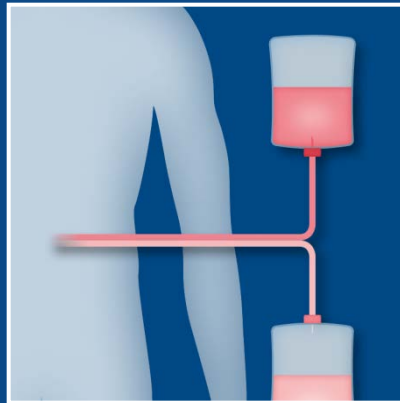


Nephro Update Europe 2018

5-6 October, Budapest

Peritoneal Dialysis



An De Vriese, Belgium

Conflicts of Interest

Research Support: Amgen, Fresenius Medical Care

Lecturing: Amgen, Fresenius Medical Care

Consulting activities: Alexion, Achillion, Ablynx

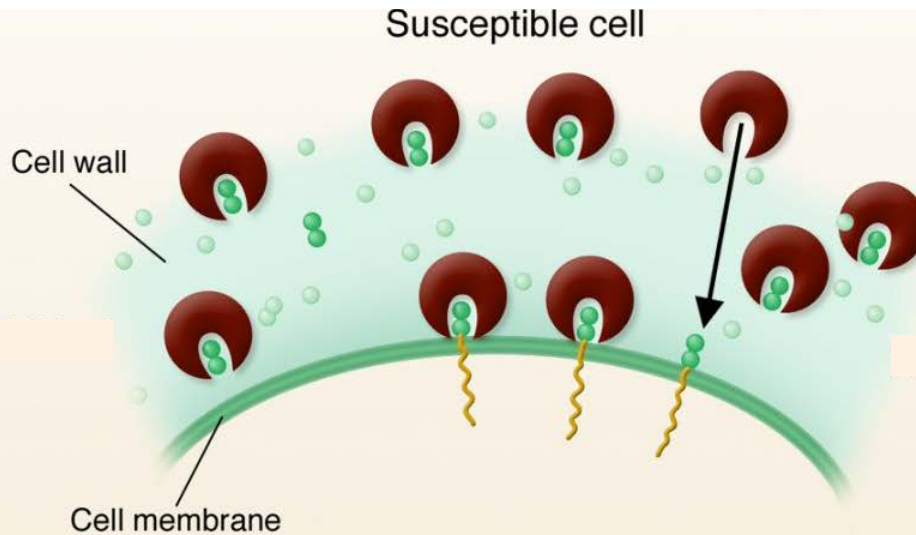
Infection Control

- Choice, dose and mode of administration of antibiotics
- PD discontinuation during peritonitis

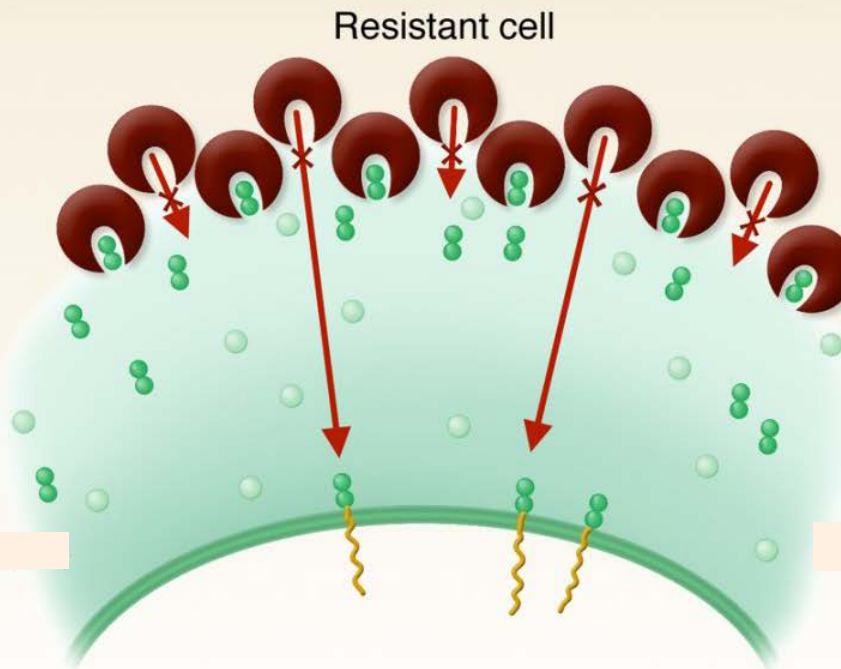
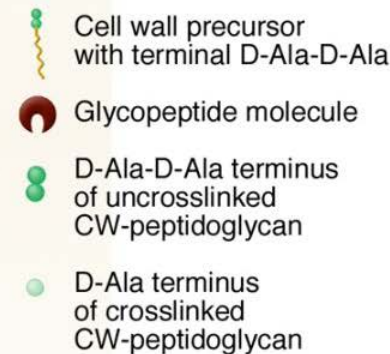
ISPD PERITONITIS RECOMMENDATIONS: 2016 UPDATE

- We suggest that IP vancomycin be administered intermittently and the serum vancomycin level be kept above 15 µg/mL (2C).
- We suggest that IP cephalosporin be administered either continuously (in each exchange) or on a daily intermittent basis (2C).

VISA



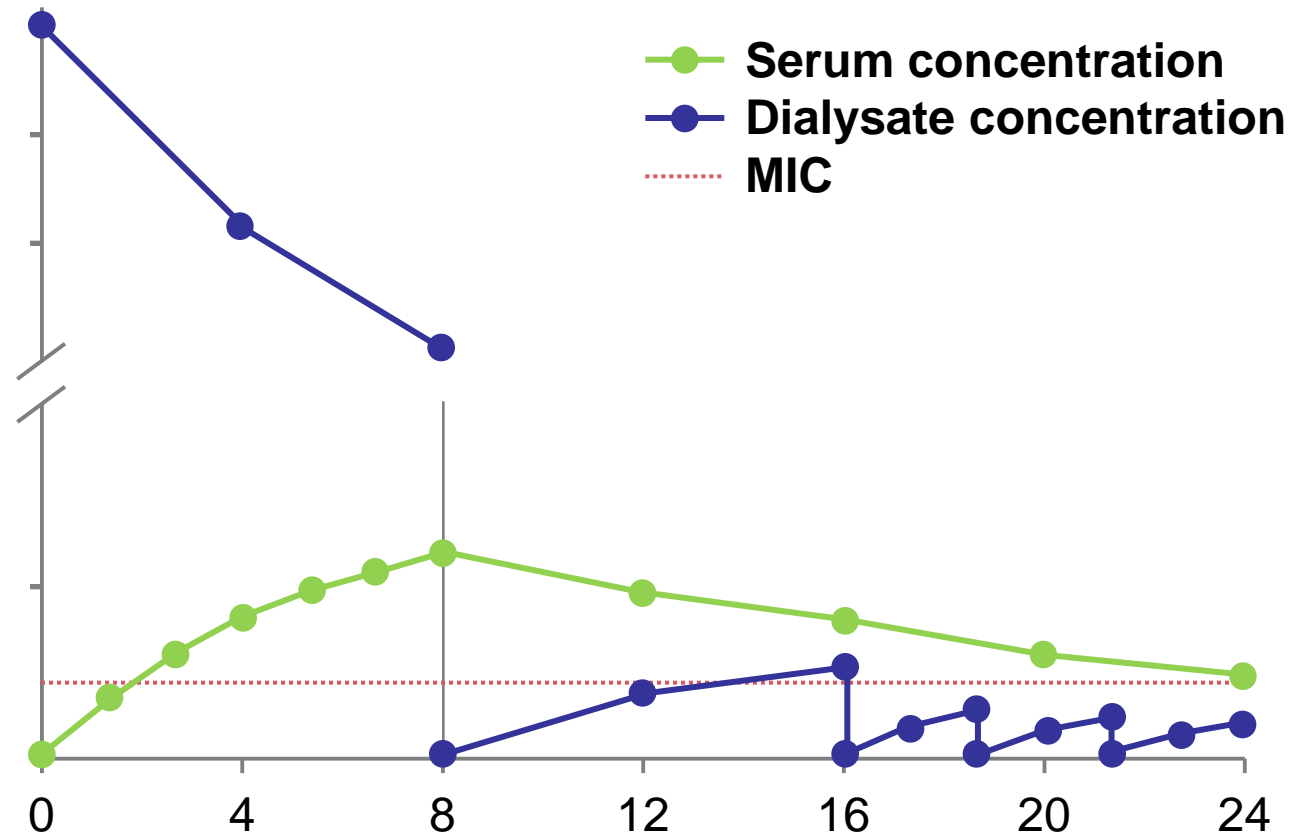
- Thickened cell wall with more peptidoglycan layers.
- Vancomycin never reaches the surface of the cytoplasmic membrane to affect the synthesis of peptidoglycan.



