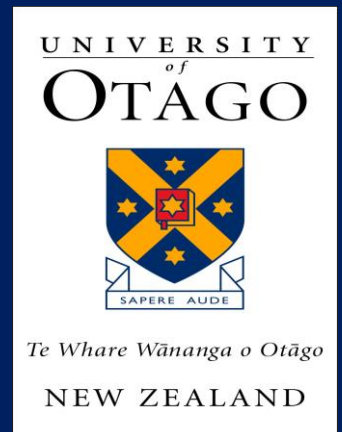


Is there any evidence for using
oral and intravenous antibiotics in
bowel preparation for elective
colorectal surgery?



Te Whatu Ora
Health New Zealand



Are there advantages in using MBP + OA + IV?

RCT data

- A series of RCT and meta-analyses have shown that MBP+IV+OA have better outcomes than MBP+IV. Chen et al 2016 DCR (reduced wound infection)

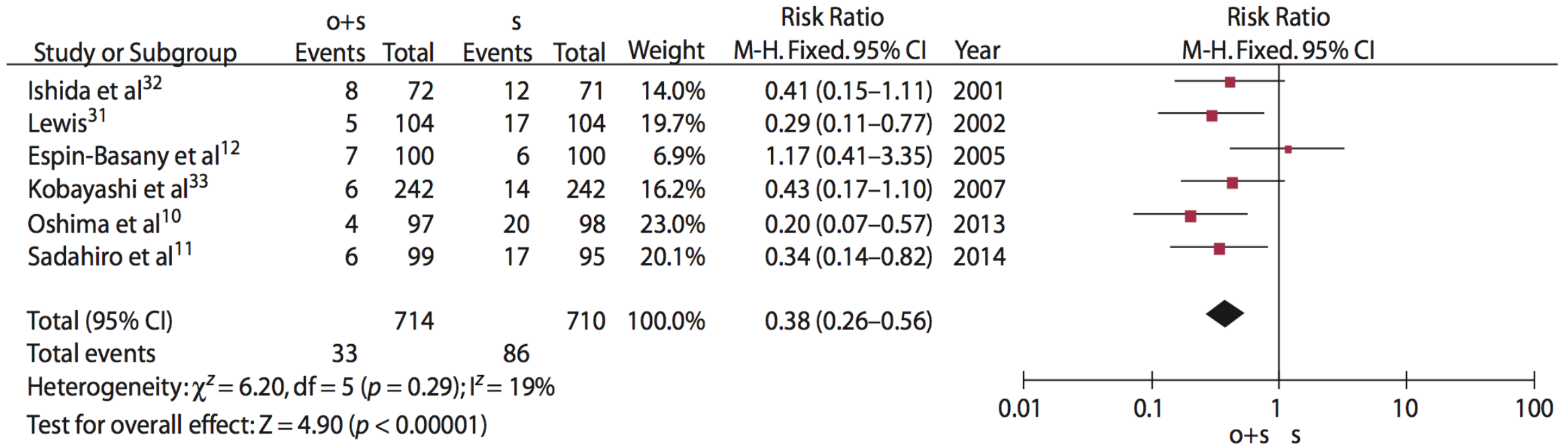


FIGURE 3. Forest plot for incisional surgical site infection (SSI) after surgery. A Mantel–Haenszel fixed-effects model was used for meta-analysis. Risk ratios are shown with 95% CIs. o = oral antibiotics; s = systemic antibiotics; df = degrees of freedom.

The importance of antibiotic cover

- Microbiology and clinical studies have strongly demonstrated that prophylactic cover in colorectal surgery should cover both aerobic and anaerobic bacteria
- A 'problem' with RCTs comparing MBP+IV+OA with MBP+IV (or IV) is when they often do not have good intravenous antibiotic cover.
 - Sometimes adding oral antibiotics resulted in the MBP+IV+OA group having better antibiotic cover than MBP+IV
 - Is the improvement due to the additional use of OA or a better spectrum of antibiotic cover?

Are there advantages in using MBP + OA + IV?

