Surgical Antibiotic Prophylaxis Utility

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Prophylactic Antibiotics
Questions

- **Which cases benefit?**
- **Which drug should you use?**
- **When should you start?**
- **How much should you give?**
- **How long should antibiotics be continued?**

Relative Benefit from Antibiotic Surgical Prophylaxis

Operation	Prophylaxis (%)	Placebo (%)	NNT*
Colon	4-12	24-48	3-5
Other (mixed) GI	4-6	15-29	4-9
Vascular	1- 4	7-17	10-17
Cardiac	3-9	44-49	2-3
Hysterectomy	1-16	18-38	3-6
Craniotomy	0.5-3	4-12	9-29
Spinal operation	2.2	5.9	27
Total joint repl	0.5-1	2-9	12-100
Brst & hernia ops	3.5	5.2	58

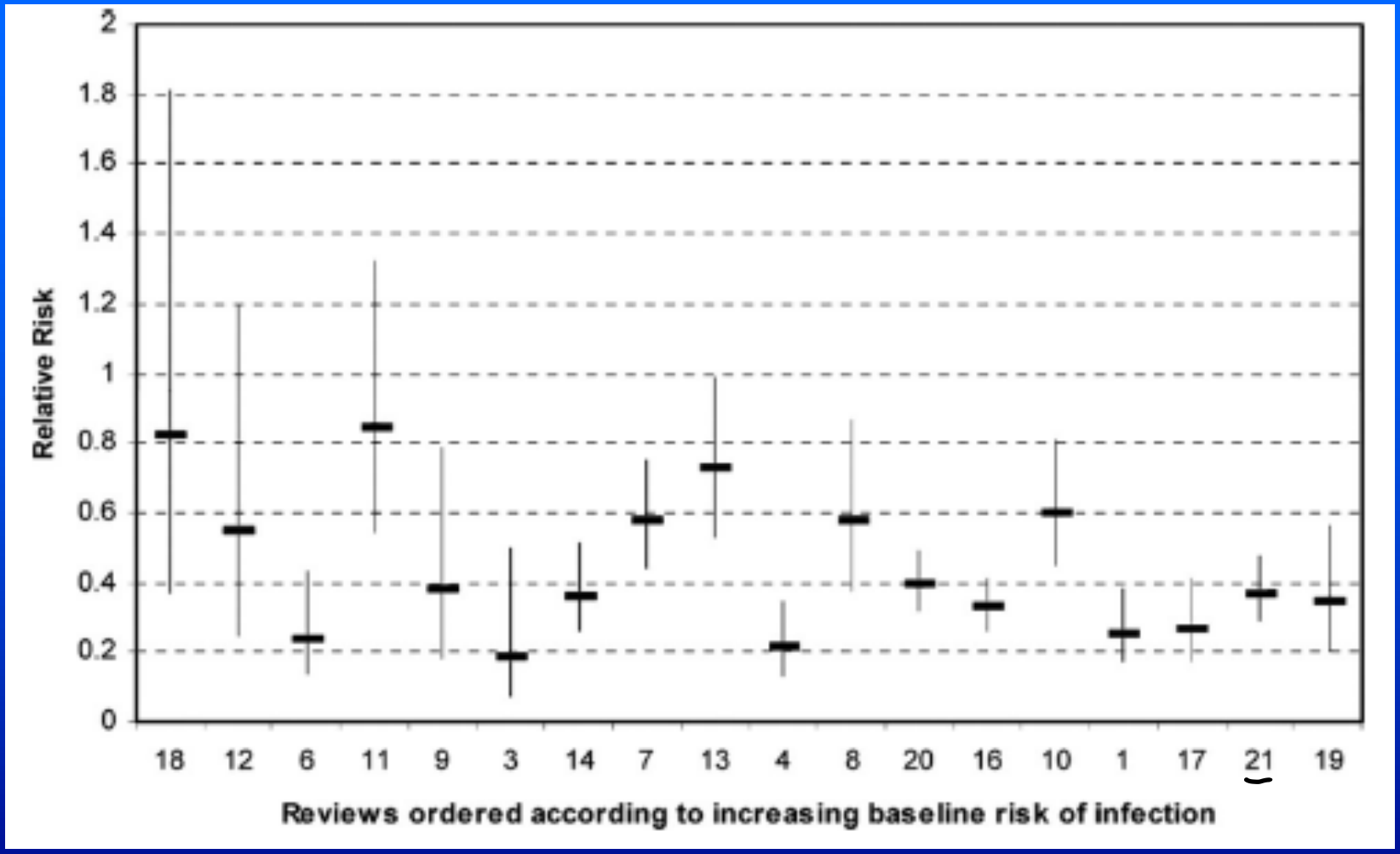
% Reduction extreme range: 12 – 90%

Antibiotic Prophylaxis
Demonstrated Benefit: All Procedures??

- **Review of prophylaxis meta-analyses suggests that there is a consistent relative risk of wound infection less than one (20-80%) associated with antibiotic prophylaxis.**
- **This is independent of the type of operation or the baseline (placebo) rate of infection.**

Bowater. *Ann Surg 2009;249: 551–556*

Relative Effect of Prophylactic Antibiotics arranged by Baseline Risk



Bowater. *Ann Surg 2009;249: 551–556*

Prophylaxis for Elective Inguinal Hernia Repair?

Meta-Analysis, 11 RCTs, 2790 pts

	Proph	Placebo	P
SSI	3.1%	5.3%	0.004
Odds ratio	0.59 (0.41 - 0.84)		

Tian. International Wound J 2023;20: 1191-1204

Prophylaxis for Open Inguinal or Femoral Hernia Repair?

Cochrane Review, 22 RCTs, 6443 pts

	Proph	Placebo
SSI (superficial & deep)	3.3%	5.5%
Odds ratio	0.61 (0.48 - 0.78)	

Orelio. Cochrane Syst Rev 2020; 4:Cd003769

Prophylaxis for Laparoscopic Cholecystectomy?

Meta-Analysis, 22 RCTs, 5168 pts

	Proph	Placebo
SSI	2.1%	3.1%
Odds ratio	0.71 (0.51 - 0.99)	
Overall Infections	2.3%	4.6%
Odds ratio	0.50 (0.34 – 0.75)	

Matsui. BMJ Open 2018; 8: e016666

Prophylaxis for Elective Laparoscopic Cholecystectomy?

