SUPPLEMENT

METHODS: Literature screening and data extraction

All returned articles were consolidated in a database (Sourcerer, Covalence Research Ltd, London UK), and duplicate studies were removed.[1] Title and abstract screening (using criteria detailed in Supplementary Table 2) was performed independently by RS and RFP. Full-text versions of all non-excluded articles were retrieved by MM and reviewed independently by RS and RFP using the inclusion criteria in Supplementary Table 2. Data were extracted from all articles included after abstract and full-text review. Extracted data included the number of patients with events and the population at risk, in addition to items required to assess article quality and bias. This was performed independently by RS and RFP and checked by MM and MMS. All extracted endpoint data were reviewed by JL and MMS for clinical utility. The aim was to ensure that all synthesized data relate to clinically equivalent endpoints.

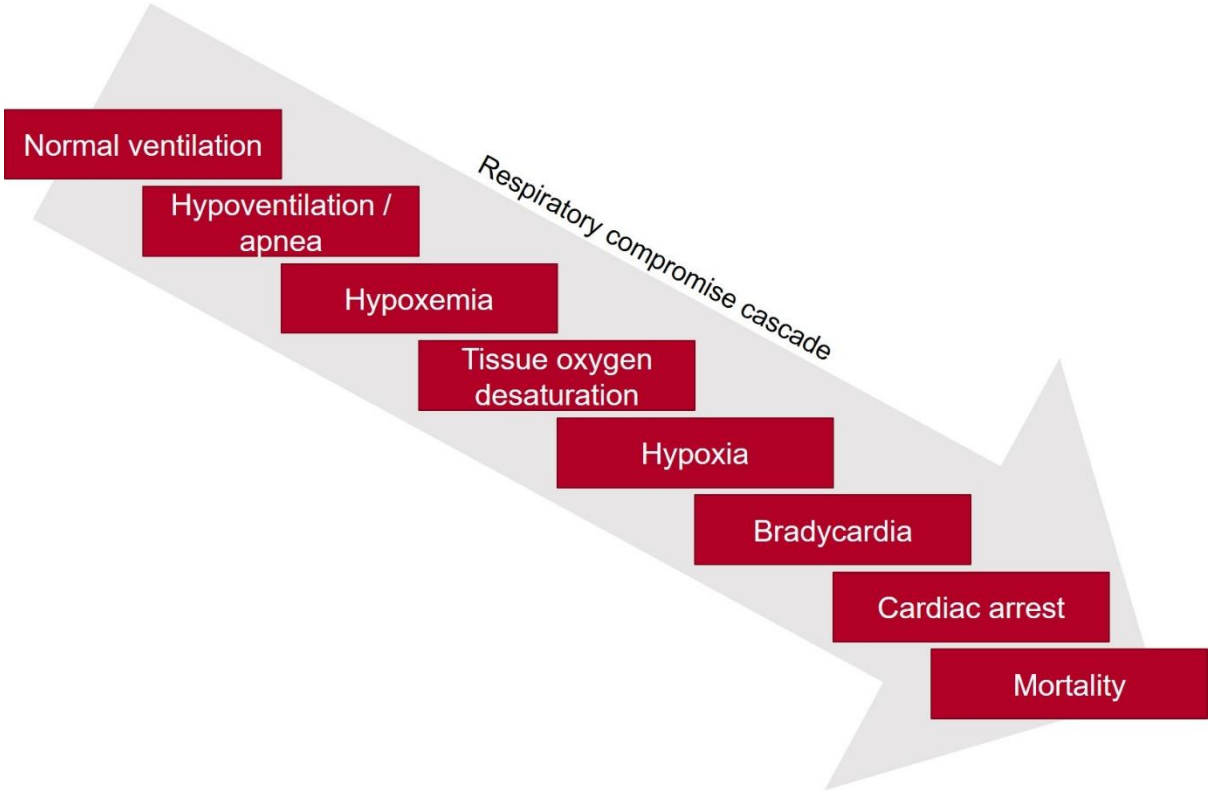
RESULTS: Supplemental oxygen

Although not a target endpoint in the protocol, eight studies reported the requirement for oxygen supplementation. When analyzing all available data, the RR was 0.93 (95% CI 0.75–1.15). Five studies were classified as high-quality and the analysis returned evidence of heterogeneity (I^2 = 36) and a RR of 0.98 (95% CI 0.78–1.23; Supplementary Figure 5).

RESULTS: Hypotension

Eight studies reported the outcome in nine populations. The risk of hypotension was equivalent between capnography and control arms in all studies, and the between study heterogeneity was low (I^2 = 8%). The pooled RR was close to one (1.02, 95% CI 0.78–1.33; Supplementary Figure 6). There was no evidence of capnography monitoring influencing the risk of this sedation-related adverse event.

