Supplementary Online Content

Toh JWT, Phan K, Hitos K, et al. Association of mechanical bowel preparation and oral antibiotics before elective colorectal surgery with surgical site infection: a network meta-analysis. *JAMA Netw Open*. 2018;1(6):e183226. doi:10.1001/jamanetworkopen.2018.3226

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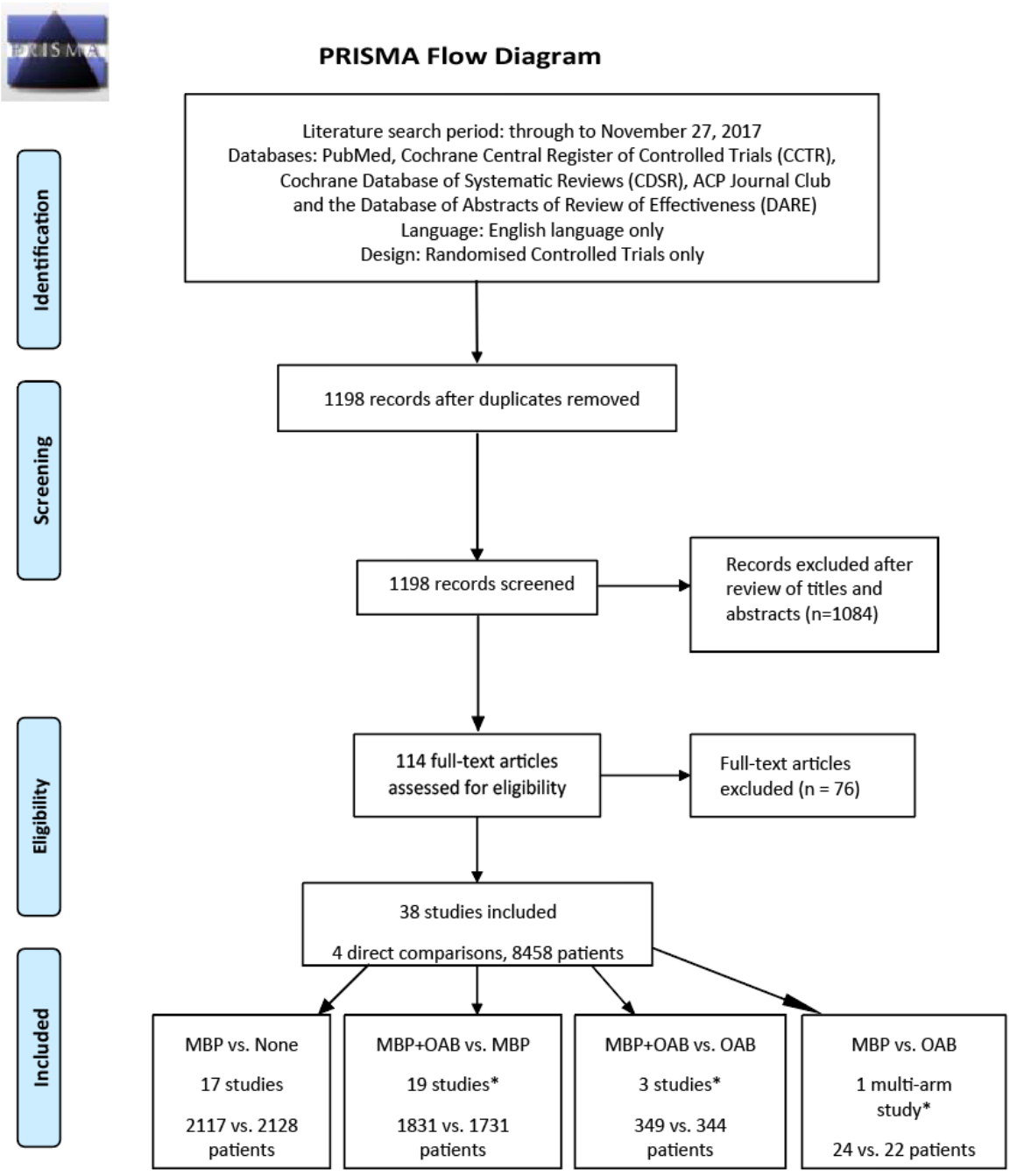
This supplementary material has been provided by the authors to give readers additional information about their work.