Meta-Analysis, 14 RCTs, 4360 pts

	Proph	Placebo
SSI	1.9%	2.9%
Odds ratio	0.66 (0.45 - 0.98)	
Overall Infections	2.3%	4.0%
Odds ratio	0.57 (0.40 – 0.80)	

Yang. Surg Endoscopy 2021; 35: 6397-6412

Prophylaxis for Clean procedures?

- Relative reduction of SSI with prophylaxis is the same for all procedures (30-70%)
- Absolute reduction is less if baseline rate with placebo is less.
- Decision on whether to use depends on cost of prophylaxis ($, side effects, generating resistance) and cost of infection ($, disability, etc).

Prophylactic Antibiotics
Questions

- Which cases benefit?
- Which drug should you use?
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Surgical Antibiotic Prophylaxis

My Choices

Bacteroides expected

- Cefazolin 2 g + Metronidazole 1g, IV in OR
- Repeat cefazolin q 3 h during procedure

Bacteroides not expected

- Cefazolin 2 g, IV in OR
- Repeat q 3 h during procedure

Alternatives

Cefazolin

- Other first generation cephalosporin
- Cefuroxime, cefamandole, cefonicid
- Oxacillin, etc

Cefazolin plus metronidazole

- Ertapenem
- Aminoglycoside or quinolone plus clindamycin or metronidazole

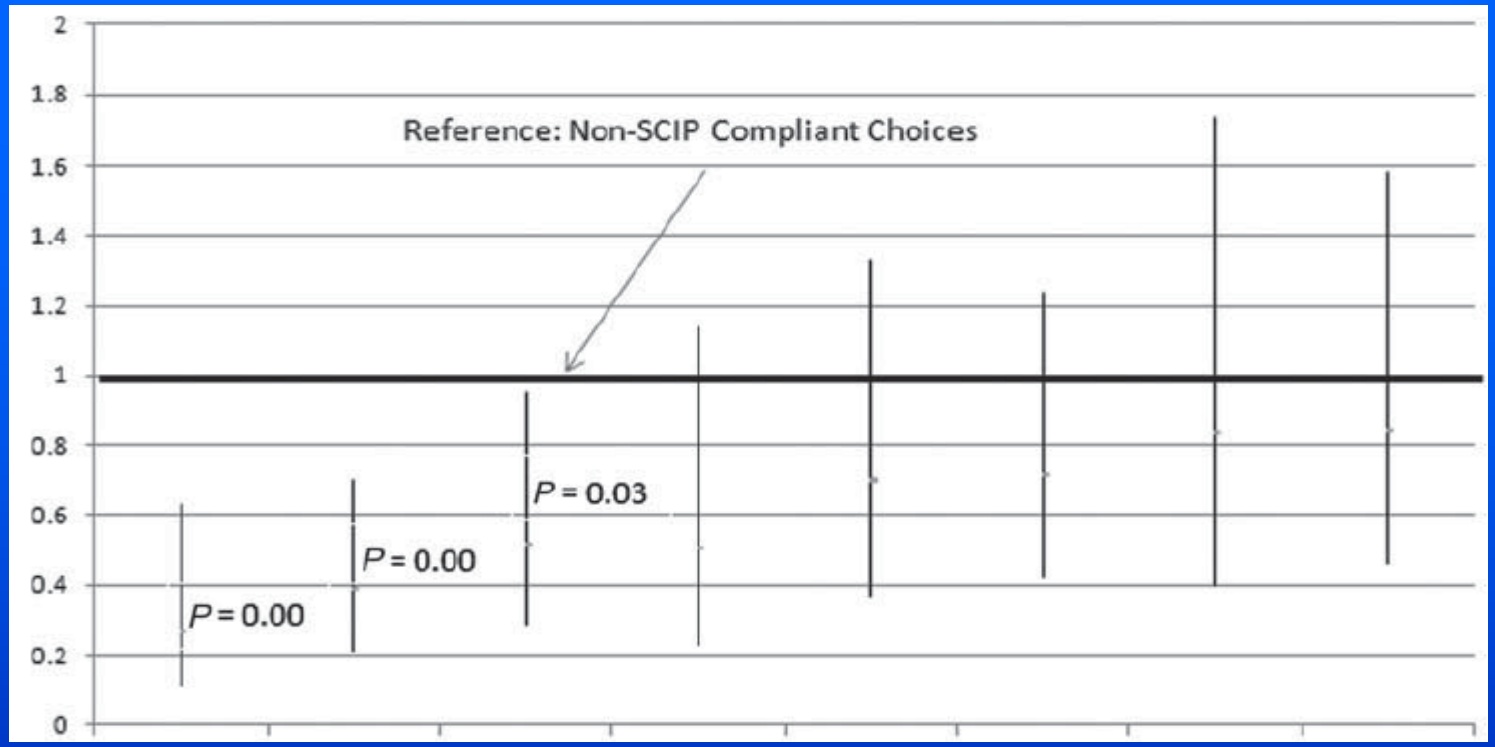
Antibiotic Choice & SSI After Colectomy - Multivariate Analysis

Premier Data Base, n = 4634

Agent	O.R.	Range
Cefoxitin	1.0	
Ertapenem	0.53	0.34 - 0.82
Cefazolin/Metron	0.58	0.33 - 1.04
Levo/Metron	0.59	0.30 - 1.14
Amp/sulbactam	0.62	0.33 - 1.15
Cefotetan	0.86	0.45 - 1.67

Eagye. Surg Infect 2011; 12: 451-7

Antibiotic Choice & SSI After Colectomy



Hendren. Ann Surg 2013;257.469

Antibiotic Choice & SSI After Open Colectomy - Multivariate Analysis

Premier Data Base, 2006-2013
445 Hospitals, 90,725 patients

Agent	O.R.	Range
Cefoxitin	1.0	
Amp/sulbactam	0.71	0.63 – 0.82
Ertapenem	0.65	0.58 - 0.71
Cefazolin/Metron	0.56	0.49 – 0.64
Other	0.56	0.49 - 0.64

48% got antibiotics after D.O.S. without benefit

Poeran. Dis Colon Rectum 2016; 59: 733-42

Cefoxitin & Cefotetan Have Been Standards for Decades for Colorectal Surgery

They are no longer effective prophylactics in this setting due to short half-life (cefoxitin) and poor anaerobic activity (both).