Supplementary Figure 1 The respiratory compromise cascade



Supplementary Table 1 Literature search strategy for PubMed (used as a basis for searching other literature databases)

Search	Search string	Results returned in PubMed
#1	Capnogra*[tiab] OR ETCO2[tiab] OR (("end-tidal"[tiab] OR monitor*[tiab]) AND ("carbon dioxide"[tiab] or CO2[tiab])) OR sidestream[tiab] OR mainstream[tiab] OR microstream[tiab] OR "Capnography"[Mesh] OR (("Monitoring, Physiologic"[Mesh] OR "Monitoring, Intraoperative"[Mesh] OR "Intraoperative Care"[Mesh]) AND ("carbon dioxide"[tiab] or CO2[tiab]))	22,689
#2	"Conscious Sedation"[Mesh] OR "Deep Sedation"[Mesh] OR "procedural sedation"[tiab] OR "moderate sedation"[tiab] or "conscious sedation"[tiab] or "deep sedation"[tiab] or sedati*[tiab] or anesthes*[tiab]	203,272
#3	"Randomized Controlled Trials as Topic"[Mesh] OR "Randomized Controlled Trial"[Publication Type] OR RCT[tiab] OR ((random*[tiab] OR clinic*[tiab]) AND control*[tiab] AND (trial[tiab] OR study[tiab]))	869,135
#4	#1 AND #2 AND #3	454
#5	#4 AND "1995/01/01"[PDAT] : "2016/12/31"[PDAT]	391

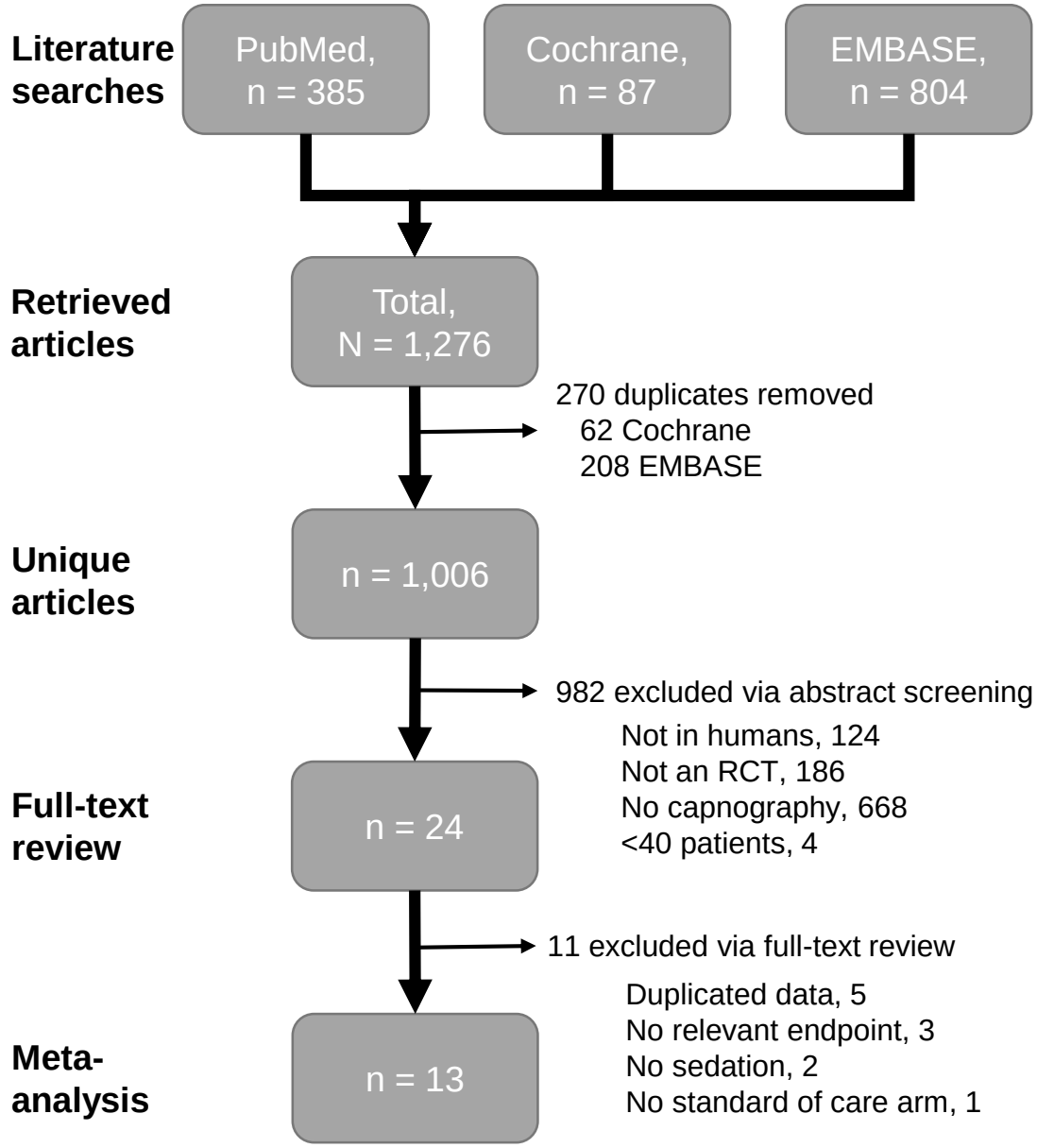
Supplementary Table 2 Study exclusion and inclusion criteria

