Gastrointestinal bleeding

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https://lacolon.com/article/gastrointestinal-bleeding

Objectives

By the end of the lecture the student should be able to:

1. Explain the pathophysiology of shock from upper gastrointestinal bleeding.

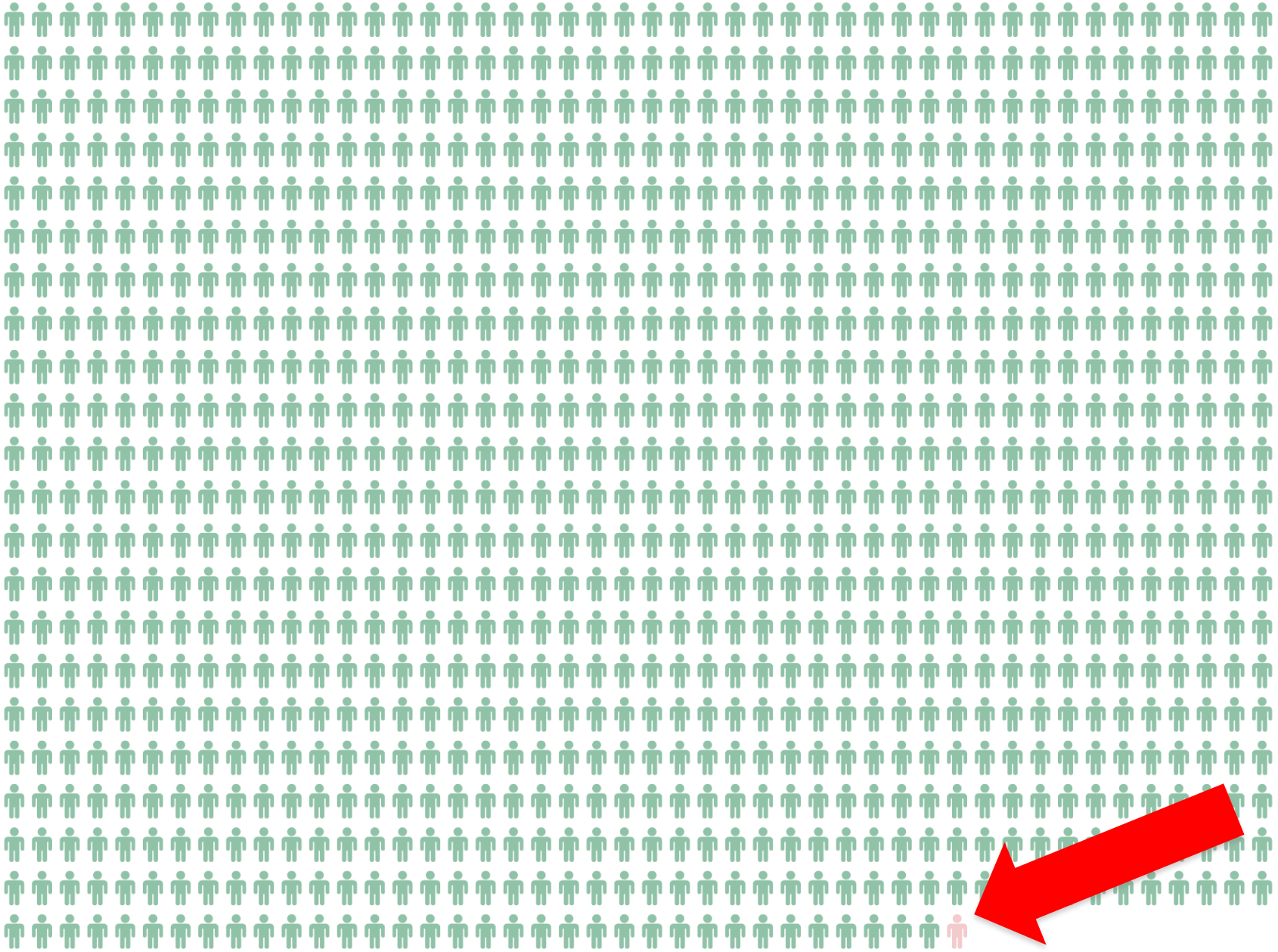
2. Outline the proper investigation of patients presenting with upper gastrointestinal bleeding and an appropriate deferential diagnosis.

Objectives

3. Outline the proper initial management of patients presenting with upper gastrointestinal bleeding

4. Recognize the differences in the approach of upper gastrointestinal bleeding from a variceal vs. non-variceal source.

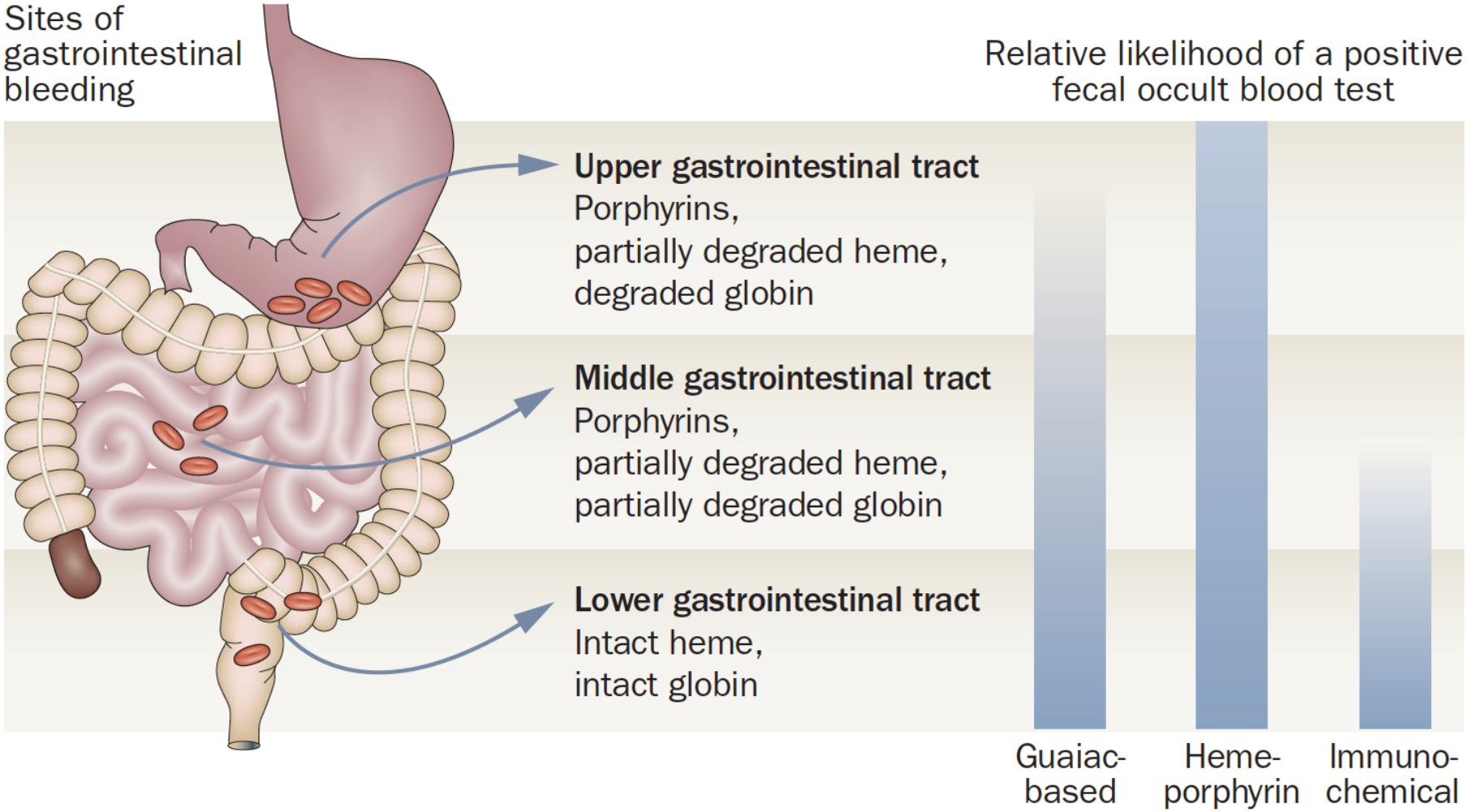
Incidence; 57-78 cases per 100,000 population



Clinical manifestations of UGIB

	Sources of GI Bleeding					
	Esophagus	Stomach	Duodenum	Small Intestine[a]	Right Colon	Left Colon
Hematemesis	X	X	X	—	—	—
Coffee-ground emesis	X	X	X	—	—	—
Melena	X	X	X	X	X	—
Guaiac-positive stool	X	X	X	X	X	X
BRBPR	(If severe)	(If severe)	(If severe)	(If severe)	X	X

Simon TG, et al. Gastrointestinal endoscopy clinics of North America 2015;25:429-42.



Rockey DC. Nat Rev Gastroenterol Hepatol. 2010 May;7(5):265-79.

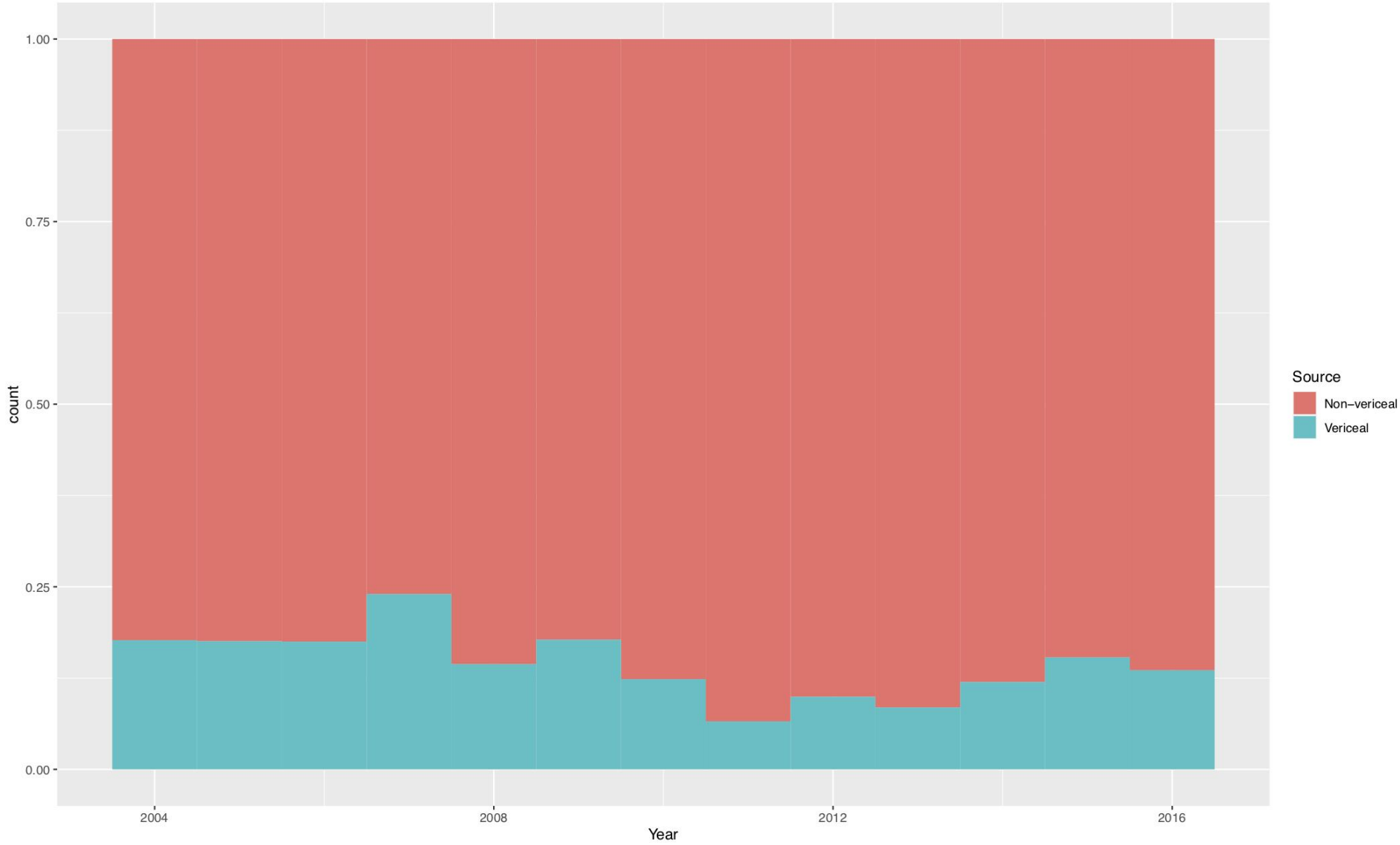
Causes of UGIB

Table 1
Frequency of common causes of upper gastrointestinal bleeding

Diagnosis	Frequency (Percentage)
Peptic ulcer disease, including duodenal and gastric ulcer	28–59
Variceal bleeding	4–14
Mucosal erosive disease, including esophagitis, gastritis, and duodenitis	1–31
Mallory-Weiss tear	4–8
Malignancy	2–4
Arteriovenous malformation	3
Gastric antral vascular ectasia	~1
Dieulafoy lesion	~1

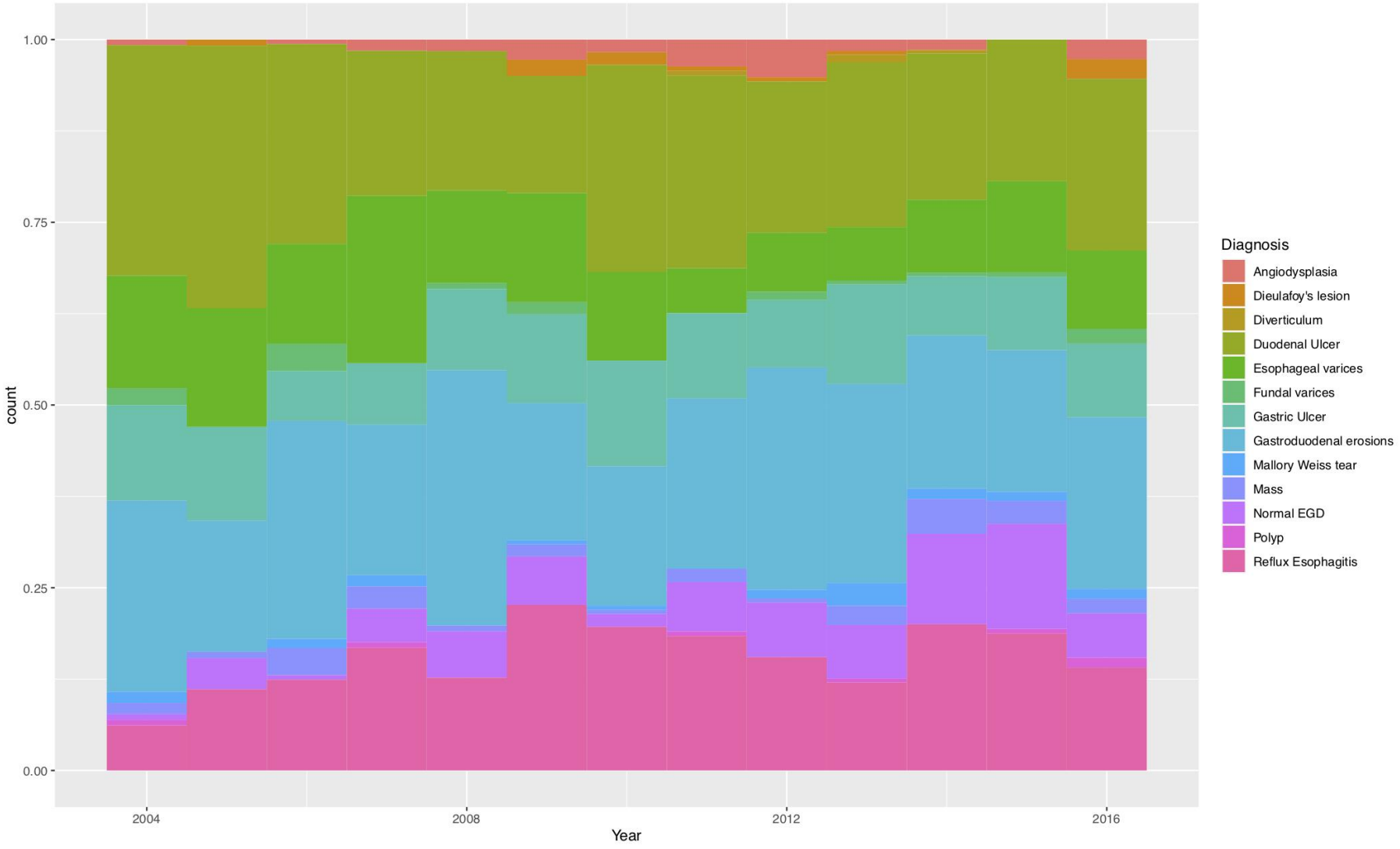
Gibson et al. Gastrointest Endosc Clin N Am 2011;21:583-96.

Time trends comparing variceal and non-variceal source of upper gastrointestinal bleeding



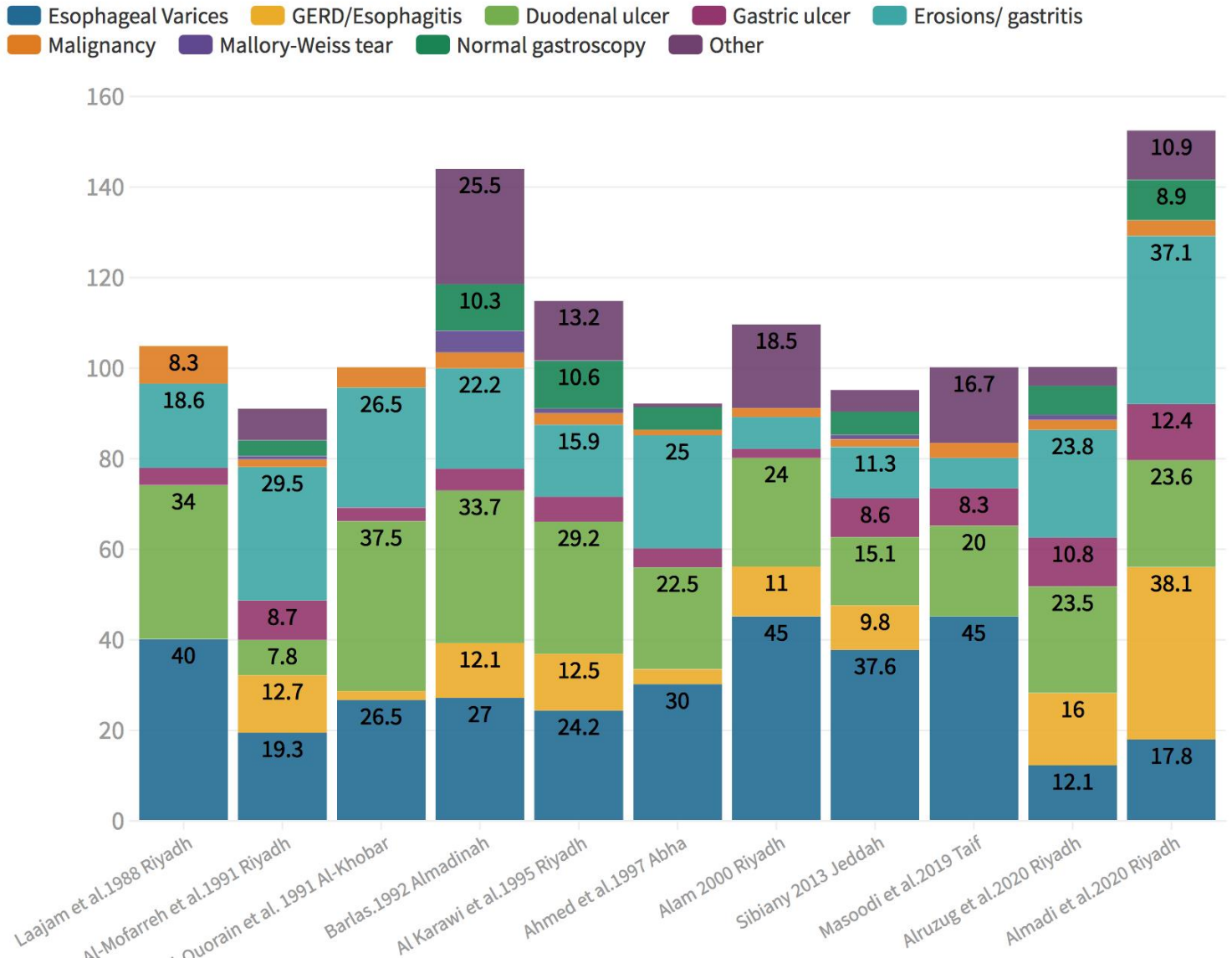
Alruzug IM, et al. Saudi J Gastroenterol. 2020 Oct 12

Time trends comparing different endoscopic diagnoses of upper gastrointestinal bleeding



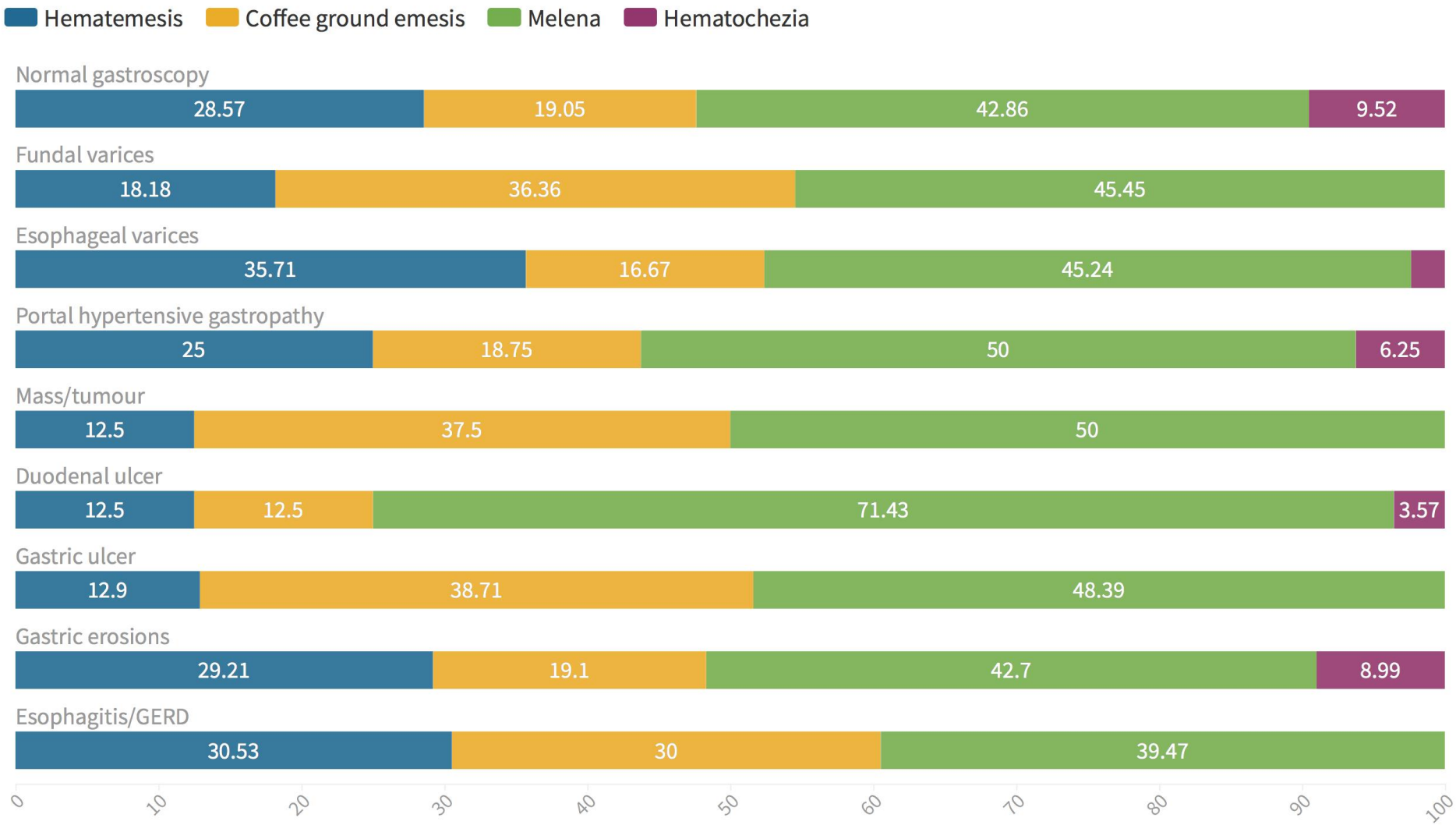
Alruzug IM, et al. Saudi J Gastroenterol. 2020 Oct 12

Proportion of Causes of Upper Gastrointestinal Bleeding Based on Different Studies in KSA



