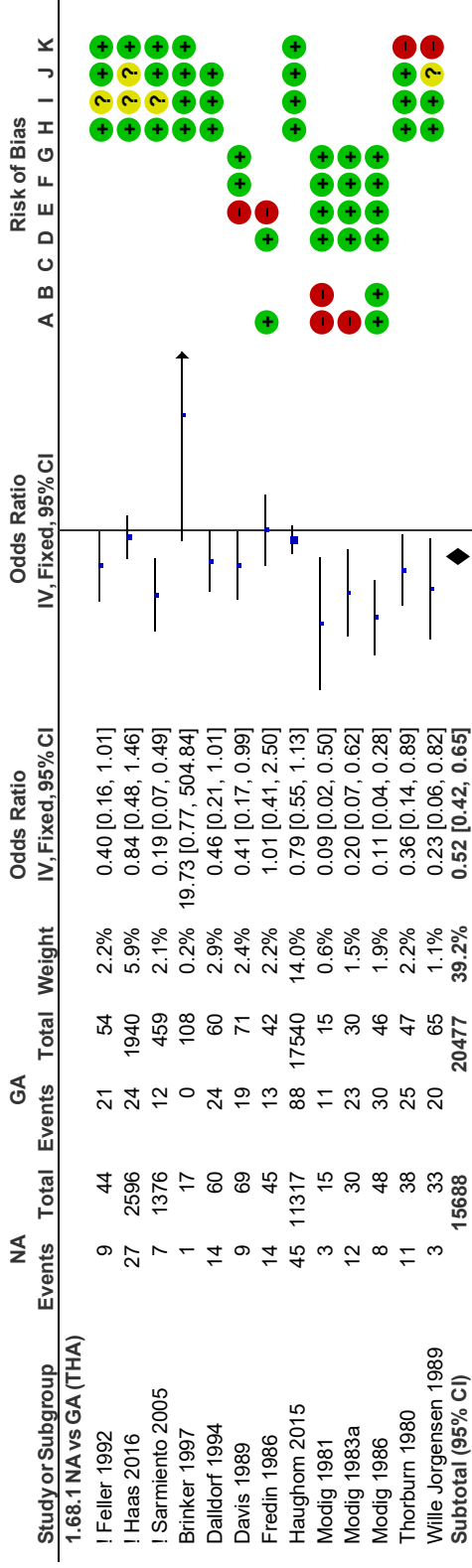
1.67 Urinary tract infection



Risk of bias legend

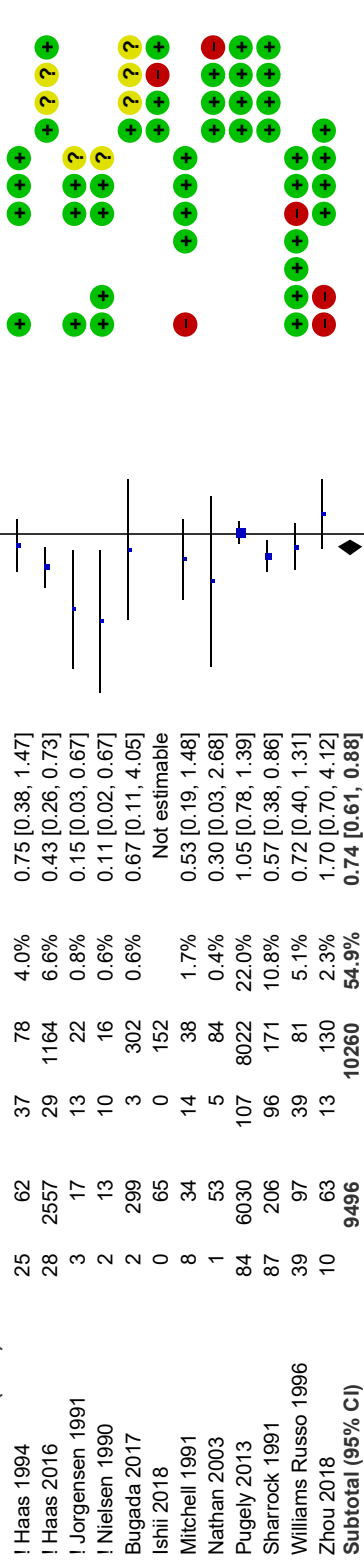
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
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1.68 Deep venous thrombosis (DVT)



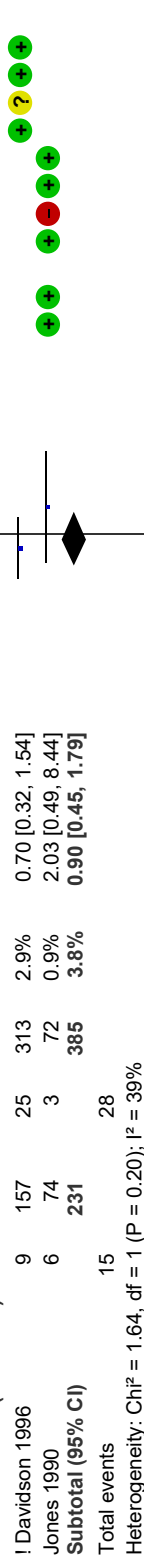
Total events 163
 Heterogeneity: Chi² = 39.25, df = 12 (P < 0.0001); I² = 69%
 Test for overall effect: Z = 5.94 (P < 0.00001)

1.68.2 NA vs GA (TKA)

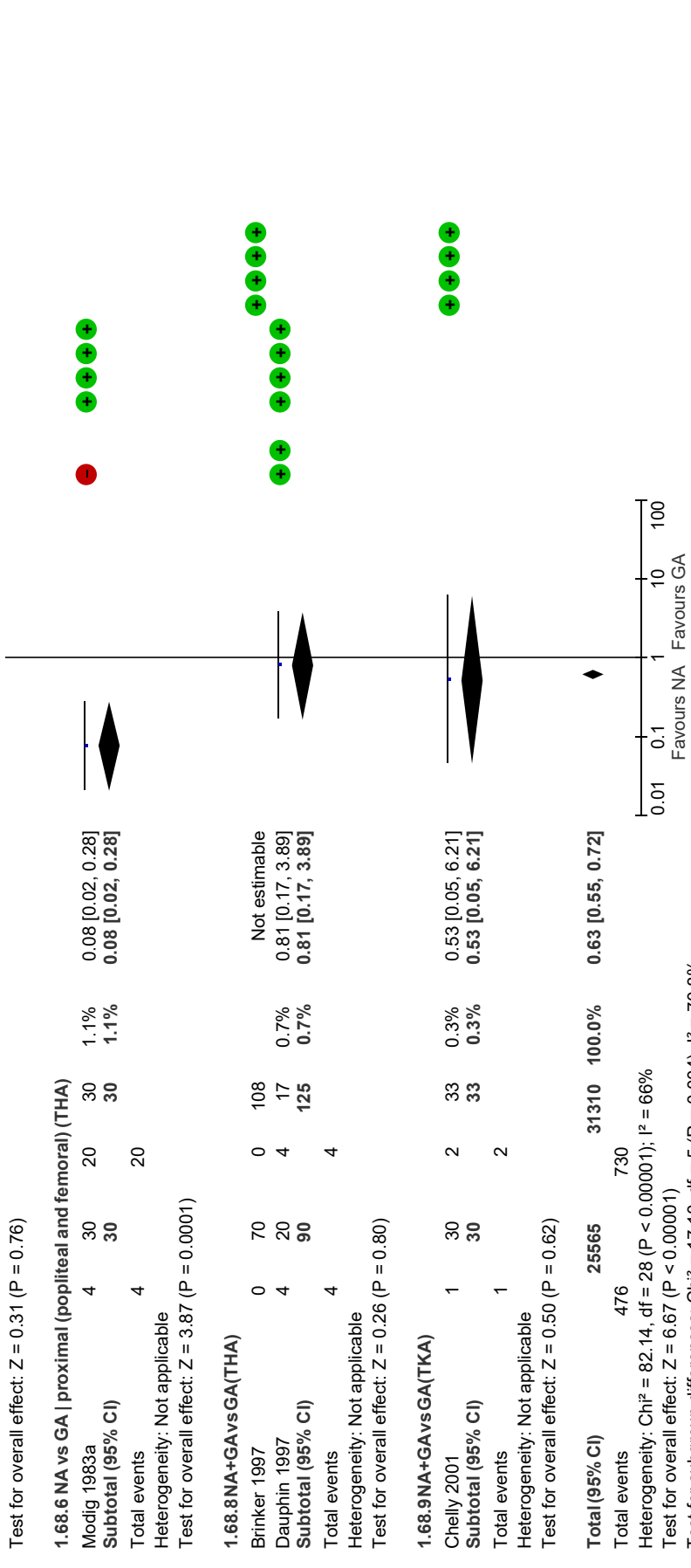


Total events 289
 Heterogeneity: Chi² = 24.15, df = 10 (P = 0.007); I² = 59%
 Test for overall effect: Z = 3.29 (P = 0.001)