Exclusion criteria	Inclusion criteria
Research not in humans [120, 124]	Presents data for sedation (procedural, moderate, or deep) during ambulatory surgery
Not a randomized, controlled trial [207, 186]	Reports at least one of the following outcomes (apnea, aspiration, bradycardia, desaturation/hypoxia, hypotension, mortality)
Does not include capnography as the intervention [647, 668]	Uses time capnography (as opposed to volumetric)
Includes fewer than 40 patients in either arm† [6, 4]	Is specific to the hospital setting

Numbers in brackets provide the number of articles assigned that reason for exclusion by each of the two independent reviewers (RS, RFP)

† Small sample size in clinical trials can limit the generalizable nature of results and the exclusion of trials enrolling fewer than 40 patients per arm formed part of the analysis protocol. The value of 40 was calculated using the equation for statistical superiority design from Zhong 2009 and data from Qadeer *et al.* 2009. If, as reported by Qadeer *et al.*, 31% of patients complete without hypoxemia using standard of care and 54% complete without hypoxemia using capnography, then the trial size must be >71 patients. For the purposes of the present study, we rounded this to 80 which can be achieved if at least 40 patients are enrolled per arm.

Supplementary Figure 2 Literature review flow diagram



Full details of exclusion criteria provided by both independent reviewers during abstract screening are presented in Table 2.

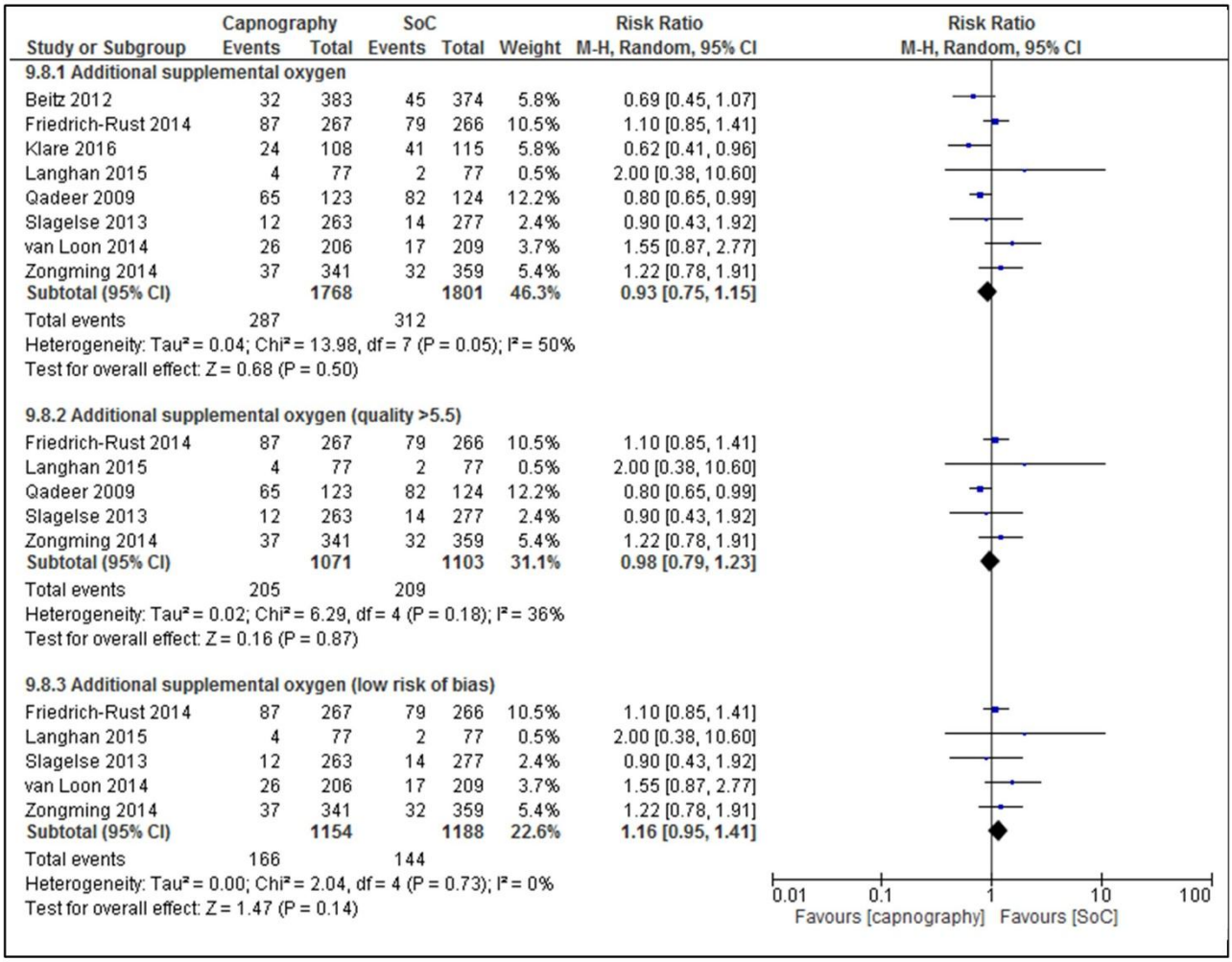
Supplementary Table 3 Endpoint definitions within included studies

