SR寫作經驗分享：
如何有效的進行系統性文獻回顧

台中榮總藥學部 張雁霖藥師

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BMJ Open Gastroenterology

Efficacy of second-line regimens for *Helicobacter pylori* eradication treatment: a systemic review and network meta-analysis

- 如何開始SR這段旅程?
- 文獻評讀注意事項
- 有效的進行SR

講者介紹

- 擅長Cohort study研究設計
- 碩班研究
  - ✓ 病歷回溯
  - ✓ 藥物動力學、藥物效力學研究
- 藥學部相關研究
  - ✓ 介入型研究、精準藥學
  - ✓ **系統性文獻回顧與統合分析**

怎麼開始踏入SR?

Clinical and Experimental Medicine (2018) 18:383–390
https://doi.org/10.1007/s10238-018-0497-2

ORIGINAL ARTICLE

Good glycaemic control is associated with a better prognosis in breast cancer patients with type 2 diabetes mellitus

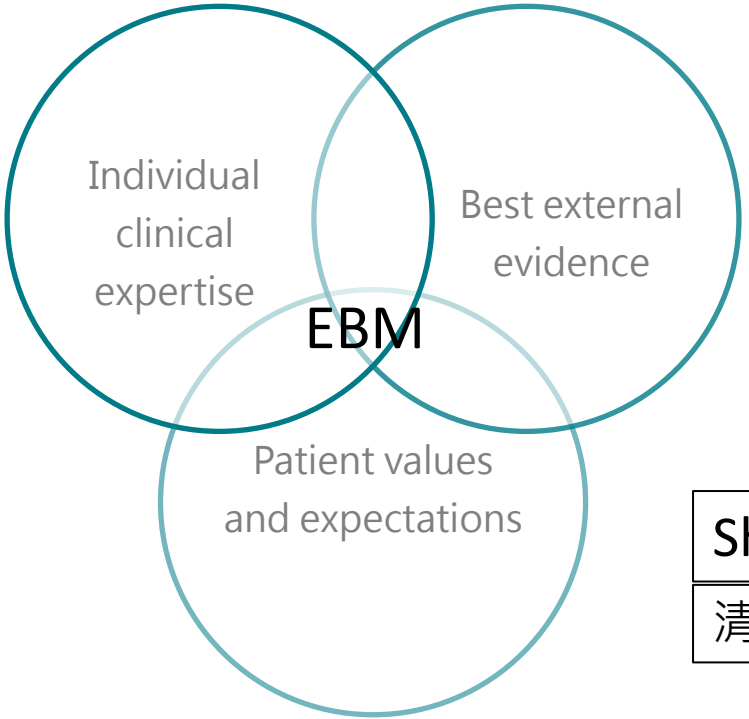
Yen-Lin Chang[1] · Wayne Huey-Herng Sheu[2,4,5,6] · Shih-Yi Lin[3,6] · Wen-Shyong Liou[1,7]

- 將introduction 視為一個小的Review
- 訂好研究主題與初步搜尋相關文獻
- 請教專家
- 孺子可教

Evidence-Based Knowledge Translation

Guideline

專家對益生菌的重要性有共識



Systematic Review

比起七天含鉍劑四合一治療，增加使用益生菌治療效果明顯更好

Shared Decision Making

清除率與經濟考量

系統性文獻回顧流程

確定題目(PICO)

計畫(Protocol)

搜尋文獻

篇名與摘要文獻篩檢

全文文獻篩檢

擷取資料

評讀文獻品質

資料合併/統合分析

PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses

1. 流程圖(flowchart)

- 如何篩選文章,如何找到你要回顧的那幾篇文章。
- “eligibility criteria”與“ study selection ”

2. Checklist表格

- 包含哪些資訊(你看了這些文章,你要整理那些東西?)
- 最主要的是“ data extraction ” “ risk of bias ”以及“ data synthesis ”

肝膽腸胃科
許斯淵醫生

Principal Investigator
Network meta-analysis
Writing

埔里分院藥劑部主任
董侑淳藥師

Systematic Reviews

藥學部
張雁霖藥師

Systematic Reviews
Writing

完成文章須要的圖表

Systemic Review

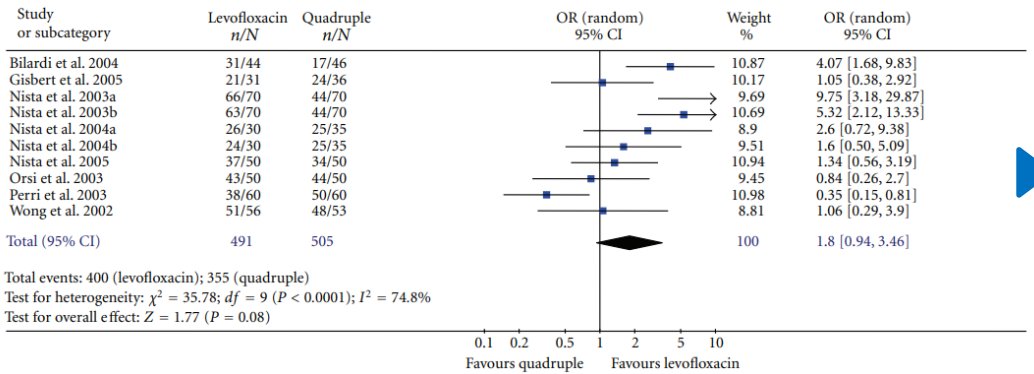
- Electronic Database Searching Strategy
- PRISMA 2009 flow diagram
- Narrations of enrolled trials
- Characteristics of enrolled trials
- Assessment of risk of bias in randomized controlled trials by ROB 2.0 assessment tool
- PRISMA Checklist

Network meta-analysis

- 網絡圖
- 直接比較
- 網絡森林圖
- SUCRA
- 漏斗圖
- 不一致性分析(Egger test、Loop inconsistency
- 次族群分析附錄圖表

如何選題?

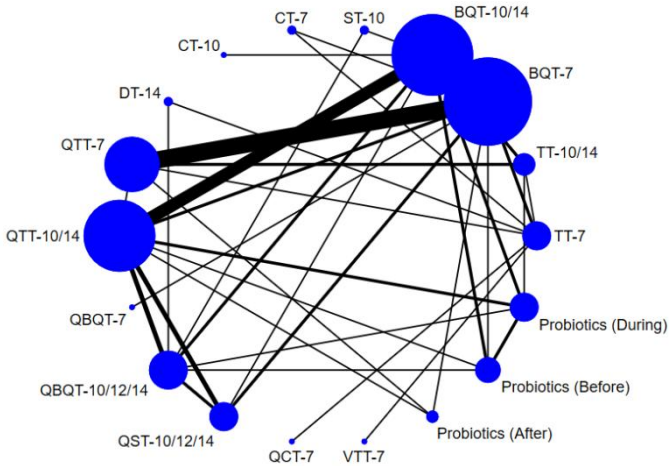
建議1. 適合作network meta-analysis的主題



Study or subcategory	Levofloxacin n/N	Quadruple n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
Bilardi et al. 2004	31/44	17/46		10.87	4.07 [1.68, 9.83]
Gisbert et al. 2005	21/31	24/36		10.17	1.05 [0.38, 2.92]
Nista et al. 2003a	66/70	44/70		9.69	9.75 [3.18, 29.87]
Nista et al. 2003b	63/70	44/70		10.69	5.32 [2.12, 13.33]
Nista et al. 2004a	26/30	25/35		8.9	2.6 [0.72, 9.38]
Nista et al. 2004b	24/30	25/35		9.51	1.6 [0.50, 5.09]
Nista et al. 2005	37/50	34/50		10.94	1.34 [0.56, 3.19]
Orsi et al. 2003	43/50	44/50		9.45	0.84 [0.26, 2.7]
Perri et al. 2003	38/60	50/60		10.98	0.35 [0.15, 0.81]
Wong et al. 2002	51/56	48/53		8.81	1.06 [0.29, 3.9]
Total (95% CI)	491	505		100	1.8 [0.94, 3.46]

Total events: 400 (levofloxacin); 355 (quadruple)
Test for heterogeneity: $\chi^2 = 35.78$; $df = 9$ ($P < 0.0001$); $I^2 = 74.8\%$
Test for overall effect: $Z = 1.77$ ($P = 0.08$)

0.1 0.2 0.5 1 2 5 10
Favours quadruple Favours levofloxacin



建議2. 搜尋有無相關發表 (不幸,有!)

Meta-Analysis > J Gastroenterol Hepatol. 2019 Jan;34(1):59-67. doi: 10.1111/jgh.14462. Epub 2018 Oct 11.

Systematic review and network meta-analysis: Comparative effectiveness of therapies for second-line Helicobacter pylori eradication

Yee Hui Yeo [1 2], Chia-Chen Hsu [3], Chiao-Chin Lee [3], Hsiu J Ho [1], Jaw-Town Lin [4 5], Ming-Shiang Wu [6], Jyh-Ming Liou [6], Chun-Ying Wu [1 4 7 8 9 10], Taiwan Gastrointestinal Disease and Helicobacter Consortium

Affiliations + expand

PMID: 30169908 DOI: 10.1111/jgh.14462

建議3.尋找破口

找更適合臨床運用分組

Regimen abbreviations:

BQT-7: bismuth-containing quadruple therapy for 7 days

BQT-10/14: bismuth-containing quadruple therapy for 10-14 days

TT-10/14: triple therapy for 10-14 days

ST-10: sequential therapy for 10 days

CT-7: concomitant therapy for 7 days

CT-10: concomitant therapy for 10 days

DT-14: high-dose dual therapy for 14 days

QTT-7: quinolone-based triple therapy for 7 days

QTT-10/14: quinolone-based triple therapy for 10-14 days

QBQT-10/12/14: quinolone-based bismuth-containing quadruple therapy for 10-14 days

QST-10/12/14: quinolone-based sequential therapy for 10-14 days

QCT-7: quinolone-based concomitant therapy for 7 days

RTT-7: rifabutin-based triple therapy for 7 days

Probiotics (After): probiotic add-on therapy after second-line antibiotic regimens

Probiotics (Before): probiotic add-on therapy before second-line antibiotic regimens

Probiotics (During): probiotic add-on therapy during second-line antibiotic regimens

重新定義時間切點

1. According to ACG and Maastricht V Guidelines
2. Asia-Pacific area published data

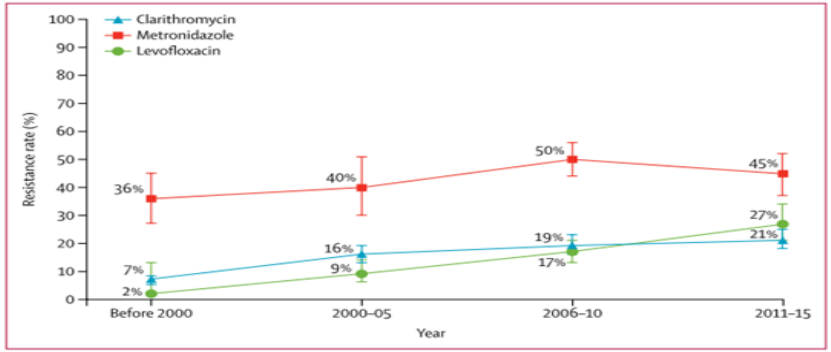


***Figure 2*: Prevalences of primary clarithromycin, metronidazole, and levofloxacin resistance in the Asia-Pacific region**
Error bars represent 95% CIs.