1.68.3 NA vs GA (THA/TKA)



Total events 15
 Heterogeneity: Chi² = 1.64, df = 1 (P = 0.20); I² = 39%



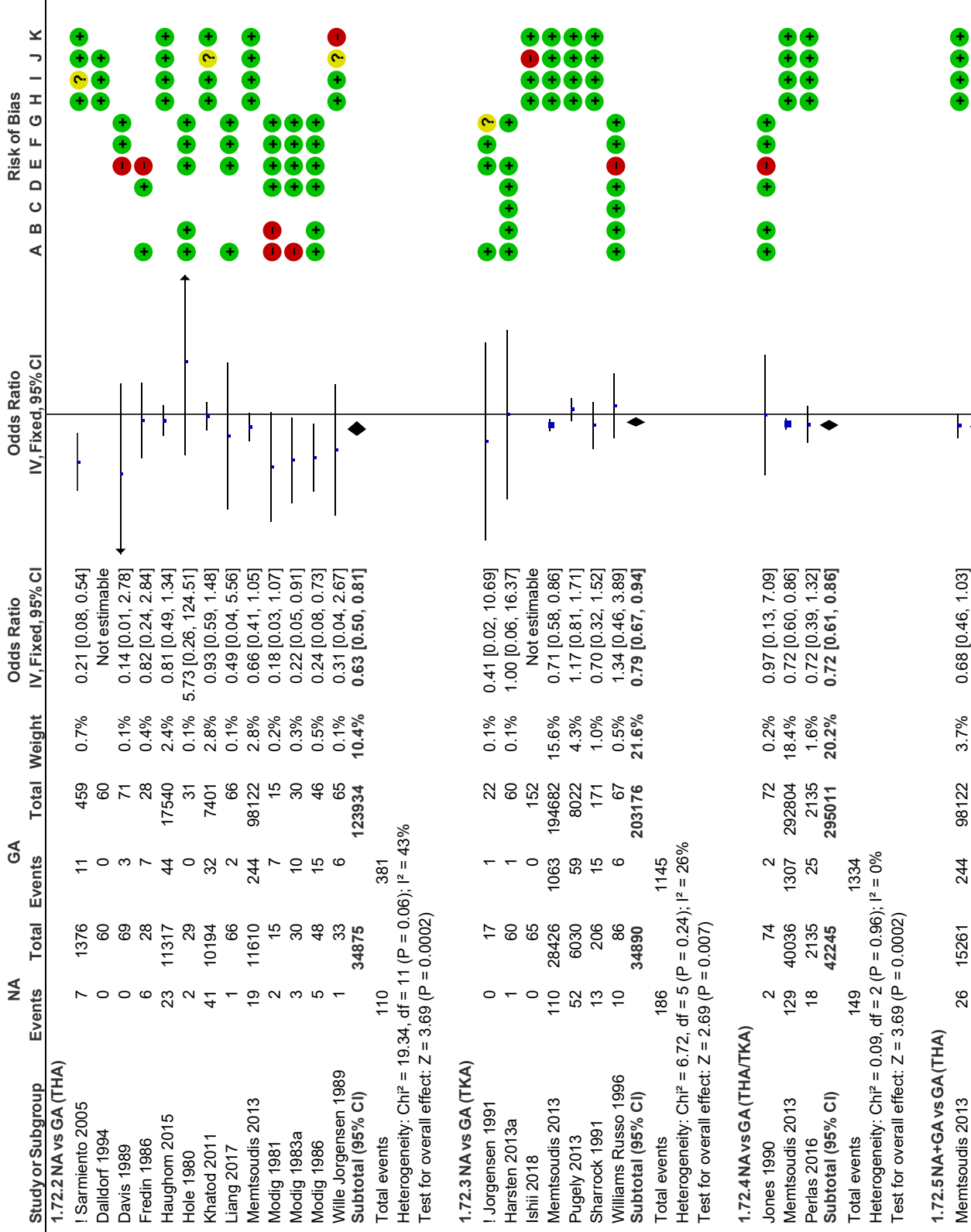
Test for overall effect: $Z = 0.31$ ($P = 0.76$)

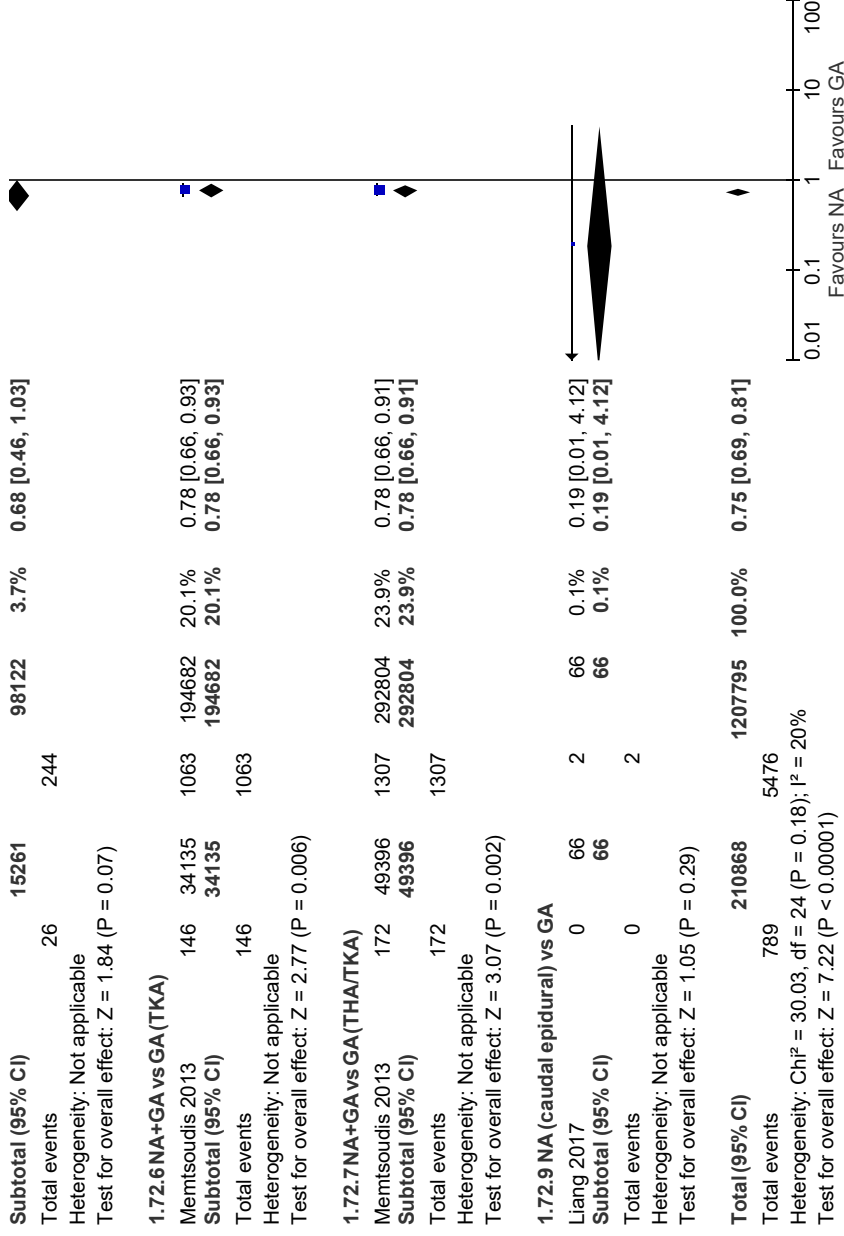
Heterogeneity: $\text{Chi}^2 = 82.14$, $\text{df} = 28$ ($P < 0.00001$); $I^2 = 66\%$
 Test for overall effect: $Z = 6.67$ ($P < 0.00001$)
 Test for subgroup differences: $\text{Chi}^2 = 17.10$, $\text{df} = 5$ ($P = 0.004$), $I^2 = 70.8\%$

Risk of bias legend

- (A) Random sequence generation (selection bias)
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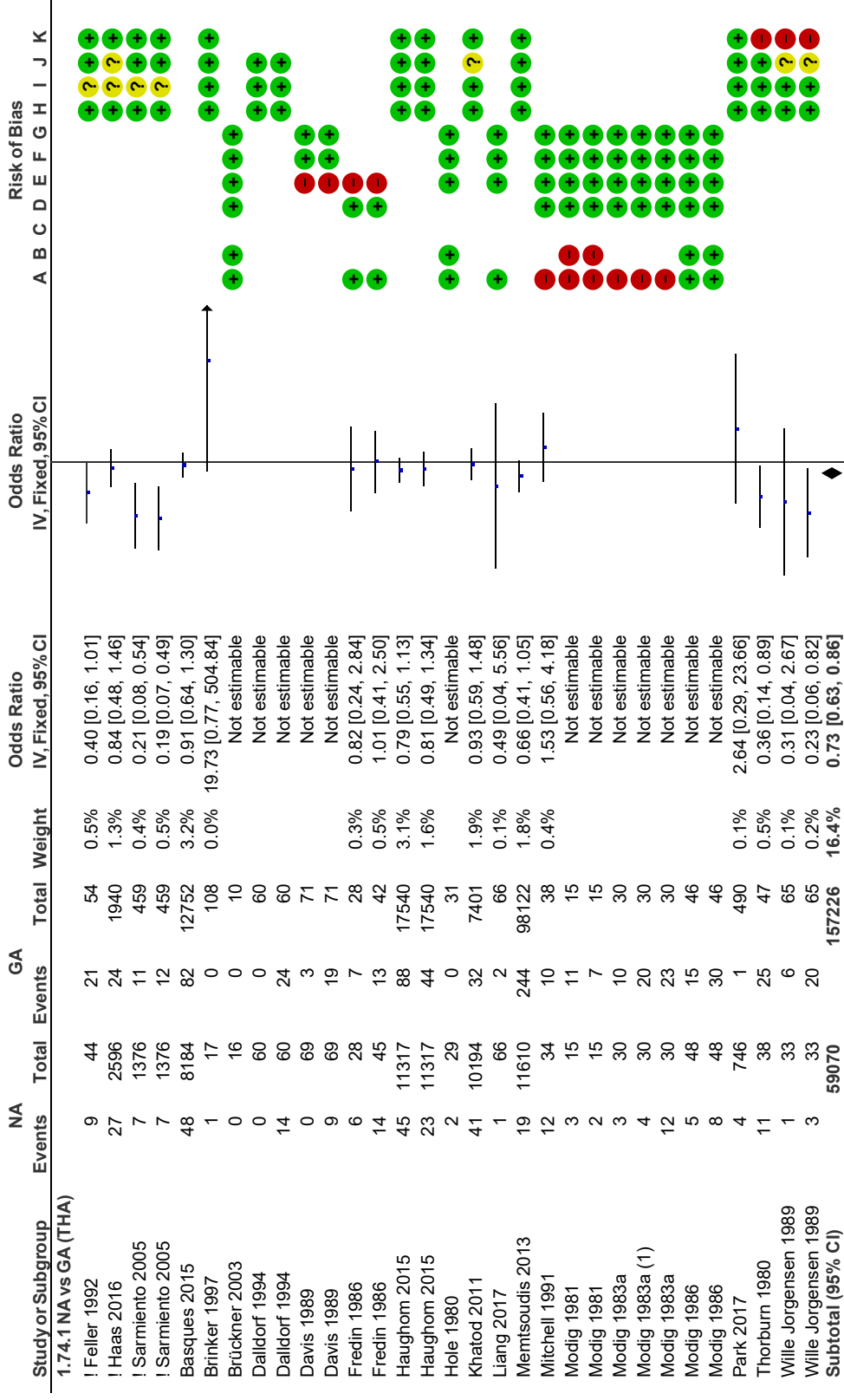
1.72 Pulmonary embolism (PE)





