台中榮民總醫院

參賽編號 BC00107

團隊成員

翁碩駿醫師

李維馨藥師

張瓊云藥師

Taichung Veterans General Hospital

臨床情境

55歲林先生長期旅居國外，因缺血性中風開始服用Aspirin，半年後因胃出血做了胃鏡後，發現有胃潰瘍改成**Plavix(保栓通)**，現在使用Plavix一年後，胃潰瘍已未再發作，林先生覺得Plavix太貴，想知道是否一定要持續使用？或者有其他選擇？

PICO1

P	Middle-aged man, ischemic stroke, UGI bleeding
I	Other treatment (aspirin + antiulcerant)
C	Clopidogrel
O	Benefit：Stroke prevention (2nd prevention) Harm：UGI bleeding, economic

PICO2

P	Middle-aged man, suspected osteoporosis
I	Calcium supplement
C	Placebo, Other Tx
O	Benefit：prevent osteoporosis and fructure Harm：prostate cancer risk

Background knowledge

Antiplatelet therapy for secondary prevention of stroke(2009)

So far therapeutic strategy:

- **Aspirin**, **clopidogrel**, and the combination of **aspirin plus extended-release dipyrudamole** (ER-DP) (Aggrenox) are all acceptable options for preventing recurrent noncardioembolic ischemic stroke.
- using either **clopidogrel** (75 mg daily) as monotherapy, or the **combination of aspirin plus ER-DP** (25 mg/200 mg twice a day), rather than aspirin (**Grade 2A**).
- **Aggrenox** contains aspirin and should not be used in patients who cannot tolerate aspirin. **Clopidogrel** (75 mg/day) is an obvious alternative for patients who cannot tolerate aspirin.

Ticlopidine should be reserved for patients intolerant of aspirin and clopidogrel.

Focused PICO

P	Middle-aged man, ischemic stroke, UGI bleeding
I	Treatment (Aspirin, anticoagulant…) + antiulcerant (antacid, PPI…)
C	Antiplatelet drug (Clopidogrel, Ticlopidine)
O	Benefit：Stroke prevention (secondary prevention), prevent cardiovascular risk Harm：UGI bleeding, economic

- 問題型態：

  治療型

- 檢索策略：

  SR/MA/RCTs

關鍵字

	關鍵字	替代字
P	Middle-aged man, ischemic stroke, UGI bleeding	Middle-aged man, ischemic cerebrovascular disease, gastrointestinal hemorrhage
I	Treatment + antiulcerant	Aspirin, anticoagulant + Anti-Ulcer Agents, antacid, proton pump inhibitor
C	Antiplatelet drug	Platelet Aggregation Inhibitors, Clopidogrel, Ticlopidine
O	Benefit：Stroke prevention (2nd prevention), prevent cardiovascular risk Harm：UGI bleeding, economic	Benefit: recurrent stroke Harm: Gastrointestinal Hemorrhage, cost

檢索策略

- Database:
  - Cochrane for SR
  - PubMed for potential SR/MA/RCTs
- Boolean searching

PubMed.gov
U.S. National Library of Medicine
National Institutes of Health

PubMed Search

earch	Most Recent Queries	Time	Result
#29	Search (((((((#5) OR #21) OR #17) OR #7) OR) OR (#26 OR #15)) AND #11 Limits: Meta-Analysis, Randomized Controlled Trial, Middle Aged: 45-64 years, published in the last 5 years Field: Title/Abstract	22:35:25	73
#28	Search (((((((#5) OR #21) OR #17) OR #7) OR) OR (#26 OR #15)) AND #11	22:33:40	3514
#26	Search ("Proton Pump Inhibitors"[Mesh] OR "Proton Pump Inhibitors "[Pharmacological Action])	22:16:54	1269
#24	Search ("Antacids"[Mesh] OR "Antacids "[Pharmacological Action] OR "Anti-Ulcer Agents"[Mesh])	22:16:03	25857
#21	Search "Platelet Aggregation Inhibitors"[Mesh] OR Platelet Aggregation Inhibitors OR Antiplatelet	22:13:55	106676
#17	Search "clopidogrel "[Substance Name]OR CLOPIDOGREL	22:11:39	5362
#15	Search "Gastrointestinal Hemorrhage"[Mesh] OR Gastrointestinal Hemorrhage OR Gastrointestinal BLEEDING	22:09:53	47445
#11	Search Ischemia, brain[MULTI] AND STROKE	22:04:15	40127
#7	Search ("Anticoagulants"[Mesh] OR "Anticoagulants "[Pharmacological Action] OR "Coumarins"[Mesh] OR "Antithrombins"[Mesh]) OR ANTICOAGULANT	22:01:55	189163
#5	Search ("Aspirin"[Mesh] OR "aspirin, dipyridamole drug combination "[Substance Name]) OR ASPIRIN	21:59:47	45911