如何搜尋納入文獻?

建議1. 看別人關鍵字都怎麼下

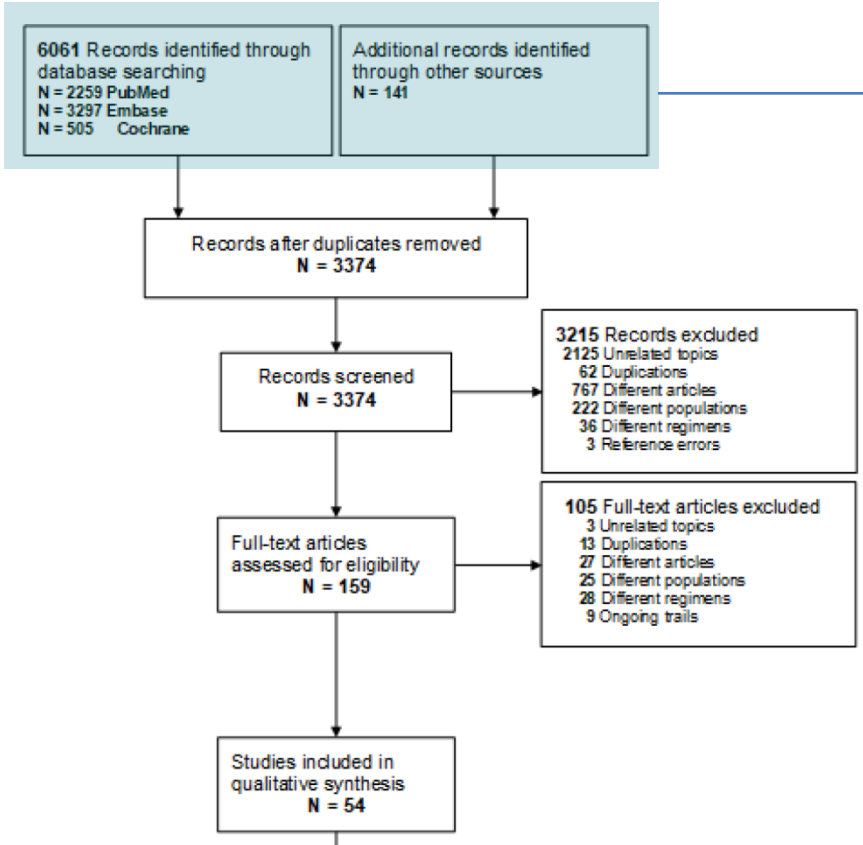
建議2. 善用圖書館資源

建議3. 不要限縮文獻類型

Supplementary Table 1. Electronic Database Searching Strategy

Electronic search strategy		
PubMed search		
Population / Helicobacter infection	#1	("Helicobacter"[Mesh] OR Helicobacter)
Intervention/ Second-line therapy	#2	(Retreatment [Mesh] OR "Salvage Therapy"[Mesh] OR "second line" OR "second-line" OR rescue OR salvage OR retreat* OR re-treat* OR fail*)
Filters	#3	Publication date from 2000/01/01 to 2018/12/31
Search algorithm	#4	#1 AND #2 AND #3
Embase search		
Population / Helicobacter infection	#1	('helicobacter pylori'/exp OR 'campylobacter pylori' OR 'campylobacter pyloridis' OR 'campylobacter pyloris' OR 'helicobacter nemestrinae' OR 'helicobacter pylori') OR ('helicobacter'/exp OR helicobacter OR 'gastrospirillum' OR 'helicobacter') OR ('helicobacter infection'/exp OR 'helicobacter gastritis' OR 'helicobacter infection' OR 'helicobacter infections' OR 'helicobacter pylori gastritis' OR 'helicobacter pylori infection')
Intervention/ Second-line therapy	#2	('salvage therapy'/exp OR 'salvage procedure' OR 'salvage therapy') OR ('retreatment'/exp OR retreatment OR 'retreatment') OR ('second line therapy'/exp OR 'second line therapy') OR ('second line':ti,ab,kw) OR (rescue:ti,ab,kw) OR (failure:ti,ab,kw) OR (failed:ti,ab,kw) OR (failing:ti,ab,kw) OR (retreated:ti,ab,kw OR 're treated':ti,ab,kw OR retreating:ti,ab,kw OR 're treating':ti,ab,kw OR retreatments:ti,ab,kw OR 're treatments':ti,ab,kw))
Filters	#3	[2000-2018]/py
Search algorithm	#4	#1 AND #2 AND #3
Cochrane clinical trial search		
Population/ Helicobacter infection	#1	MeSH descriptor Helicobacter explode all trees OR Helicobacter
Intervention/ Second-line therapy	#2	MeSH descriptor Retreatment explode all trees OR MeSH descriptor Salvage Therapy explode all trees OR "second line" OR "second-line" OR rescue OR salvage OR retreat* OR re-treat* OR fail*
Search algorithm	#3	#1 AND #2

如何將文獻整理至Excel?



匯入endnote

移除重複
References > Find Duplicates

自製一個符合需求的Output Style

匯出txt檔

txt檔轉excel 檔

no.	Authors	Title	Year	Journal	DOI	Abstract	是否納入分析 (1= Yes, 0= No)	Reasons for exclusion
1	D. Tang, L. Yuan, C. Yue, T. Cai, Y. Yao and F. Wang	[Efficacy of bismuth containing quadruple therapies on Helicobacter pylori eradication in patients with history of antibiotic treatment]	2018	Zhong Nan Da Xue Xue Bao Yi Xue Ban	10.11817/j.issn.1672-7347.2018.07.012	OBJECTIVE: To investigate the efficacy of bismuth containing quadruple therapies on Helicobacter pylori (Hp) eradication in patients with history of antibiotic treatment. Methods: Hp infected patients (n=327) were allocated into 3 groups. Group A (n=52), patients had no antibiotic history and they took medicine of proton pump inhibitors (PPI) and livzon triple (clarithromycin, tinidazole, and bismuth); group B (n=80), patients had the antibiotic history except for amoxicillin and clarithromycin, and they were treated with PPI, amoxicillin, clarithromycin, and bismuth; group C (n=195), patients suffered failures of Hp therapy or with history of antibiotic abuse, and they were treated with PPI, doxycycline, furazolidone, and bismuth. Results: Both the intention-to-treat (ITT) analysis (group A 63.5%, group B 76.2%, group C 82.6%, P<0.05) and the pre-protocol (PP) analysis (group A 76.7%, group B 92.4%, group C 96.4%, P<0.05) showed significant difference among the 3 groups, revealing higher elimination in group B and C. The side-effects (20.2%) were mild and tolerable (group A, 28.0%; group B, 10.7%; group C, 22.0%). Conclusion: Proton pump inhibitors together with the livzon triple regimen have a low rate of Hp eradication and a higher incidence of adverse reactions. The quadruple therapy containing clarithromycin and metronidazole drugs can achieve the satisfactory outcomes based on patient's antibiotic history. For patients with multiple antibiotics, the quadruple therapy containing furazolidone and doxycycline may achieve the satisfactory outcomes, but the adverse resction would be relatively higher.	1	

如何初步篩選納入文獻?

建議1. 記錄文獻排除的理由

Reasons for exclusion :

- Unrelated topics
- Duplications
- Different type of articles
- Different populations
- Different regimens

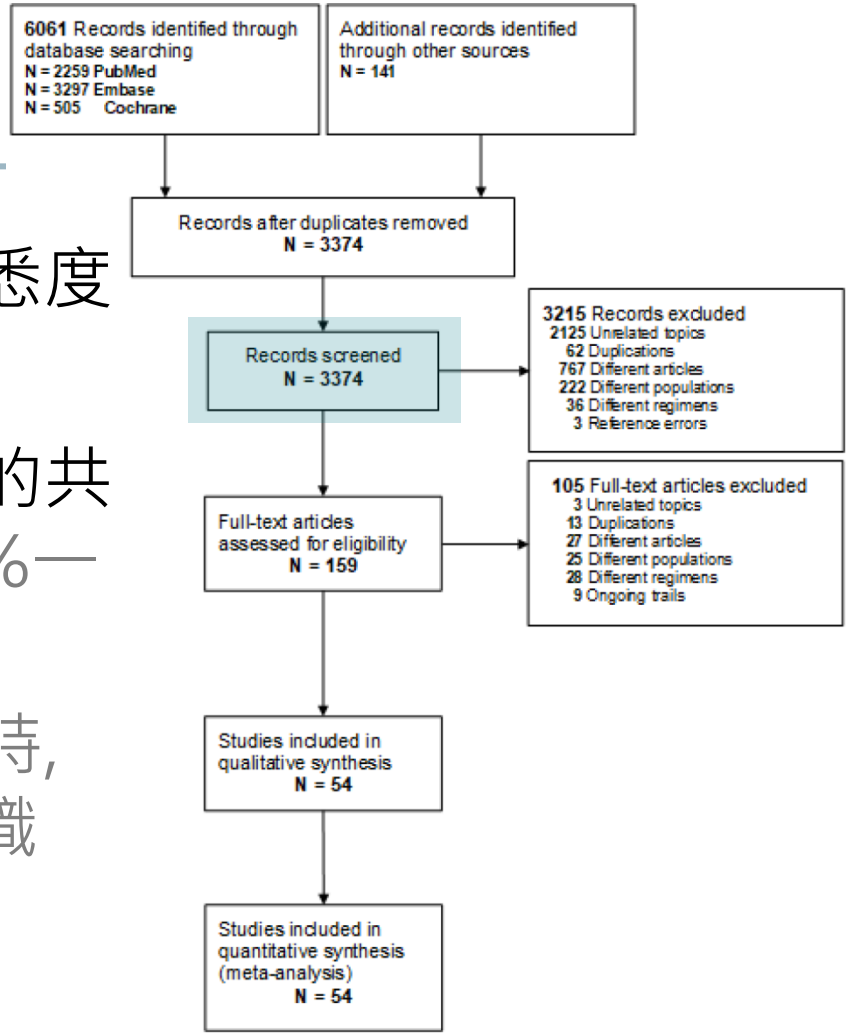
在初篩文獻時, RCT 與Cohort study兩種文獻類型我們都有納入

建議2. 對研究設計要有一定的熟悉度

建議3. 初篩時盡量不要找全文

建議4. 兩位文獻篩選者要有一定的共識(我們抓10%的文章, 至少有80%一致性)

