SUPPLEMENTARY INFORMATION

A Meta-Analysis of 80% Fraction of Inspired Oxygen on Surgical Site Infection in Patients Undergoing Surgery

Rifaldy Nabiel Erisadana[*]*, Achmad Ilham Tohari*, Yehuda Tri Nugroho Supranoto*, Wiwien Sugih Utami**, Laksmi Indreswari**

[*]Faculty of Medicine University of Jember, Jember, Indonesia
[**]Department of Parasitology, Faculty of Medicine University of Jember, Jember, Indonesia
***Department of General Surgery, Soebandi General Hospital, Faculty of Medicine University of Jember, Jember, Indonesia

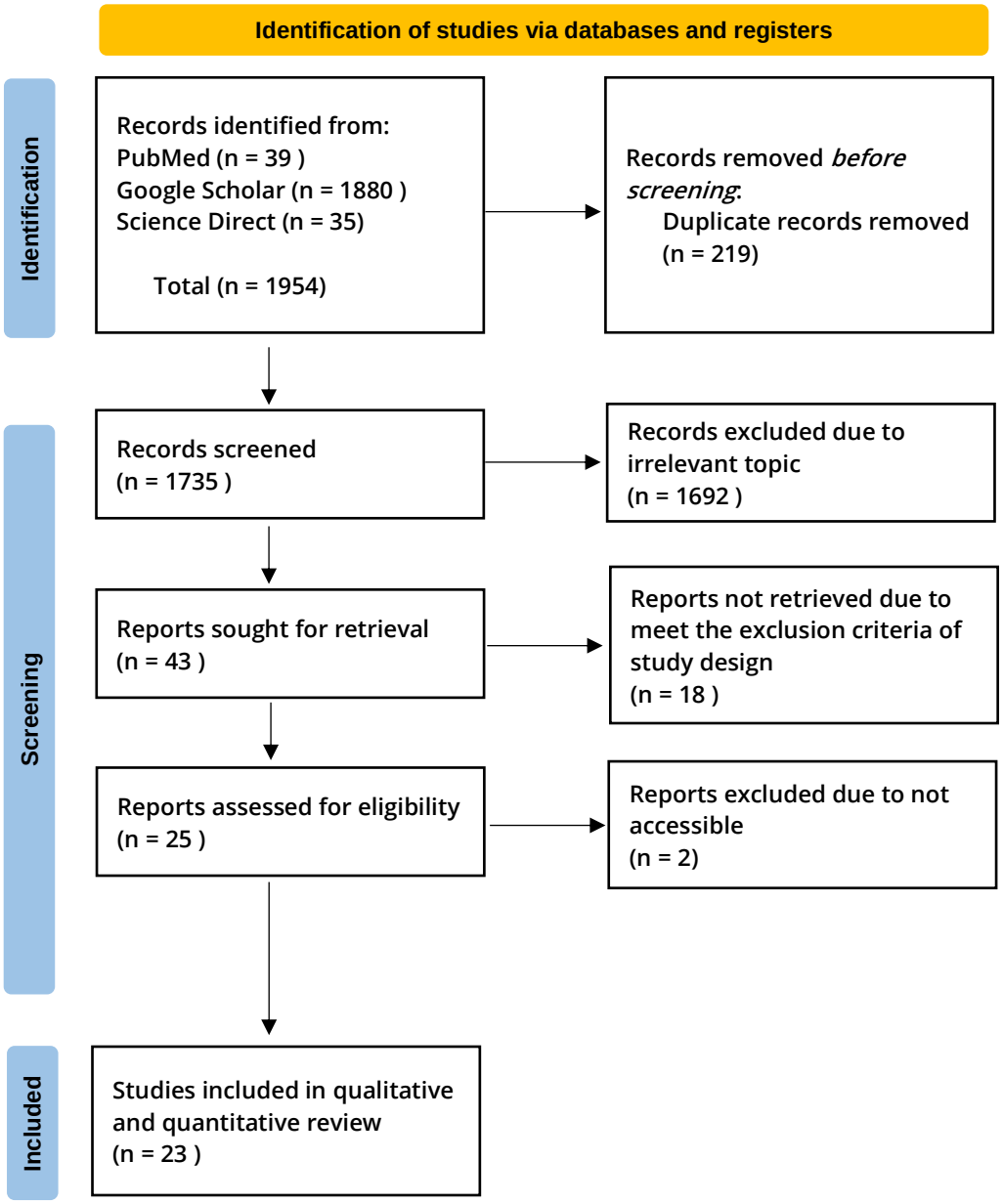
✉Correspondence: rifaldydana@gmail.com

ABSTRACT

Introduction: WHO recommended the use of 80% FiO2 in patients undergoing general anesthesia with endotracheal intubation (ETI) to prevent surgical site infection (SSI). However, the ongoing debate regarding efficacy and safety raises because further trials have been published. We conducted a review based on recommendations in terms of SSI as the primary outcome and adverse events as the secondary outcome in both patients with or without ETI.
Methods: A literature search was carried out by PubMed, ScienceDirect, and Google Scholar for RCTs in all-type surgical patients who administrated 80% FiO2 compared with 30–35% FiO2. Pooled relative risks with a 95% confidence interval were conducted for meta-analysis
Results: Based on 23 RCTs included in the analysis, there were no significant differences in terms of SSI (RR,0.85; 95%CI, 0.72 to 1.01; p=0.07), sepsis (RR,1.47; 95%CI, 0.78 to 2.76; p=0.23), postoperative hospitalization days (PHD) (RR,0.16; 95%CI, -0.67 to 0.98; p=0.71), ICU admission (RR,0.94; 95%CI, 0.78 to 1.13; p=0.50), reoperation required (RR,0.78; 95%CI, 0.30 to 2.06; p=0.62), and 30-days mortality (RR,1.18; 95%CI, 0.76 to 1.84; p=0.45). In contrast, even though the subgroup analysis showed association that PHD longer in high FiO2 group for colorectal surgery (RR,0.80; 95%CI, 0.24 to 1.35; p=0.005), the high FiO2 significantly reduced SSI and anastomotic leakage in abdominal surgery (RR,0.78; 95%CI, 0.62 to 0.99; p=0.04 and RR,0.55; 95%CI, 0.36 to 0.85; p=0.008).
Conclusion: This meta-analysis provides evidence that administration of 80% FiO2 even though association with longer of PHD in colorectal surgery, it is associated with a reduction in SSI and anastomotic leakage in patients who underwent abdominal surgery. It contrasts for sepsis, ICU admission, reoperation required, 30-day mortality, SSI, and PHD in all-type surgery.
Keywords: adverse events; meta-analysis; oxygen; SSI; surgery