挑選文獻

	搜尋文獻	不符合PICO	符合PICO篇數			
			SR	RCT	PG	合計
Cochrane	39	38	1	0	0	1
PubMed	73	71	0	2	0	2

Esomeprazole With Aspirin Versus Clopidogrel for Prevention of Recurrent Gastrointestinal Ulcer Complications. KAM–CHUEN LAI, et al. Clinical Gastroenterology and hepatology 2006;4:860–865

Clopidogrel plus omeprazole compared with aspirin plus omeprazole for aspirin-induced symptomatic peptic ulcers/erosions with low to moderate bleeding/re-bleeding risk — a single-blind, randomized controlled study. NG FH et al Aliment Pharmacol Ther 2004; 19: 359–365.

Oral anticoagulants versus antiplatelet therapy for preventing further vascular events after transient ischaemic attack or minor stroke of presumed arterial origin (Review)

Algra A, De Schryver ELLM, van Gijn J, Kappelle LJ, Koudstaal PJ

	情境患者	RCT- Kam-Kuenm 2006	RCT- NG FH 2004
P	Middle-aged man, ischemic stroke, UGI bleeding	18.8–53.6 y/o, GU, DU Aspirin 100mgday	18-85 y/o, 2nd prevention for CAD, PAOD, ischemic stroke, TIA GU, DU, Aspirin 100mgday Plavix 75mg/day
I	Treatment + antiulcerant	20mg esomeprazole	20mg omeprazole/day
C	Antiplatelet drug	Plavix 75mg/day	Placebo
O	Benefit：Stroke prevention (2nd prevention) Harm：UGI bleeding, economic	Recurrent ulcer complication	Treatment success rate
T		8 wks later UGI scope (after HP eradication	8 wks later UGI scope
S		RCT (double blind)	RCT (single blind)

嚴格評估

評讀工具：NHI **Critical Appraisal Skills Programme (CASP) - RCT**

效度**(validity)**分析**:**

	Kam-Kuenm 2006	NG FH 2004
此篇研究是否可回答我們的問題?	Y	Y
病人的治療分派是隨機的嗎？	Y	Y
病人、醫生、研究員是否對治療不知情？	Y	N
是否所有的病人都被放到原先分派的組別中做分析？	Y	Y
所有組別是否被平等對待？	Y	Y
病人數量是否足夠？	Y	Y
Level of Evidence	1b	1C

嚴格評估

評讀工具：NHI **Critical Appraisal Skills Programme (CASP) - RCT**

效益(Impact)分析:	Kam-Kuenm 2006	NG FH 2004
結果數據的影響力	**Ulcer treatment success rates** **Aspirin were 95% (57/60)** **Clopidogrel 94% (62/66)** **AE: No adverse**	**Recurrent ulcer complication** **Aspirin were 0% (0/100)** **Clopidogrel 14% (14/100)** **AE: No adverse**
結果精確度	**OR: 0.03, 95% CI 0.03-0.50, P=0 .039).**	**OR: 0.013, 95% CI 6.3%–20.9%; P=0 .0019).**

NNT (Kam-Kuenm 2006) – 100
NNT (NG FH 2004) – 7.14

	Placebo (control)	Intervention (experiment)	
Hearing improve	a	b	Control event rate (CER)=a/(a+c)=
Hearing no improve	c	d	Experiment event rate (EER)=b/(b+d)=
Relative risk reduction (RRR) = (CER-EER)/(CER) =			
Absolute risk reduction (ARR) = CER-EER =			
Number needed to treat (NNT)= 1/ARR =			
Relative risk (RR) =EER/CER =			
Confidence Intervals on the ARR:			

