

# What is the most appropriate antibiotic duration for treatment of intra-abdominal infections?

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# Reviews

- Mazuski J et al, *Surgical Infections* 2002
- Solomkin JS et al, *Clinical Infectious Diseases* 2003

# Defining the population

# Established infections

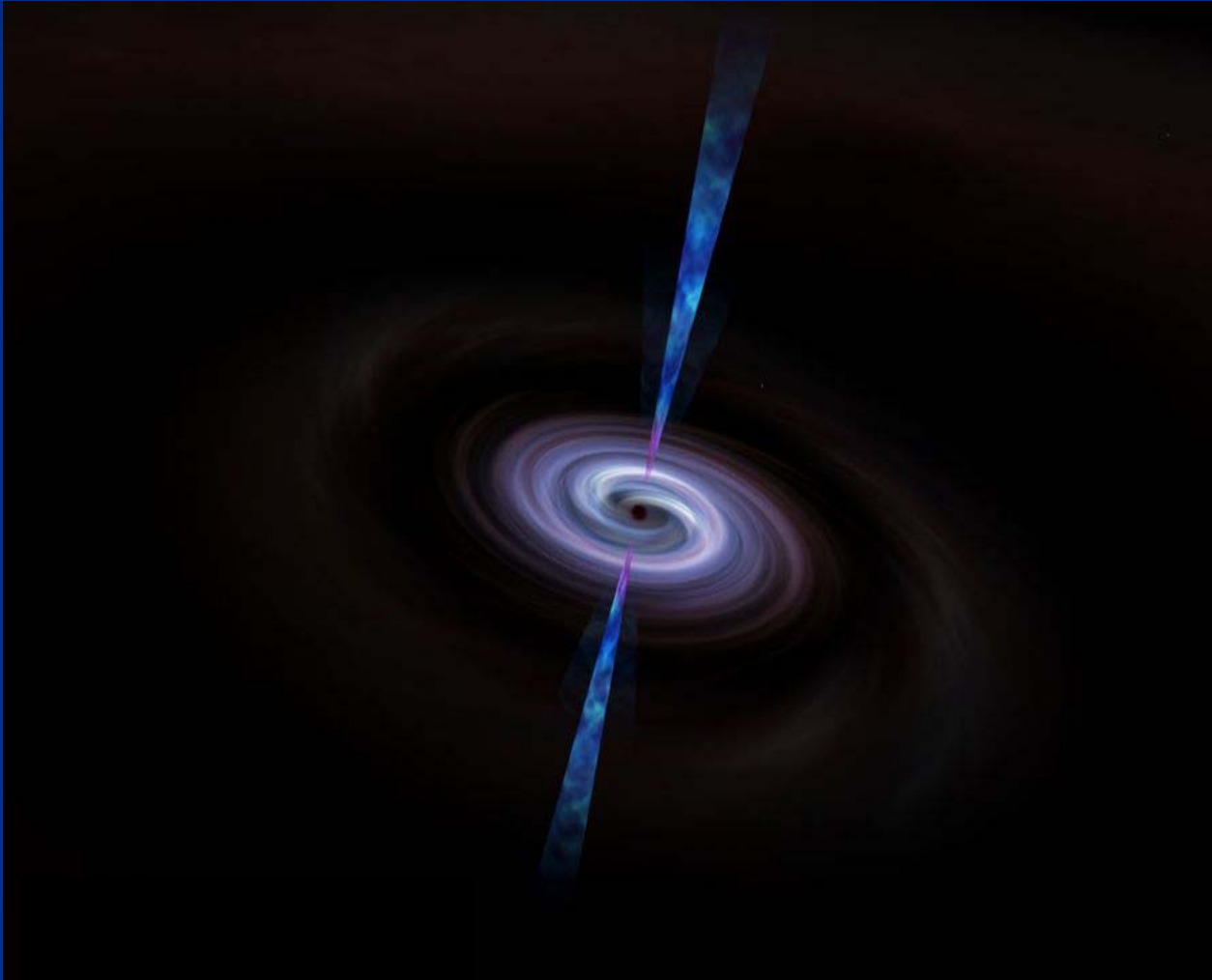
- Excludes diseases where brief contamination has occurred and treatment with antibiotic therapy  $\leq 24$  hours is adequate
  - Peptic gastroduodenal perforations or traumatic bowel injuries  $< 12$  hours old
  - Any intra-operative contamination
  - Phlegmonous/ gangrenous appendicitis or cholecystitis without perforation
  - Resection of necrotic, non-perforated bowel

# Established infections

- A very broad range of conditions, ranging from a peri-appendiceal abscess to infected pancreatic necrosis
- 2 common determinants of duration of antibiotics
  - Until clinical status improves or normalizes
  - Fixed duration decided upon at initiation of treatment

No prospective studies  
specifically of duration of  
therapy for a broad  
range of infections

# Class I evidence (“definitive”)



# Why so little data?

- Heterogeneity of patient populations makes the study complicated (and daunting)
- Need for large numbers
- Who would pay for it?

