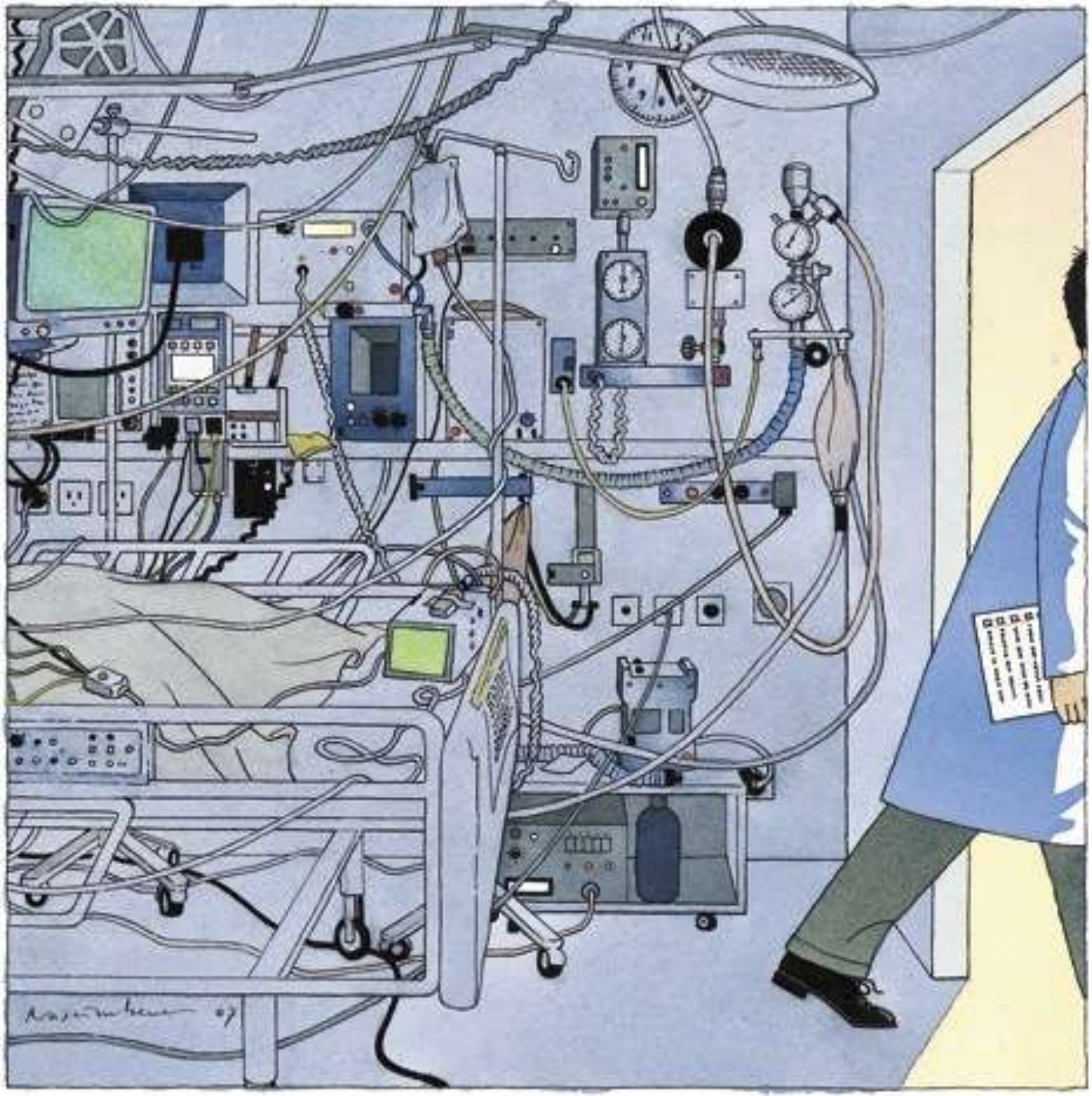
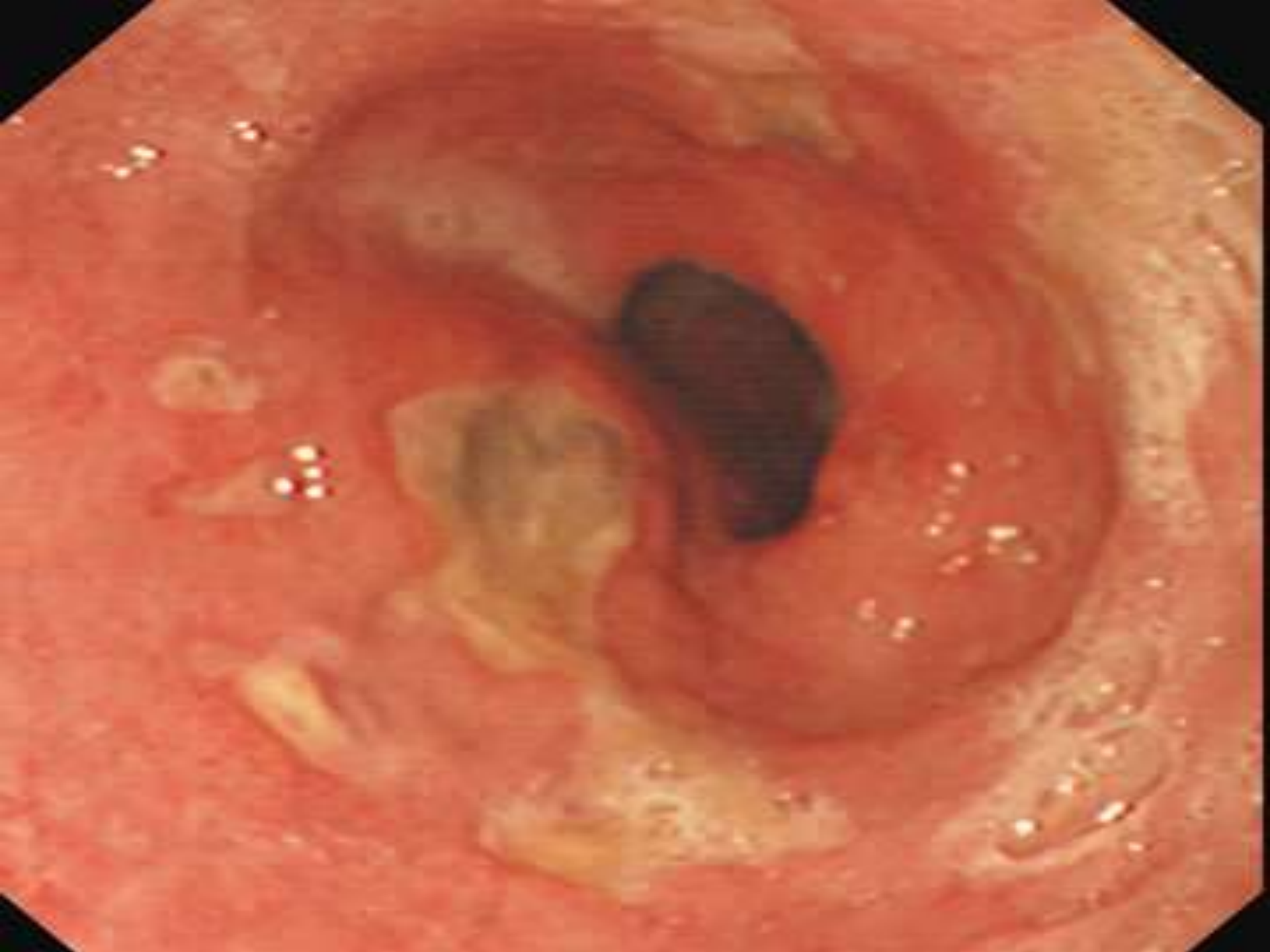


Stressulcusprophylaxe

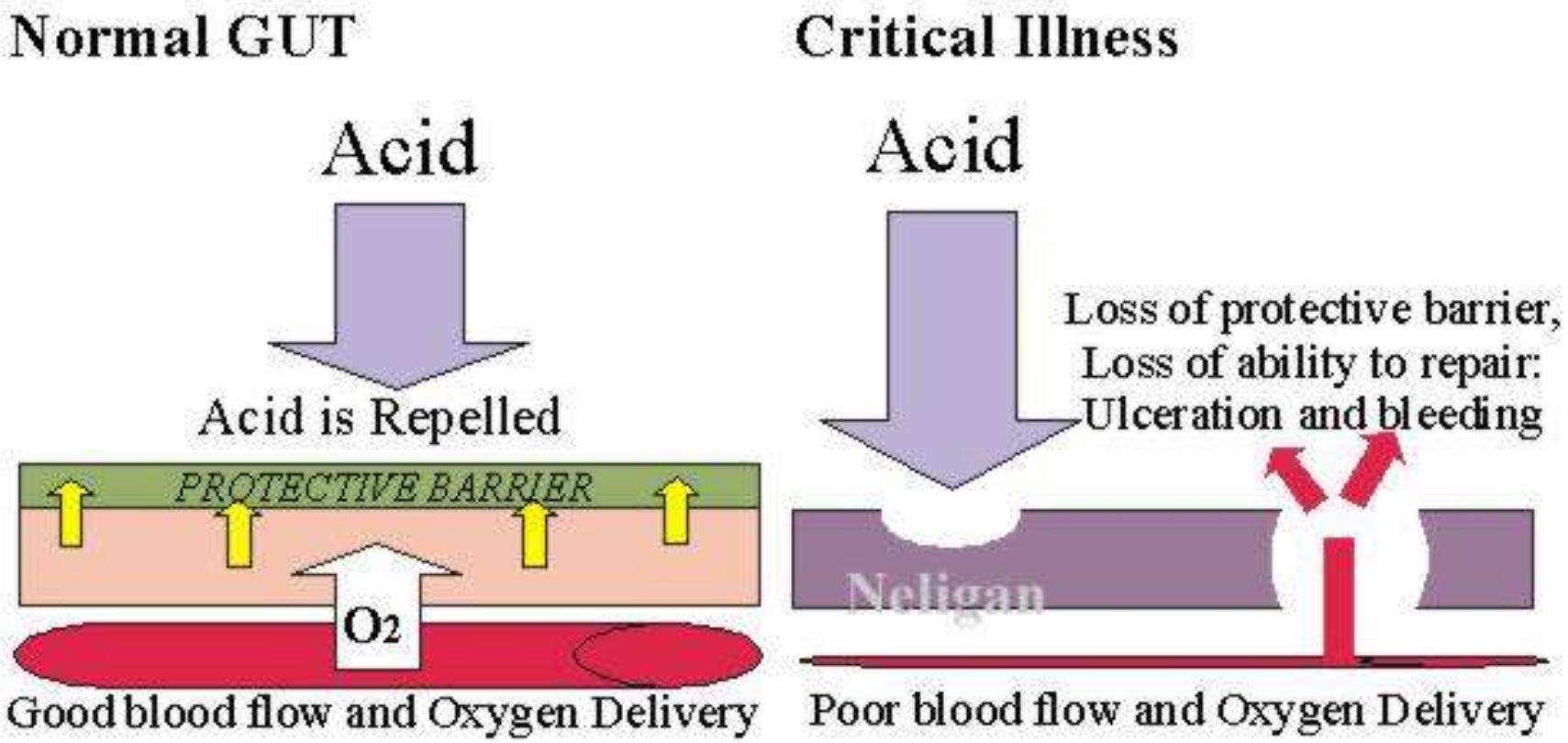
- Was ist ein Stressulcus?
- Wie hoch ist die Inzidenz?
- Prognose, Relevanz?
- Welche Risikofaktoren gibt es?
- Welche Prophylaxe?
- Wer braucht eine Prophylaxe?