Targeted Prophylactic Antibiotic Choice for Specific Settings

- Local carriage rate for ESBLs for patients having colectomy
- Pancreatico-biliary operations for patient with biliary stents-Prophylaxis targeted to preop bile cultures
- Rectal swabs predict ESBL in biliary stent
- Prophylaxis targeted to flora found in prior SSIs at same institution

Targeted Prophylaxis for ESBL

- Colectomy patients screened for ESBL due to local prevalence and high SSI rate
- ESBL carriers randomized to cefuroxime/metronidazole vs. ertapenem

	Any SSI	ESBL SSI
Cef/metron	56/247 (22.7%)	16/247 (6.5%)
Ertapenem	35/221 (15.8%)	2/221 (0.9%)

Nutman. Clin Inf Dis 2020; 70: 1891-91

Targeted Prophylaxis for Flora of Preoperative Bile Culture

HepatoPancreaticoBiliary surgical patients with biliary stents had PreOp bile cultures

Pts randomized to "standard" proph (cefmetazole) or targeted proph based on cultures

	Any SSI
Cefmetazole	44/62 (71%)
Targeted	27/62 (44%)
	p=0.002

Okamura. J Hepatobiliary Pancreat Sci 2017; 24: 382-93

Targeted Prophylaxis for Bile Flora Based on Rectal Cultures

Pancreatectomy patients screened preoperatively with rectal swab looking for ESBL, carbapenemase producers, and VRE

Intraoperative bile cultures obtained in 181 pts

In 157 patients (87%) positive and negative results from rectal swabs and intraoperative bile cultures were consistent

De Pastena. HPB 2018; 20: 555-62

Patients With Prior History of Postoperative Infection

- Should our preoperative history ask about any prior postoperative infections?
- Should we look for prior infections and target prophylaxis according to prior pathogens?

Patients With Prior History of Postoperative Infection

First Op

758 Pts	114 (15%) with infection

Second Op (mean 366 days later)

No prior inf (644)	61 (9.5%) with infection
Prior inf (114):	26 (22.8%) with infection
	50% resistant to proph

Feldt. J Amer Coll Surg 2022; 235: 285-92

Targeted Prophylaxis for Flora of Prior SSIs at Hospital

Pathogens in SSI and Susceptibilities for 58 HepatoPancreaticoBiliary surgical patients identified

Prophylaxis for next 58 patients targeted to these data

	Any SSI
Early Group	27/58 (47%)
Targeted Group	14/58 (24%)
	p=0.012

Kondo. J Hepatobiliary Panc Sci 2013; 20: 286-93

Prophylactic Antibiotics Questions

Which cases benefit?

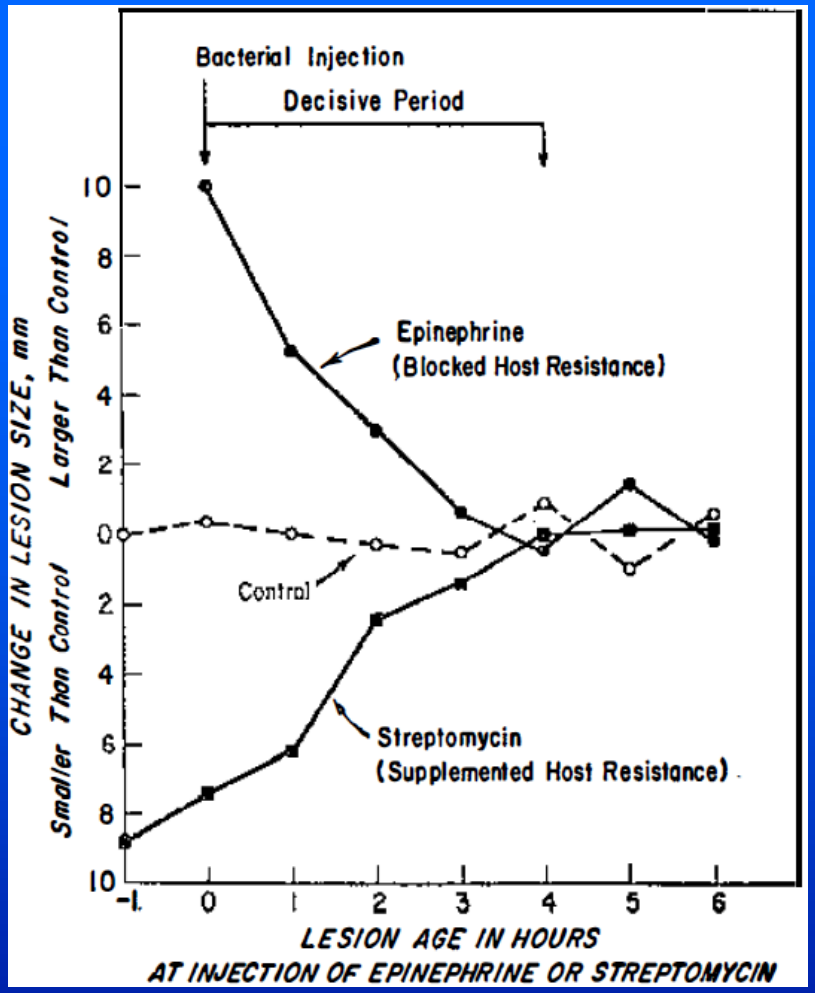
Which drug should you use?

When should you start?

How much should you give?

