Reference: Sung JJ, et al. Continuation of low-dose aspirin therapy in peptic ulcer bleeding. Ann Intern Med. 2010;152:1-9.

Clinical question posed by this trial: In a patient with a history of CHD or CVA who has just achieved homeostasis following a peptic ulcer bleed, does the continuation of low-dose aspirin versus withholding aspirin for 2 months increase the risk of short-term re-bleeding?

Methodology

Study design	Non-inferiority RCT
Sequence generation	Appropriate (computer-generated list of random #s)
Allocation concealment	Adequate (independent staff dispensed consecutive sealed bottles of study dryg)
Blinding	Identical matching placebo (patient, clinician, adjudicator blinded)
Loss to follow-up	0%? (3 patients total terminated early)
Population analyzed	Intention-to-treat (no dropouts)
Intervention	• ASA 80 mg/day + All received endoscopy ≤24h of onset of UGIB, including epinephrine injection & thermal coagulation + All received panto 80 mg bolus + 8mg/h IV x72h, followed by panto 40 mg PO daily

Outcomes	• **All-cause mortality over 8 weeks**
	• **CVD, CVA, GI death**
	• **Recurrent peptic ulcer bleeding ≤ 30** days of endoscopic treatment (1º outcome)
	  ○ ≥1 of the following + endoscopic confirmation
	  ○ Recurrent hematemesis of fresh blood
	  ○ Melena after a normal stool
	  ○ Decrease in Hb ≥20 g/L ≤24h despite ≥2 units of blood transfused
	  ○ Unstable hemodynamic status (SBP≤90, HR≥110) after achieving stabilization
	• **Recurrence of ACS or CVA**
	• **Requirement of blood transfusion**
	• **Duration of hospital stay**
	• **Requirement of surgery**

Duration	8 weeks
Funding	Non-industry

Participants

Setting	Single-centre (Hong Kong tertiary care)
Inclusion criteria	• Peptic ulcer showing active bleeding, visible blood vessels, or adherent clots that were successfully treated with endoscopy • Continued requirement for low-dose ASA (≤325mg/day) for prophylaxis of CVD
Relevant exclusion criteria	• Receiving ASA for primary prevention • Unsuccessful endoscopic hemostasis of bleeding ulcers • Gastric outlet obstruction • Ulcer perforation • Previous partial gastrectomy or vagotomy • Receiving anticoagulants, corticosteroids or NSAIDs • Pregnancy
Study size	156 patients (78 on ASA, 78 on placebo)

"Average" patient	• Male 62%
	• Indication for ASA
	  ○ CHD 50-60%
	  ○ CVA 30-40%
	  ○ Both 10%
	• Age mean 74y
	• Previous ulcer bleeding 12%
	• Mean baseline Hb ~85-90
	• Location of bleed
	  ○ Gastric 55%
	  ○ Duodenal 45%
	• Endoscopic stigmata
	  ○ Active bleeding 30-35%
	  ○ Visible vessel 40-45%
	  ○ Adherent clot ~25%
	• Previous NSAID use ~15%

No clinically-relevant baseline between-group differences

Results

	Aspirin	Placebo	RR	ARD
Death (at 2 months)	1.3%	12.9%	0.10 (0.01-0.76)	11.6% (NNT 5-28)
from CV complications	1.3%	6.4%		
From GI complications	0%	3.9%		
from pneumonia	0%	2.6%		
Recurrent non-fatal ischemic events	5.1%	2.6%	0.50 (0.09-2.65)	
Confirmed recurrent bleed	10.3%	5.4%	2.00 (0.63-6.37)	+4.9% (-3.6% to +13.4%)
	**did not meet non-inferiority criteria (lower bound of ARD >10%)*			
Median units of blood transfused	2	3		
Median hospital stay (days)	5	4.5		

Major Limitations:

Methods

- **Baseline differences**: More smokers in placebo group, more ASA grade 3 patients in ASA group

Results

- Mortality reduction with ASA in context **of failure to show NI in re-bleed** (1^{o} outcome)
  - Despite a very generous MCID
- **Low # of events, mortality reduction may be due to chance**
  - Lower mortality from GI complications and pneumonia not explained by ASA pharmacology
- **Re-bleeding rates were much higher in both groups at 2 months compared to 1-year re-bleed rates in previous RCT by Chan et al.**
  - Differences in baseline characteristics do not explain this.

Generalizability

- Conducted in **tertiary care setting with skilled endoscopists** – endoscopic intervention and ulcer identification may not be as good in real-world setting
- Conducted in **single Hong Kong hospital** – GI risk/CV benefit of restarting ASA may be different in other ethnic groups
- Unknown benefit/harm of restarting ASA immediately after achieving homeostasis (as per study protocol) compared to restarting "once CV benefit outweighs risk, usually within 7 days" (expert consensus).

Conclusions:

- This study, though limited by sample size, provides some reassurance that following a peptic ulcer bleed, starting aspirin immediately after achieving homeostasis is as safe, and potentially safer, than withholding aspirin.