Study	Desaturation, mild, SpO_2 %	Desaturation, severe, SpO_2 %	Apnea	Bradycardia, HR beats/minute	Hypotension, SBP mm Hg	Supplemental oxygen
Beitz 2012	<90	≤85		<50	<90	>2 L/min
Deitch 2010	<93 for ≥15 seconds					
Friedrich-Rust 2014	<90 for ≥15 seconds	<85		<50	<100	>2 L/min
Langhan 2015	<95					
Lightdale 2006	<95					
Qadeer 2009	<90 for ≥15 seconds	≤85	No capnogram for ≥15 seconds		Not defined	Any use
Slagelse 2013	<92					Any increase
van Loon 2014	<91	<81				Any increase
Zongming 2014	<90	≤85		<50	<90	>3 L/min
Campbell 2016	<90				<100	
Klare 2016	<90	<85	Not defined for SoC, no capnogram for ≥15 seconds	<50	<90	Any increase
Mehta 2016 colon	<90 for ≥10 seconds	<85	No capnogram for ≥5 seconds	≤60	<90	Any use
Mehta 2016 EGD	<90	<85	No capnogram for ≥5 seconds	≤60	<90	Any use

Study	Desaturation, mild, SpO_2 %	Desaturation, severe, SpO_2 %	Apnea	Bradycardia, HR beats/minute	Hypotension, SBP mm Hg	Supplemental oxygen
Riphaus 2016	<90		No capnogram for ≥15 seconds	<50	<90	>2L/min