VRSA

- *VanA* gene=high-level vancomycin resistance
- D-ala-D-ala → D-ala-D-lac

HYPOTHETICAL SERUM AND DIALYSATE ANTIBIOTIC LEVELS IN CCPD



Current Guidelines and Suggested Vancomycin Dosing Schedule

	Dose type	
	Loading	Maintenance
ISPD guideline		
CAPD intermittent		15-30 mg/kg every 5-7 days
CAPD continuous	1000 mg/L	25 mg/L
CCPD intermittent	30 mg/kg	15 mg/kg every 3-5 days
Our proposal		
CAPD or CCPD continuous	25 mg/kg	25 mg/L

=higher local concentrations → less failure / VISA

=lower systemic exposure → less side effects

Residual Kidney Function and PD Peritonitis Treatment Outcomes

Table 4. Clinical outcomes among episodes of Gram-positive and culture-negative peritonitis

Urinary Creatinine Clearance, ml/min	<i>n</i> Participants (<i>n</i> Episodes)	Unadjusted OR (95% CI)	<i>P</i> Value	Adjusted OR (95% CI)	<i>P</i> Value
Treatment failure					
>5	17 (27)	2.52 (1.18 to 5.41)	0.02	6.80 (2.37 to 19.6)	<0.01
>0–5	10 (14)	1.39 (0.59 to 3.24)	0.45	2.87 (1.12 to 7.35)	0.03
0	17 (20)	1.0 (Reference)		1.0 (Reference)	
Relapse and recurrence					
>5	13 (17)	2.33 (0.94 to 5.78)	0.07	6.76 (1.90 to 23.8)	<0.01
>0–5	5 (8)	1.26 (0.40 to 3.95)	0.69	2.95 (0.90 to 9.62)	0.07
0	9 (12)	1.0 (Reference)		1.0 (Reference)	
OR, odds ratio; 95% CI, 95% confidence interval.					

ENTEROCOCCAL PERITONITIS: STATE OF THE ART

Enterococcus *Species* **Faecalis
Faecium**

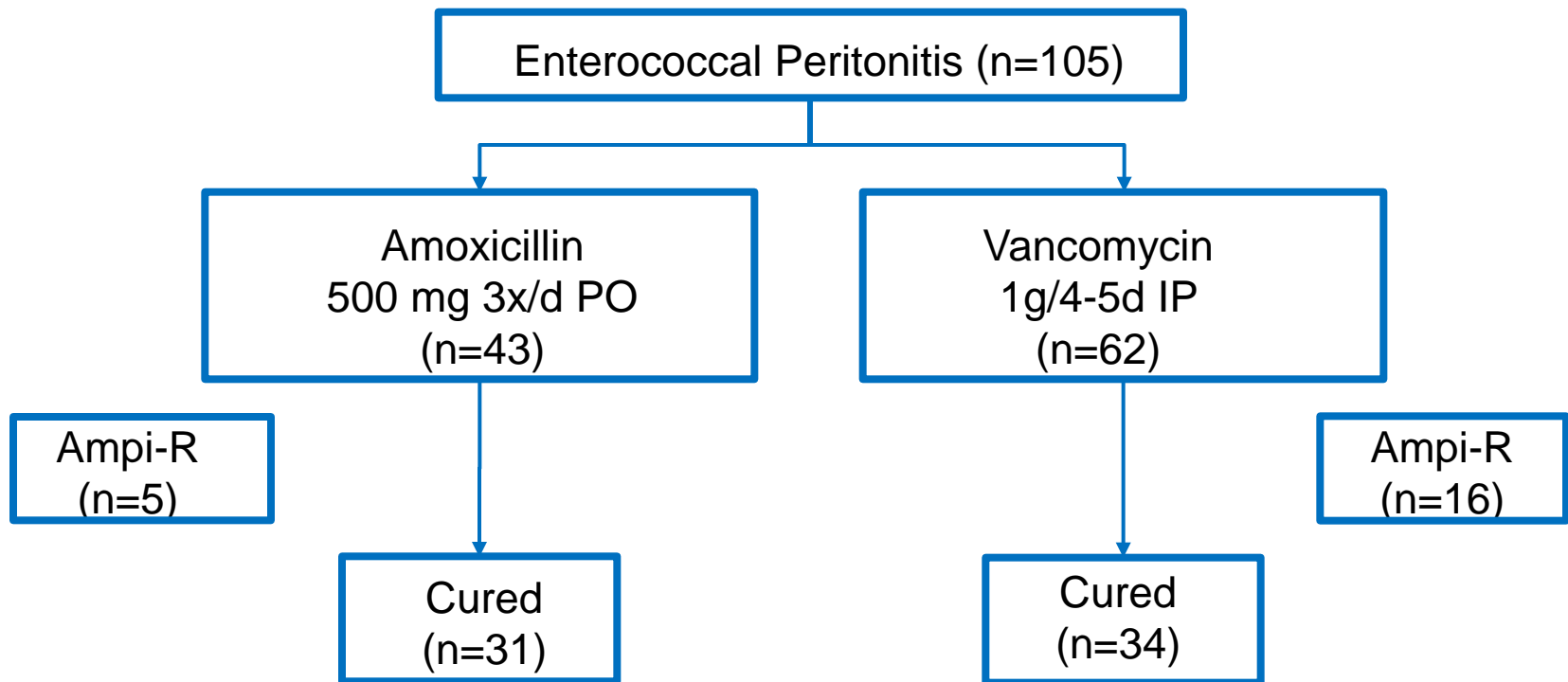
~~Cephalosporins~~

- We suggest that enterococcal peritonitis be treated for 3 weeks with IP vancomycin (2C).
- We suggest adding IP aminoglycoside for severe enterococcal peritonitis **(2D)**.
- For peritonitis due to vancomycin-resistant Enterococcus (VRE), we suggest treatment for 3 weeks with IP ampicillin if the organism is susceptible or with alternative antibiotics (linezolid, quinupristin/dalfopristin, daptomycin or teicoplanin, based on antimicrobial susceptibilities) if the organism is ampicillin-resistant **(2D)**.