SUPPLEMENTARY INFORMATION

PRISMA Flow Diagram



SUPPLEMENTARY INFORMATION

Characteristic of Included Studies Part I

Study	Sample Size	Type of surgery	Age		Duration of surgery		Intervention		Patients outcomes
			High FiO_2	Low FiO_2	High FiO_2	Low FiO_2	High FiO_2	Low FiO_2	
Greif et al, (2000) Austria	500	Elective open colorectal resection	57±15	57±15	3.1±1.4 (h)	3.1±1.4 (h)	80% O_2 with 20% N_2O	30% O_2 with 70% N_2O	SSI, POHD, ICU admission
Pryor et al, (2004) USA	160	Major abdominal surgery	54±16	57±15	233±83 (min)	208±91 (min)	80% O_2	35% O_2	SSI, POHD, ICU admission
Belda et al, (2005) Spain	291	Elective colorectal resection	64.2±11.8	62.3±12.5	161±62 (min)	159±61 (min)	80% O_2	30% O_2	SSI, POHD, ICU admission
Mayzler et al, (2005) Israel	38	Elective colorectal surgery	67±10	69±9	140±40 (min)	135±40 (min)	80% O_2 with 20% N_2O	30% O_2 with 70% N_2O	SSI, anastomotic leakage
Myles et al, (2007) Multicenter	2012	Mixed surgeries	55.8±17	54.6±16	3.3±2.0 (h)	3.3±2.0 (h)	80% O_2 with 20% N_2O	30% O_2 with 70% N_2O	SS, ICU admission, 30-days mortality
Gardella et al, (2008) USA	143	Caesarean section	31 (19–46)	28 (16–47)	48 (26–87) (min)	52 (20–141) (min)	80% O_2	30% O_2	SSI
Meyhoff et al, (2009) Denmark	1386	Acute or elective laparotomy	64 (27–85)	64 (34–84)	128 (38–310) (min)	132 (35–295) (min) \	80% O_2	30% O_2	SSI, ICU admission, anastomotic leakage, POHD, re 30-days mortality
	633	Colorectal surgery	NR	NR	NR	NR	80% O_2	30% O_2	SSI
Bickel et al, (2011) Israel	210	Open appendectomy	28.5±12.3	27.6±10.8	33.04±10.6 (min)	32.75±10.3 (min)	80% O_2 with 20% air	30% O_2 with 70% N_2O	SSI, POHD
Scifres et al, (2011) USA	585	Caesarean section	27.5±6.4	27.8±5.9	57.4±20.5 (min)	60.6±26.1 (min)	80% O_2	25-35% O_2	SSI
Thibon et al, (2012) France	434	Abdominal, gynecologic, breast (Mixed surgeries)	52.1±13.7	51.8±13.3	89±61 (min)	84±58 (min)	80% O_2	30% O_2	SSI
Chen et al, (2013) Hong Kong	60	Open colorectal surgery	62±12	60±15	A/199±76 (min)	A/184±85 (min)	80% O_2	30% O_2	SSI, POHD
Duggal et al, (2013) USA	831	Caesarean section	29.2±5.6	29.5±5.8	NR	NR	80% O_2	30% O_2	SSI and/or endometritis
Schietroma et al, (2013) Italy	171	gastrectomy and subsequent esophagojejunal anastomosis	68.4 (51–84)	67.8 (48–82)	175 (100–250) (min)	180 (118–270) (min)	80% O_2	30% O_2	SSI, anastomotic leakage, reoperation required
Stall et al (2013) USA	235	Open reduction and internal fixation	42.3±12.1	42.5±12.2	233±88 (min)	228±88 (min)	80% O_2	30% O_2	SSI
William et al, (2013) USA	160	Caesarean section	24.6024	24.8961	51.2048 (min)	52.2467 (min)	80% O_2	30% O_2	SSI
Kurz et al, (2015) Multicenter	586	Colorectal resection	54±16	51±17	3.5±1.5 (h)	3.5±1.8 (h)	80% O_2	30% O_2	SSI, POHD, 30-days mortality

Wasnik et al, (2015) India	64	Open Appendectomy	27.15± 10.46	28.56± 12.22	61.87± 10.6 (min)	61.4±12.5 (min)	80% O_2	30% O_2	SSI, POHD
Fariba et al, (2016) Iran	122	Caesarean section	29.70± 5.4	29.26± 4.6	57.5±14.2 (min)	60±10.4 (min)	80% O_2	30% O_2	SSI
Schietroma et al, (2016a) Italy	239	Open perforated peptic ulcer surgery	58.3 (35–80)	57.8 (30–82)	63.2 (38–104) min	58.7 (33–102) min	80% O_2	30% O_2	SSI
Schietroma et al, (2016b) Italy	85	Open colorectal resection	71.4 (55–92)	68.6 (49–86)	200 (95–410) min	195 (100–385) min	80% O_2	30% O_2	SSI, anastomotic leakage, reoperation required
Mayank et al, (2019) India	94	Elective colorectal surgery	57.02± 12.94	53.36± 14.45	233.51 ±87.65 (min)	207.66 ±103.53(min)	80% O_2 with 20% N_2O	33% O_2 with 66% N_2O	SSI, POHD, anastomotic leakage
Ferrando et al, (2020) Multicenter	740	Abdominal sutgery	64.2±12.8	63.9±13.9	214.2± 93.3 (min)	209.2± 89.7 (min)	80% O_2	30% O_2	SSI, POHD, 30-days mortality
Xue-Fei Li et al, (2020) China	251	Abdominal surgery	54±14	53±13	190 (154–245) min	200 (146–258) min	80% O_2	30% O_2	SSI, sepsis, ICU admission

