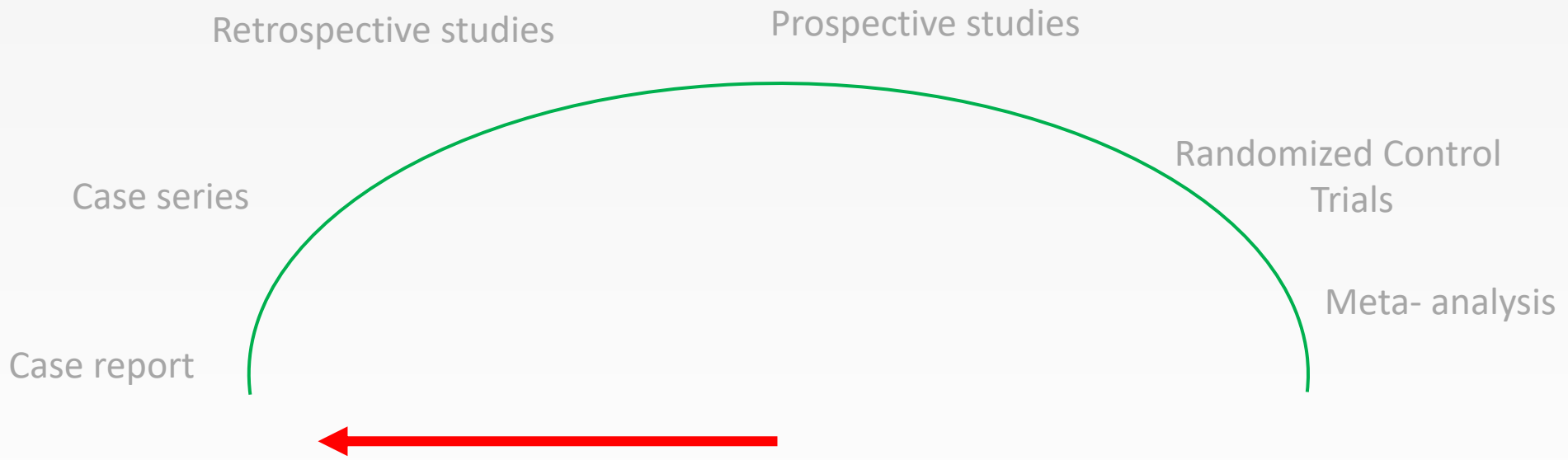
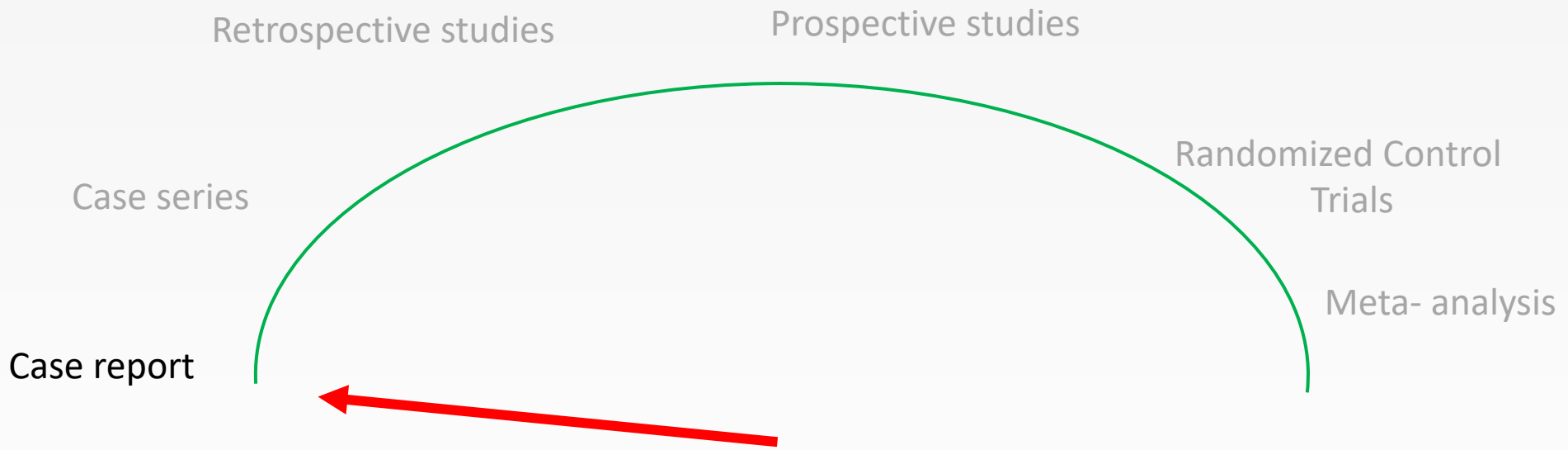
Study designs explained

Rajvinder Singh
Professor of Medicine
Director of Gastroenterology
Lyell McEwin Hospital/ University of Adelaide
Past Chair of the Australian Gastrointestinal Endoscopic Association (AGEA)
AUSTRALIA

Evidence Barometer



Evidence Barometer: Case report



Case report

- Purely descriptive
- Often used in ‘new’ disease/intervention describing salient features
- Difficult to publish…

A case of a false target sign

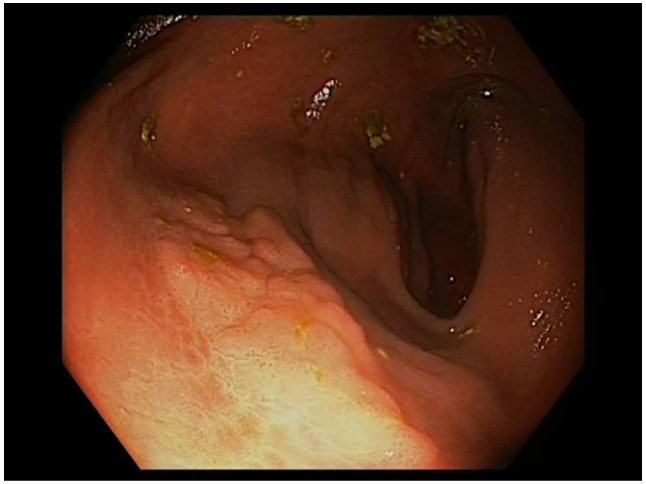


Figure 1 ••.

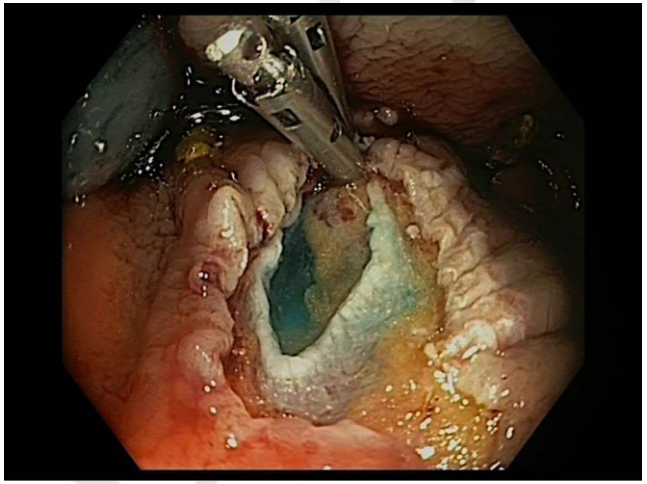


Figure 3 ••.

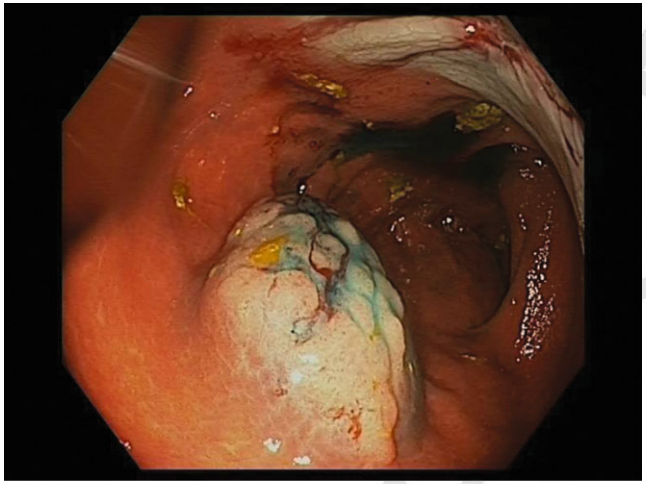


Figure 2 ••.

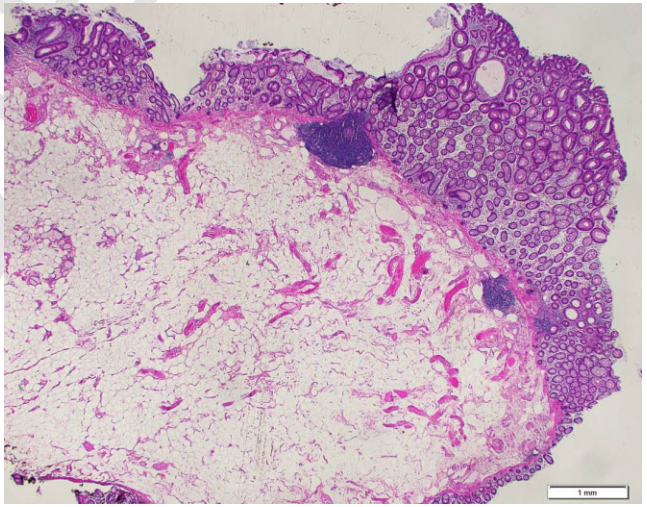


Figure 4 ••.