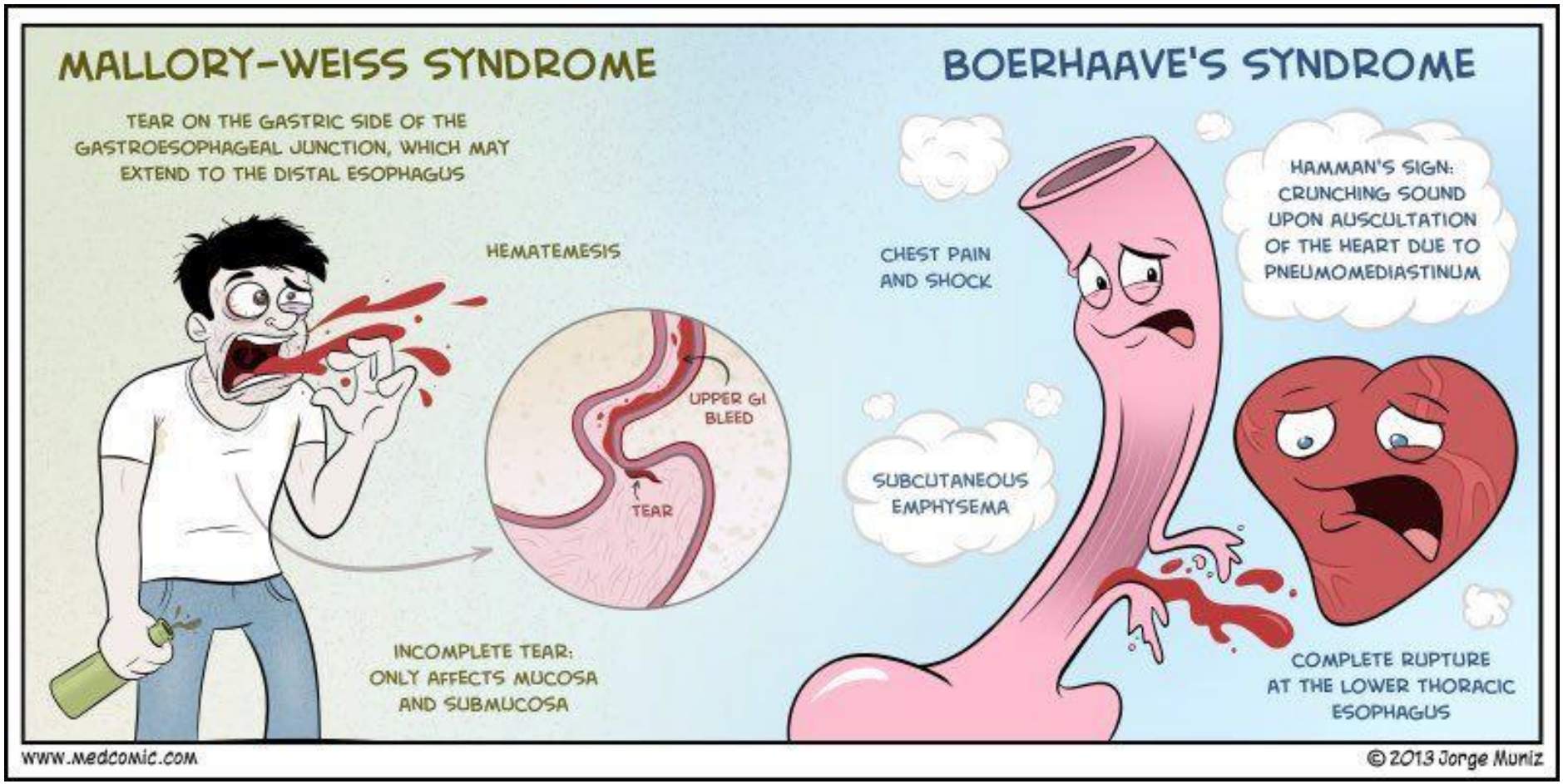
Almadi MA, et al. Saudi J Gastroenterol. 2020 Oct 12

Causes of Upper Gastrointestinal Bleeding in a Tertiary Care Center in Riyadh



Almadi MA, et al. Saudi J Gastroenterol. 2020 Oct 12

PUD 36-50% of UGIB


MALLORY-WEISS SYNDROME
TEAR ON THE GASTRIC SIDE OF THE GASTROESOPHAGEAL JUNCTION, WHICH MAY EXTEND TO THE DISTAL ESOPHAGUS
HEMATEMESIS
UPPER GI BLEED
TEAR
INCOMPLETE TEAR: ONLY AFFECTS MUCOSA AND SUBMUCOSA
BOERHAAVE'S SYNDROME
CHEST PAIN AND SHOCK
HAMMAN'S SIGN: CRUNCHING SOUND UPON AUSCULTATION OF THE HEART DUE TO PNEUMOMEDIASTINUM
SUBCUTANEOUS EMPHYSEMA
COMPLETE RUPTURE AT THE LOWER THORACIC ESOPHAGUS
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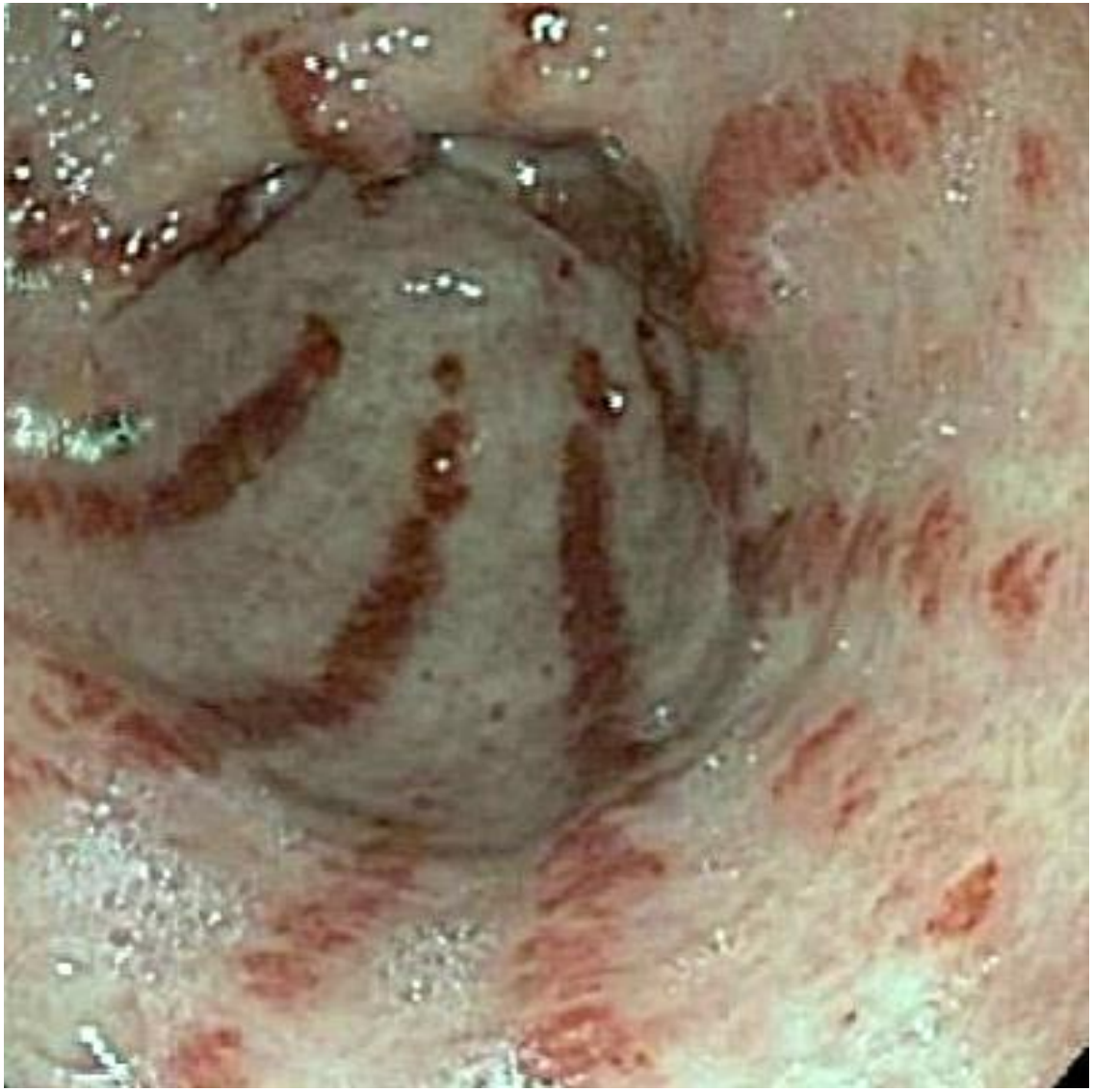
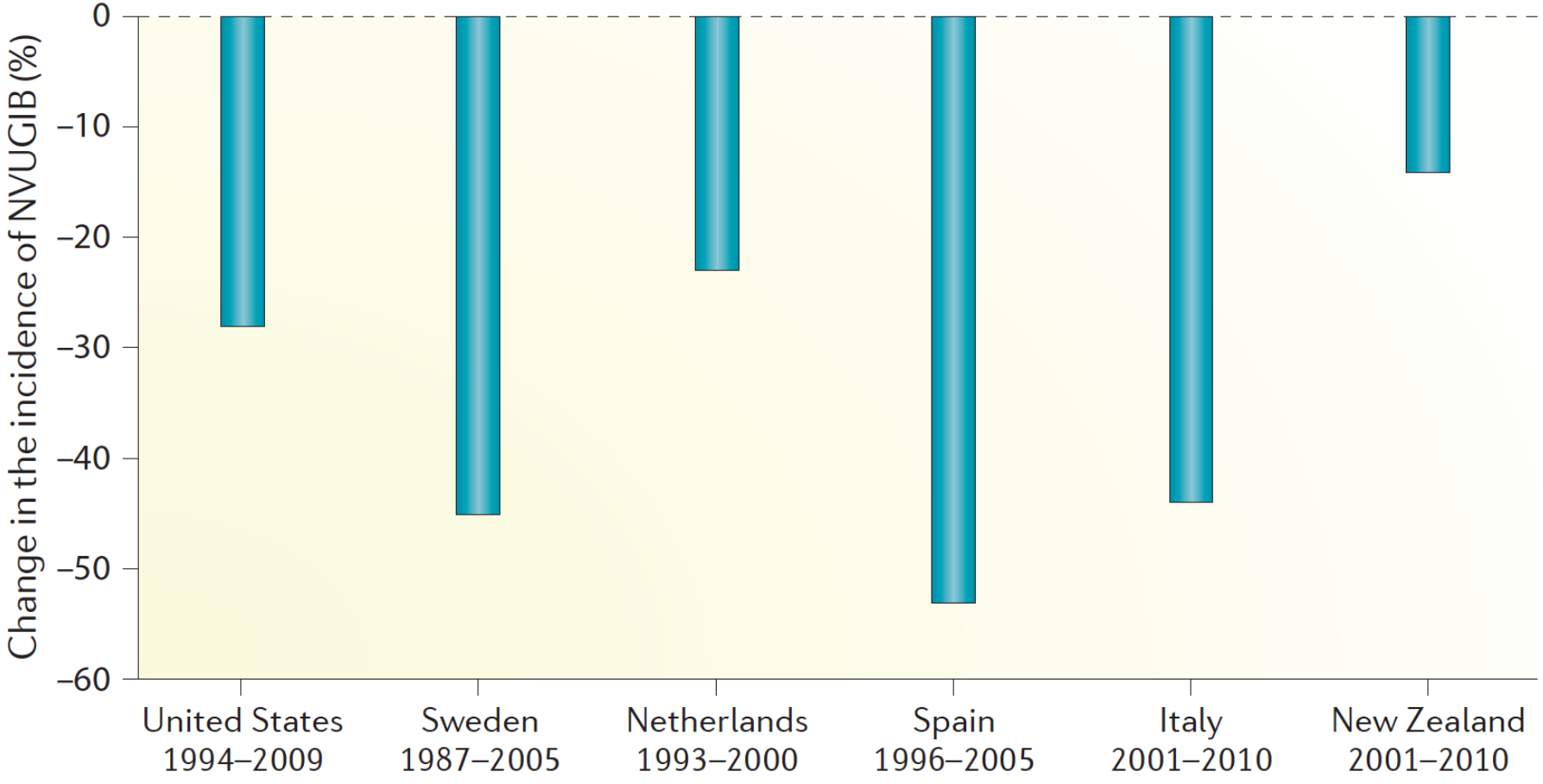
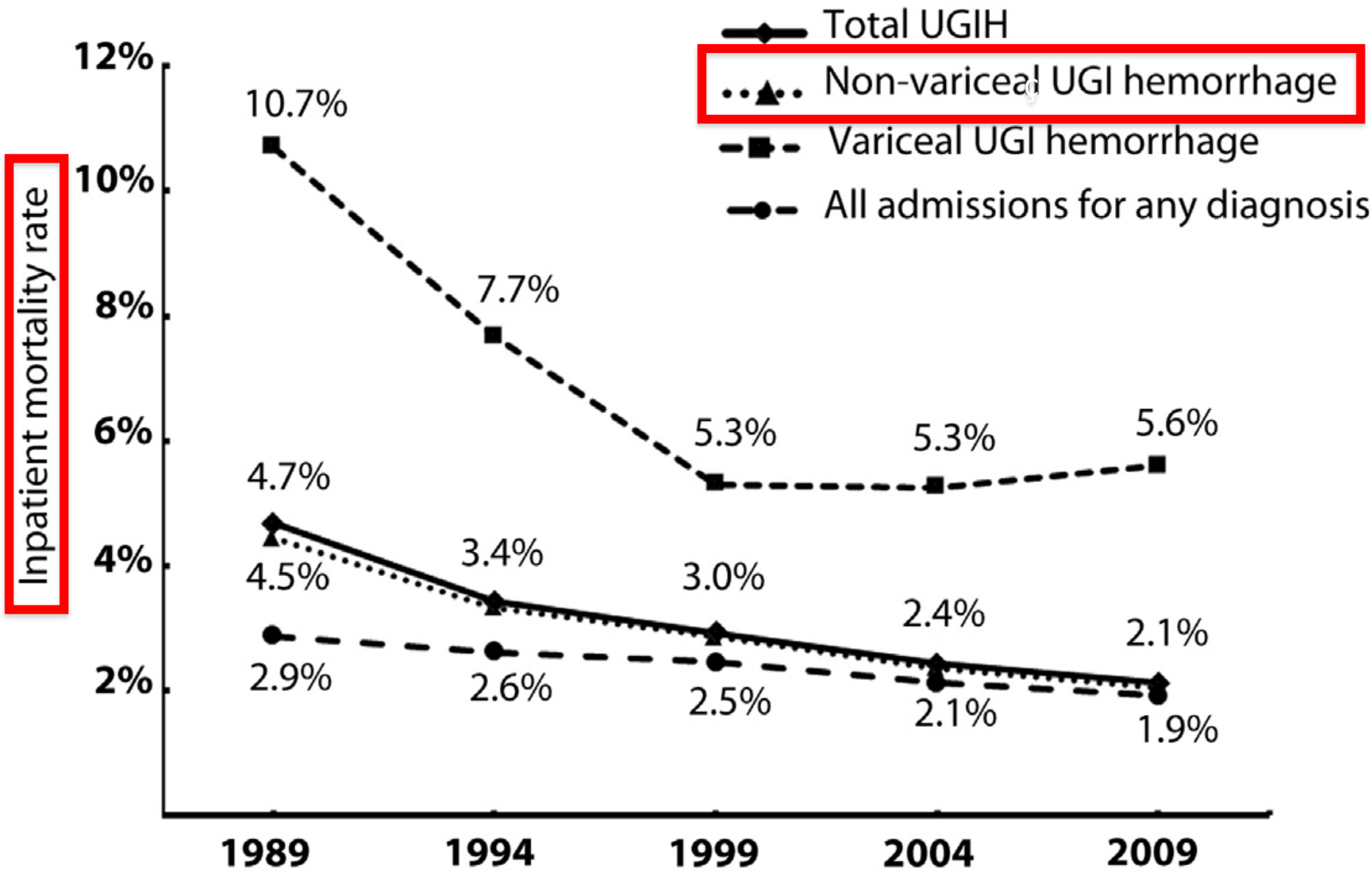
GAVE



The decline in incidence of NVUGIB over time

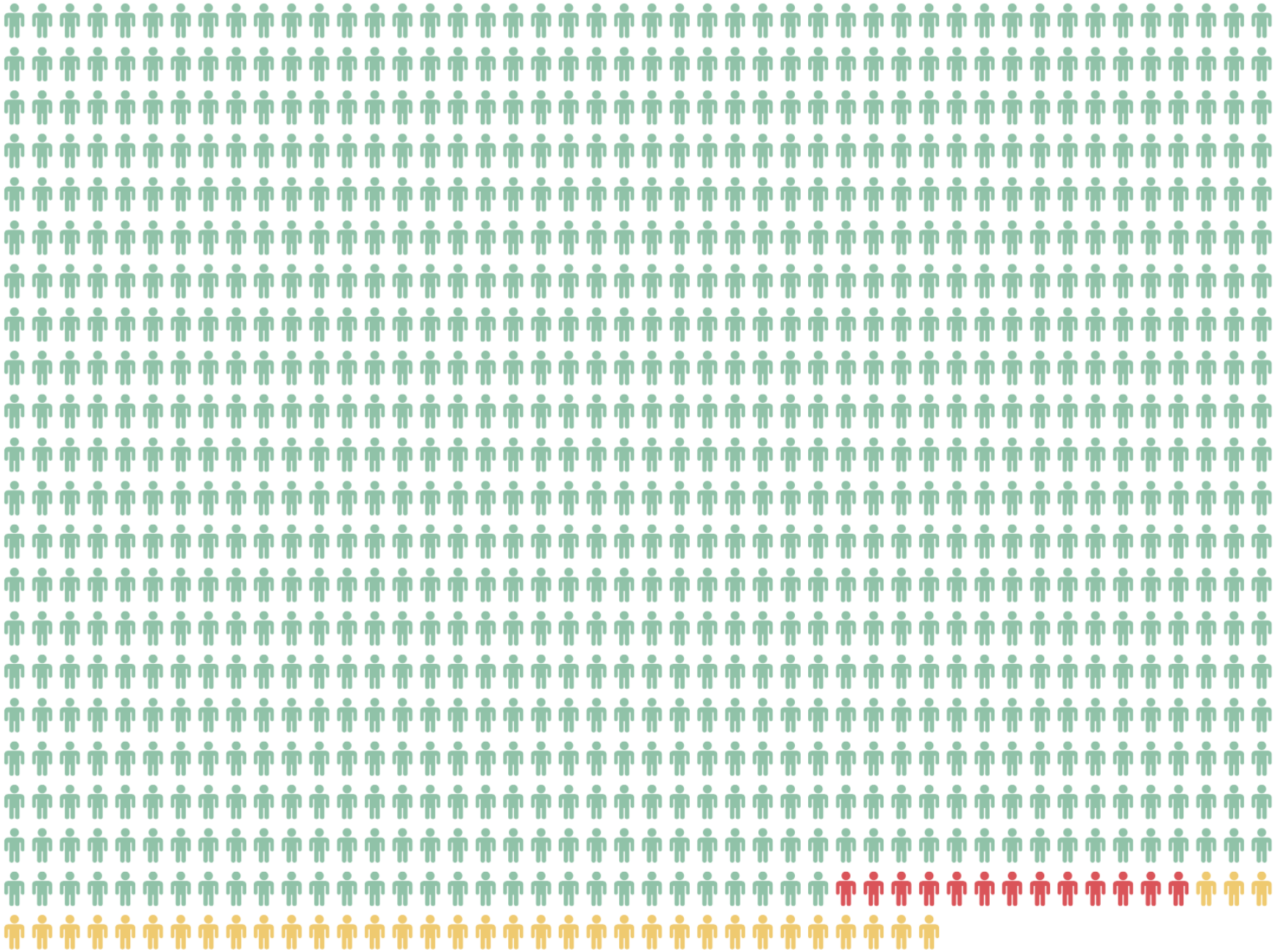


Lanas A, et al. Nat Rev Dis Primers. 2018 Apr 19;4:18020.

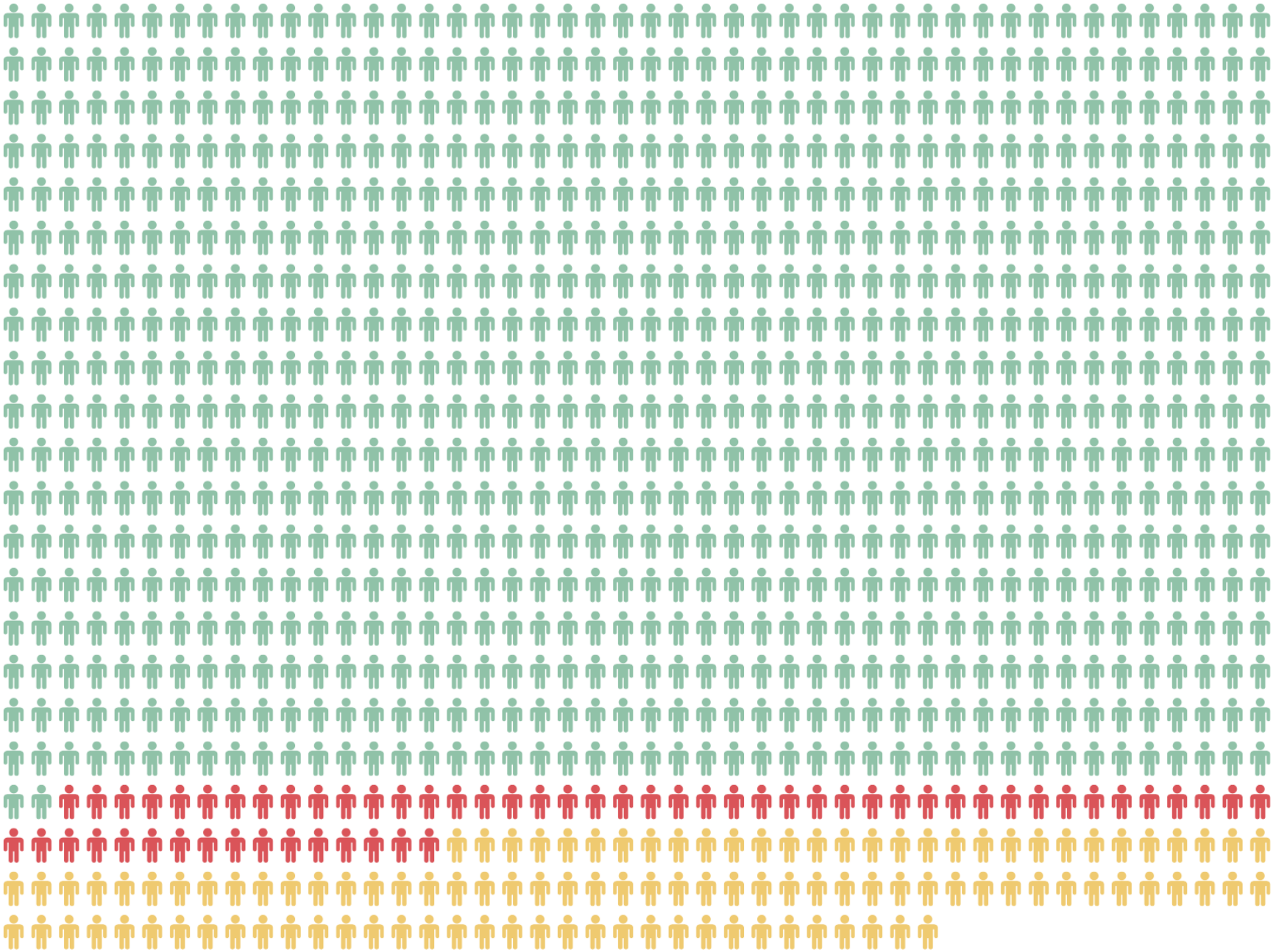


Tielleman T, et al. Gastrointestinal endoscopy clinics of North America 2015;25:415-28.