Large database data

- Since 2010 there have been a series of publications [all from the same NSQIP database] showing that MBP+IV+OA has
- A lower rate of ISSI
- A lower rate of anastomotic leaks
- A lower rate of ileus
- A shorter LOS and fewer readmissions



All about
50%
better

Combined Preoperative Mechanical Bowel Preparation With Oral Antibiotics Significantly Reduces Surgical Site Infection, Anastomotic Leak, and Ileus After Colorectal Surgery

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Cody Chiuzan, PhD,† David Estrada, MD,* and Kenneth Forde, MD**

Problems with Large database data

1. No randomisation

➤ Tables looking at risk factors show a better ASA profile, better functional status and less comorbidities (hypertension, SOB, ascites, renal failure and disseminated cancer) and more laparoscopic surgery *all in favour of the MBP+IV+OA group*

2. No documentation of IV antibiotic use or on the overall adequacy of aerobic and anaerobic antibiotic cover in the NSQIP database

A Network Meta-analysis of Antibiotics and Bowel Preparation in Elective Colorectal Surgery



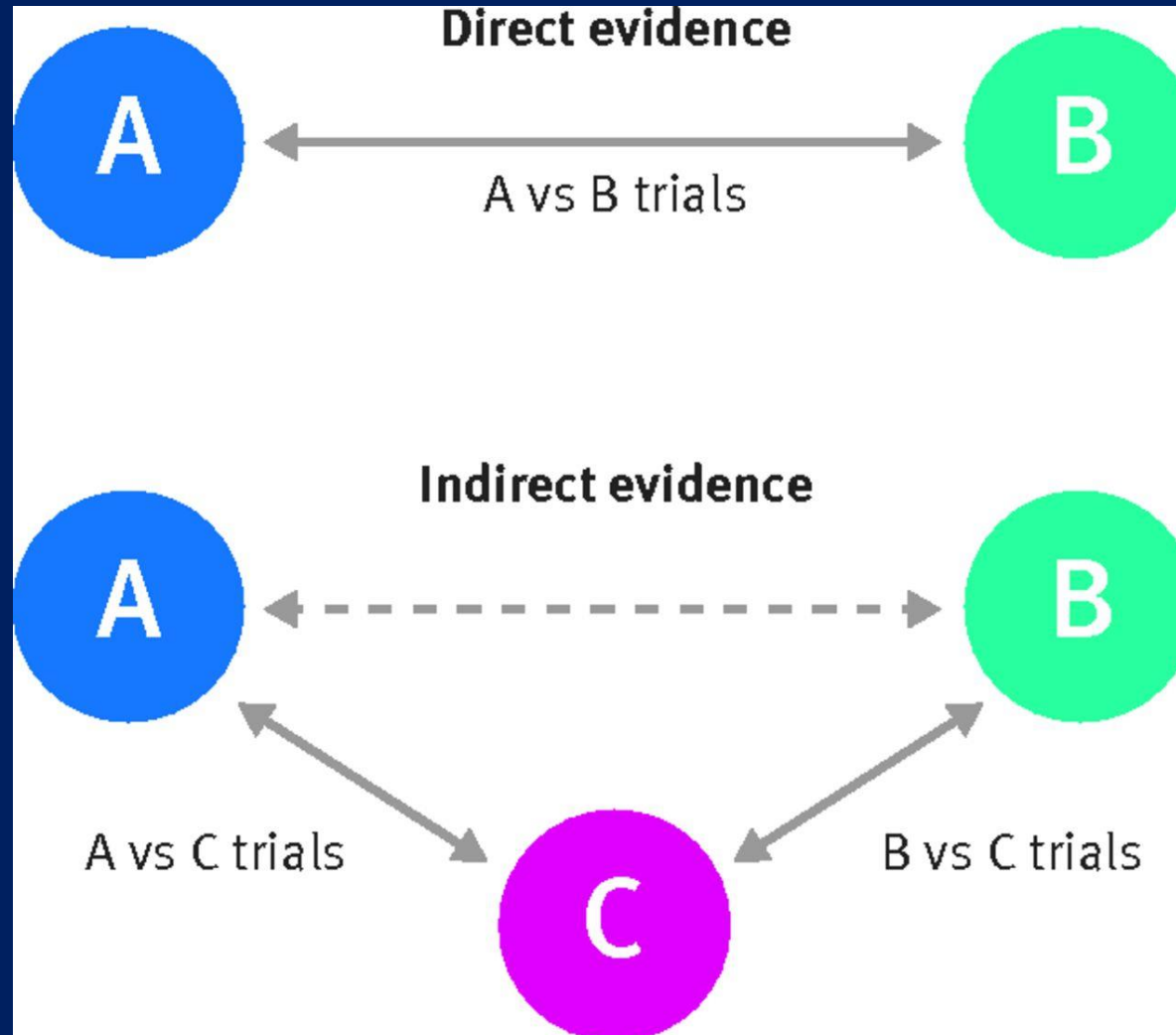
Aims

1. To summarise all the RCT data in studies with good antibiotic cover (*in all groups being compared*)
2. To identify how different strategies for elective preparation rank in terms of their risks and benefits

Inclusion criteria

- Randomised controlled trials In adults
- Undergoing elective colorectal surgery
- Good aerobic and anaerobic cover in all groups being compared
- Comparing different combinations of
 - IV antibiotics (IV)
 - Oral antibiotics (OA)
 - Mechanical bowel preparation (MBP)
 - Enemas (E)

Network Meta-Analysis: Direct and indirect evidence



Outcomes

Primary

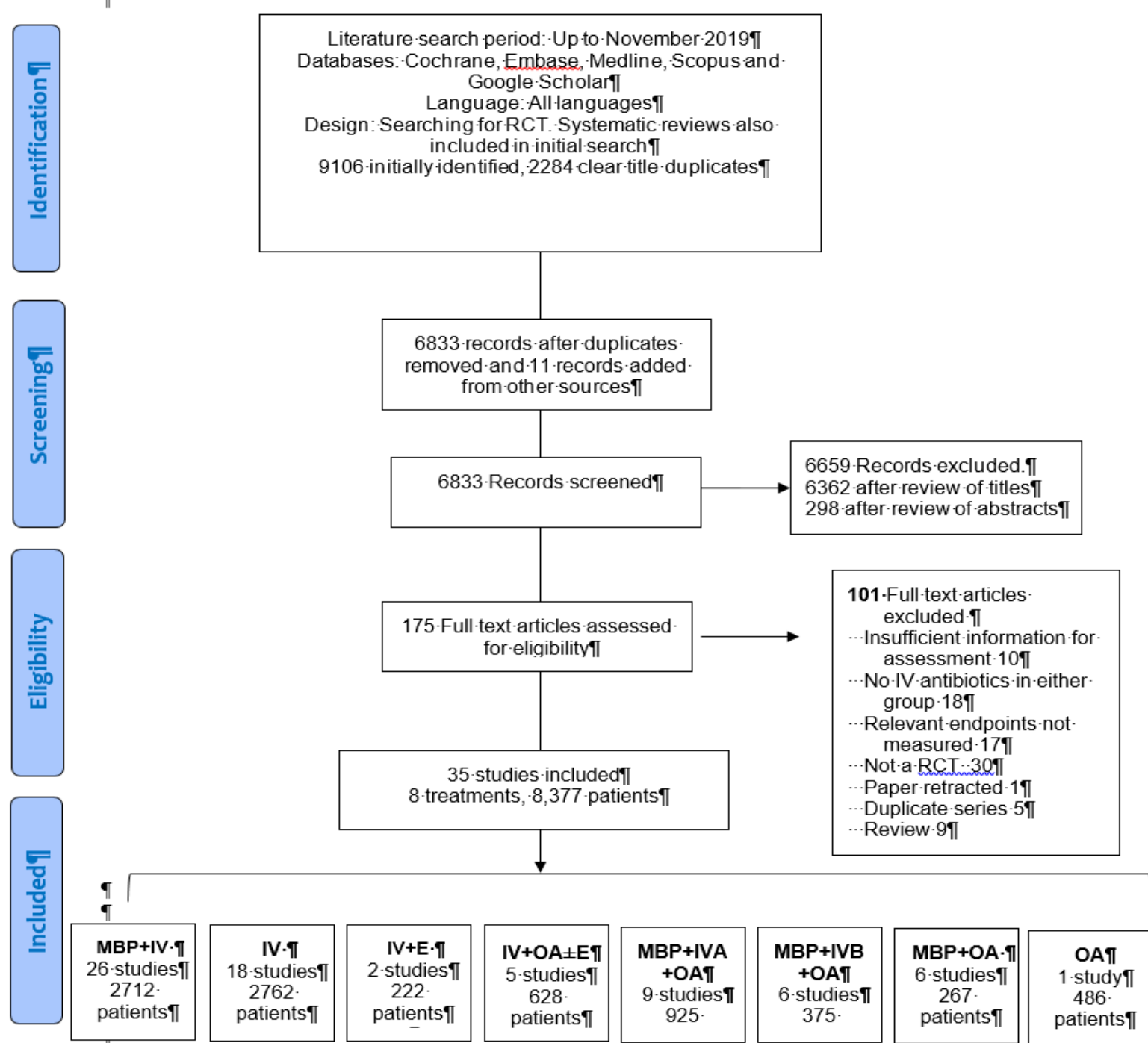
- Incisional Surgical site infection (Wound infection)
- Anastomotic leak