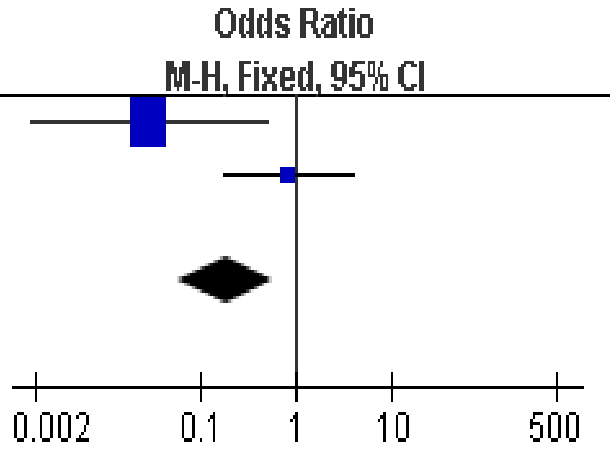
Recurrent ulcer complication – Aspirin+PPI vs clopidogrel+PPI

c/c+d a/a+b OR = a/a+b ÷ c/c+d

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Kam-Chuem 2006	0	100	14	100	79.9%	0.03 [0.00, 0.50]
Ng FH 2004	3	60	4	66	20.1%	0.82 [0.17, 3.80]
Total (95% CI)		**160**		**166**	**100.0%**	**0.19 [0.06, 0.59]**
Total events	3		18			

Heterogeneity: $Chi^2 = 5.13$, $df = 1$ ($P = 0.02$); $I^2 = 81\%$

Test for overall effect: $Z = 2.87$ ($P = 0.004$)



Weighting (wi) = 1/ variance 變異數

Overall estimate: log (RR) = $\Sigma W_i * \log(RR_i) / \Sigma W_i$

Review Manage 5

Taichung Veterans General Hospital

Systematic review
- Anticoagulant vs antiplatelet
2nd prevention

Oral anticoagulants versus antiplatelet therapy for preventing further vascular events after transient ischaemic attack or minor stroke of presumed arterial origin (Review)

Algra A, De Schryver ELLM, van Gijn J, Kappelle LJ, Koudstaal PJ

嚴格評估

		是否與PICO相符
P	Previous transient ischaemic attack or minor stroke of presumed arterial origin	Y
I	Oral anticoagulant	Y
C	Antiplatelet drug	Y
O	Recurrent stroke, death, bleeding	Y
T	> 6 month	Y
S	Meta-analysis	Y
搜尋文章要求:RCT		
搜尋資料庫對象: Cochrane/medline/EBMbase (最後檢索時間2005/02)		
檢索結果: 5篇RCT (共4076位受試者)		