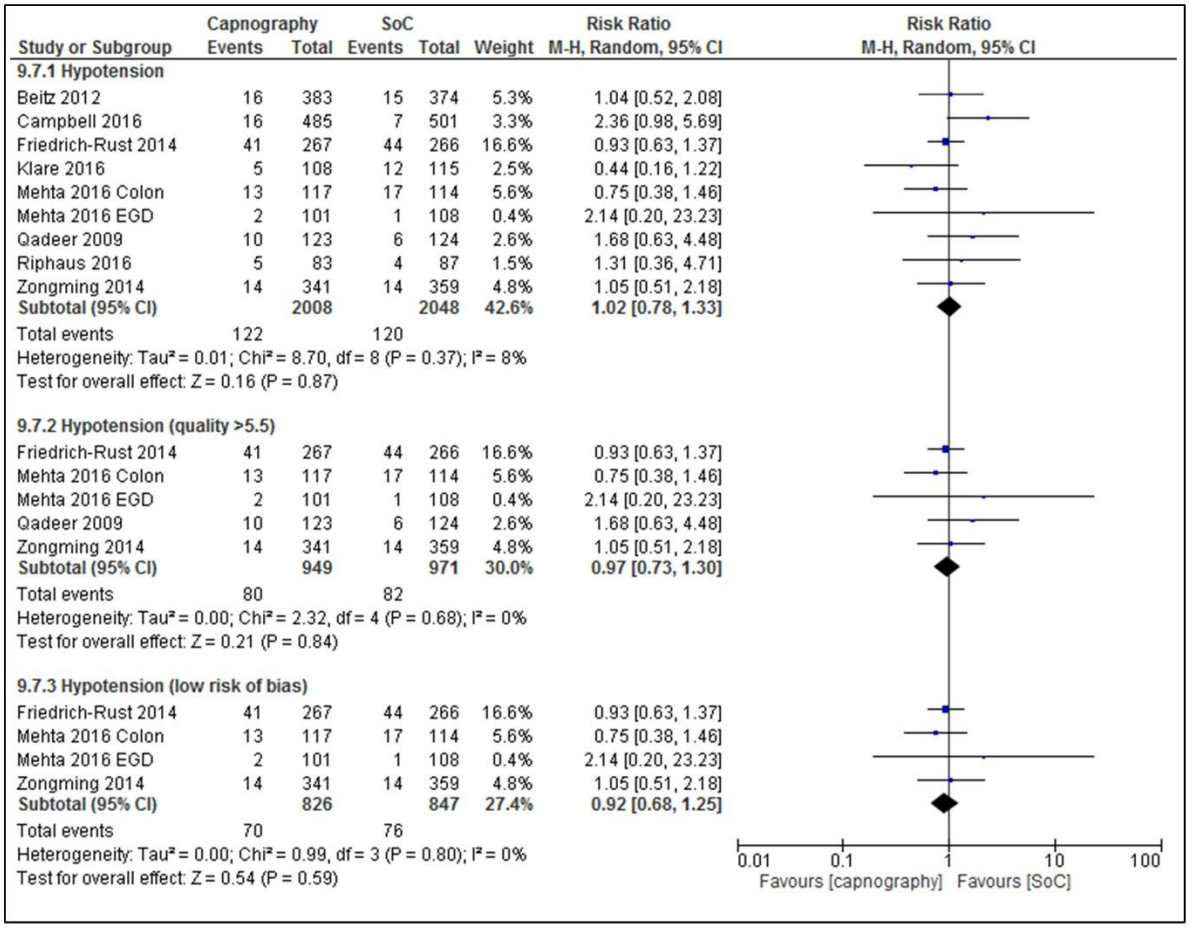
HR, Heart rate; SBP, Systolic blood pressure; SpO_2, Oxygen saturation

Supplementary Figure 3 Results for the need for supplemental oxygen



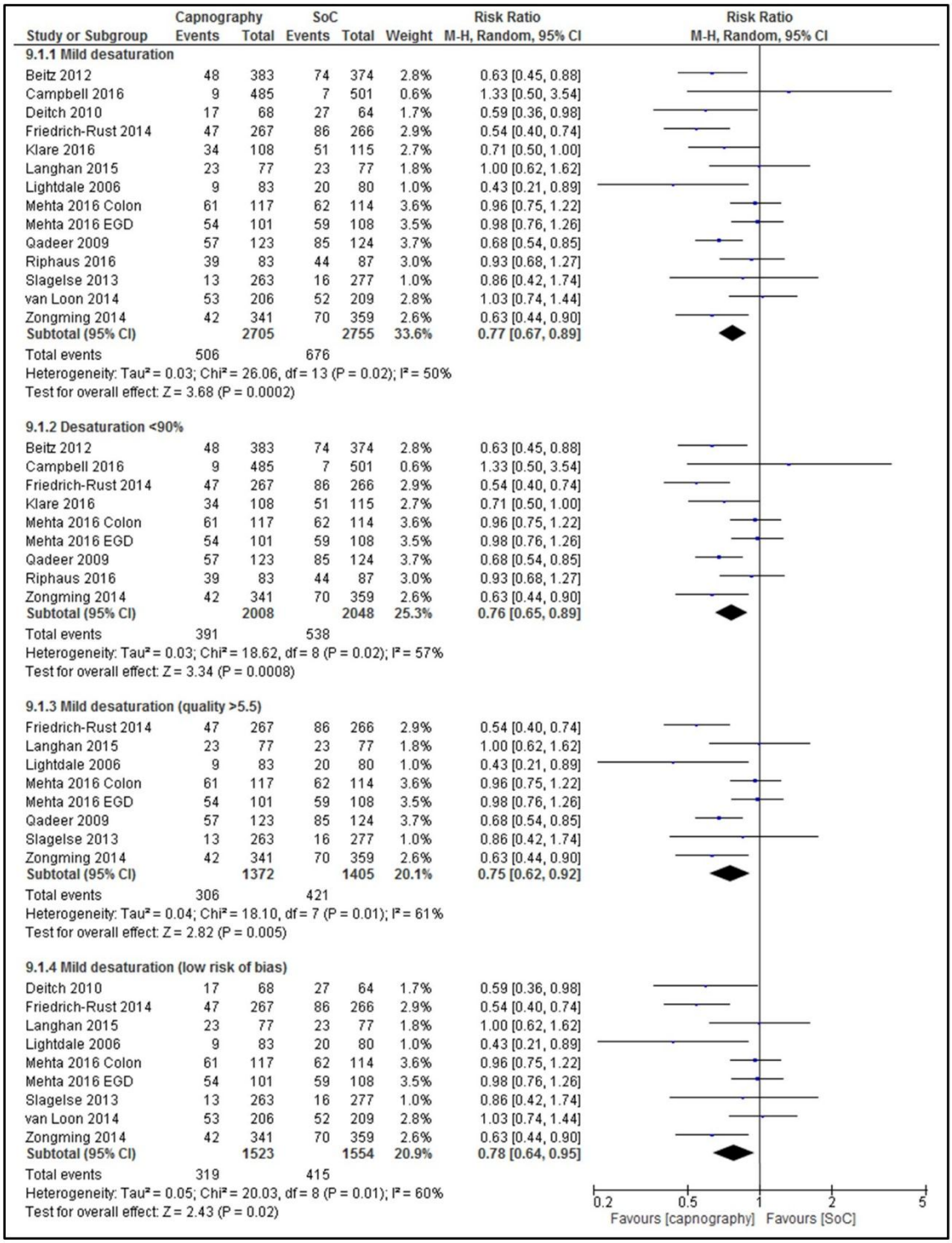
The risk ratios for the supplemental oxygen endpoint are presented for all studies, high-quality studies (quality >5.5), and studies with low risk of bias. CI, Confidence interval; M-H, Mantel-Haenszel