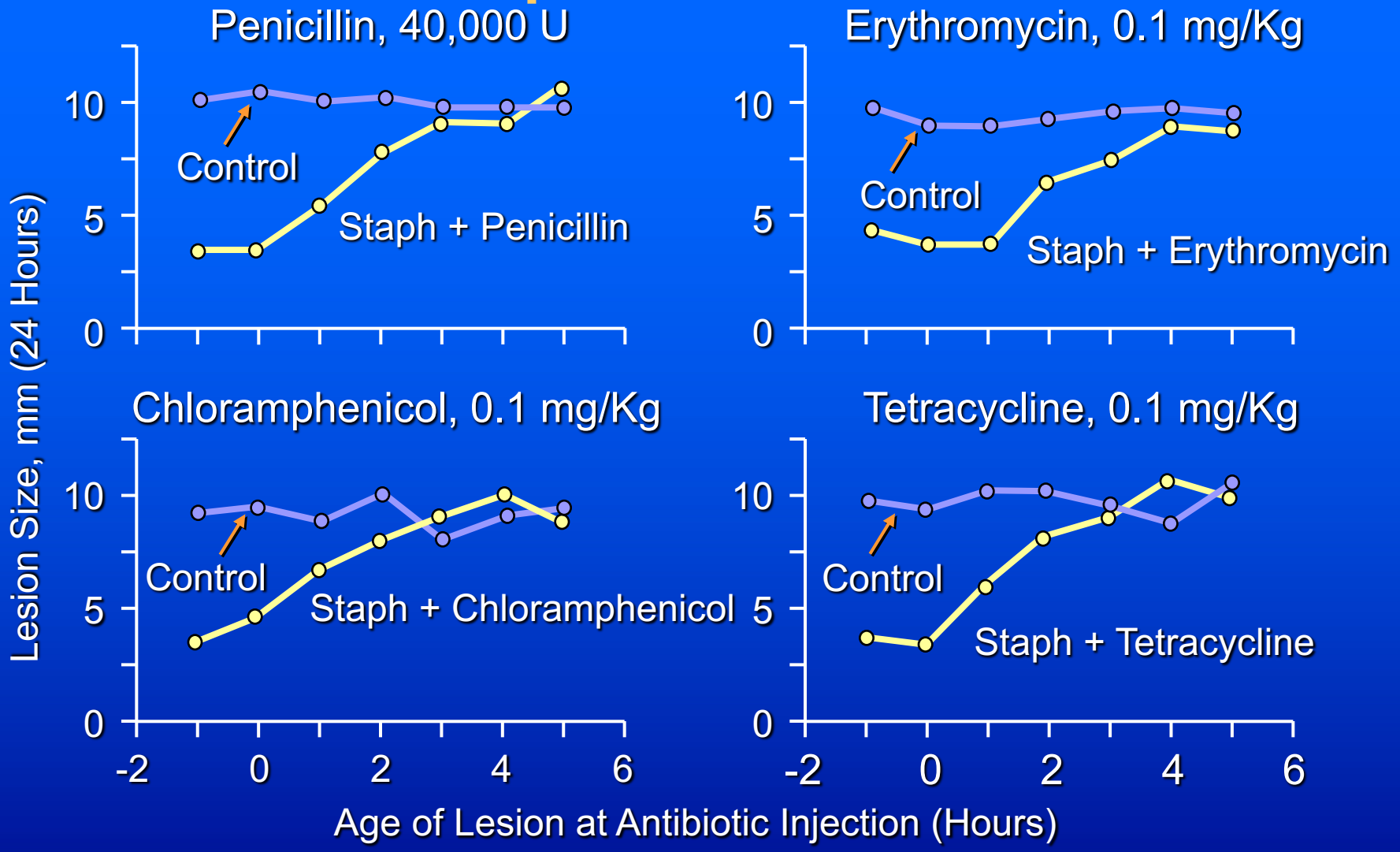
How long should antibiotics be continued?

Decisive Period For Development Of Wound Infection



Burke. Annual Rev Med 1973; 24: 289-94

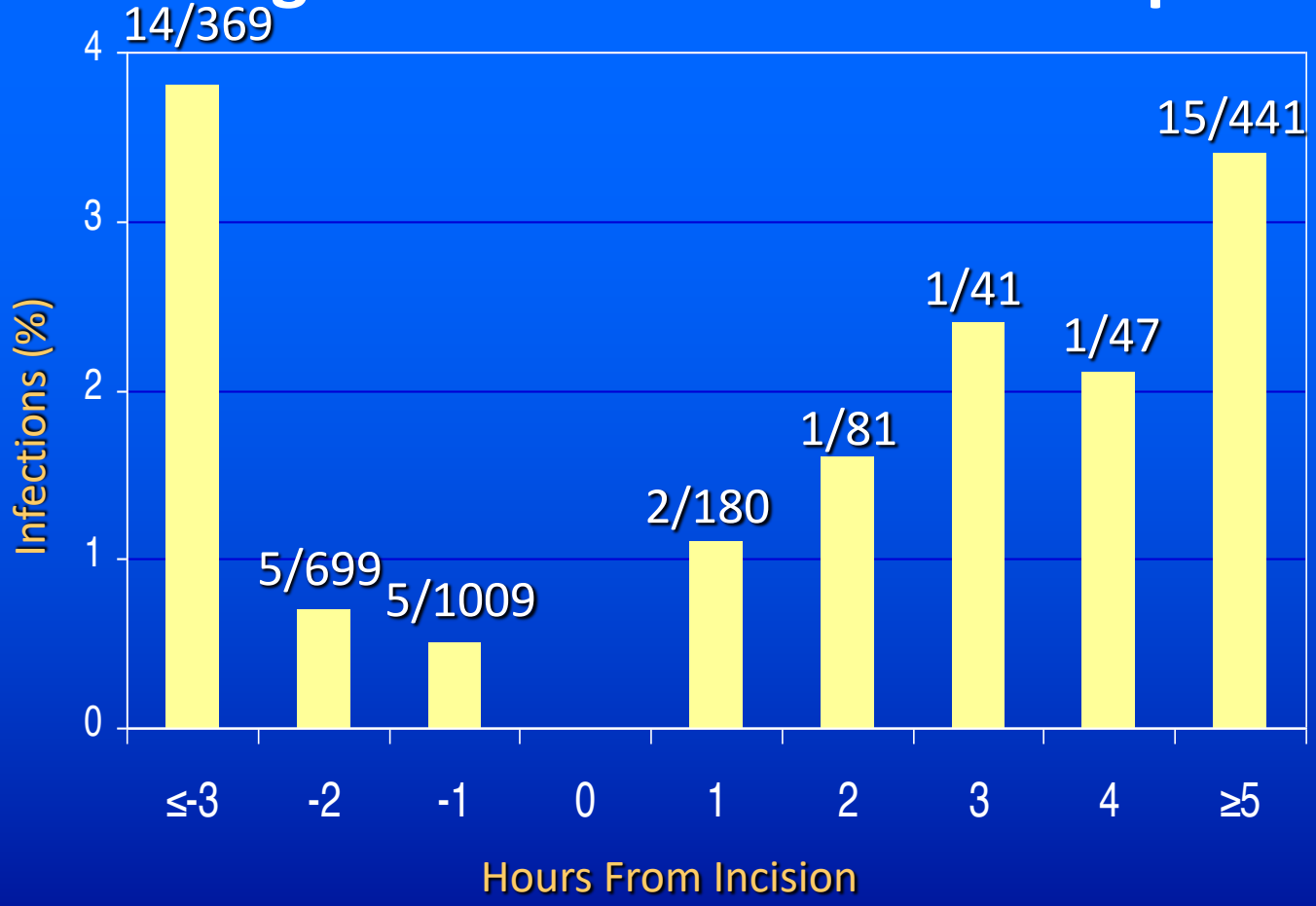
Efficacy Of Prophylaxis Is Independent Of The Specific Antibiotic