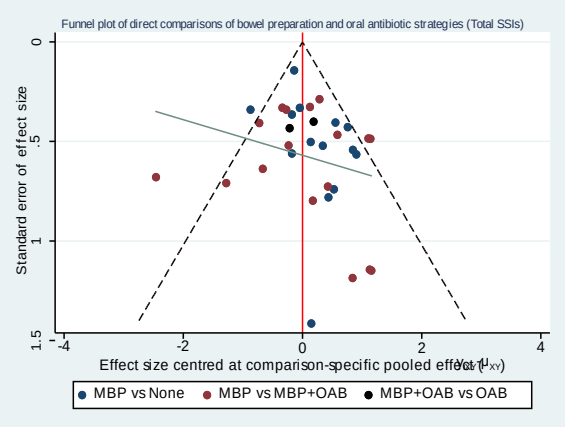
eFigure 1. PRISMA Flow Diagram

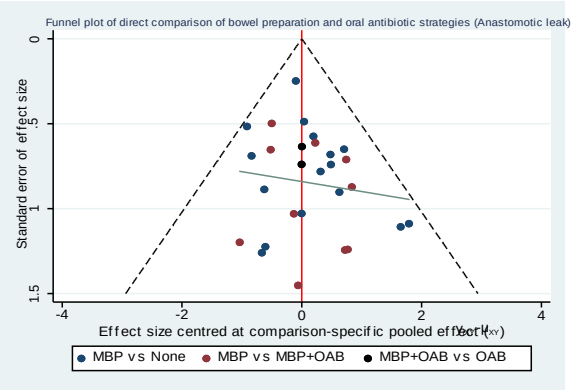


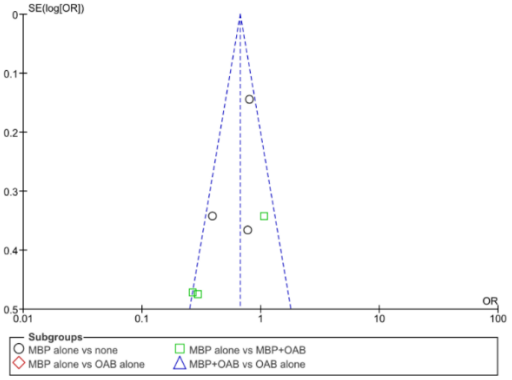
From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

* Multi-arm study comparing three different bowel preparation approaches

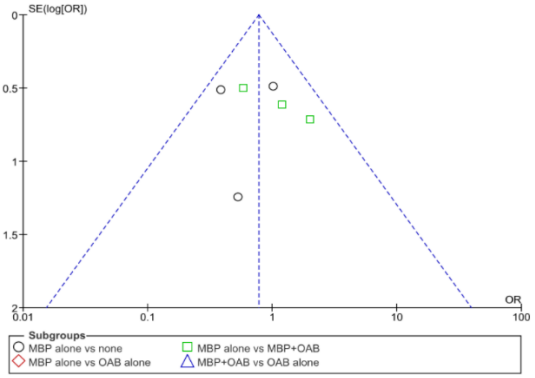
eFigure 2. Funnel Plots







Funnel plot of direct comparisons of bowel preparation and oral antibiotic strategies (laparoscopic / mixed studies only) (Total SSI)



Funnel plot of direct comparisons of bowel preparation and oral antibiotic strategies (laparoscopic / mixed studies only) (Anastomotic leak)

eAppendix. Search Strategy, Selection Process and Data Extraction and Method of Network Analysis