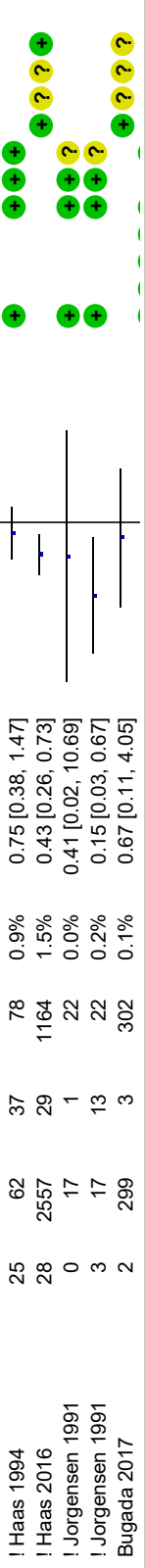
- Risk of bias legend**
- (A) Random sequence generation (selection bias)
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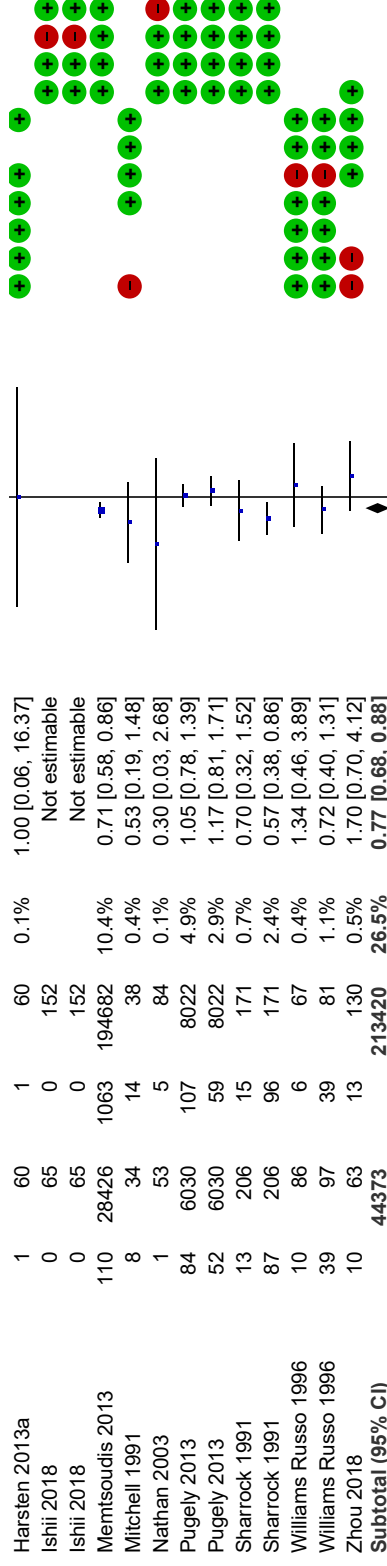
1.74 Thrombembolism (DVT + PE)



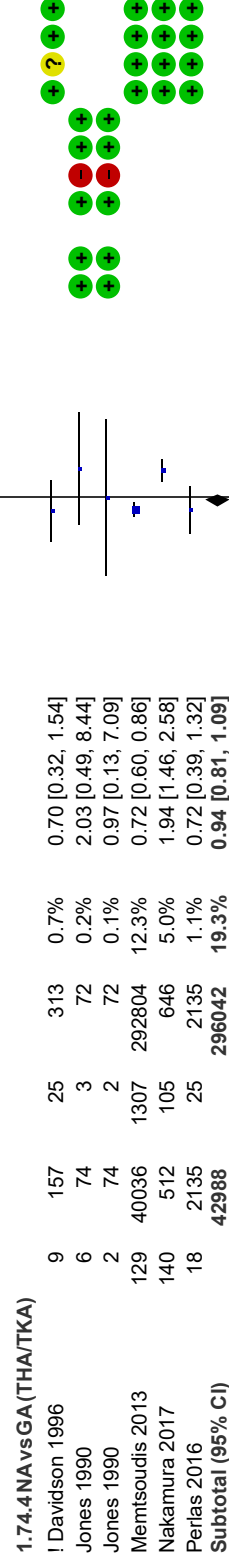
Heterogeneity: Chi² = 33.56, df = 17 (P = 0.010); I² = 49%
 Test for overall effect: Z = 3.87 (P = 0.0001)

1.74.3 NA vs GA (TKA)

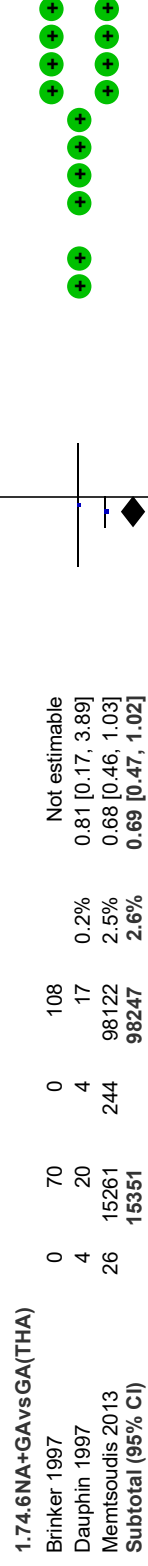




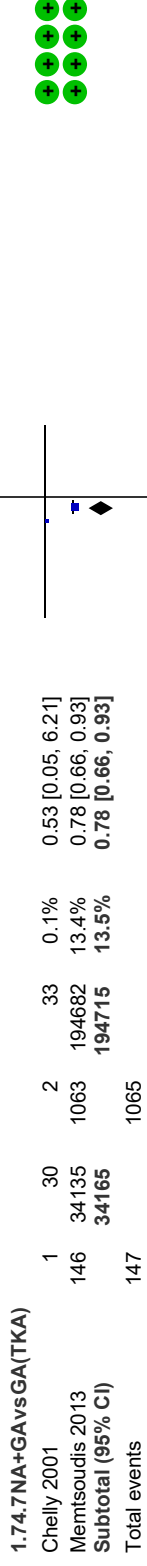
Total events 473 1501
 Heterogeneity: Chi² = 26.77, df = 15 (P = 0.03); I² = 44%
 Test for overall effect: Z = 4.05 (P < 0.0001)



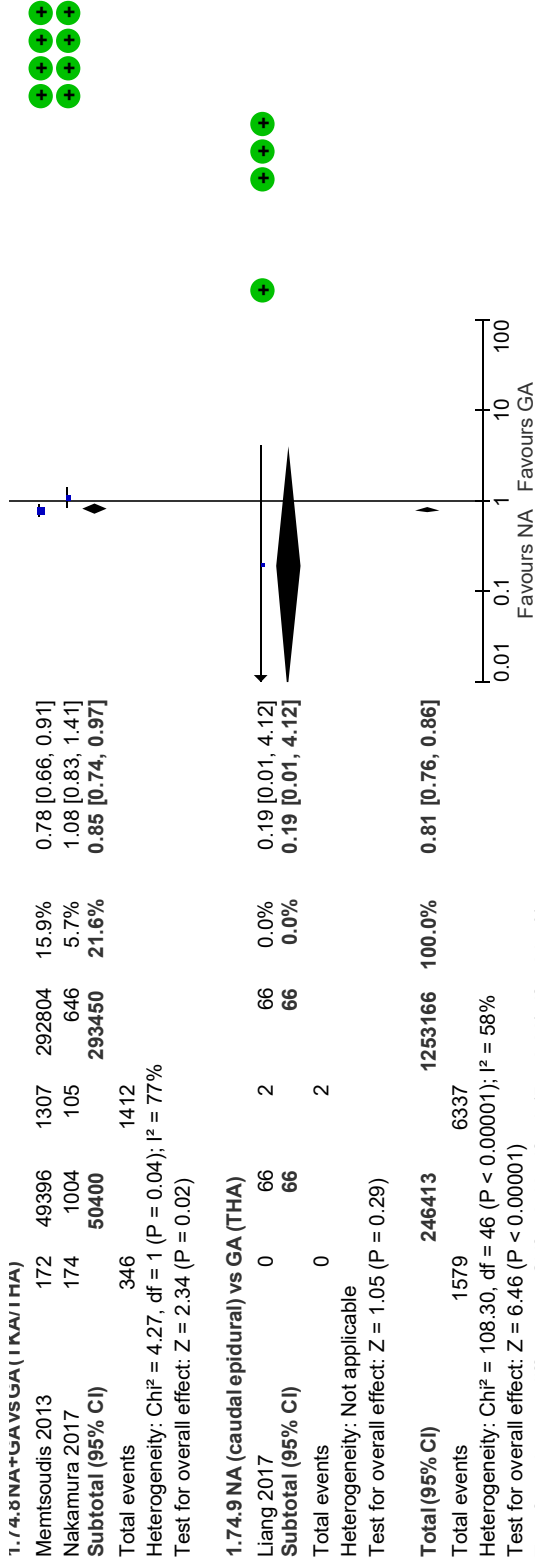
Total events 304 1467
 Heterogeneity: Chi² = 35.38, df = 5 (P < 0.00001); I² = 86%
 Test for overall effect: Z = 0.84 (P = 0.40)