Was ist ein Stressulcus

- oberflächliche Mucosaläsionen → ↓ Blutungsrisiko
- tiefere Ulcera → ↑ Blutungsrisiko

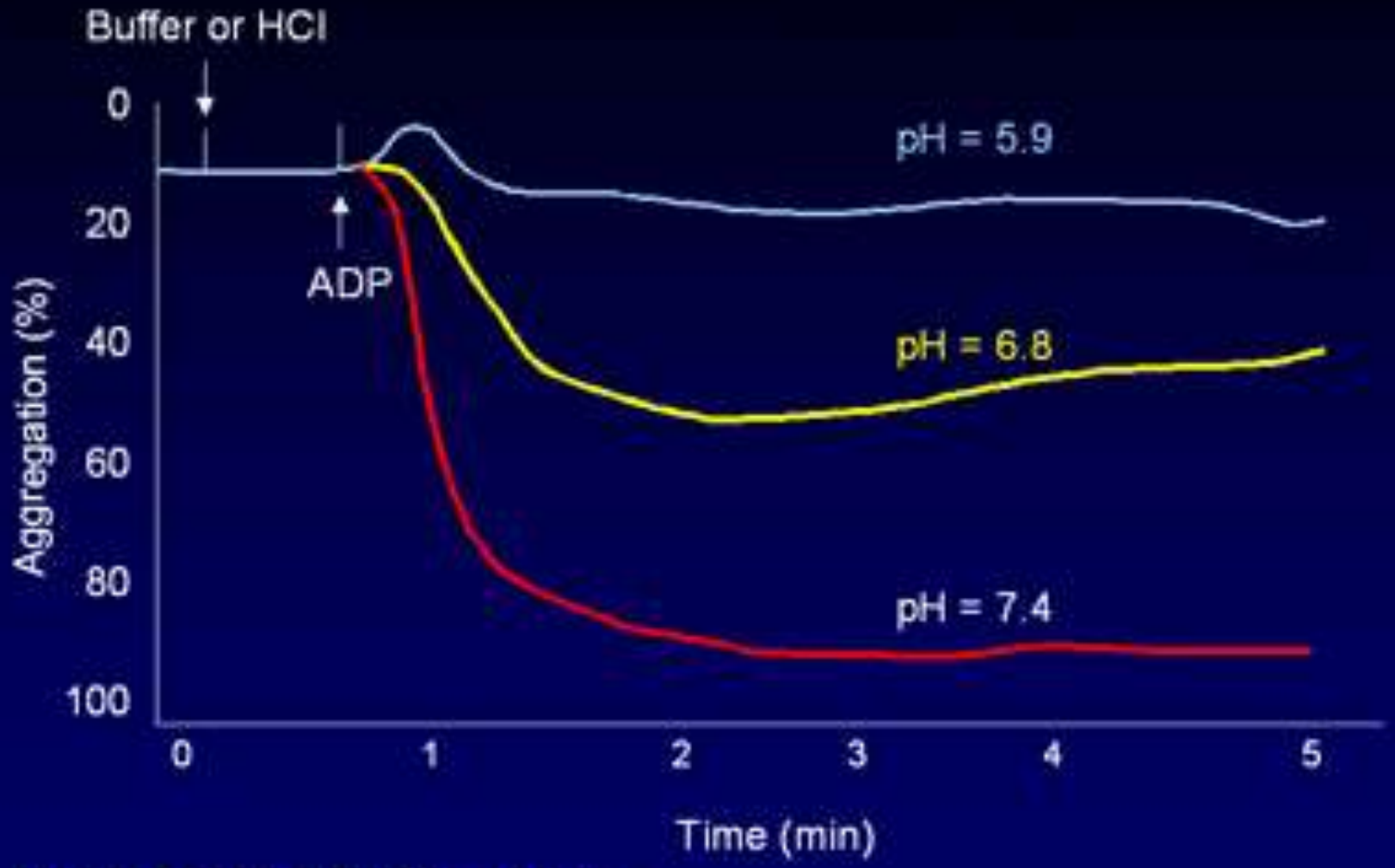
Was ist ein Stressulcus?



1. Reduktion der Mucosadurchblutung: Produktion von NO, free radicals, v.a. während Reperfusion
2. Reduktion der lokalen Prostaglandinsekretion
3. 1&2 führen zu fehlender Schutzschicht über der Mucosa
4. Auch bei geringer Säuresekretion entsteht ein Mucosaschaden
5. Fehlende Reparationsmechanismen
6. Tiefer Mucosa-pH aktiviert Pepsin und fördert die Fibrinolyse

Reilly J. Pathophysiology of the upper gastrointestinal tract in the critically ill patient: Rationale for the therapeutic benefit of acid suppression. JPharm Prac 1998; 11: 418-432

pH and Platelet Aggregation



ADP = adenosine diphosphate

Green FW et al. Gastroenterology. 1978;74:38-43.

Wie hoch ist die Inzidenz?

- 75-100% zeigen Mucosaläsionen 24 h nach IPS-Eintritt

  Reilly J. JPharm Prac 1998; 11: 418-432

- 3 mögliche Arten „Stress“ bedingter Mucosablutungen
  - okkulter Blutverlust (Inzidenz ?)
  - makroskopischer Blutverlust (Inzidenz 5%-8%)
  - grosser makroskopischer Blutverlust (hämodynamische Instabilität od. Transfusionsbedarf; Inzidenz 1-4%)

Reilly J. Pathophysiology of the upper gastrointestinal tract in the critically ill patient: Rationale for the therapeutic benefit of acid suppression. JPharm Prac 1998; 11: 418-432

Cook DJ. Risk factors for gastrointestinal bleeding in critically ill patients. N Engl J Med 1994; 330: 377-381 **(31/847; 3.7% with RF – 0.1% without RF)**

Zandstra DF. The virtual absence of stress-ulceration related bleeding in critically ill patients receiving prolonged mechanical ventilation without any prophylaxis. Intens Care Med 1994; 20: 335-340

Pimentel M. Clinically significant gastrointestinal bleeding in critically ill patients in an era of prophylaxis. Am J Gastroenterol 2000; 95: 2801-2806

Cook DJ. The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients. Crit Care 2002; 5: 368-375

Faisy C. Clinically significant gastrointestinal bleeding in critically ill patients with and without stress-ulcer prophylaxis. Intens Care Med 2003; 29: 1306-1313

Maury E. An observational study of upper gastrointestinal bleeding in intensive care units: is Helicobacter pylori the culprit? Crit Care Med 2005; 1513-1518

Wie hoch ist die Inzidenz?

Patient Group and Risk Factor	Bleeding	No Bleeding	Percent with Bleeding*
All patients			
Neither	2	1403	0.1
Respiratory failure	8	384	2.0
Coagulopathy	1	191	0.5
Both	22	241	8.4
Total	33	2219	1.5

Cook DJ. Risk factors for gastrointestinal bleeding in critically ill patients.
N Engl J Med 1994; 330: 377-381

Overall 33/2219 (1.5%)
Ohne RF: 2/1403 (0.1%)
Mit RF: 31/ 847 (3.7%)

Welche Risikofaktoren gibt es?

prospective multicenter observational. n = 2252 (multivariate logistic regression)

Risk Factor	Simple Regression		Multiple Regression	
	Odds ratio	P value	Odds ratio	P value
Respiratory failure	25.5	<0.001	15.6	<0.001
Coagulopathy	9.5	<0.001	4.3	<0.001
Hypotension	5.0	0.03	3.7	0.08
Sepsis	7.3	<0.001	2.0	0.17
Hepatic failure	6.5	<0.001	1.6	0.27
Renal failure	4.6	<0.001	1.6	0.26
Enteral feeding	3.8	<0.001	1.0	0.99
Glucocorticoid administration	3.7	<0.001	1.5	0.26
Organ transplantation	3.6	0.006	1.5	0.42
Anticoagulant therapy	3.3	0.004	1.1	0.88

Cook DJ. Risk factors for gastrointestinal bleeding in critically ill patients. N Engl J Med 1994; 330: 377-381

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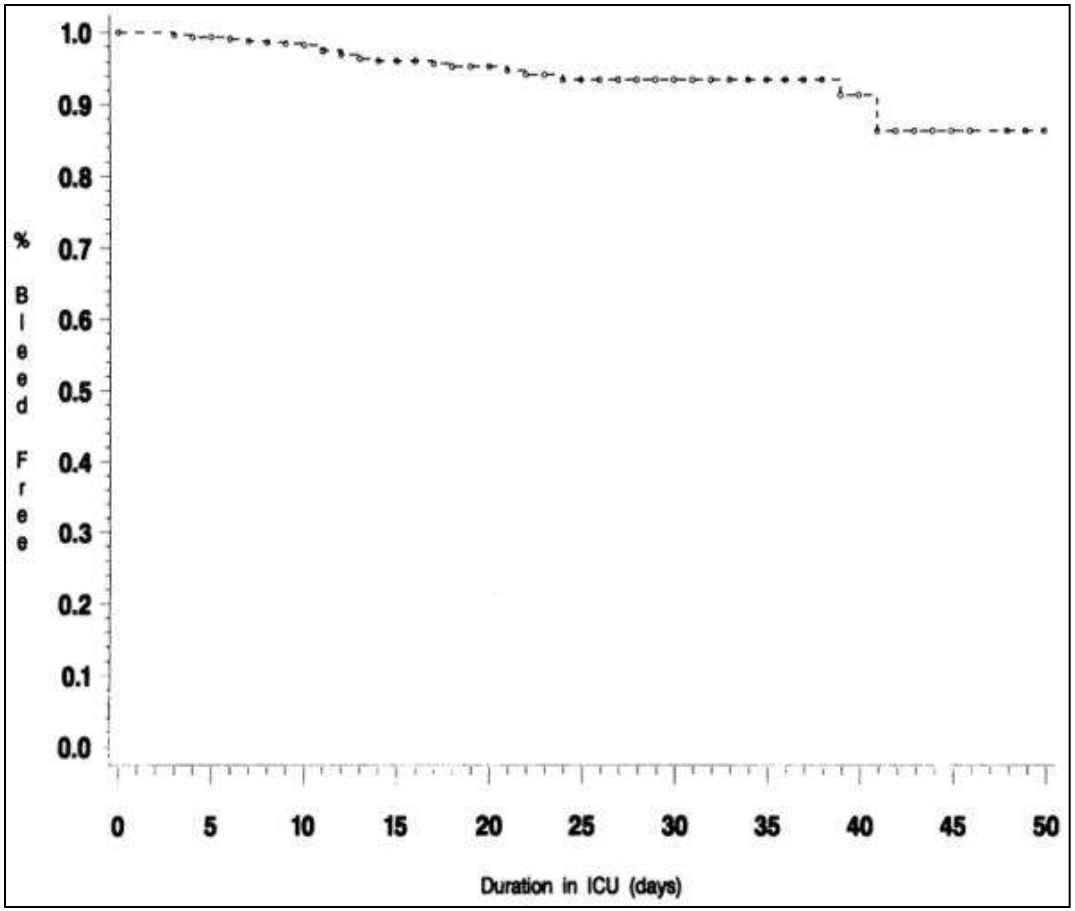
Welche Risikofaktoren gibt es?



Proportion der blutungsfreien Patienten

Cook DJ. Risk factors for clinically important upper gastrointestinal bleeding in critically ill patients requiring mechanical ventilation. Crit Care Med 1999; 27: 2812-2817

Welche Risikofaktoren gibt es?

prospective observational (dabase RCT Sucralfate vs. Ranitidine; NEJM 1998).
n = 1077 ventilated > 48 h (cox regression)

Risk Factor	Univariable Regression		Multivariable Regression	
	Risk Ratio (95% CI)	*p*	Risk Ratio (95% CI)	*p*
Platelet count < 50,000	2.58 (1.19–5.57)	.02		
Maximum serum creatinine	1.19 (1.06–1.35)	.01	1.16 (1.02–1.32)	.023
Maximum MOD score	1.11 (1.01–1.21)	.04		
Renal domain of MOD score	1.46 (1.14–1.87)	.002		
Pulmonary domain of MOD score	1.56 (0.99–2.47)	.04		
Hepatic domain of MOD score	1.37 (1.04–1.77)	.008		
Enteral nutrition	0.35 (0.16–0.76)	.002	0.30 (0.13–0.67)	.004
Ranitidine	0.40 (0.18–0.89)	.02	0.39 (0.17–0.83)	.024

CI, confidence interval; MOD, multiple organ dysfunction (representing six organs).

The renal domain indicates a categorical description of serum creatinine; the pulmonary domain indicates a categorical description of Pao_2/Fio_2 ratio; the hepatic domain indicates a categorical description of serum bilirubin; the relative risk of maximum serum creatinine corresponds with a 100-μmol/L increment; the relative risk of all MOD scores corresponds with a 1-unit increment.

Cook DJ. Risk factors for clinically important upper gastrointestinal bleeding in critically ill patients requiring mechanical ventilation. Crit Care Med 1999; 27: 2812-2817

Welche Risikofaktoren gibt es?