Search Strategy

We performed a comprehensive literature according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[1,2] Five electronic databases were searched including PubMed, Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR), ACP Journal Club and the Database of Abstracts of Review of Effectiveness (DARE) from database inception to current (November 27, 2017). To minimise the risk of overlooking relevant studies and given the wide variety of procedural nomenclature, it was necessary to combine a large number of key words and MeSH terms. This constituted the terms "mechanical bowel preparation", "oral antibiotics", "colon", "rectal", "colorectal", "surgery". We also used ClinicalTrials.gov to identify recently completed trials and PROSPERO to identify recently completed systematic reviews.

Number	Search
1	colon.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw, nm, fx, kf, px, rx, an, ui, sy]
2	rectal.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw, nm, fx, kf, px, rx, an, ui, sy]
3	colorectal.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw, nm, fx, kf, px, rx, an, ui, sy]
4	surgery.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw, nm, fx, kf, px, rx, an, ui, sy]
5	mechanical bowel preparation.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw, nm, fx, kf, px, rx, an, ui, sy]
6	antibiotic.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw, nm, fx, kf, px, rx, an, ui, sy]
7	(1 or 2 or 3) and 4 and (5 or 6)
8	Duplicates removed

Selection process and data extraction

Two independent reviewers assessed the eligibility of each study for inclusion, with any disagreements being resolved by review and consensus. The following data were extracted for each study: author, year of publication, study period, journal, study design, status of mechanical bowel preparation and oral antibiotics, bowel preparation used, right vs. left side of resection, laparoscopic/open/mixed cohort, type of intravenous antibiotics used and type of

oral antibiotics used. The data for primary and secondary outcomes were then extracted for each study.

Network Meta-analysis

We conducted a network meta-analysis using Bayesian Markov Chain Monte Caro (MCMC) method in WinBUGS 1.4.3 (MRC Biostatistics Unit, Cambridge, UK) through the conduit of the Microsoft Excel based macro NetMetaXL 1.6.1 (Canadian Agency for Drugs and Technologies in Health). [3] A convergence test for each analysis was conducted by checking whether the Monte Carlo error was less than 5% of the standard deviation of the effect estimates or the variance between the studies. Convergence was achieved for all analyses at 20,000 "burn in" runs and 30,000 model runs. A random effects model with informative priors was used to best minimise the impact of the diversity of the assorted patient populations and designs for each study.

Clinical post-operative outcomes were examined calculating the pooled estimates of odds ratios (OR) and 95% confidence interval (CI) of direct comparisons between any 2 of bowel preparation and oral antibiotic strategies. Direct and indirect evidence for all MBP and OAB strategies were combined to estimate the examined outcomes, with a 95% equal tail credible interval (CrI). Bayesian analysis was implemented because of its ability to simultaneously compare multiple treatment options. We used NetMetaXL in order for rank probabilities to be plotted against the possible ranks for a treatment to result in the production of a graphical "rankogram". This method of visually representing probabilities was combined with a surface under the cumulative ranking line for each surgical intervention (SUCRA). For example, a SUCRA of 0.5 means that there is a 50% chance that the respective intervention is the best option in achieving the lowest rate of an undesirable clinical outcome.

All results were presented as relative effects and Bayesian estimates of the probability of each technique being the best to the worst relating to every studied outcome with rankograms, league tables and forest plots.