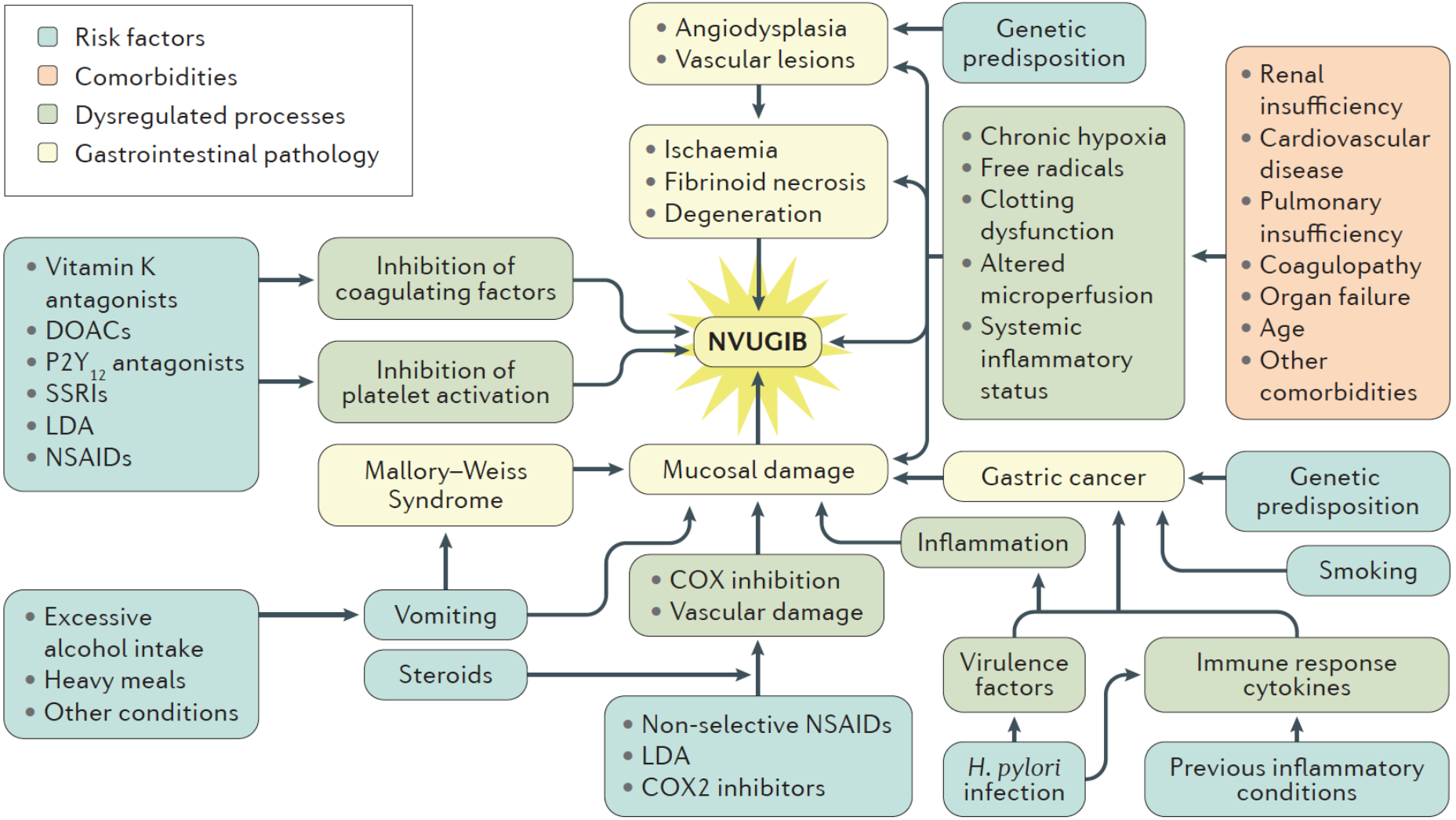
In-hospital mortality 1.7−3.7%



30-day mortality 6−11%

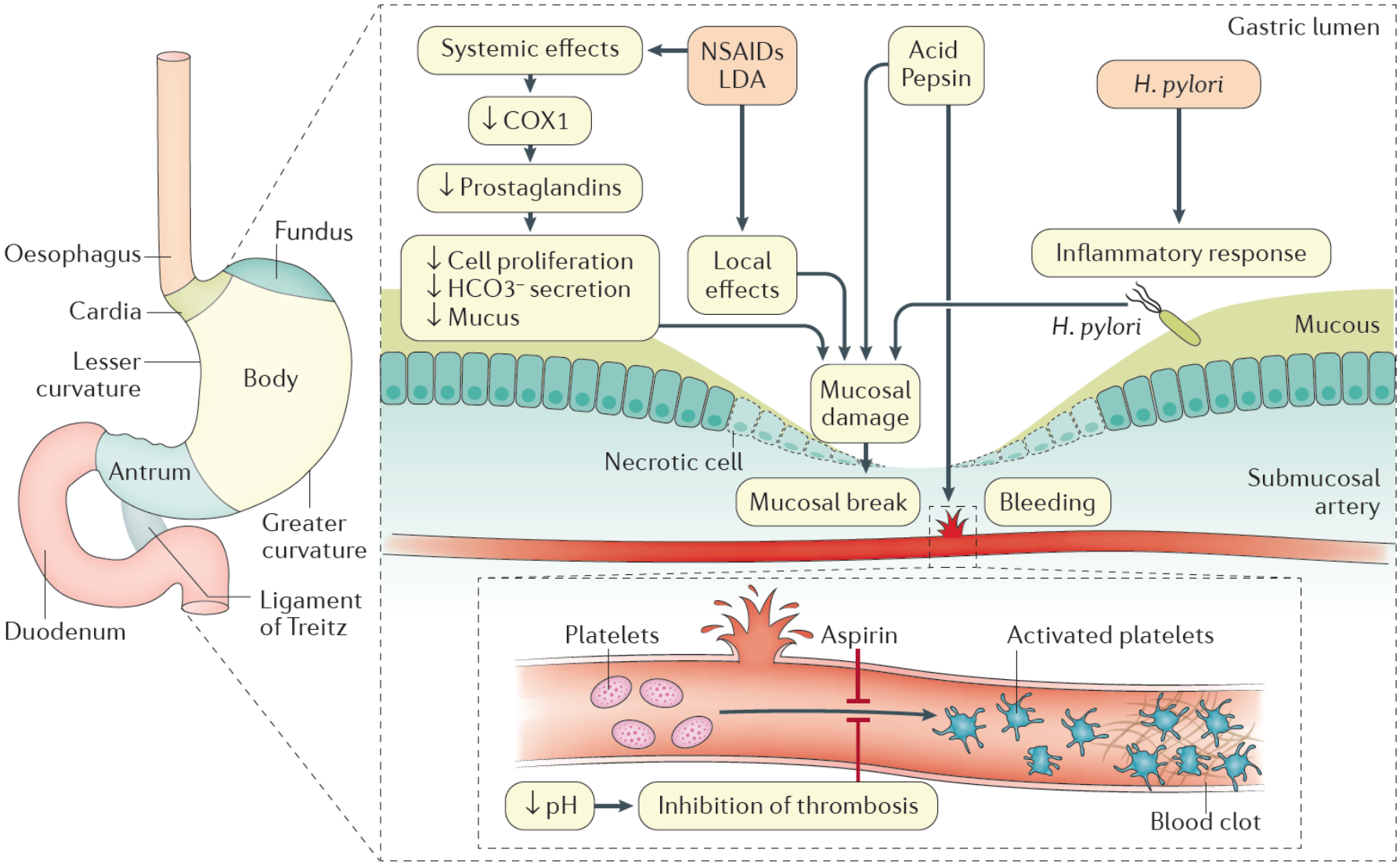


Complex pathophysiology of NVUGIB



Lanas A, et al. Nat Rev Dis Primers. 2018 Apr 19;4:18020.

Mechanisms of upper gastrointestinal bleeding induced by NSAIDs, Low dose Aspirin or H pylori



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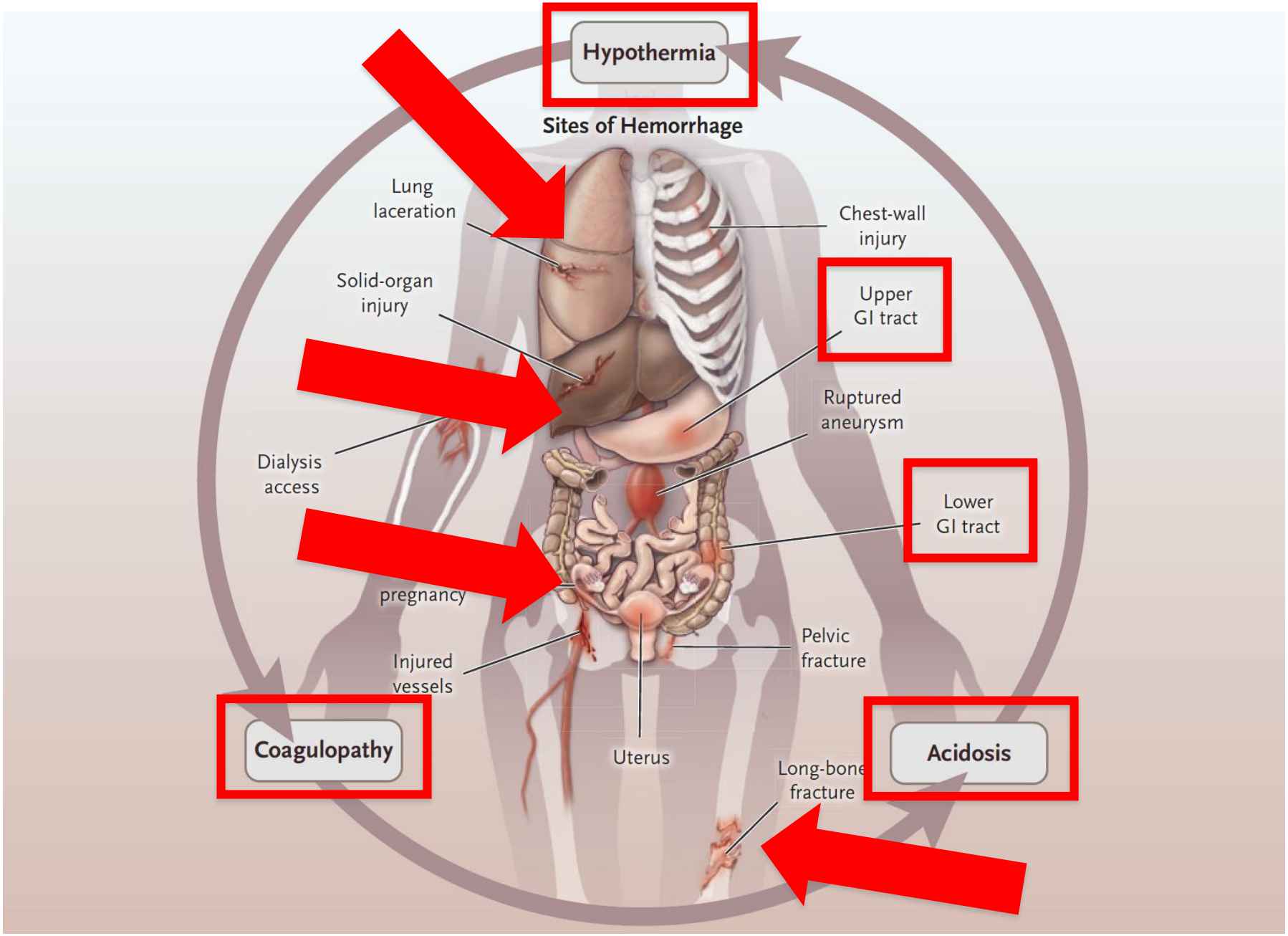
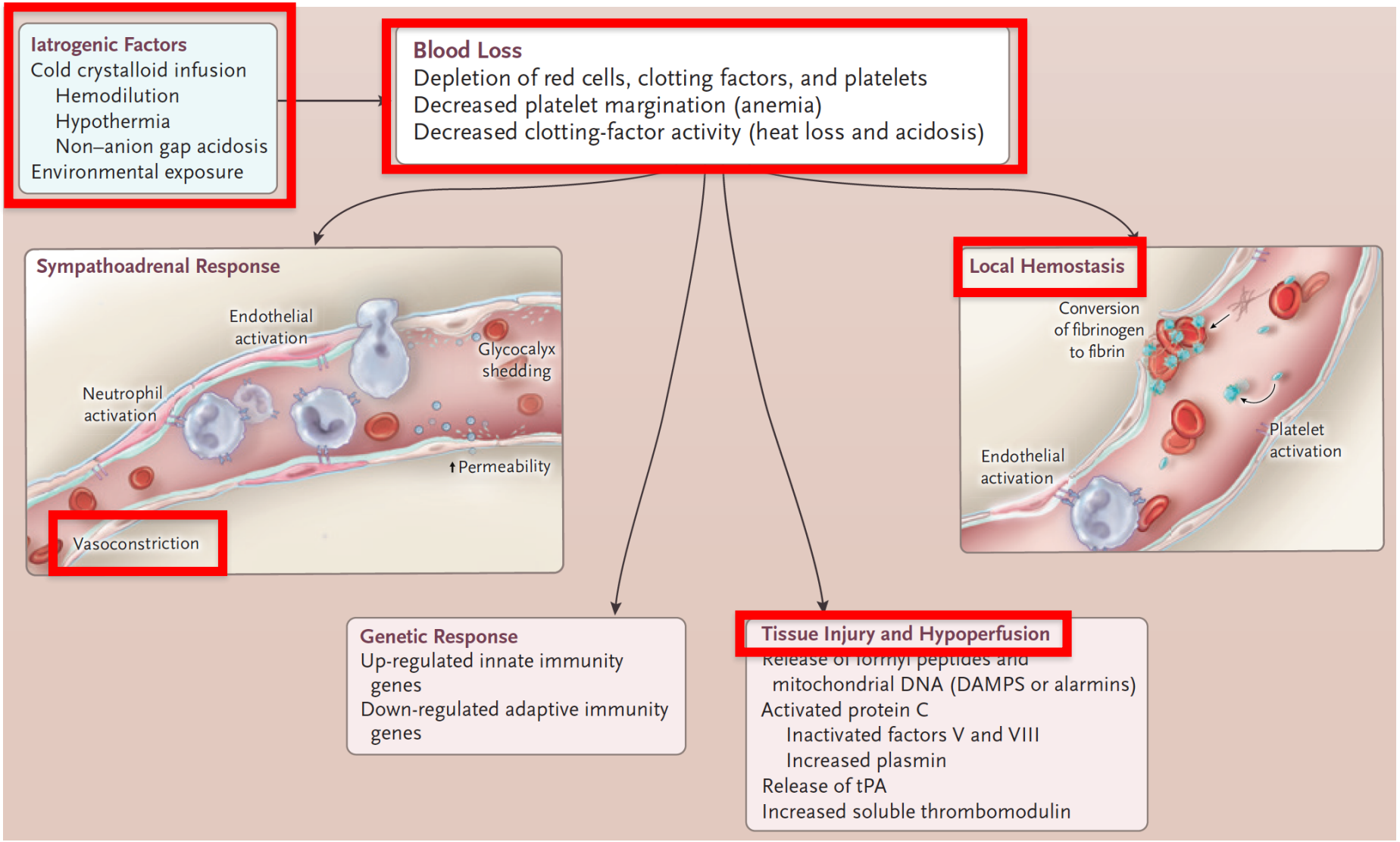


Cannon JW. N Engl J Med 2018; 378:370-379



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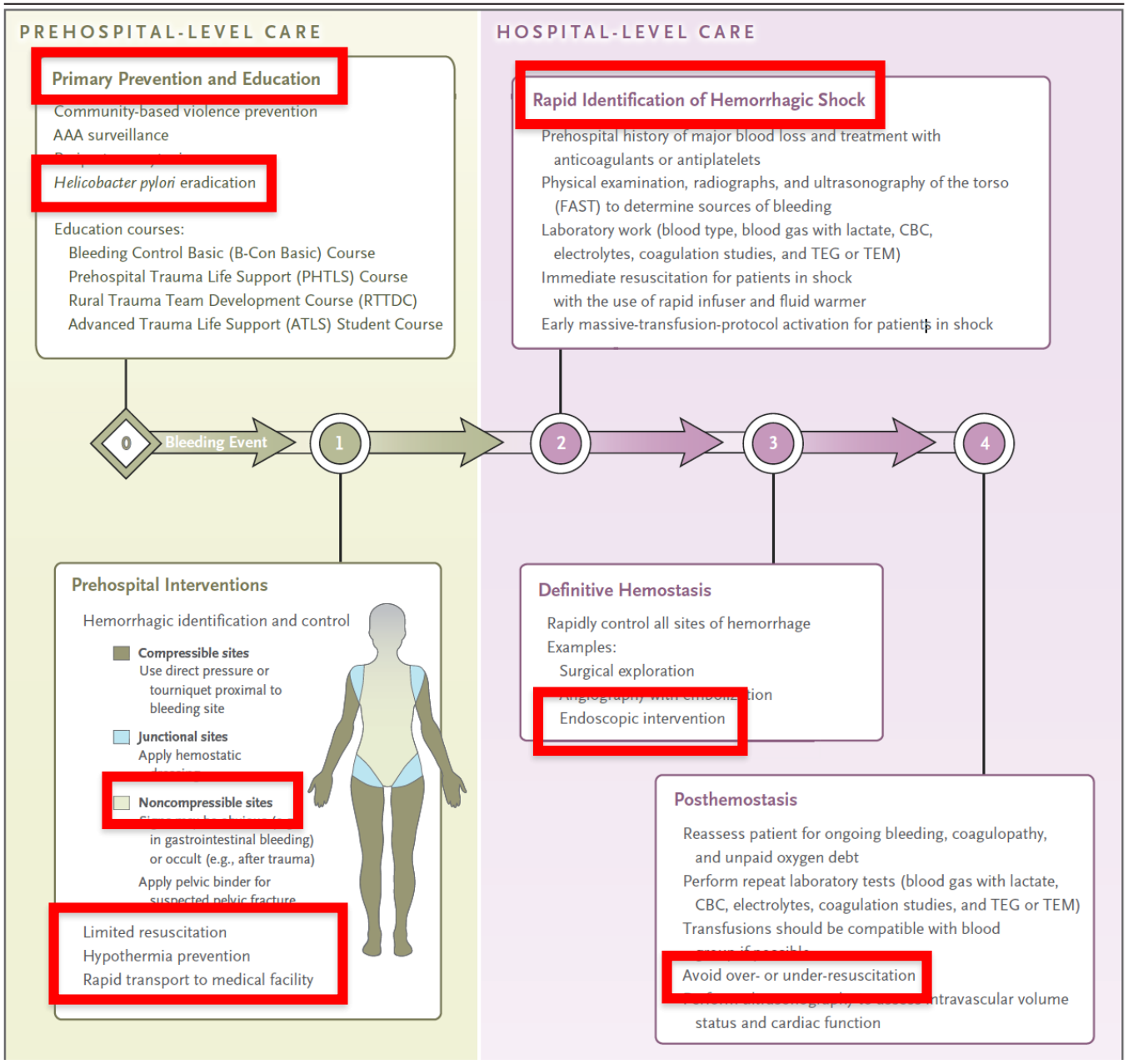


Cannon JW. N Engl J Med 2018; 378:370-379

Table 1. Estimated Hemorrhage-Related Deaths per Year and Years of Life Lost in the United States and Worldwide, According to the Cause of Hemorrhage.

Cause of Hemorrhage	Deaths from Hemorrhage*	U.S. Cases of Hemorrhage		Global Cases of Hemorrhage	
		No. of Deaths per Yr	Yr of Life Lost	No. of Deaths per Yr	Yr of Life Lost
	percent				
Abdominal aortic aneurysm	100	9,988†	65,273‡	191,700§	2,881,760¶
Maternal disorder	23§	138‖	7,572**	69,690‖	4,298,240**
Peptic ulcer disease	60††	1,860‖	38,597**	141,000‖	3,903,600**
Trauma	30‡‡	49,440‖	1,931,786**	1,481,700‖	74,568,000**
Total		61,426	2,043,228	1,884,090	85,651,600

Cannon JW. N Engl J Med 2018; 378:370-379

https://lacolon.com/article/gastrointestinal-bleeding

Hypovolemic shock: symptoms, signs and fluid replacement

Blood loss (mL)	<750	750–1500	1500–2000	>2000
Blood loss (%)	<15	15–30	30–40	>40
Pulse rate	<100	>100	>120	>140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal or increased	Decreased	Decreased	Decreased
Respiratory rate	14–20	20–30	30–40	>35
Urine output (mL)	>30	20–30	5–15	Negligible
Mental status	Slightly anxious	Mildly anxious	Anxious and confused	Confused and lethargic
Fluid replacement	Crystalloid	Crystalloid	Crystalloid and blood	Crystalloid and blood

Table 2. Classification of Hemorrhagic Shock.*

Shock Class	Blood Loss†	Heart Rate	Blood Pressure	Pulse Pressure	Respiratory Rate	Mental Status
	ml (%)	*beats/min*			*breaths/min*	
I	<750 (15)	<100	Normal	Normal	14–20	Slightly anxious
II	750–1500 (15–30)	100–120	Normal	Narrowed	20–30	Mildly anxious
III	1500–2000 (30–40)	120–140	Decreased	Narrowed	30–40	Anxious, confused
IV	>2000 (>40)	>140	Decreased	Narrowed	>35	Confused, lethargic

* Data are from the American College of Surgeons Committee on Trauma.[42]
† Blood-loss volume and percentage of total blood volume are for a male patient with a body weight of 70 kg.

Cannon JW. N Engl J Med 2018; 378:370-379

Pre-endoscopic management

Risk stratification

- Low vs. high risk
- Early identification
- Appropriate intervention
- Minimizes morbidity and mortality

Barkun et al. Ann Intern Med 2010;152:101-13.

Gastroenterology

Interventional Rad.

YOU ARE NOT ALONE

Intensive Care

Surgery

Table 1 | Glasgow–Blatchford score assessment criteria

	Risk factors at presentation	Threshold	Score
Urea	Blood urea nitrogen (mmol/l)	6.5–7.9	2
		8.0–9.9	3
		10.0–24.9	4
		≥25.0	6
CBC	Hemoglobin for men (g/l)	120–130	1
		100–119	3
		<100	6
	Hemoglobin for women (g/l)	100–120	1
		<100	6
Physical	Systolic blood pressure (mmHg)	100–109	1
		90–99	2
		<90	3
	Heart rate (bpm)	>100	1
History	Melena	Present	1
	Syncope	Present	2
	Hepatic disease	Present	2
	Cardiac failure	Present	2

Total score (0–23). Patients with scores >0 are considered to be at high risk. Permission obtained from Elsevier Ltd © Blatchford, O. *et al*. *Lancet* **356**, 1318–1321 (2000).

Bardou et al. Nat Rev Gastroenterol Hepatol 2012;9:97-104.



IV Fluid Resuscitation



Then


Zebra Technologies
Blood Center
O
Rh Positive
VOLUNTEER DONOR
RED BLOOD CELLS
15 APR 2019

Comparison of flow rates through IV catheters

Type and Diameter of Venous Catheter	Maximum Flow Rate
20-gauge	60 mL/min
18-gauge	105 mL/min
16-gauge	220 mL/min
Triple lumen catheter	
Medial (blue)/proximal (white) lumen (18-gauge)	26 mL/min
Distal (brown) lumen (16-gauge)	52 mL/min
Cordis: 8.5 French (100 mm)	126 mL/min 333 mL/min under pressure[a]
Intraosseous line	80 mL/min 150 mL/min under pressure[a]

Simon TG, et al. Gastrointestinal endoscopy clinics of North America 2015;25:429-42.


TRAUMA
MANAGEMENT
Fluid Resuscitation &
Permissive Hypotension

Patients receiving anticoagulants

Correction of coagulopathy is recommended

Endoscopy should not be delayed for a high INR unless the INR is supratherapeutic

Barkun et al. Ann Intern Med 2010;152:101-13.

Initial resuscitation

- Maintain airway, breathing, and circulation
- Ensure large-bore intravenous access and consider monitored setting
- Resuscitate initially with crystalloid solution
- Send blood work including CBC, coagulation studies, and type and cross-matching

Transfusion requirements

- Transfuse red blood cells only if hemoglobin <70g/L, unless symptoms of anemia or significant cardiac disease
- Transfuse platelets only if platelet count $<50 \times 10^9$/L or $<100 \times 10^9$/L with suspected platelet dysfunction

Pre-endoscopic therapy

- Provide erythromycin intravenously 30 minutes prior to endoscopy
- High-dose intravenous proton pump inhibitors should be initiated
- The routine use of nasogastric lavage and/or tranexamic acid is not recommended

Fortinsky KJ, et al. Gastrointestinal endoscopy clinics of North America 2015;25:463-78.

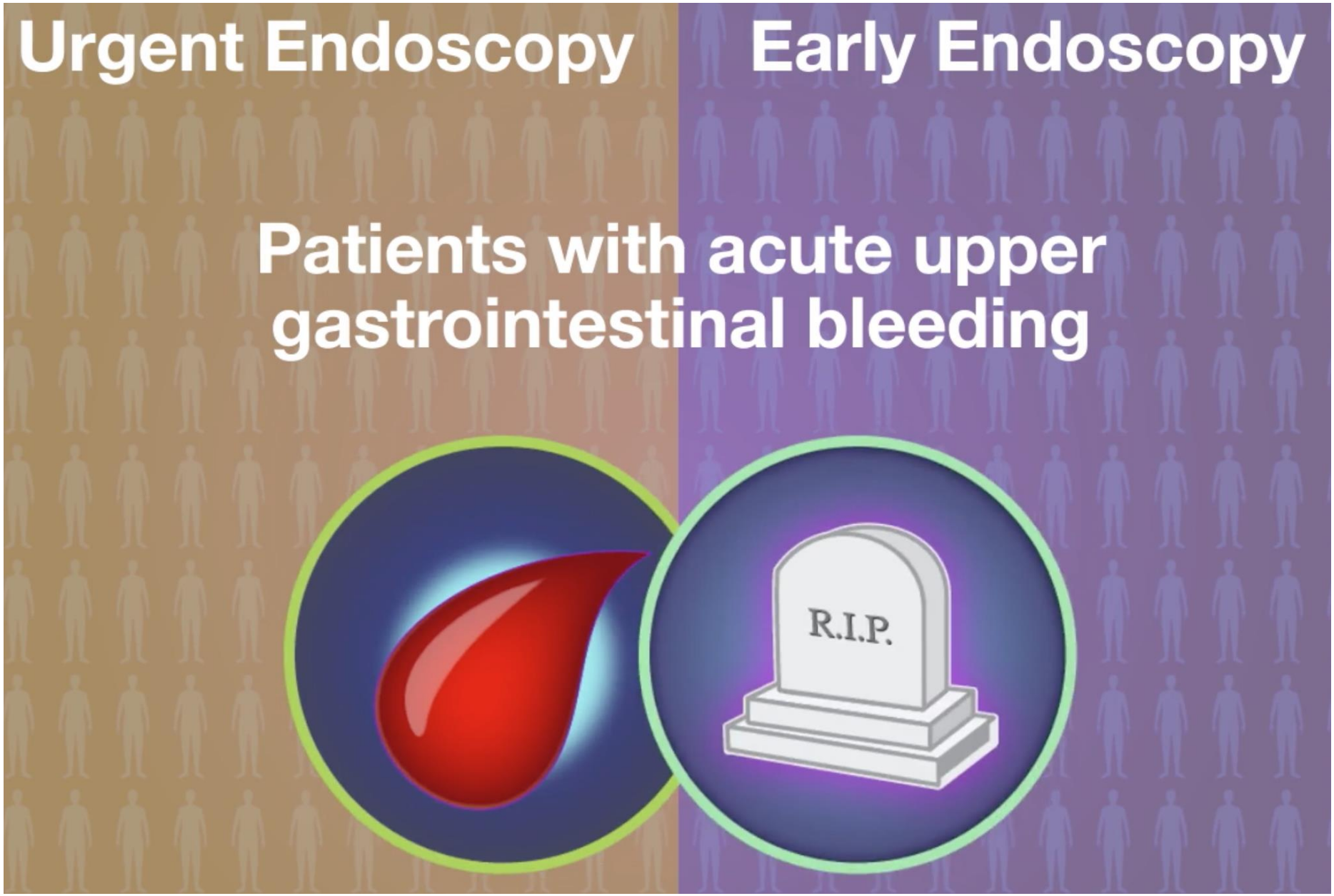
Endoscopic management

Timing and need for early endoscopy

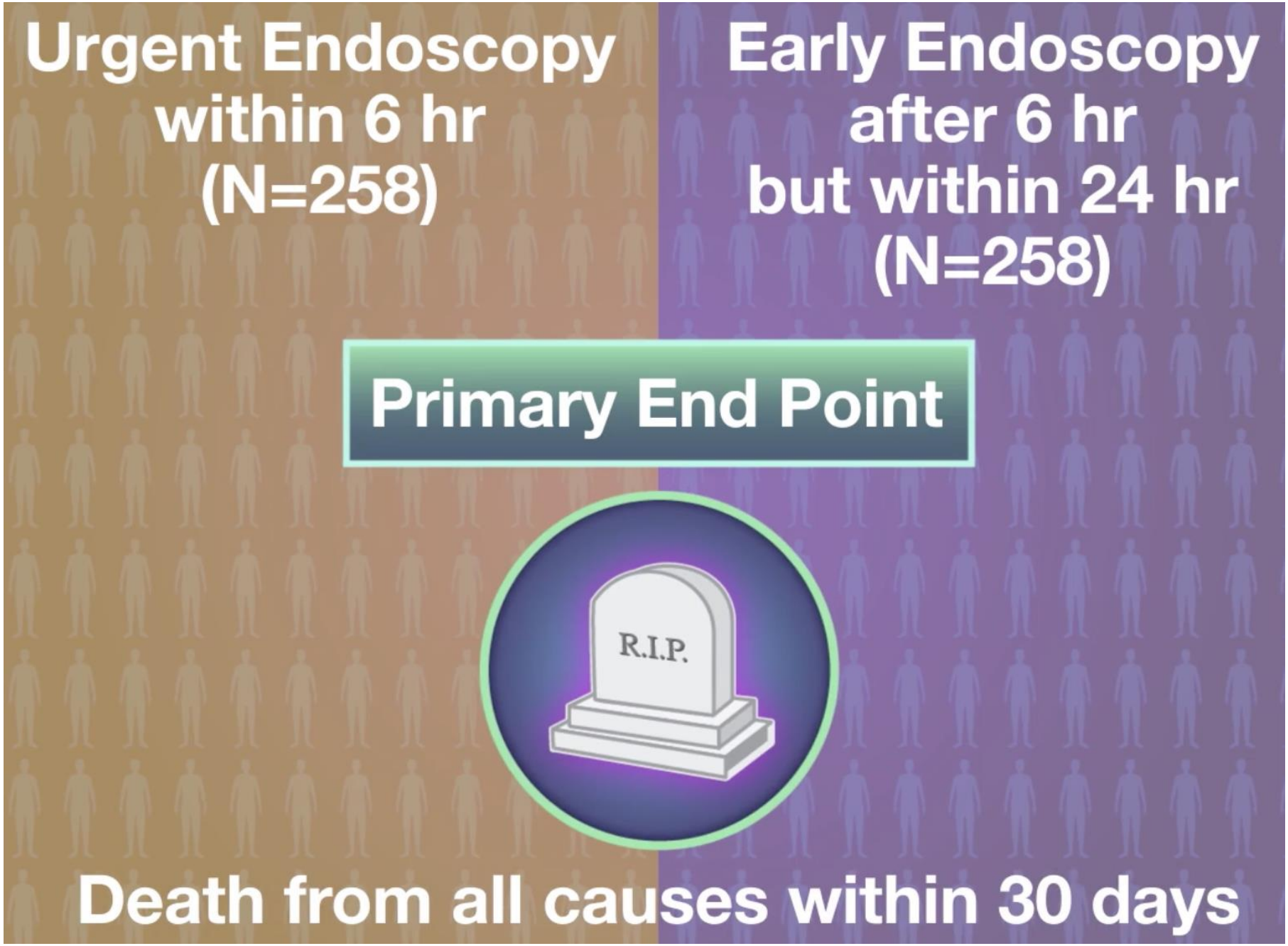
- Definition of early endoscopy
  - Ranges from 2 to 24 hours AFTER INITIAL PRESENTATION

- May need to be delayed or deferred:
  - Active acute coronary syndromes
  - Suspected perforation

Barkun et al. Ann Intern Med 2010;152:101-13.