ENTEROCOCCAL PERITONITIS: PRACTICAL PROBLEMS

- Aminoglycosides should not be added to the same bag with penicillins because of chemical incompatibility
- Ampicillin has little *in vitro* activity when added to common PD solutions
- Vancomycin is less effective than ampicillin for *Enterococci* that are penicillin-sensitive

Treatment of Enterococcal PD Peritonitis by Oral Amoxicillin or IP Vancomycin: a Retrospective Study



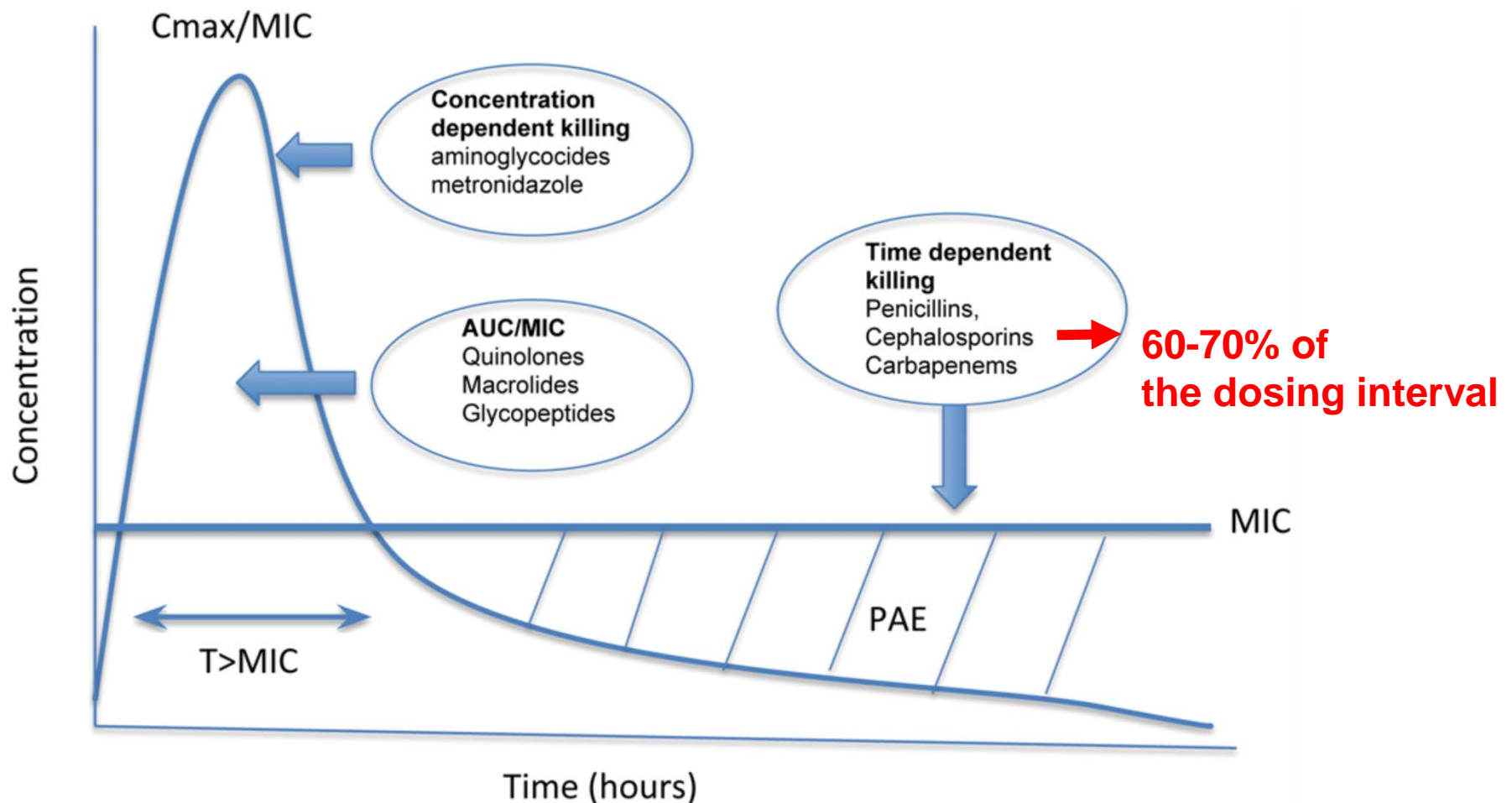
ENTEROCOCCAL PERITONITIS: TAKE-HOME MESSAGE

- Oral amoxicillin is a convenient therapeutic option for Enterococcal peritonitis
- Validity? (comparison with suboptimal Vancomycin IP)

ISPD PERITONITIS RECOMMENDATIONS: 2016 UPDATE

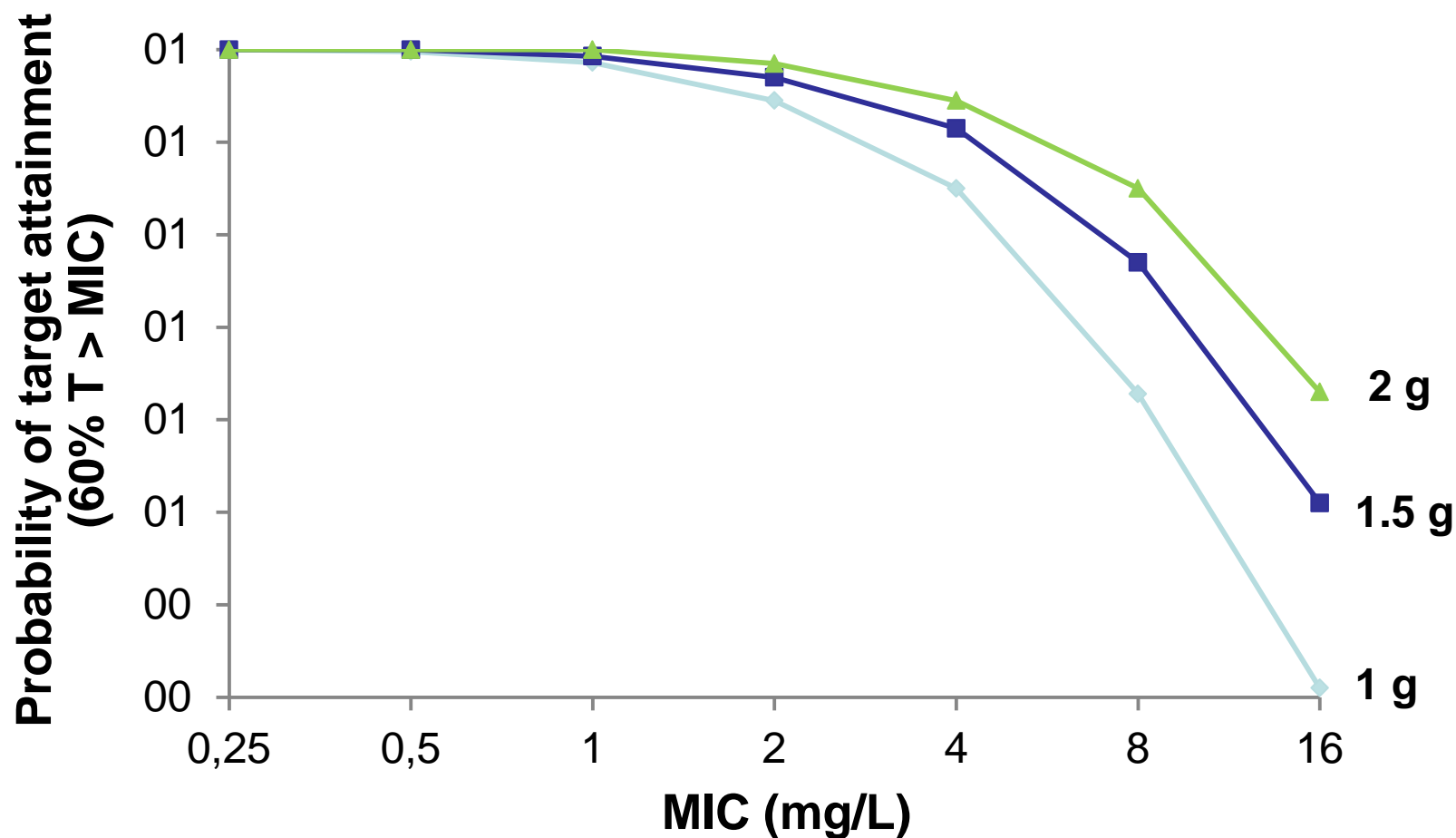
- We suggest that IP vancomycin be administered intermittently and the serum vancomycin level be kept above 15 µg/mL (2C).
- We suggest that IP cephalosporin be administered either continuously (in each exchange) or on a daily intermittent basis (2C).