Burke JF. Surgery. 1961;50:161.

Perioperative Prophylactic Antibiotics

Timing of Administration – 2867 patients



Classen. NEJM. 1992;328:281.

Prophylactic Antibiotics
Timing - Cefazolin

	Serum Levels (mg/L)	
	On Call	Anesth
Incision	87	148
1 hour	37	57
2 hours	25	39

DiPiro. Arch Surg 1985;120:829

Prophylactic Antibiotics Timing – Cefazolin

	Muscle Levels	
	On Call	Anesth
Incision	9	17
Wound closure	7	11
No Drug Dectectable	38%	14%

DiPiro JT et al. Arch Surg. 1985;120:829-832.

Prophylactic Antibiotics
Administration in the O.R.
Drugs Given I.V. Push over 5-10 Min

Cefazolin

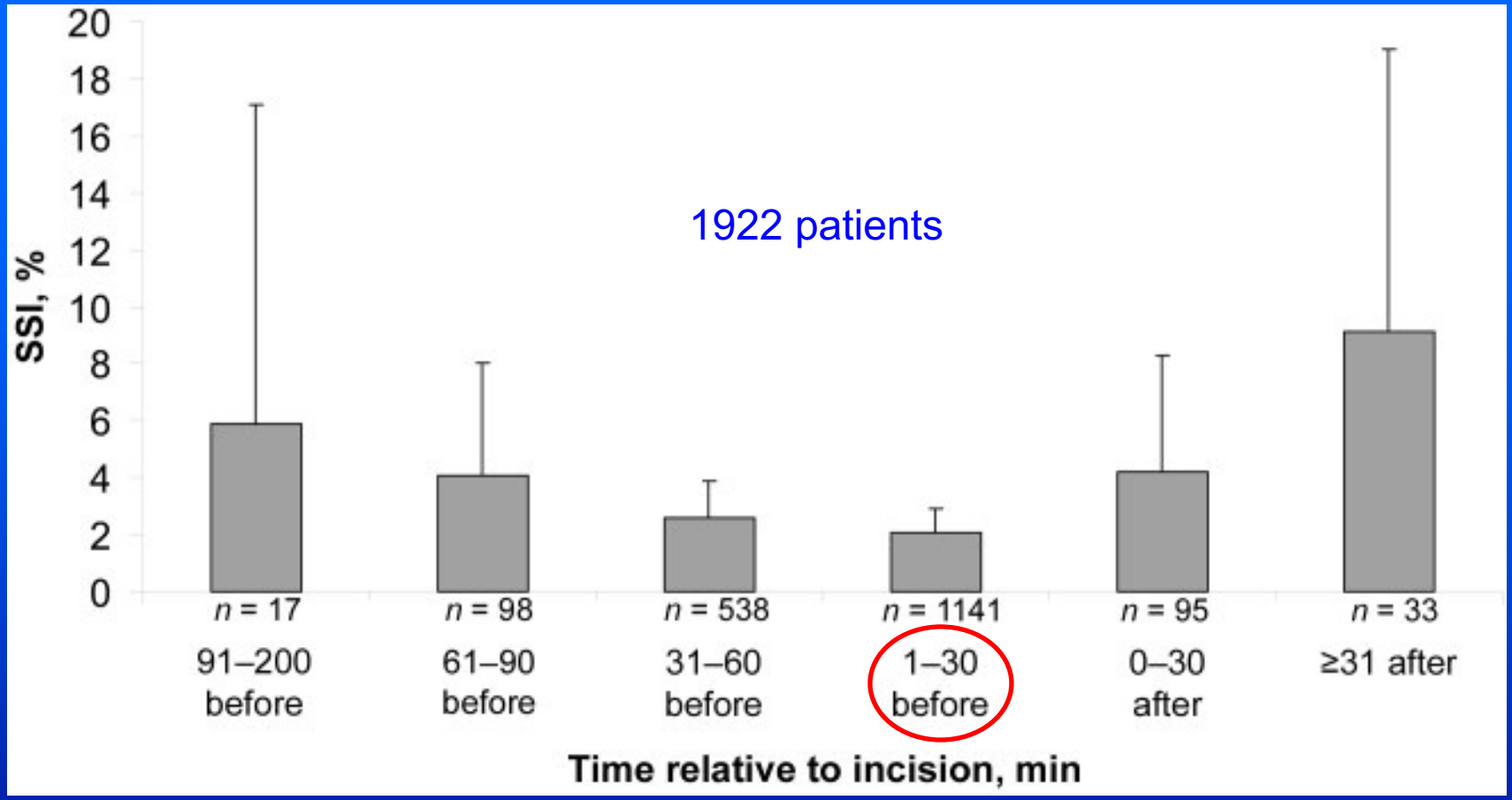
Drug to incision	17 (7-29)	min
Muscle levels	76 (9-245)	mg/kg