Lau JYW, et al. N Engl J Med. 2020 Apr 2;382(14):1299-1308.



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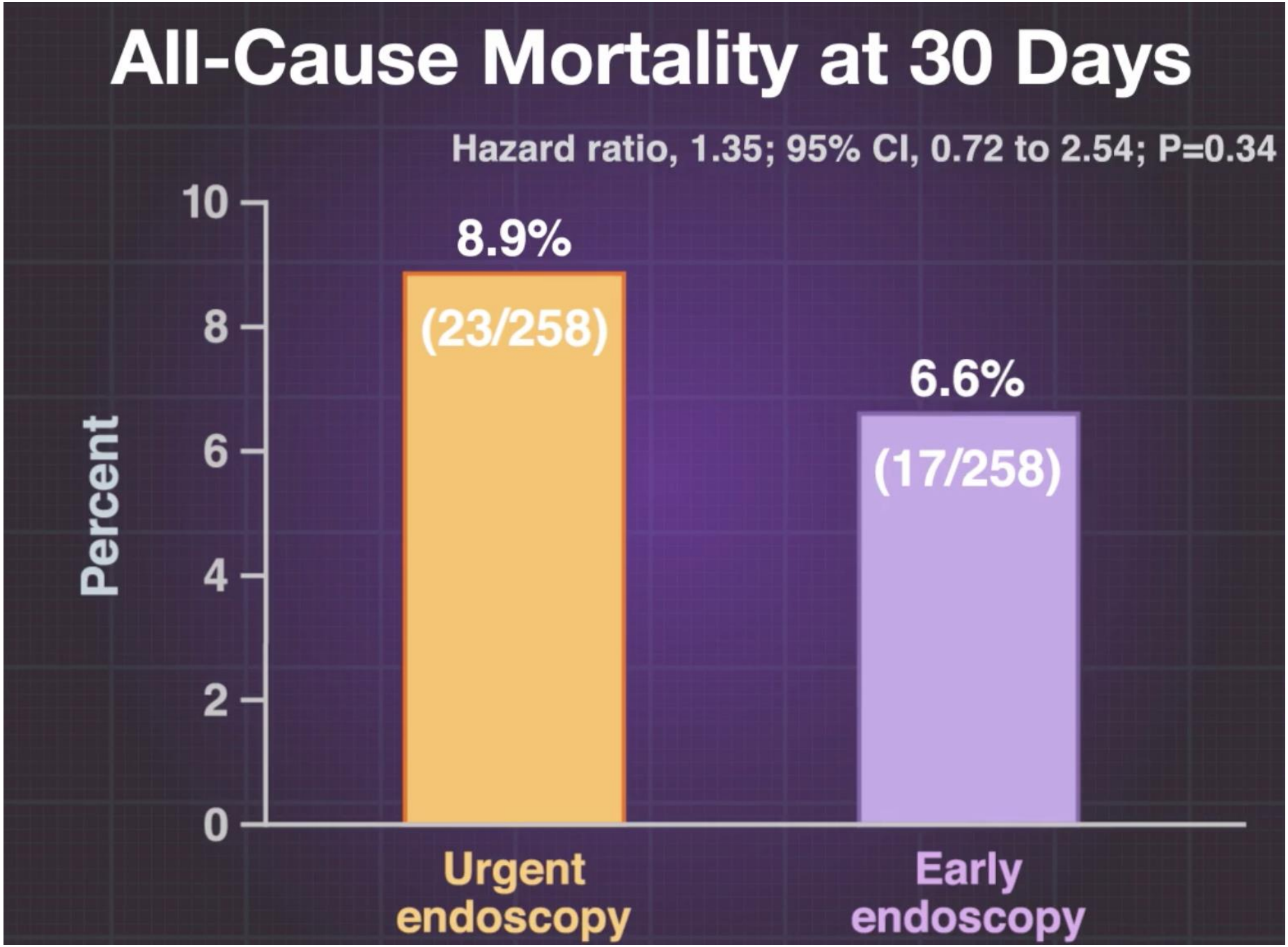

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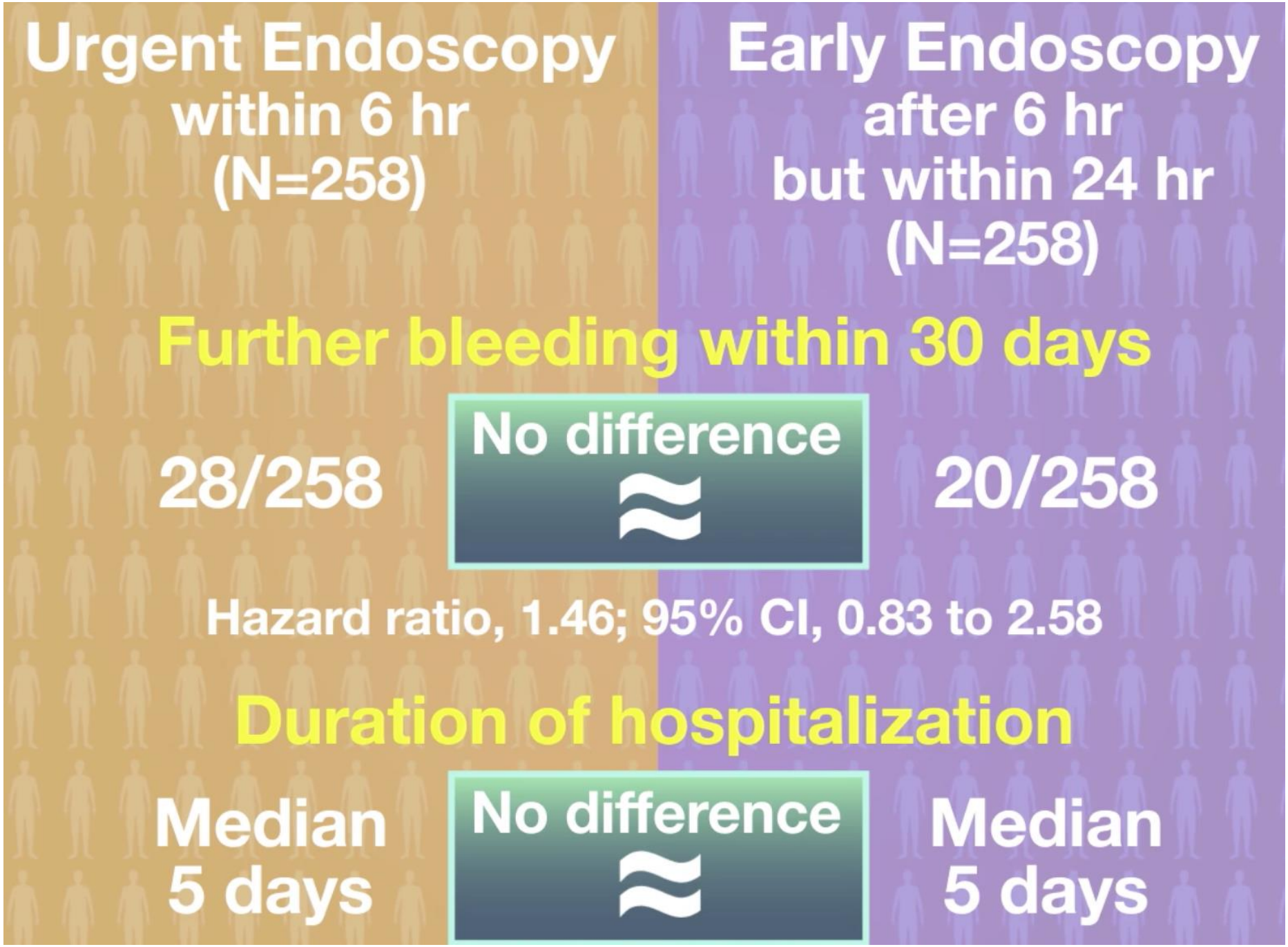

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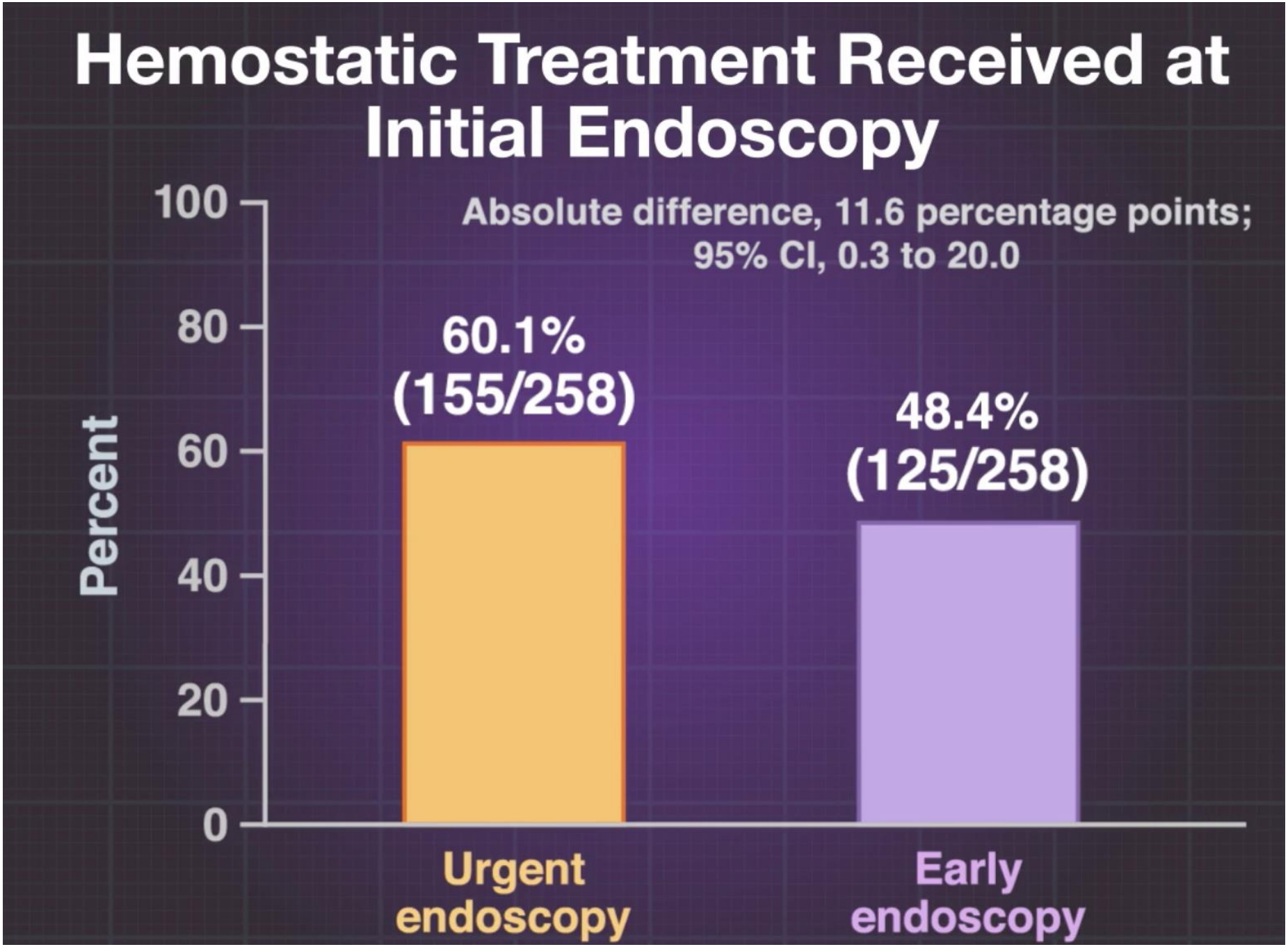

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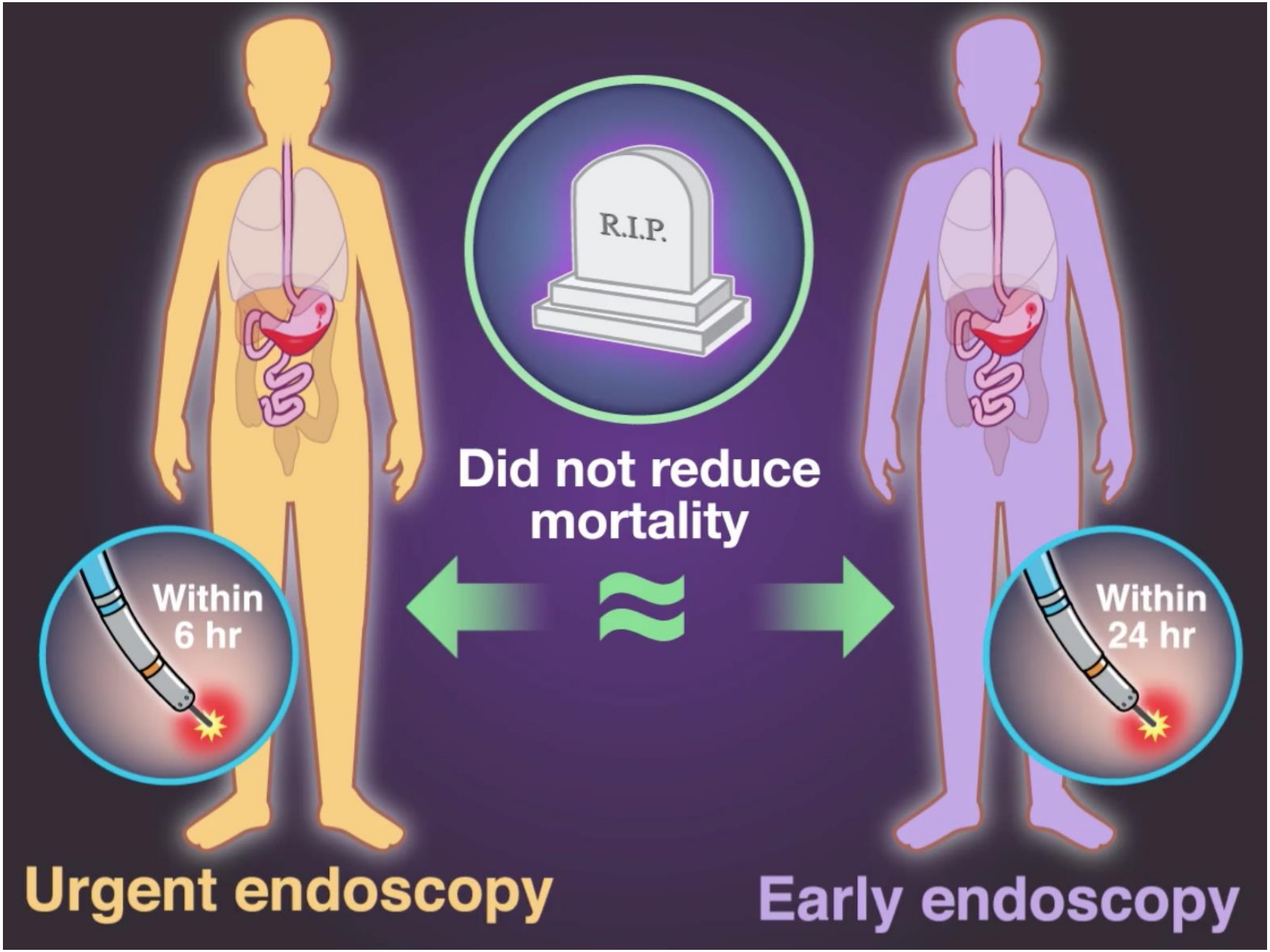
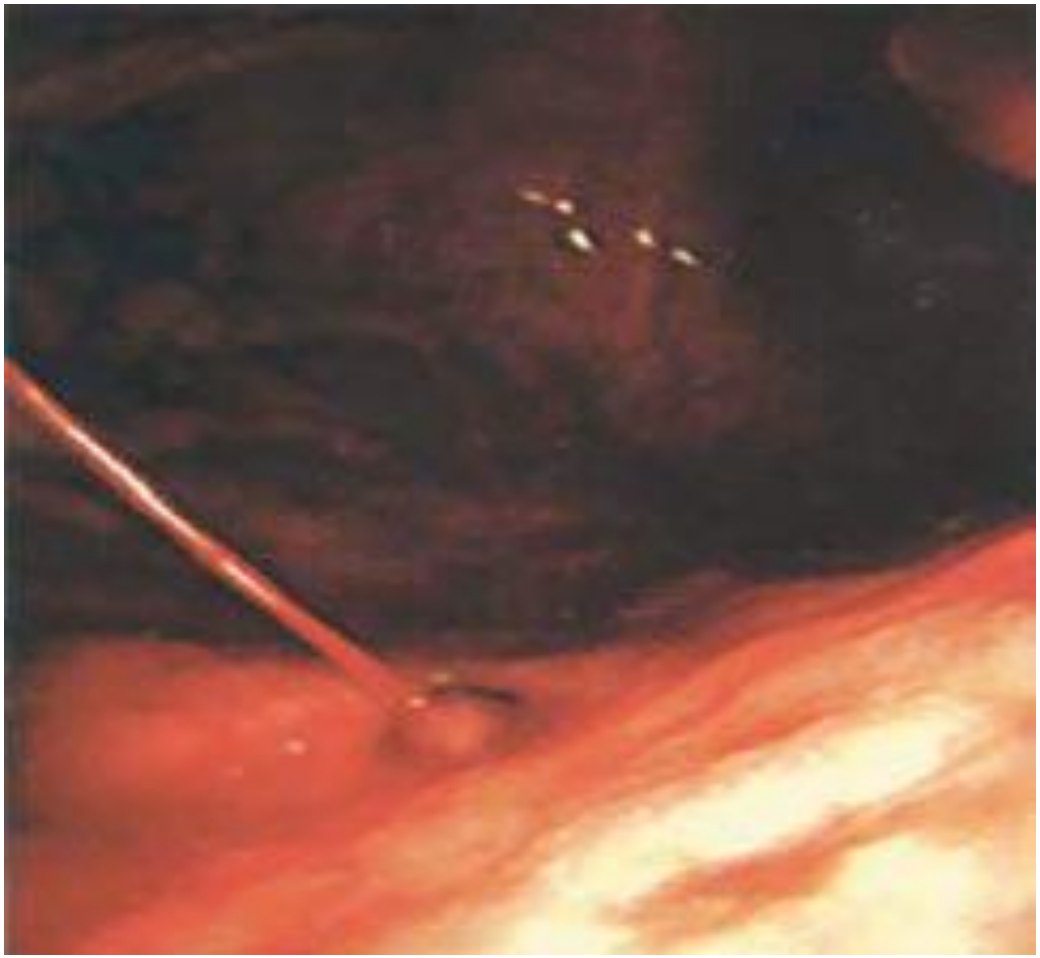


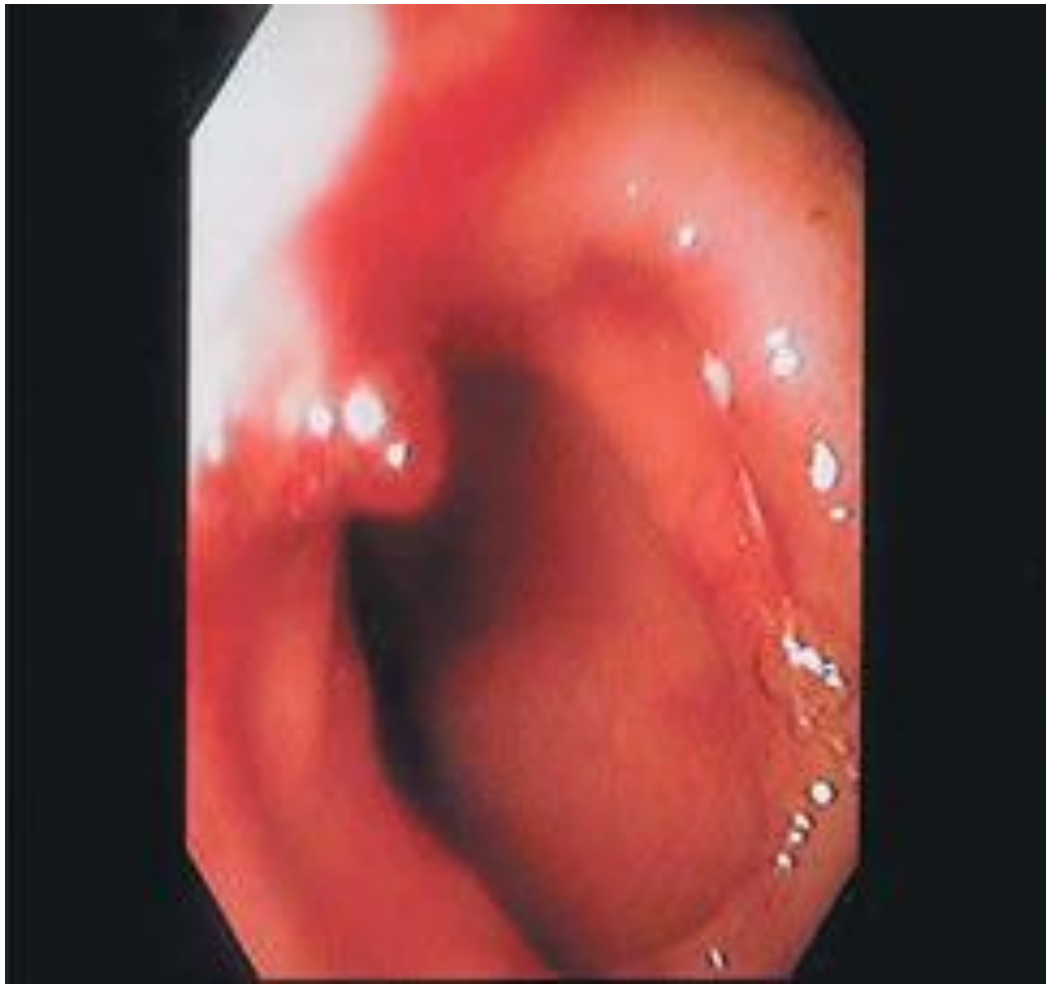
Lau JYW, et al. N Engl J Med. 2020 Apr 2;382(14):1299-1308.