Clinical characteristics of ICU patients with negative and positive *H. pylori* antigen detection

Characteristic	Hp⁻ ($n = 1,665$)	Hp⁺ ($n = 111$)
Age (years)	[illegible]	[illegible]
Male/female (%)	65/35	55/45*
SAPS II	39.9 ± 16.5	43.3 ± 15.6*
Patients with mechanical ventilation (%)	77.0	77.5
Duration of mechanical ventilation (days)	12.1 ± 14.0	12.3 ± 12.1
Patients with sepsis (%)	21.3	22.7
Patients receiving antibiotics on admission (%)	27.8	29.7
Creatinine on admission (μmol/l)	144 ± 185	156 ± 182
Ulcer prophylaxis (%)	15.9	11.7
Hemoglobin on admission (g/dl)	12.4 ± 7.8	11.5 ± 2.6
Patients with hematocrit fall (%)	13.6	12.6
Patients requiring red blood transfusion (%)	28.0	29.7
Red blood transfusion in patients requiring transfusion (units)		
Mean ± SD	5.5 ± 6.7	3.9 ± 3.8
Median (range)	3 (1–69)	3 (1–43)
Death (%)	23.4	20.0

Hp⁻, negative for *H. pylori* antigen; Hp⁺, positive for *H. pylori* antigen; SAPS, Simplified Acute Physiology Score. * $p < 0.05$.

Robert R. Helicobacter pylori infection is not associated with an increased hemorrhagic risk in patients in the intensive care unit. Crit Care 2006; 10: R77

Welche Risikofaktoren gibt es?

prospective observational an 1776 IPS-Patienten (multivariate log. regression)

Table 3

Main clinical characteristics of patients with and without bleeding during their ICU stay

Characteristic	Bleeding patients ($n = 223$)	Non-bleeding patients ($n = 1,469$)
Age (year)	61.2	61.0
Male sex (%)	68.2	63.4
SAPS II	44.7 ± 17.8	39.2 ± 15.9[a]
Patients with mechanical ventilation (%)	78	77
Patients with sepsis (%)	27.4	20.3[b]
Shock on admission (%)	35.9	21.2[a]
Creatinine on admission (µmol/l)	180 ± 176	135 ± 175[b]
Positivity of *H. pylori* antigen (%)	5.4	6.3
Death (%)	30.9	18.6[a]

The patients with documented extra-digestive bleeding were excluded from this analysis.
[a]Statistical significance: $p < 0.01$ with univariate analysis. [b]Statistical significance: $p < 0.05$ with univariate analysis.

Robert R. Helicobacter pylori infection is not associated with an increased hemorrhagic risk in patients in the intensive care unit. Crit Care 2006; 10: R77

Prognose, Relevanz?

prospective observational an 1666 IPS-Patienten aus zwei Datenbanken (Cook DJ. NEJM 1994, Cook DJ. NEJM 1998). Drei statistische Modelle.

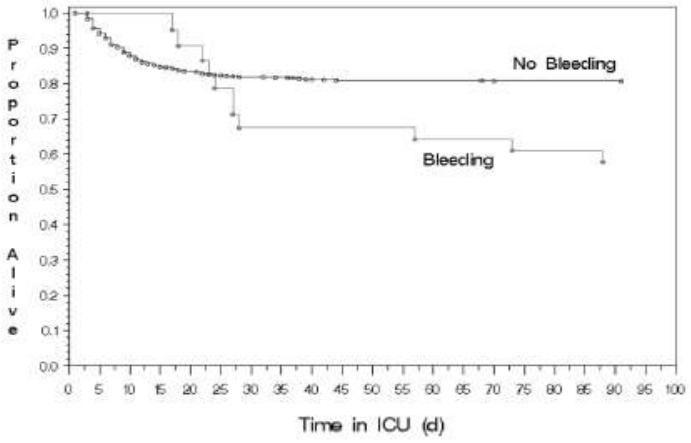
Intensive care unit (ICU) mortality attributable to clinically important gastrointestinal bleeding

ICU mortality	Relative risk (95% confidence interval)	Absolute risk (95% confidence interval)
Crude comparison	2.2 (1.6–2.9)	24.0 (11.3–36.6)
Matched cohort method	2.9 (1.6–5.5)	30.3 (15.2–45.3)
Model-based matched cohort method	1.8 (1.1–2.9)	20.3 (4.3–36.4)
Regression method	4.1 (2.6–6.5)	–
Adjusted*	1.0 (0.6–1.7)	–

The model-based matched cohort probably yields the best estimate of the attributable mortality. See Table 3 for advantages and disadvantages of these methods. * Adjusted for age, APACHE II score, admitting diagnosis, duration of ventilation, Multiple Organ Dysfunction Score, and bleeding status.

Cook DJ. The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients. Crit Care 2001; 5: 368-375

Prognose, Relevanz?



The survival curves for patients with and without clinically important gastrointestinal bleeding. ICU, intensive care unit; d, days.

prospective observational
an 1666 IPS-Patienten
aus zwei Datenbanken
(Cook DJ. NEJM 1994,
Cook DJ. NEJM 1998).
Drei statistische Modelle.

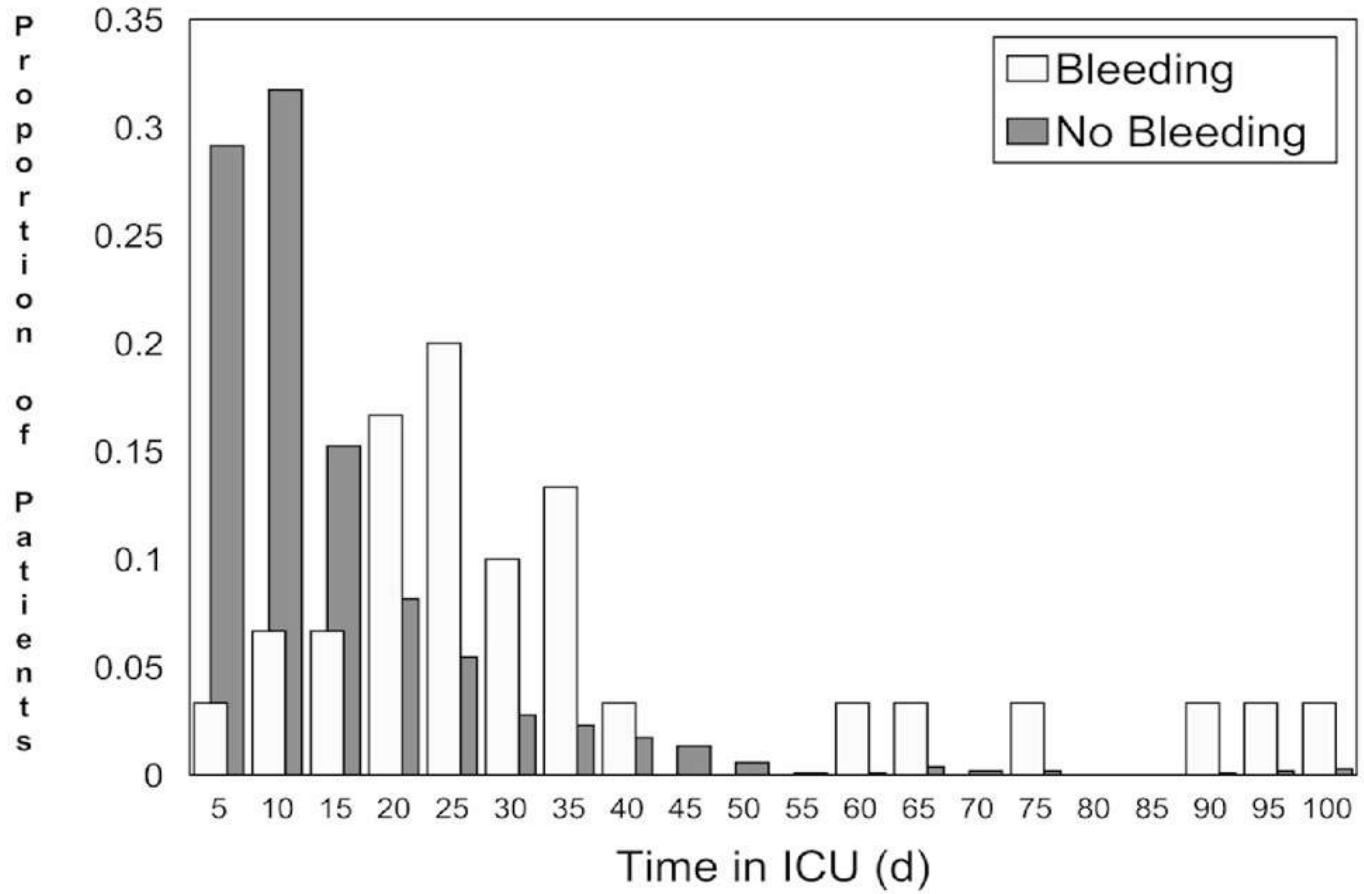
Zeit nach IPS-Eintritt	RR f. Mortalität	CI (95%)
2 Wochen	0.4	0.06 – 2.0
3 Wochen	1.6	0.6 – 4.0
4 Wochen	7.4	1.7 – 32.2

Je später die Blutung eintritt, desto ungünstiger ist sie!

Cook DJ. The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients. Crit Care 2001; 5: 368-375

Prognose, Relevanz?

prospective observational an 1666 IPS-Patienten aus zwei Datenbanken (Cook DJ. NEJM 1994, Cook DJ. NEJM 1998). Drei statistische Modelle.



Cook DJ. The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients. Crit Care 2001; 5: 368-375

Critical Care

Welche Prophylaxe?

Randomisierte, doppelblind, placebo kontrollierte Multicenterstudie an 1200 Patienten (Cook DJ. NEJM 1998).

Ranitidine (H2-B) vs. Sucralfat

Welche Prophylaxe?

Randomisierte, doppelblind, placebo kontrollierte Multicenterstudie an 1200 Patienten (Cook DJ. NEJM 1998).

Blutung	Ranithidine	Sucralfate	RR	CI 95%	p
Non adj.	10/596 (1.7%)	23/604 (3.8%)	0.44	0.21 – 0.92	0.002
Adj.			0.45	0.22 – 0.92	0.003

Cook DJ. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in Patients recquiring mechanical ventilation. N Engl J Med 1998; 338: 791-797

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Adj.			0.45	0.22 – 0.92	0.003
Pneumonie					
Non adj.	114/596 (19.1%)	98/604 (16.2%)	1.18	0.92 – 1.51	0.19
Adj.			1.14	0.91 – 1.44	0.26

Cook DJ. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in Patients recquiring mechanical ventilation. N Engl J Med 1998; 338: 791-797

Welche Prophylaxe?

TABLE 3. PATIENTS WITH VENTILATOR-ASSOCIATED PNEUMONIA.*

DIAGNOSTIC CRITERIA USED	RANITIDINE GROUP	SUCRALFATE GROUP	DIFFERENCE IN RISK (95% CI)†	RELATIVE RISK (95% CI)	P VALUE
	no.		%		
Adjudication rate	114	98	2.9 (−1.4 to 7.2)	1.18 (0.92 to 1.51)	0.19
Bedside clinicians' assessment	153	133	3.7 (−1.2 to 8.5)	1.17 (0.95 to 1.43)	0.14
CDC	140	120	3.6 (−1.0 to 8.3)	1.18 (0.95 to 1.47)	0.13
Clinical suspicion	132	107	4.4 (−0.1 to 9.0)	1.25 (0.95 to 1.57)	0.06
Probable pneumonia	58	54	0.8 (−2.5 to 4.1)	1.09 (0.77 to 1.55)	0.64
Definite pneumonia	5	0	0.8 (0.1 to 1.6)	Undefined	0.03

Cook DJ. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in Patients recquiring mechanical ventilation. N Engl J Med 1998; 338: 791-797

Welche Prophylaxe?