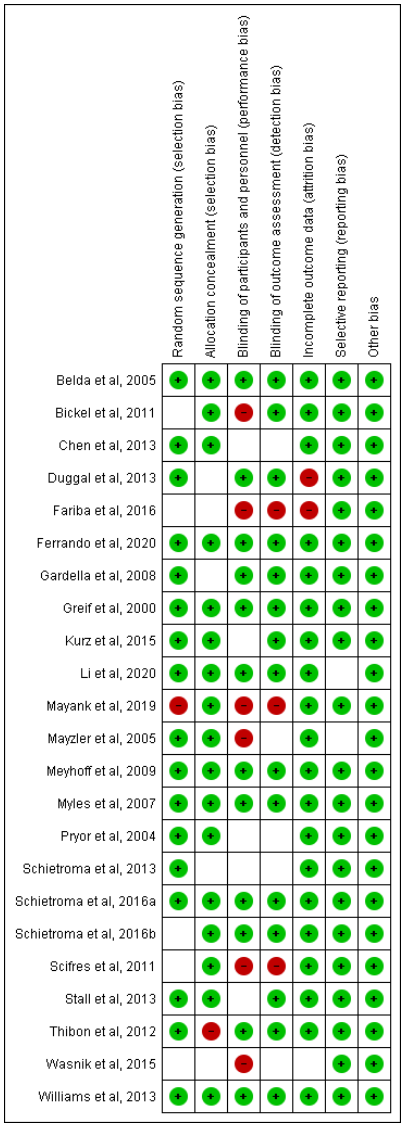
SUPPLEMENTARY INFORMATION

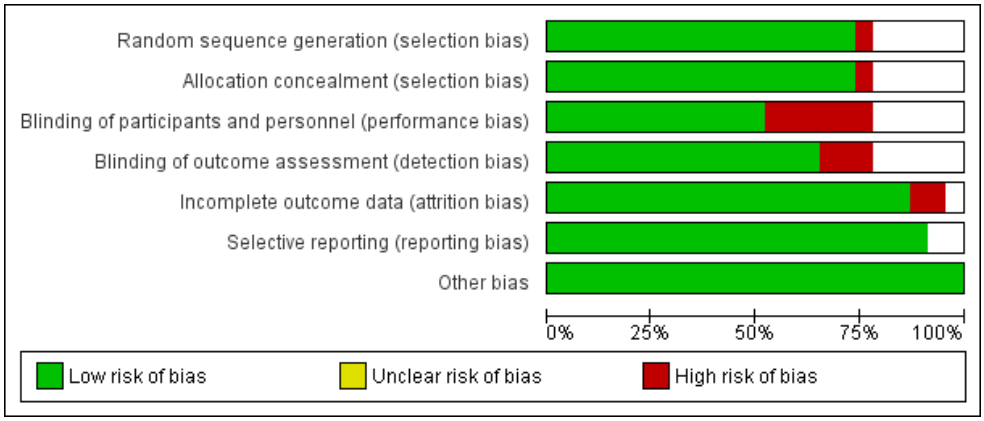
Characteristic of Included Studies Part II

Study	Type of SSI Assesment	Type of anaesthesia	Post-operative oxygenation	Follow up for SSI Assesment	Bacterial culture
Greif et al, (2000) Austria	ASEPSIS scores	General	2 h by NRBM	15 days	*Escherichia coli* Enterococcus *Pseudomonas aeruginosa* *Staphylococcus aureus* *S. epidermidis* Enterobacter
Pryor et al, (2004) USA	NR	General	2 h by CN for low group and NRBM for high group	14 days	*Escherichia coli* *Bacteroides fragilis* *Enterococcus faecalis* *Coagulase-negative staphylococcus* No species identified
Belda et al, (2005) Spain	ASEPSIS scores and CDC criteria	General	6 h by NRBM	14 days	NR
Mayzler et al, (2005) Israel	NR	General	2 h by face mask	30 days	NR
Myles et al, (2007) Multicenter	NR	General	NR	30 days	NR
Gardella et al, (2008) USA	NR	Regional	2 h by NRBM	14 days	Group B streptococcus
Meyhoff et al, (2009) Denmark	ASEPSIS scores and CDC criteria	General	2 h by NRBM	14 days	NR
Bickel et al, (2011) Israel	ASEPSIS scores	General	2 h by CN for low group and NRBM for high group	14 days	NR
Scifres et al, (2011) USA	NR	Regional	2 h by CN for low group and NRBM for high group	28 days	Group B streptococcus
Thibon et al, (2012) France	CDC criteria	General	NR	30 days	*Staphylococcus aureus* coagulasenegative staphylococcal species *Pseudomonas aeruginosa* Gram-negative bacteria
Chen et al, (2013) Hong Kong	ASEPSIS scores and CDC criteria	General	24 h by facemask	30 days	NR
Duggal et al, (2013) USA	NR	Regional	1 h by facemask	14 days	NR
Schietroma et al, (2013) Italy	NR	General	6 h by facemask with reservoir	NR	NR
Stall et al (2013) USA	ASEPSIS scores and CDC criteria	General	2 h by CN for low group and NRBM for high group	12 weeks	NR
William et al, (2013) USA	CDC criteria	Regional	2 h by aerosol mask	6 weeks	NR
Kurz et al, (2015) Multicenter	CDC criteria	General	1 h by NRBM	30 days	NR
Wasnik et al, (2015) India	ASPESIS scores	NR	2 h	10 days	NR
Fariba et al, (2016) Iran	ASEPSIS scores	Regional	6 h by normal mask for low group and venturi mask for high group	14 days	NR
Schietroma et al, (2016a) Italy	ASEPSIS scores and CDC criteria	General	6 h by NRBM with a reservoir	14 days	NR
Schietroma et al, (2016b) Italy	NNIS, SENIC scales, and ASEPSIS scores	General	6 h by NRBM	14 days	NR
Mayank et al, (2019) India	ASEPSIS score and CDC criteria	General	6 h by standard venturi mask for low group and NRBM venturi face mask for high group	48 h ssi	NR
Ferrando et al, (2020) Multicenter	CDC criteria	General and Regional	3 h by venturi mask for low group and NRBM with a reservoir for high group	30 days	NR
Xue-Fei Li et al, (2020) China	CDC criteria	General	NR	7 days	NR