Spurting Blood



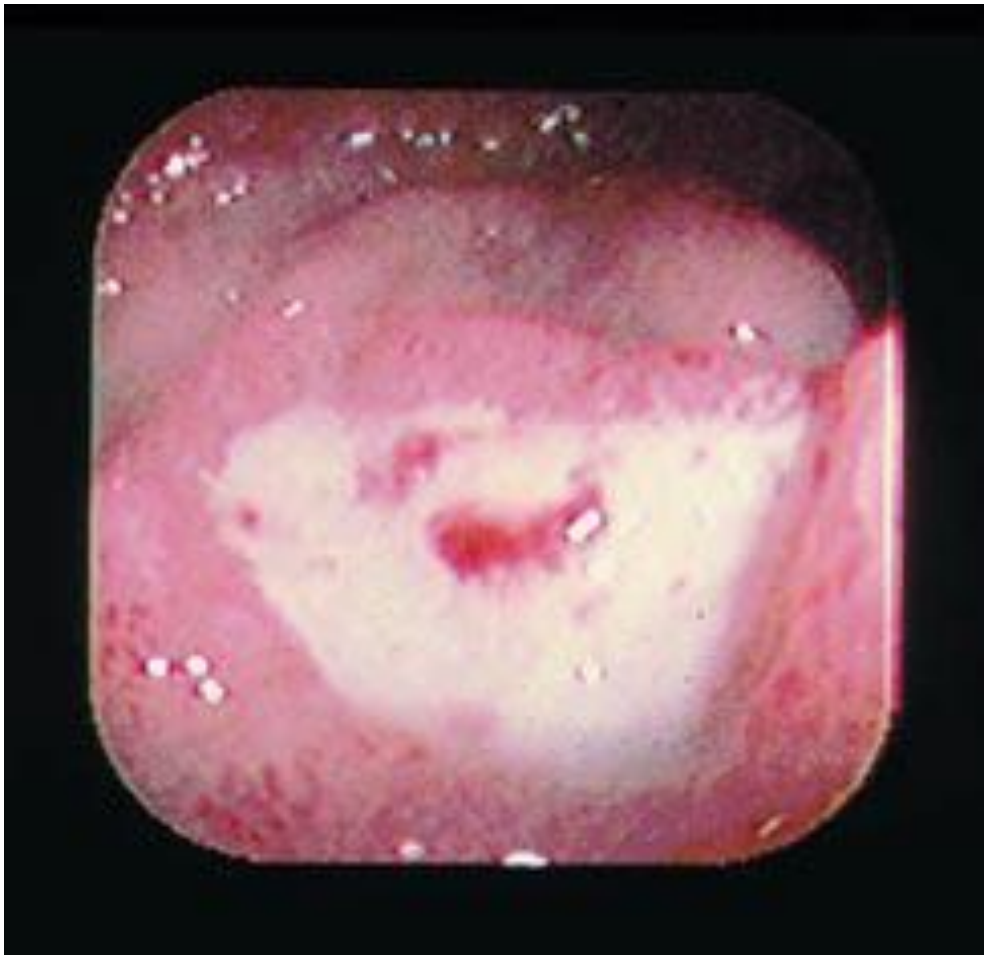
Gralnek et al. N Engl J Med 2008;359:928-37.

Non-bleeding Visible Vessel



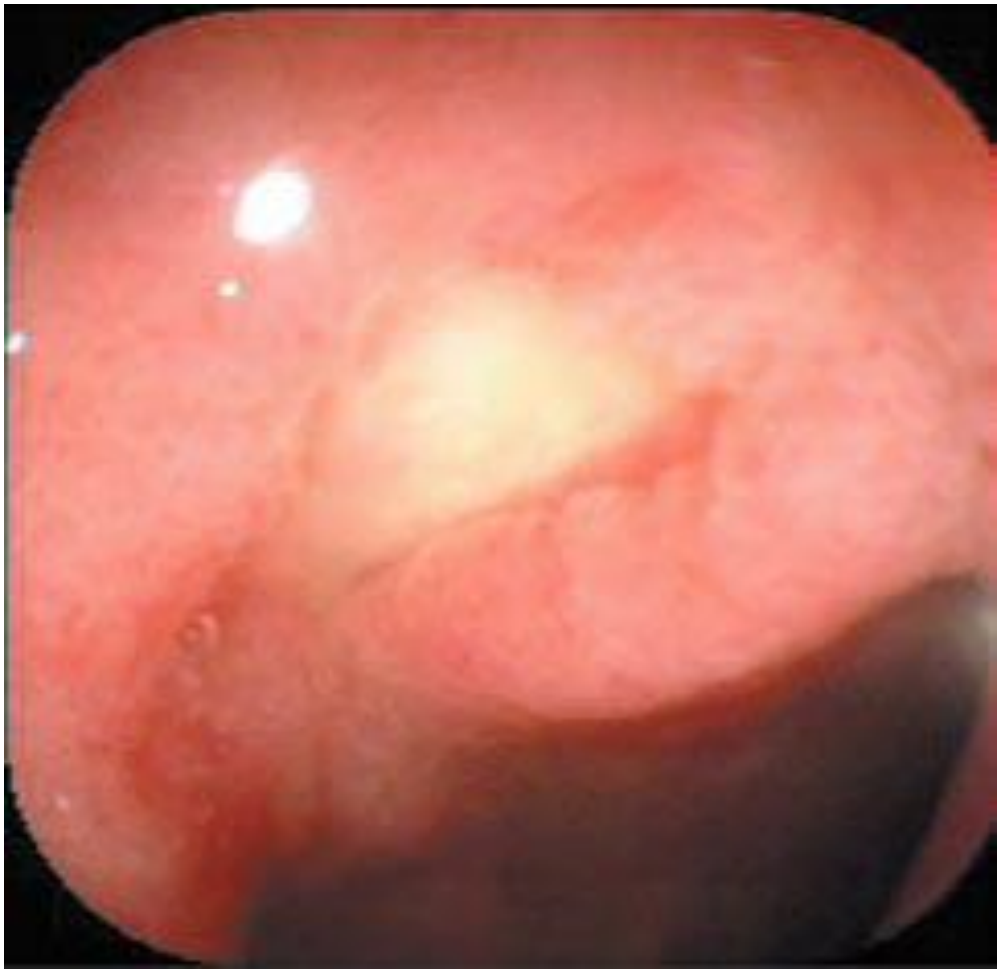
Gralnek et al. N Engl J Med 2008;359:928-37.

Flat, Pigmented Spot



Gralnek et al. N Engl J Med 2008;359:928-37.

Clean Base



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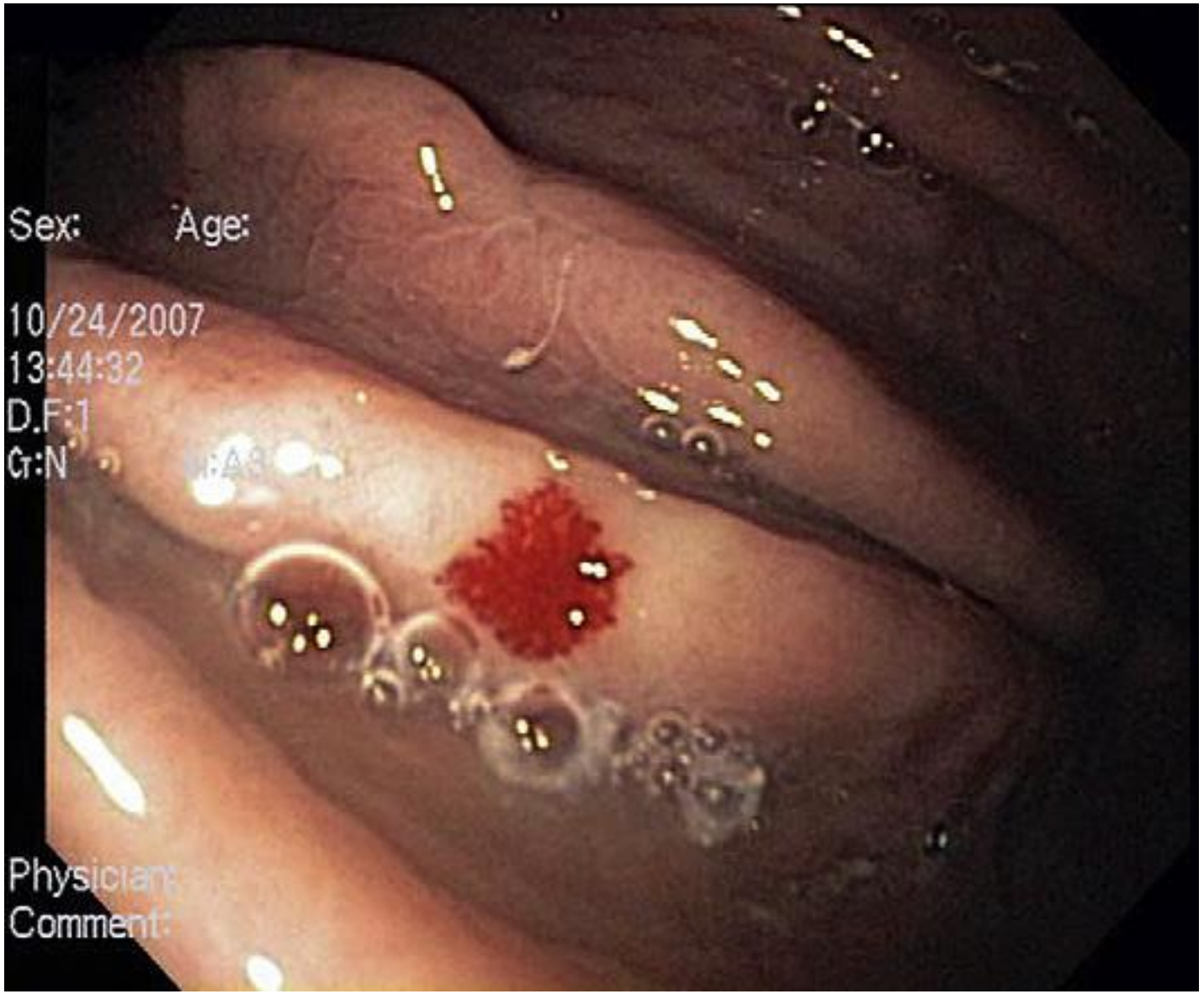
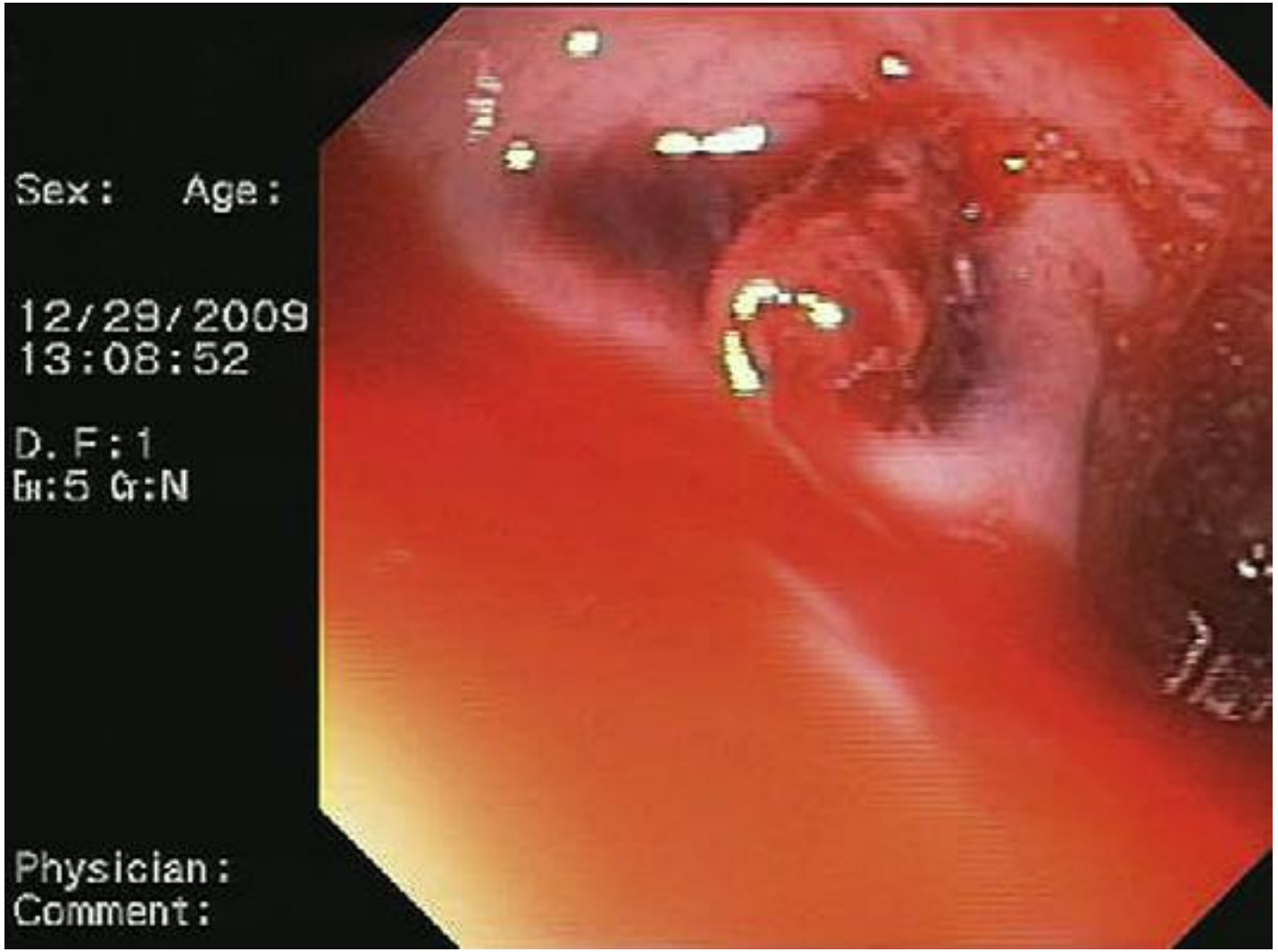
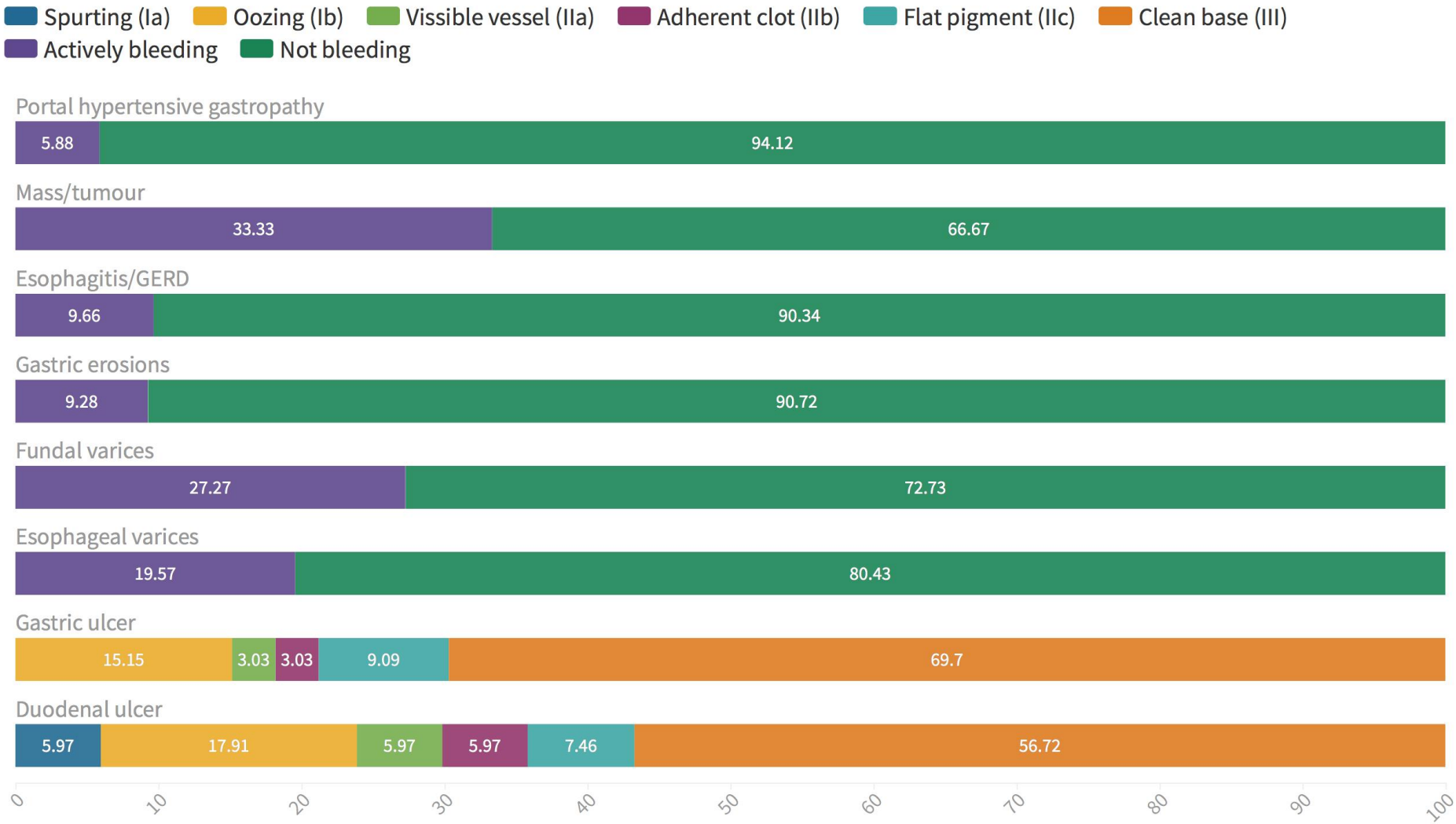


Acosta et al. Gastrointest Endosc Clin N Am 2011;21:555-66.

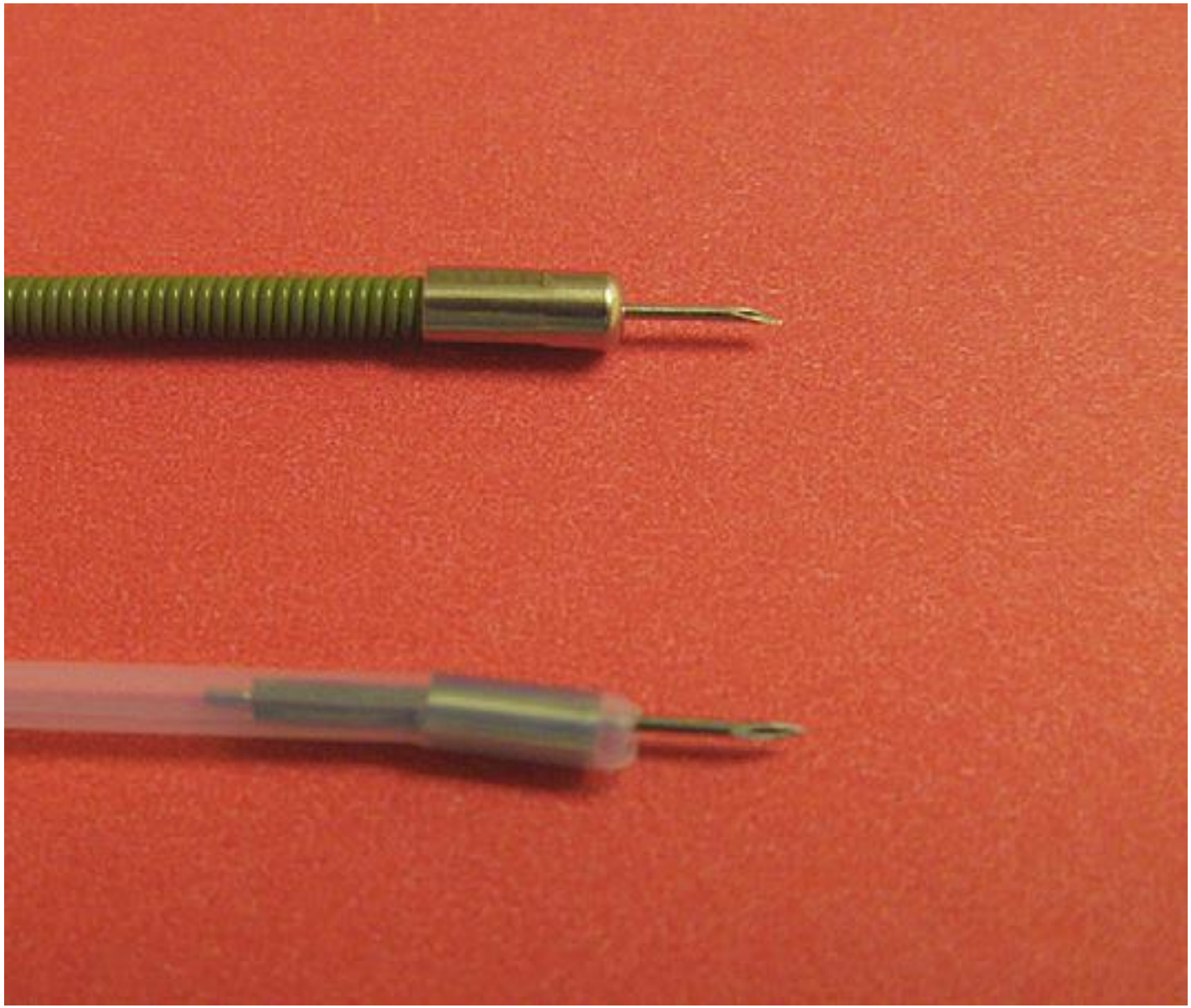


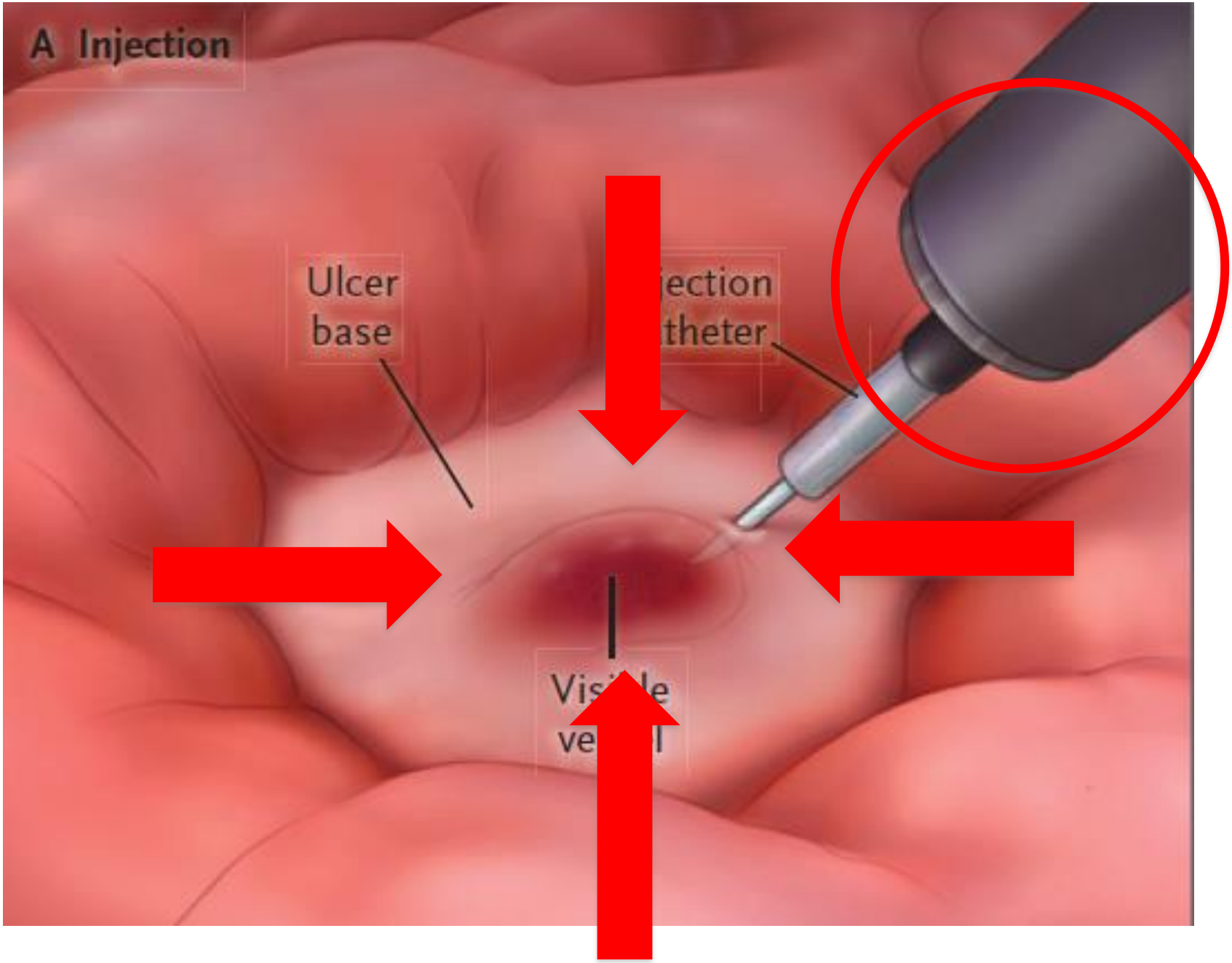
Acosta et al. Gastrointest Endosc Clin N Am 2011;21:555-66.