建議5. 當文獻篩選者意見不一致時, 應進一步作較深入討論以取得共識



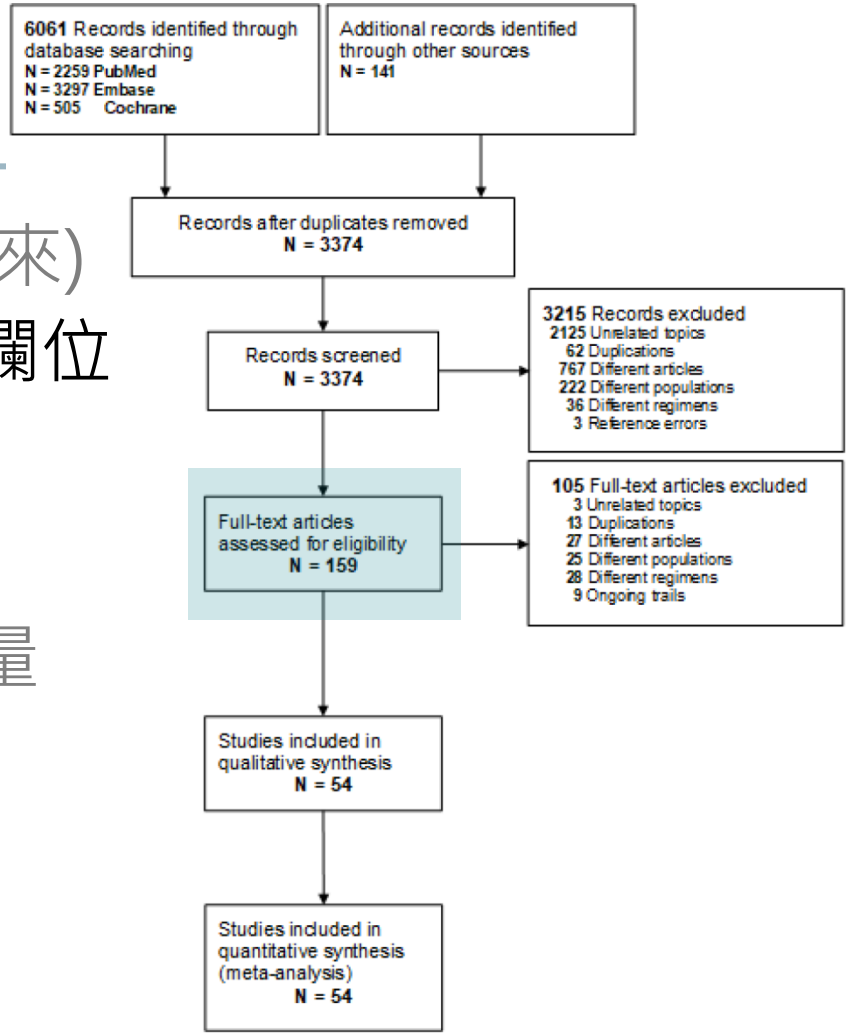
如何篩選合格文獻?

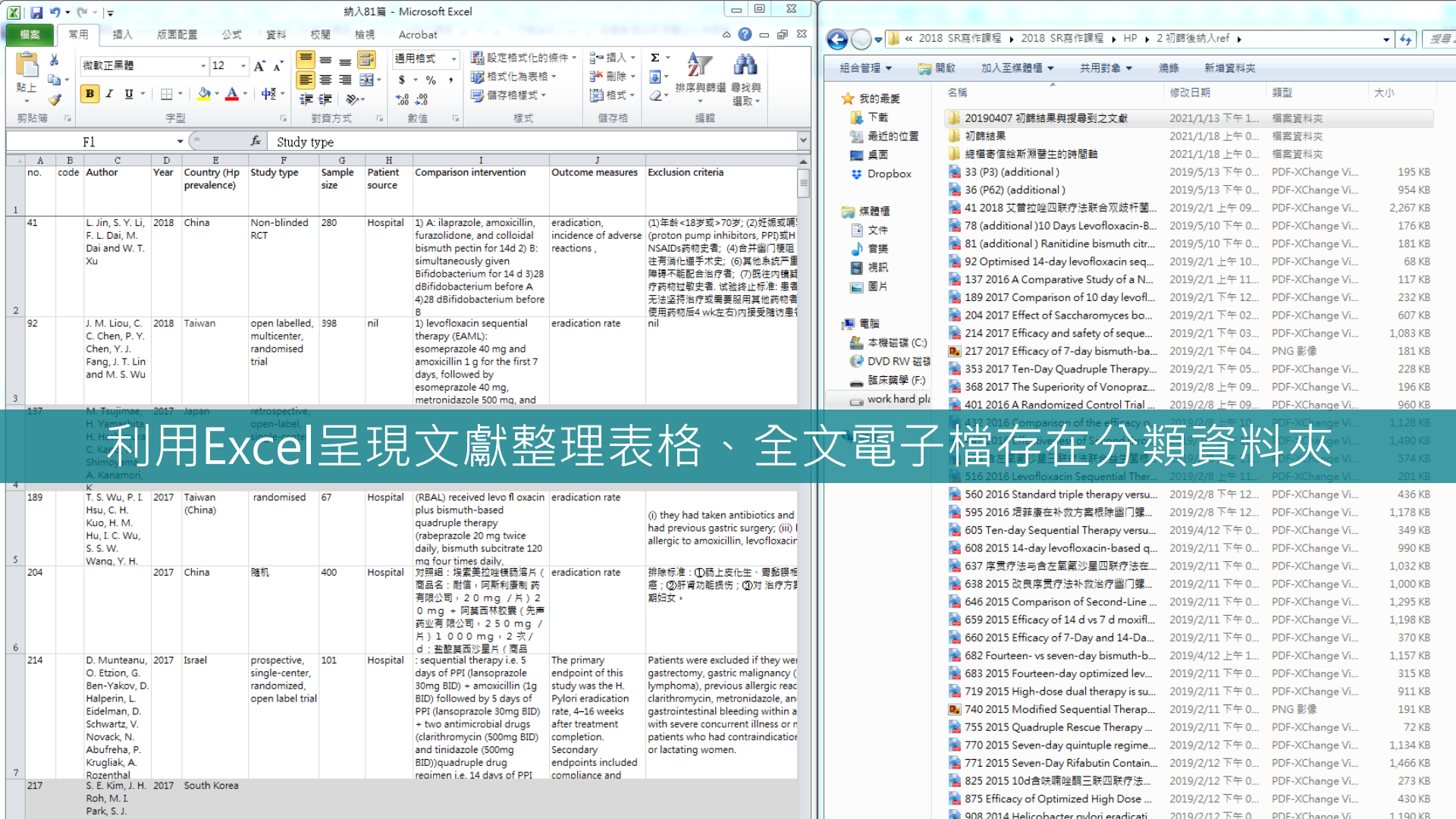
建議1. 下載全文細讀(可以印出來)

建議2. 開始思考設定模板相關欄位

- 研究特徵擷錄
- 研究對象特質擷錄
- 研究結果指標擷錄

建議3. 次族群資料是否納入考量





利用Excel呈現文獻整理表格、全文電子檔存在分類資料夾

Supplementary Table 3. Narration of Enrolled Trials

Author	Year	Country	Study type	Sample size	Comparison intervention	Outcome measures	Inclusion criteria
Jin L, et al.[1]	2018	China	Non-blinded RCT (multi-center)	280	BQT-14 vs P + BQT-14 vs BQT-14 (P)	UBT	Chronic non-atrophic gastritis +/- erosions; non-bismuth eradication therapy
Liou JM, et al.[2]	2018	Taiwan	Non-blinded RCT (multi-center)	379	BQT-10 vs QST-14	NA	NA

Supplementary Table 4A. Characteristics of Enrolled Trials

Author	Mean age (years)	Male (%)	Diagnostic methods	First-line regimen	Intervention group	Intervention group 1		Intervention group 2		Intervention group 3	
						Event/Total	Eradication rate by ITT (%)	Event/Total	Eradication rate by ITT (%)	Event/Total	Eradication rate by ITT (%)
Jin L, et al.[1]	39	57.1	UBT	NA	BQT-14 vs P + BQT-14 vs BQT-14 (P)	44/70	62.9	107/140	76.4	50/70	71.4
Liou JM, et al.[2]	NA	NA	NA	NA	BQT-10 vs QST-14	172/189	91.0	169/190	88.9	NA	NA

Supplementary Table 4B. Characteristics of Enrolled Trials

Author	Intervention groups	Intervention group 1	Intervention group 2	Intervention group 3
Jin L, et al.[1]	BQT-14 vs P + BQT-14 vs BQT-14 (P)	[PPI (bid) + Colloidal bismuth pectin 200mg (bid) + Amo 1g (bid) + Furazolidone 100mg (bid)] x 14	[Bifidobacterium x 28] + [PPI (bid) + Colloidal bismuth pectin 200mg (bid) + Amo 1g (bid) + Furazolidone 100mg (bid) +/- Bifidobacterium] x 14	[PPI (bid) + Colloidal bismuth pectin 200mg (bid) + Amo 1g (bid) + Furazolidone 100mg (bid) + Bifidobacterium] x 14
Liou JM, et al.[2]	BQT-10 vs QST-14	[PPI (bid) + Bismuth tripotassium dicitrate 300mg (qid) + Met 500mg (tid) + Tet 500mg (qid)] x 10	[PPI (bid) + Amo 1g (bid)] x 7 + [PPI (bid) + Lev 250mg (bid) + Met 500mg (bid)] x 7	NA

如何進行資料萃取?

建議1. 模板建置完整

建議2. 資料萃取後**重複核對檢視**

建議3. 定期服用葉黃素

No.	Year	Study	Treat 1	Treat 2	Treat 3	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	t[,1]	t[,2]	t[,3]	na[]
92	2018	1	BQT-10	QST-14	NA	172	189	169	190	NA	NA	4	11	NA	2
189	2017	2	QTT-10	QBQT-10	NA	23	38	28	35	NA	NA	10	13	NA	2
214	2017	3	BQT-14	ST-10	NA	23	50	20	51	NA	NA	4	5	NA	2
353	2017	4	QTT-10	QBQT-10	NA	36	52	49	50	NA	NA	10	13	NA	2
368	2017	5	TT-7	VTT-7	NA	119	146	174	216	NA	NA	1	14	NA	2
401	2016	6	QTT-10	QST-10	NA	66	82	74	82	NA	NA	10	11	NA	2
432	2016	7	QTT-14	QBQT-14	QTT-14 + P	29	48	33	48	79	96	10	13	15	3
455	2016	8	QTT-14	QBQT-14	QTT-14 + P	29	48	33	48	79	96	10	13	15	3
516	2016	9	QTT-10	QST-10	NA	2[illegible]	[illegible]53	300	NA	NA	10	11	NA	2
637	2015	10	ST-10	QBQT-12	NA	60	85	61	82	NA	NA	5	13	NA	2
638	2015	11	QBQT-14	T-10+QST	NA	49	65	120	130	NA	NA	13	11	NA	2
646	2015	12	CT-10	BQT-10	NA	55	61	58	63	NA	NA	7	4	NA	2
825	2014	13	TT-10	BQT-10	NA	28	40	36	40	NA	NA	2	4	NA	2
1075	2013	14	BQT-10	QBQT-10	NA	59	74	60	76	NA	NA	4	13	NA	2
1102	2013	15	QBQT-14	DT-14	NA	44	48	41	45	NA	NA	13	8	NA	2
1103	2013	16	QST-12	QBQT-10	NA	60	73	68	75	NA	NA	11	13	NA	2
1158	2013	17	QTT-14	BQT-14	NA	308	426	169	222	NA	NA	10	4	NA	2
1293	2012	18	BQT-7	QST-10	NA	35	49	44	49	NA	NA	3	11	NA	2
1157	2013	19	QTT-7	BQT-7	NA	38	56	48	57	NA	NA	9	3	NA	2
1379	2012	20	TT-14	QTT-7	NA	48	64	50	64	NA	NA	2	9	NA	2
1407	2012	21	QTT-14	BQT-14	NA	43	51	43	50	NA	NA	10	4	NA	2
1570	2011	22	QTT-7	TT-14	NA	31	45	38	45	NA	NA	9	2	NA	2

篩選文獻相關參數,開始利用統計軟體 Stata跑network meta-analysis

評讀工具

評讀工具	評讀項目
Risk of bias tool (RoB 2.0) from Cochrane	RCT
Risk of bias in non-randomised studies of interventions (ROBINS-I) from Cochrane	Non-randomized study
Critical Appraisal Skills Programme (CASP)	SR, RCT, Cohort, Case Control, Diagnostics, Economics, Qualitative Researches
Critical Appraisal Tools (CAT) from Oxford CEBM	SR, RCT, Diagnostics, Prognostic
A MeaSurement Tool to Assess systematic Reviews (AMSTAR)	SR
Appraisal of Guidelines for REsearch and Evaluation (AGREE)	Guideline development and the quality of reporting

如何進行文獻評讀?