A Shaikh, R Singh et al JGH 2015

False sense of security: a case of retroperitoneal perforation after colonic EMR

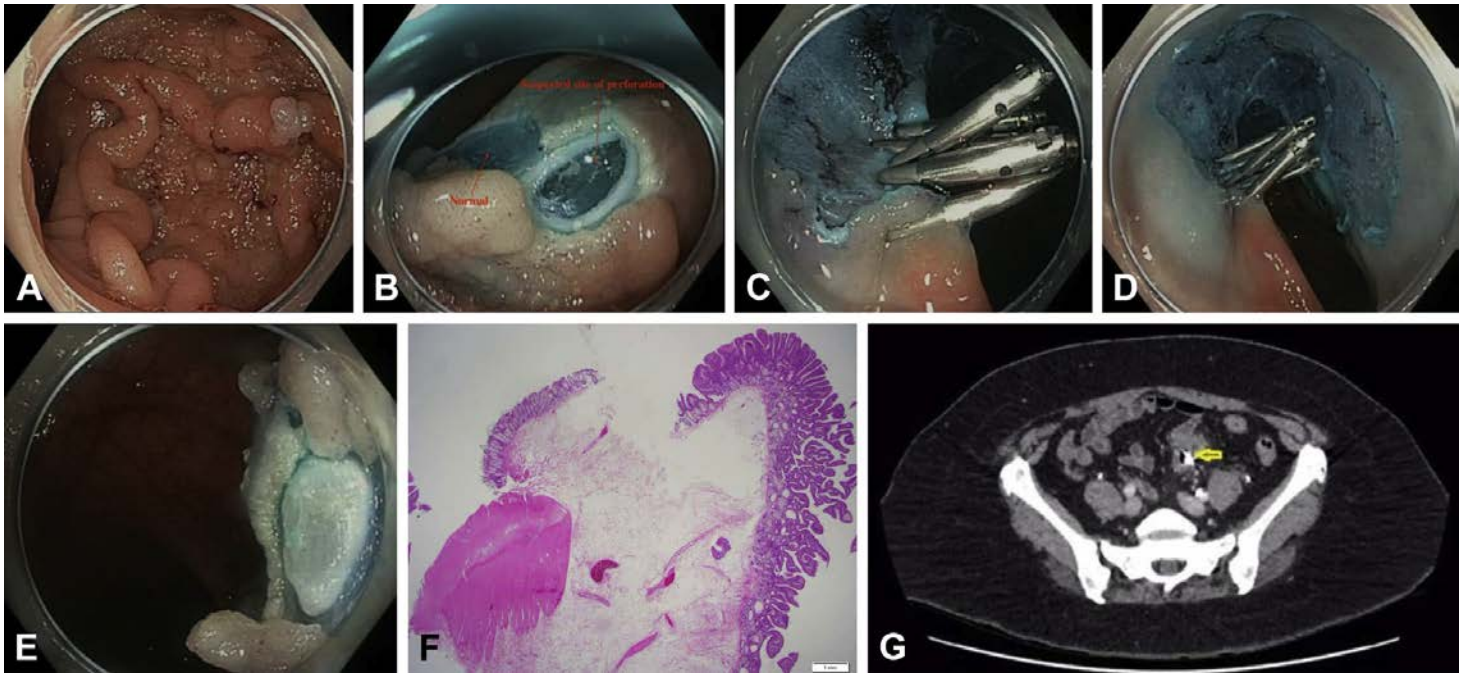
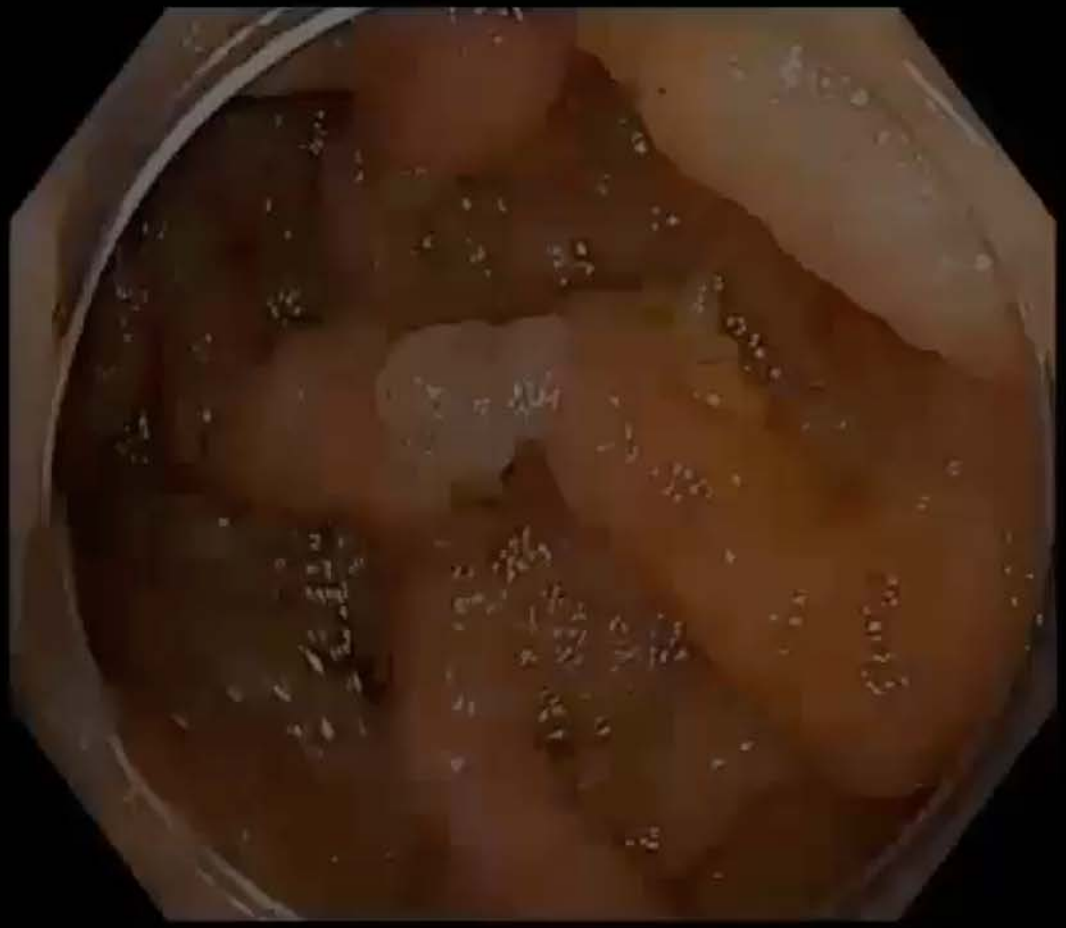
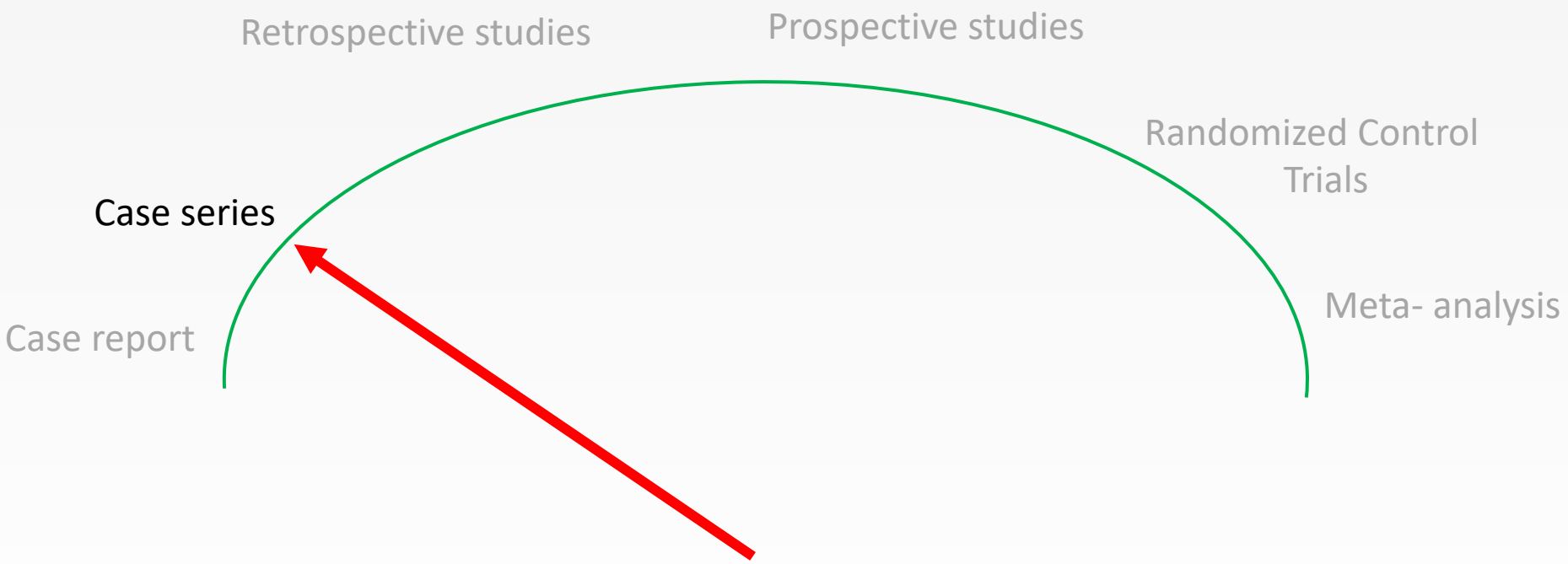


Figure 1. A, Laterally spreading tumor at the rectosigmoid junction. **B,** Suspected site of perforation, with a whitish circular ring and bluish base. **C,** Closure of perforation with 6 hemoclips. **D,** Resection of remainder of the polyp. **E,** Resected specimen showing the target sign. **F,** Histology slide showing the muscularis propria, confirming the perforation. **G,** Abdominal CT view showing no evidence of perforation. *Yellow arrow* indicates endoscopic clips.

LST



Evidence Barometer: Case series



Case series

- Purely descriptive study
- Often used in ‘new’ diseases/intervention
- Multiple cases of a condition combined and analyzed
- No control group
- Generally retrospective (with prospectively collected data increasingly becoming ‘the ‘flavor)

GASTROENTEROLOGY IN MOTION

Ralf Kiesslich and Thomas D. Wang, Section Editors

Expanding the Boundaries of Endoscopic Resection: Circumferential Laterally Spreading Lesions of the Duodenum

Amir Klein, Nicholas Tutticci, Rajvinder Singh, and Michael J. Bourke

Department of Gastroenterology and Hepatology, Westmead Hospital, Sydney, Australia

Table 1. Patient, Lesion, Procedure Characteristics, and Outcomes

Characteristic	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11
Age, y (sex)	72 (F)	75 (F)	79 (F)	66 (F)	59 (M)	70 (F)	78 (F)	58 (F)	80 (M)	77 (F)	73 (F)
Location	D2+	D2+	D2+	D1-D2	D2-D3	D2	D2+	D3	D2+	D2+	D2+
Longitudinal extent (mm)	60	70	60	80	60	60	80	80	80	80	80
Circumferential extent (%)	80	100	90	100	100	80	80	95	100	100	100
Histology	TVA+LGD	TVA+LGD	TVA+LGD	TVA+LGD	TVA+LGD	TVA+LGD	TVA+LGD	TVA+LGD	Whipple - TVA+HGD	Whipple - invasive CA	Whipple - invasive CA
Endoscopic resection attempted	Yes (C)	Yes (IC)	Yes (C)	Yes (C)	Yes (C)	Yes(C)	Yes (C)	Yes (C)	No (luminal stenosis – surgery)	No (luminal stenosis + non lifting – surgery)	No (depressed area with altered pit-pattern – surgery)
Procedure time (min)	180		250	180	120		180		NA	NA	NA
Intra-procedural bleeding	Yes (minor)	Yes (minor)	Yes (minor)	Yes (minor)	Yes (minor)	Yes (minor)	Yes (minor)	Yes (minor)	NA	NA	NA
Delayed bleeding	Minor melena and HB drop – no Tx.	Hematemesis on POD1. Spurting vessel on endoscopy treated with coagulation graspers. PCX2	Nil	Melena and HB drop POD 1. Spurting vessel on endoscopy – treated with injection and clip.	Hematemesis POD 10. Spurting vessel on endoscopy treated with coagulation grasper	Nil	Nil	Nil	NA	NA	NA
Days in hospital post procedure	3	15	3	9	7	2	4	3	NA	NA	NA
Stenosis (# of dilatations)	Nil	Nil	Nil	Yes (3)	Yes (3)	Nil	Yes (1)	Nil	NA	NA	NA
SE1	Diminutive residual – treated	Residual – treated endoscopically	Two foci of residual. Treated endoscopically	Clear	Clear	Clear	Clear	Clear	NA	NA	NA

Klein, Tutticci, Singh, Bourke. Gastroenterology 2017

Lessons from this case series

- Large Duodenal LST's are uncommon, mostly in D2 and do not harbor invasive disease
- Wide field single session EMR in duodenal LST's possible
- High risk of delayed bleeding : 37%
- High risk of strictures: warn patient and prepare to dilate sequentially
- Risk of recurrence common but easily dealt with

Endoscopic journals which accepts case reports/reviews..