Secondary

- Deep peritoneal infection (Space SSI)
- Mortality
- LOS
- Ileus
- Distant infections (UTI, pneumonia, PUO)
- Side effects (MBP and antibiotics)



Main Results



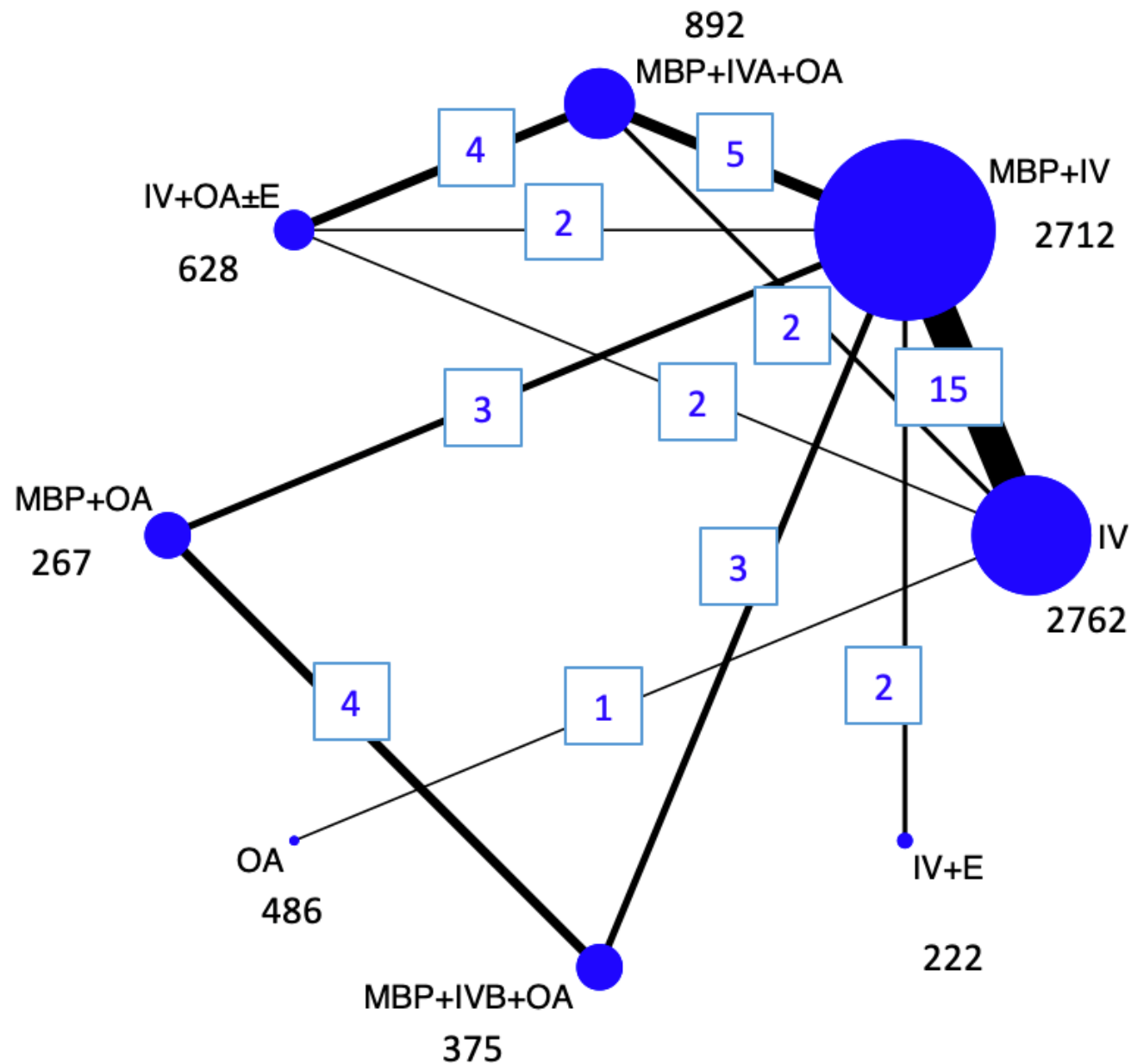
6834 Titles

472 abstracts

175 Papers

35 RCT selected
(8377 patients)

Network Plot



Incisional Surgical site infection Treatment effect

	OR(95% CI) for Incisional SSI	
	IV+OA	MBP+IV+OA
OA	0.14 (0.06,0.33)	0.19(0.08,0.43)
MBP+OA	0.10 (0.04,0.25)	0.14 (0.07,0.31)