- Revised tool for Risk of Bias (RoB2.0)
- Cochrane RoB tool is very widely used
  - 100 out of 100 Cochrane reviews from 2014 (100%)
  - 31 out of 81 non-Cochrane review (38%)
- >2700 citations from non-Cochrane sources.

Syst Rev. 2016 May 10;5:80.

1. 隨機化過中的偏誤

2. 偏離既定干預的偏誤

3. 結局數據缺失的偏誤

4. 結局測量的偏誤

5. 結果選擇性報告的偏誤

6. 整體偏誤評估

1.1 Was the allocation sequence random?	Y / PY / PN / N / NI	[Description]
1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	Y / PY / PN / N / NI	[Description]
1.3 Were there baseline imbalances that suggest a problem with the randomization process?	Y / PY / PN / N / NI	[Description]
Risk of bias judgement	Low / High / Some concerns	[Support]
Optional: What is the predicted direction of bias arising from the randomization process?		[Rationale]
2.1. Were participants aware of their assigned intervention during the trial?	Y / PY / PN / N / NI	[Description]
2.2. Were carers and trial personnel aware of participants' assigned intervention during the trial?	Y / PY / PN / N / NI	[Description]
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	NA / Y / PY / PN / N / NI	[Description]
2.4. If Y/PY to 2.3: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	NA / Y / PY / PN / N / NI	[Description]
2.5 Were any participants analysed in a group different from the one to which they were assigned?	Y / PY / PN / N / NI	[Description]
2.6 If Y/PY/NI to 2.5: Was there potential for a substantial impact (on the estimated effect of intervention) of analysing participants in the wrong group?	NA / Y / PY / PN / N / NI	[Description]
Risk of bias judgement	Low / High / Some concerns	[Support]
Optional: What is the predicted direction of bias due to deviations from intended interventions?		[Rationale]
3.1 Were outcome data available for all, or nearly all, participants randomized?	Y / PY / PN / N / NI	[Description]
3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across intervention groups?	NA / Y / PY / PN / N / NI	[Description]
3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NA / Y / PY / PN / N / NI	[Description]
Risk of bias judgement	Low / High / Some concerns	[Support]
Optional: What is the predicted direction of bias due to missing outcome data?		[Rationale]
4.1 Were outcome assessors aware of the intervention received by study participants?	Y / PY / PN / N / NI	[Description]
4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NA / Y / PY / PN / N / NI	[Description]
Risk of bias judgement	Low / High / Some concerns	[Support]
Optional: What is the predicted direction of bias due to measurement of the outcome?		[Rationale]
Are the reported outcome data likely to have been selected, on the basis of the results, from...		
5.1. ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	Y / PY / PN / N / NI	[Description]
5.2 ... multiple analyses of the data?	Y / PY / PN / N / NI	[Description]
Risk of bias judgement	Low / High / Some concerns	[Support]
Optional: What is the predicted direction of bias due to selection of the reported result?		[Rationale]
Risk of bias judgement	Low / High / Some concerns	[Support]
Optional: What is the overall predicted direction of bias for this outcome?		[Rationale]

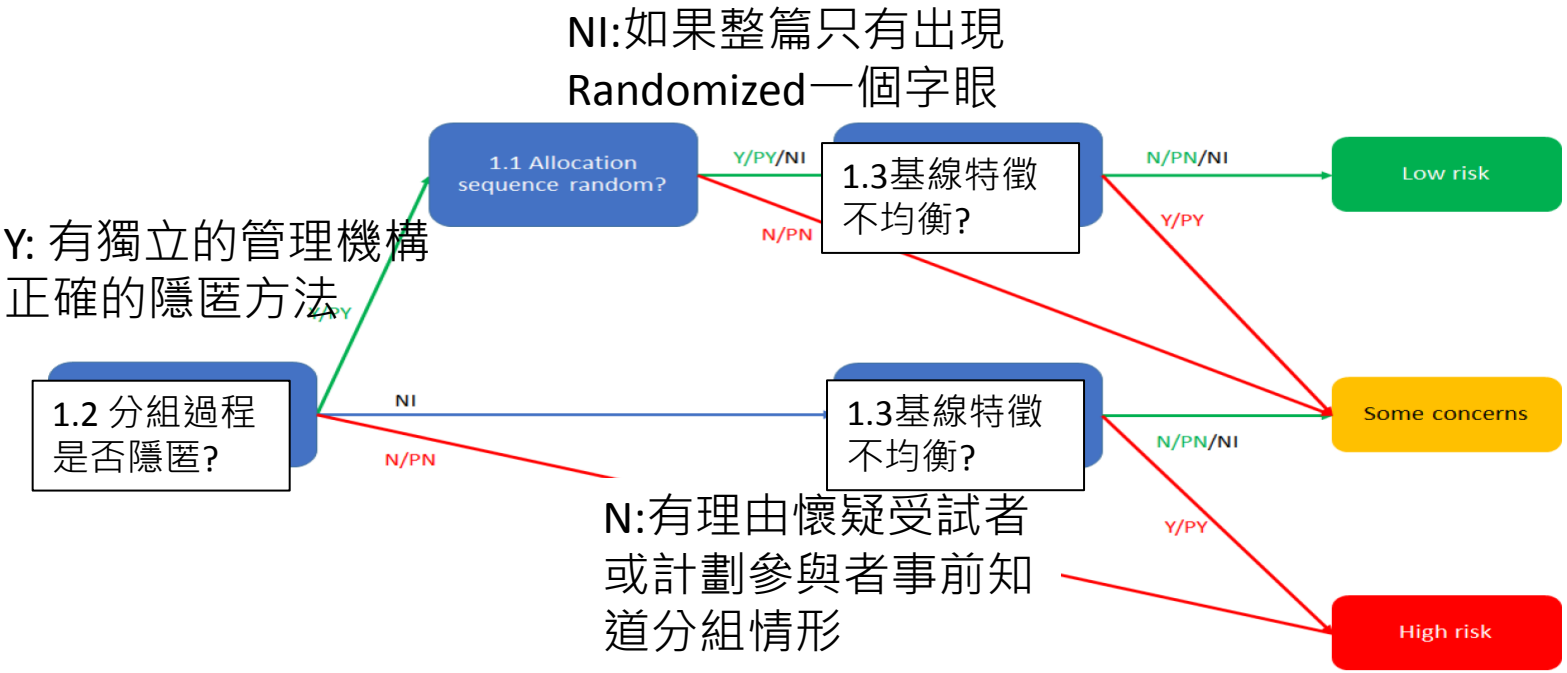
Supplementary Table 7. Risk of Bias for Randomised Trials of Second-line *H. pylori* Eradication Therapies

Author	Year	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
Munteanu D, et al.[9]	2017	Some concerns	Some concerns	High risk	Low risk	Low risk	High risk
Hsu PI, et al.[6]	2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Chuah SK, et al.[7]	2016	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kwon YH, et al.[8]	2016	High risk	Low risk	Low risk	Low risk	Low risk	High risk
Peng W, et al.[9]	2016	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Liou JM, et al.[10]	2016	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Yu H, et al.[11]	2016	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Wang JX, et al. [12]	2015	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Zeng LN, et al.[13]	2015	Some concerns	High risk	High risk	Low risk	Some concerns	High risk
Jheng GH, et al.[14]	2015	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Hung IF, et al.[15]	2015	Some concerns	Some concerns	Low risk	Low risk	Some concerns	Some concerns
Huang H, et al.[16]	2014	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Wang F, et al.[17]	2014	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Kuo CH, et al.[18]	2013	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Lu Q, et al.[19]	2013	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Calhan T, et al. [20]	2013	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Liu X, et al.[21]	2013	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Moon JY, et al. [22]	2013	Some concerns	High risk	Low risk	Low risk	Low risk	High risk
Bago J, et al.[23]	2013	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Yoon JH, et al.[24]	2012	Some concerns	Some concerns	Low risk	Low risk	Some concerns	Some concerns
He Y, et al.[25]	2012	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Ojetti V, et al.[26]	2012	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Chuah SK, et al.[27]	2012	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Chuah SK, et al.[28]	2012	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns
Yoon H, et al.[29]	2011	Some concerns	Some concerns	Low risk	Low risk	Low risk	Some concerns
Hu TH, et al.[30]	2011	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

1 Randomization process
2 Deviations from intended interventions
3 Missing outcome data
4 Measurement of the outcome
5 Selection of the reported result
6 Overall Bias

接下來依照本篇研究內容進行RoB 2.0 評讀, 歡迎大家共同討論指導。

1. Randomization process



Algorithm for suggested judgement of risk of bias arising from the randomization process

Results

The CONSORT flow diagram and study flow chart are depicted in Fig 1 and Fig 2 respectively. A total of 101 patients from the SUMC Gastroenterology clinic were randomized to receive either ST (50 patients) or QR (51 patients), between January 1st 2012 to June 31st 2015. The baseline demographic and clinical characteristics of patients in this study are listed in Table 1. Mean age (43 in both groups), gender distribution (35–40% male) and comorbidities were similar between the 2 arms.