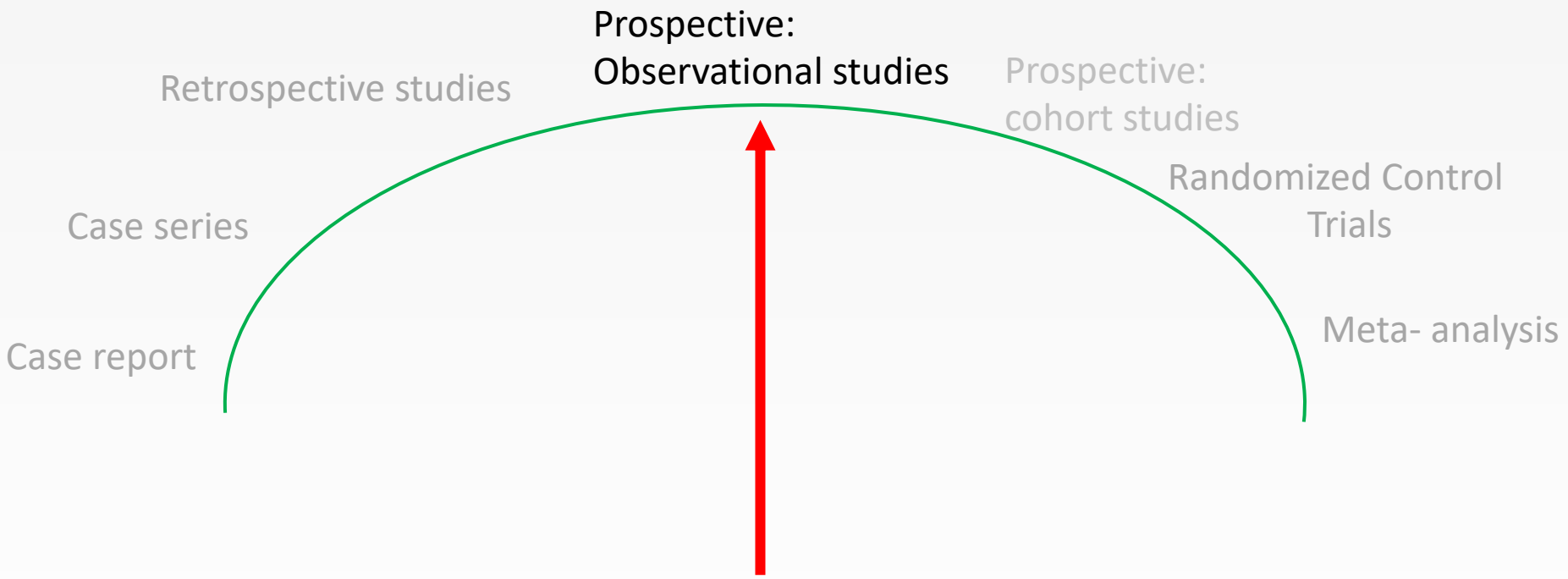
- Gastroenterology
- Endoscopy
- GIE
- JGH
- Digestive Endoscopy
- Video GIE

Evidence Barometer: Retrospective studies

Case control studies

- Compares group with disease vs. group without
- Looks for exposure or risk factors
- Opposite of cohort study
- Main outcome is odds ratio (OR):
  Odds of disease in exposed Odds of disease in unexposed
- Advantages: quick, cheap(er) and easy to perform, better for rare diseases, minimal/no loss to follow up
- Disadvantages: Recall bias, if onset of disease preceded exposure to disease, **causation cannot be inferred**

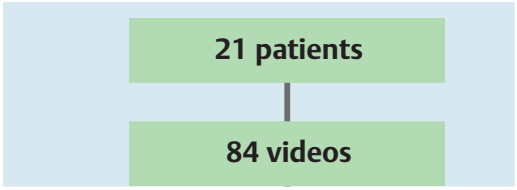
Evidence Barometer: Prospective observational studies

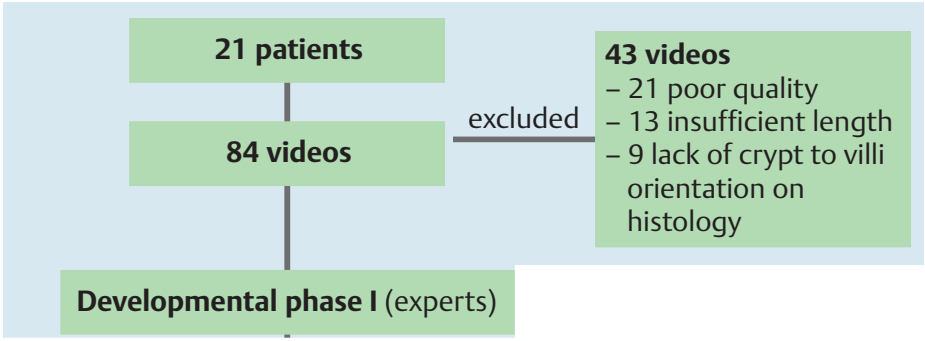


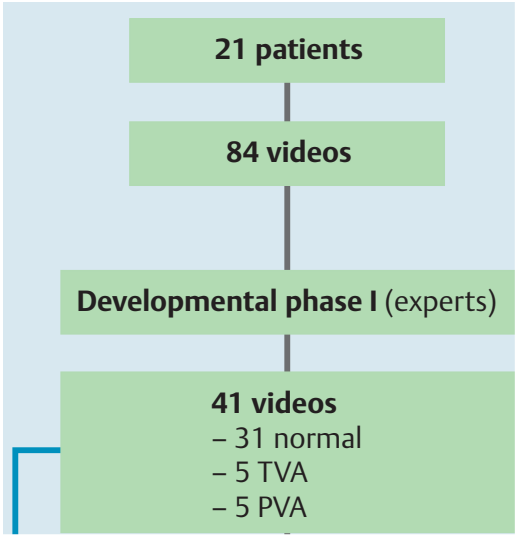
Narrow-band imaging in the evaluation of villous morphology: a feasibility study assessing a simplified classification and observer agreement

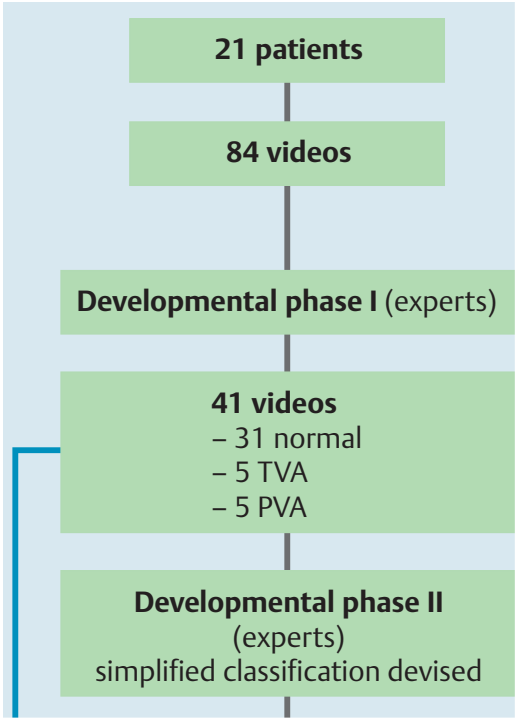
Authors R. Singh[1,2], G. Nind[1,3], G. Tucker[4], N. Nguyen[2,3], R. Holloway[2,3], J. Bate[3], M. Shetti[1], B. George[1], W. Tam[1,2,3]

Institutions
[1] The Lyell McEwin Hospital, Adelaide, South Australia, Australia
[2] University of Adelaide, South Australia, Australia
[3] The Royal Adelaide Hospital, Adelaide, South Australia, Australia
[4] Epidemiology Unit, SA Health, Adelaide, South Australia, Australia


21 patients
84 videos


21 patients
84 videos
excluded
43 videos
– 21 poor quality
– 13 insufficient length
– 9 lack of crypt to villi orientation on histology
Developmental phase I (experts)


21 patients
84 videos
Developmental phase I (experts)
41 videos
– 31 normal
– 5 TVA
– 5 PVA


21 patients
84 videos
Developmental phase I (experts)
41 videos
– 31 normal
– 5 TVA
– 5 PVA
Developmental phase II
(experts)
simplified classification devised

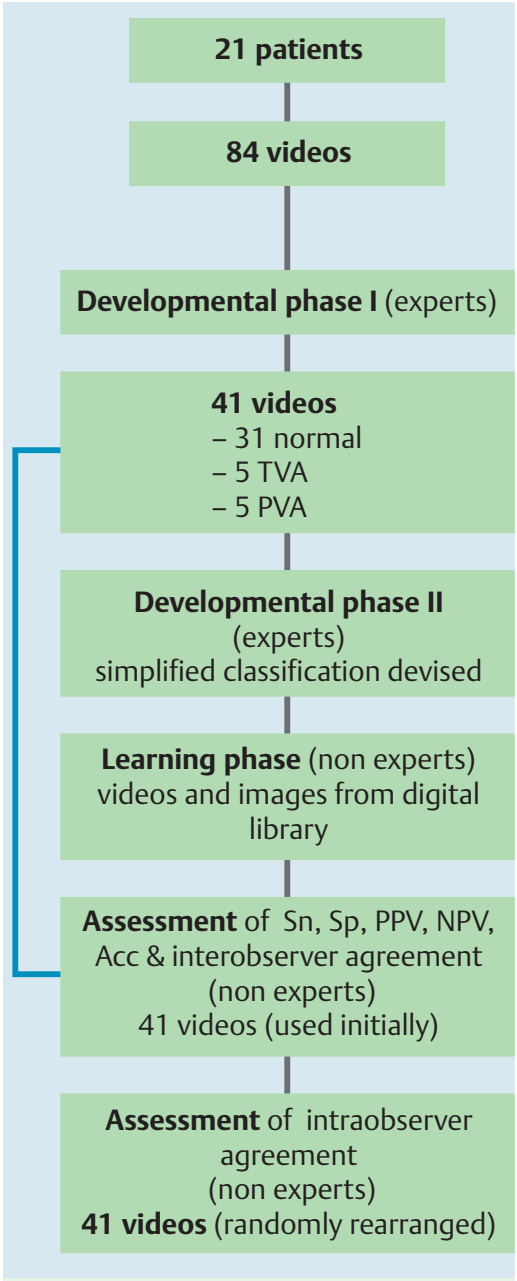
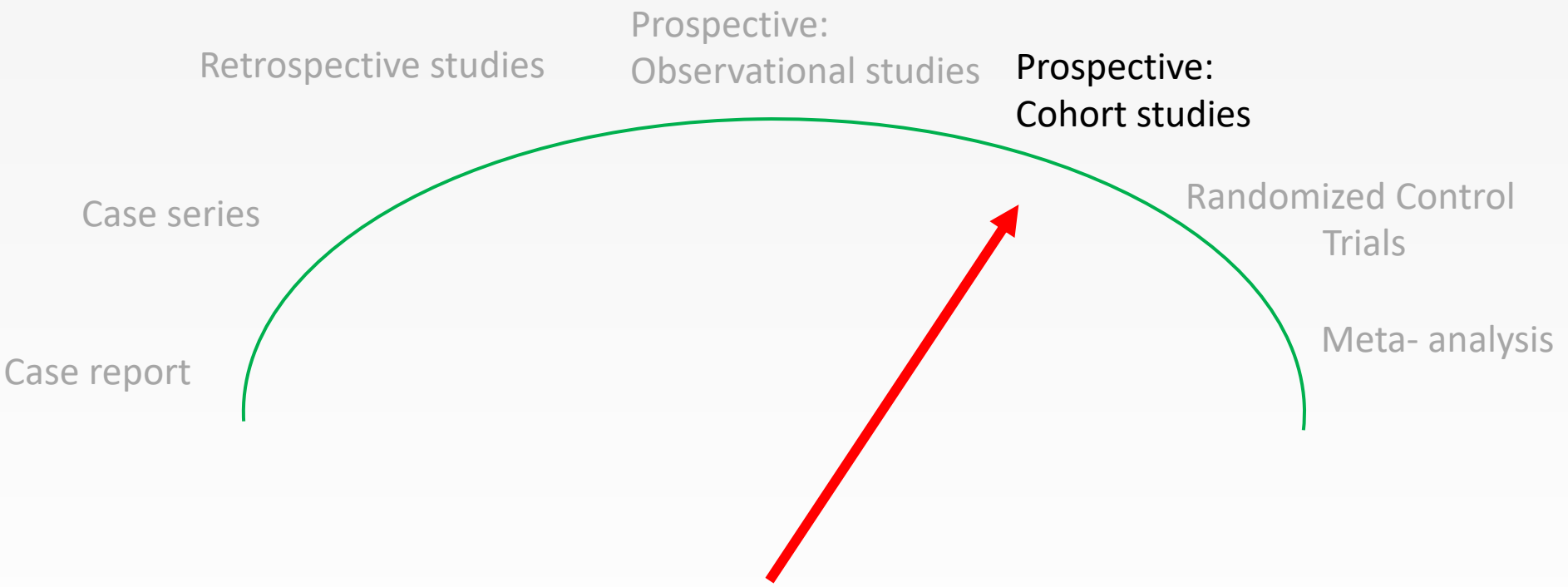


Fig. 1 Flow chart of study design.