Cefoxitin

Drug to incision	22 (14-27)	min
Muscle levels	24 (13-45)	mg/kg

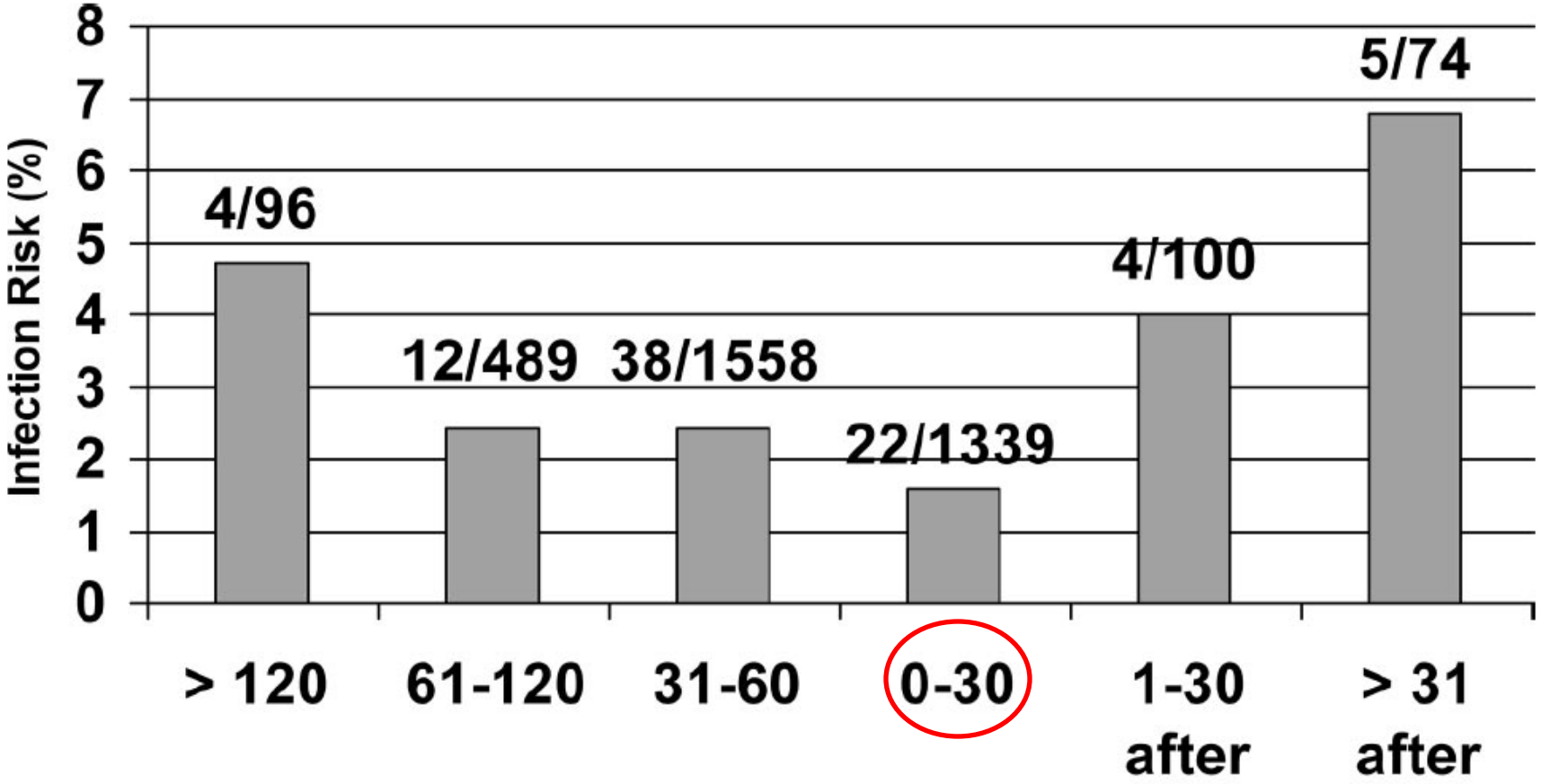
DiPiro. Arch Surg 1985;120:829
DiPiro. Personal Communication

Timing of Prophylactic Antibiotic Administration for Total Hip Arthroplasty



van Kasteren. Clin Infect Dis 2007; 44:921

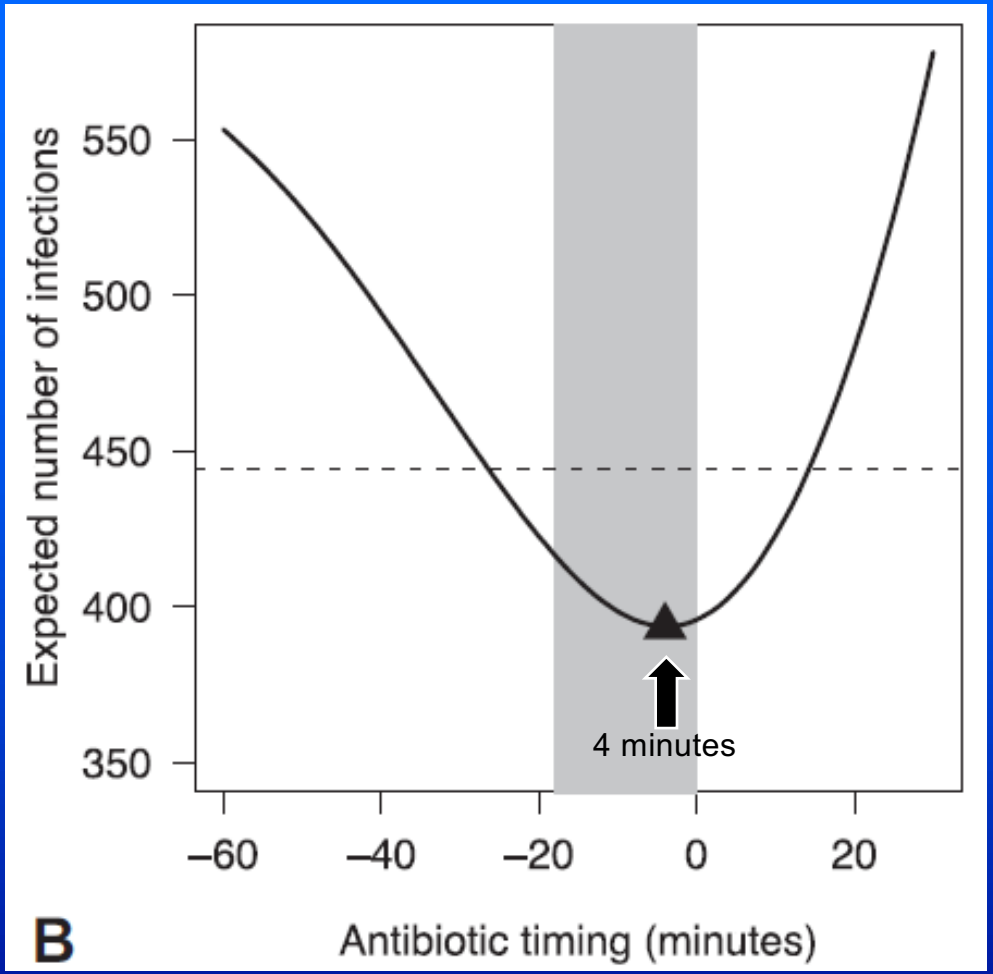
Timing of Prophylactic Antibiotic Administration – Cardiac, Arthroplasty, Hysterectomy – 3656 patients