Total events 30 248
 Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%
 Test for overall effect: Z = 1.84 (P = 0.07)



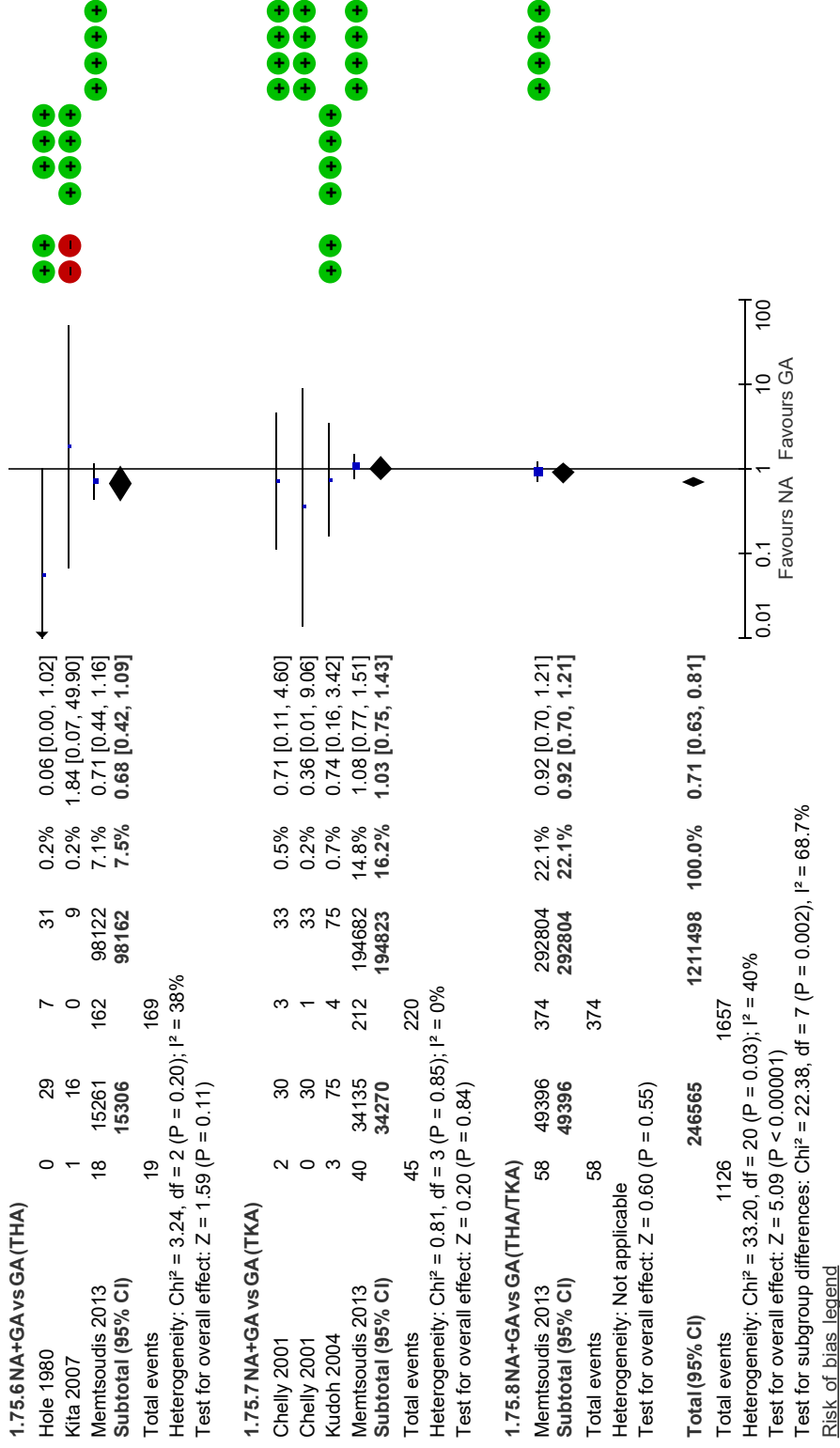
Total events 147 1065
 Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%
 Test for overall effect: Z = 2.80 (P = 0.005)



Risk of bias legend

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- (K) Observational Study: Failure to adequately control for confounding