SUPPLEMENTARY INFORMATION

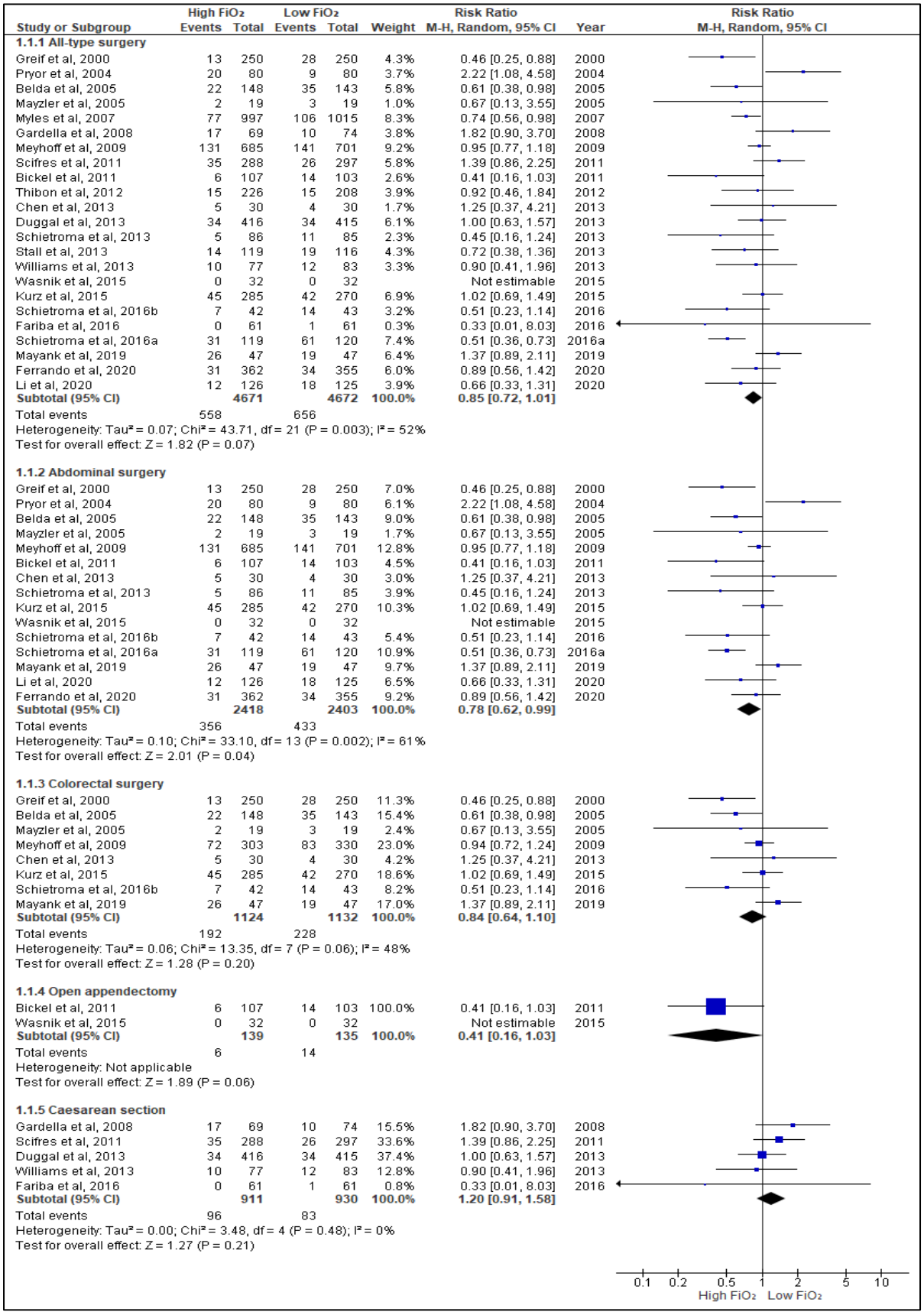
Risk of Bias Assessment based on Risk of Bias 2 (RoB 2) Tools (Recommended by Cochrane Handbook for Systematic Review of Intervention)



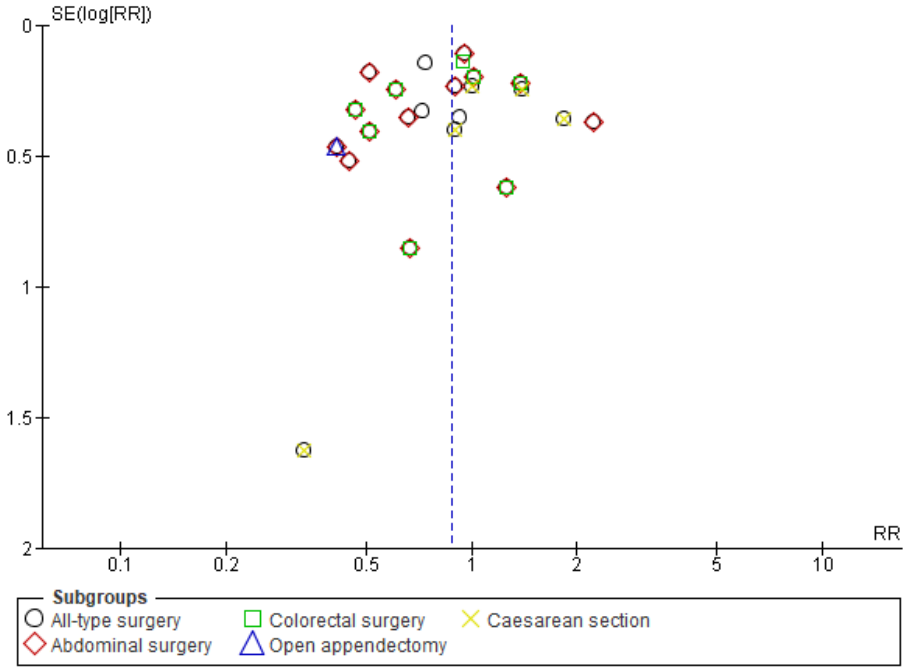


SUPPLEMENTARY INFORMATION

Forest Plot and Funnel Plot for Incidence of Surgical Site Infection (SSI) between High FiO_2 Group and Low FiO_2 Group