1.2 =NI
1.3 基線特徵不均衡?
•Baseline characteristics ≥ 5種、p>0.05 = N
•Baseline characteristics < 5種、p>0.05 = PN

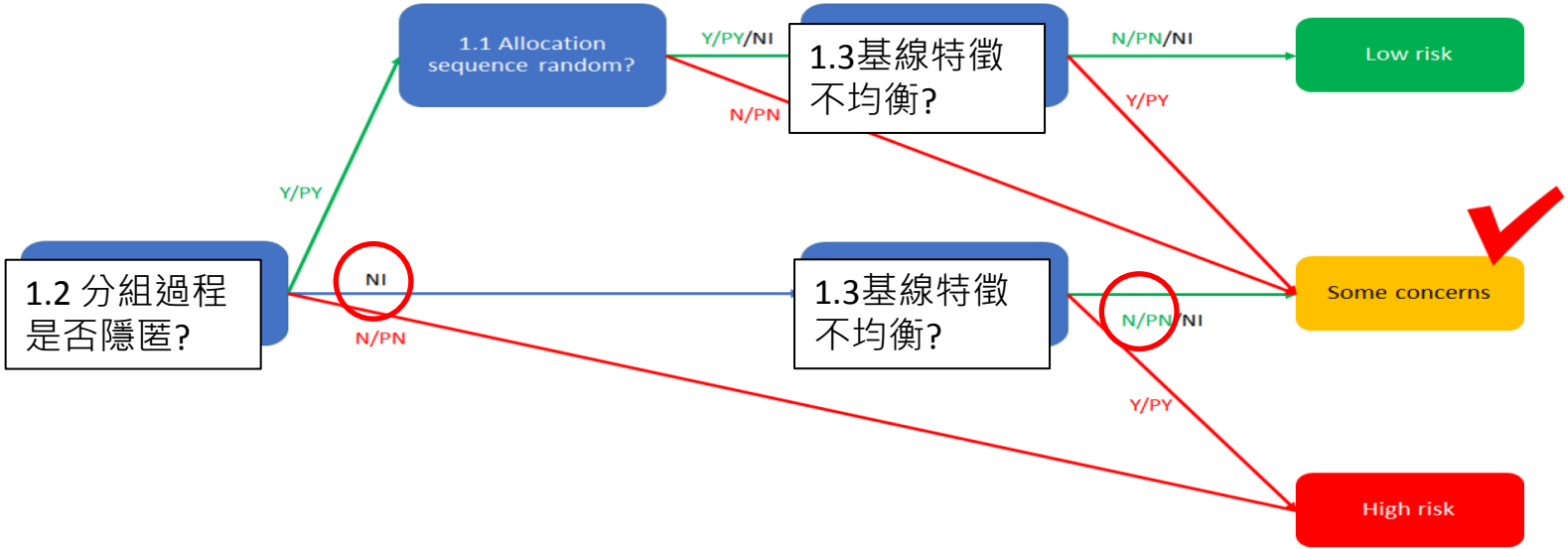
Table 1. Patient baseline characteristics.

		**Sequential (n = 50)	*Quadruple (n = 51)
Age (mean ± SD)		43.94 ± 15.75	43.75 ± 17.08
Gender	Male (n, %)	20 (40%)	18 (35.3%)
Comorbidities			
Family history of gastric cancer (n, %)		1 (2%)	5 (9.8%)
Alcohol or drug abuser (n, %)		2 (4%)	1 (2%)
Anemia (n, %)		11 (22%)	12 (24%)
Smoker (n, %)		9 (18%)	4 (8%)
Diabetes (n, %)		1 (2%)	7 (13.7%)
Chronic medications			
Aspirin (n, %)		3 (6%)	6 (12%)
Anticoagulation (n, %)		1 (2%)	1 (2%)
Other medications (n, %)		19 (38%)	20 (40%)

* The quadruple therapy is the recommended second line of treatment for *H. pylori* infection and includes 14 days of PPI+ bismuth + metronidazole + tetracycline/doxycycline.

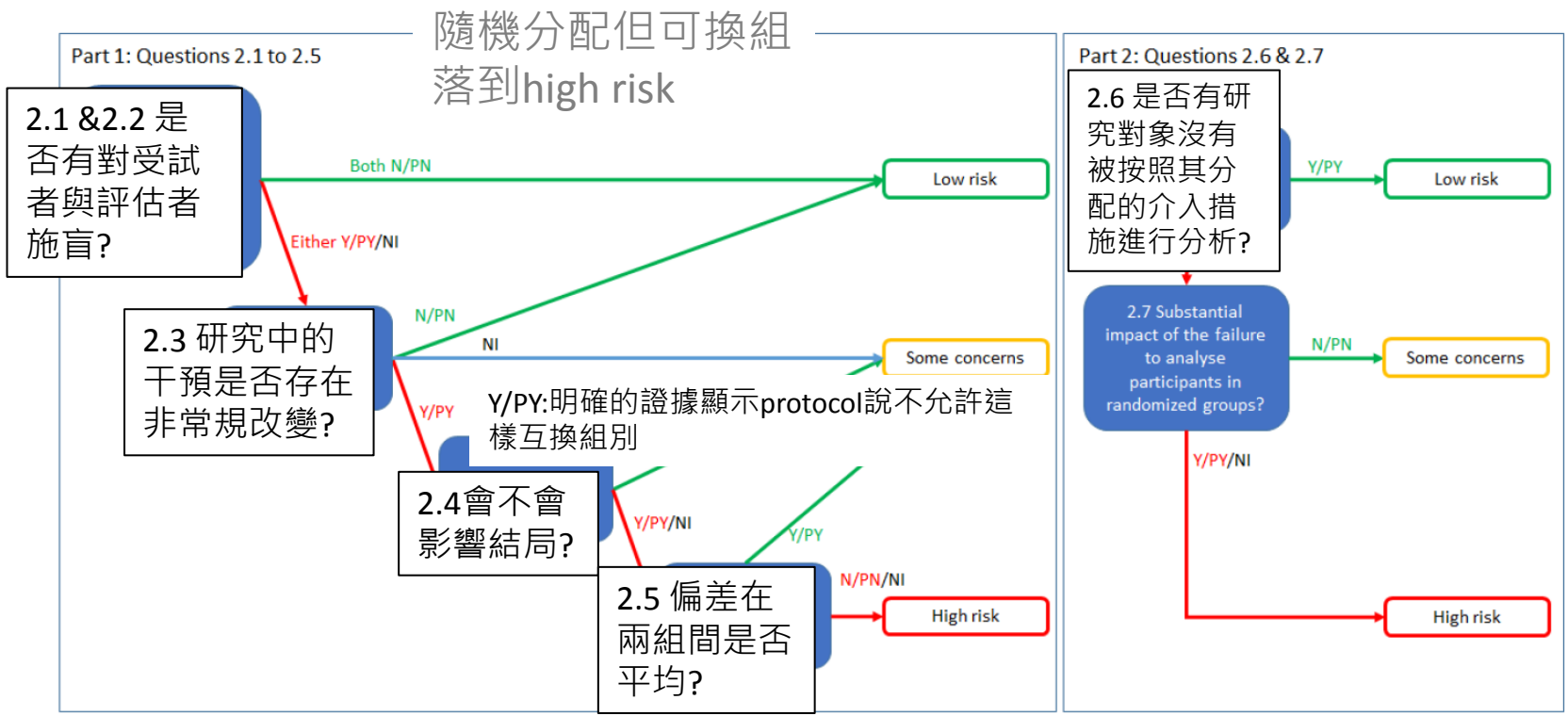
** The ST regimen includes 5 days of PPI + amoxicillin followed by 5 days of PPI + two antimicrobial drugs (clarithromycin and tinidazole).

Ex.Randomization process



Algorithm for suggested judgement of risk of bias arising from the randomization process

2. Deviations from intended interventions



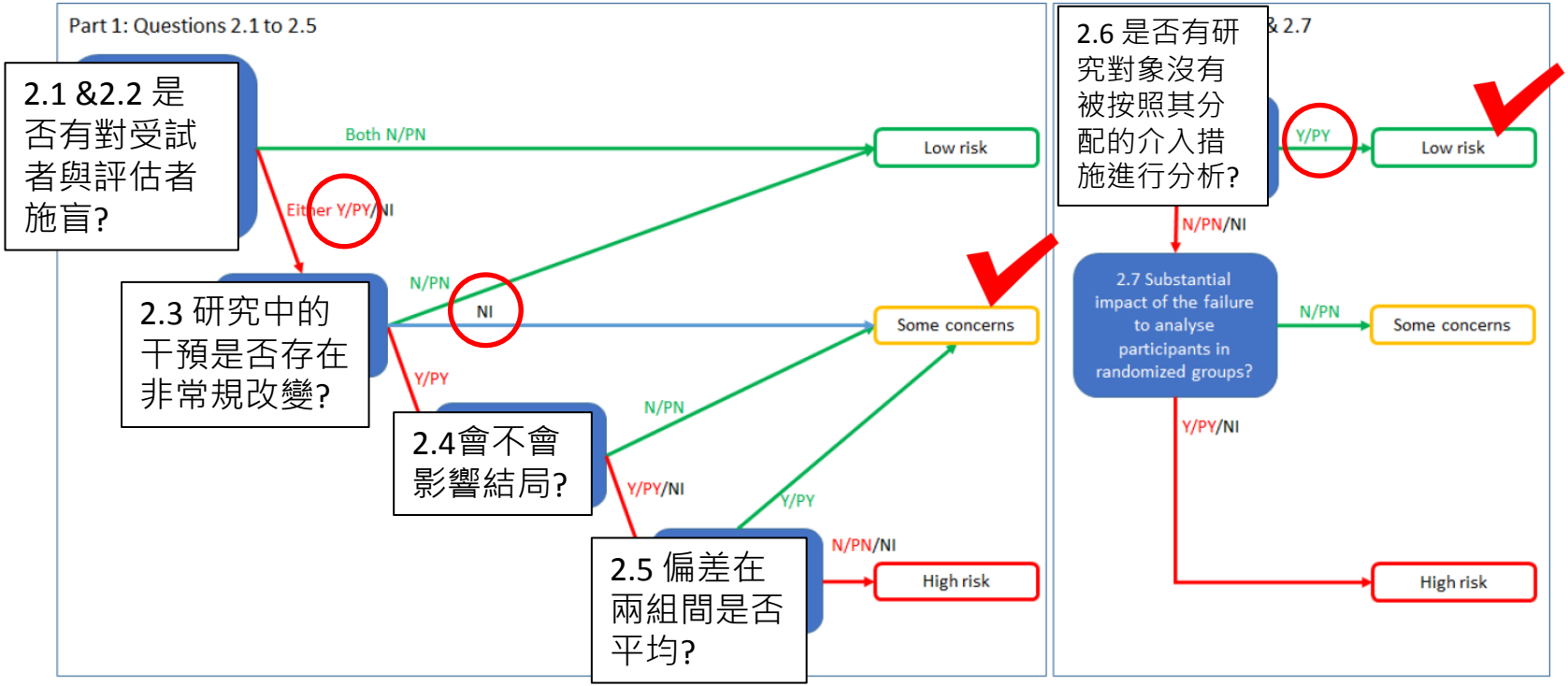
Supplementary Table 3. Narration of Enrolled Trials