MBP+IVB+OA	0.18 (0.08,0.41)	0.25 (0.12,0.51)
MBP+IV	0.22 (0.12,0.40)	0.31 (0.20,0.48)
IV	0.27 (0.15,0.50)	0.38 (0.24,0.62)
IV+E	0.26 (0.11,0.63)	0.37 (0.17,0.81)
MBP+IV+OA	0.71 (0.41,1.21)	
IV+OA ±E		1.41 (0.83, 2.42)

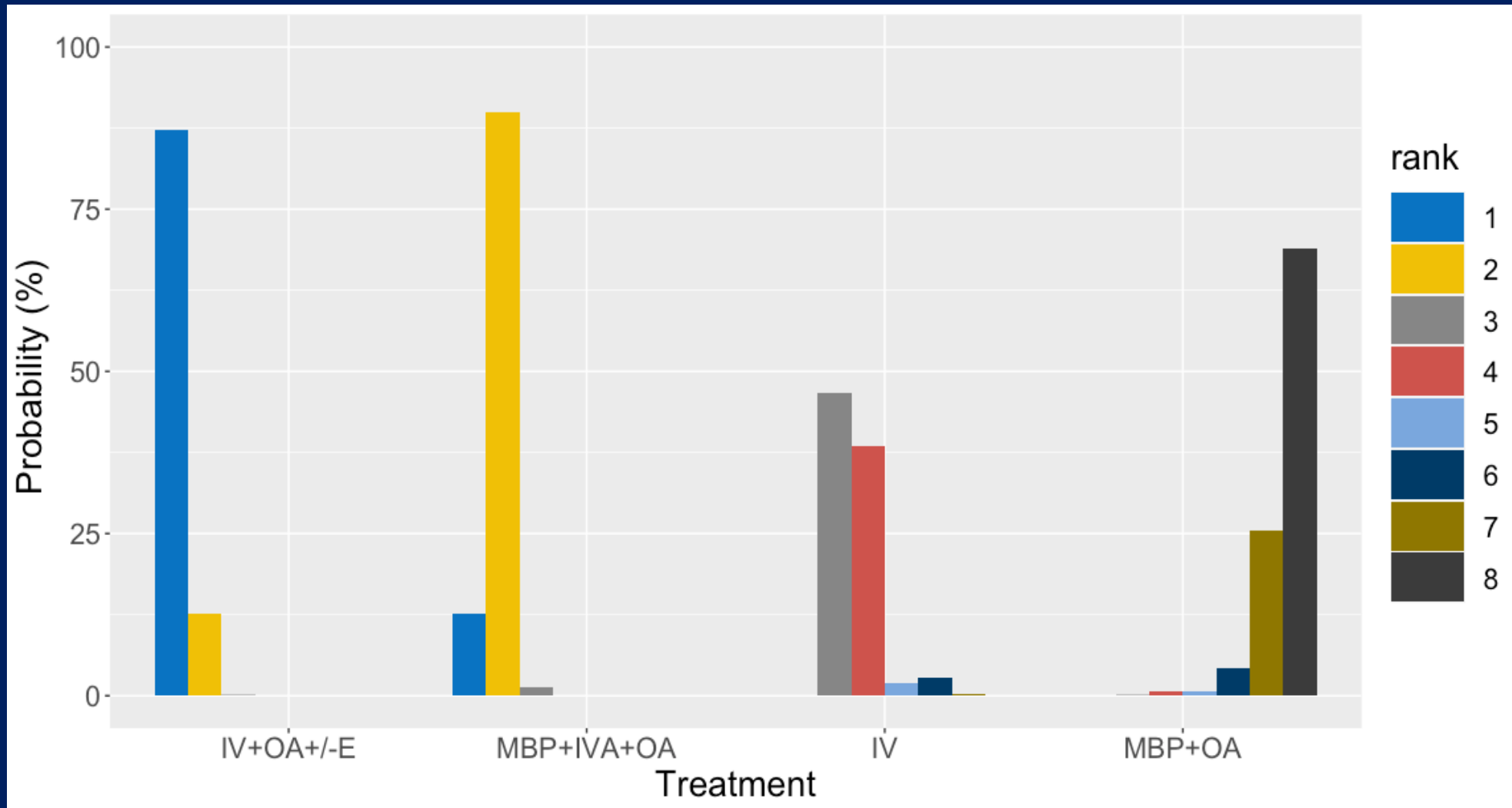
The two bowel preparation options including intravenous and oral antibiotics (IV+OA and MBP+IV+OA) were significantly better than all other methods of bowel preparation at reducing incisional surgical site infection (By > 50%)