# Class II evidence (hints)

- Lennard 1980 Arch Surg
- 31 patients treated for intra-abdominal infection who were afebrile at the time of cessation of antibiotic therapy
- 12 had normal WBC, 19 elevated WBC when antibiotics stopped
- Infectious complication rates were 8% and 68%, respectively

# Class II evidence (hints)

- Lennard 1982 Ann Surg
- 51 patients with intra-abdominal infection
- 13% infection rate if normal WBC at cessation of antibiotics, 43% if WBC elevated
- 79% of 14 patients who were febrile ( $T > 37.6^{\circ} \text{C}$ ) at the cessation of antibiotics developed infectious complications

# Class II evidence (hints)

- Smith 1985 J Hosp Infect
- 23 patients with peritonitis from non-appendiceal source assigned to a minimum of four days of antibiotics
- Antibiotics stopped when 3 major criteria and 2 of 4 minor criteria achieved
- Reduced doses from 28 to 21 with similar wound infection rate (30%) compared to historic controls

# Class II evidence (hints)

- Andaker 1987 Acta Chir Scand
- 99 patients with intestinal perforation
- All assigned to 5 days of post-operative antibiotics
- Overall infectious complication rate was 8%
- Comparable to historical studies using longer durations

# Class II evidence (hints)

- Schein 1994 Br J Surg
- Etiology based treatment protocol
- 48 patients with localized infection or > 12 hour old peptic perforation or traumatic injury treated for 48 hours
- 23 patients with diffuse established purulent peritonitis treated for 3 to 5 days

# Class II evidence (hints)

- Schein 1994 Br J Surg (continued)
- 12% infectious complication in the group receiving 48 hours of antibiotics
- 22% infectious complication in the group receiving 3 to 5 days of antibiotics
- Outcomes similar to reported series using 5 to 10 days or more of treatment

# Class II evidence (hints)

- Visser 1998 Eur J Surg
- 58 patients with intra-abdominal infection managed with an open technique
- Scoring system to predict the recurrence of peritonitis relied on fever, leukocytosis, etiology of infection, duration of antibiotics, and inotrope requirements
- 0-3 points, no recurrence; > 5 points, 89% recurrence

# Class II evidence (hints)

- Taylor 2000 Am Surg
- 94 patients with complicated appendicitis
- 46 patients assigned to a minimum of 5 days of antibiotics, 48 had no fixed duration
- Duration: 5.9 days and 4.3 days, respectively;  $p < 0.05$
- 6 infectious complications in each group

# Class III evidence (opinions)

- Multiple publications of expert opinion, including Bohnen/SIS 1992 Arch Surg; Mazuski/SIS 2002 Surg Infect; Solomkin/IDSA 2003 CID
- Schein, Wittmann, Lorenz 1996 Eur J Surg and Am J Surg
- Emphasis placed on shortening the duration of antimicrobial use

# *E. g.*, Schein M et al 1996

- Recommendation for established infections:
  - 2 to 5 days for established infections which cannot be easily eradicated or resected
  - More than 5 days of antibiotics for cases where source control cannot be insured, *e. g.*, necrotizing pancreatitis, and continue based on clinical response