Ceftazidime: Intermittent regimen: 1000-1500 mg/d
 Continuous regimen: LD 500 mg/L, MD 125 mg/L

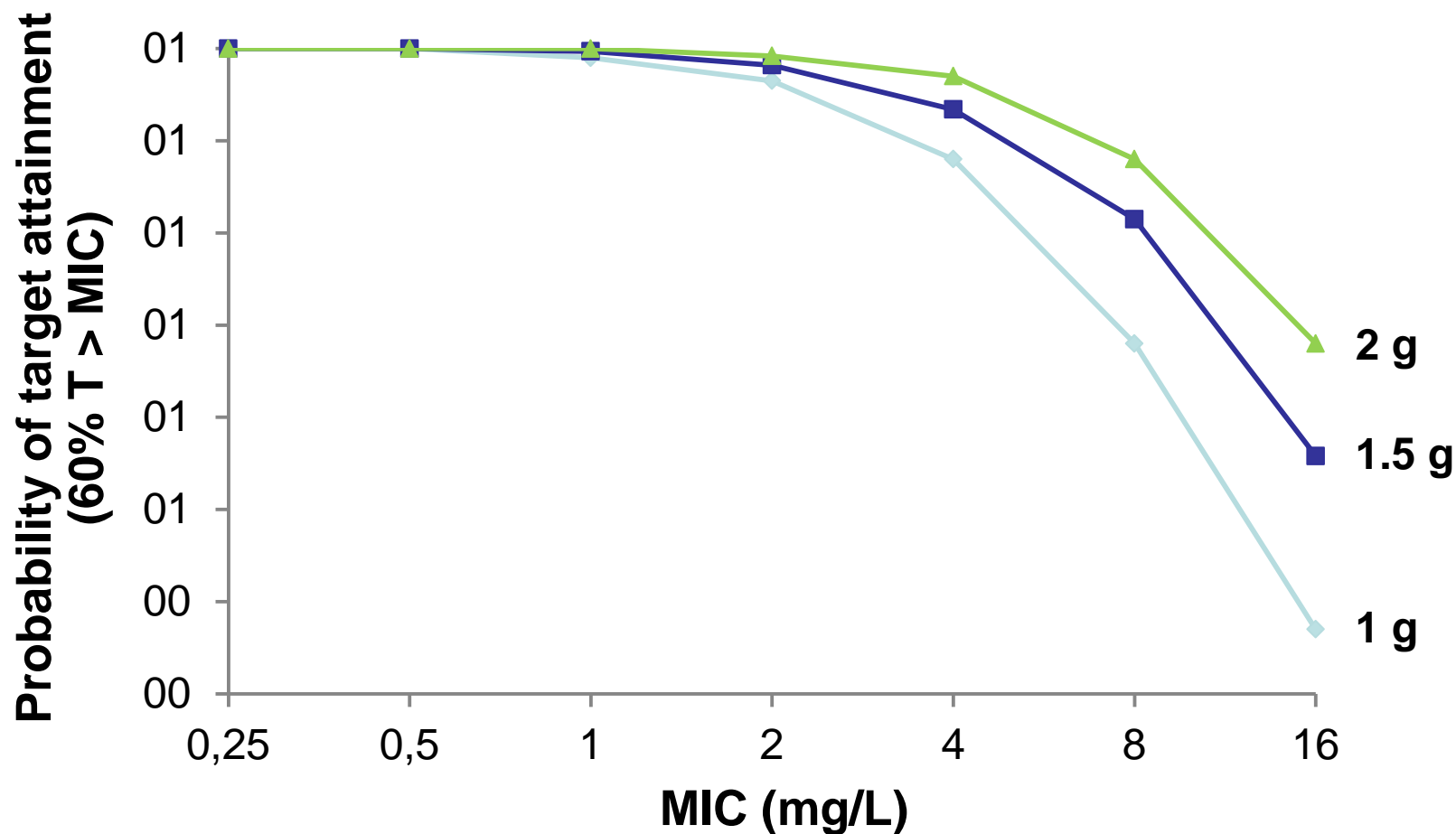


Johnson et al. BJA Educ. 2016;17(4):111-116. doi:10.1093/bjaed/mkw059

Probability of Target Attainment (60% T>MIC) for IP Ceftazidime Day 1



Probability of Target Attainment (60% T>MIC) for IP Ceftazidime during Entire Dosing Interval



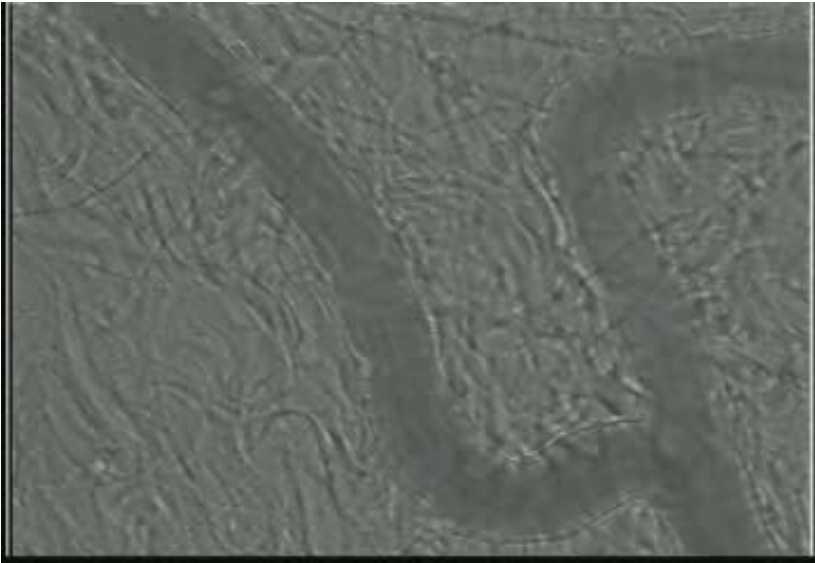
CEFTAZIDIME IP: TAKE-HOME MESSAGE

- 3g IP loading dose is required for a 90% probability of achieving $\geq 60\%$ T>MIC in the peritoneal cavity at MIC 8 mg/L during the first 24 h
- 1-2g IP q24h provide adequate exposure in the peritoneal cavity following this loading dose

Infection Control

- Choice, dose and mode of administration of antibiotics
- PD discontinuation during peritonitis