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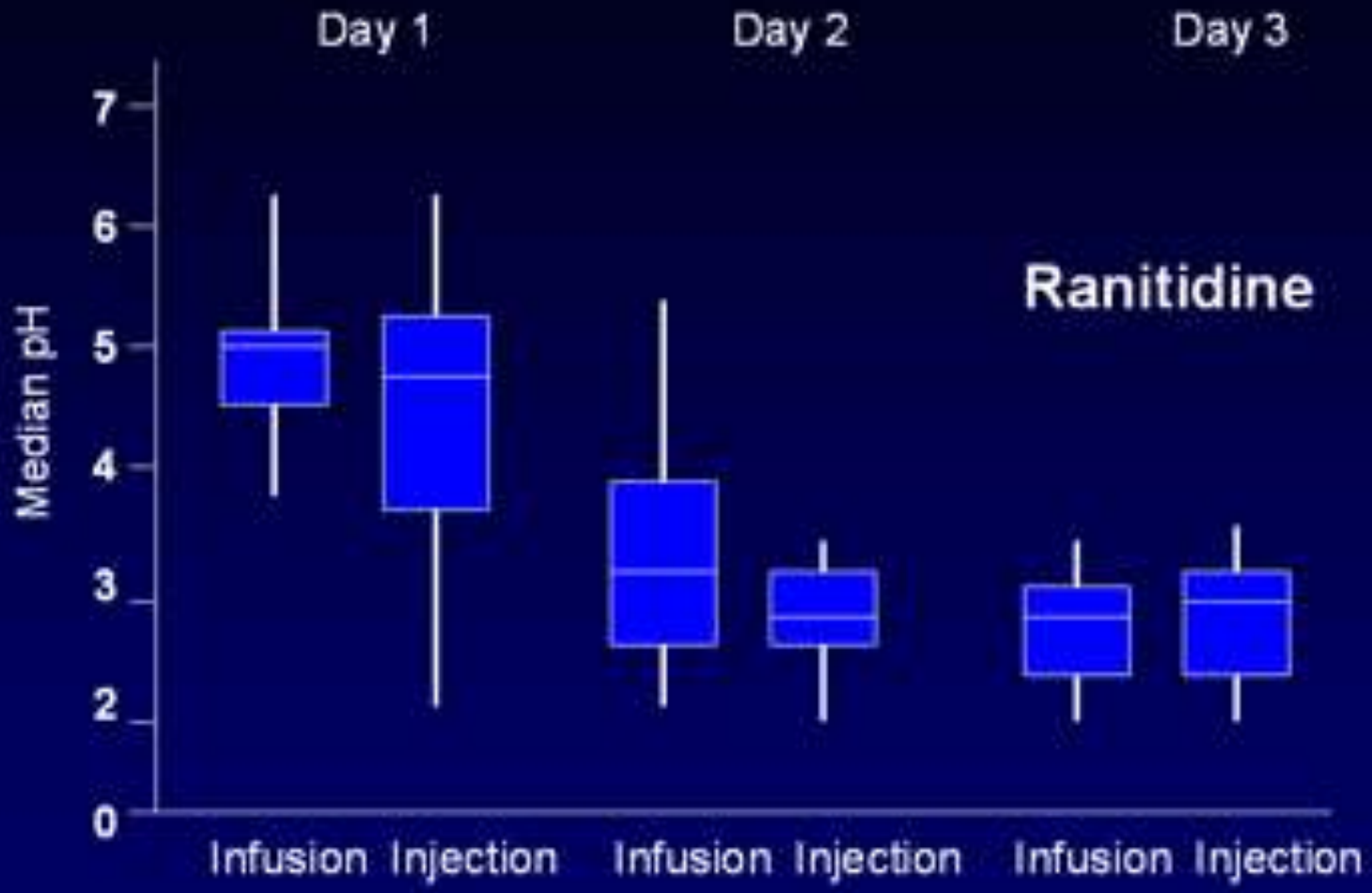
Pneumonie					
Non adj.	114/596 (19.1%)	98/604 (16.2%)	1.18	0.92 – 1.51	0.19
Adj.			1.14	0.91 – 1.44	0.26
Mortalität	140/596 (23.5%)	138/604 (22.8%)	1.03	0.84 – 1.26	0.79

Cook DJ. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in Patients recquiring mechanical ventilation. N Engl J Med 1998; 338: 791-797

Injection or Infusion



Netzer P et al. *Am J Gastroenterol.* 1999;94:351-357.

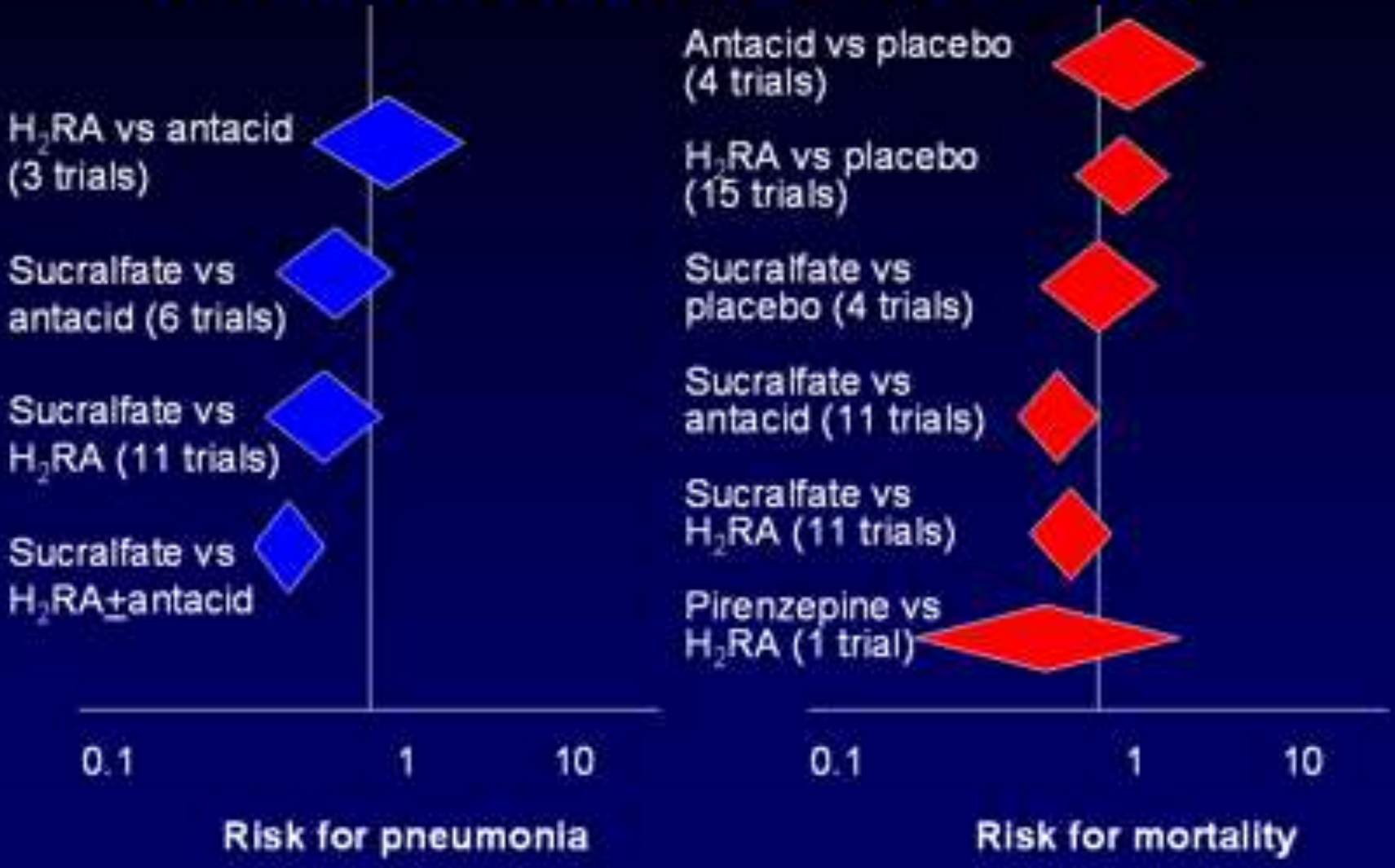
Welche Prophylaxe?

prospective observational (dabase RCT Sucralfate vs. Ranitidine; NEJM 1998). n = 1077 ventilated > 48 h (cox regression with an nonproportional hazard model)

Ranitidin	**HR**	**CI**
D5	0.18	0.04 – 0.70
D10	0.26	0.07 – 1.02
D15	0.40	0.10 – 1.65
D20	0.59	0.12 – 2.92

Cook DJ. Risk factors for clinically important upper gastrointestinal bleeding in critically ill patients requiring mechanical ventilation. Crit Care Med 1999; 27: 2812-2817

Pneumonia and Mortality



Welche Prophylaxe?

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PPI vs. H2-B

Welche Prophylaxe?

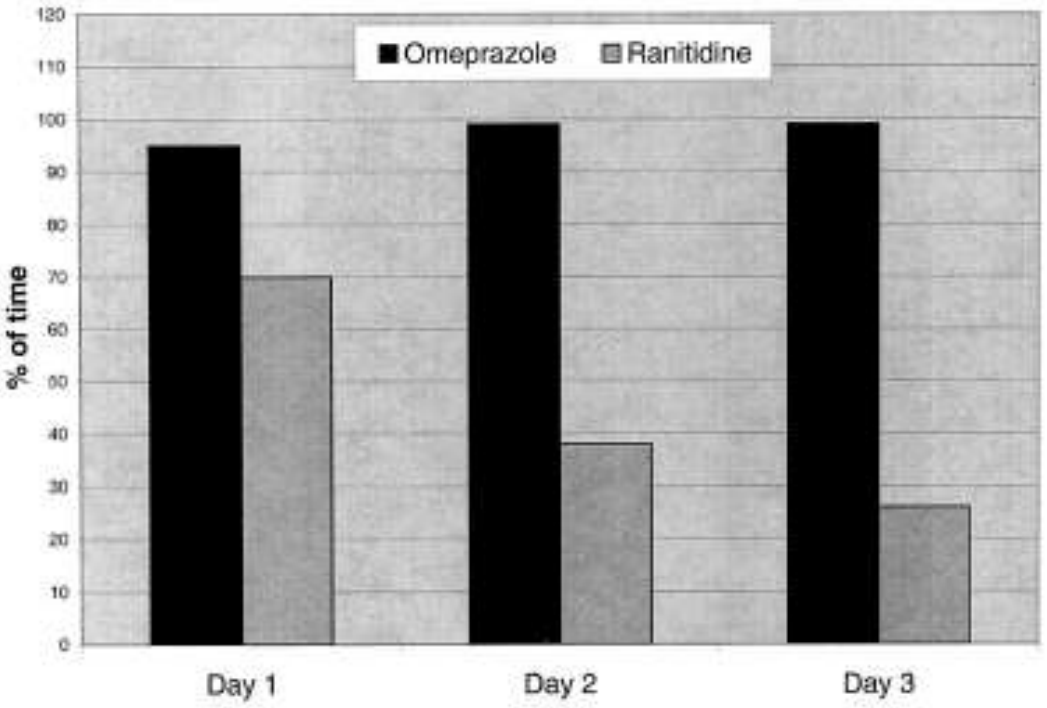
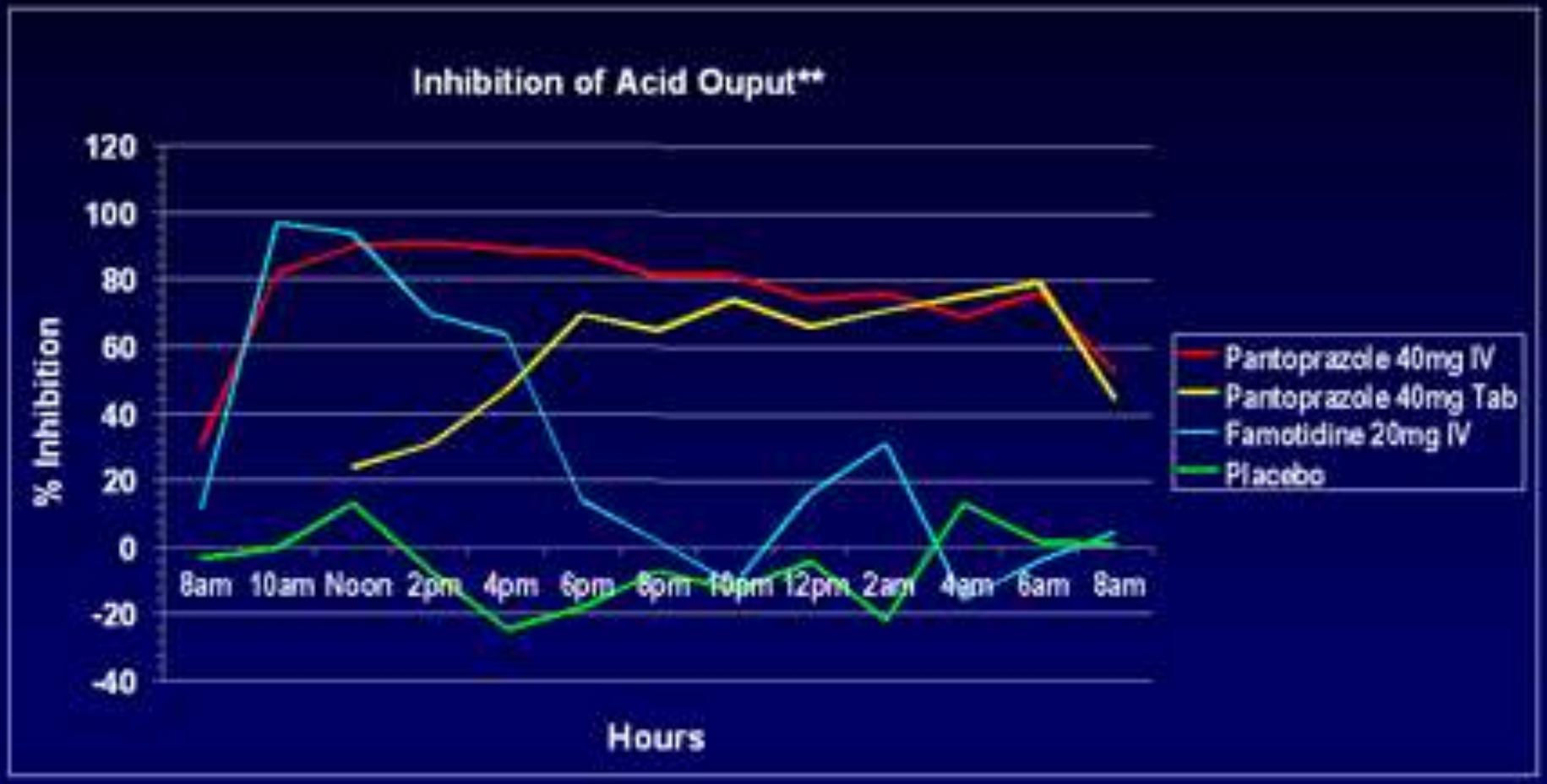