Odds Ratio (95% CI) for comparison of treatment effects. If OR<1 the outcome is less likely for treatment in the top row

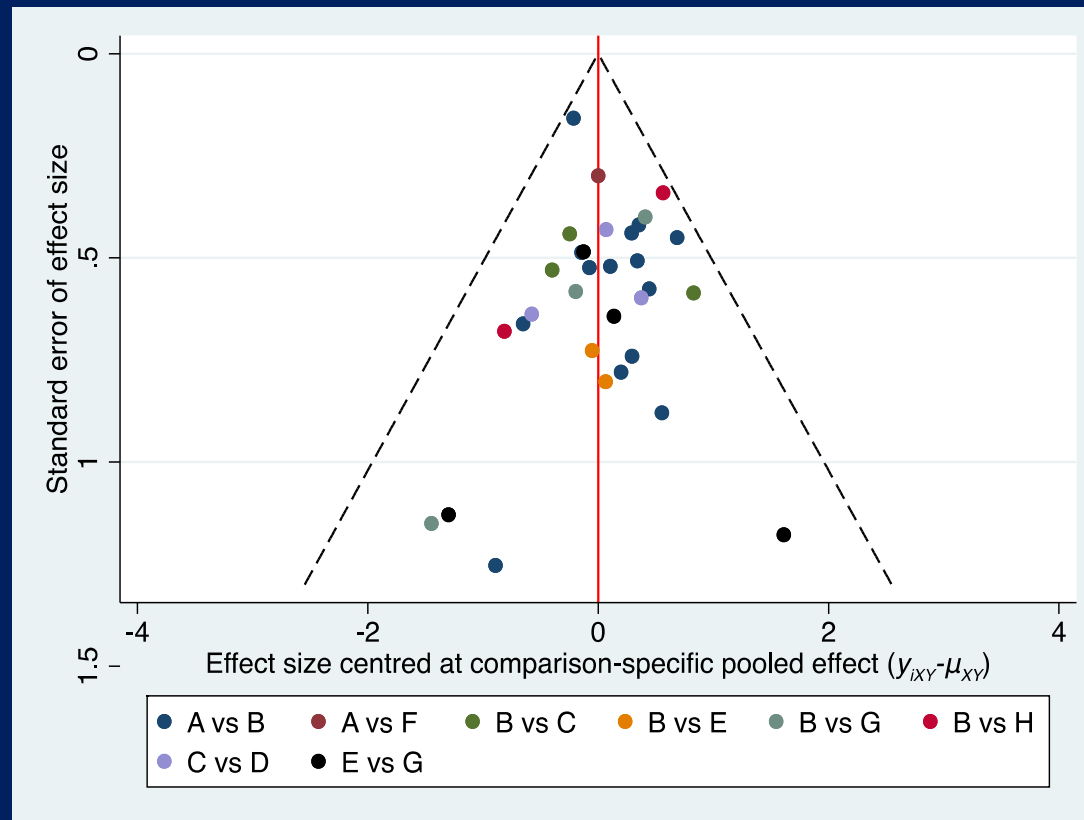
Incisional Surgical site infection Ranking