Control t=0 min

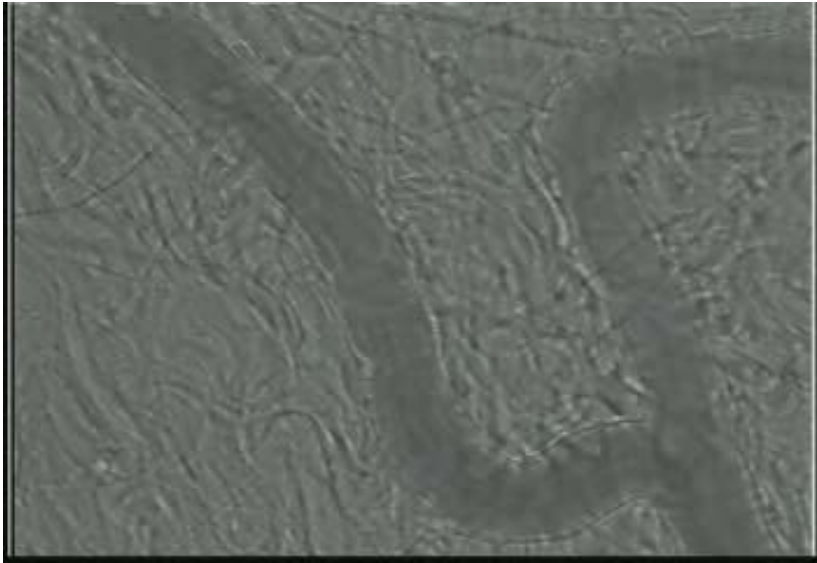


Dialysate t=0 min

Control t=150 min after LPS

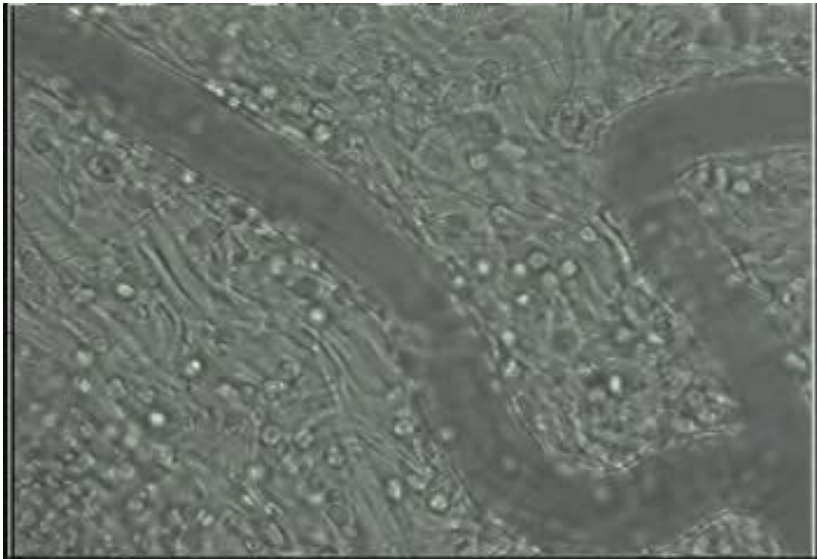
Dialysate t=150 min after LPS

Control t=0 min



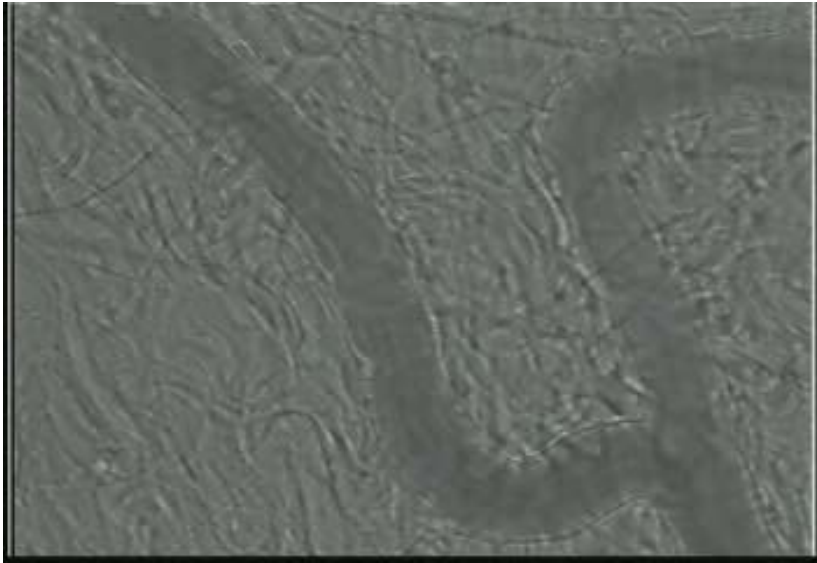
Dialysate t=0 min

Control t=150 min after LPS

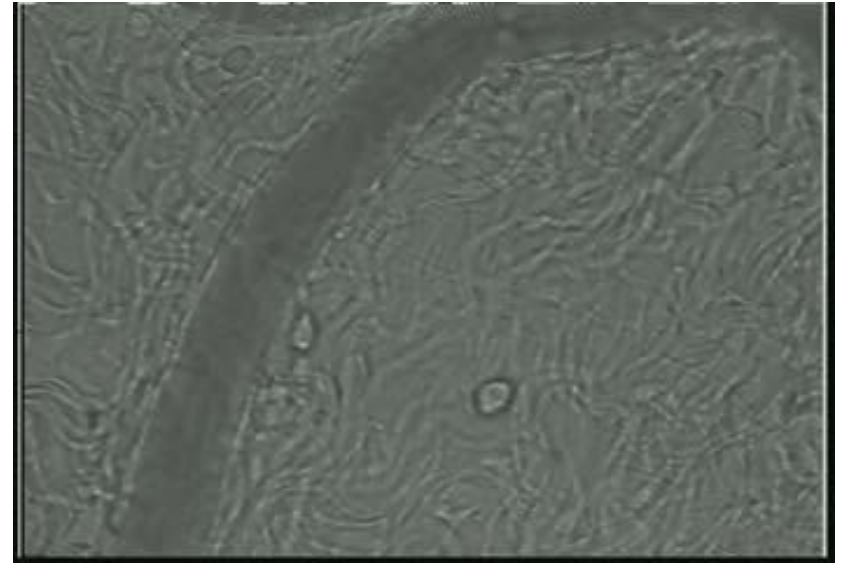


Dialysate t=150 min after LPS

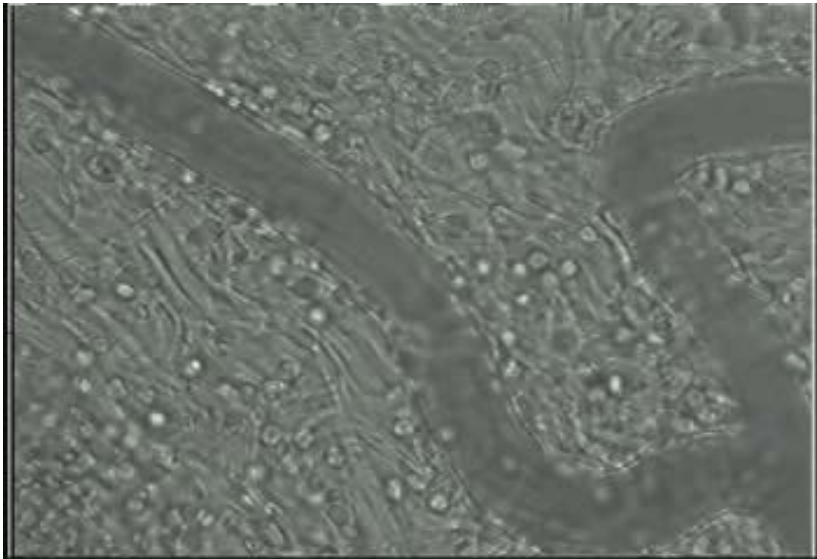
Control t=0 min



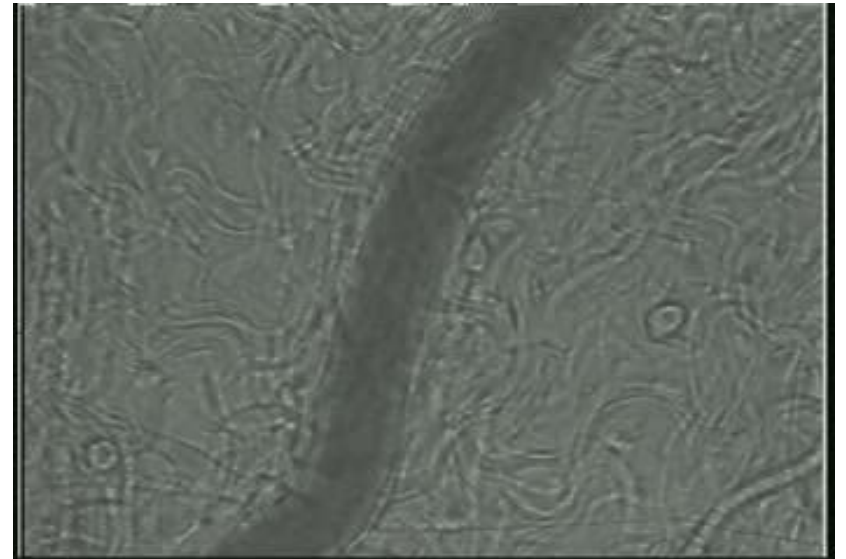
Dialysate t=0 min



Control t=150 min after LPS



Dialysate t=150 min after LPS



Enteric Microorganism Peritonitis

UMCU

MeroRest=

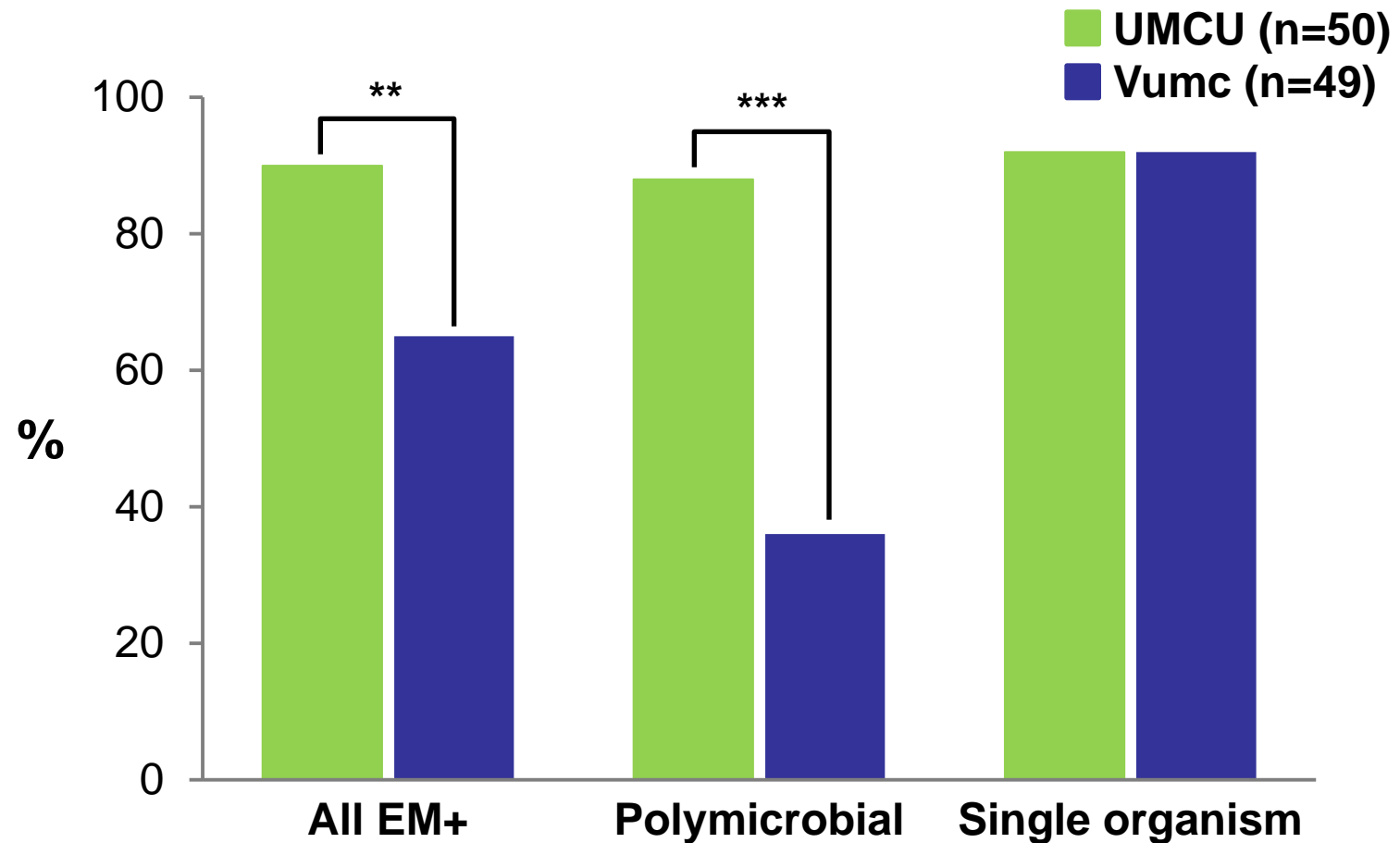
- stop PD without removal PD catheter**
- Meropenem IV 500 mg/d**
- Meropenem catheter lock 125 mg in 25 ml saline/d**

VUmc

Standard PD peritonitis treatment

NB: Enteric microorganisms were defined as pathogens commonly found in the gut, including *Enterobacteriaceae*, enterococci, and anaerobic bacteria.

Primary Cure Rate of Enteric Microorganism Peritonitis



P<0.01; *P<0.001

MANAGEMENT OF PERITONITIS: TAKE-HOME MESSAGE

- Vancomycin: continuous regimen is preferable
- Oral amoxicilline for Enterococcal peritonitis?
- Ceftazidime 3g IP loading dose
- Improved outcome of polymicrobial EM peritonitis by discontinuation of PD without catheter removal + IV and IC meropenem

Technical Issues

- Peritoneal access: method of insertion
- Peritoneal access: type of catheter

PERITONEAL ACCESS: STATE OF THE ART

Guideline 4.4: The Implantation Technique (1A):

Rationale: There is no RCT evidence to support one method of insertion over another; however, the method needs be determined by patient characteristics. For more complicated patients, including those with previous significant abdominal surgery, a technique that involves direct vision is necessary, such as laparoscopic or open insertion (19).

PERITONEAL ACCESS: METHODS OF INSERTION

A: Open surgery

B: Laparoscopy: basic, advanced

C: Percutaneous: blind (Trocars or Seldinger)