未施盲

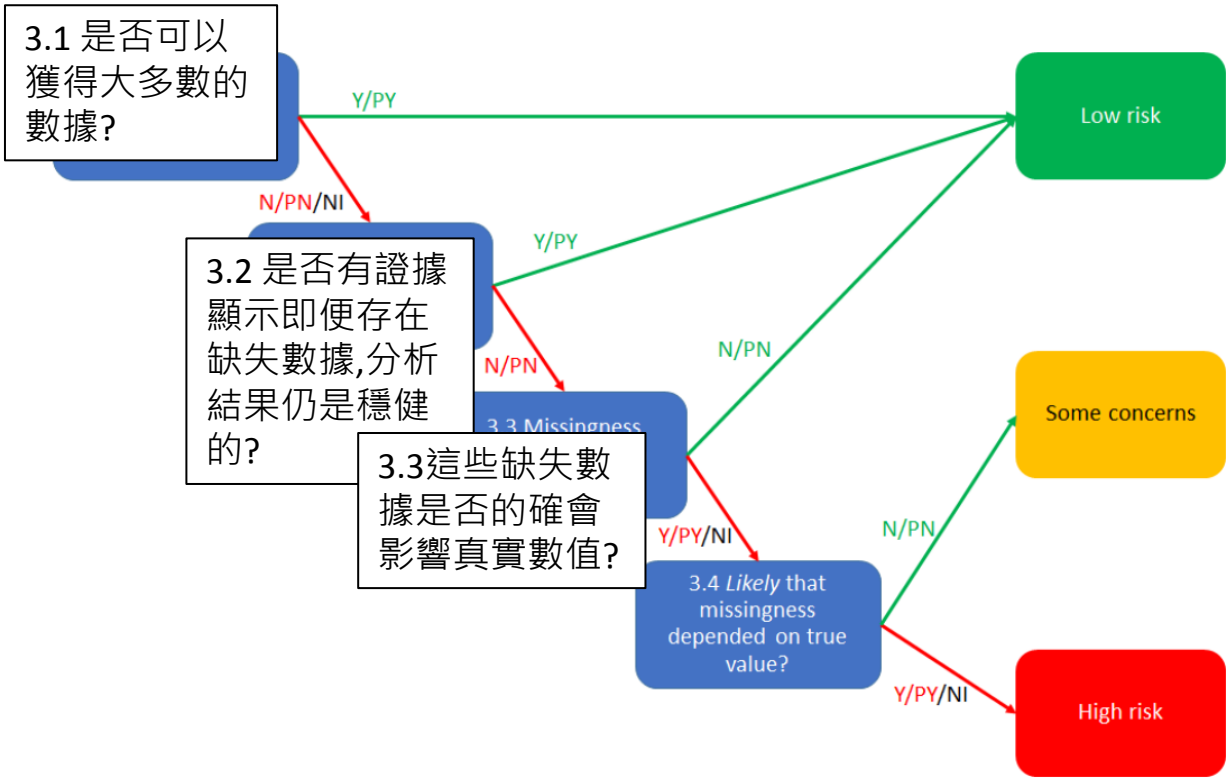
Author	Year	Country	Study type	Sample size	Comparison intervention	Outcome measures	Inclusion criteria
Jin L, et al.[1]	2018	China	Non-blinded RCT (multi-center)	280	BQT-14 vs P + BQT-14 vs BQT-14 (P)	UBT	Chronic non-atrophic gastritis +/- erosions; non-bismuth eradication therapy
Liou JM, et al.[2]	2018	Taiwan	Non-blinded RCT (multi-center)	379	BQT-10 vs QST-14	NA	NA
Wu TS, et al.[3]	2017	Taiwan	Non-blinded RCT (multi-center)	73	QTT-10 vs QBQT-10	RUT, H, C	PUD
Lu JH, et al.[4]	2017	China	Non-blinded RCT (multi-center)	400	QTT-14 vs QTT-14 (P)	UBT	Chronic gastritis
Munteanu D, et al.[5]	2017	Israel	Non-blinded RCT (single center)	101	ST-10 vs BQT-14	UBT, SAT	NA

No.	Year	Study	Treat 1	有無嚴重度分類	Number of adverse events 1 (person)	Number of patients at risk1	Any GI AEs1	備註	Treat 2	Number of adverse events 2 (person)	Number of patients at risk2	Any GI AEs2	備註	Treat 3	CLA resistance	CLA resistance (1 < 15%, 2 >= 15%)	MET resistance	MET resistance (0= unknown, 1 < 50%, 2	LEV resistance	LEV resistance (0= unknown,
41	2018	48	BQT-14		10	61	10	失去追蹤者3,退出治療6	P + BQT-14	9	127	9	失去追蹤者7,退出治療6	BQT-14 (P)	37	2	77	2	33	2
189	2017	2	QTT-10		0	33	有GIAE	未接受任何治療4,失去追蹤者+退出治療1	QBQT-10	3	32	有GIAE	未接受任何治療2,失去追蹤者+退出治療1	NA	26	2	31	1	15	1
204	2017	49	QTT-14		27	151	27	失去追蹤者37,退出治療12	QTT-14 (P)	15	157	15	失去追蹤者28,退出治療15	NA	37	2	77	2	33	2
214	2017	3	BQT-14		65(27)	33	45	失去追蹤者4, 退出治療18	ST-10	44(19)	42	27	失去追蹤者3,退出治療8	NA	47	2	57	2	5	1

Ex. Deviations from intended interventions



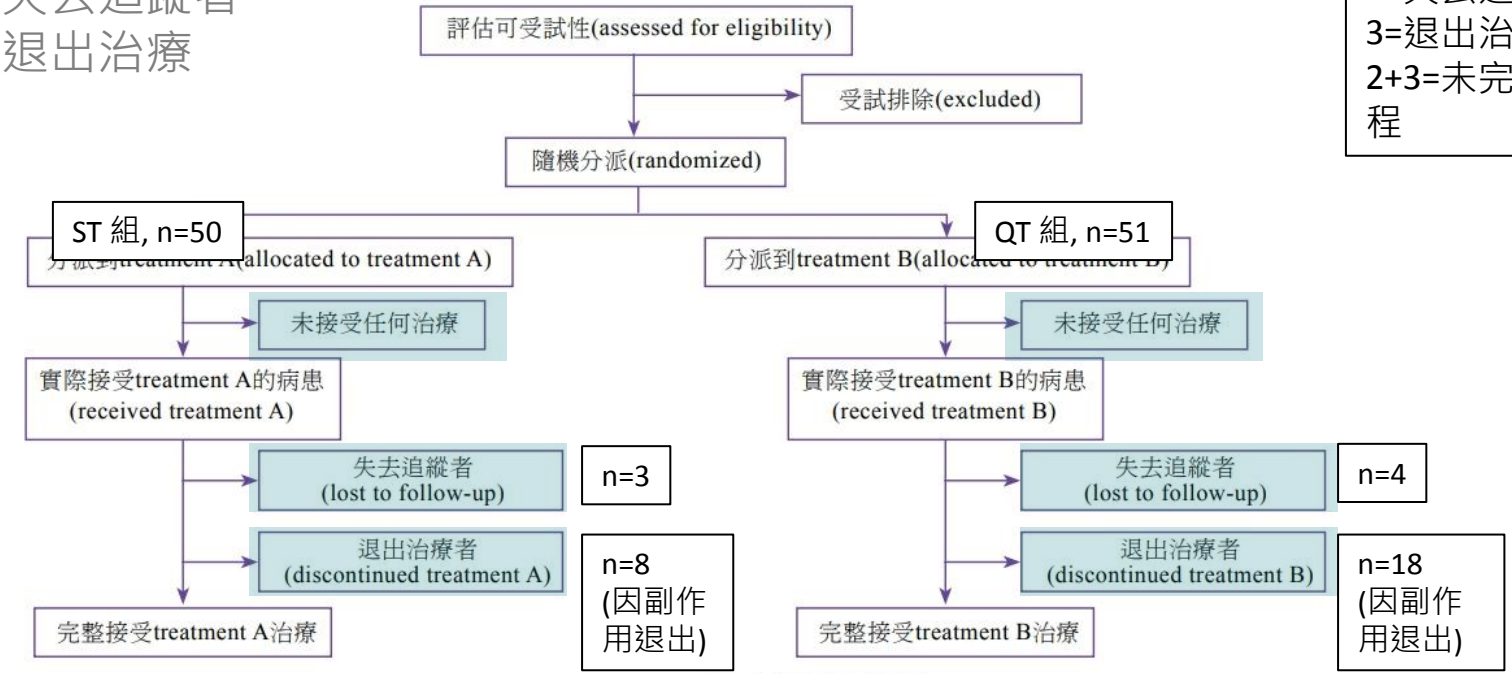
3. Missing outcome data



Algorithm for suggested judgement of risk of bias due to missing outcome data

Missing outcome data=1+2+3
1=未接受任何治療
2=失去追蹤者
3=退出治療

備註定義:
1=未接受任何治療
2=失去追蹤者
3=退出治療
2+3=未完成整個規程



說明病患治療分析方式：
1.意圖治療分析法(intention-to-treat analysis)
2.改良式意圖治療分析法(modified intention-to-treat analysis)
3.實際接受治療分析法(per-protocol analysis)

圖2 典型的RCT研究的病患受試流程圖

Missing outcome data=1+2+3
1=未接受任何治療
2=失去追蹤者
3=退出治療

ST regiment (n=50)

	有完成療程	未完成療程 (=退出治療)
有作治療結果確認	23/39	0/0
沒有作治療結果確認 (=loss follow up)	3	8

ITT=23/50 =46%
PP=23/39= 59.0%

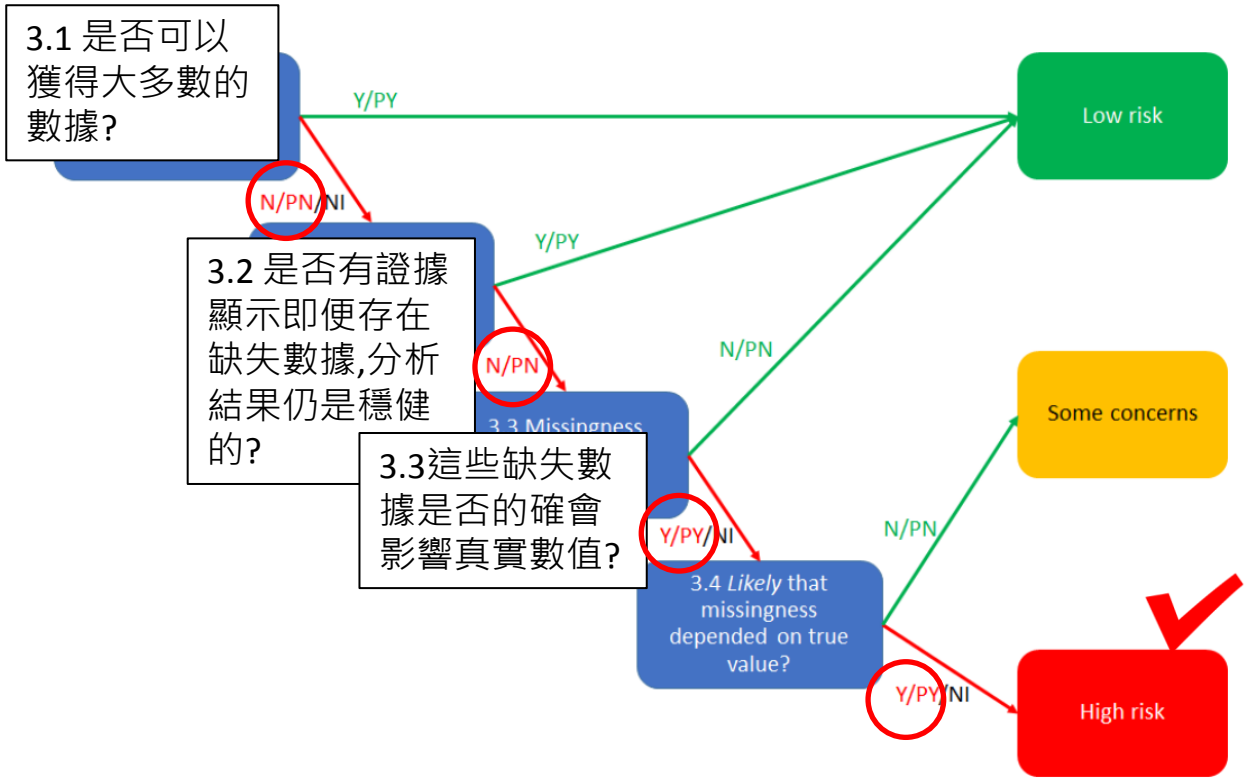
QT regiment (n=51)