Bowel Preparation	Ranking
IV+OA +/- E	1 [Probability 86%]
MBP+IV+OA	2 [Probability 85%]
IV	3
IV+E	4
MBP+IV	5
OA +/-E	7
OA+MBP	8 [Probability 68%]

Surgical site infection Ranking



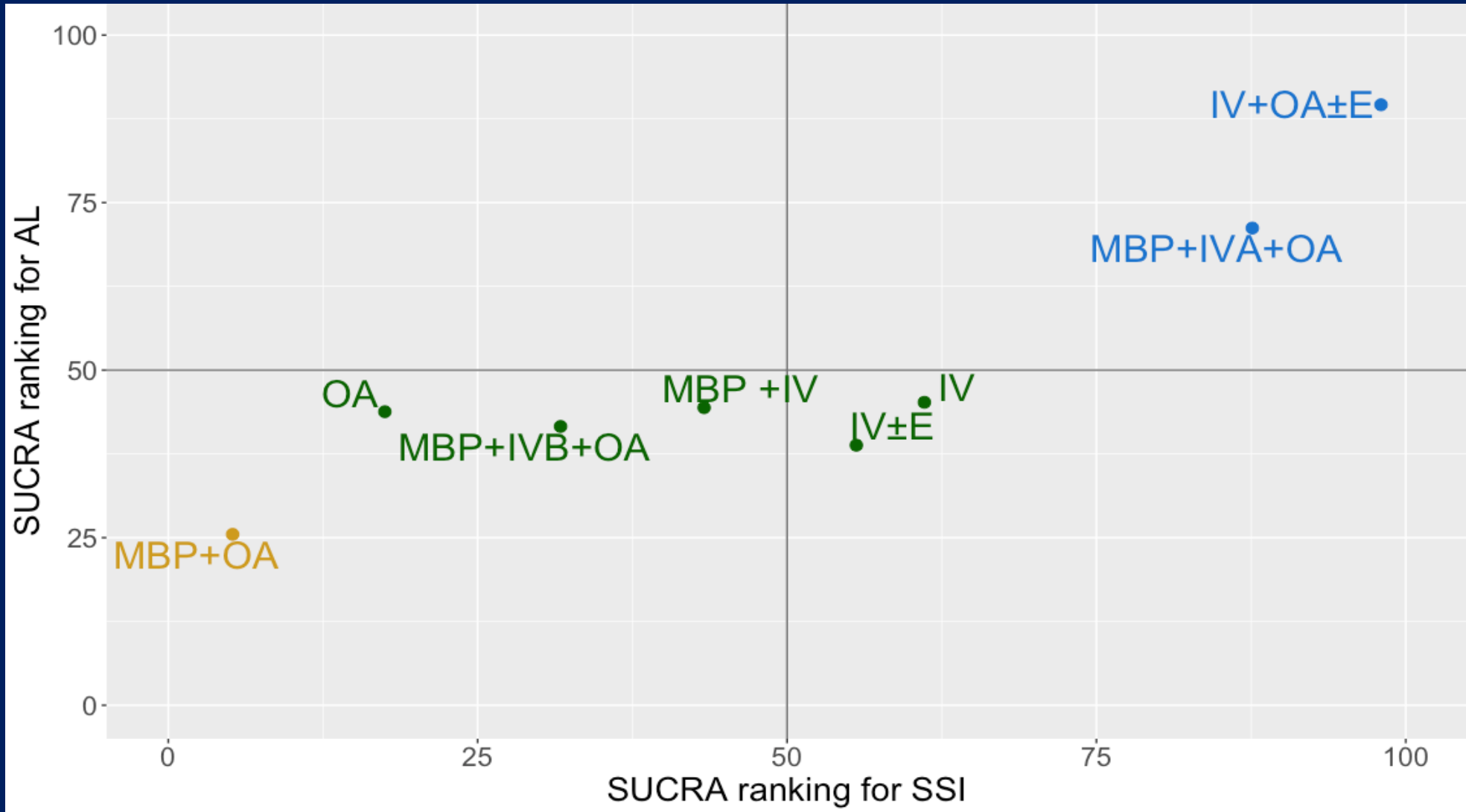
No evidence of publication bias



Other endpoints

- Anastomotic leak – No significant differences between groups
- Ileus – No significant differences between groups
- Other secondary endpoints – No significant differences between groups

SUCRA Clustered Ranking Plot (for primary Outcomes)



SUCRA: Gives a % of the cumulative surface area under the ranking curve for each type of bowel preparation

Conclusion of NMA

1. The addition of OA significantly reduces incisional surgical site infection by >50%
 - The best option for colonic surgery is either IV+OA+/-Enema or MBP+IV+OA
 - In rectal surgery MBP+IV+OA is effective. IV+OA +/-Enema has not been assessed
 2. There are no significant differences in anastomotic leak or other end points
- ❖ There is sufficient evidence to add OA into our protocol

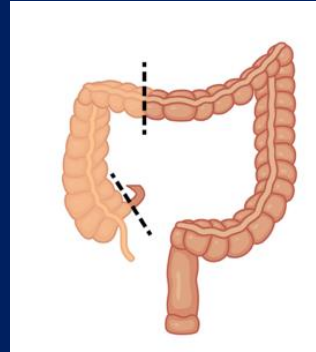
Weaknesses in the study

1. Limited number of patients for some of the bowel preparation options – including those options combining IV and oral antibiotics