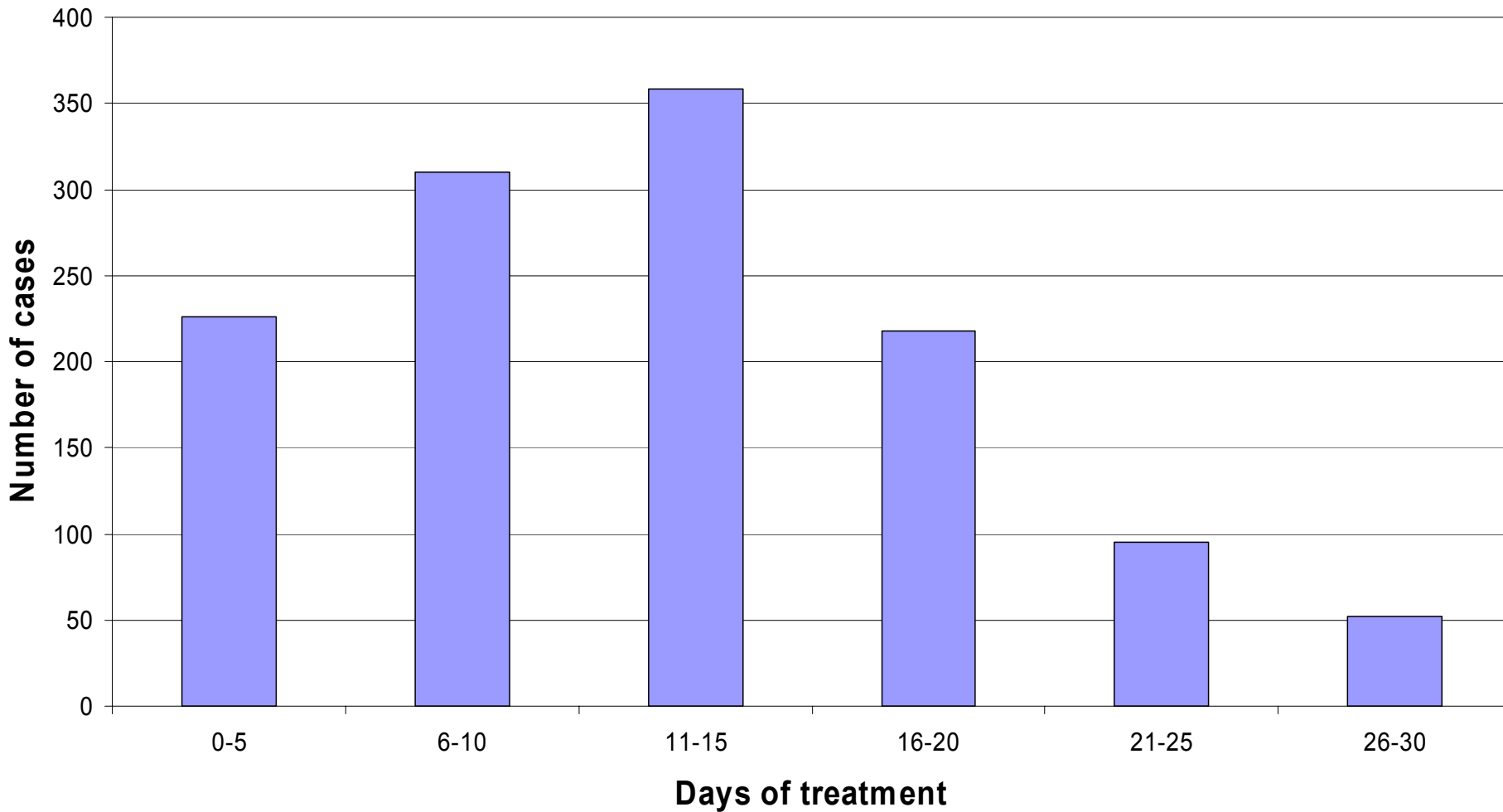
**Are we  
doing a  
good job?**

**No**

# University of Virginia data

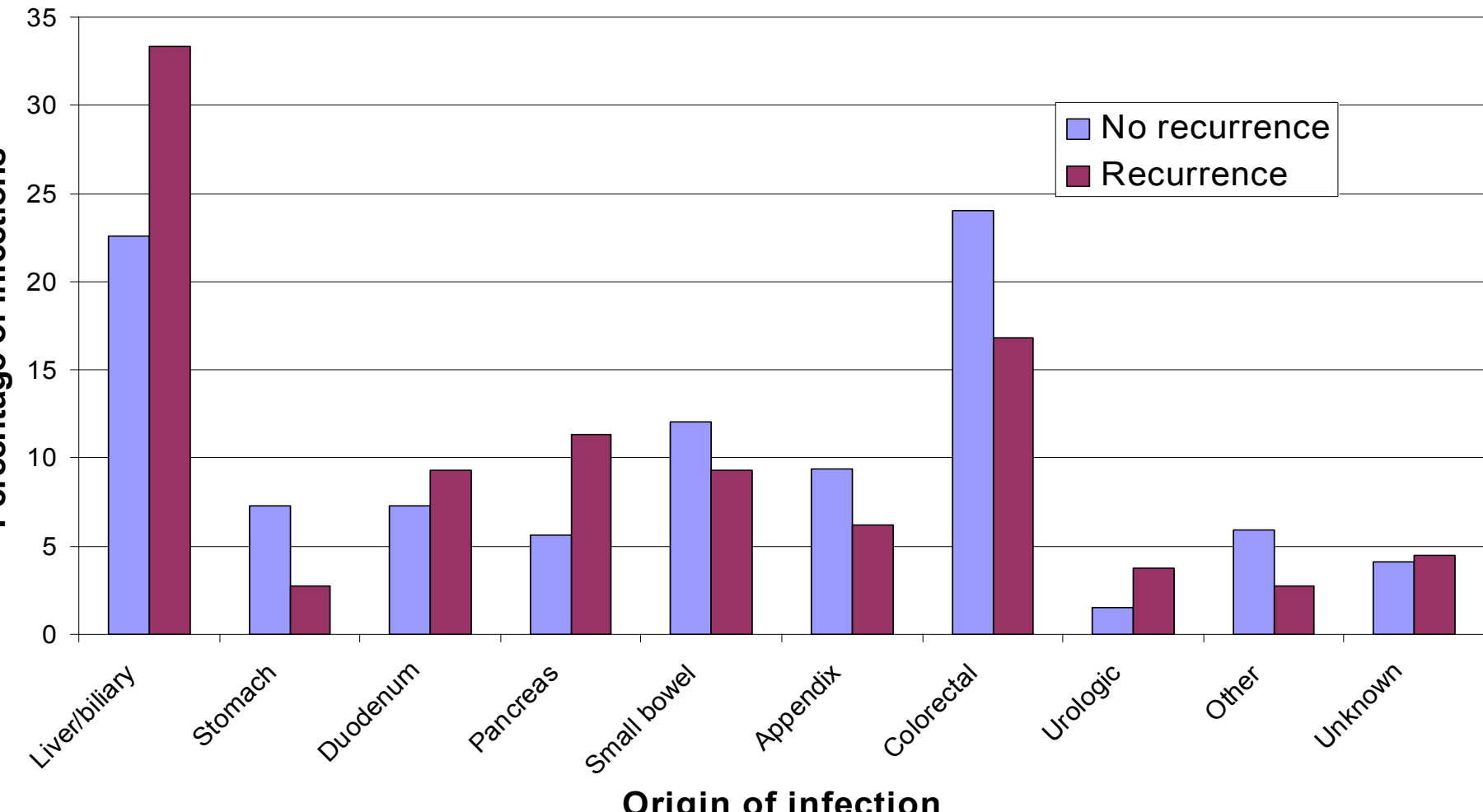
- Six year period
- 1,343 consecutive intra-abdominal infections treated on the general surgery services
- No guidelines for management
- 1,052 treated without recurrence
- 291 recurred (22%)
- $14.5 \pm 0.4$  days of antibiotic treatment

# Distribution of days of treatment



**Can we predict  
who will recur?**

# Origin of infection



# Origin and recurrence

- Why the liver?
- Why the pancreas?
- Why not the colon?