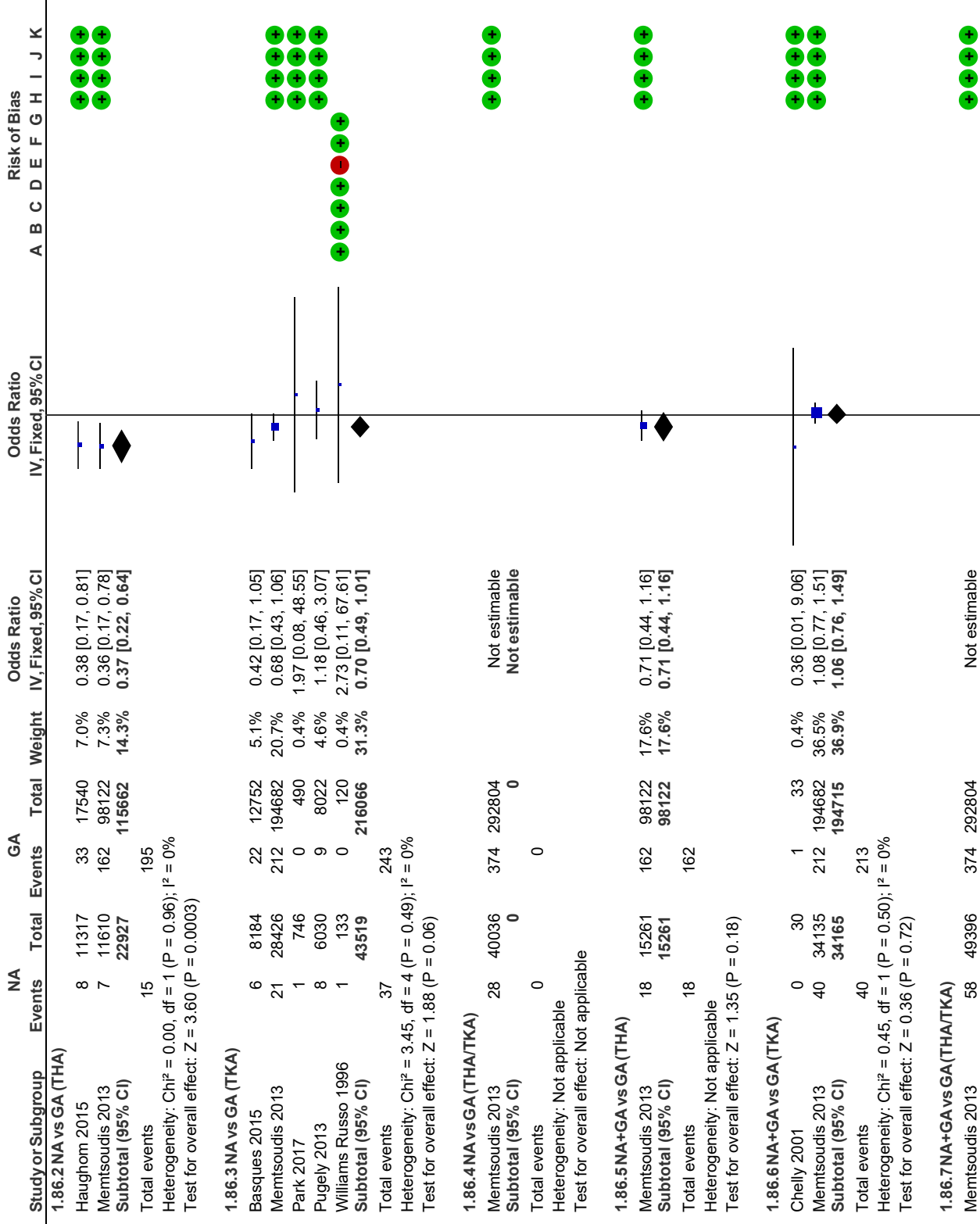
(1) popliteal and femoral

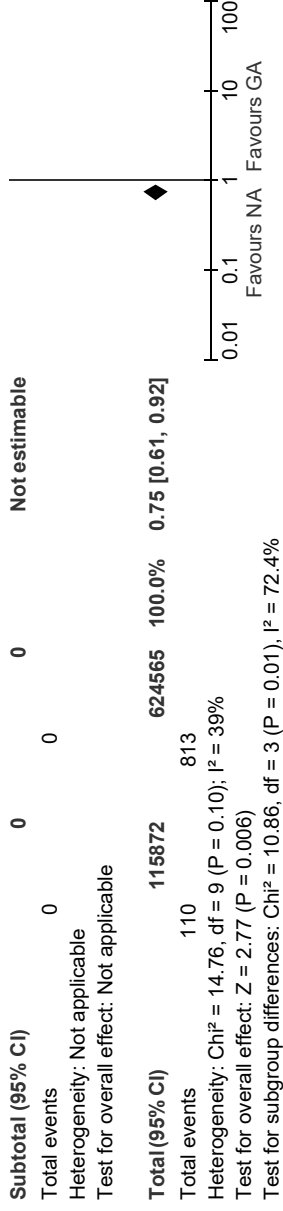


Risk of bias legend

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1.86 Stroke

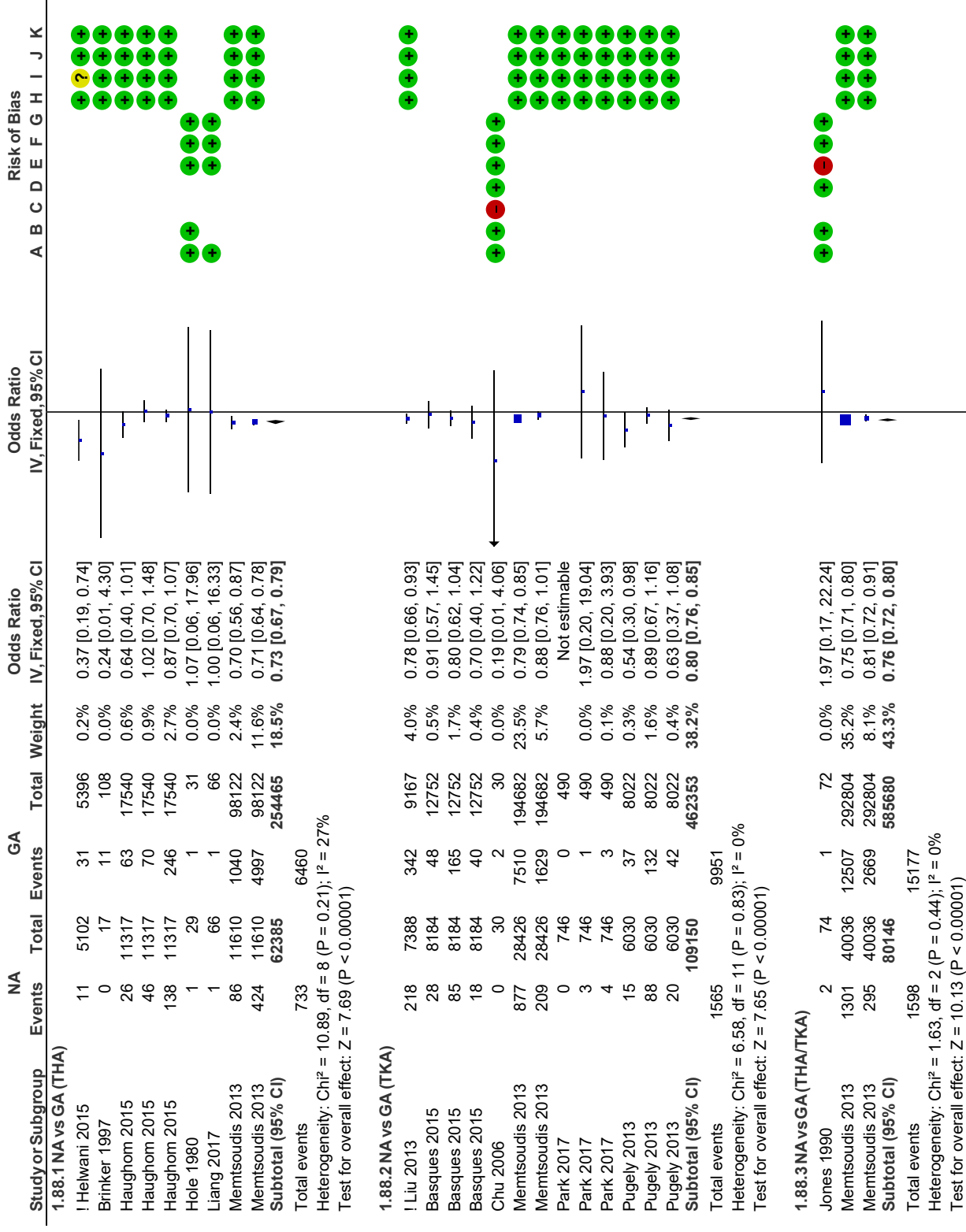


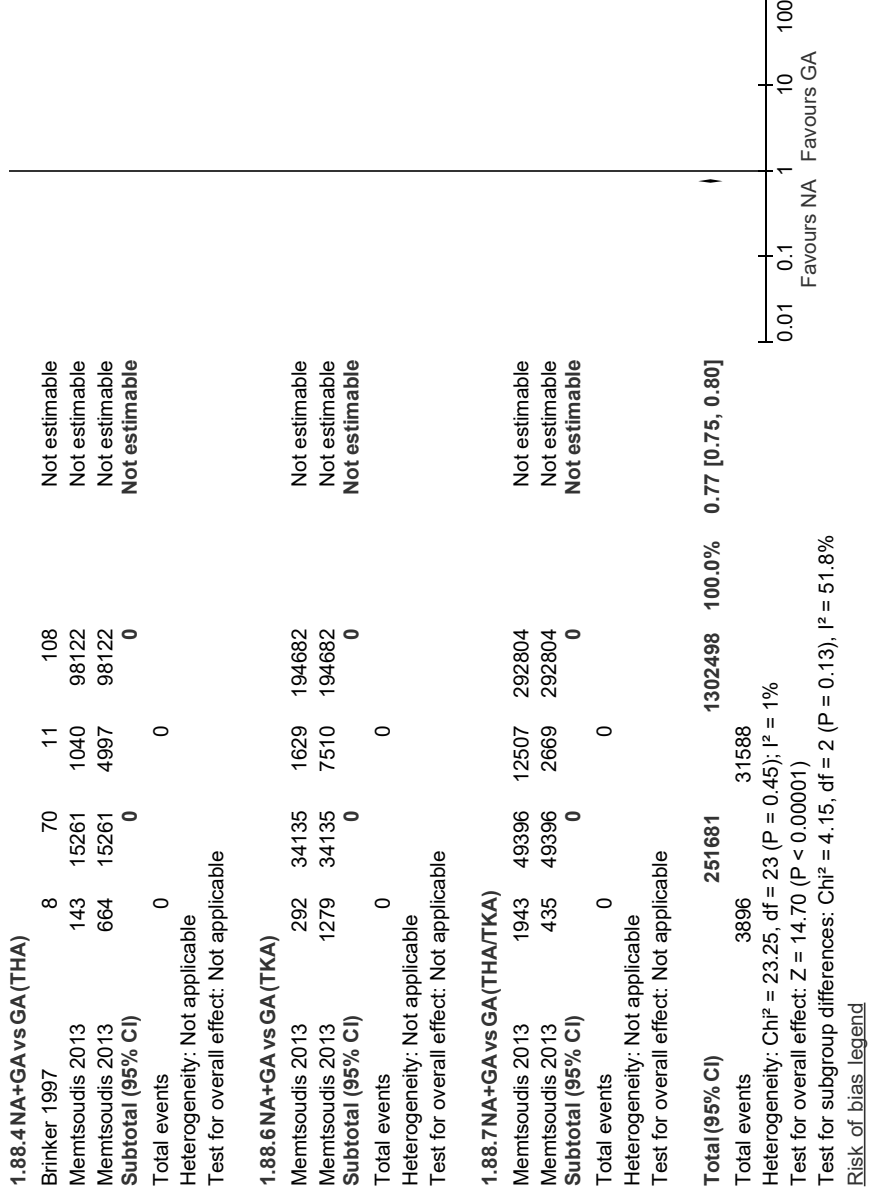


Risk of bias legend

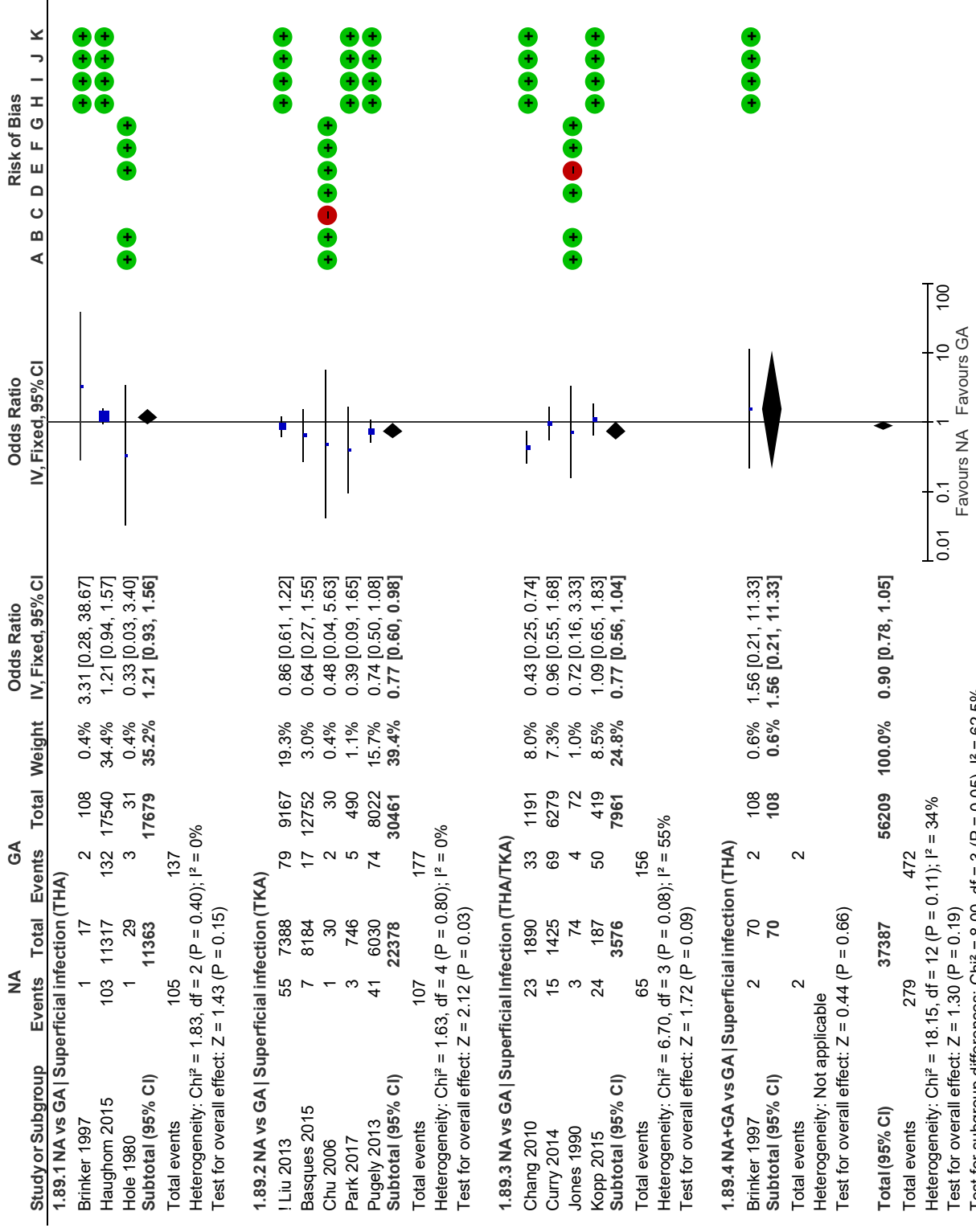
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