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eTable 1. Cochrane Collaboration Risk-of-Bias Tool (Version 5.0.1): Risk of Bias in the Individual Randomized Controlled Trials Assessed by Cochrane Risk of Bias Checklist

First author	Random sequence allocation	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Incomplete outcomes data
MBP+ OAB- versus MBP- OAB-					
Ali[1]	Unclear	Unclear	High	High	Unclear
Bertani[2]	Low	Unclear	High	High	Unclear
Bhat[3]	Low	Low	Low	High	Low
Bhattacharjee[4]	Low	Low	High	High	Unclear
Bretagnol[5]	Low	Low	Low	High	Low
Bucher[6]	Low	Low	Low	High	Low
Burke[7]	Low	Unclear	Low	Unclear	Low
Contant[8]	Low	Low	Low	Low	Low
Fa-Si-Oen[9]	Low	Low	Unclear	Unclear	Low
Khan[10]	Unclear	Unclear	High	High	Unclear
Miettinen[11]	Unclear	Unclear	High	High	Unclear
Pena-Soria[12]	Low	Unclear	Low	High	Low
Platell[13]	Low	Low	Unclear	Unclear	Low
Ram[14]	Unclear	High	Unclear	Unclear	Low
Saha[15]	High	High	High	High	High
Santos[16]	Unclear	High	High	High	High
Sasaki[17]	Unclear	Unclear	High	High	High
MBP+ OAB+ vs MBP- OAB+					
Reddy[18]	Low	Unclear	High	High	Low
Zmora (2003)[19]	Low	High	High	High	High
Zmora (2006)[20]	Low	High	High	High	High
MBP+OAB+ vs MBP+OAB-					
Beggs[21]	Unclear	High	Low	High	High
Dion[22]	Low	Low	Low	Low	High
Espin-Basany[23]	Unclear	Unclear	High	Low	Low
Hata[24]	Low	Low	High	High	Low
Ikeda[25]	Unclear	Unclear	High	Low	Low
Ishida[26]	Low	Low	High	High	Low
Kling[27]	Unclear	High	High	High	High
Kobayashi[28]	Low	High	High	High	Low
Lau[29]	Low	High	High	Low	Low
Lazorthes[30]	Unclear	High	High	High	Low
Lewis[31]	Low	Low	Low	Low	Low
Oshima[32]	Low	High	High	Low	High
Playforth[33]	Unclear	High	High	High	Low

Raahave[34]	Low	Low	High	High	Low
Reddy[18]	Low	Unclear	High	High	Low
Sadahiro[35]	Low	Low	High	Unclear	Low
Stellato[36]	Low	High	Low	Low	High
Weaver[37]	Unclear	High	High	High	Low
Yabata[38]	Low	Unclear	High	High	High
MBP+ OAB- vs MBP- OAB+					
Reddy[18]	Low	Unclear	High	High	Low

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eTable 2. Presentation of Outcome Data for Total Surgical Site Infection, by Included Study

Direct comparison of mechanical bowel preparation and oral antibiotic strategies

Study	MBP			None			MBP+OAB			OAB		
	Events, n	Patients, n		Events, n	Patients, n		Events, n	Patients, n		Events, n	Patients, n	
Bertani	16	114	14%	20	115	17%						
Bhat	6	98	6%	8	104	8%						
Bhattacharjee	14	38	37%	7	33	21%						
Bretagnol	18	89	20%	35	89	39%						
Bucher	11	78	14%	5	75	7%						
Burke	4	82	5%	3	87	3%						
Contant	105	670	16%	128	684	19%						
Fa-Si-Oen	9	125	7%	7	125	6%						
Miettinen	5	138	4%	3	129	2%						
Pena-Soria	19	65	29%	11	64	17%						
Platell	20	147	14%	22	147	15%						
Ram	17	164	10%	11	165	7%						
Saha	16	32	50%	15	31	48%						
Sasaki	1	38	3%	1	41	2%						
Reddy	5	24	21%				6	42	14%	3	22	14%
Zmora (2003)							14	187	7%	13	193	7%
Zmora (2006)							10	120	8%	14	129	11%
Beggs	5	51	10%				6	46	13%			
Dion	4	39	10%				1	39	3%			
Espin-Basany	10	100	10%				22	200	11%			
Hata	37	290	13%				21	289	7%			
Ikeda	20	256	8%				20	255	8%			
Ishida	17	71	24%				8	72	11%			
Kling	3	27	11%				1	27	4%			
Kobayashi	26	242	11%				17	242	7%			