Supplementary Figure 4 Capnography monitoring resulted in no change in the risk of hypotension relative to standard of care



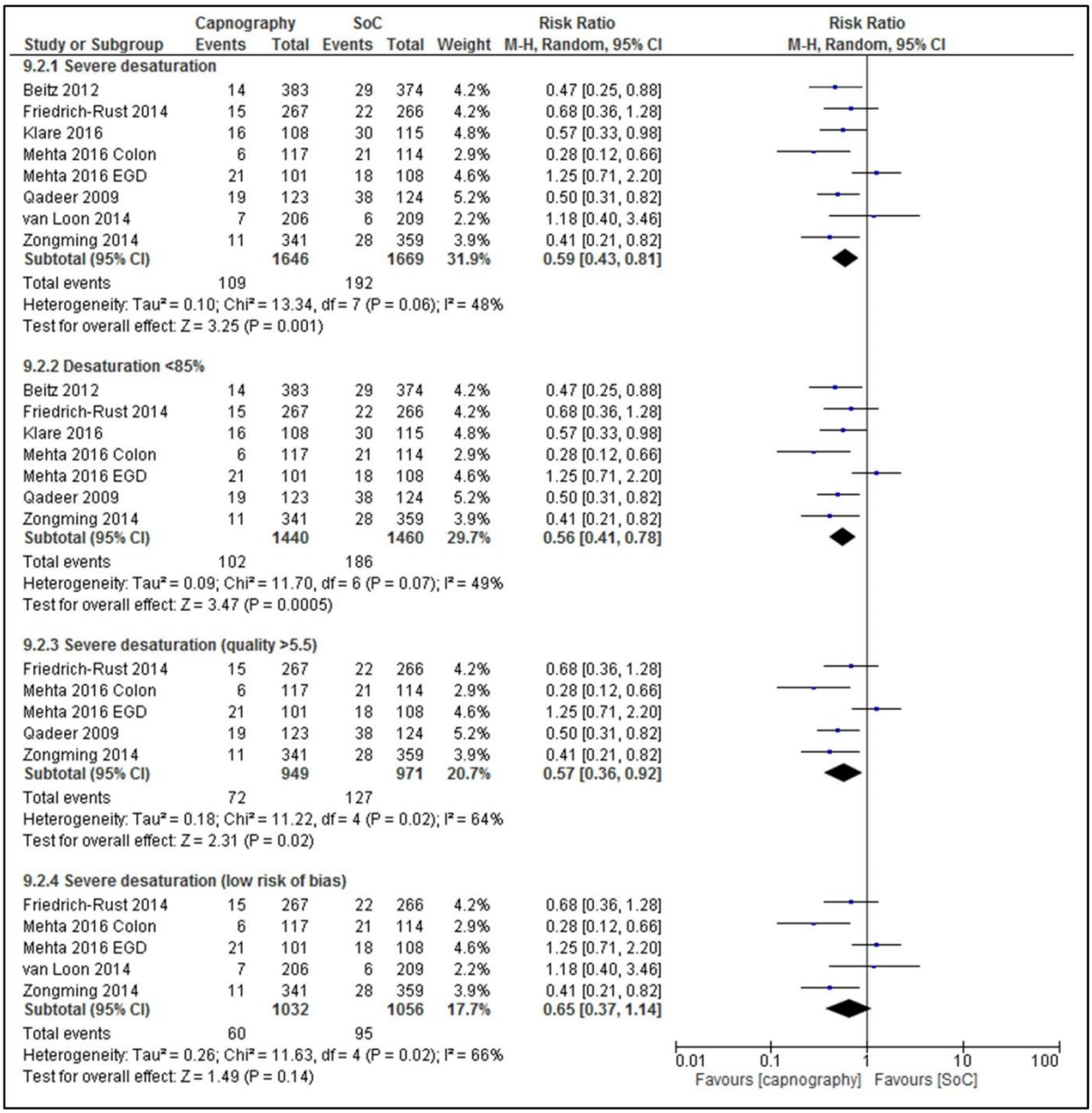
The risk ratios for hypotension are presented for all studies, high-quality studies (quality >5.5), and studies with low risk of bias. CI, Confidence interval; M-H, Mantel-Haenszel