Figure 1. Comparison of the percentage of time that omeprazole and ranitidine maintained the intragastric pH at >4. Healthy volunteers were randomized to receive either intravenous ranitidine or omeprazole as a bolus injection, followed by continuous infusion over 72 hrs. Adapted with permission (19).

Netzer P. Effect of repeated injection and continuous infusion of omeprazole and ranithidine on intragastric pH over 72 hours. Am J Gastroenterol 1999; 94: 351-357

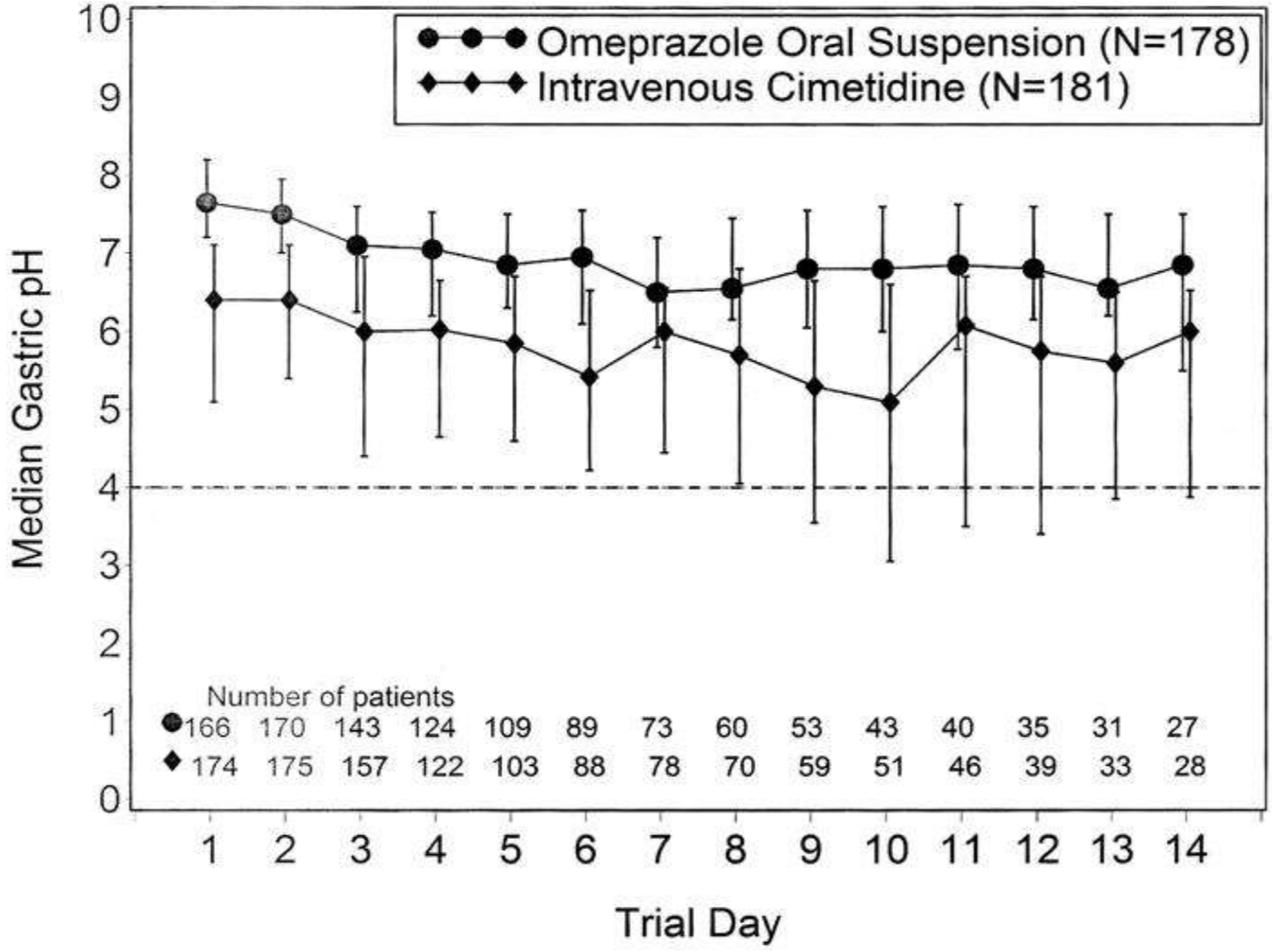
Pantoprazole Effect on Acid Output

40 mg Oral and IV vs Famotidine, 20 mg IV



*Pentagastrin stimulated

Welche Prophylaxe?



Conrad SA. Randomized, double-blind comparison of immediate-release omeprazole oral suspension versus Intravenous cimetidine for the prevention of upper gastrointestinal bleeding in critically ill patients. Crit Care Med 2005; 33: 760-765

Welche Prophylaxe?

Protonenpumpenhemmer sind nicht besser (aber auch nicht schlechter!) als H2-Ant.

Table 2. Results in the intent-to-treat population

	Omeprazole Oral Suspension (n = 178)	Intravenous Cimetidine (n = 181)	Confidence Interval for the Difference in Rates, %
Clinically significant bleeding, n (%)	7 (3.9)	10 (5.5)	−100.0, 2.8[a]
Any overt bleeding, n (%)	34 (19.1)	58 (32.0)	−21.9, −4.0[b]
Inadequate pH control, n (%)	32 (18.0)	105 (58.0)	−49.2, −30.9[c]

Any overt bleeding included both end point and non-end point bleeding. Inadequate pH control was defined as two consecutive gastric pH determinations of ≤4 at least 1 hr apart on any given day of treatment; tabulated patients experienced inadequate pH control at least once during the trial. The difference in rates was calculated as omeprazole-cimetidine.

[a]Noninferiority analysis, one-sided 97.5% confidence interval; [b]two-sided 95% confidence interval, $p = .005$; [c]two-sided 95% confidence interval, $p < .001$.

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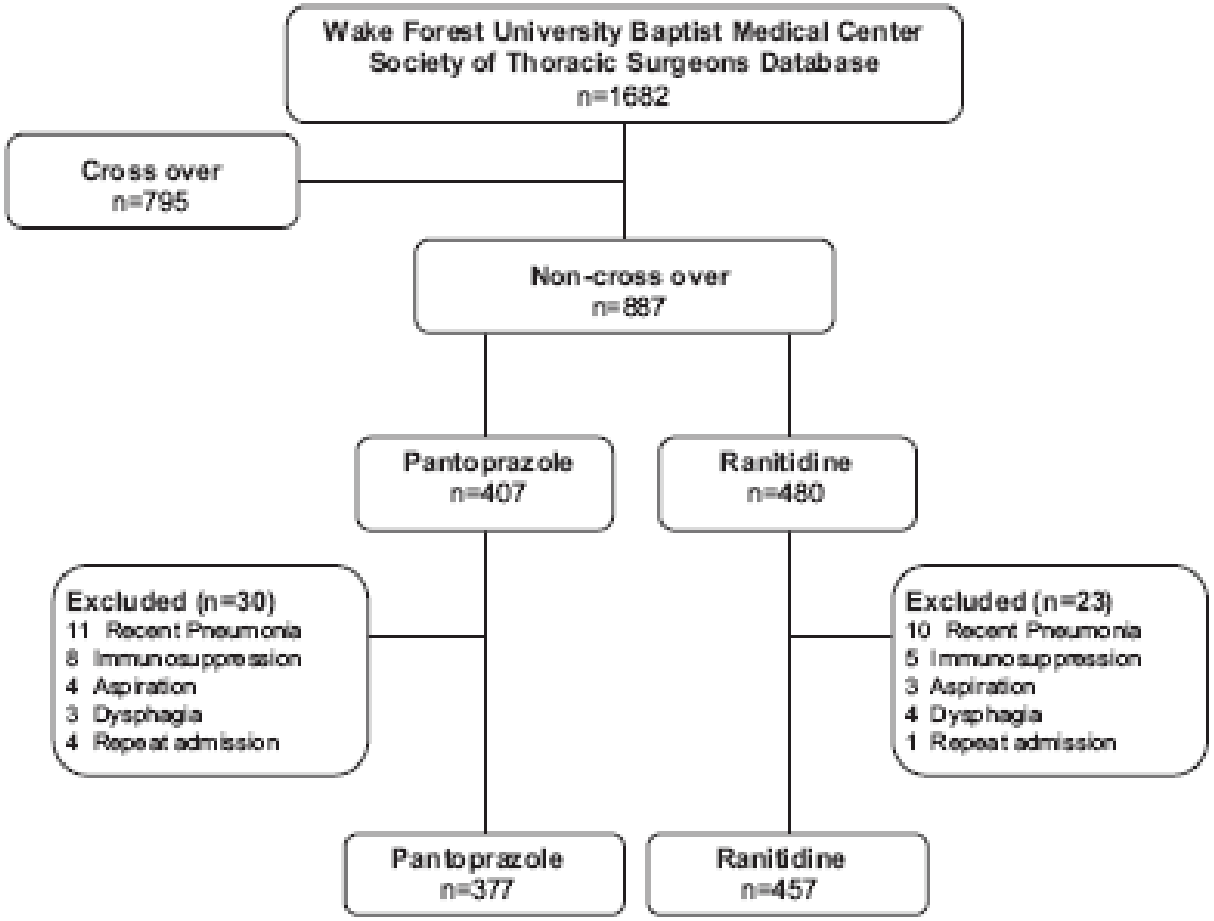
Welche Prophylaxe?