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1.88 All infections (including pneumonia and sepsis)





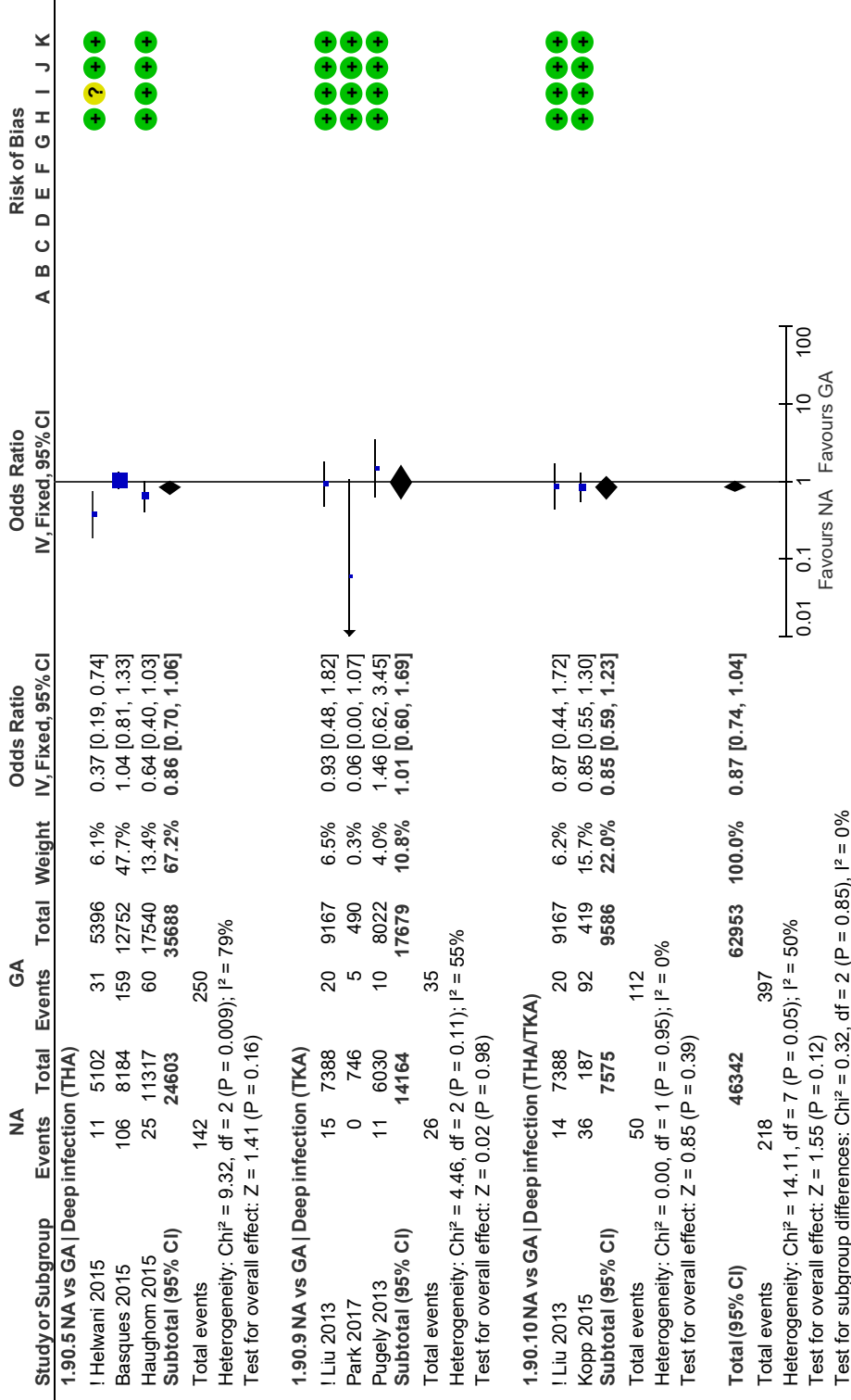
1.89 Wound complications | Superficial infection



Risk of bias legend

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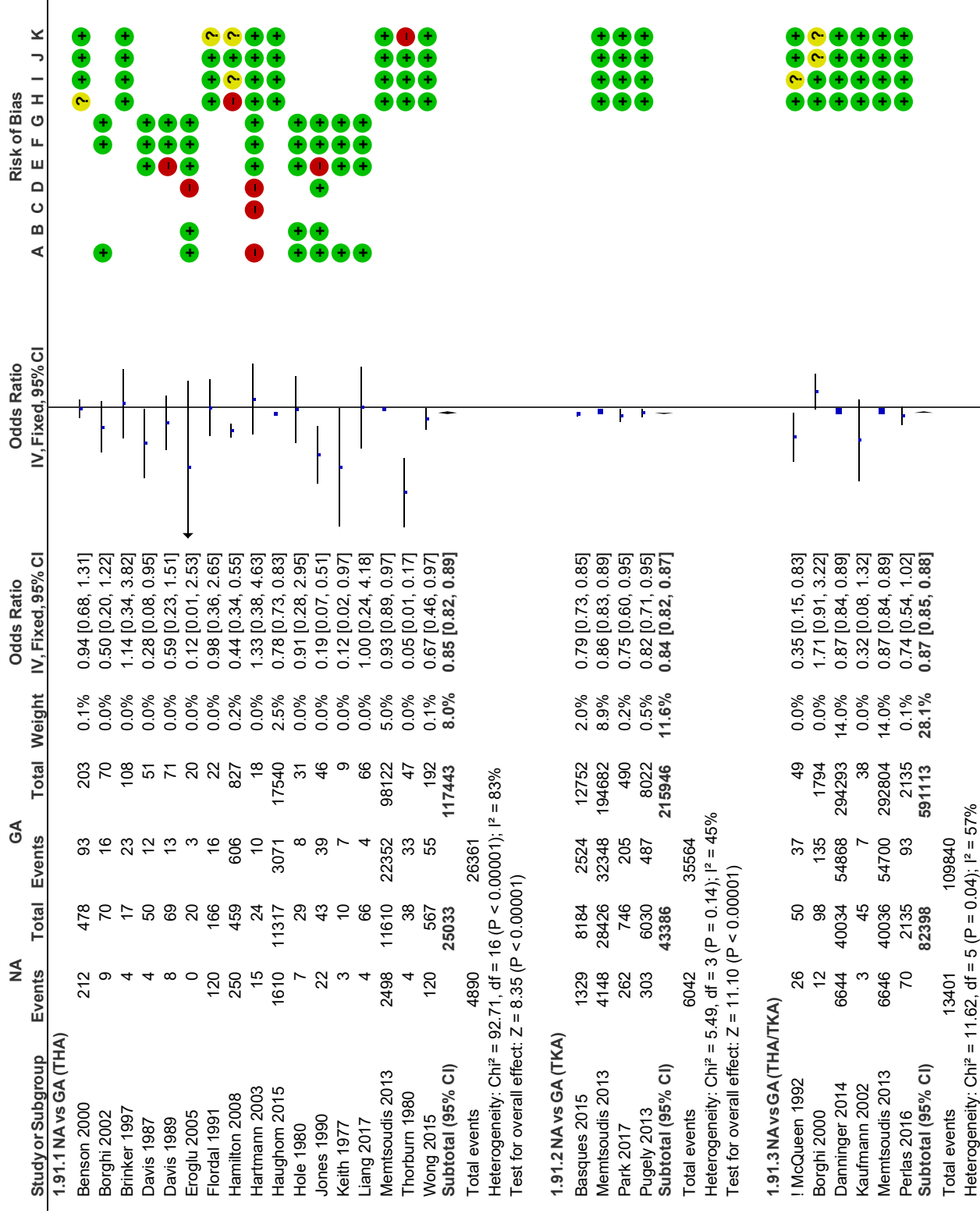
1.90 Wound complications | Deep infection