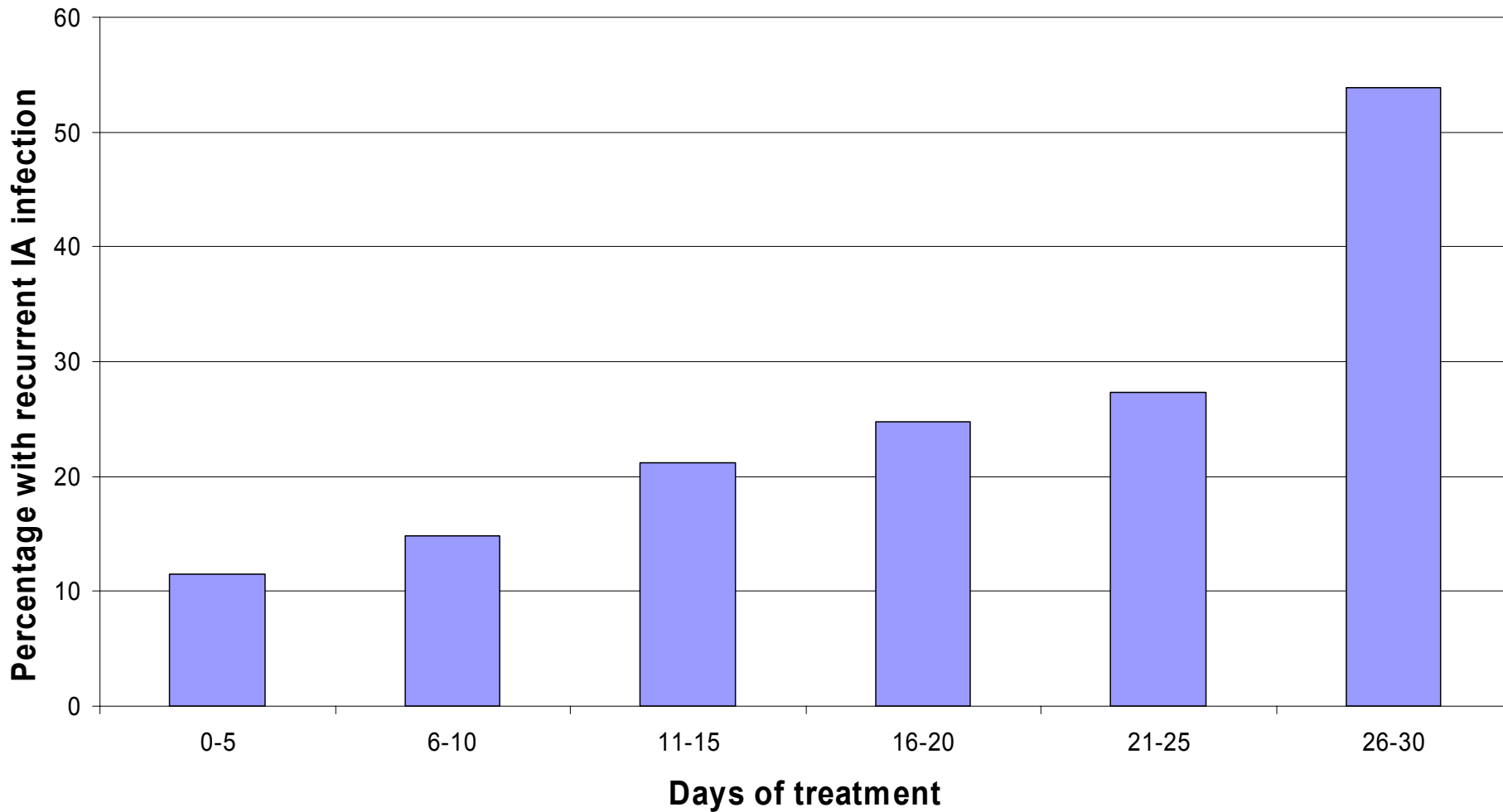
# Origin and recurrence

Recurrence is frequently a product of mechanical failure (source control)

**Is duration of  
treatment associated  
with recurrence?**

**Yes**

# Treatment duration vs. recurrence rate



**Can we figure anything out  
from this larger data set of  
non-interventional (free  
range) data?**

# Hedrick et al, *Surg Infect* in press

	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Patients	218	217	246	248
Days- Range	0 – 7d	8 – 12d	13 – 17d	> 17d
Days- Mean	4.5 ± 0.1	10.0 ± 0.1	14.8 ± 0.1	29.5 ± 1.8
APACHE II	10.1 ± 0.4	11.9 ± 0.4*	13.3 ± 0.4†	14.4 ± 0.5†
Recurrence or death after completion of antibiotics	23 (10.6%)	35 (16.1%)	53 (21.5%)	86 (34.7%)

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## Adjusted Odds Ratio

0.50 0.75 1.50 2.50 4.00

Quartile 2 vs. Quartile 1



Quartile 3 vs. Quartile 1



Quartile 4 vs. Quartile 1



Odds ratio adjusted for APACHE II score, age, prior transfusion, ventilator dependence and gender

**Do I believe it?**

**Yes**

**Do I think it proves  
anything?**

**No**

# Where are we now?

- Many non-randomized or retrospective studies imply 5-7 days of antibiotics have outcomes as good as historical series using longer durations
- A lot of smart people think 5 days should be OK (eminence based medicine)
- It will take time for more definitive data to accumulate

# Questions?