Stigmata of Upper Gastrointestinal Bleeding in a Tertiary Care Center in Riyadh



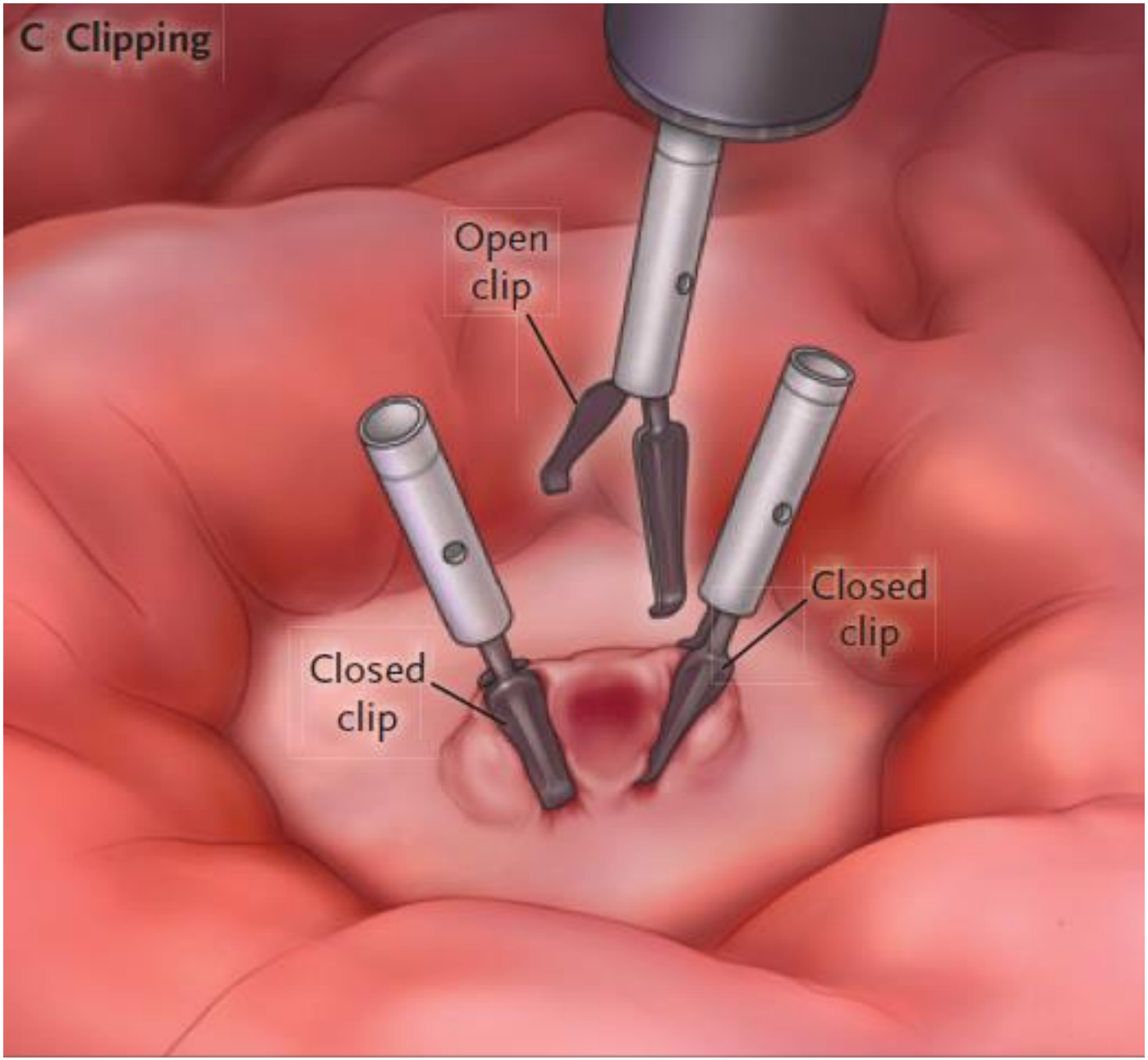
Almadi MA, et al. Saudi J Gastroenterol. 2020 Oct 12





NEJM 2016

Kovacs et al. Gastrointest Endosc Clin N Am 2011;21:681-96.



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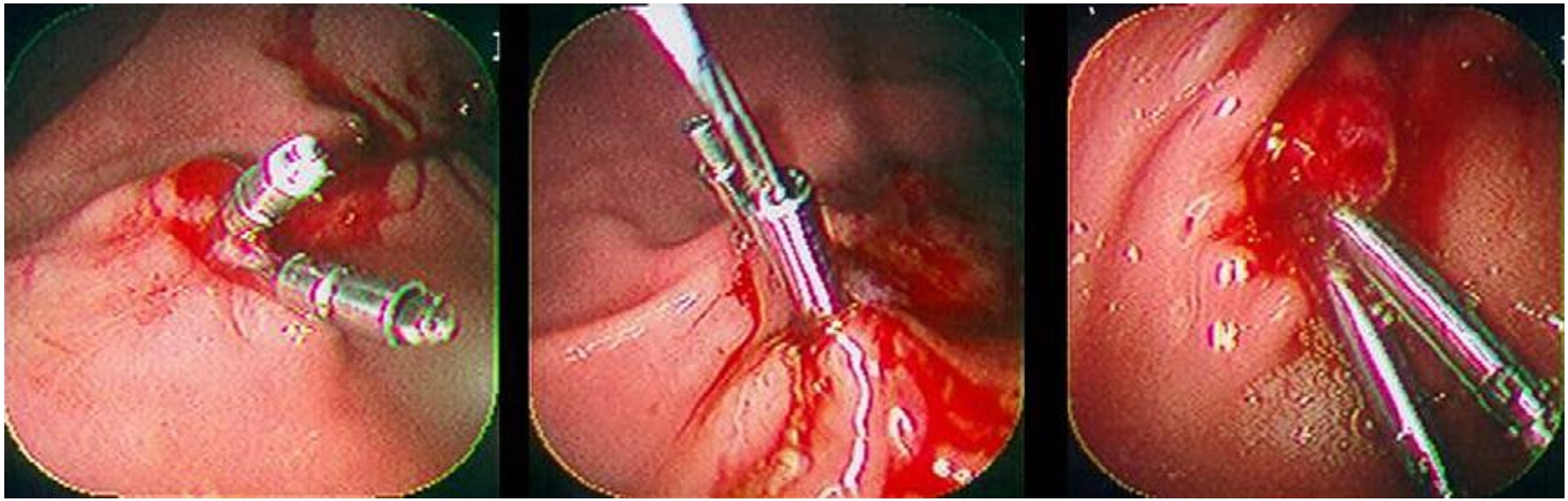

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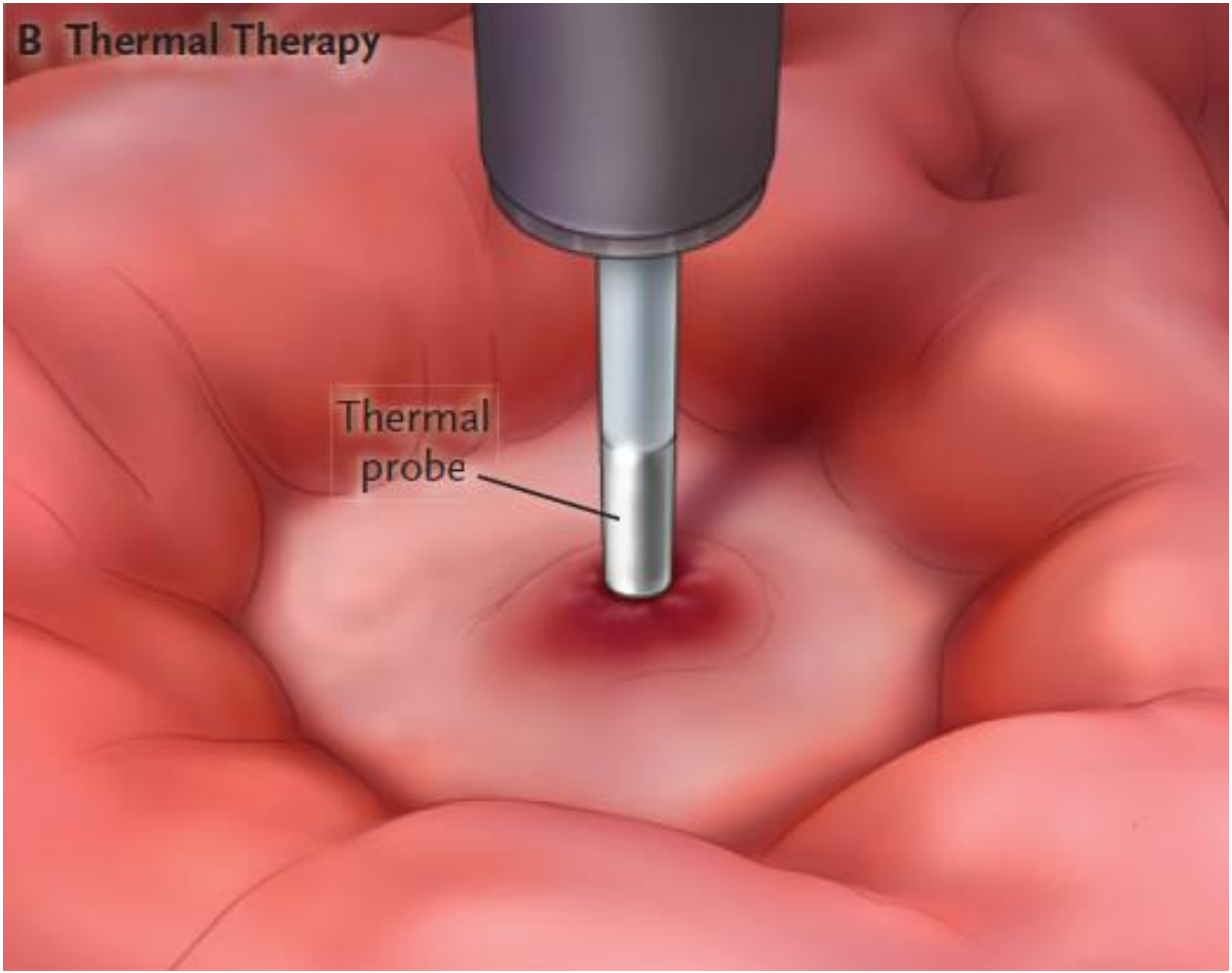

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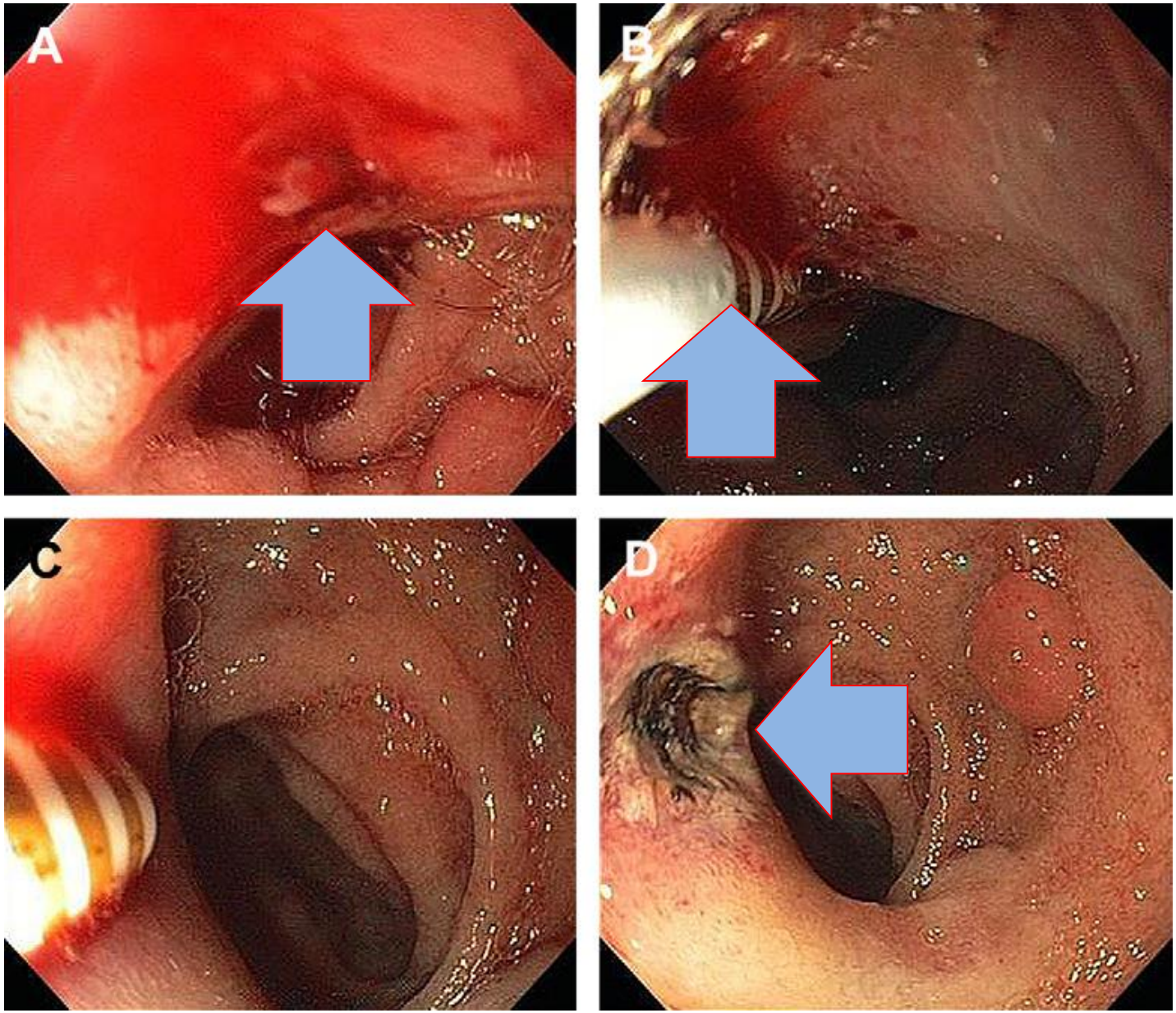
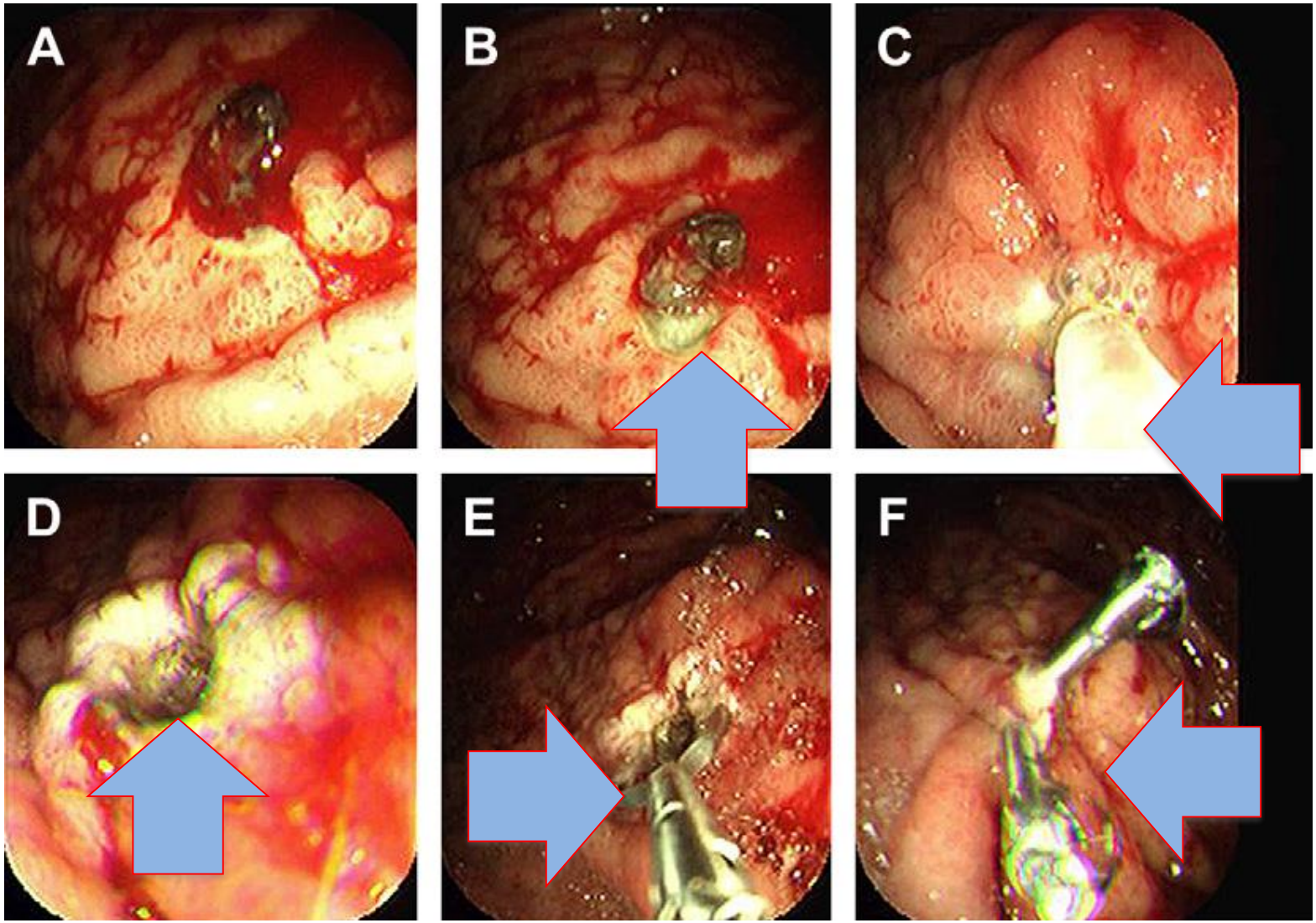
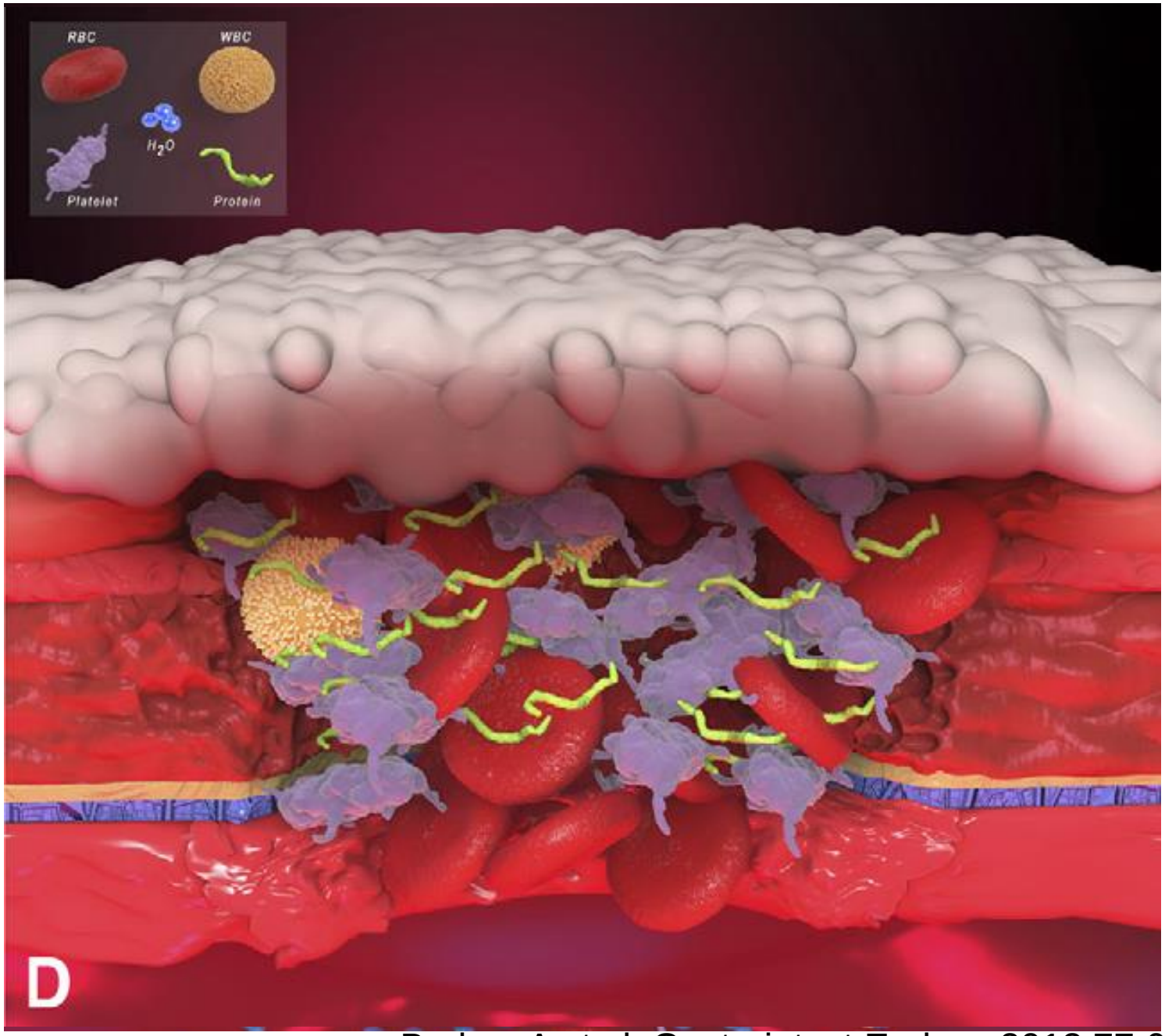


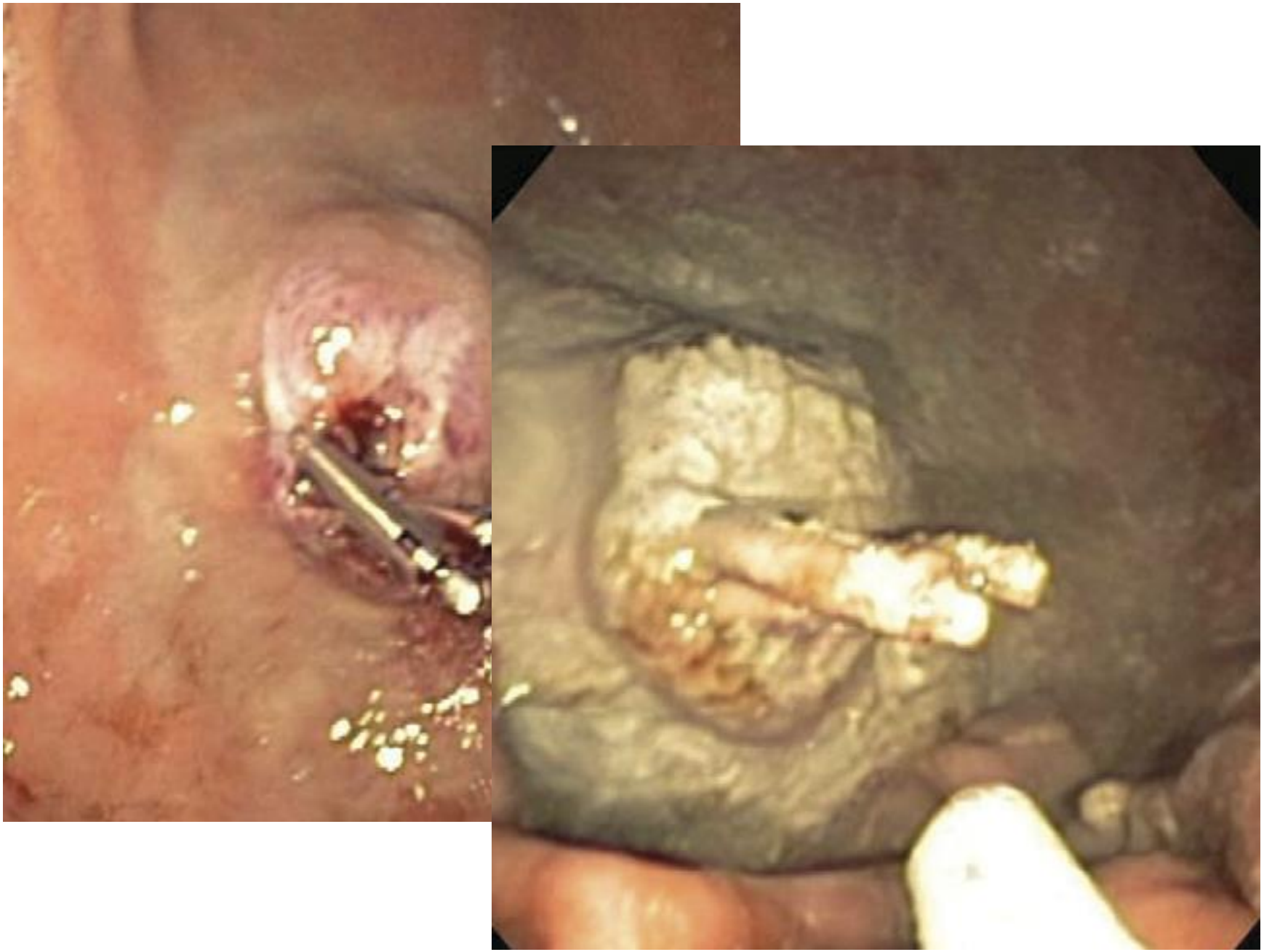
Kovacs et al. Gastrointest Endosc Clin N Am 2011;21:681-96.



Kovacs et al. Gastrointest Endosc Clin N Am 2011;21:681-96.

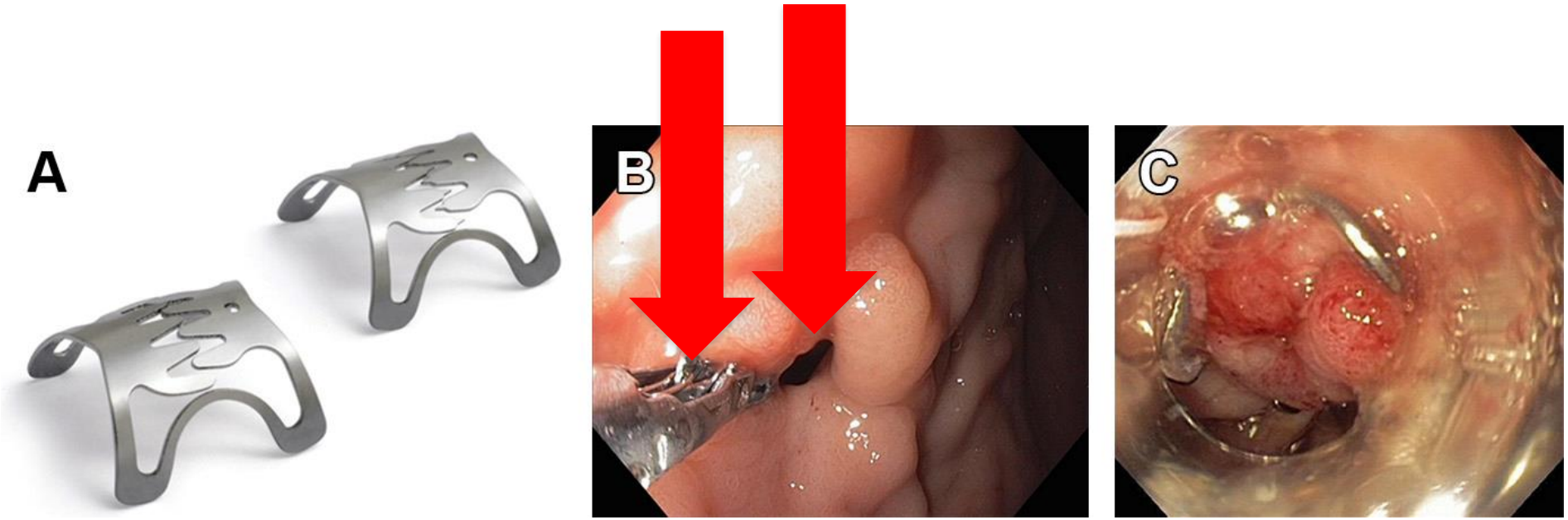


Barkun A et al. Gastrointest Endosc 2013;77:692-700



Barkun A et al. Gastrointest Endosc 2013;77:692-700

Over The Scope Clip (OTSC)



Brock AS, et al. Gastrointestinal endoscopy clinics of North America 2015;25:523-33.