Results

	Histology		Sn, %	Sp, %	PPV, %	NPV, %	Acc, %	Intra-OA	Inter-OA
	N	VA							
Endoscopist 1									
N	31	1	90	100	100	96.9	97.6	0.93	
VA	0	9							
Endoscopist 2									0.82
N	30	0	100	96.8	90.9	100	97.6	0.77	
VA	1	10							
Endoscopist 3									
N	30	1	90	96.8	90.0	96.8	95.1	0.87	
VA	1	9							

Evidence Barometer: Prospective observational studies

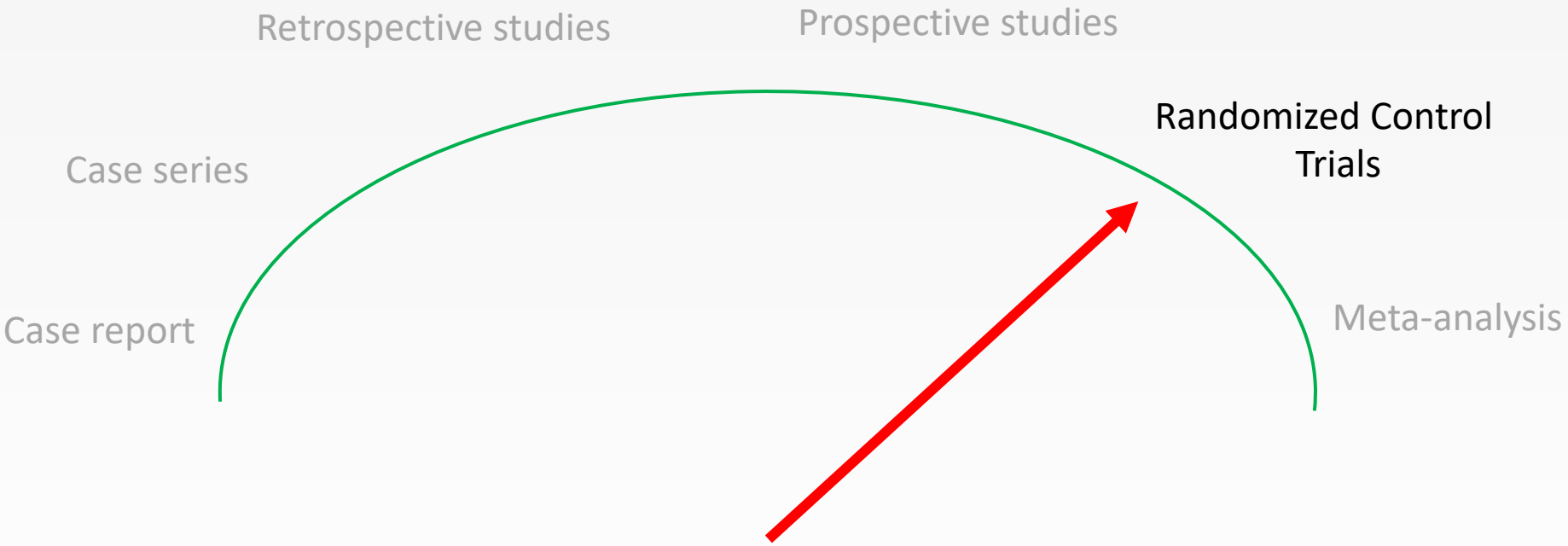


Cohort studies

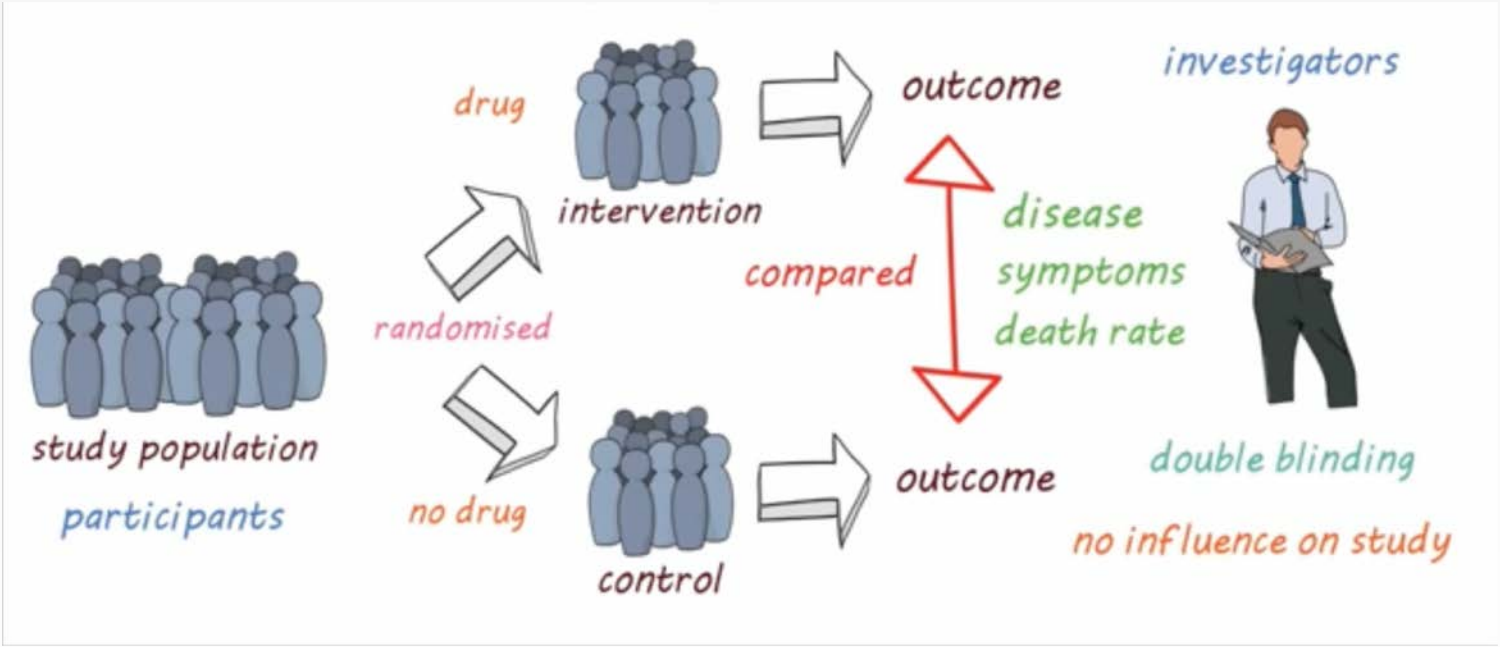
- Compares group with exposure vs. group without….over a period of time
- ‘Healthy entrants’
- Did exposure change likelihood of disease?
- Main outcome measure is the relative risk (RR): how much does exposure/intervention increase or decrease the risk/progression
- Advantages: Exposure can be measured over a range of time frames - time sequence can be assessed
- Problems:

1. over a long period of time
2. difficult to maintain consistency
3. individuals may ‘modify’ their behavior
4. can be costly
5. does not work in rare diseases

Evidence Barometer: RCT



RCT- simplified



RCT

- Advantages:

- Randomization = equal chance
- Blinding
- Causality

- Disadvantages:

- Expensive
- Many participants: recruitment can be difficult

RCT : CONSORT

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item
Title and abstract		
	1a	Identification as a randomised trial in the title
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts[21 31])
Introduction		
Background and objectives	2a	Scientific background and explanation of rationale
	2b	Specific objectives or hypotheses

RCT : CONSORT

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item
Title and abstract		
	1a	Identification as a randomised trial in the title
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts[21 31])
Introduction		
Background and objectives	2a	Scientific background and explanation of rationale
	2b	Specific objectives or hypotheses
Methods		
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons
Participants	4a	Eligibility criteria for participants
	4b	Settings and locations where the data were collected
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
	6b	Any changes to trial outcomes after the trial commenced, with reasons

RCT : CONSORT

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item
Title and abstract		
	1a	Identification as a randomised trial in the title
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts[21 31])
Introduction		
Background and objectives	2a	Scientific background and explanation of rationale
	2b	Specific objectives or hypotheses
Methods		
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons
Participants	4a	Eligibility criteria for participants
	4b	Settings and locations where the data were collected
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
	6b	Any changes to trial outcomes after the trial commenced, with reasons
Sample size	7a	How sample size was determined
	7b	When applicable, explanation of any interim analyses and stopping guidelines
Randomisation:		
Sequence generation	8a	Method used to generate the random allocation sequence
	8b	Type of randomisation; details of any restriction (such as blocking and block size)
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how
	11b	If relevant, description of the similarity of interventions
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses

RCT: CONSORT

Results		
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome
	13b	For each group, losses and exclusions after randomisation, together with reasons
Recruitment	14a	Dates defining the periods of recruitment and follow-up
	14b	Why the trial ended or was stopped
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[28])

RCT: CONSORT

Results		
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome
	13b	For each group, losses and exclusions after randomisation, together with reasons
Recruitment	14a	Dates defining the periods of recruitment and follow-up
	14b	Why the trial ended or was stopped
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[28])
Discussion		
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses
Generalisability	21	Generalisability (external validity, applicability) of the trial findings
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence

RCT: CONSORT

Results		
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome
	13b	For each group, losses and exclusions after randomisation, together with reasons
Recruitment	14a	Dates defining the periods of recruitment and follow-up
	14b	Why the trial ended or was stopped
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[28])
Discussion		
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses
Generalisability	21	Generalisability (external validity, applicability) of the trial findings
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
Other information		
Registration	23	Registration number and name of trial registry
Protocol	24	Where the full trial protocol can be accessed, if available
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders

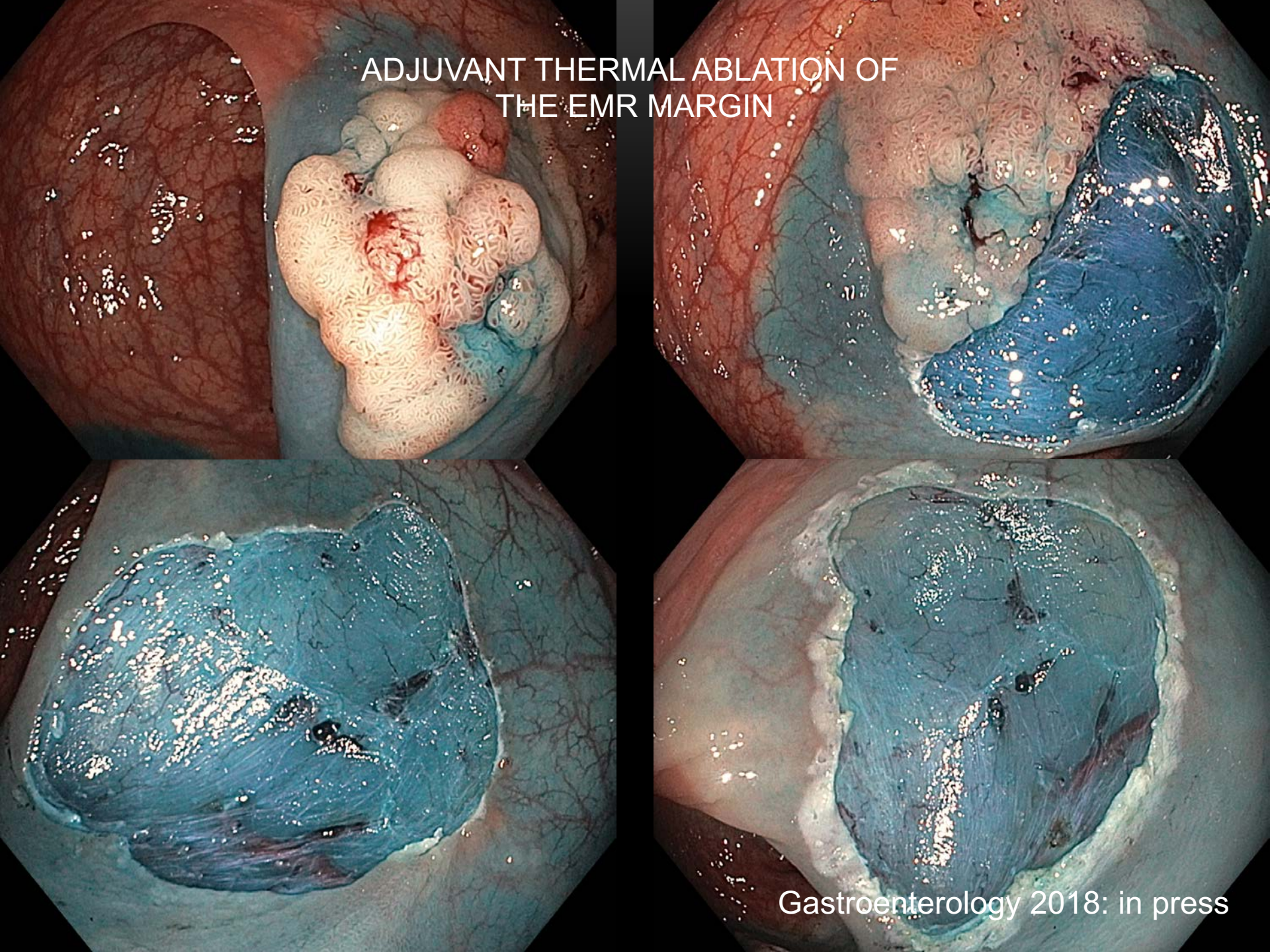
A MULTI-CENTRE RANDOMIZED CONTROL TRIAL OF SNARE TIP SOFT COAGULATION FOR THE PREVENTION OF ADENOMA RECURRENCE FOLLOWING COLONIC EMR

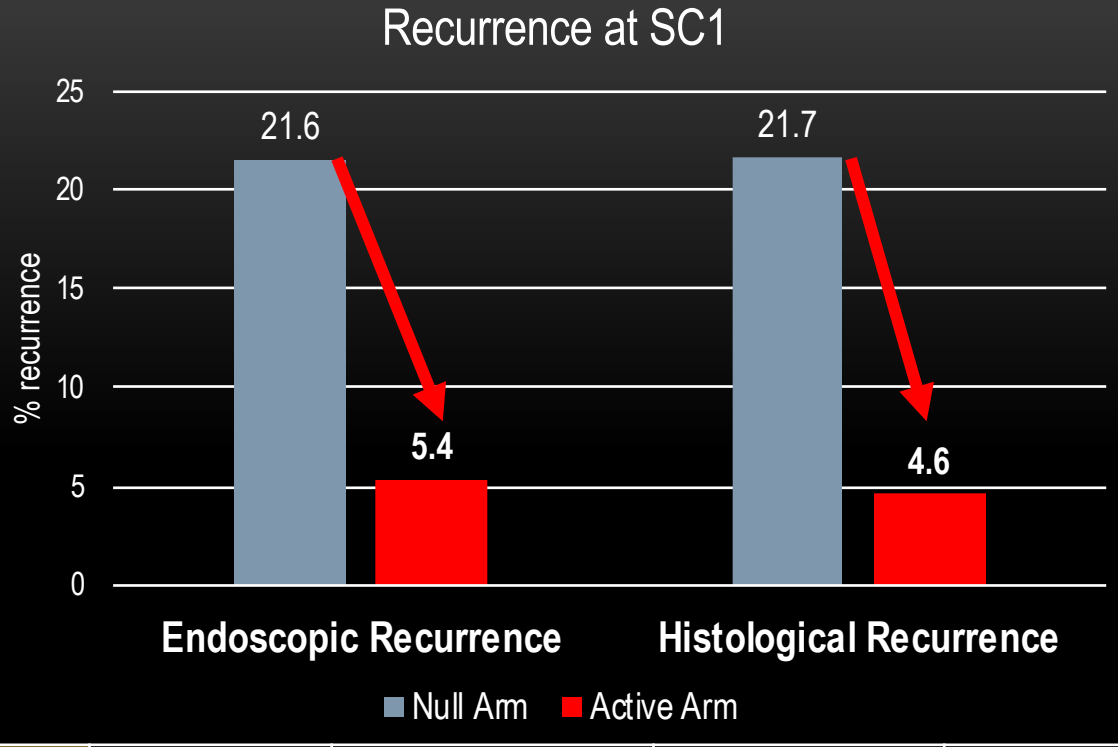
RESULTS FROM THE "SCAR" STUDY

Amir Klein[1], Vanoo Jayasekeran[1], Luke Hourigan[3], Rajvinder Singh[5], Gregor Brown[4], David J Tate[1]
Farzan F Bahin[1,2], Nicholas Burgess[1,2], Stephen J Williams[1], Eric Lee[1], Michael J Bourke[1,2]

[1]Department of gastroenterology and hepatology, Westmead hospital Sydney; [2]University of Sydney; [3]Department of gastroenterology and hepatology Princess Alexsandra Hospital Brisbane; [4]Department of gastroenterology and hepatology Alfred Hospital Melbourne; [5]Department of gastroenterology and hepatology Lyell McEwin Hospital Adelaide

Gastroenterology 2018: in press


ADJUVANT THERMAL ABLATION OF
THE EMR MARGIN
Gastroenterology 2018: in press

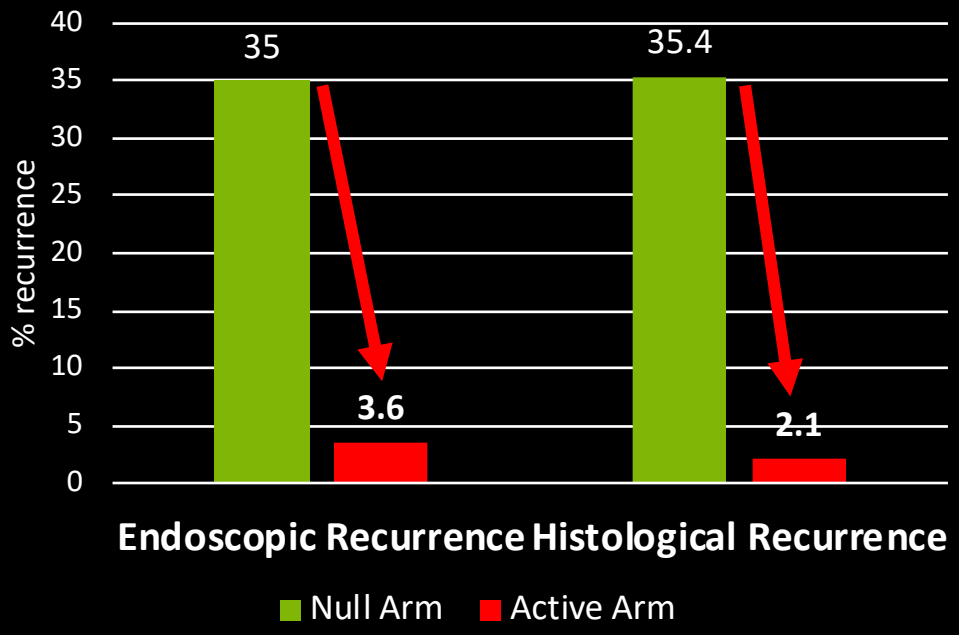


SC1	Null arm	Active arm	RR	NNT	p
Endoscopic recurrence	21.6% (33/153)	5.4% (9/167)	0.25	6.17	< 0.001
Histological recurrence	21.7% (26/120)	4.6% (6/131)	0.21	5.89	< 0.001

Gastroenterology 2018: in press

RESULTS – SUBGROUP ANALYSIS LSL > 40MM

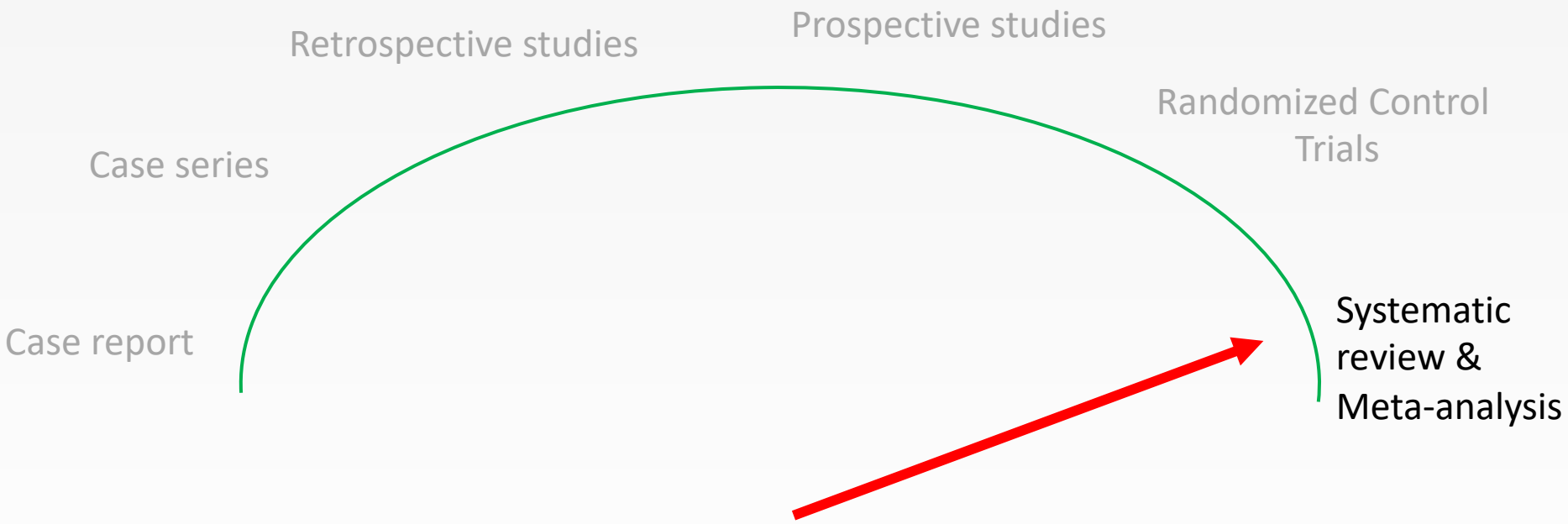
- Lesions >= 40mm
- n=151 (115 completed SC1), median size 50 mm
- Recurrence rate at SC1