D: Percutaneous: peritoneoscope guidance

E: Percutaneous: fluoroscopic (\pm ultrasound) guidance

F: Mixed

Meta-analyses

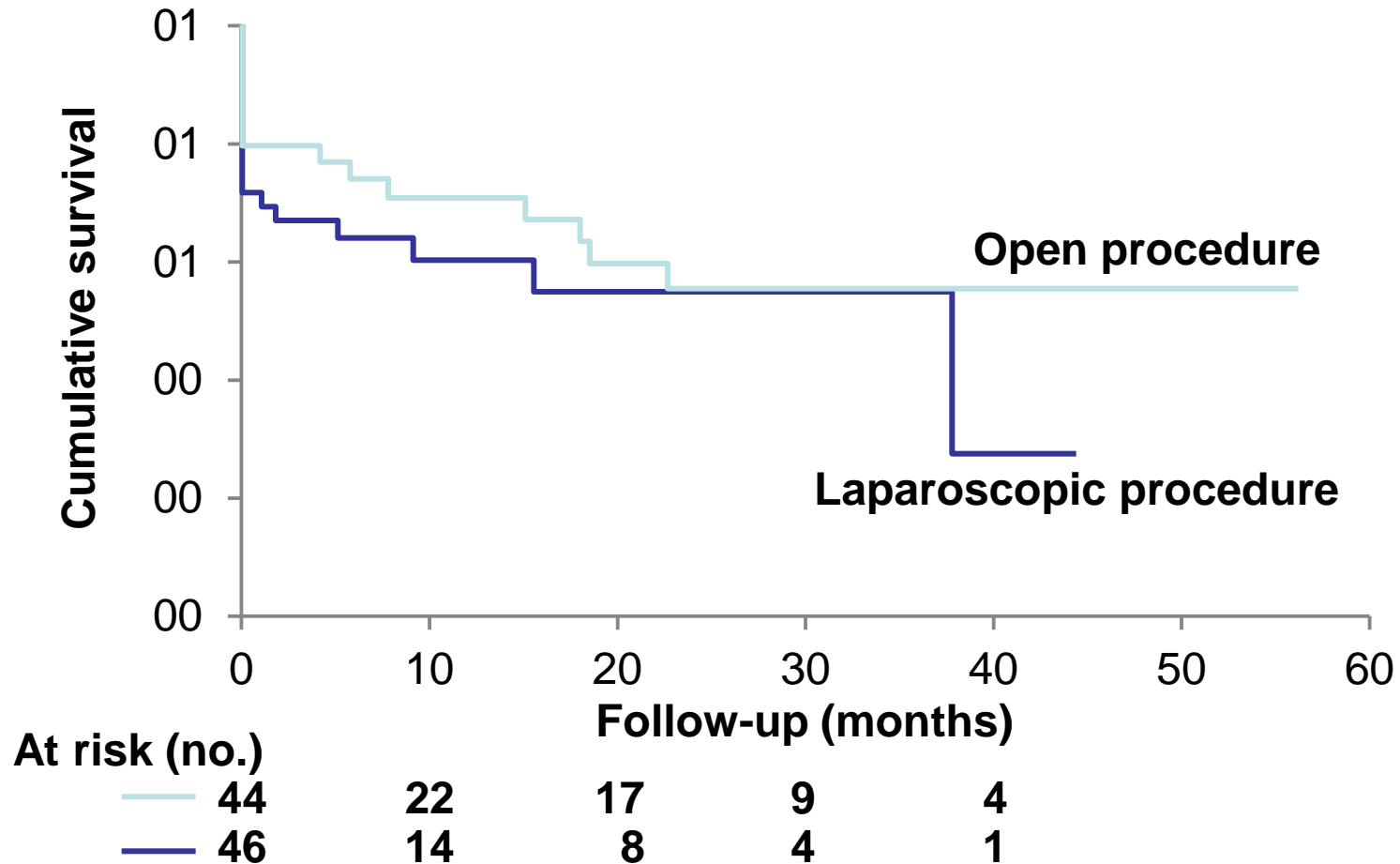
Percutaneous versus Surgical Procedures

Reference	Studies	Outcome
Boujelbane 2015	1 RCT + 12 cohort	No difference

Laparoscopic versus Open Procedures

Reference	Studies	Outcome
Xie 2012	4 RCT + 10 cohort	No difference
Hagen 2013	3 RCT + 8 cohort	Laparoscopy better
Chen 2015	4 RCT + 10 cohort	Laparoscopy better
Qao 2016	5 RCT + 11 cohort	Laparoscopy better

RCT: Survival of Open and Laparoscopic Procedures



RCT: Reasons for Failure of PD Catheter

	Open surgery group	Laparoscopic group
Total	10	14
Omental wrapping	4	7
Malpositioning of catheter between bowel	3	3
Adhesions	1	1
Peritonitis (>6 wk from operation)	1	1
Bleeding (and removal of catheter)	—	1
Dialysate leakage	—	1
Death	1	—

Clinical Success of PD Catheter Insertion

	Open surgery group			Laparoscopic group			P
	Functioning catheter			Functioning catheter			
	No.	No.	%	No.	No.	%	
Total	44	34	77	46	32	70	0.48
Virgin abdomen	21	16	76	24	15	63	0.36
Previous abdominal operation	23	18	78	22	17	77	1.00
Previous median laparotomy	6	3	50	16	11	69	0.62
Previous PD catheter	6	5	83	8	7	88	1.00

Laparoscopic Procedures

➤ Basic:

- Laparoscope is used to verify the position of the PD catheter

➤ Advanced:

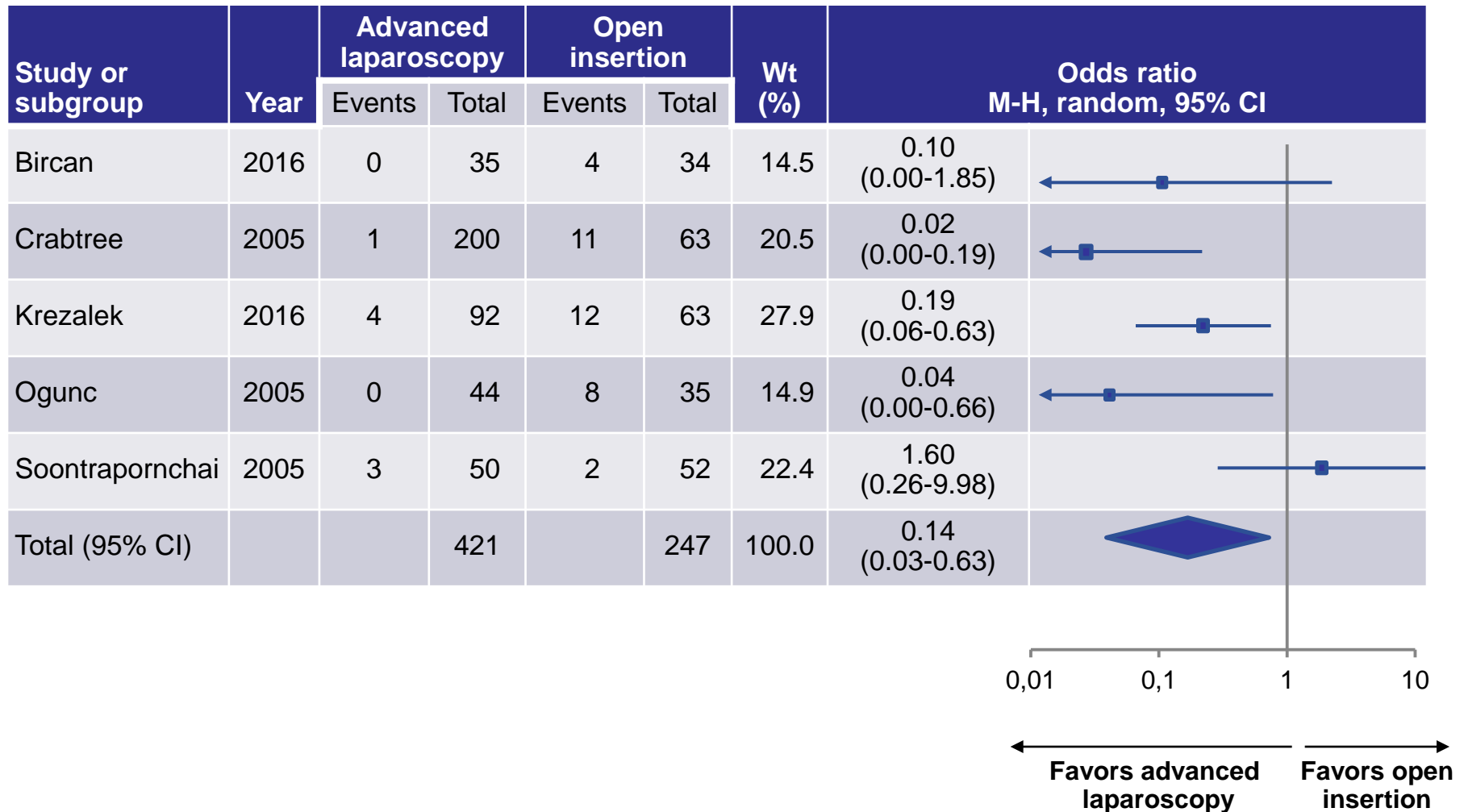
- Adjunctive procedures: omentopexy, adhesiolysis, excision of appendix epiploica, ...