Pharmacological therapy

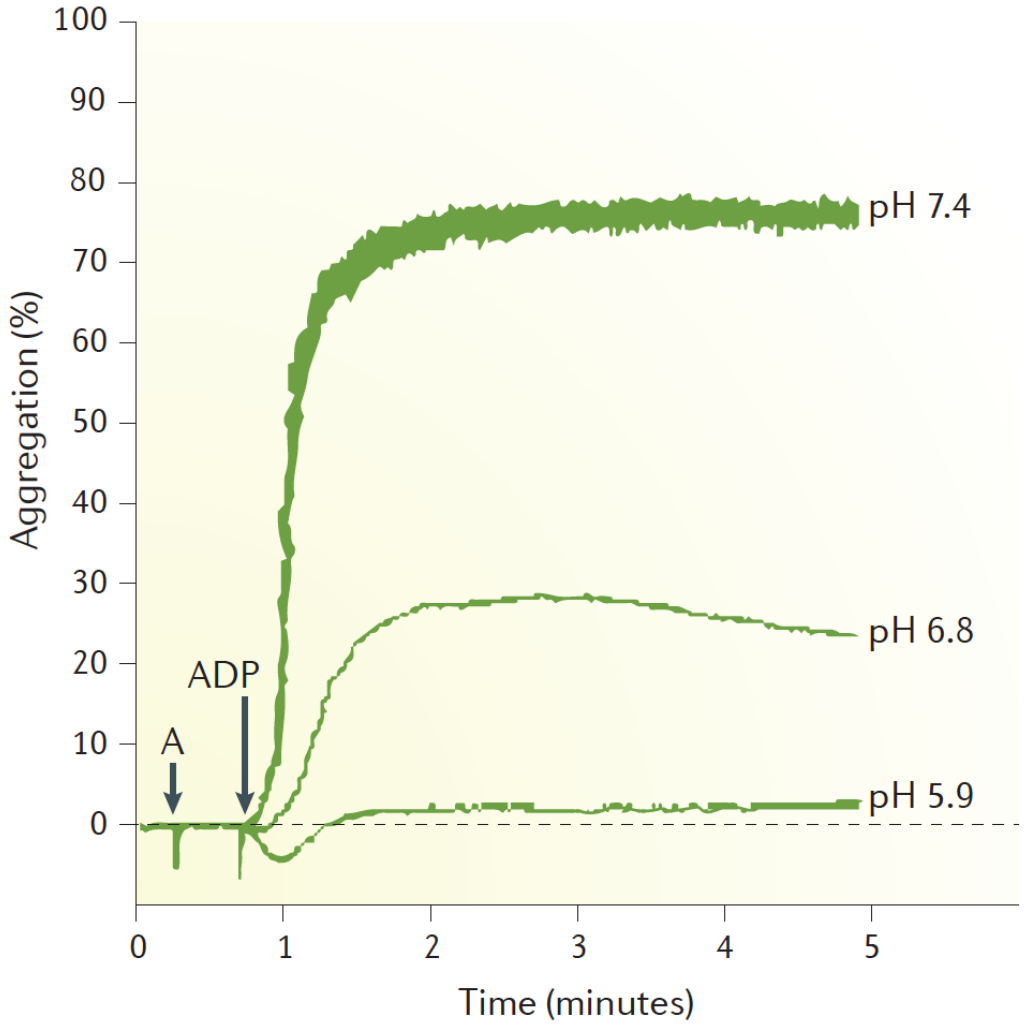
Hospitalizaton

- It takes 72 hours for most high-risk lesions to become low-risk lesions AFTER endoscopic therapy

- 60% - 76% of patients who had rebleeding within 30 days AFTER endoscopic hemostasis PLUS high-dose PPI therapy did so within the first 72 hours

Barkun et al. Ann Intern Med 2010;152:101-13.

Effects of an acidic environment on platelet aggregation



Lanas A, et al. Nat Rev Dis Primers. 2018 Apr 19;4:18020.

Admission to a monitored setting

- For at least the first 24 hours on the basis of risk or clinical condition
  - Hemodynamic instability
  - Increasing age
  - Severe comorbidity
  - Active bleeding at endoscopy
  - Large ulcer size (>2 cm)

Barkun et al. Ann Intern Med 2010;152:101-13.

EDITORIAL | Annals of Internal Medicine

Aspirin Withdrawal in Acute Peptic Ulcer Bleeding: Are We Harming Patients?

Barkun et al. Ann Intern Med 2010;152:52-3, W-12.

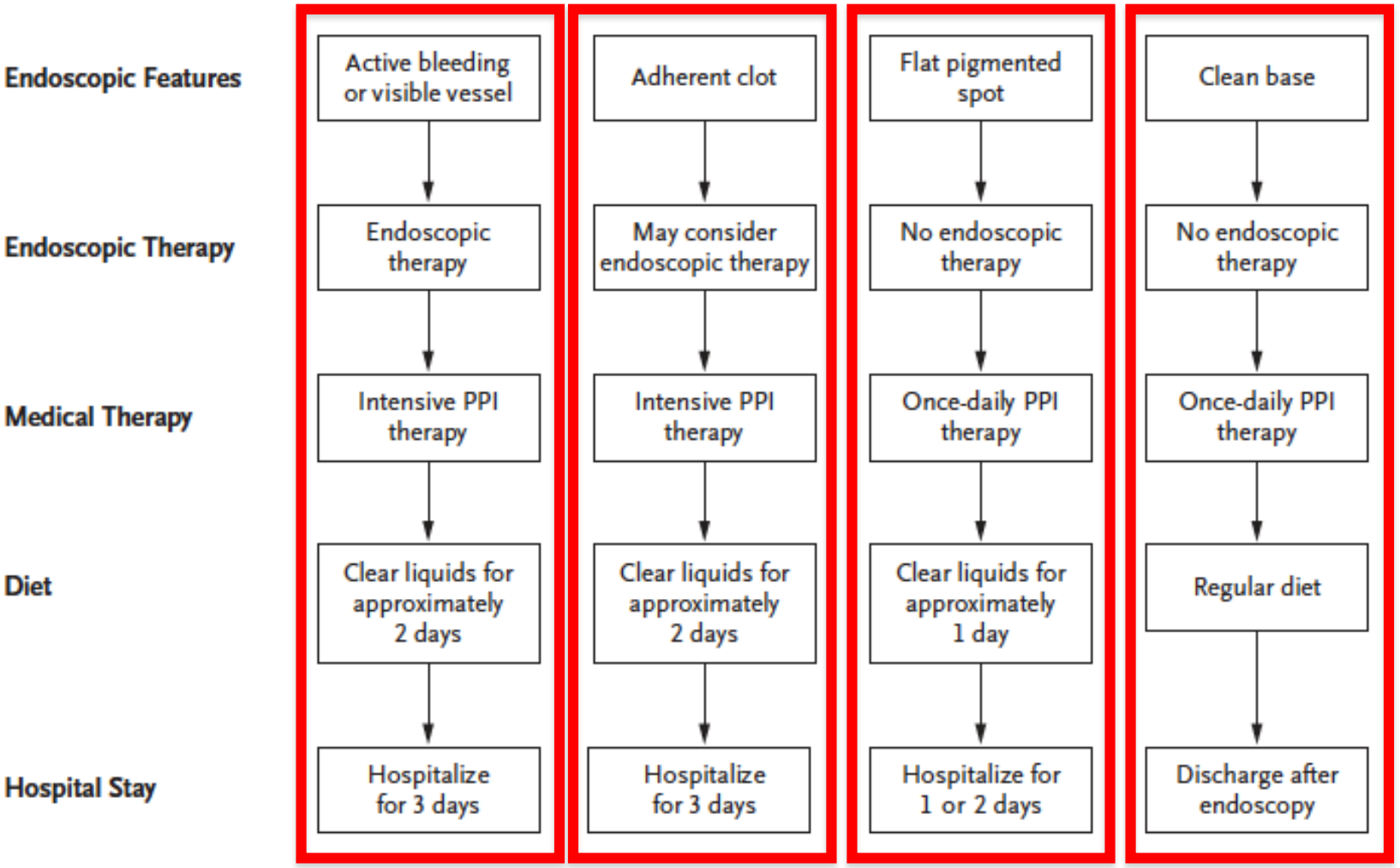
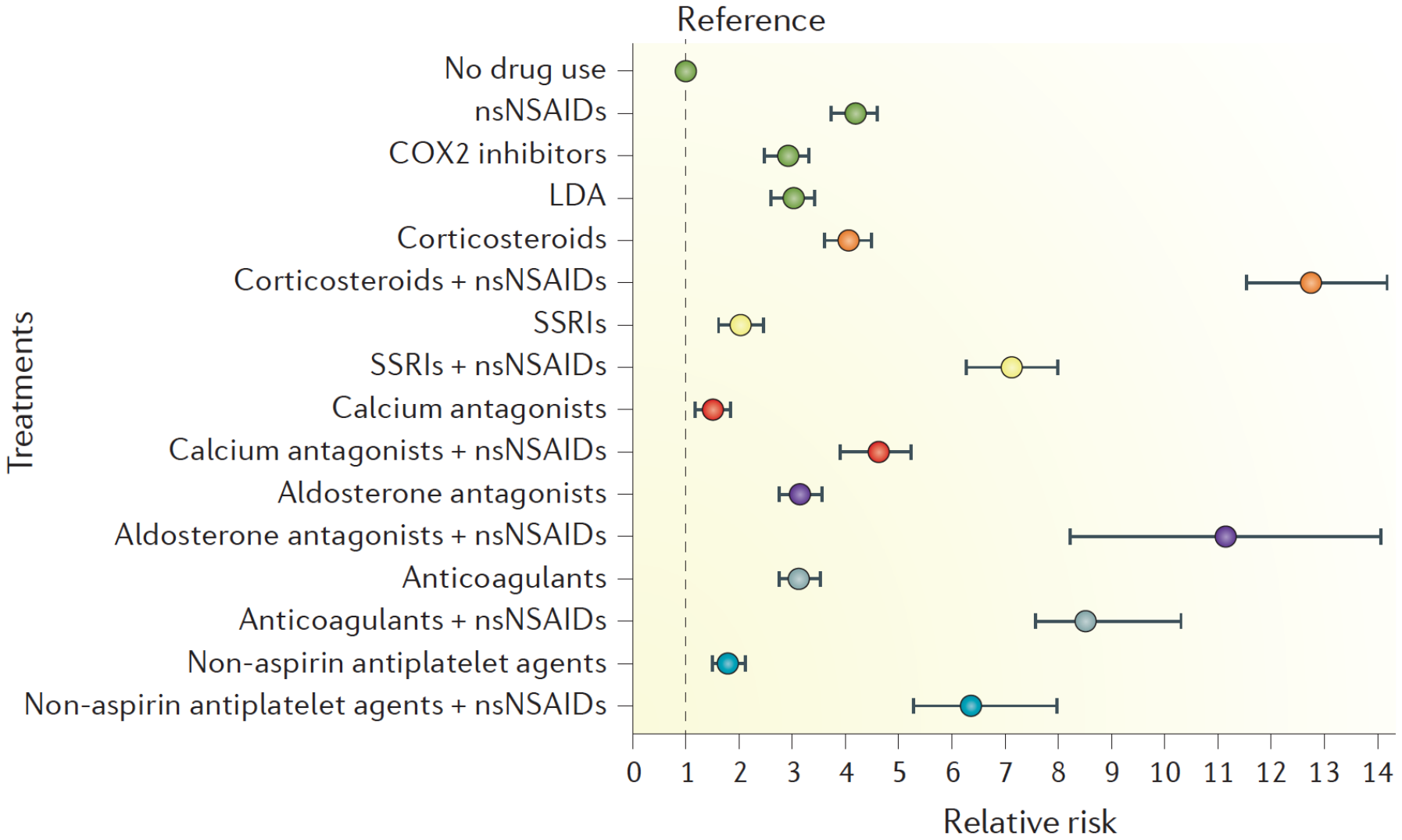


Figure 1. Initial Treatment of Patients with Ulcer Bleeding, According to the Endoscopic Features of the Ulcer.

Intensive proton-pump inhibitor (PPI) therapy is an intravenous bolus (80 mg) followed by an infusion (8 mg per hour) for 72 hours or an oral or intravenous bolus (e.g., 80 mg) followed by intermittent high-dose PPI therapy (e.g., 40 to 80 mg twice daily) for 3 days.[11] The diets shown are diets after endoscopy in patients who do not have nausea or vomiting. The duration of hospital stay after endoscopy is shown in patients who are in stable condition and do not have further bleeding or concurrent medical conditions requiring hospitalization.

NEJM 2016

Risk of developing NVUGIB associated with certain drugs



Lanas A, et al. Nat Rev Dis Primers. 2018 Apr 19;4:18020.

***H pylori*-associated ulcer:**

- No need for continuing PPI therapy after eradication of *H pylori*

NSAID-induced ulcer:

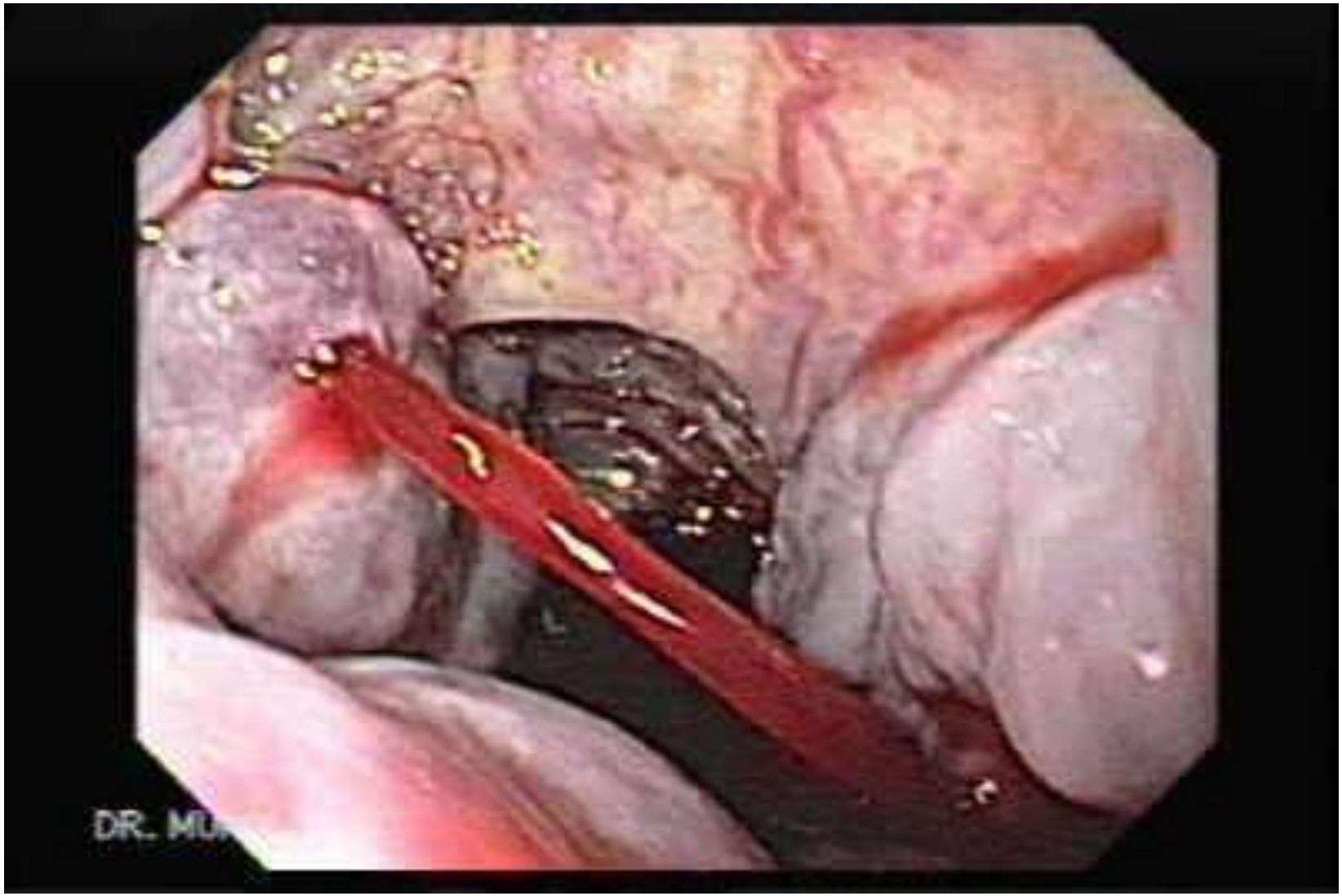
- No need for continuing PPI therapy after discontinuation of NSAID
- If NSAID required, consider COX-2 inhibitor with PPI therapy
- Use PPI with low-dose ASA if needed for secondary prevention

Idiopathic ulcers:

- PPI therapy should be prescribed indefinitely

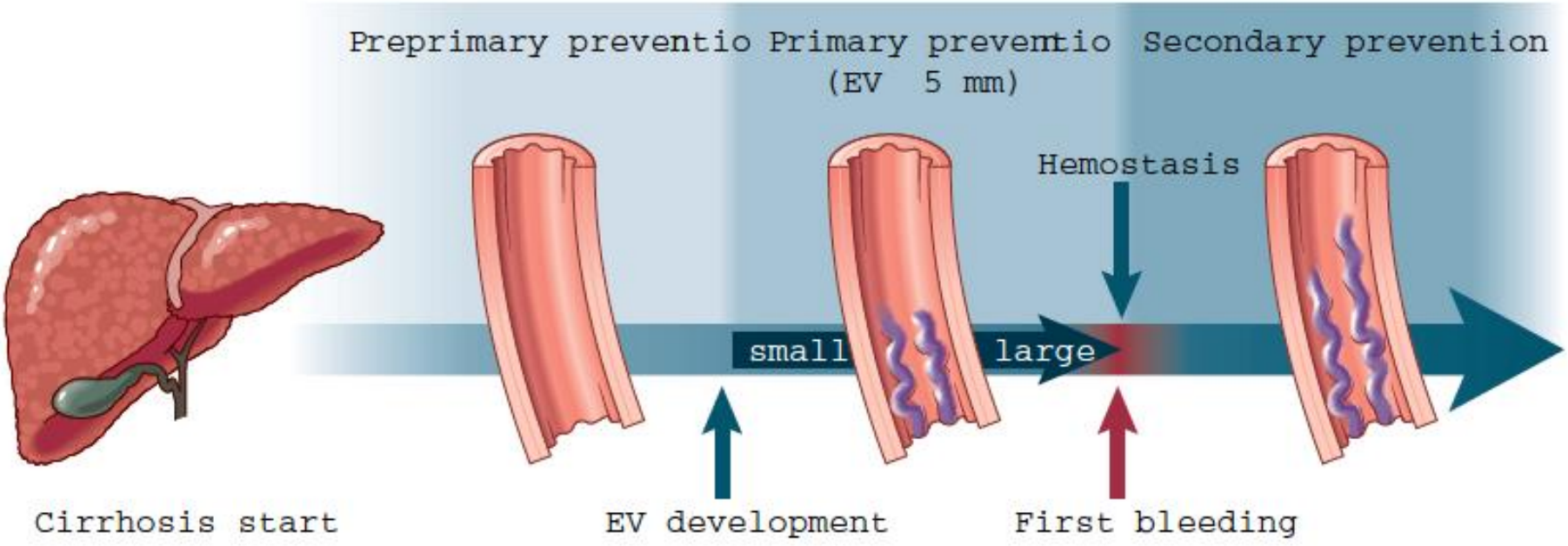
Fortinsky KJ, et al. Gastrointestinal endoscopy clinics of North America 2015;25:463-78.

Variceal Hemorrhage



50% of patients with Cirrhosis

85% of patients with Child C



CMAJ, 2006

Kapoor A, et al. Gastrointestinal endoscopy clinics of North America 2015;25:491-507

Management of Patients With Moderate/Large Varices That Have Not Bled

Therapy	Dose	Therapy goals	Maintenance/follow-up evaluation
Propranolol[a]	20 mg orally twice a day Adjust every 2–3 days until treatment goal is achieved[a] Maximal daily dose should not exceed 320 mg	Maximum tolerated dose Aim for resting heart rate of 50–55 beats per minute	At every outpatient visit make sure that patient is appropriately β-blocked Continue indefinitely No need for follow-up EGD
Nadolol[a]	40 mg orally once a day Adjust every 2–3 days until treatment goal is achieved[a] Maximal daily dose should not exceed 160 mg	As for propranolol	As for propranolol
Carvedilol	Start with 6.25 mg once a day After 3 days increase to 12.5 mg Maximal dose should not exceed 12.5 mg/day (except in patients with arterial hypertension)	Systolic arterial blood pressure should not decrease <90 mm Hg	
EVL[b]	Every 2–4 weeks until the obliteration of varices	Obliteration varices Eradication of new varices after initial obliteration	First EGD performed 1–3 months after obliteration and every 6–12 months thereafter

NOTE. Only 1 of the 4 therapies shown in the table are recommended.

[a]Dose titration is feasible in 1–2 weeks in settings where a medical assistant is available to check the patient's heart rate. In the case of carvedilol, the dose is fixed at a maximum of 12.5 mg/day so no titration is necessary.

[b]EVL is unlikely to prevent other complications of portal hypertension.

Most Commonly Used Vasoactive Agents in the Management of Acute Hemorrhage

Drug	Standard dosing	Duration	Mechanism of action
Somatostatin	Initial IV bolus 250 mcg (can be repeated in the first hour if ongoing bleeding) Continuous IV infusion of 250–500 mcg/h	Up to 5 days	nhibits vasodilator hormones similar to glucagon, causing splanchnic vasoconstriction and reduces portal blood flow Facilitates adrenergic vasoconstriction
Octreotide (somatostatin analogue)	Initial IV bolus of 50 mcg (can be repeated in first hour if ongoing bleeding) Continuous IV infusion of 50 mcg/h	Up to 5 days	Same as somatostatin, longer duration of action
Terlipressin (vasopressin analogue)	Initial 48 hours: 2 mg IV every 4 hours until control of bleeding Maintenance: 1 mg IV every 4 hours to prevent re-bleeding	Up to 5 days	Splanchnic vasoconstriction The active metabolite lysine-vasopressin is released gradually over several hours in tissue, thus decreasing typical systemic vasopressin side effects

Pharmacologic therapy in the management of acute esophageal variceal hemorrhage

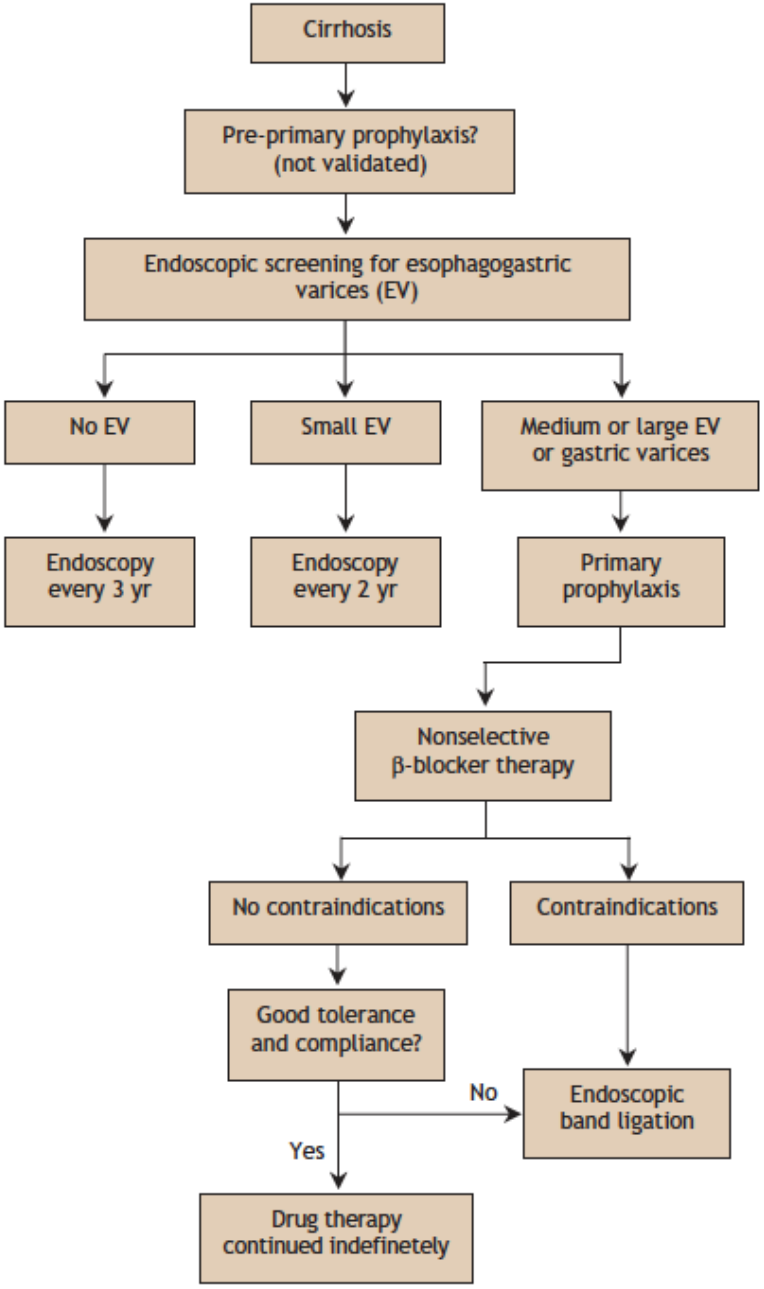
Regimen	Dose	Duration	Follow-up
Vasoconstrictor			
Octreotide	Intravenous 50-μg bolus, followed by infusion of 50 μg/h	2–5 d	Bolus can be repeated in first hour if variceal hemorrhage uncontrolled; if rebleeding occurs during therapy, consider TIPS
Terlipressin	2 mg given intravenously every 4 h for first 48 h, followed by 1 mg given intravenously every 4 h	2–5 d	If rebleeding occurs during therapy, consider TIPS
Somatostatin	Intravenous 250-μg bolus, followed by infusion of 250–500 μg/h	2–5 d	Bolus can be repeated in first hour if variceal hemorrhage uncontrolled; if rebleeding occurs during therapy, consider TIPS
Antibiotic			
Ceftriaxone	Intravenous ceftriaxone at a dose of 1 g once a day	5–7 d or until discharge	No long-term antibiotics unless spontaneous bacterial peritonitis develops
Norfloxacin	400 mg given orally twice a day	5–7 d or until discharge	No long-term antibiotics unless spontaneous bacterial peritonitis develops

Bhutta AQ, et al. Gastrointestinal endoscopy clinics of North America 2015;25:479-90.