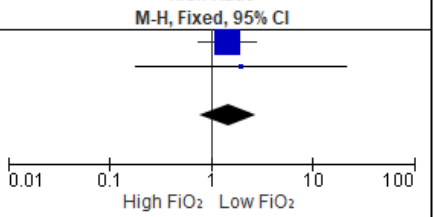
SUPPLEMENTARY INFORMATION

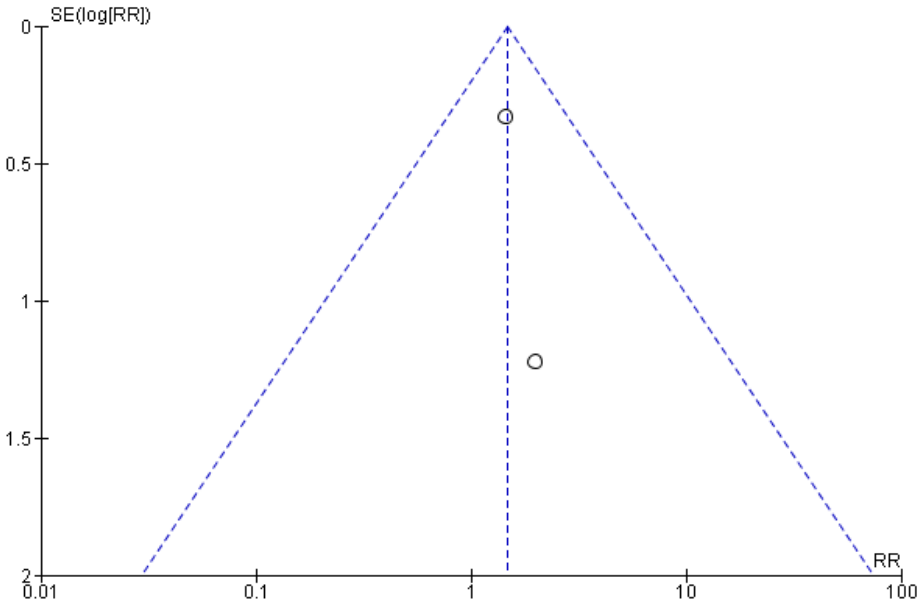


Forest Plot and Funnel Plot for Incidence of Sepsis between High FiO_2 Group and Low FiO_2 Group

Study or Subgroup	High FiO_2 Events	Total	Low FiO_2 Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Meyhoff et al, 2009	21	685	15	701	93.7%	1.43 [0.74, 2.76]	2009
Li et al, 2020	2	126	1	125	6.3%	1.98 [0.18, 21.60]	2020
Total (95% CI)		**811**		**826**	**100.0%**	**1.47 [0.78, 2.76]**	
Total events	23		16				

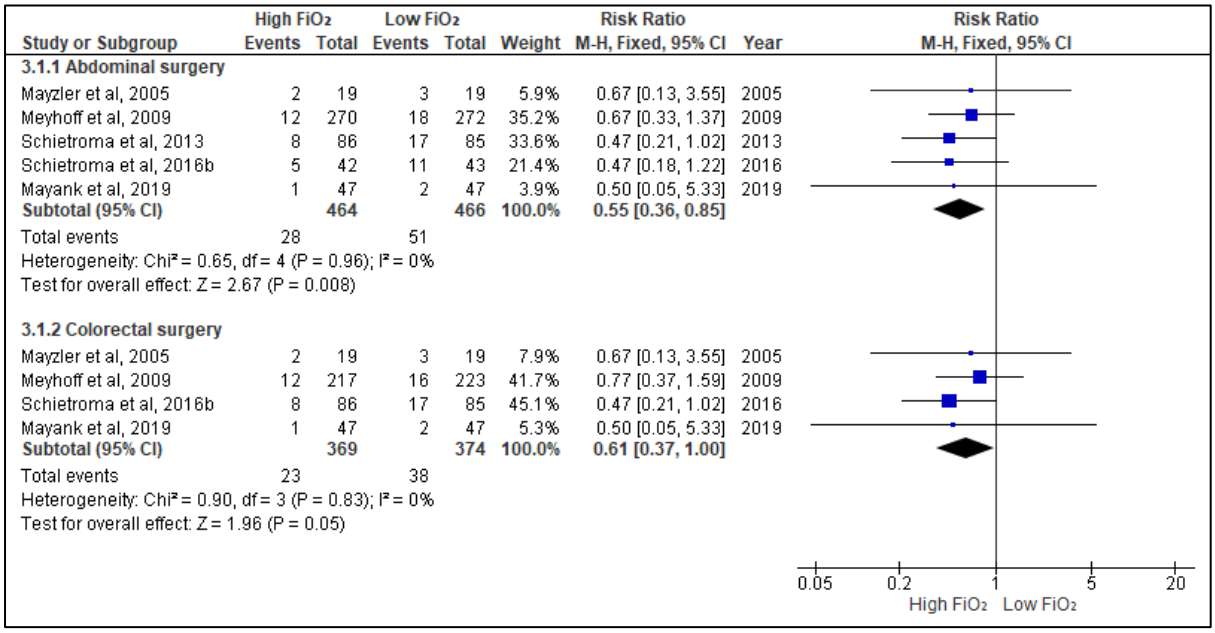
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.80); I² = 0%
Test for overall effect: Z = 1.19 (P = 0.23)