LSL>= 40mm	Null arm	Active arm	RR	p
Endoscopic Recurrence	35.0% (21/60)	3.6% (2/55)	0.10	<0.001
Histological Recurrence	35.4% (17/48)	2.1% (1/47)	0.06	<0.001

Gastroenterology 2018: in press

Evidence Barometer: Meta-analysis



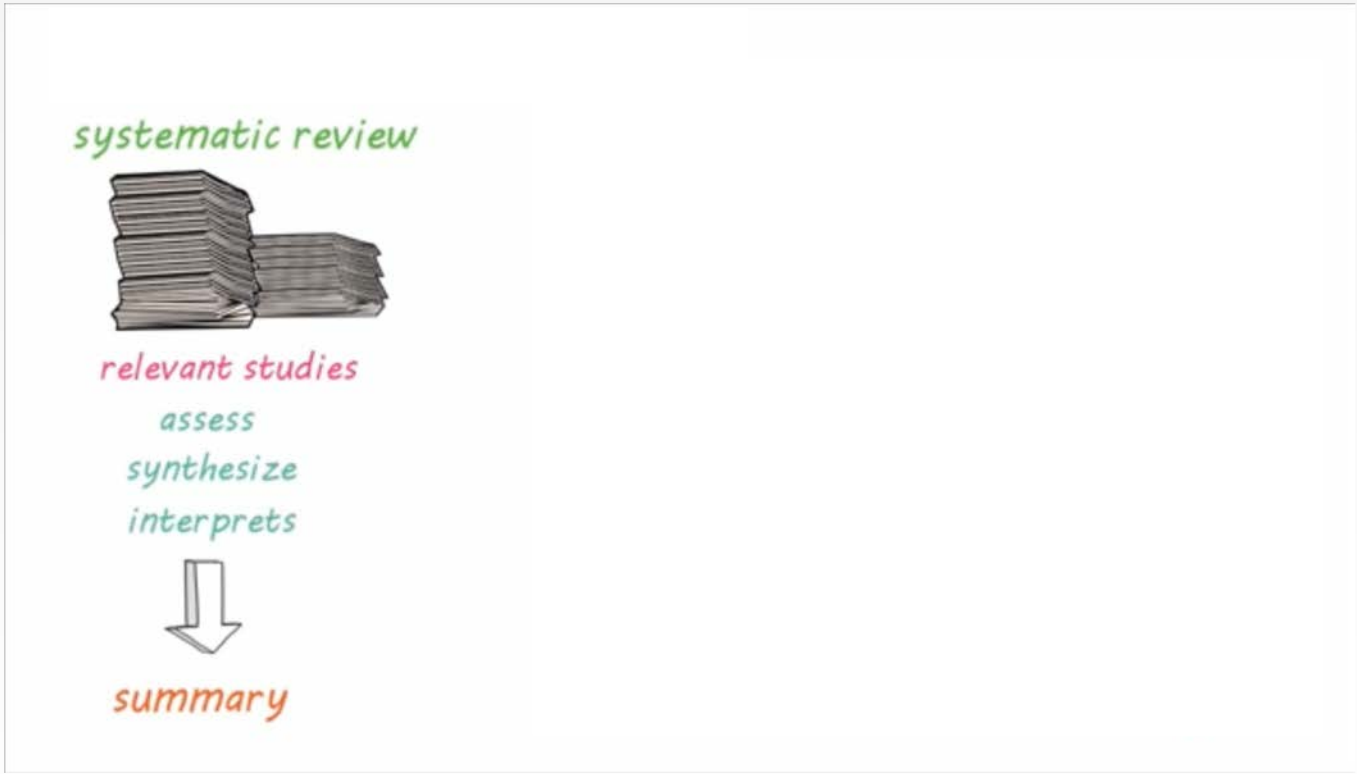
Systematic review

- Is a formalized and stringent process of combining the information from all relevant studies (published and unpublished) of the same health condition

1. Large quantities of information refined and reduced to a manageable size
2. Usually quicker and less costly to perform than a new study (may prevent others embarking on unnecessary studies)
3. Generalizable to a larger population
4. Consistencies (and inconsistencies) of different studies assessed

- Main difference from meta-analysis is it relies on interpretation of data instead of combining statistical results

Systematic review- simplified



Surgery versus radical endotherapies for early cancer and high grade dysplasia in Barrett's oesophagus (Review)

Bennett C, Green S, Barr H, Bhandari P, DeCaestecker J, Ragunath K, Singh R, Tawil A, Jankowski J

THE COCHRANE COLLABORATION®

Why perform this review?

- To examine the effectiveness of endotherapies (the intervention) compared with surgery (the control), in two groups of people with Barrett's oesophagus;
  - Early neoplasia (HGD) vs. Early cancer

1) In patients with either HGD or early cancer, who received either endotherapies or surgery, what are the overall survival rates at 1, 5 or more years?

2) In HGD, the effect of the therapies on rates of progression to cancer and for people having early cancer, progression to more invasive cancer

Gastrointestinal Endoscopic Society of Australia (GESA)

Carbapenemase-Producing Enterobacteriaceae (CPE) Infection Control in Endoscopy Consensus Statement

JGH 2018: in press

Carbapenemase-Producing Enterobacteriaceae (CRE/CPE)

- Confer broad resistance to most ß-lactam antibiotics including “last-line” carbapenems
- Serious infections: Intra-abdominal infection, pneumonia, UTI, device related infections
- US: 9000 health-care associated infections→ 600 deaths/year
- Limited selection of treatment strategies
- Asymptomatic colonisation
- “Urgent public health threat”

Delphi Methodology

- Statements formulated and randomly distributed to committee members (3 pairs of two)
- Extensive literature review
- Statements voted on anonymously
- 1st electronically (Survey Monkey)
- 2nd Face to face meeting (www.multimeter.com)
- Statements reviewed/revised/appraised:
  - Acceptance or rejection of statement
  - Level of supporting evidence
  - Grading of the recommendation
- Consensus statement accepted if 5/6 of votes were ‘completely accepted’ or ‘accept with some reservation’

Statement Grading and Recommendation

Level/grade	Description
Evidence level	
I-A	Evidence from meta-analysis of RCTs
I-B	Evidence from at least 1 RCT
II-A	Evidence from at least 1 controlled study without randomization
II-B	Evidence from at least 1 other type of quasi-experimental study
III	Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both
Recommendation grade	
A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated recommendation from category I evidence
C	Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D	Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence
Voting on recommendation	
A	Accept completely
B	Accept with some reservation
C	Accept with major reservation
D	Reject with reservation
E	Reject completely

Adapted from Shekelle et al.[2]

1. Evidence Level
2. Recommendation Grade
3. Voting on the Recommendation

Shekelle PG, Woolf SH, Eccles M et al.
West J Med 1999;170:348-51

‘Expert’ consensus

Guidelines

OPEN ACCESS

Asia-Pacific working group consensus on non-variceal upper gastrointestinal bleeding: an update 2018

Joseph JY Sung,[1] Philip CY Chiu,[1] Francis K L Chan,[1] James YW Lau,[1] Khean-lee Goh,[2] Lawrence HY Ho,[3] Hwoon-young Jung,[4] Jose D Sollano,[5] Takuji Gotoda,[6] Nageshwar Reddy,[7] Rajvinder Singh,[8] Kentaro Sugano,[9] Kai-chun Wu,[10] Chun-Yin Wu,[11] David J Bjorkman,[12] Dennis M Jensen,[13] Ernst J Kuipers,[14] Angel Lanas[15]

Gut 2017

Methodology

- The Asia-Pacific Working Group of upper GI bleeding comprises key opinion leaders in the region/countries of Asia and Australasia: (Australia, China, Hong Kong, India, Japan, Korea, Malaysia, Philippines, Singapore and Taiwan). International experts from Europe and North America were also invited to share new scientific data and discuss the consensus statements

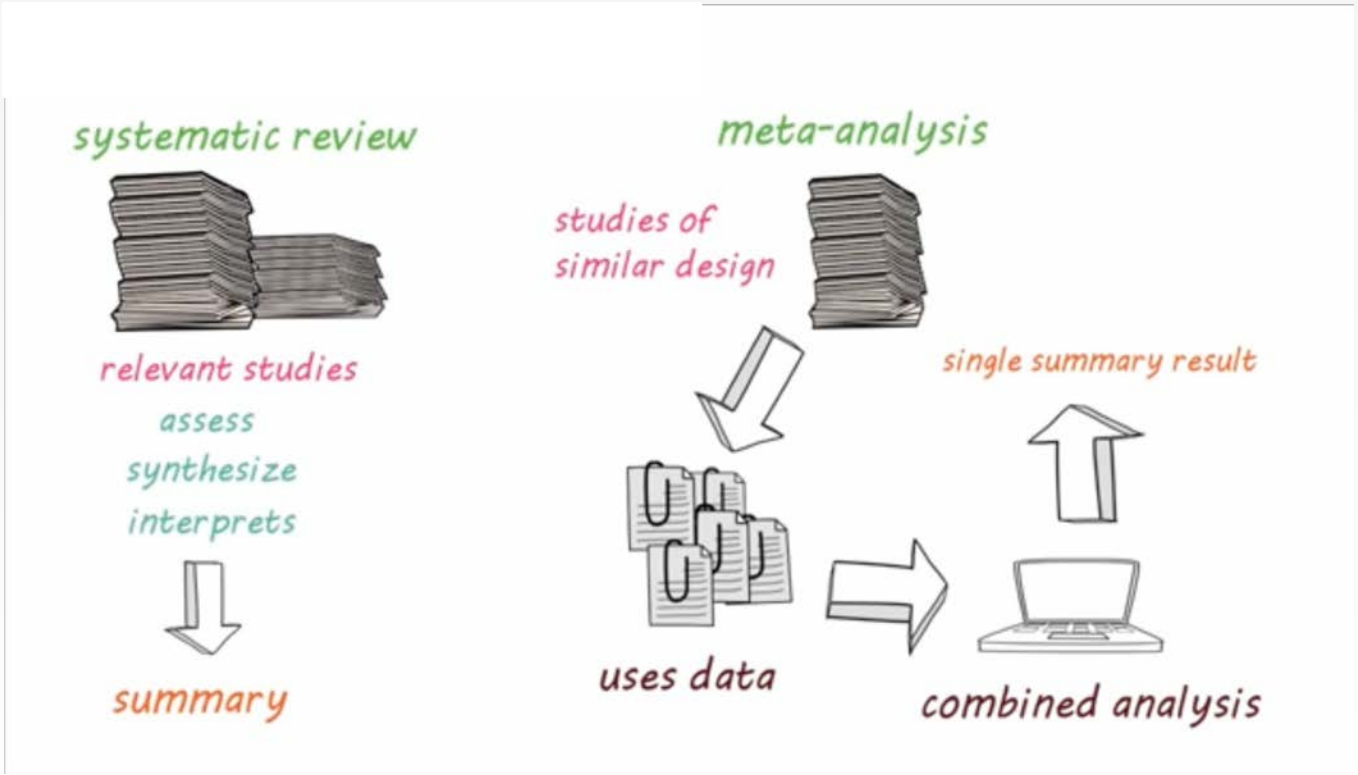
- Literature search include Medline, EMBASE, the Cochrane Central Register of Controlled Trials and ISI Web of Knowledge with manual searches of bibliographies of key articles and abstracts of major gastroenterology conferences held in the past 5 years, 2012–2017: APDW, DDW, UEGW