Supplementary Figure 5 Mild desaturation is reduced with capnography monitoring



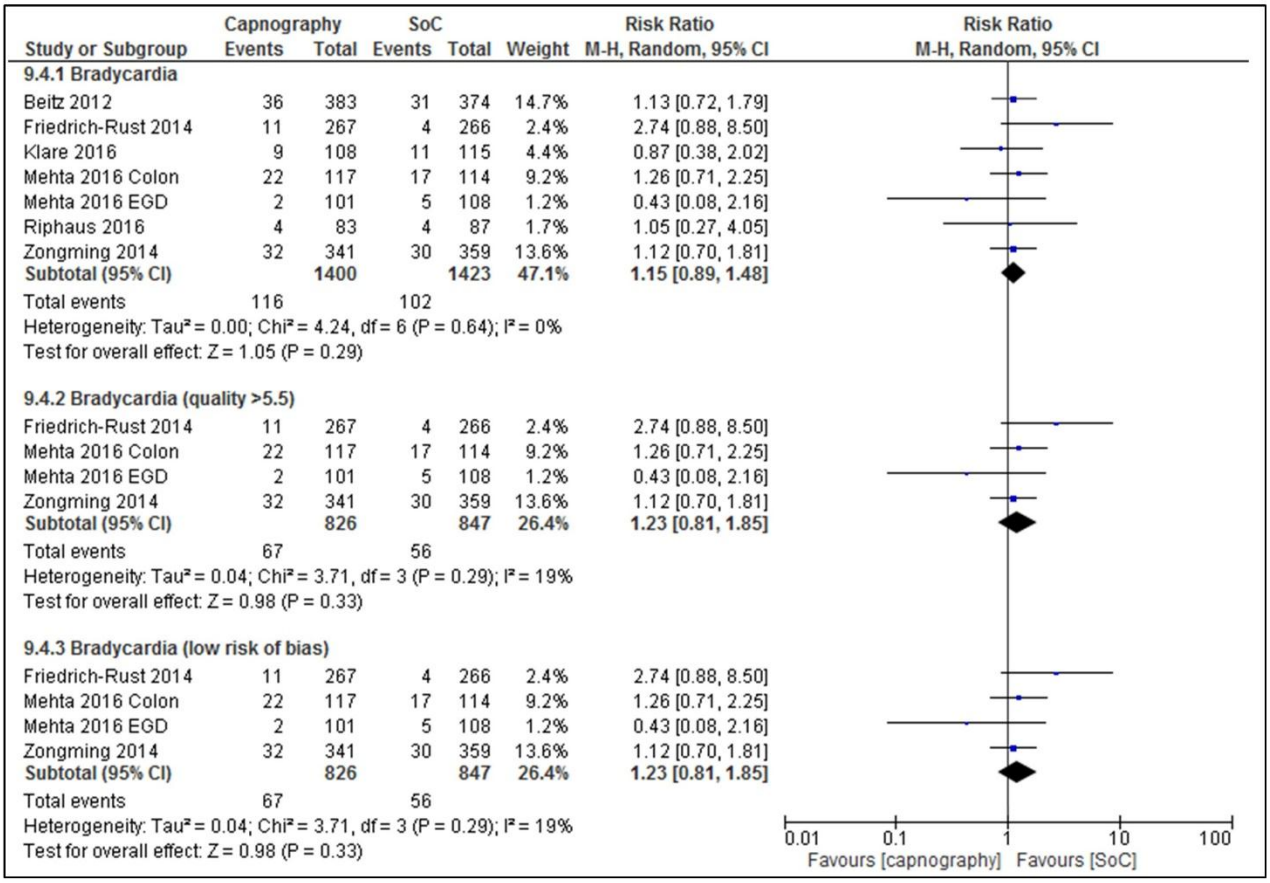
The risk ratios for the mild desaturation endpoint are presented for all studies, studies with an endpoint of <90%, high-quality studies (quality >5.5), and studies with low risk of bias. CI, Confidence interval; M-H, Mantel-Haenszel