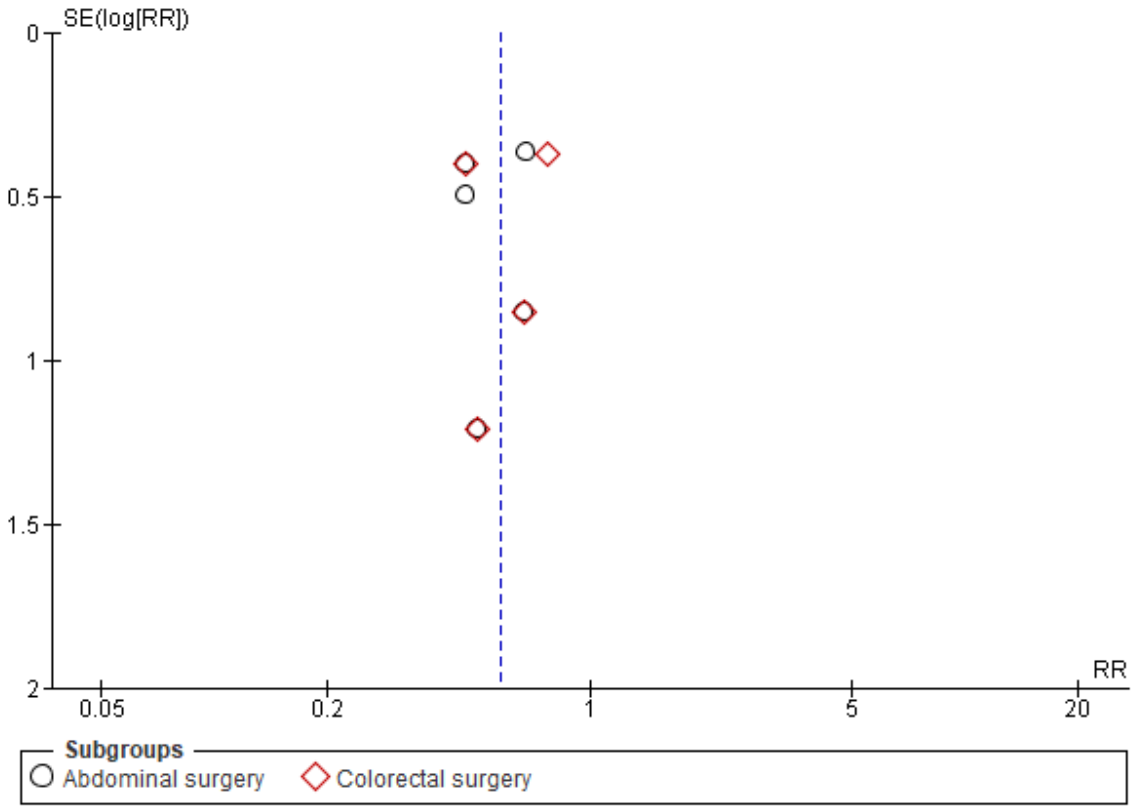




SUPPLEMENTARY INFORMATION

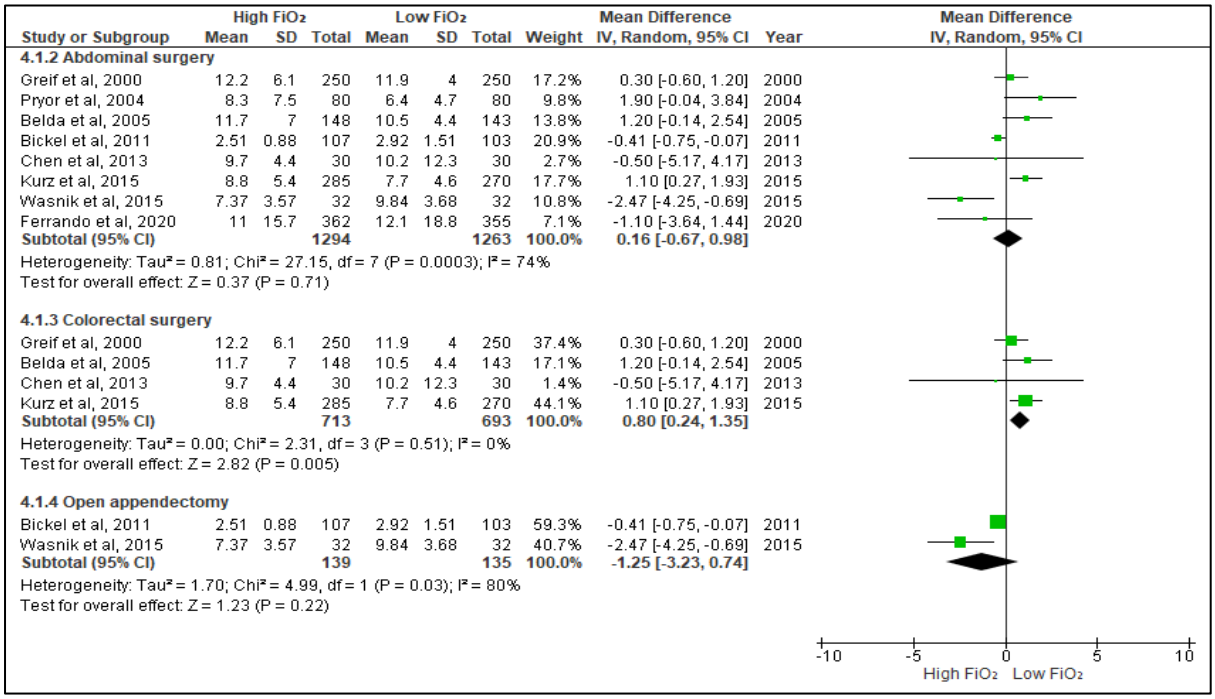
Forest Plot and Funnel Plot for Incidence of Anastomotic Leakage between High FiO_2 Group and Low FiO_2 Group



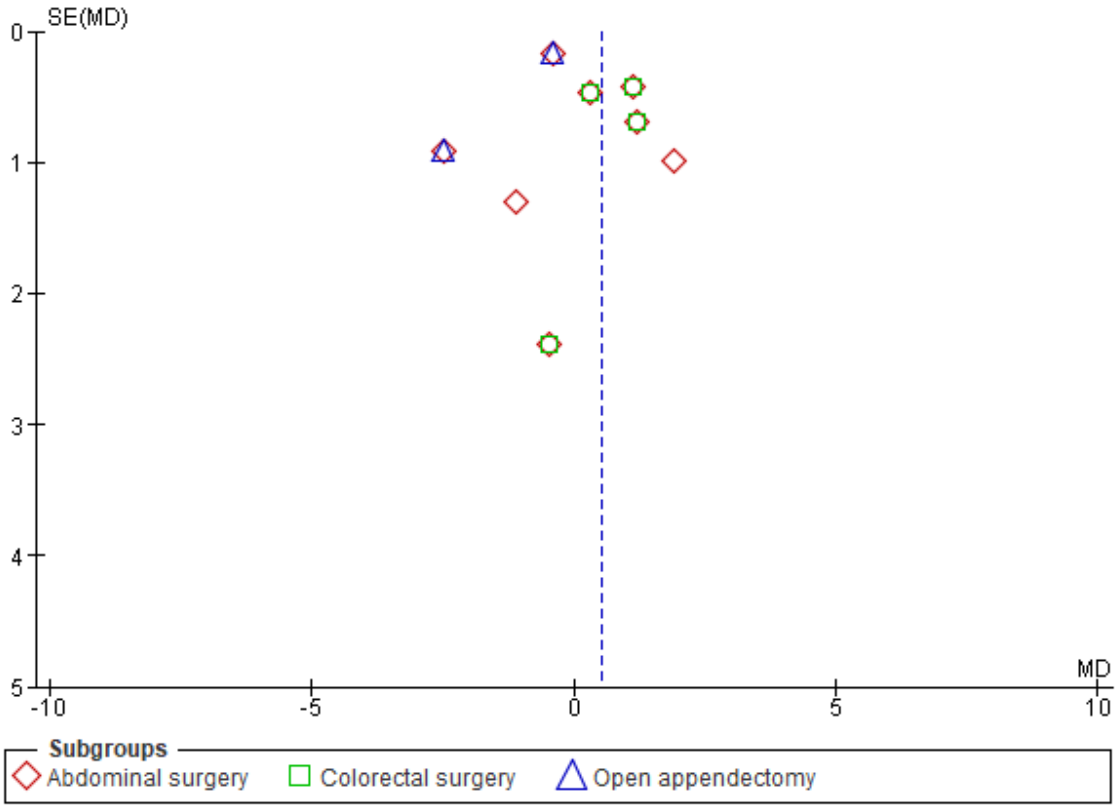


SUPPLEMENTARY INFORMATION

Forest Plot and Funnel Plot for Postoperative Hospitalization Days (PHD) between High FiO_2 Group and Low FiO_2 Group