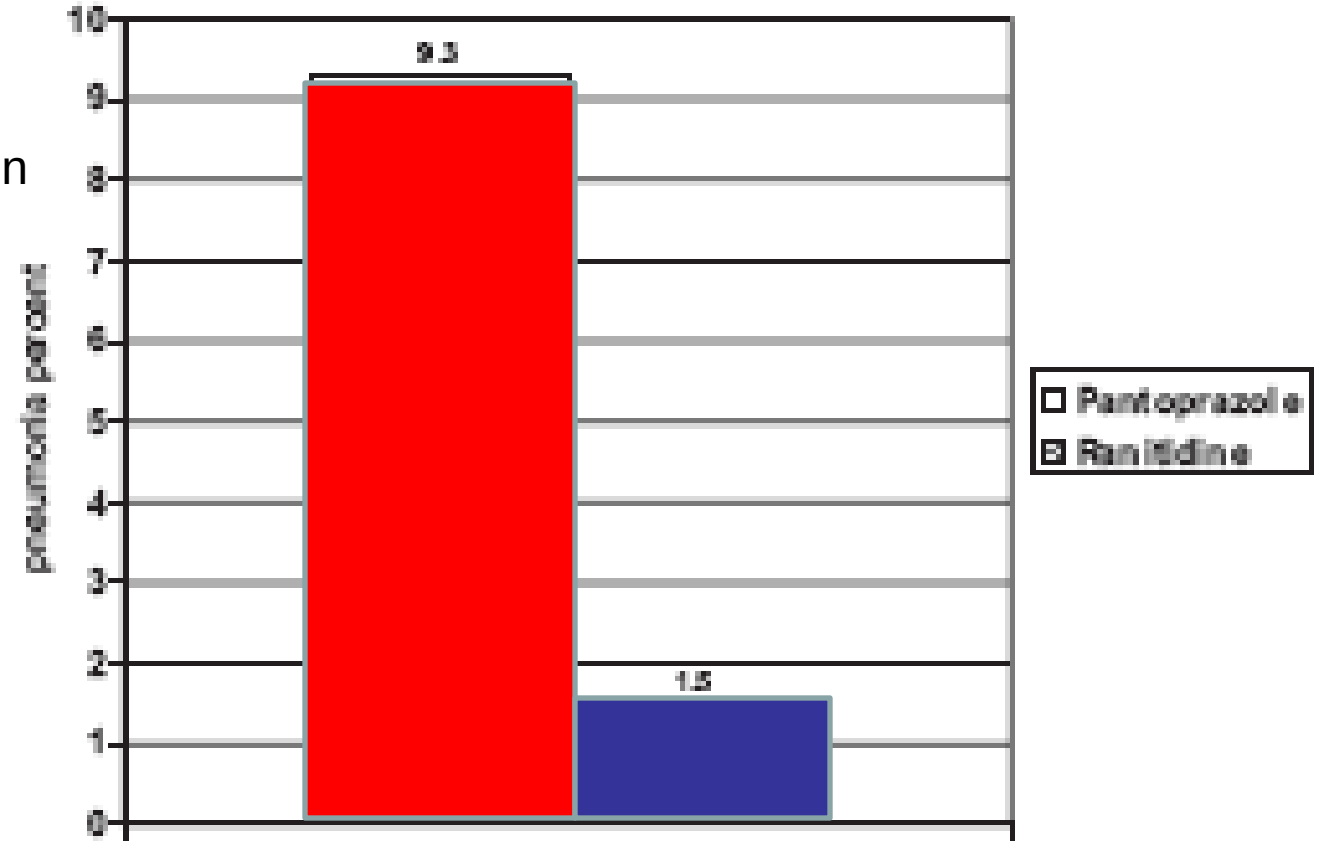


Retrospektive Studie an kardiochirurgischen Patienten in der Intensivstation welche Ranitidin oder Pantoprazol erhielten. Multivariate logistische Regression einschliessl. Korrektur für Wahrscheinlichkeit einer Gabe von Pantoprazol. (propensity score)

Miano T.A. Nosocomial pneumonia risk and stress ulcer prophylaxis. A comparison of pantoprazole vs Ranithidine in cardiothoracic surgery patients. Chest 2009; 136: 440-447

Welche Prophylaxe?

% pneumonien



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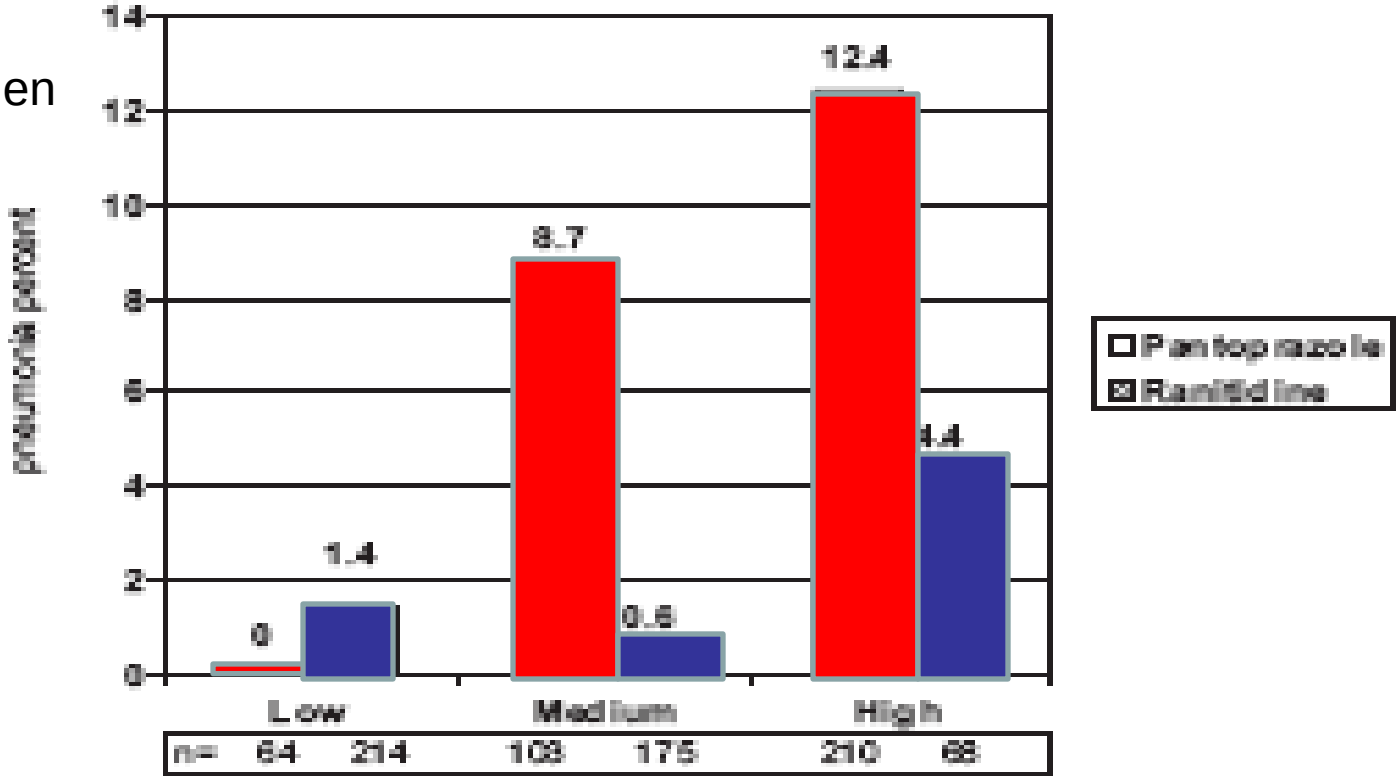
Welche Prophylaxe?

% pneumonien



Multivariante logistische Regression mit Propensity Score: OR 2.7, CI 1.1-6.7, p=0.034

Miano T.A. Nosocomial pneumonia risk and stress ulcer prophylaxis. A comparison of pantoprazole vs Ranitidine in cardiothoracic surgery patients. Chest 2009; 136: 440-447

Welche Prophylaxe?

Retrospective, nested cohort, n=364‘683

	No. (%)		Unadjusted OR	Adjusted OR (95% CI)*
	Cases	Controls		
Use of acid-suppressive drugs				
Current	183 (38.5)	1361 (27.4)	1.28	1.27 (1.06-1.54)
Recent (<30 days ago)	28 (5.9)	243 (4.9)	1.12	1.08 (0.78-1.50)
Past (30-180 days ago)	34 (7.2)	346 (7.0)	0.96	1.00 (0.74-1.36)
Distant past (>180 days ago)	230 (48.4)	3010 (60.7)	1.00	
Drug classes				
Current PPIs	99 (20.8)	697 (14.1)	1.79	1.73 (1.33-2.25)
Current H_2RAs	48 (10.1)	417 (8.4)	1.43	1.59 (1.14-2.23)
Current use of H_2RAs and PPIs	36 (7.6)	247 (5.0)	1.89	1.76 (1.18-2.61)
Recent use of H_2RAs or PPIs	28 (5.9)	243 (4.9)	1.47	1.44 (0.94-2.21)
Past plus distant past use of H_2RAs or PPIs	264 (55.6)	3356 (67.7)	1.00	

Laheij R.J.F. Risk of community-acquired pneumonia and use of gastric acid-suppressive drugs. JAMA 2004; 292: 1955-1960

Welche Prophylaxe?

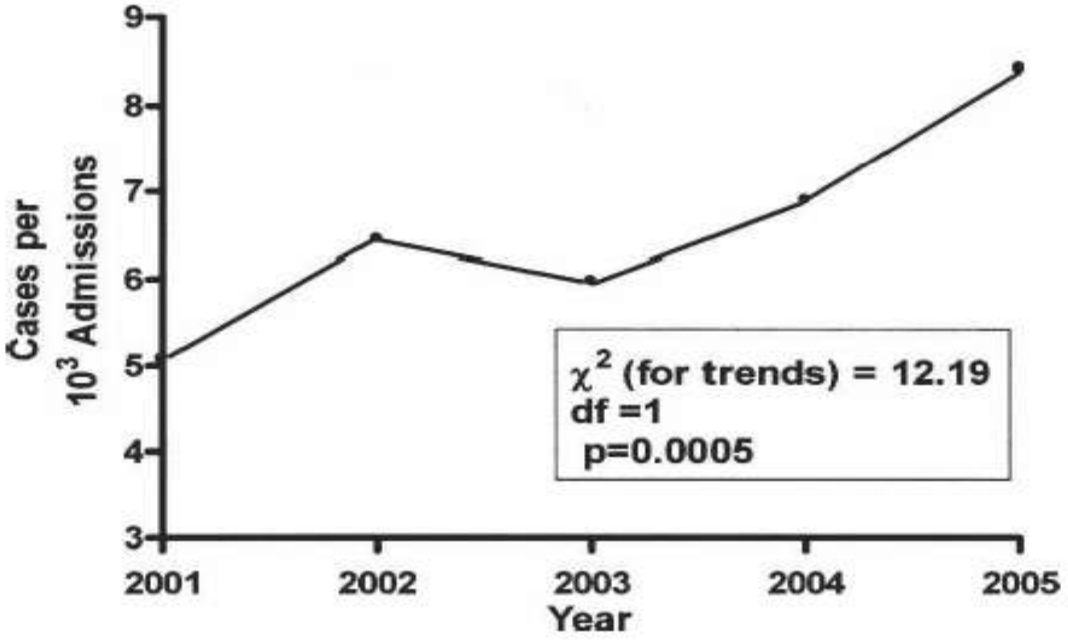


Fig. 1. Change in annual incidence of CDAD during the period from 2001 to 2005.

Jayatilaka S. Clostridium difficile infection in an urban medical center: Five-year analysis of infection Rates among adult admissions and association with the use of proton pump inhibitors.
Ann Clin Lab Sci 2007; 37: 241

Welche Prophylaxe?

B. Adjusted Odds Ratios for GARD, controlled for antibiotic use as a confounding variable

Variable	OR (95% CI)	p value
	PPI Use pre- or during admission	
Any Antibiotic[a]	2.75 (1.68-4.52)	0.0001
Fluoroquinolones	2.56 (1.58-4.16)	0.0001
	PPI use post-admission	
Any Antibiotic[a]	1.88 (1.07-3.31)	0.0283
Fluoroquinolones	1.82 (1.06-3.14)	0.0301
	H2A use pre- or during admission	
Any Antibiotic[a]	0.95 (0.39-2.34)	0.9153
Fluoroquinolones	0.89 (0.36-2.19)	0.8040
	H2A use post-admission	
Any Antibiotic[a]	0.73 (0.26-2.06)	0.5520
Fluoroquinolones	0.74 (0.26-2.12)	0.5818

[a] Excluding vancomycin and metronidazole

Jayatilaka S. Clostridium difficile infection in an urban medical center: Five-year analysis of infection Rates among adult admissions and association with the use of proton pump inhibitors.
Ann Clin Lab Sci 2007; 37: 241

Welche Prophylaxe?