Steinberg. TRAPE. Ann Surg 2009; 250:10

Timing of Prophylactic Antibiotic Administration and Risk of SSI – General Surgery Cases

4,453 patients



Observed=444

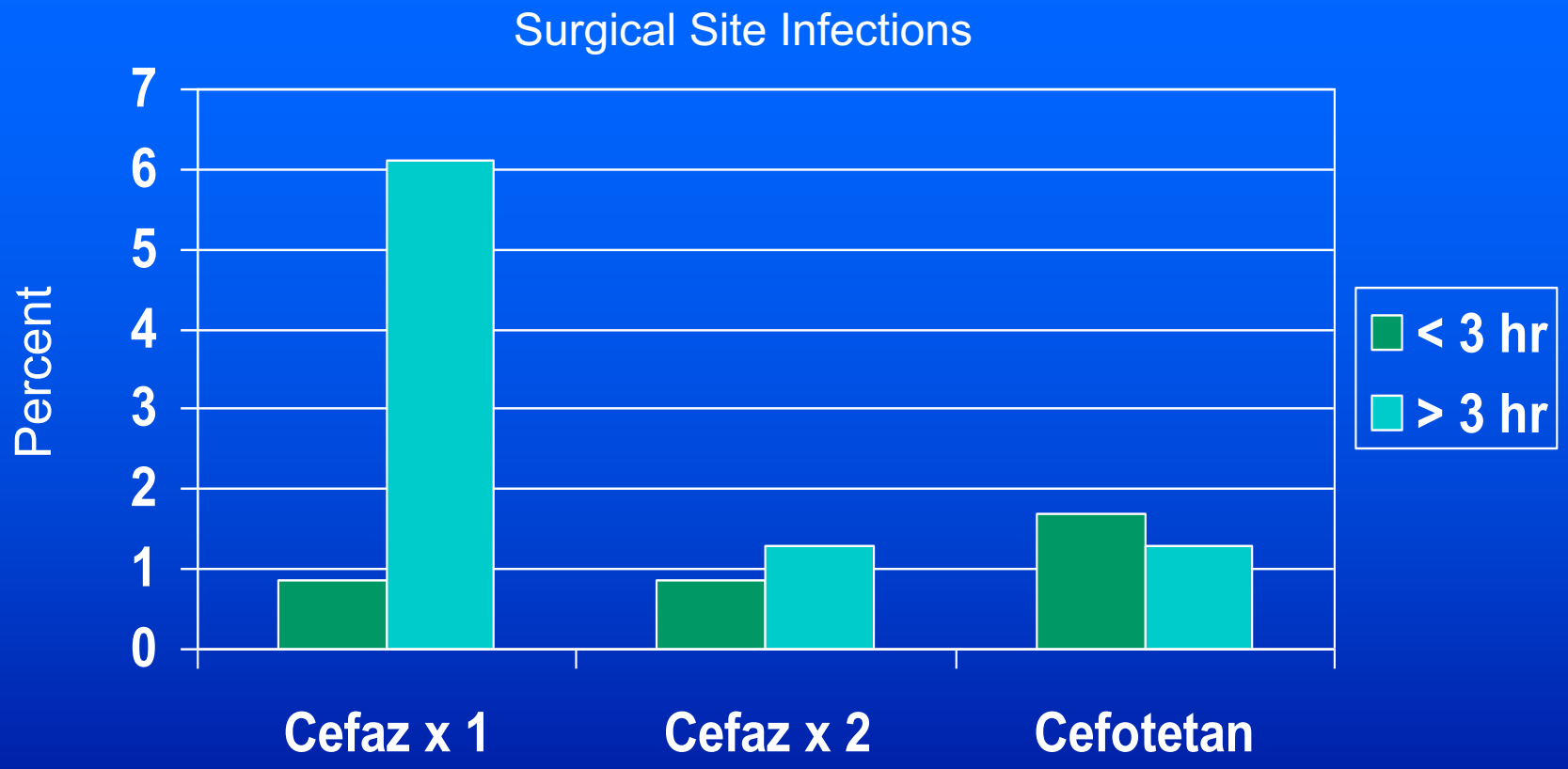
Koch.JACS 2013; 217: 628-35

Timing, Dose, Redose, Weight

All the evidence suggests that having effective drug levels in tissue and blood (more is better) during the entire operation reduces SSI risk.

Dosing close to incision, redosing, and using weight based dosing are logical ways to accomplish this.