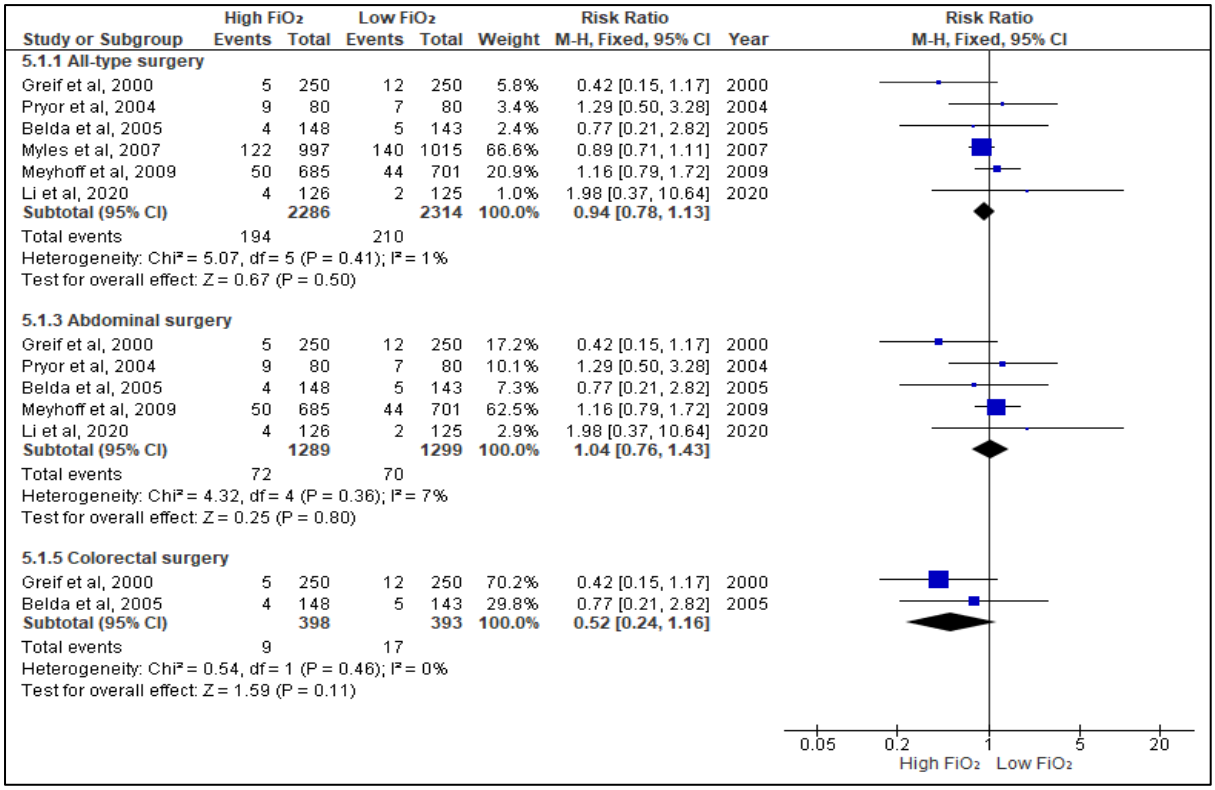


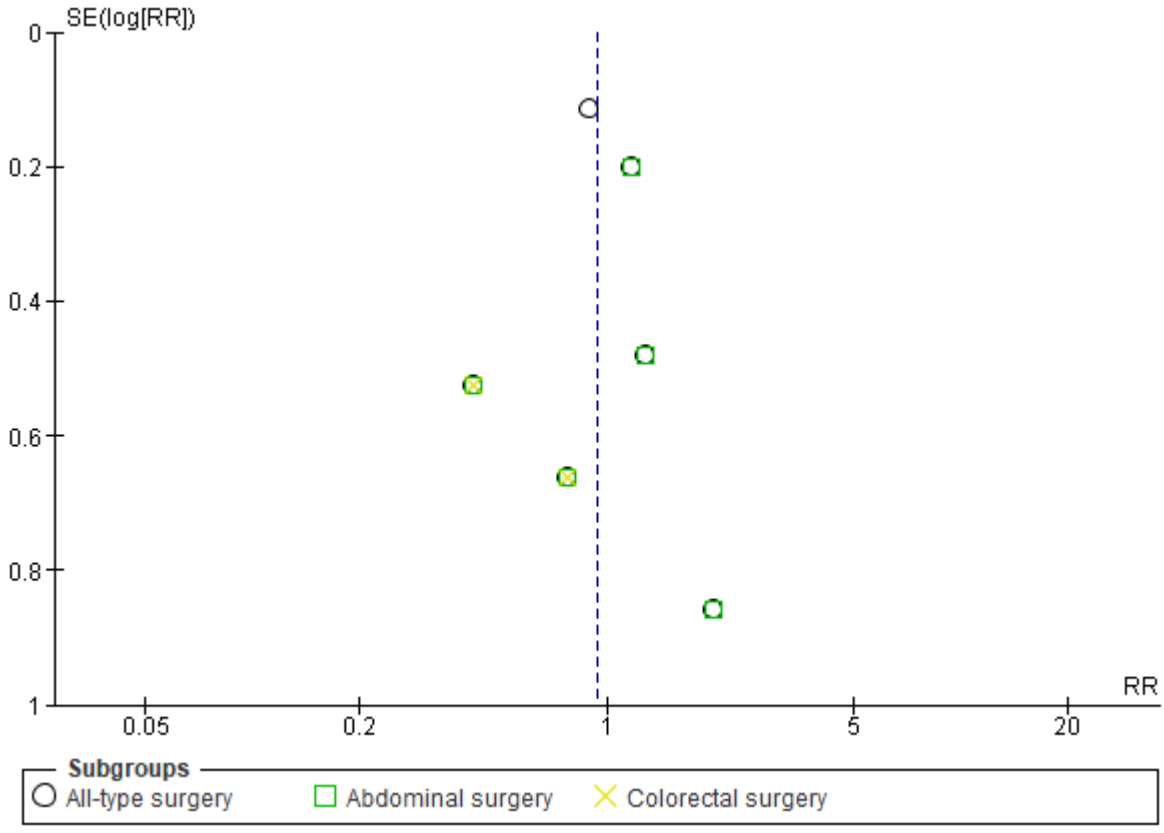
Study or Subgroup	High FiO_2 Mean	SD	Total	Low FiO_2 Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
4.1.2 Abdominal surgery									
Greif et al, 2000	12.2	6.1	250	11.9	4	250	17.2%	0.30 [-0.60, 1.20]	2000
Pryor et al, 2004	8.3	7.5	80	6.4	4.7	80	9.8%	1.90 [-0.04, 3.84]	2004
Belda et al, 2005	11.7	7	148	10.5	4.4	143	13.8%	1.20 [-0.14, 2.54]	2005
Bickel et al, 2011	2.51	0.88	107	2.92	1.51	103	20.9%	-0.41 [-0.75, -0.07]	2011
Chen et al, 2013	9.7	4.4	30	10.2	12.3	30	2.7%	-0.50 [-5.17, 4.17]	2013
Kurz et al, 2015	8.8	5.4	285	7.7	4.6	270	17.7%	1.10 [0.27, 1.93]	2015
Wasnik et al, 2015	7.37	3.57	32	9.84	3.68	32	10.8%	-2.47 [-4.25, -0.69]	2015
Ferrando et al, 2020	11	15.7	362	12.1	18.8	355	7.1%	-1.10 [-3.64, 1.44]	2020
Subtotal (95% CI)			**1294**			**1263**	**100.0%**	**0.16 [-0.67, 0.98]**	
Heterogeneity: $Tau^2 = 0.81$; $Chi^2 = 27.15$, df = 7 (P = 0.0003); $I^2 = 74\%$									
Test for overall effect: Z = 0.37 (P = 0.71)									
4.1.3 Colorectal surgery									
Greif et al, 2000	12.2	6.1	250	11.9	4	250	37.4%	0.30 [-0.60, 1.20]	2000
Belda et al, 2005	11.7	7	148	10.5	4.4	143	17.1%	1.20 [-0.14, 2.54]	2005