	有完成療程	未完成療程 (=退出治療)
有作治療結果確認	20/29	0/3
沒有作治療結果確認 (=loss follow up)	4	15

ITT=20/51 =39.2%
PP=20/29 =69.0%

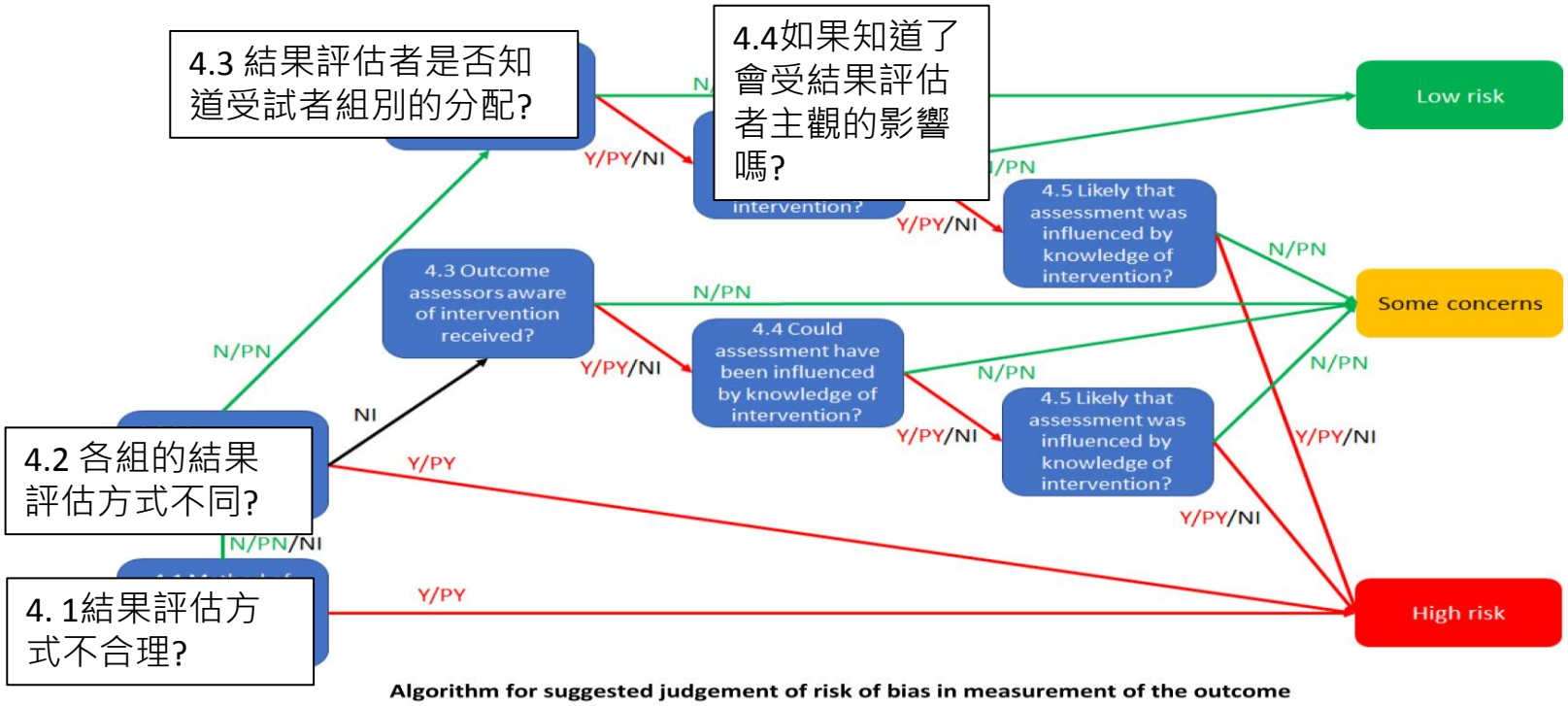
3.4 組間缺失的數據不平衡=Y

Ex. Missing outcome data



Algorithm for suggested judgement of risk of bias due to missing outcome data

4. Measurement of the outcome



Algorithm for suggested judgement of risk of bias in measurement of the outcome

Measurements in our review literature

Author	Year	Country	Study type	Sample size	Comparison intervention	Outcome measures	Inclusion criteria
Jin L, et al.[1]	2018	China	Non-blinded RCT (multi-center)	280	BQT-14 vs P + BQT-14 vs BQT-14 (P)	UBT	Chronic non-atrophic gastritis +/- erosions; non-bismuth eradication therapy
Liou JM, et al.[2]	2018	Taiwan	Non-blinded RCT (multi-center)	379	BQT-10 vs QST-14	NA	NA
Wu TS, et al.[3]	2017	Taiwan	Non-blinded RCT (multi-center)	73	QTT-10 vs QBQT-10	RUT, H, C	PUD
Lu JH, et al.[4]	2017	China	Non-blinded RCT (multi-center)	400	QTT-14 vs QTT-14 (P)	UBT	Chronic gastritis
Munteanu D, et al.[5]	2017	Israel	Non-blinded RCT (single center)	101	ST-10 vs BQT-14	UBT, SAT	NA
Hsu PI, et al.[6]	2017	Taiwan	Non-blinded RCT (multi-center)	102	QTT-10 vs QBQT-10	UBT	PUD
Chuah SK, et al.[7]	2016	Taiwan	Non-blinded RCT (single center)	164	QTT-10 vs QST-10	UBT, RUT, H	Gastritis; PUD

- 結果評估方式可能不同 =PY
- 結果評估方式相同 =N
- 結果評估方式相似 =PN (敏感性、特異性相似)

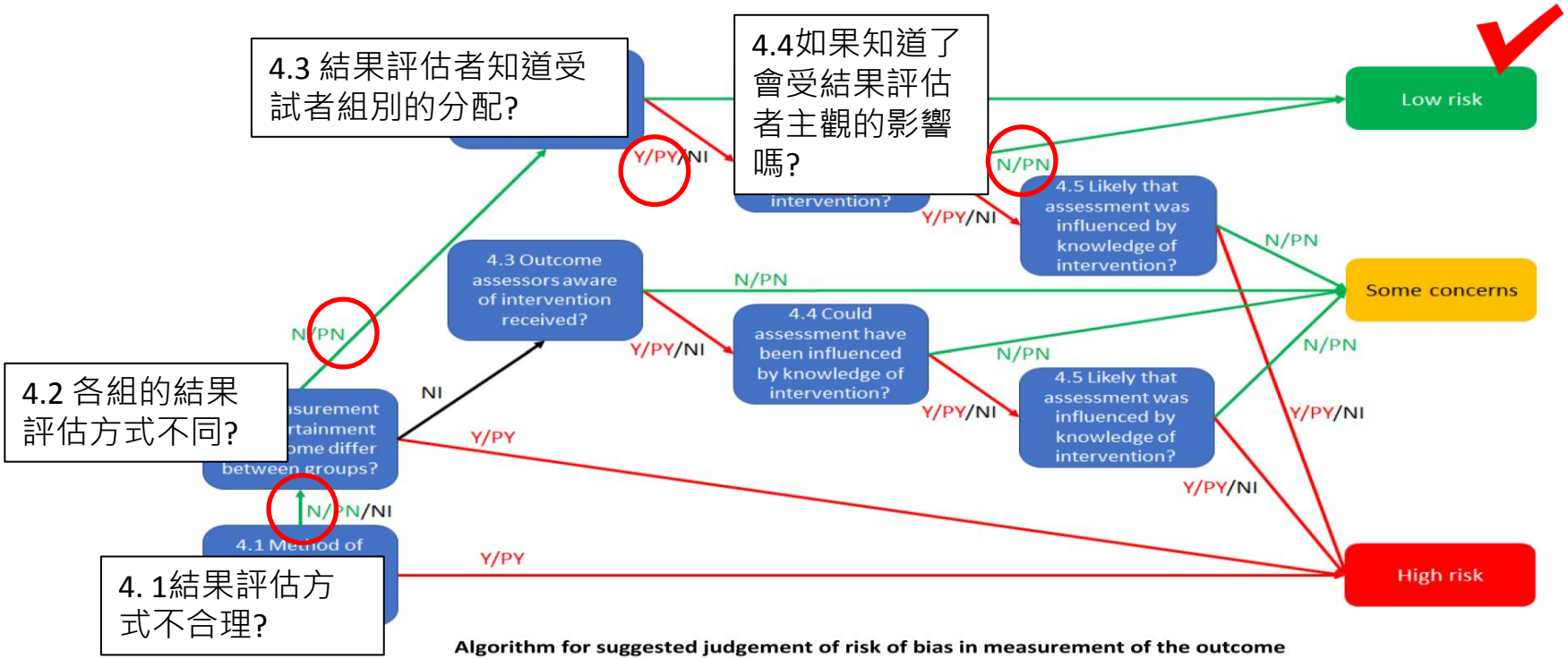
Table 6: Diagnostic test for *H. pylori* infection.

Diagnostic test	Sensitivity [18, 21]	Specificity [18, 21]	Advantages	Disadvantages
Direct test				
Histology	95%	99%	High accuracy, a possibility to send specimens at room temperature, and combination with IHC increase accuracy.	Low sensitivity for patients with gastric atrophy or intestinal metaplasia, time and cost, dependent on the operator skills, and interobserver variability.
Culture	69–98%	100%	Direct detection of *H. pylori*, excellent specificity, and allowing determination of antibiotic sensitivities.	Limited sensitivity, time-consuming procedure, and need of a special transport.
RUT	90%	93%	Inexpensive and provides rapid results, adding the number and increasing the size of biopsy specimens will increase the accuracy.	Sensitivity significantly reduced by bismuth, PPI and antibiotics, and formalin contamination of biopsy forceps generate false negative.
Indirect test				
UBT	95%	95%	Higher accuracy than serology and SAT, having a new portable type.	Atrophy, bismuth, PPI and antibiotics induce false-negative and need a local validation.
SAT	94%	92%	More economical than UBT and monoclonal antibody showed better accuracy.	Differences in the antigens may affect the accuracy, influence by bismuth, PPI, and antibiotics, and accuracy was influenced by stool condition.
Serology	90%	80%	Inexpensive, widely available, and the most efficient method in particular condition.	Less accurate than UBT and SAT and the cut-off values should be validated locally and cannot distinguish between current and past infections.