 2. Wide range of frequency of complications for the same endpoints (some studies tried harder to identify endpoints events than others)
 3. The difference in wound infection when OA is used is greater than one would 'expect'
- Additional high-quality studies will help to clarify ongoing questions

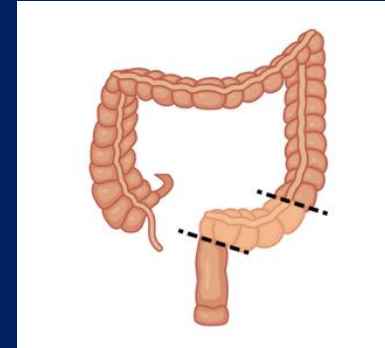
Practical Application

Recommendation: In terms of bowel preparation add OA to what you currently do

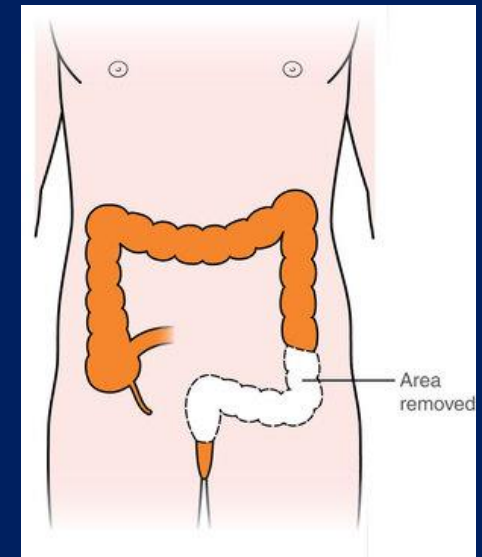
➤ R hemicolectomy: Change from IV antibiotics alone to IV+OA



➤ Left sided colon tumors: Change from IV+E to IV+OA+E



➤ Low Rectal: Change from MBP + IV to MBP+IV+OA



Choice of oral antibiotic

- There is a wide range of antibiotics used at different doses and for different durations of time in the RCT data
- Most frequently used oral antibiotics (in >90 RCT studies) were...
 - Anaerobes: Metronidazole 26, tinidazole 6
 - Aerobic cover: Neomycin 28, Erythromycin 18, kanamycin 13, doxycycline 3, cotrimoxazole 2, tobramycin 2, quinolones 3
- Usually given as three doses on the preoperative day
- Oral neomycin is not 'available for human use' in NZ – Getting this approved by Pharmac would be very helpful