Supplementary Figure 6 Severe desaturation is reduced with capnography monitoring



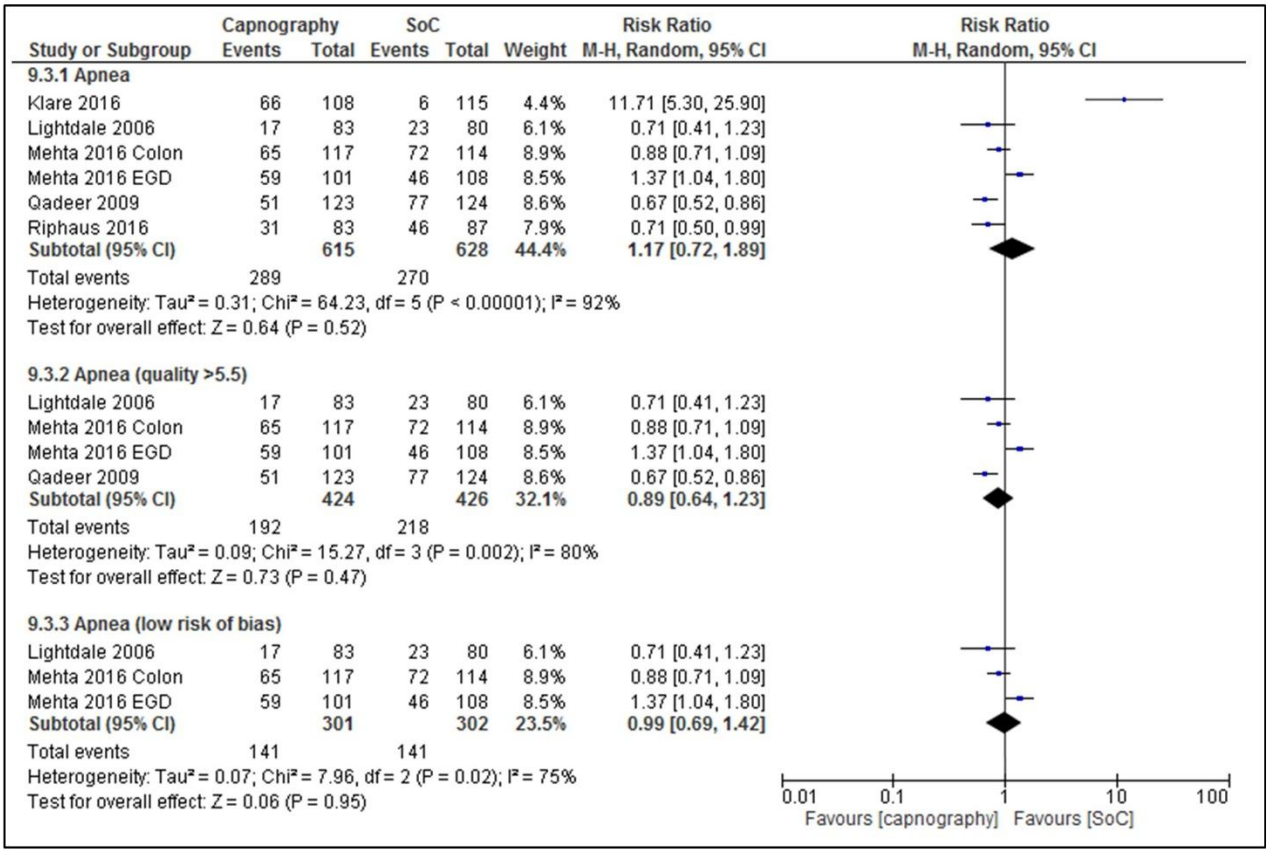
The risk ratios for the severe desaturation endpoint are presented for all studies, studies with an endpoint of <85%, high-quality studies (quality >5.5), and studies with low risk of bias. CI, Confidence interval; M-H, Mantel-Haenszel

Supplementary Figure 7 Capnography monitoring resulted in no change in the risk of bradycardia relative to standard of care



The risk ratios for bradycardia are presented for all studies, high-quality studies (quality >5.5), and studies with low risk of bias. CI, Confidence interval; M-H, Mantel-Haenszel

Supplementary Figure 8 Capnography monitoring resulted in no change in the risk of apnea relative to standard of care



The risk ratios for apnea are presented for all studies, high-quality studies (quality >5.5), and studies with low risk of bias. CI, Confidence interval; M-H, Mantel-Haenszel

SUPPLEMENT REFERENCES

[1] Sourcerer. Covalence Research Ltd, London, UK. Available at https://sourcerer.pro/