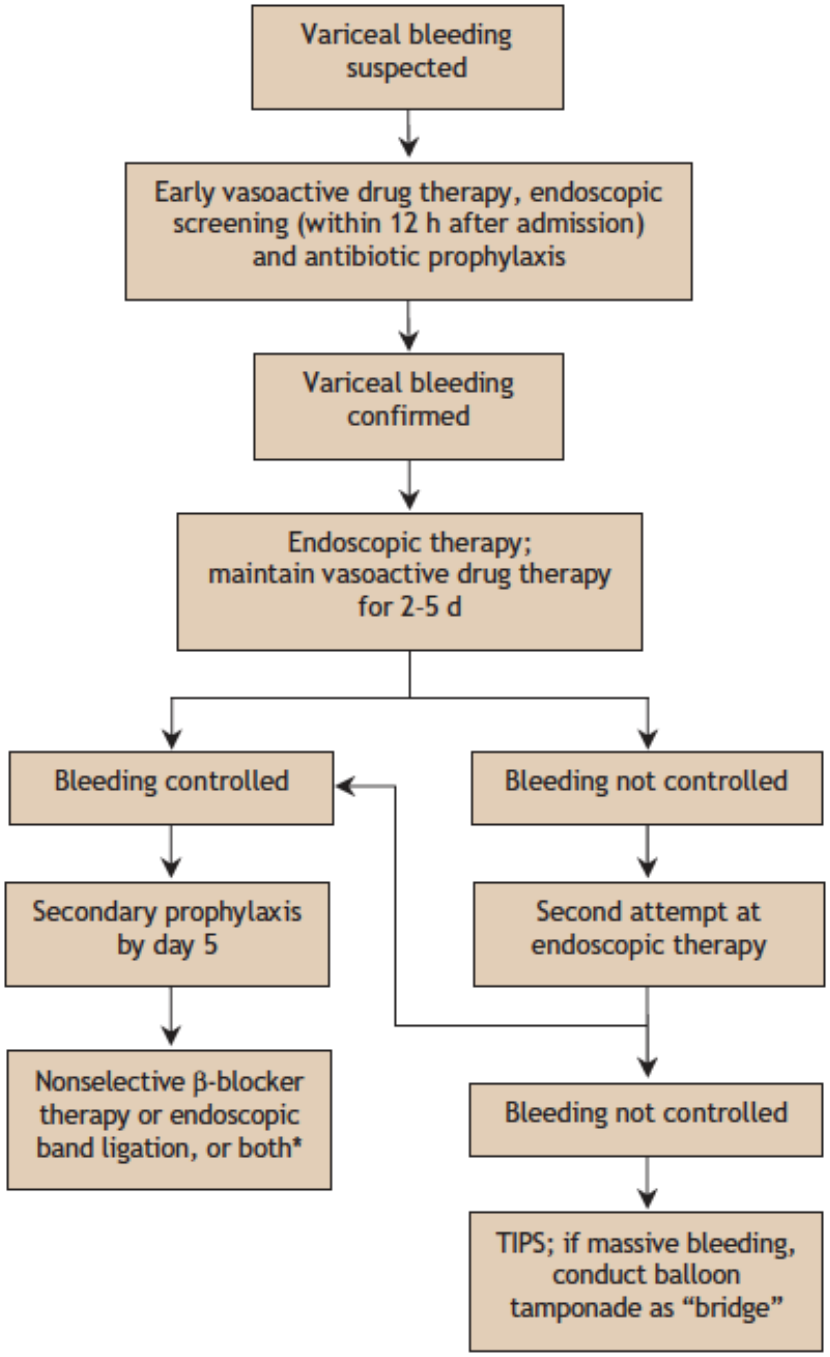
Management of Patients Who Have Bled From Varices and in Whom the Goal Is to Prevent Recurrence of Hemorrhage

Therapy	Starting dose	Therapy goals	Maintenance/follow-up evaluation
Propranolol	20 mg orally twice a day Adjust every 2–3 days until treatment goal is achieved Maximal daily dose should not exceed 320 mg	Maximum tolerated dose Aim for resting heart rate of 50–55 beats per minute	At every outpatient visit make sure that patient is appropriately β-blocked Continue indefinitely In patients with refractory ascites reduce dose or discontinue if SBP < 90 mm Hg, serum sodium <130, or with acute kidney injury
Nadolol	40 mg orally once a day Adjust every 2–3 days until treatment goal is achieved Maximal daily dose should not exceed 160 mg		
EVL	Every 2–4 weeks until the obliteration of varices	Obliteration varices Eradication of new varices after initial obliteration	First EGD performed 1–3 months after obliteration and every 6–12 months thereafter

NOTE. Combination of 1 nonselective β-blocker (propranolol or nadolol) plus EVL is recommended.
SBP, spontaneous bacterial peritonitis.


Cirrhosis
Pre-primary prophylaxis? (not validated)
Endoscopic screening for esophagogastric varices (EV)
No EV
Small EV
Medium or large EV or gastric varices
Endoscopy every 3 yr
Endoscopy every 2 yr
Primary prophylaxis
Nonselective β-blocker therapy
No contraindications
Contraindications
Good tolerance and compliance?
No
Endoscopic band ligation
Yes
Drug therapy continued indefinetely

CMAJ, 2006


Variceal bleeding suspected
Early vasoactive drug therapy, endoscopic screening (within 12 h after admission) and antibiotic prophylaxis
Variceal bleeding confirmed
Endoscopic therapy; maintain vasoactive drug therapy for 2-5 d
Bleeding controlled
Bleeding not controlled
Secondary prophylaxis by day 5
Second attempt at endoscopic therapy
Nonselective β-blocker therapy or endoscopic band ligation, or both*
Bleeding not controlled
TIPS; if massive bleeding, conduct balloon tamponade as "bridge"

CMAJ, 2006

Conclusions

- Resuscitation should be initiated prior to any diagnostic procedure
- Gastrointestinal endoscopy allows visualization of the stigmata, accurate assessment of the level of risk and treatment of the underlying lesion
- Intravenous PPI therapy after endoscopy is crucial to decrease the risk of cardiovascular complications and to prevent recurrence of bleeding
- *Helicobacter pylori testing should be performed in the acute setting*

Bardou et al. Nat Rev Gastroenterol Hepatol 2012;9:97-104.

the bmj Visual summary

Management of upper gastrointestinal bleeding

This visual summary presents a practical approach to initial management of patients with upper gastrointestinal bleeding. Peptic ulcers are the most common cause of serious bleeding from the oesophagus, stomach, and duodenum, and can be identified with simple diagnostic tests.

Initial assessment

Check circulatory status to assess need for immediate interventions

Blood pressure may remain normal initially, so increased heart rate is a more sensitive measure of circulatory status

Haemodynamically stable

Signs of current bleeding

- Hematochezia
- Haematemesis

Urgent intensive care involvement required for:

- Haemodynamically unstable
- Airway compromise
- Hypoxia
- Reduced level of consciousness

Actions in parallel

- Obtain blood chemistry
- Obtain medical history

Initial resuscitation

- 2 x Large bore intravenous access
- Urinary catheter (if required)
- Intravenous fluids
- Pharmacological treatment (proton pump inhibitor)

Risk stratification

Glasgow-Blatchford Score (GBS)

Systolic blood pressure mmHg		Blood urea mmol/L		Haemoglobin g/dL			Pulse ≥ 100	1
100–109	1	6.5–7.9	2	Men	Women		Melaena	1
90–99	2	8.0–9.9	3	12.0–12.9	10.0–11.9	1	Syncope	2
< 90	3	10.0–24.9	4	10.0–11.9		3	Hepatic disease	2
		≥ 25.0	6	< 10.0	< 10.0	6	Cardiac failure	2

Total score

- 0 – 1: Low risk of death. Can be considered for outpatient management.
- 5+: Increased risk of 30-day mortality
- 7+: Predicts need for endoscopic haemostatic intervention, but needs individual evaluation

Total score 0 – 1

Early discharge

Endoscopy in outpatient clinic

Total score 2+

Haemodynamically stable

Endoscopy within 24 hours

Proton pump inhibitor

Eradication of any *Helicobacter pylori* infection

Haemodynamically unstable

Emergency endoscopy

Successful haemostasis

Not successful haemostasis

Embolisation therapy

Transcatheter arterial embolisation should be considered as the next alternative after unsuccessful endoscopy, because it is effective and associated with less risk of major complications than surgery

Surgery

If transcatheter arterial embolisation is unsuccessful or not available, surgery is the only remaining treatment to stop peptic ulcer bleeding. A minimal surgical approach with over-sewing of the ulcer is preferable, but depending on size and location of ulcer, open surgery may be required.

Annals of Internal Medicine

CLINICAL GUIDELINE

Management of Nonvariceal Upper Gastrointestinal Bleeding: Guideline Recommendations From the International Consensus Group

Alan N. Barkun, MD; Majid Almadi, MD; Ernst J. Kuipers, MD; Loren Laine, MD; Joseph Sung, MD; Frances Tse, MD; Grigorios I. Leontiadis, MD; Neena S. Abraham, MD; Xavier Calvet, MD; Francis K.L. Chan, MD; James Douketis, MD; Robert Enns, MD; Ian M. Gralnek, MD; Vipul Jairath, MD; Dennis Jensen, MD; James Lau, MD; Gregory Y.H. Lip, MD; Romaric Loffroy, MD; Fauze Maluf-Filho, MD; Andrew C. Meltzer, MD; Nageshwar Reddy, MD; John R. Saltzman, MD; John K. Marshall, MD; and Marc Bardou, MD

Description: This update of the 2010 International Consensus Recommendations on the Management of Patients With Nonvariceal Upper Gastrointestinal Bleeding (UGIB) refines previous important statements and presents new clinically relevant recommendations.

Methods: An international multidisciplinary group of experts developed the recommendations. Data sources included evidence summarized in previous recommendations, as well as systematic reviews and trials identified from a series of literature searches of several electronic bibliographic databases from inception to April 2018. Using an iterative process, group members formulated key questions. Two methodologists prepared evidence profiles and assessed quality (certainty) of evidence relevant to the key questions according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach. Group members reviewed the evidence profiles and, using a consensus process, voted on recommendations and determined the strength of recommendations as strong or conditional.

Recommendations: *Preendoscopic management:* The group suggests using a Glasgow Blatchford score of 1 or less to identify patients at very low risk for rebleeding, who may not require hospitalization. In patients without cardiovascular disease, the suggested hemoglobin threshold for blood transfusion is less than 80 g/L, with a higher threshold for those with cardiovascular disease. *Endoscopic management:* The group suggests that patients with acute UGIB undergo endoscopy within 24 hours of presentation. Thermocoagulation and sclerosant injection are recommended, and clips are suggested, for endoscopic therapy in patients with high-risk stigmata. Use of TC-325 (hemostatic powder) was suggested as temporizing therapy, but not as sole treatment, in patients with actively bleeding ulcers. *Pharmacologic management:* The group recommends that patients with bleeding ulcers with high-risk stigmata who have had successful endoscopic therapy receive high-dose proton-pump inhibitor (PPI) therapy (intravenous loading dose followed by continuous infusion) for 3 days. For these high-risk patients, continued oral PPI therapy is suggested twice daily through 14 days, then once daily for a total duration that depends on the nature of the bleeding lesion. *Secondary prophylaxis:* The group suggests PPI therapy for patients with previous ulcer bleeding who require antiplatelet or anticoagulant therapy for cardiovascular prophylaxis.

Ann Intern Med. doi:10.7326/M19-1795 **Annals.org**

For author affiliations, see end of text.

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PRIMEVIEW

NON-VARICEAL UPPER GI BLEEDING

nature REVIEWS DISEASE PRIMERS

For the Primer, visit doi:10.1038/nrdp.2018.20

Non-variceal upper gastrointestinal bleeding (NVUGIB) is an often life-threatening bleeding event that develops in the oesophagus, stomach or proximal duodenum. Peptic ulcers, caused by *Helicobacter pylori* infection or use of NSAIDs or low-dose aspirin (LDA), are the most common causes.

MECHANISMS

NSAIDs and LDA have direct and systemic effects on the gastrointestinal mucosa. They can change the characteristics of the mucus layer in the upper gastrointestinal tract, increase gastrointestinal permeability, lower levels of prostaglandins (which are involved in mucus, bicarbonate and acid secretion, cell proliferation and mucosal blood flow) through systemic inhibition of cyclooxygenases and inhibit the prothrombotic effects of platelets.

Exposure of the blood vessel is the consequence of disruption of the mucosal barrier or structural abnormalities

H. pylori infection induces a strong immune response in the host

MUCOSAL DAMAGE

BLEEDING

DIAGNOSIS

NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

The clinical presentation of NVUGIB varies from asymptomatic, potentially with melena (black faeces owing to the presence of blood), to an emergency condition in which patients present with large volume haematemesis (vomiting of blood), severe hypotension and a compromised airway. Each patient presenting with NVUGIB should have pre-endoscopic risk assessment aimed at predicting the need for interventions and risk of complications or death. Early endoscopy within 24 hours of admission is necessary to evaluate signs of recent haemorrhage (including active bleeding, visible vessels or presence of clots) to stratify the risks of re-bleeding, need for surgery and risk of death.

NVUGIB is a medical emergency and mortality rates are in the range ~1–5%

The acidic pH in the upper gastrointestinal tract further erodes the blood vessel wall, inhibits coagulation and activates the proteolytic enzyme pepsin

MANAGEMENT

PPI therapy aims to maintain gastric pH at >6

The management of individuals presenting with NVUGIB is focused on stabilization protocols to restore and protect the airway and to maintain circulation. Pre-endoscopic intravenous administration of high-dose proton pump inhibitors (PPIs) is recommended to stabilize blood clots and reduce the effects of recent haemorrhage, thereby reducing the need for endoscopic management. Various modalities for endoscopic management aimed at stopping active bleeding are available. Post-endoscopic medical treatment to reduce risk of rebleeding, which occurs in 10–15% of patients, involves high-dose PPIs (oral or intravenous).

How to treat NVUGIB in those receiving antiplatelet agents and anticoagulants is complicated; the decision to continue or discontinue treatment before endoscopic management and when to resume treatment should balance the risk of adverse cardiovascular events and the risk of further bleeding or rebleeding of the NVUGIB.

EPIDEMIOLOGY

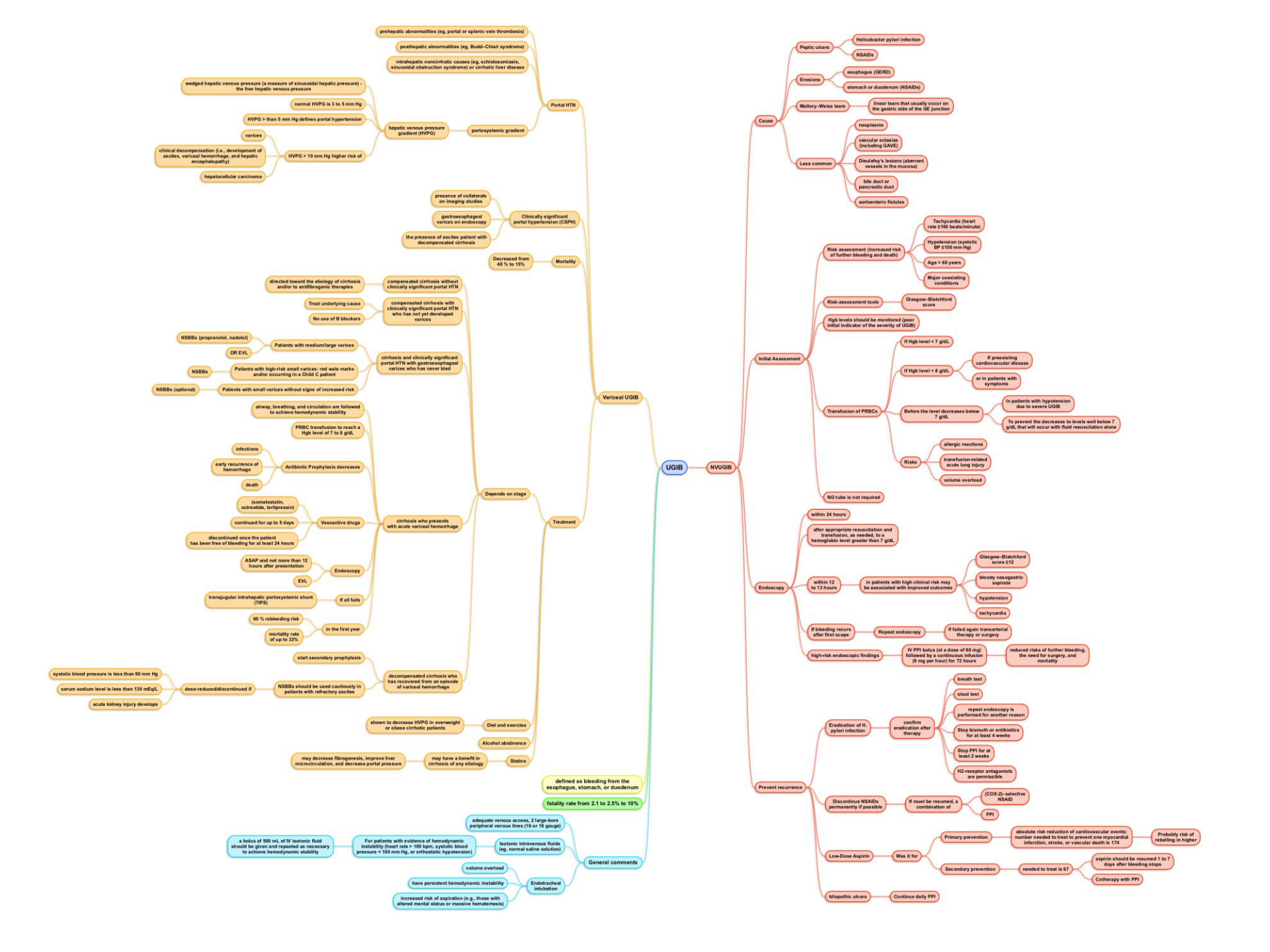
NVUGIB is a common clinical problem; an annual incidence of ~67 per 100,000 individuals has been estimated in the United States in 2012. The incidence has decreased over the past two decades owing to the implementation of successful preventive measures including administration of PPIs and *H. pylori* eradication in those at increased risk of developing NVUGIB, for example, those taking NSAIDs. The most common cause of NVUGIB are peptic ulcers followed by erosions associated with gastritis, vascular lesions, Mallory–Weiss syndrome (lacerations associated with recurrent vomiting) and neoplastic lesions.

QUALITY OF LIFE

Health-related quality of life is impaired during the bleeding event, but often follows an upward trajectory following hospital discharge. However, similar quality of life levels as in the general population are almost never reached, owing to pre-existing comorbidities and treatments. Anaemia, which is associated with fatigue, heart palpitations and shortness of breath, is a common long-term consequence of NVUGIB.

Written by Liesbet Lieben; designed by Laura Marshall

Article number: 18021; doi:10.1038/nrdp.2018.21; published online 19 Apr 2018


UGIB
defined as bleeding from the esophagus, stomach, or duodenum
fatality rate from 2.1 to 2.5% to 10%
NVUGIB
Cause
Peptic ulcers
Helicobacter pylori infection
NSAIDs
Erosions
esophagus (GERD)
stomach or duodenum (NSAIDs)
Mallory–Weiss tears
linear tears that usually occur on the gastric side of the GE junction
Less common
neoplasms
vascular ectasias (including GAVE)
Dieulafoy's lesions (aberrant vessels in the mucosa)
bile duct or pancreatic duct
aortoenteric fistulas
Initial Assessment
Risk assessment (increased risk of further bleeding and death)
Tachycardia (heart rate ≥100 beats/minute)
Hypotension (systolic BP ≤100 mm Hg)
Age > 60 years
Major coexisting conditions
Risk-assessment tools
Glasgow–Blatchford score
Hgb levels should be monitored (poor initial indicator of the severity of UGIB)
Transfusion of PRBCs
If Hgb level < 7 g/dL
If Hgb level < 8 g/dL
If preexisting cardiovascular disease
or in patients with symptoms
Before the level decreases below 7 g/dL
In patients with hypotension due to severe UGIB
To prevent the decreases to levels well below 7 g/dL that will occur with fluid resuscitation alone
Risks
allergic reactions
transfusion-related acute lung injury
volume overload
NG tube is not required
Endoscopy
within 24 hours
after appropriate resuscitation and transfusion, as needed, to a hemoglobin level greater than 7 g/dL
within 12 to 13 hours
in patients with high clinical risk may be associated with improved outcomes
Glasgow–Blatchford score ≥12
bloody nasogastric aspirate
hypotension
tachycardia
If bleeding recurs after first scope
Repeat endoscopy
If failed again transarterial therapy or surgery
high-risk endoscopic findings
IV PPI bolus (at a dose of 80 mg) followed by a continuous infusion (8 mg per hour) for 72 hours
reduced risks of further bleeding, the need for surgery, and mortality
Prevent recurrence
Eradication of H. pylori infection
confirm eradication after therapy
breath test
stool test
repeat endoscopy is performed for another reason
Stop bismuth or antibiotics for at least 4 weeks
Stop PPI for at least 2 weeks
H2-receptor antagonists are permissible
Discontinue NSAIDs permanently if possible
If must be resumed, a combination of
(COX-2)–selective NSAID
PPI
Low-Dose Aspirin
Was it for
Primary prevention
absolute risk reduction of cardiovascular events; number needed to treat to prevent one myocardial infarction, stroke, or vascular death is 174
Probably risk of rebelling in higher
Secondary prevention
needed to treat is 67
aspirin should be resumed 1 to 7 days after bleeding stops
Cotherapy with PPI
Idiopathic ulcers
Continue daily PPI
Variceal UGIB
Portal HTN
prehepatic abnormalities (eg, portal or splenic vein thrombosis)
posthepatic abnormalities (eg, Budd–Chiari syndrome)
intrahepatic noncirrhotic causes (eg, schistosomiasis, sinusoidal obstruction syndrome) or cirrhotic liver disease
portosystemic gradient
hepatic venous pressure gradient (HVPG)
wedged hepatic venous pressure (a measure of sinusoidal hepatic pressure) - the free hepatic venous pressure
normal HVPG is 3 to 5 mm Hg
HVPG > than 5 mm Hg defines portal hypertension
HVPG > 10 mm Hg higher risk of
varices
clinical decompensation (i.e., development of ascites, variceal hemorrhage, and hepatic encephalopathy)
hepatocellular carcinoma
Clinically significant portal hypertension (CSPH)
presence of collaterals on imaging studies
gastroesophageal varices on endoscopy
the presence of ascites patient with decompensated cirrhosis
Mortality
Decreased from 40 % to 15%
Treatment
Depends on stage
compensated cirrhosis without clinically significant portal HTN
directed toward the etiology of cirrhosis and/or to antifibrogenic therapies
compensated cirrhosis with clinically significant portal HTN who has not yet developed varices
Treat underlying cause
No use of B blockers
cirrhosis and clinically significant portal HTN with gastroesophageal varices who has never bled
Patients with medium/large varices
NSBBs (propranolol, nadolol)
OR EVL
Patients with high-risk small varices: red wale marks and/or occurring in a Child C patient
NSBBs
Patients with small varices without signs of increased risk
NSBBs (optional)
cirrhosis who presents with acute variceal hemorrhage
airway, breathing, and circulation are followed to achieve hemodynamic stability
PRBC transfusion to reach a Hgb level of 7 to 8 g/dL
Antibiotic Prophylaxis decreases
infections
early recurrence of hemorrhage
death
Vasoactive drugs
(somatostatin, octreotide, terlipressin)
continued for up to 5 days
discontinued once the patient has been free of bleeding for at least 24 hours
Endoscopy
ASAP and not more than 12 hours after presentation
EVL
If all fails
transjugular intrahepatic portosystemic shunt (TIPS)
in the first year
60 % rebleeding risk
mortality rate of up to 33%
decompensated cirrhosis who has recovered from an episode of variceal hemorrhage
start secondary prophylaxis
NSBBs should be used cautiously in patients with refractory ascites
dose-reduced/discontinued if
systolic blood pressure is less than 90 mm Hg
serum sodium level is less than 130 mEq/L
acute kidney injury develops
Diet and exercise
shown to decrease HVPG in overweight or obese cirrhotic patients
Alcohol abstinence
Statins
may have a benefit in cirrhosis of any etiology
may decrease fibrogenesis, improve liver microcirculation, and decrease portal pressure
General comments
adequate venous access, 2 large-bore peripheral venous lines (16 or 18 gauge)
Isotonic intravenous fluids (eg, normal saline solution)
For patients with evidence of hemodynamic instability (heart rate > 100 bpm, systolic blood pressure < 100 mm Hg, or orthostatic hypotension)
a bolus of 500 mL of IV isotonic fluid should be given and repeated as necessary to achieve hemodynamic stability
Endotracheal intubation
volume overload
have persistent hemodynamic instability
increased risk of aspiration (e.g., those with altered mental status or massive hematemesis)

https://lacolon.com/article/gastrointestinal-bleeding