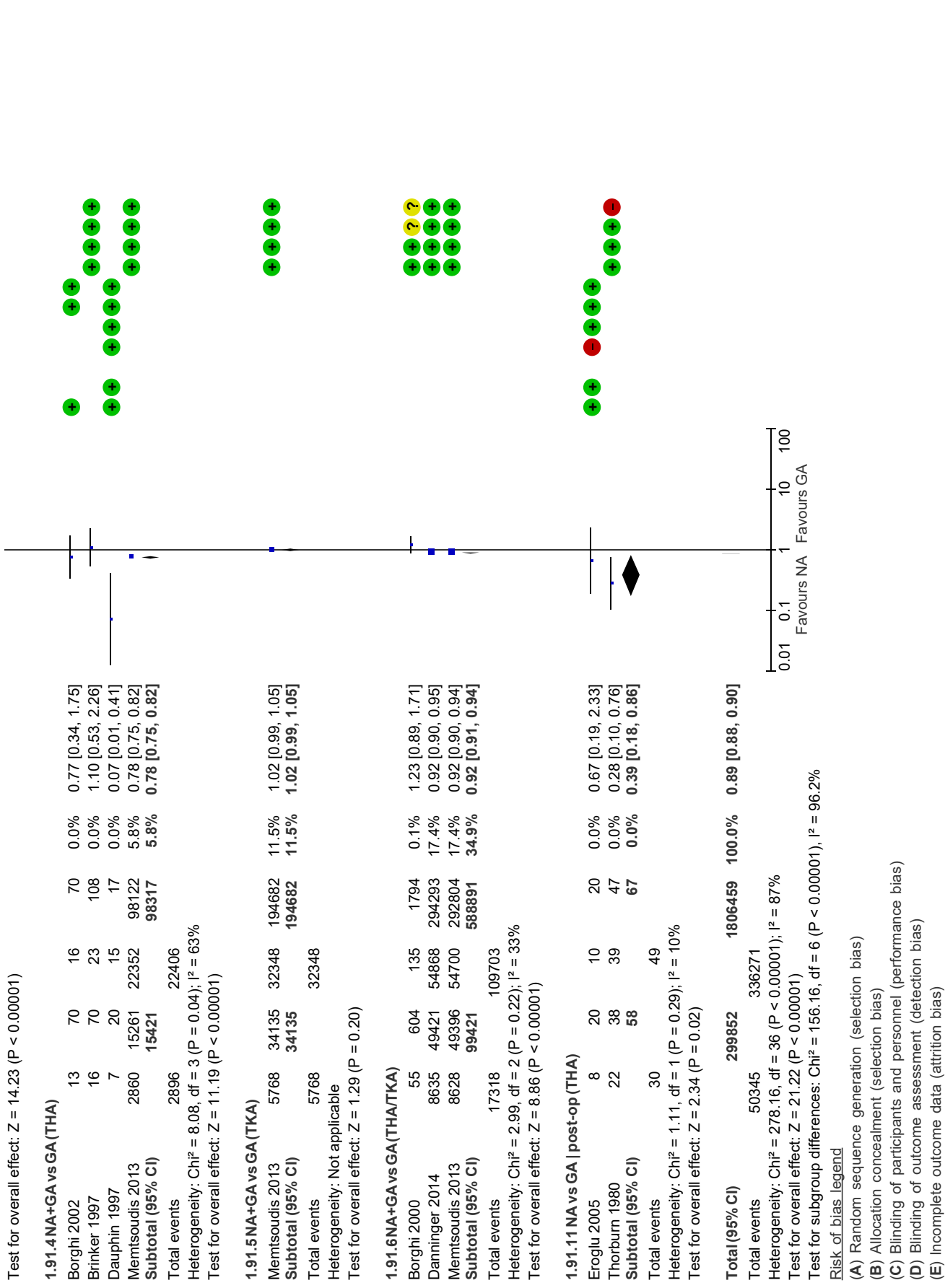


Risk of bias legend

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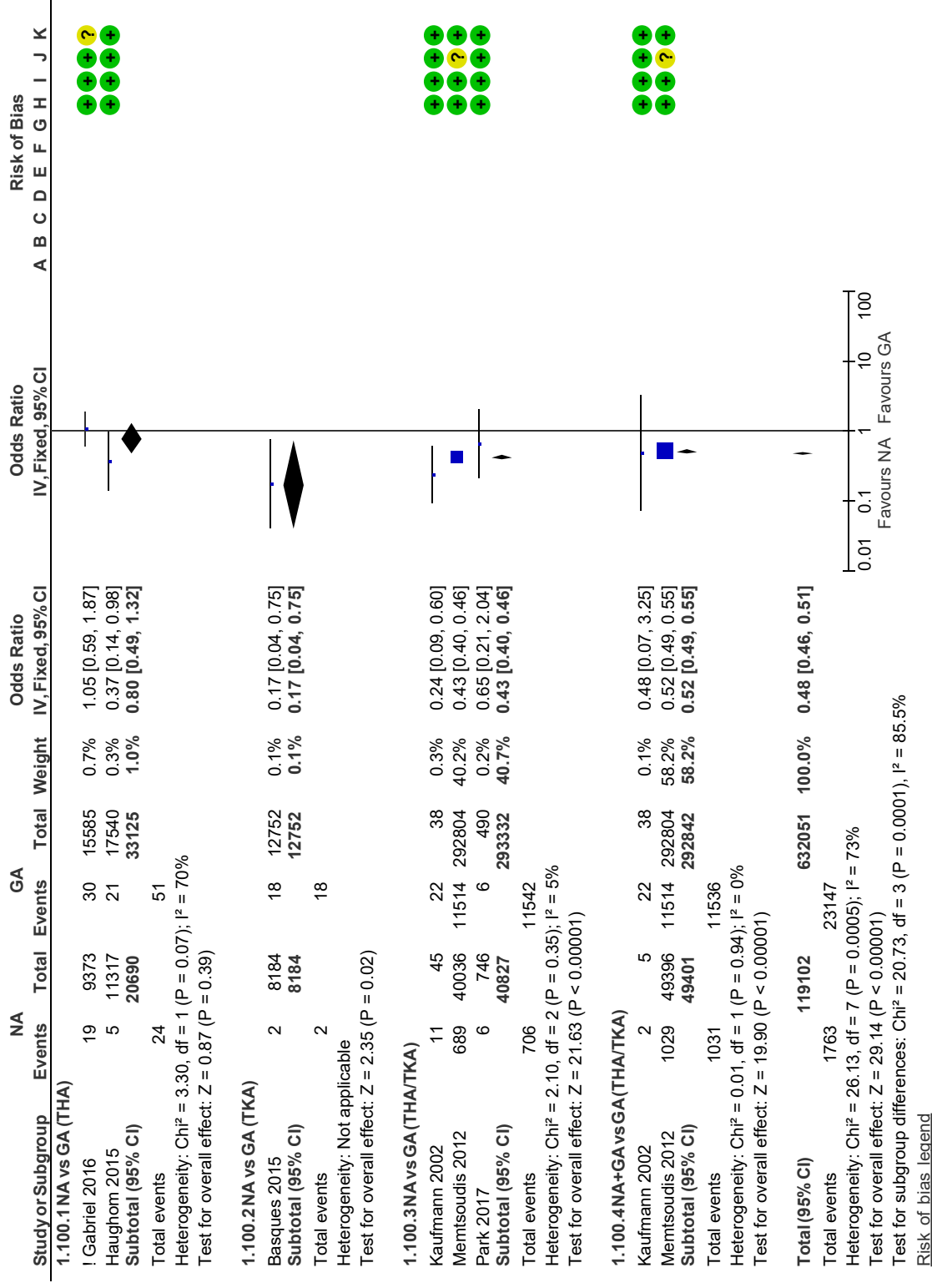
1.91 Blood transfusion





- (F) Selective reporting (reporting bias)
- (G) Other bias
- (H) Observational Study: Incomplete follow-up
- (I) Observational Study: Failure to develop and apply appropriate eligibility criteria
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1.100 Critical care admission