- Key words used included gastrointestinal bleeding, peptic ulcer disease and Asia

Methodology

- A modified Delphi process was used, and these drafted statements were sent to all group members for voting before the meeting, together with evidence-based reviews and other pertinent literature
- Each statement was assessed on a five-point Likert scale: (1) accept completely, (2) accept with some reservation, (3) accept with major reservation, (4) reject with reservation, (5) reject completely
- Results and comments were collated by emails
- A statement was accepted when supported by ≥80% of the working group (i.e., proportion of the working group voting on the 5-point scale for 1 or 2)
- Statements that did not reach consensus support during the first-round voting were modified. These modified statements were discussed during a face to face meeting, followed by a second round of voting with electronic keypads
- Participants voted anonymously on statements after discussion and provided comments on the wording of the statements, which were progressively finalised through two separate iterations.
- If this again failed to reach consensus, the statement was rejected

Systematic review vs. Meta-analysis (simplified)



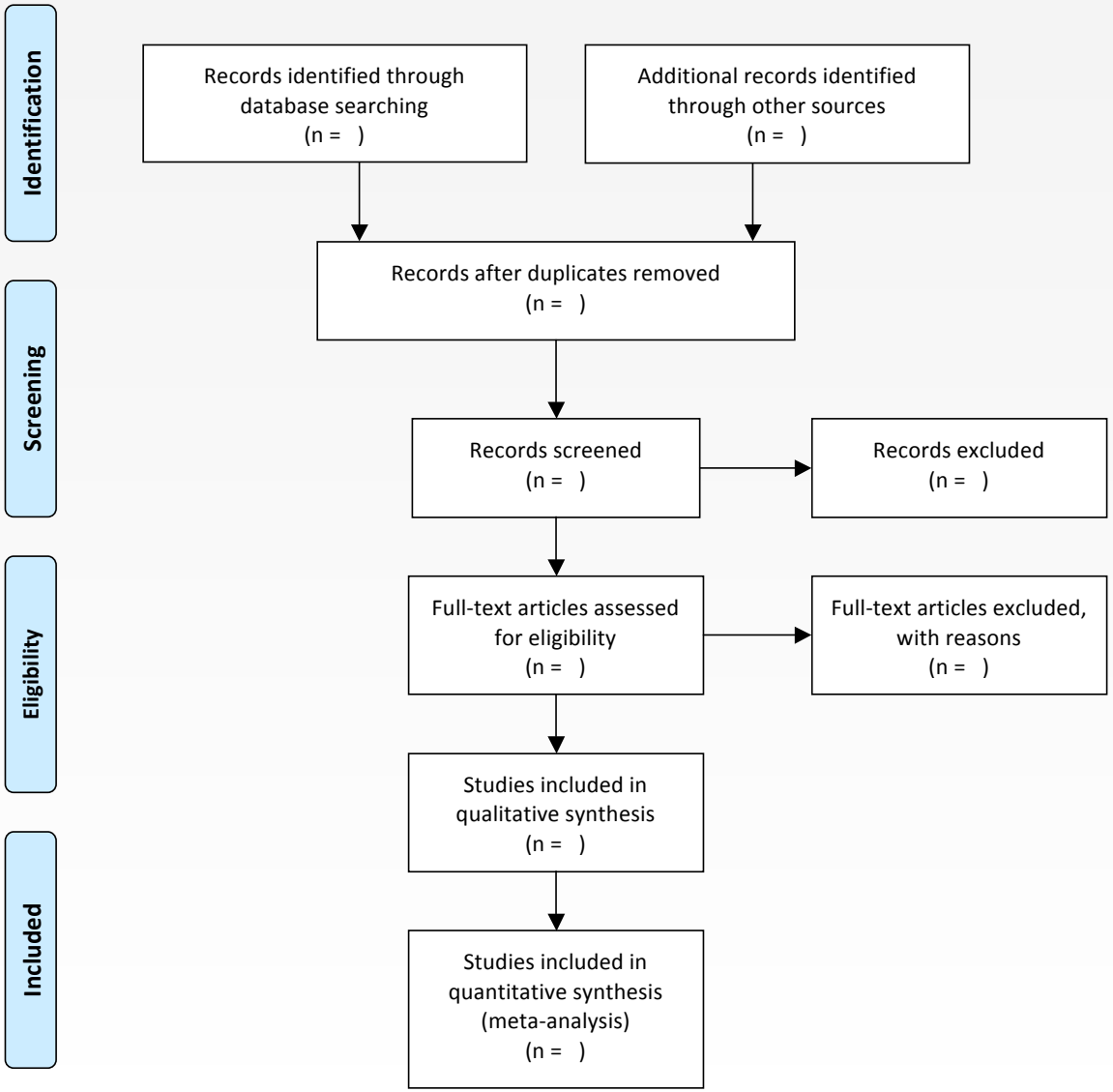
Meta-analysis

- Main aim is to compare results from individual studies to produce if appropriate an estimate of the overall effect of interest

- Advantages – similar to systematic reviews but possibly greater effect (greater precision - meta-analysis softwares)

- Improper use may lead to wrong conclusions
  - publication bias (funnel plot)
  - clinical heterogeneity (difference in patient population, outcome measures, duration etc. of each study)
  - Quality differences between studies (weighing systems?)
  - Dependence (when results of one study published in more than one occasion)

PRISMA 2009 Flow Diagram



Section/topic	#	Checklist item
TITLE		
Title	1	Identify the report as a systematic review, meta-analysis, or both.
ABSTRACT		
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
INTRODUCTION		
Rationale	3	Describe the rationale for the review in the context of what is already known.
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).

Section/topic	#	Checklist item
TITLE		
Title	1	Identify the report as a systematic review, meta-analysis, or both.
ABSTRACT		
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
INTRODUCTION		
Rationale	3	Describe the rationale for the review in the context of what is already known.
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).
METHODS		
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.

Section/topic	#	Checklist item
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
RESULTS		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).

Section/topic	#	Checklist item
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
RESULTS		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).
DISCUSSION		
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
FUNDING		
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.

Others…. Invited reviews/opinion

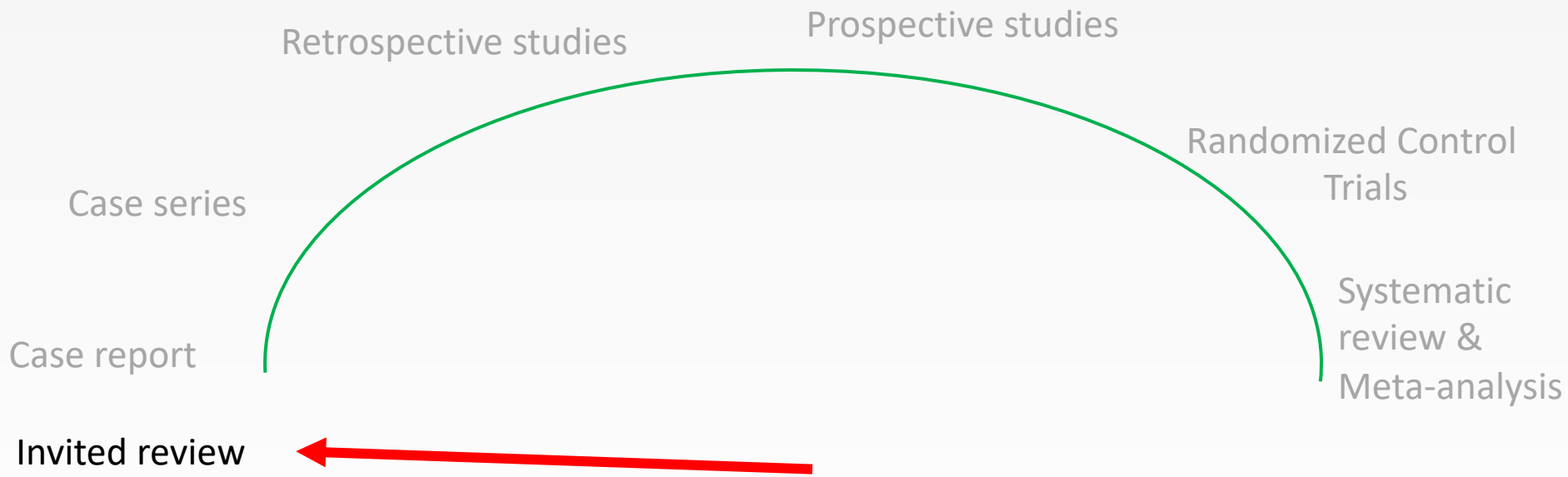
MINIREVIEWS

Sessile serrated adenoma/polyps: Where are we at in 2016?

Rajvinder Singh, Leonardo Zorrón Cheng Tao Pu, Doreen Koay, Alastair Burt

WJG 2016

Evidence Barometer



Others… Letter to the editor

Reply to Rostami et al.

R. Singh, W. Tam, G. Nind, B. George, M. Shetti, G. Tucker

We thank Rostami et al. for their interest in our paper [1]. In this feasibility study, narrow band imaging with optical magnification (NBI-Z) was clearly able to discern the villous morphology in keeping with the Marsh 3 classification.

It must be stressed that the study was performed on 21 patients suspected of having celiac disease (6 with anemia, 6 abdominal pain, 5 chronic diarrhoea, 3 bloating, and 1 with positive tissue transglutaminase [tTg]), amongst whom only three patients demonstrated the disease. We would also like to point out that all three patients were identified using the NBI-Z technology. Amongst these three, only one patient demonstrated the typical appearances on white light endoscopy as described in the critique of Rostami et al. and by other authors. NBI-Z was hence valuable in detecting two additional patients. We would therefore beg to differ with Rostami and colleagues that the Marsh 3 patients are a nonchallenging subgroup.

Furthermore, we required three NBI-naive endoscopists to grade the villous morphology after a short learning session, and were able to demonstrate relatively high accuracies (> 95 % for all three assessors) and good inter- and intraobserver agreement ($\kappa > 0.75$). This indicates that the simplified classification was not only easily learnt but also reproducible.

We agree however that this technology is unable to distinguish patients with Marsh 1 and 2 grade disease. This is mainly because of the level of magnification achieved (× 80 – 115) and hence is a drawback. Novel techniques such as endocytoscopy and confocal endomicroscopy, with magnification levels of up to × 1000 may enable this differentiation although there have been conflicting results in this regard [2 – 4].

We would therefore like to point out that NBI-Z could potentially aid the endoscopist in case-finding during routine endoscopy (as shown in our study), and the technique may also be useful for performing targeted biopsies especially in patients presenting with patchy villous atrophy. This could address the concern of Rostami et al. with regard to the frequent inadequacy of biopsy sampling by endoscopists.