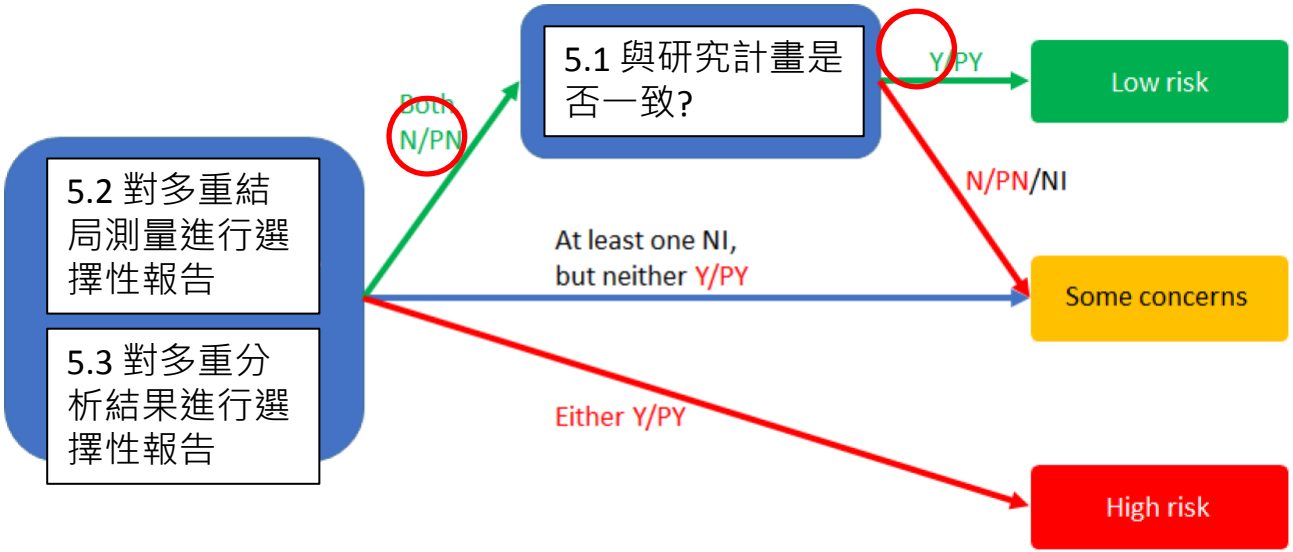
PPI: proton pump inhibitor; UBT: urea breath test; SAT: stool antigen test; RUT: rapid urease test.

Biomed Res Int. 2016;2016:4819423.

Ex. Measurement of the outcome



5. Selection of the reported result



Algorithm for suggested judgement of risk of bias in selection of the reported result

Intervention

Patients were enrolled by one of physicians of the Institute of Gastroenterology and Liver Diseases at SUMC, acting as principal or associate investigators on the study. Patients enrolled between January 1st 2012 to June 31st 2015, were randomly assigned (1:1), to receive one of the following two treatment regimens: sequential therapy i.e. 5 days of PPI (lansoprazole 30mg BID) + amoxicillin (1g BID) followed by 5 days of PPI (lansoprazole 30mg BID) + two antimicrobial drugs (clarithromycin (500mg BID) and tinidazole (500mg BID)) or, quadruple drug regimen i.e. 14 days of PPI (lansoprazole 30mg BID) + bismuth (525mg QID) + metronidazole (500mg TID) + tetracycline (500mg QID)/doxycycline (100mg BID)(during the enrollment period tetracycline was changed to doxycycline due to interruption of tetracycline drug supply). Drug adherence and adverse side effects to therapy were assessed via telephone questionnaire 1 week following completion of treatment or pill counting. *H. pylori* eradication was defined as a negative ^{13}C-urea breath or stool antigen test 4–16 weeks after completion of eradication treatment [17].

同一結果只有一種測量方式、或測量方式不同但符合指引

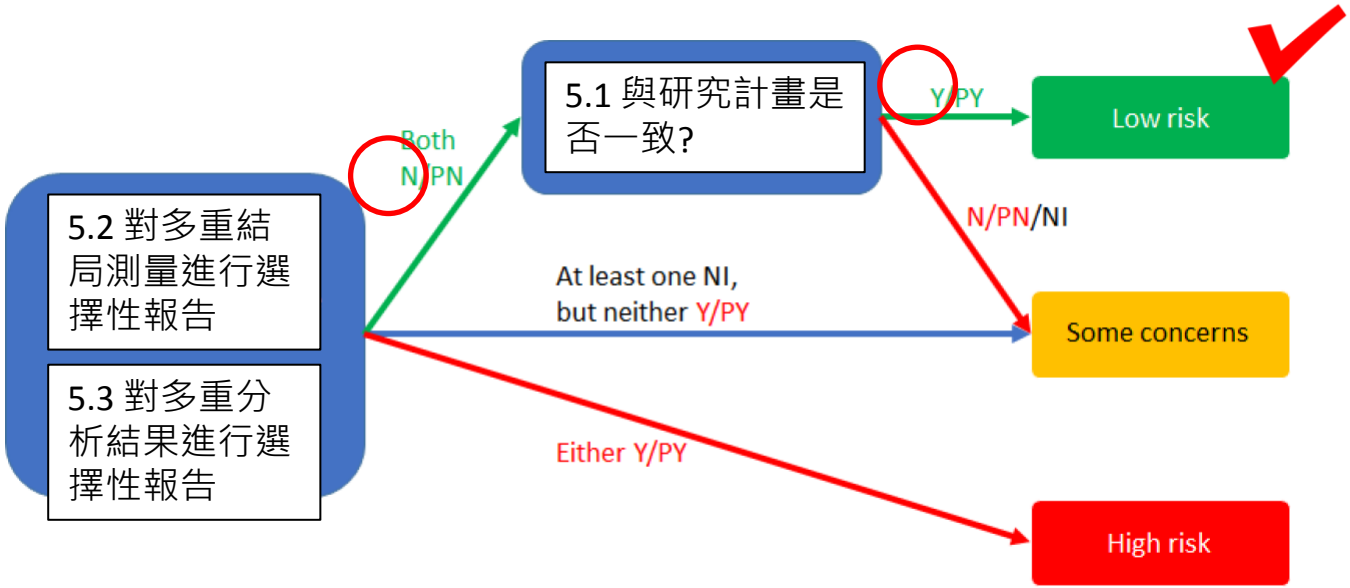
Conclusion

Sequential treatment when used as a second line regimen, was non-inferior to the standard of care quadruple regimen in achieving *Helicobacter pylori* eradication, and was associated with better compliance and fewer adverse effects. Both treatment protocols failed to show an adequate eradication rate in the population of Southern Israel.

Trial registration

ClinicalTrials.gov NCT01481844

Ex. Selection of the reported result



Algorithm for suggested judgement of risk of bias in selection of the reported result

6. Overall risk of bias judgement

Table 4. Assessment of risk of bias in randomized controlled trials by ROB 2.0 assessment tool

Author	Year	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
Munteanu D, et al.	2017	Some concerns	Some concerns	High risk	Low risk	Low risk	High risk

Low risk of bias	The study is judged to be at low risk of bias for all domains for this result.
Some concerns	The study is judged to be at some concerns in at least one domain for this result.
High risk of bias	The study is judged to be at high risk of bias in at least one domain for this result. OR The study is judged to have some concerns for multiple domains in a way that substantially lowers confidence in the result.

RoB Domains	study Processes	評讀重點	蒐集相關資料
RoB arising from randomization Process	Allocation bias	1. 是否隨機產生分組方案? 2. 分組是否隱匿? 3. Baseline是否具有可比性?	從method 、result與table 1 找
RoB due to deviations from intended intervention	Performance bias Analysis bias	Domain 2: 1. 是否有對受試者與評估者施盲? 2. 研究中的干預是否存在非常規改變? 3. 受試者有沒有按照其分配的干預組別進行分析(ITT analysis)	是否干預存在非常規改變這題須要找到protocol作為評讀依據
RoB due to missing outcome data	Attrition bias	1. 是否可以獲得全部或大多數的數據? 2. 是否有證據顯示即便存在缺失數據,分析結果仍是穩健的?	摘錄各組受試者因為什麼原因而造成變動或人員流失
RoB from measurement of outcome	Measurement bias	1. 結果測量方式是否合理? 2. 評估者是否知道受試者接受的干預?	研究特徵擷錄時蒐集結果測量方法
RoB from selective reporting	Reporting bias	1. 與研究計畫是否一致?	研究計畫書、統計分析計畫書、試驗註冊平台


“I JUST CAN'T
WAIT
TO START
SR”


從寫作到發表需要多久時間？

初學者：最快 3 個月

因此，以一個初學者來說，用一個月的時間，來建立起一篇統合分析論文的架構，再用一個月完成論文寫作，第三個月即可完成修稿與完成投稿的準備。掌握上述步調，就可以快速進行發表。

論文老手：1 個月內有機會

若對於一個熟練的老手來說，可能只要用一週收集題目，一週完成計算與圖表，再用一週就可以寫完全文，一個月內就可投稿。

理想與現實的差距

執行項目	時間																					
年	2018				2019													2020				
月	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6
選定主題進行文獻檢索		初篩平均一天看56篇																				
篇名與摘要文獻篩檢																						
全文文獻篩檢																						
研究特徵與結果指標擷錄																						
RoB 2.0 and ROBINS-I																						
Meta-analysis																						
投稿準備																						
正式投稿																						
投稿接受																						


The value of a
spiritual mentor

何鴻鋆主任

許斯淵醫生

董侑淳主任

邵時傑主任

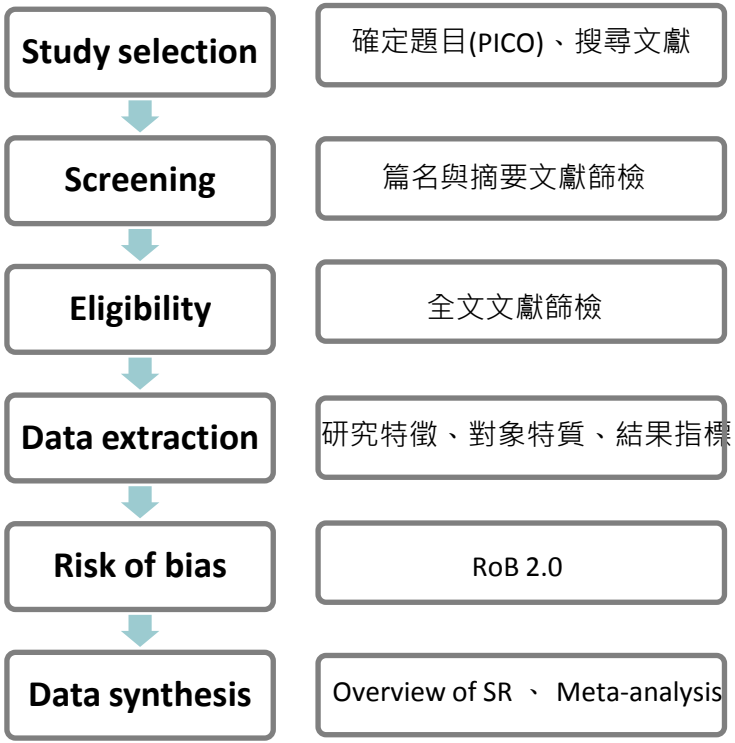
如何有效的進行SR

熟悉流程

精準評讀

時間規劃

精神指標



滿意度調查