		Clostridien –Colitis: Case/Control		
Medikament		**Yes**	**No**	**p**
PPI	**Yes**	**24**	**37**	
	No	**12**	**21**	**<0.001**
H2-B	**Yes**	**2**	**15**	
	No	**7**	**70**	**0.134**
Renal failure	**Yes**	**2**	**12**	
	No	**3**	**77**	**0.035**
Diabetes mellitus	**Yes**	**13**	**15**	
	No	**18**	**48**	**0.728**
Immunosuppr.	**Yes**	**7**	**21**	
	No	**13**	**53**	**0.229**
Malignancy	**Yes**	**1**	**10**	
	No	**7**	**76**	**0.629**
Gastroint. Disease	**Yes**	**0**	**4**	
	No	**1**	**89**	**0.375**

Aseeri M. Gastric acid suppression by proton pump inhibitors as a risk factor for Clostridium difficile-associated diarrhea in hospitalized patients. Am J Gastroenterol 2008; 103: 2308

Welche Prophylaxe?

	Sucralfat	Antacida	H2-Blocker	Esomeprazol	Lansoprazol	Omeprazol	Pantoprazol	Rabeprazol
Magen-pH↑		+	+	+++	+++	+++	+++	+++
Tolerabilität	+	+	+	+++	+++	+++	+++	+++
Bei MOF							+	
↓ Interaktionen							+	
Verabreichung								
Oral				+	+	+	+	+
i.v.			+	+		+	+	
n.g.	+	+		+	+	+		

Brett S. Science review: The use of proton pump inhibitors for gastric acid supression in critical illness. Crit Care 2005; 9: 45

Welche Prophylaxe?

CLINICAL RESEARCH Clinical Trials

Influence of Omeprazole on the Antiplatelet Action of Clopidogrel Associated With Aspirin

The Randomized, Double-Blind OCLA (Omeprazole CLopidogrel Aspirin) Study

Martine Gilard, MD,* Bertrand Arnaud, PHARMD,† Jean-Christophe Cornily, MD,* Grégoire Le Gal, MD,§ Karine Lacut, MD,‡ Geneviève Le Calvez, PHARMD,† Jacques Mansourati, MD,* Dominique Mottier, MD,§ Jean-François Abgrall, MD,† Jacques Boschat, MD*

Brest, France

JACC 2008

Welche Prophylaxe?

CLINICAL RESEARCH — Clinical Trials

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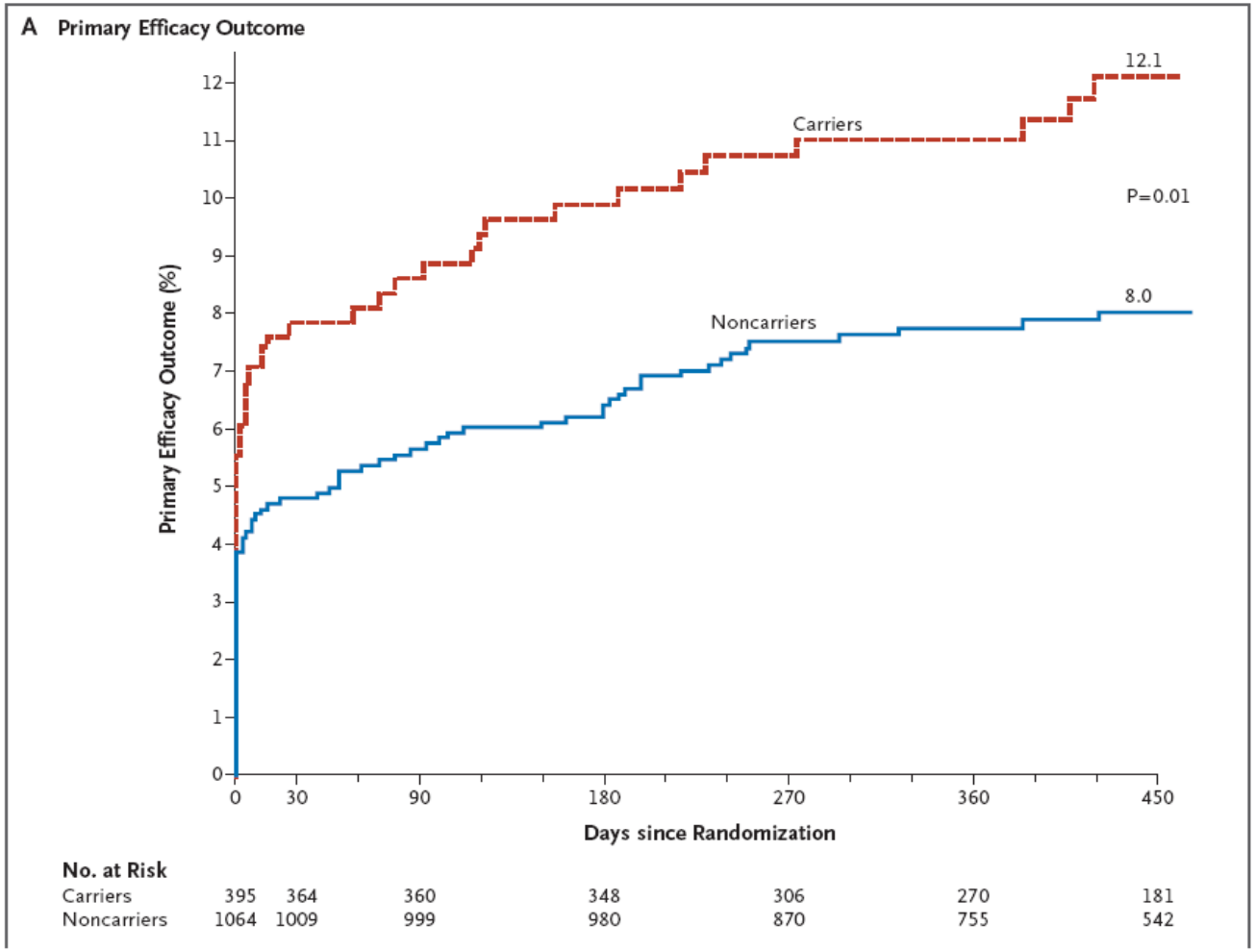
Brest, France

Risk of Adverse Outcomes Associated With Concomitant Use of Clopidogrel and Proton Pump Inhibitors Following Acute Coronary Syndrome

JAMA 2009

Welche Prophylaxe?



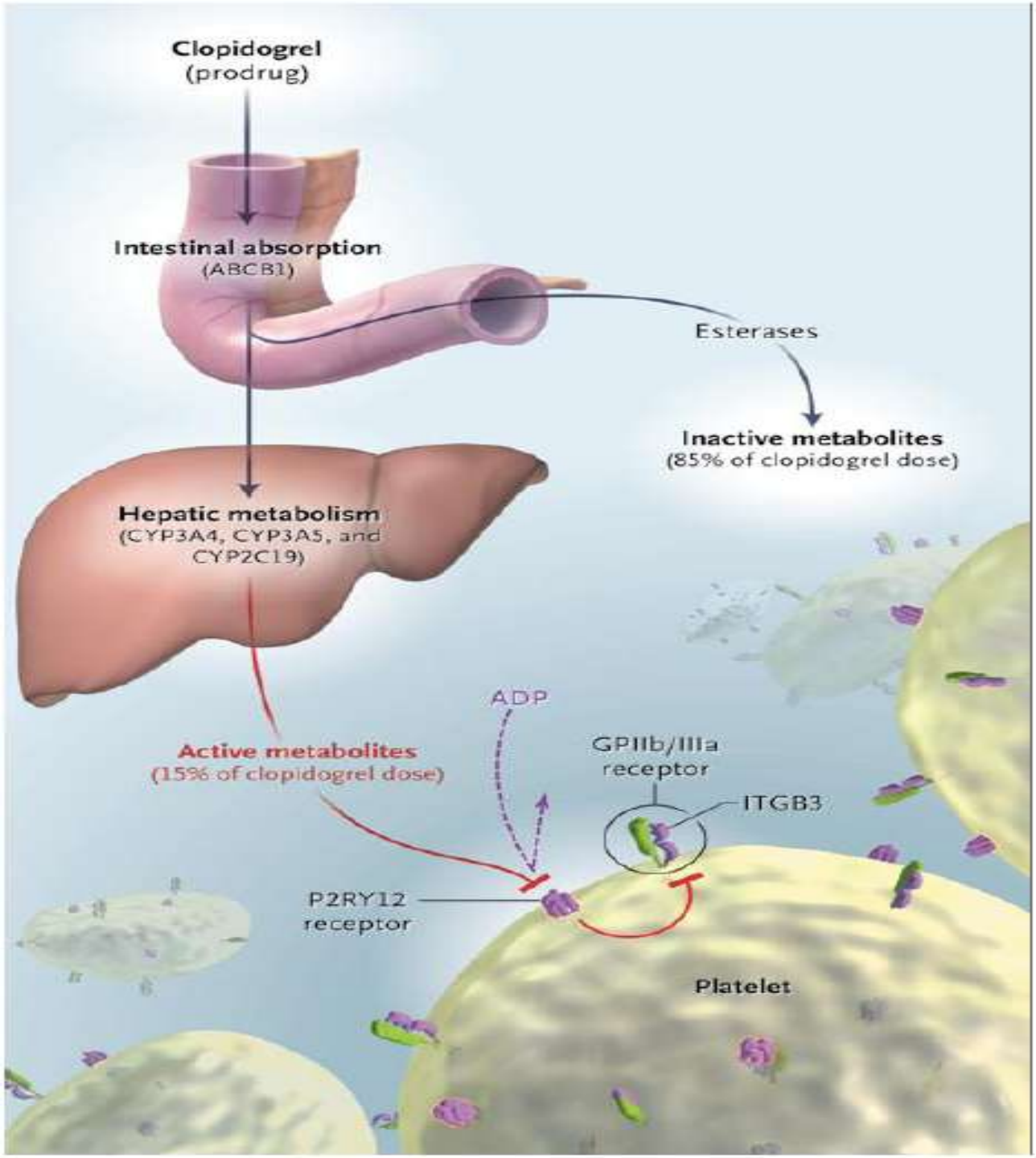
Mega J.L. Cytochrome P-450 polymorphism and response to clopidogrel. N Engl J Med 2009; 360: 354

Welche Prophylaxe?