Repeat Antibiotic Prophylaxis Doses in Gastrointestinal Procedures



Scher. American Surgeon 1997;63:59

UW Redose Paper

Observational Study – n = 3981

Mix of clean, clean-contam, contam, & dirty cases

2396 did not need redose, SSI=3.2%

1565 needed and were redosed, SSI=6.1%

20 needed but did not get redose, SSI=12.5%

Multivariate analysis – No redose when indicated, SSI odds ratio = 4.61 (1.33-15-91)
p=0.016

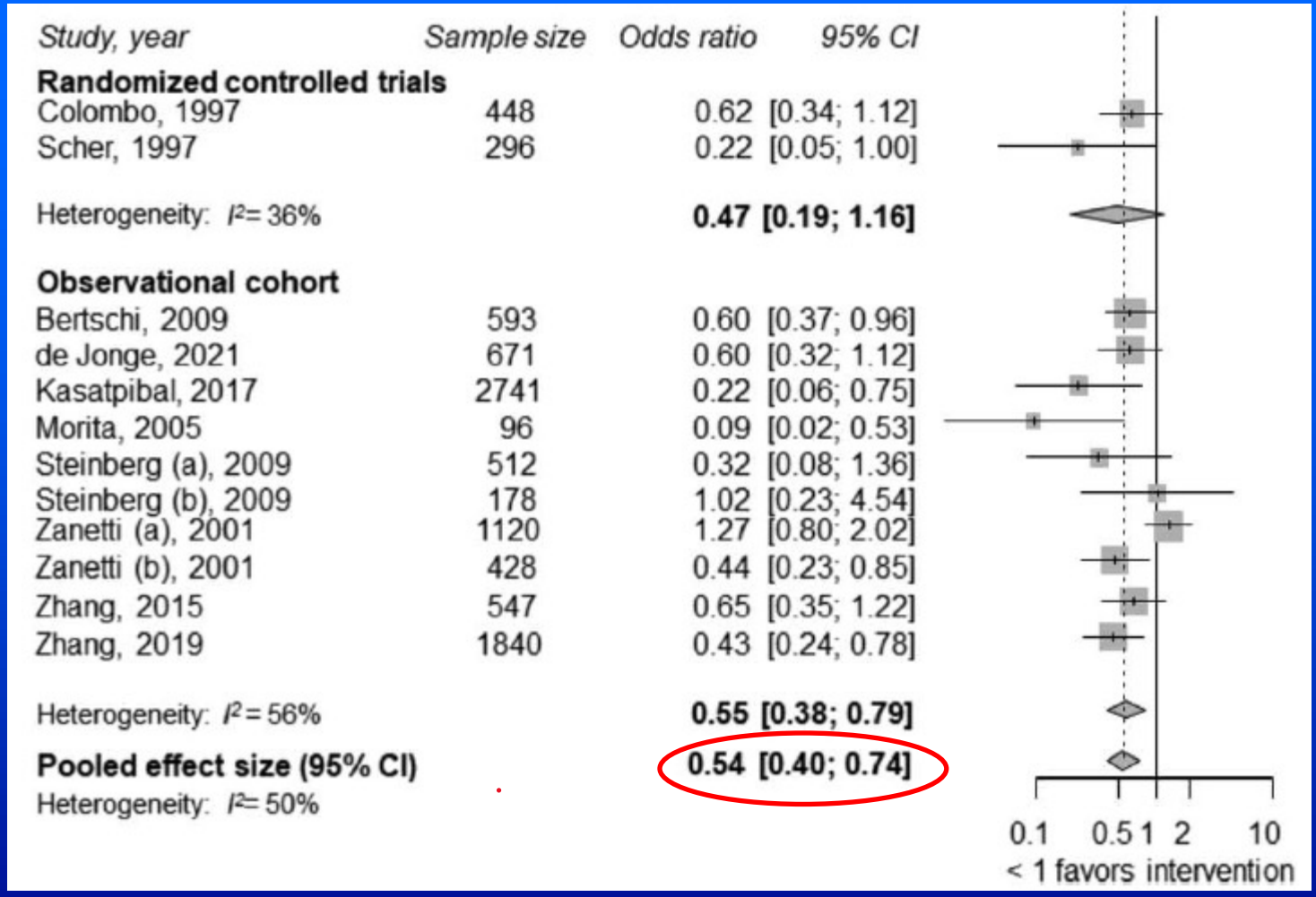
Kasatpibal. Surg Infect 2017; 18: 474-84

IntraOp Redosing vs.Single Dose Prophylaxis – 12 Studies

744

8726

9470



Wolfhagen. MetaAnalysis. Ann Surg 2022; 275:1050-7

Prophylactic Antibiotics
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Cardiac Surgery Prophylaxis
Effect of Serum Levels

Serum Level at Wound Closure	Infection
None	3/11
Present	2/175

P = .002

Goldmann. *J Thorac Cardiovasc Surg.* 1977;73:470-479.

Cardiac Surgery Prophylaxis
Effect of Atrial Appendage Levels

Infected	Cephalothin (mg/l)
Yes	6
No	13

$P = .02$

Platt. *Ann Intern Med.* 1984;101:770-774.

Prophylactic Antibiotics
Size of Patient and Size of Dose

- Morbidly obese patients having bariatric operation with a high infection rate
- Cefazolin levels lower than in non-obese patients at same dose
- Cefazolin dose changed from 1 g to 2 g

Infection rate at 1g:	16.5%
Infection rate at 2g:	5.6%

Forse RA. Surgery 1989;106:750

Gentamicin Levels and SSI Risk for Colectomy

	Closing Gent level (mg/L)	D.M. (%)	Stoma (%)	Age
SSI	1.3±1.0	29	50	59±14
No SSI	2.1±0.9	2	24	55±19
p	0.02	0.02	0.04	0.05

Gent level < 0.5 at close had 80% SSI rate (p=0.003).

Zelenitsky. Antimicrob Ag Chemother 2002;46:3026-30

Dose of Antibiotic for Prophylaxis

- Always give at least a full therapeutic dose of antibiotic.
- Consider the upper range of doses for large patients and/or long operations.
- Repeat doses for long operations.

New ASHP / IDSA / SHEA / SIS Antibiotic Prophylaxis Guidelines

Cefazolin	> 80 kg	2 g
	≥ 120 kg	3 g
Vancomycin		15 mg/kg
Gentamicin		5 mg/kg

dosing wgt = ideal wgt + 40% of excess wgt

Bratzler. Surgical Infections2013;14:73-156

Prophylactic Antibiotics

1. Risk is reduced for all procedures. Benefit depends on baseline risk and morbidity of SSI
2. Choose a drug that is effective against bugs that show up in SSI for that procedure
3. If you're going to give some, give a lot
4. Give it very shortly before the procedure
5. Repeat for long cases (2 half-lives)
6. Stop when the operation is over