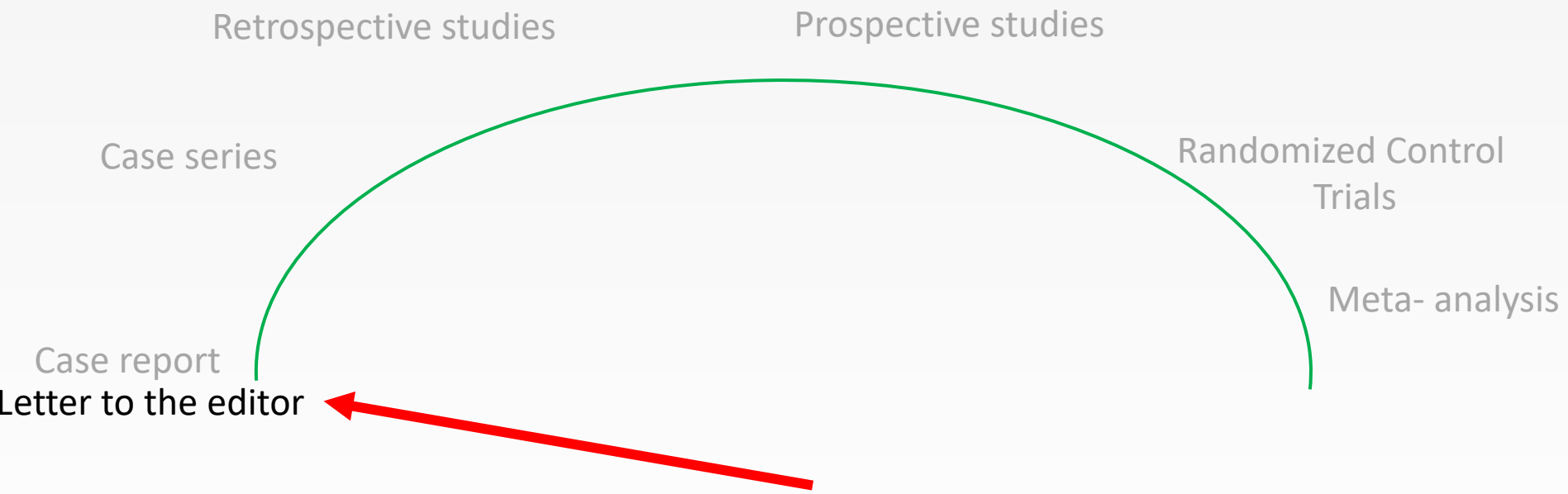
References

1 *Singh R, Nind G, Tucker G et al.* Narrow-band imaging in the evaluation of villous morphology: a feasibility study assessing a simplified classification and observer agreement. Endoscopy 2010; 42: 889 – 894
2 *Leong RW, Nguyen NG, Meredith CG et al.* In vivo confocal endomicroscopy in the diagnosis and evaluation of celiac disease. Gastroenterology 2008; 135: 1870 – 1876
3 *Pohl H, Rosch T, Tanczos B et al.* Endocytoscopy for the detection of microstructural features in adult patients with celiac sprue: a prospective, blinded endocytoscopy – conventional histology correlation study. Gastrointest Endosc 2009; 70: 933 – 941
4 *Singh R, Raju D, Chen Yi Mei SL et al.* Real-time histology with the endocytoscope. World J Gastroenterol 2010; 16: 5016 – 5019

R. Singh, MRCP, MPhil, FRACP, AM, FRCP
Lyen McEwin Hospital
University of Adelaide
Haydown Road
Elizabeth Vale SA S112
Australia
Fax: +61 8 81829837
rajvindersingh2003@yahoo.com

R Singh et al. Endoscopy 2011

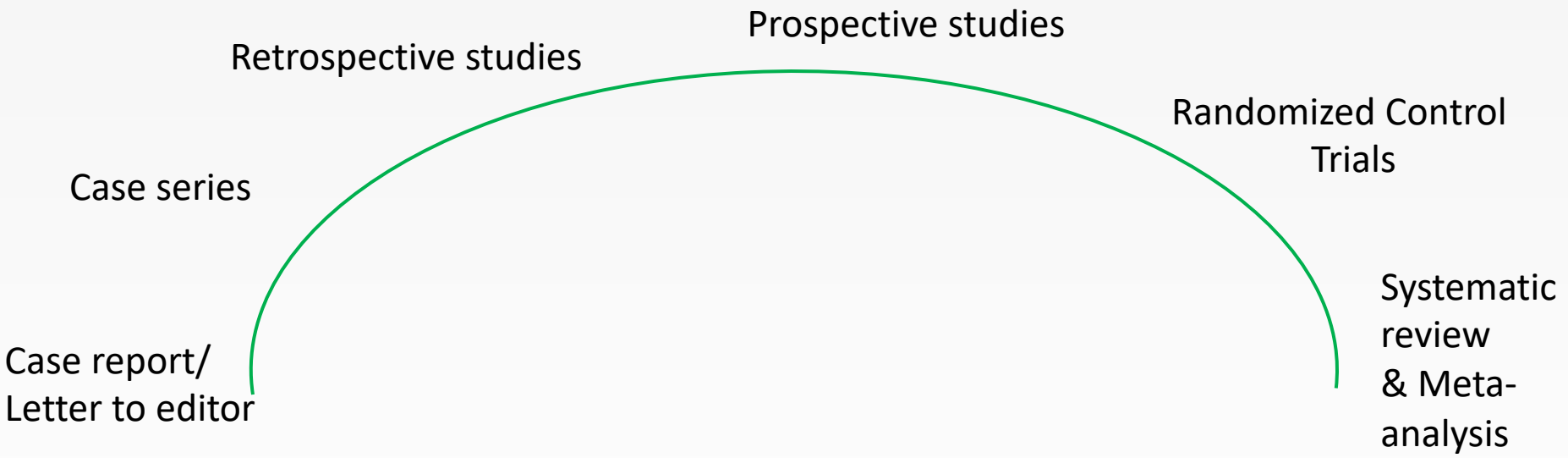
Evidence Barometer: letter to the editor



Helpful checklists

- *CONSORT statement* for RCTs
- *ARRIVE* for animal experiments
- *STROBE statement* for cross-sectional, case-control and cohort studies
- *CARE statement* for case report
- *PRISMA statement* for meta-analysis

Conclusion – study designs

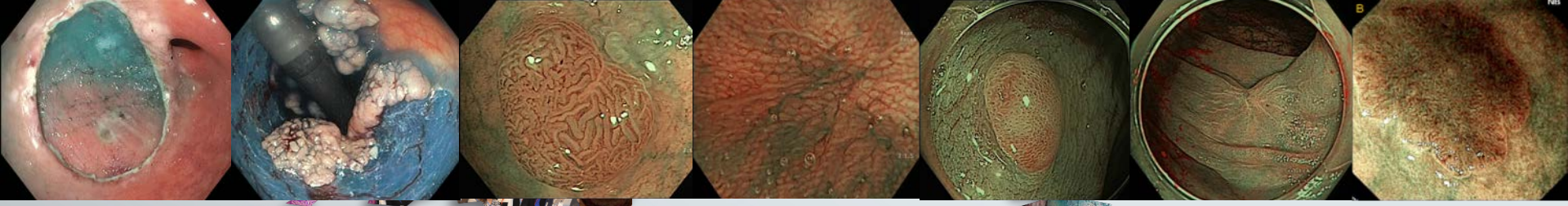


Important to select the right design…

It can be an interesting journey

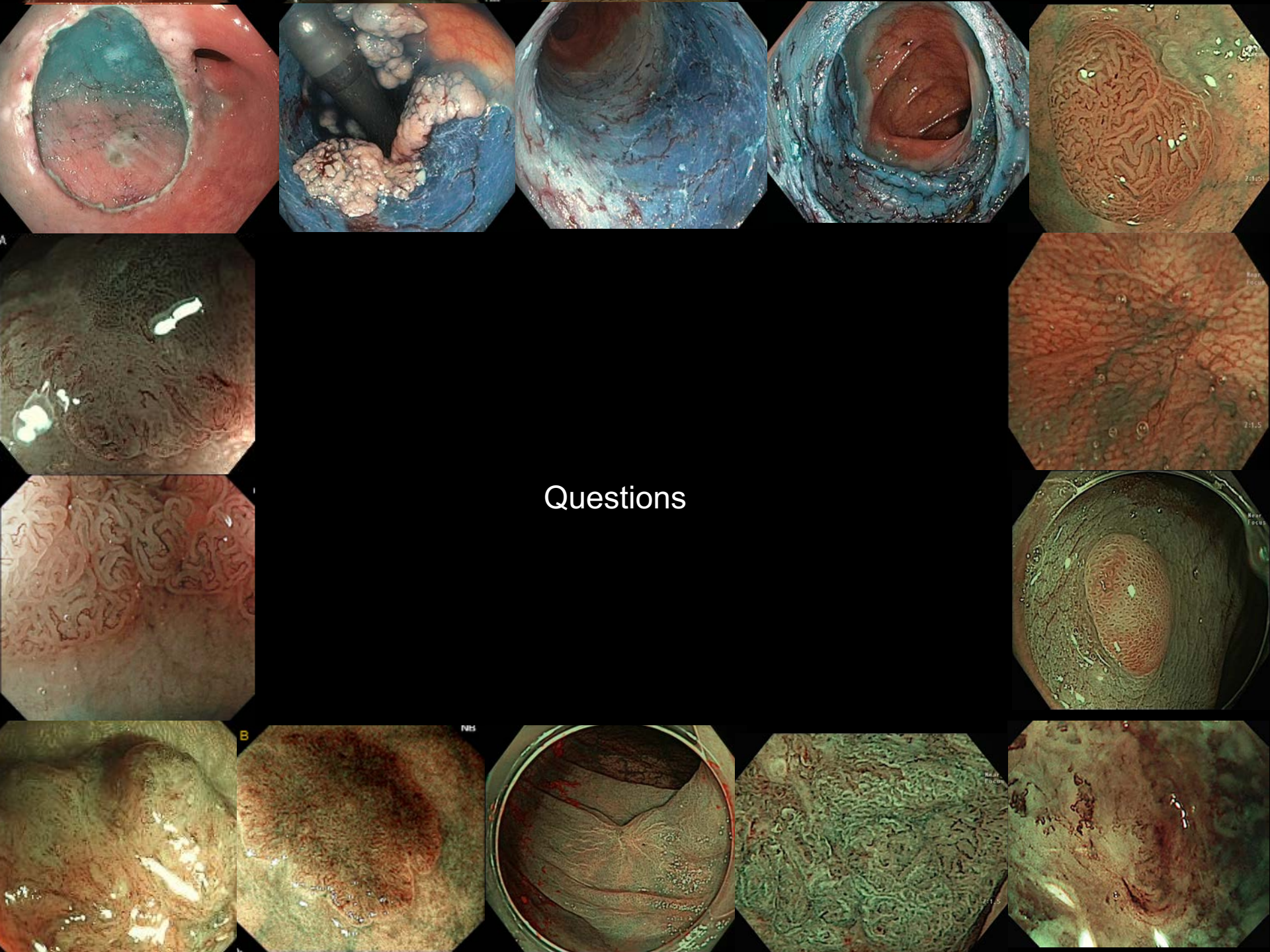
Doing research is rewarding

1. Improve clinical outcomes for your patients
2. Learn
3. Give…



Thank You

THE UNIVERSITY of ADELAIDE


Questions