Chen et al, 2013	9.7	4.4	30	10.2	12.3	30	1.4%	-0.50 [-5.17, 4.17]	2013
Kurz et al, 2015	8.8	5.4	285	7.7	4.6	270	44.1%	1.10 [0.27, 1.93]	2015
Subtotal (95% CI)			**713**			**693**	**100.0%**	**0.80 [0.24, 1.35]**	
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.31$, df = 3 (P = 0.51); $I^2 = 0\%$									
Test for overall effect: Z = 2.82 (P = 0.005)									
4.1.4 Open appendectomy									
Bickel et al, 2011	2.51	0.88	107	2.92	1.51	103	59.3%	-0.41 [-0.75, -0.07]	2011
Wasnik et al, 2015	7.37	3.57	32	9.84	3.68	32	40.7%	-2.47 [-4.25, -0.69]	2015
Subtotal (95% CI)			**139**			**135**	**100.0%**	**-1.25 [-3.23, 0.74]**	
Heterogeneity: $Tau^2 = 1.70$; $Chi^2 = 4.99$, df = 1 (P = 0.03); $I^2 = 80\%$									
Test for overall effect: Z = 1.23 (P = 0.22)									



SUPPLEMENTARY INFORMATION

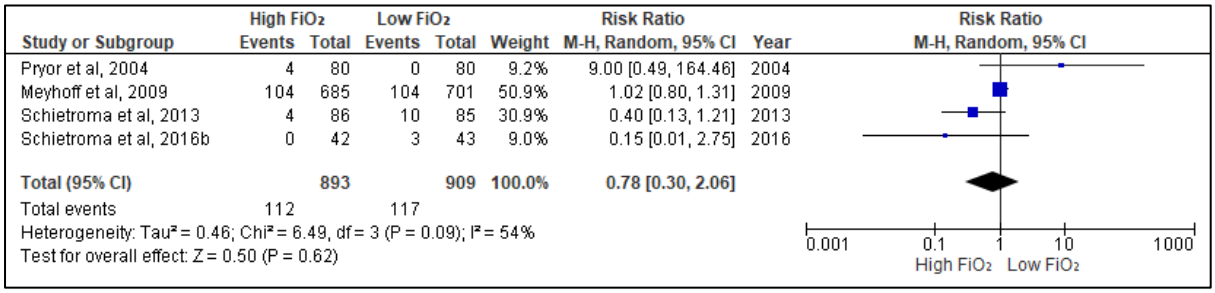
Forest Plot and Funnel Plot for ICU Admission between High FiO_2 Group and Low FiO_2 Group

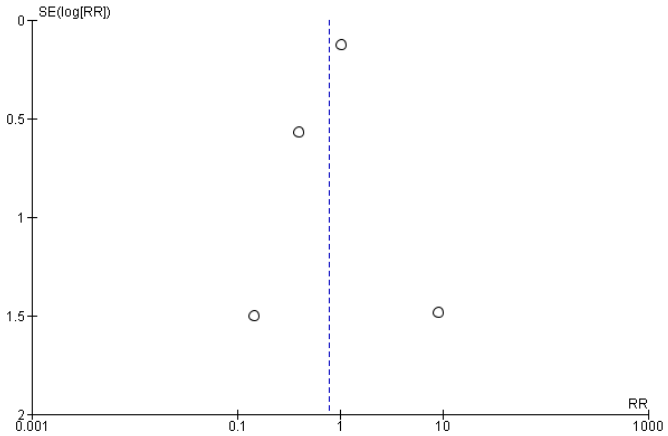




SUPPLEMENTARY INFORMATION

Forest Plot and Funnel Plot for Reoperation Required between High FiO_2 Group and Low FiO_2 Group





Forest Plot and Funnel Plot for Reoperation Required between High FiO_2 Group and Low FiO_2 Group