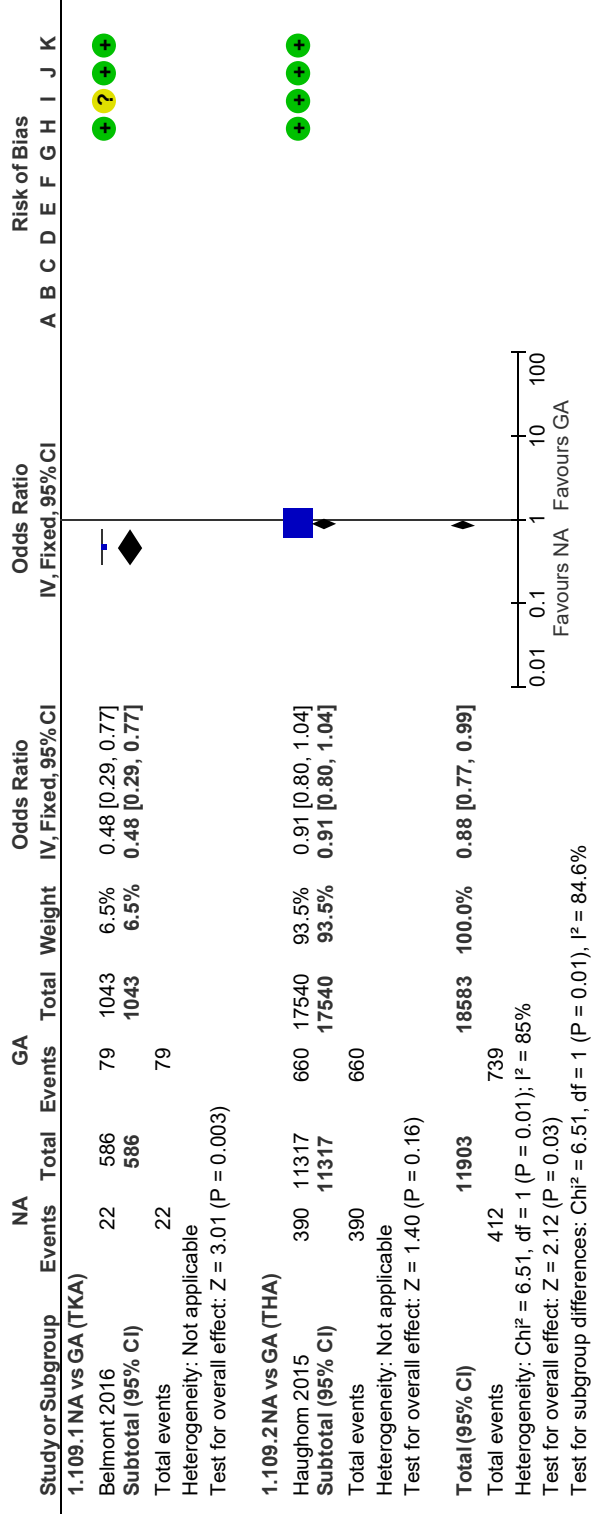


Risk of bias legend

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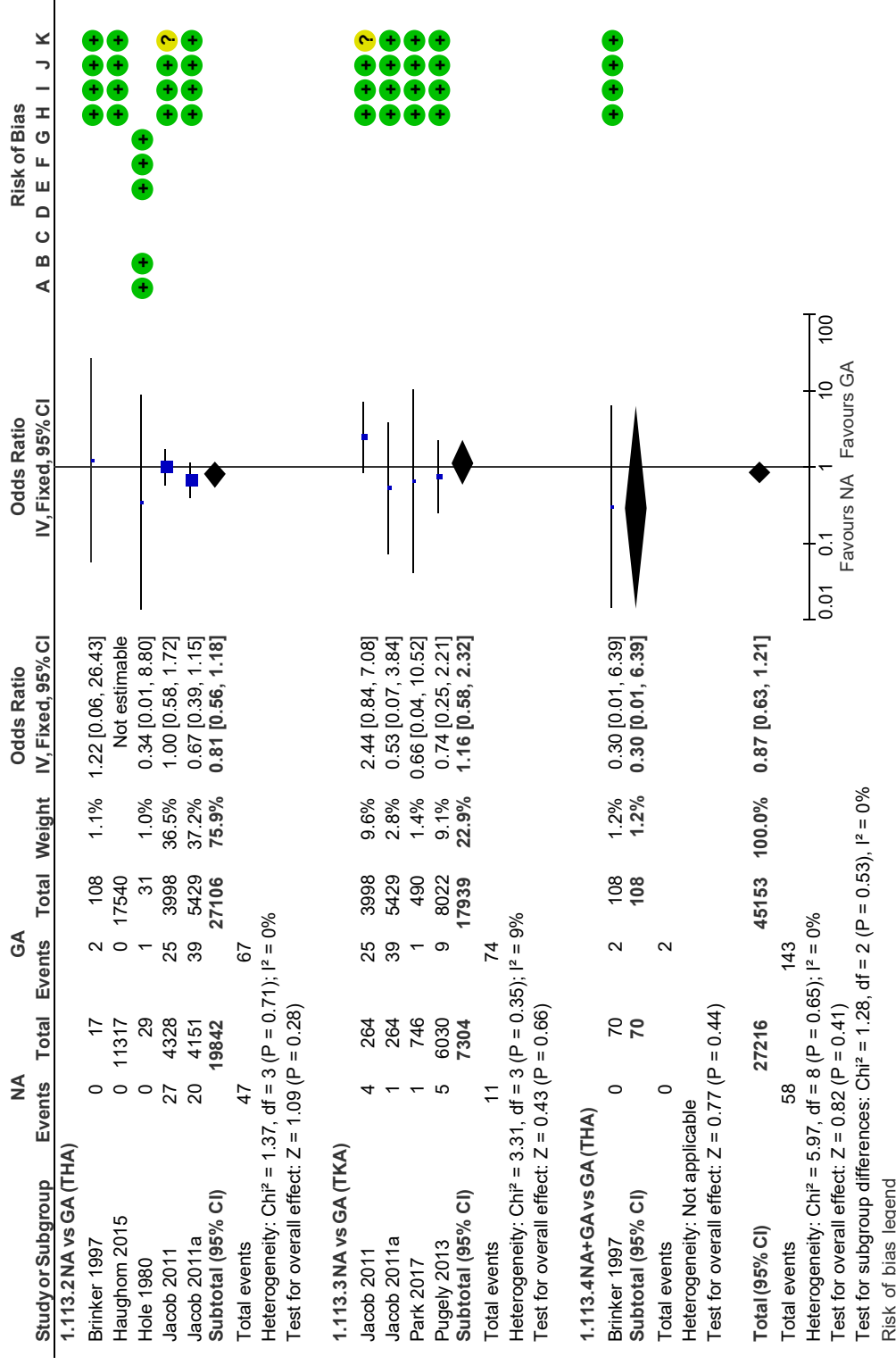
1.109 Readmission



Risk of bias legend

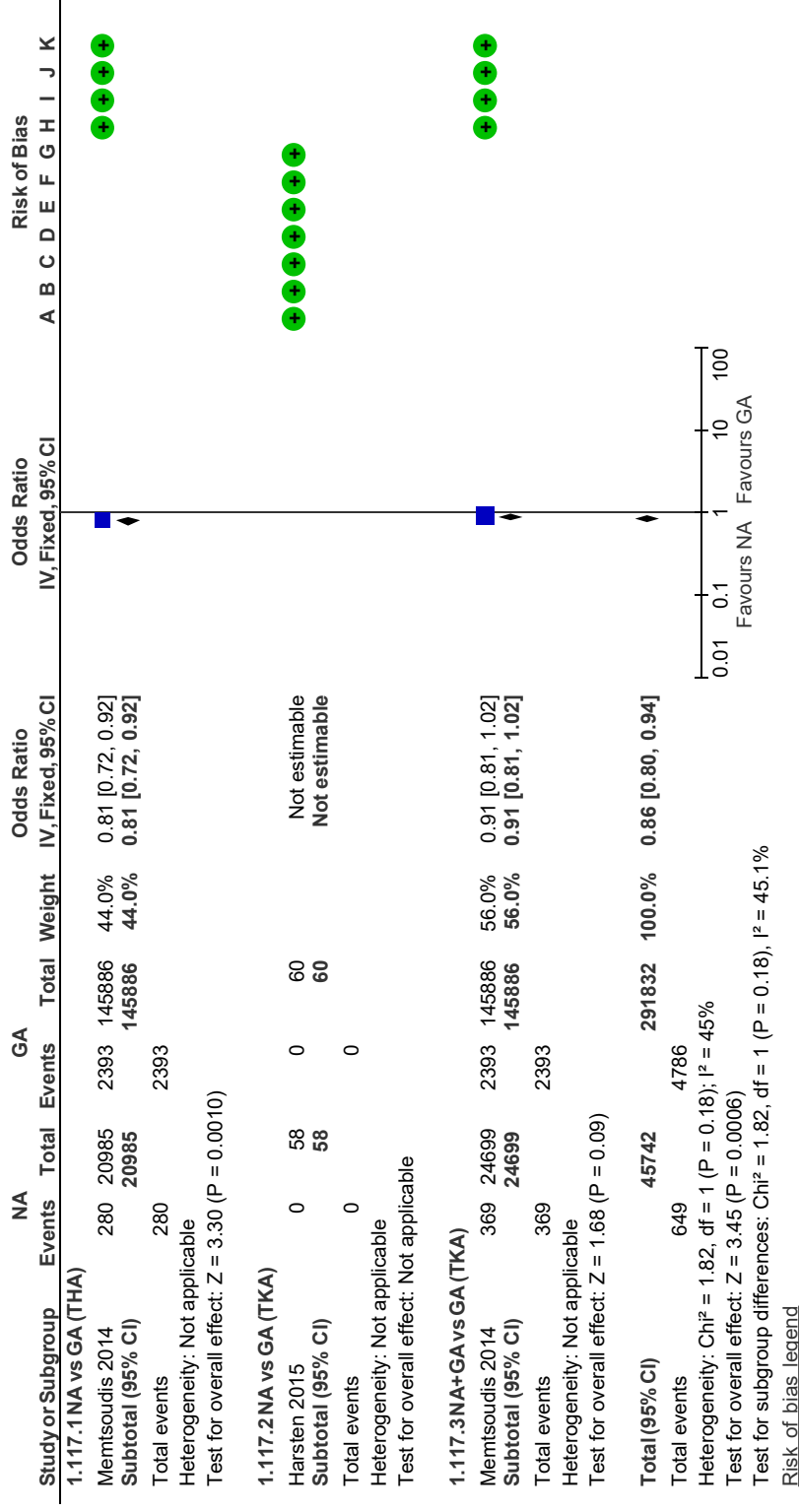
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
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1.113 Perioperative Nerve Injury



- (J) Observational Study: Flawed measurement of exposure or outcome
- (K) Observational Study: Failure to adequately control for confounding

1.117 Falls



- Risk of bias legend
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