嚴格評估

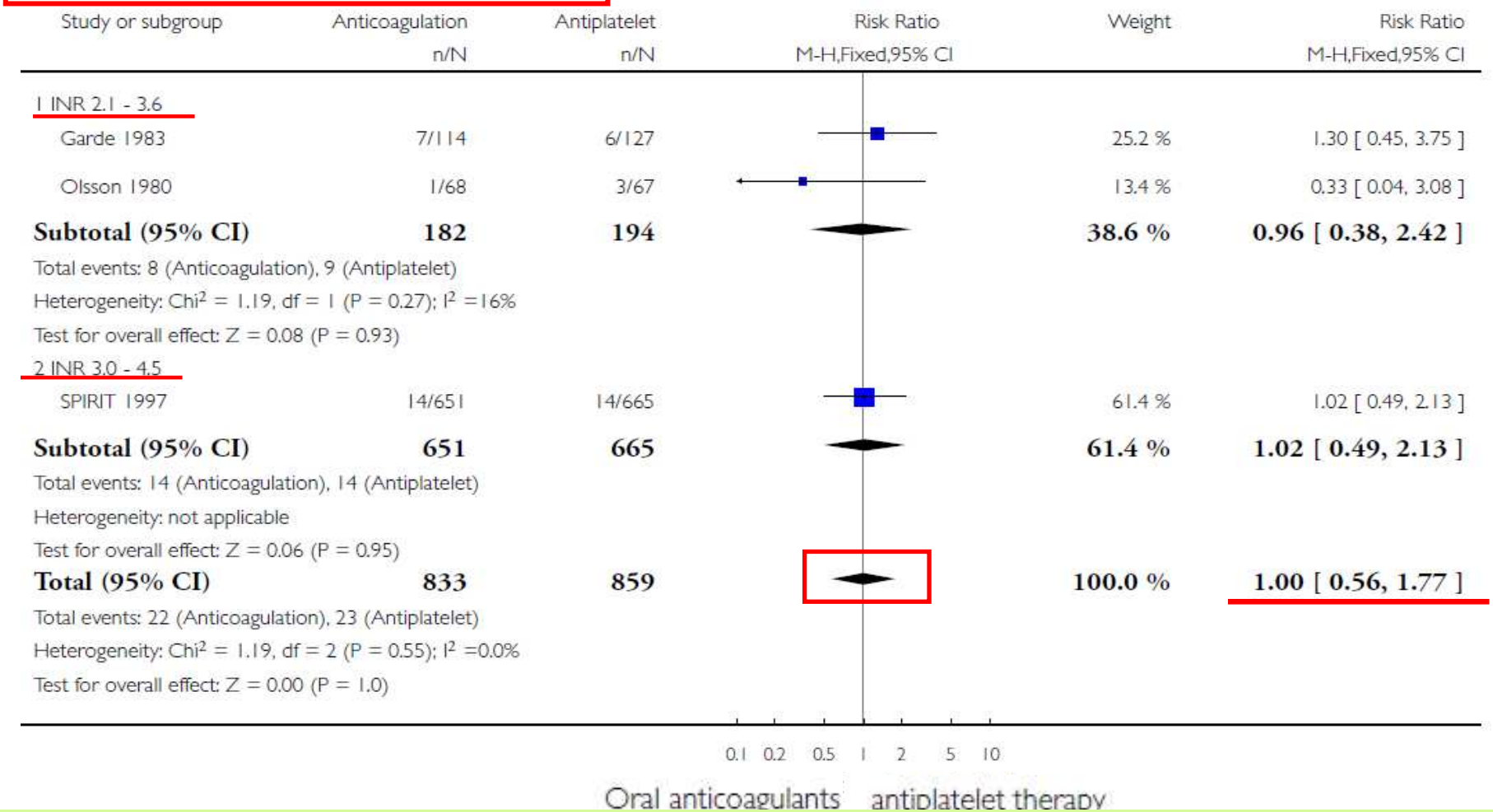
評讀工具：NHI **Critical Appraisal Skills Programme (CASP) - SR**

效度(validity)分析

此篇系統性回顧的文章是否可回答我們的問題?	Y
搜尋策略是否完整?	Y
作者是否有個別評估每個研究的效度?	Y
若有將收納研究結果綜合分析，如此做是否合理?	Y
所有收案研究就臨床與統計方法是否都一致?	Y
是否所有重要結果都有考量到?	Y
證據等級	1A