Adverse outcomes following hospital discharge for ACS

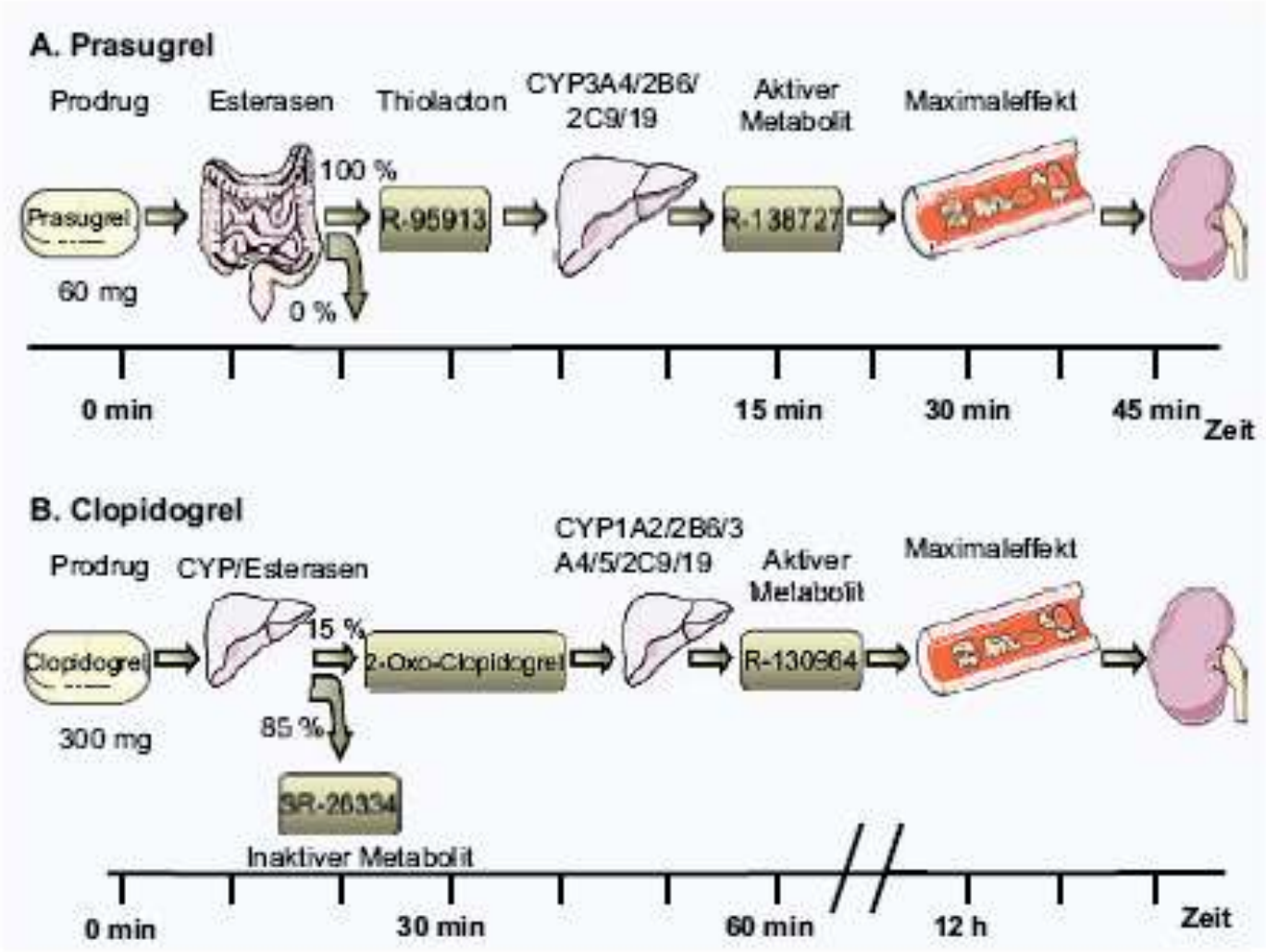
Outcome	Clopidogrel without PPI (n=2961), %	Clopidogrel with PPI (n=5244), %	Adjusted odds ratio (95% CI)
Death or rehospitalization for ACS	20.8	29.8	1.25 (1.11-1.41)
Rehospitalization for ACS	6.9	14.6	1.86 (1.57-2.20)
Revascularization procedures	11.9	15.5	1.49 (1.30-1.71)
All-cause mortality	16.6	19.9	0.91 (0.80-1.05)

Ho M.P. Risk of adverse outcomes associated with concomitant use of clopidogrel and Proton pump inhibitors following acute coronary syndrome. JAMA 2009; 301: 937

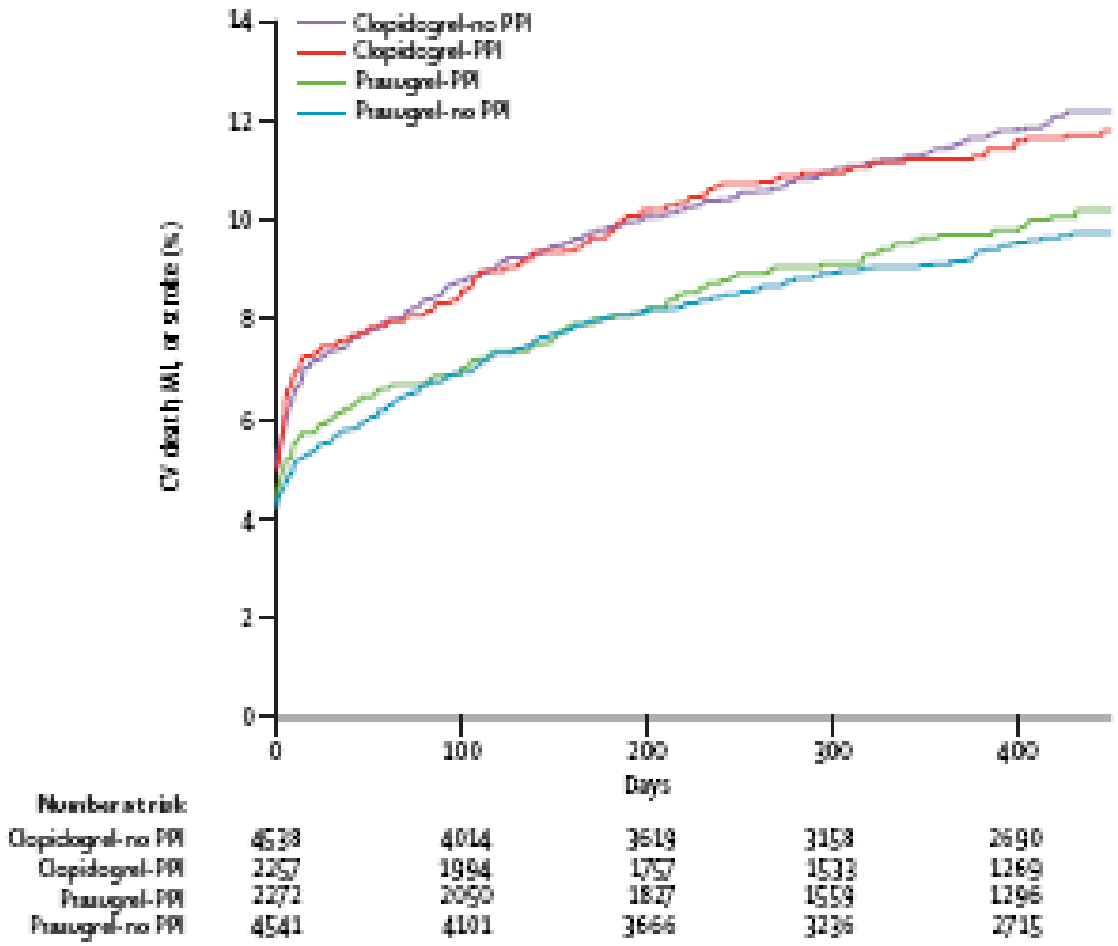


Tabassome S. Genetic determinants Of response to Clopidogrel and Cardiovascular events. N Engl J Med 2009; 360: 363

Welche Prophylaxe?



Welche Prophylaxe?



O'Donoghue M. Pharmacodynamic effects and clinical efficacy of clopidogrel and prasugrel with or without a proton-pump inhibitor: An analysis of two randomised trials. Lancet 2009; 374: 989

Welche Prophylaxe?

Table 2: Association between exposure to proton pump inhibitors and recurrent myocardial infarction among patients who started taking clopidogrel following index myocardial infarction

Exposure to proton pump inhibitor	Group; no. (%) of patients		Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
	Cases *n = 734*	Controls *n = 2057*		
None	448 (61.0)	1317 (64.0)	1.00	1.00
Current (< 30 days)	194 (26.4)	424 (20.6)	1.32 (1.08–1.62)	1.27 (1.03–1.57)
Pantoprazole	46 (6.3)	125 (6.1)	1.06 (0.74–1.52)	1.02 (0.70–1.47)
Other	148 (20.2)	299 (14.5)	1.43 (1.14–1.80)	1.40 (1.10–1.77)
Previous (31–90 days)	63 (8.6)	195 (9.5)	0.94 (0.70–1.28)	0.86 (0.63–1.19)
Pantoprazole	16 (2.2)	39 (1.9)	1.13 (0.62–2.06)	0.89 (0.48–1.67)
Other	47 (6.4)	156 (7.6)	0.90 (0.64–1.27)	0.86 (0.60–1.23)
Remote (91–180 days)	17 (2.3)	68 (3.3)	0.78 (0.45–1.34)	0.81 (0.46–1.41)
Pantoprazole	6 (0.8)	10 (0.5)	1.97 (0.71–5.45)	2.09 (0.74–5.92)
Other	11 (1.5)	58 (2.8)	0.58 (0.30–1.12)	0.60 (0.31–1.17)

Note: CI = confidence interval, OR = odds ratio

Juurlink D.N. A population-based study of the drug interaction between proton pump Inhibitors and clopidogrel. CMAJ 2009; 180: 713

Welche Prophylaxe?

Comparison of Intravenous Pantoprazole and Famotidine for Stress Ulcer Prophylaxis

This study is currently recruiting participants.
Verified by Far Eastern Memorial Hospital, October 2007

First Received: February 6, 2009 No Changes Posted

Sponsor:	Far Eastern Memorial Hospital
Information provided by:	Far Eastern Memorial Hospital
ClinicalTrials.gov Identifier:	NCT00839488

Estimated Enrollment:	120
Study Start Date:	April 2008
Estimated Study Completion Date:	January 2011
Estimated Primary Completion Date:	December 2010 (Final data collection date for primary outcome measure)

Welche Prophylaxe?

• Wirksamkeit:	-↑ pH im Magen	PPI >>> H2-B > Antacida > Sucralfat
	-↓ Blutung	PPI = H2-B > Sucralfat
	-↓ Mortalität	no effect
• Komplikationen:	-nosokom. Pn.	PPI > H2-B ≥ Sucralfat
	-Clostridien-Colitis	PPI > H2-B
	-adv. Events	H2-B > PPI > Sucralfat
• Interaktionen:	-pharmakodynam .	H2-B > PPI
	-phamakokinet.	Sucralfat > PPI

Wer braucht eine Prophylaxe?

prospective observational. n = 2252 (multivariate logistic regression)

Risk Factor	OR	P
Respiratory failure (MV >48h)	15.6	<0.001
Coagulopathy	4.3	<0.001
Hypotension	3.7	0.08
Sepsis	2.0	0.17
Hepatic Failure	1.6	0.27
Renal Failure	1.6	0.26
Enteral feeding	1.0	0.99
Glucocorticoids	1.5	0.26

n tot = 816
bleed. 31(3.8%)
+ proph. = 369
bleed. 22 (5.9%)
-proph. = 447
bleed. 9 (2.0%)

n = 1403
bleed. 2 (0.1%)
+ proph. = 283
bleed. 1 (0.4%)
-proph. = 1121
bleed. 1 (0.1%)

Cook DJ. Risk factors for gastrointestinal bleeding in critically ill patients. N Engl J Med 1994; 330: 377-381

Wer braucht eine Prophylaxe?

Was wissen wir bis jetzt?

-nur zwei signifikante Risikofaktoren

-Blutungen sind immer seltener

-Stress Ulkus-Prophylaxe ↓ Blutungen um 50%

-Stress Ulkus-Prophylaxe red. Mortalität nicht

-Blutende Patienten haben aber eine ↑ Mortalität

-H2-Antagonisten reduzieren Blutungen besser

-H2-Antagonisten ↑ die VAP-Rate evt. (minimal)

-Protonenpumpenhemmer sind gleich wirksam wie H2-Antagonisten

Wer braucht eine Prophylaxe?

We recommend that stress ulcer prophylaxis using H2 blocker (grade 1A) or proton pump inhibitor (grade 1B) be given to patients with severe sepsis to prevent upper gastrointestinal (GI) bleed. The benefit of prevention of upper GI bleed must be weighed against the potential effect of an increased stomach pH on development of ventilator-associated pneumonia.

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008
Crit Care Med 2008; 36: 296-327

Wer braucht eine Prophylaxe?

Beatmung > 48 h & 1 od. mehrere Punkte

-Gerinnungsstörung

-hämodynamische Instabilität

-Niereninsuffizienz

-fehlende enterale Ernährung

od. frühere obere GIB

Prophylaxe stoppen sobald keine RF mehr

Pantoprazole

Wer braucht (k)eine Prophylaxe?

Hospital-acquired gastrointestinal bleeding outside the critical care unit: risk factors, role of acid suppression, and endoscopy findings.

Of 17,707 patients admitted to the General Medicine ward over a 4-year period, 73 (0.41%) met the case definition.

The main risk factor for nosocomial GIB was treatment with full dose anticoagulants or clopidogrel (OR = 5.4; 2.6-11.7; P < .0001).

Use of aspirin, nonsteroidal anti-inflammatory medications, and glucocorticoids did not differ significantly between cases and controls.

De novo acid-suppressive prophylaxis was not protective (OR = 1.0; 95% CI: 0.4-2.4; P = 0.97).

Routine use of acid suppressant medications for prophylaxis is unnecessary in most hospitalized patients.

Quadeer MA. Hospital acquired gastrointestinal bleeding outside the critical care unit: risk factors, role of acid supression,and endoscopy findings. J Hosp Med 2006; 1: 13-20

"Say ... what's a mountain goat doing
way up here in a cloud bank?"