Lau	9	67	13%				8	65	12%			
Lazorthes	4	30	13%				1	30	3%			
Lewis	21	106	20%				6	109	6%			
Oshima	22	98	22%				6	97	6%			
Raahave	3	50	6%				7	50	14%			
Sadahiro	22	95	23%				22	100	22%			
Stellato	7	45	16%				3	38	8%			
Weaver	4	31	13%				16	29	55%			

MBP – mechanical bowel preparation; OAB – oral antibiotics

eTable 3. Presentation of Outcome Data for Anastomotic Leak, by Included Study

Direct comparison of mechanical bowel preparation and oral antibiotic strategies												
Study	MBP			None			MBP+OAB			OAB		
	Events, n	Patients, n		Events, n	Patients, n		Events, n	Patients, n		Events, n	Patients, n	
Ali	6	109	6%	1	101	1%						
Bertani	9	114	8%	9	115	8%						
Bhat	2	98	2%	4	104	4%						
Bhattacharjee	4	38	11%	2	33	6%						
Bretagnol	6	89	7%	14	89	16%						
Bucher	5	78	6%	1	75	1%						
Contant	32	670	5%	37	684	5%						
Fa-Si-Oen	7	125	6%	6	125	5%						
Khan	6	51	12%	4	51	8%						
Miettinen	5	138	4%	3	129	2%						
Pena-Soria	4	65	6%	3	64	5%						
Platell	3	147	2%	7	147	5%						
Ram	1	164	1%	2	165	1%						
Saha	2	32	6%	2	31	6%						
Santos	7	72	10%	4	77	5%						
Sasaki	1	38	3%	2	41	5%						
Zmora (2003)							7	187	4%	4	193	2%
Zmora (2006)							5	120	4%	3	129	2%
Beggs	1	51	2%				1	46	2%			
Hata	6	290	2%				5	289	2%			
Ikeda	6	256	2%				3	255	1%			
Ishida	2	71	3%				1	72	1%			
Lau	2	67	3%				1	65	2%			

Lewis	1	106	1%				3	109	3%			
Playforth	4	58	7%				7	61	11%			
Raahave	5	40	13%				2	33	6%			
Sadahiro	7	95	7%				12	100	12%			
Stellato	2	45	4%				2	38	5%			

MBP – mechanical bowel preparation; OAB – oral antibiotics

eTable 4. Presentation of Outcome Data for Mortality, by Included Study

Direct comparison of mechanical bowel preparation and oral antibiotic strategies

Study	MBP			None			MBP+OAB			OAB		
	Events, n	Patients, n		Events, n	Patients, n		Events, n	Patients, n		Events, n	Patients, n	
Ali	6	109	6%	1	101	1%						
Bhat	0	98	0%	0	104	0%						
Bhattacharjee	1	38	3%	1	33	3%						
Bretagnol	1	89	1%	0	89	0%						
Bucher	0	78	0%	0	75	0%						
Burke	2	82	2%	0	87	0%						
Contant	20	670	3%	26	684	4%						
Fa-Si-Oen	2	125	2%	1	125	1%						
Miettinen	0	138	0%	0	129	0%						
Pena-Soria	3	65	5%	4	64	6%						
Platell	4	147	3%	1	147	1%						
Ram	2	164	1%	2	165	1%						
Santos	0	72	0%	0	77	0%						
Reddy	0	24	0%				0	42	0%	0	22	0%
Zmora (2003)							3	187	2%	3	193	2%
Ikeda	0	256	0%				0	255	0%			
Lazorthes	1	30	3%				1	30	3%			
Playforth	5	58	9%				6	61	10%			
Raahave	3	50	6%				0	50	0%			

MBP – mechanical bowel preparation; OAB – oral antibiotics