結果評讀

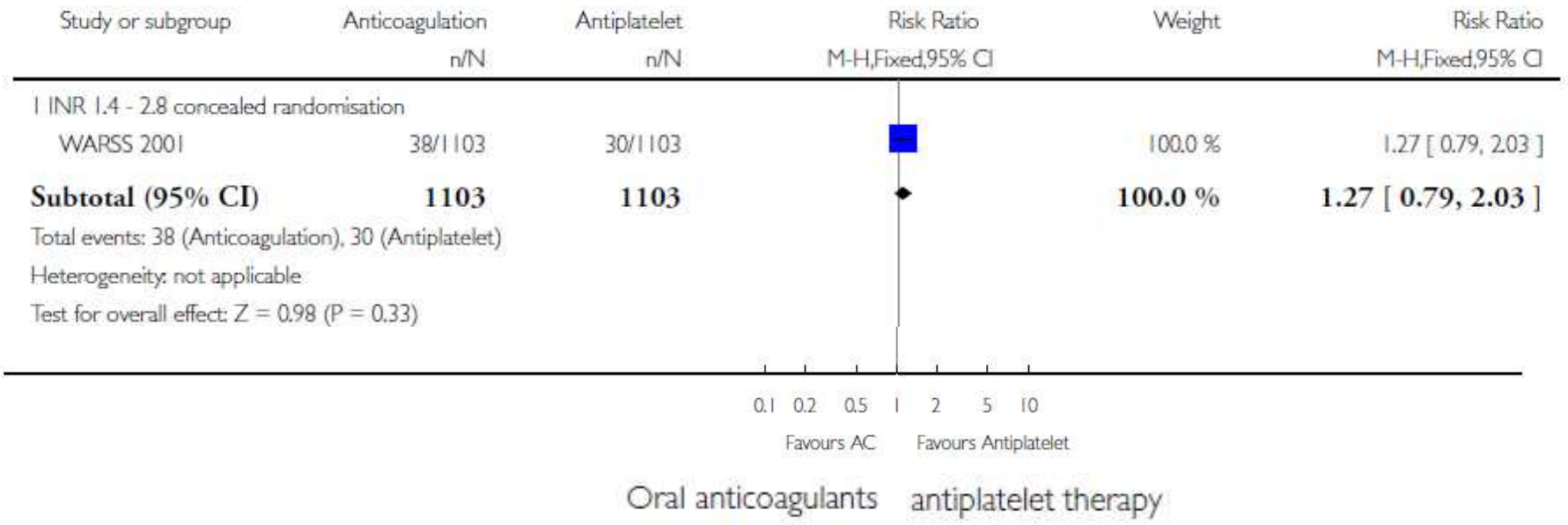
recurrent ischaemic stroke



Anticoagulants 相較於antiplatelet 在recurrent ischaemic stroke 風險 RR=1.00 (95% CI: 0.56-1.77)

結果評讀

major bleeding complication



Anticoagulants 相較於antiplatelet 在Major bleeding complication 風險 RR=1.27 (95% CI: 0.79-2.03)

回歸到臨床應用考量

- 病患狀況_1
- 採取KG FH 2004
- 結論Aspirin+ PPI比clopidogrel+PPI
  - 降低胃潰瘍復發好

(OR: 0.03, 95% CI 0.03-0.50, P=0 .039)

- 病患狀況_2
- 採取Algra 2009
- 結論Anticoagulants 比 antiplatelet
  - Recurrent ischaemic stroke 風險 RR=1.00 (0.56-1.77)
  - Major bleeding complication 風險 RR=1.27(0.79-2.03)
  - 皆無統計上差異

健保給付規定

- 消化性潰瘍及逆流性食道炎符合洛杉磯食道炎分級表
- 欲使用消化性潰瘍用藥，其使用期間以四個月為限，申報費用時需檢附四個月內有效之上消化道內視鏡檢查或上消化道X光攝影報告，其針劑限使用於消化道出血不能口服之病人急性期替代療法。(92/10/1)

EBCPG與其他治療之比較

藥物	方便性	價錢 (NTD;月)
Aspirin	100mg QD	約21
Clopidogrel	75 mg QD	約1200
Warfarin	5mg QD	約100
PPI	QD	約1200

價錢參考自健保局　　劑量參考自UpToDate

回歸到我們的病患

這個研究的結果適用於我們的病人嗎？

評估項目	
病人特性	年齡/其他疾病/personal hx.
病人順從度	病患對副作用的認同
醫療人員執行順從度	醫護照護過程人力時間資源消耗

團隊給病人之建議

使用的好處:
Aspirin+ PPI比clopidogrel+PPI降低胃潰瘍復發好 (OR: 0.03, 95% CI 0.03-0.50, P=0 .039)

使用的壞處
四個月內仍要追蹤一次胃鏡。

最後的建議: 以目前最好的證據等級同時使用Aspirin和氫離子阻斷劑可有效降低胃潰瘍及出血的發生，所以建議您換成Bokey合併氫離子阻斷劑。

與病人對話

目前最好的醫學證據，若同時使用Aspirin和氫離子阻斷劑可有效降低胃潰瘍及出血的發生，與比較其他藥物如Plavix、Warfarin等，Aspirin價格最低，副作用較少，但仍建議加上氫離子阻斷劑，所以多方面考量下建議您換成Aspirin合併氫離子阻斷劑來預防胃潰瘍和中風的復發。

Thank you for your attention

Taichung Veterans General Hospital