Meta-analysis of Advanced Laparoscopic, Basic Laparoscopic and Open PDC Insertion

Author	Year	Country	Study type	Groups	No.
Bircan	2016	Turkey	Retrospective cohort	Advanced laparoscopic Open	35 34
Krezalek	2016	USA	Retrospective cohort	Basic laparoscopic Advanced laparoscopic Open	80 92 63
Lund	2007	Denmark	Retrospective cohort	Advanced laparoscopic Open	9 13
Soontrapornchai	2005	Thailand	Prospective cohort	Advanced laparoscopic Open	50 52
Ogunc	2005	Turkey	Retrospective cohort	Advanced laparoscopic Open	44 35
Crabtree	2005	USA	Prospective cohort	Basic laparoscopic Advanced laparoscopic Open	78 200 63
Attaluri	2010	USA	Retrospective cohort	Basic laparoscopic Advanced laparoscopic	68 129

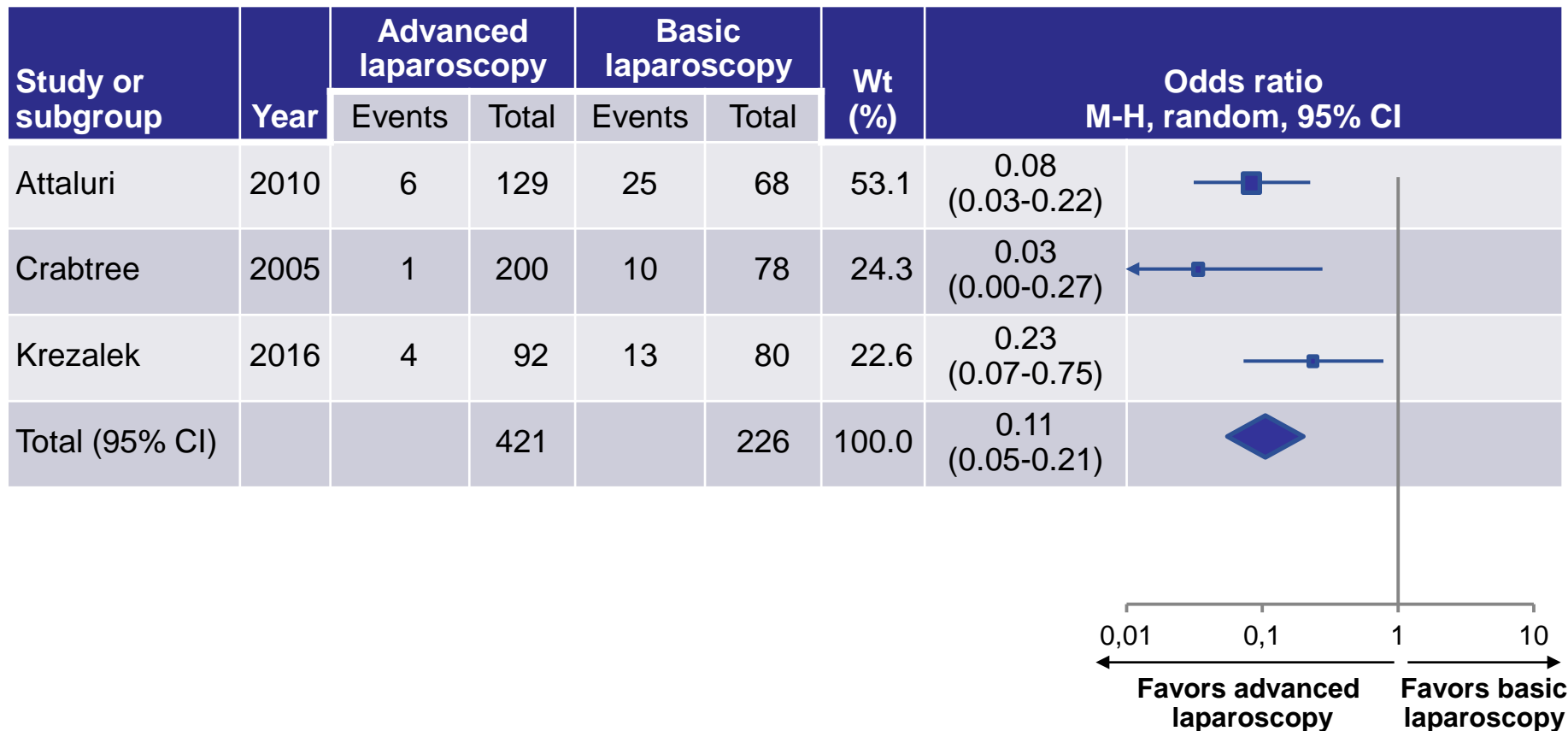
Advanced Laparoscopy vs Open Insertion

Risk of catheter obstruction



Advanced vs. Basic Laparoscopy

Risk of Catheter Obstruction



METHOD OF CATHETER INSERTION: TAKE-HOME MESSAGE

- A dedicated team and experience with a specific method of insertion is important
- Advanced laparoscopy may be superior to other methods of insertion, in particular in complex patients
- Rectus sheath tunneling

Technical Issues

- Peritoneal access: method of insertion
- Peritoneal access: type of catheter

PERITONEAL ACCESS: STATE OF THE ART

Guideline 5.2: Facilities for PD Catheter Insertion (2C):

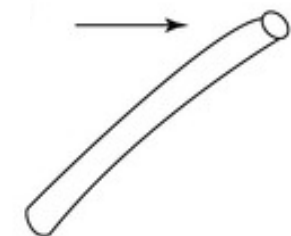
We suggest that no particular catheter type has been proven to be better than another.

-coiled vs. straight: to improve flow and reduce inflow pain, catheter migration, omental wrapping, visceral trauma

-self-locating vs. not: to reduce the risk of tip migration

-double vs. single cuff: to reduce the risk of exit-site complications and peritonitis

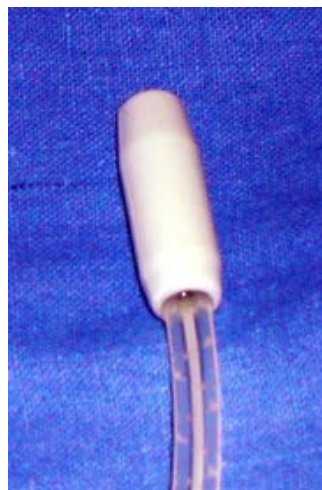
-swan neck vs. Tenckhoff: to reduce the risk of exit-site infections, tip migration, and cuff protrusion



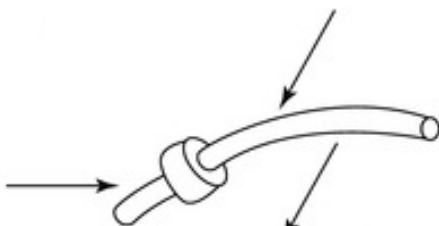
Straight tenckhoff



Coiled tenckhoff



Self-locating



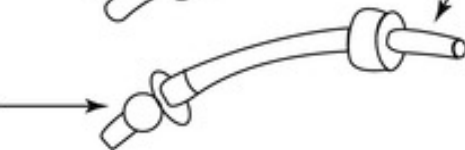
Single cuff



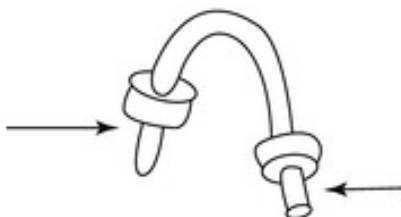
TWH cuff
Disc-bead single cuff



Double cuff



2 cuff
Disc-bead double cuff



Swan neck
(150 degree permanent bend-arcuate)

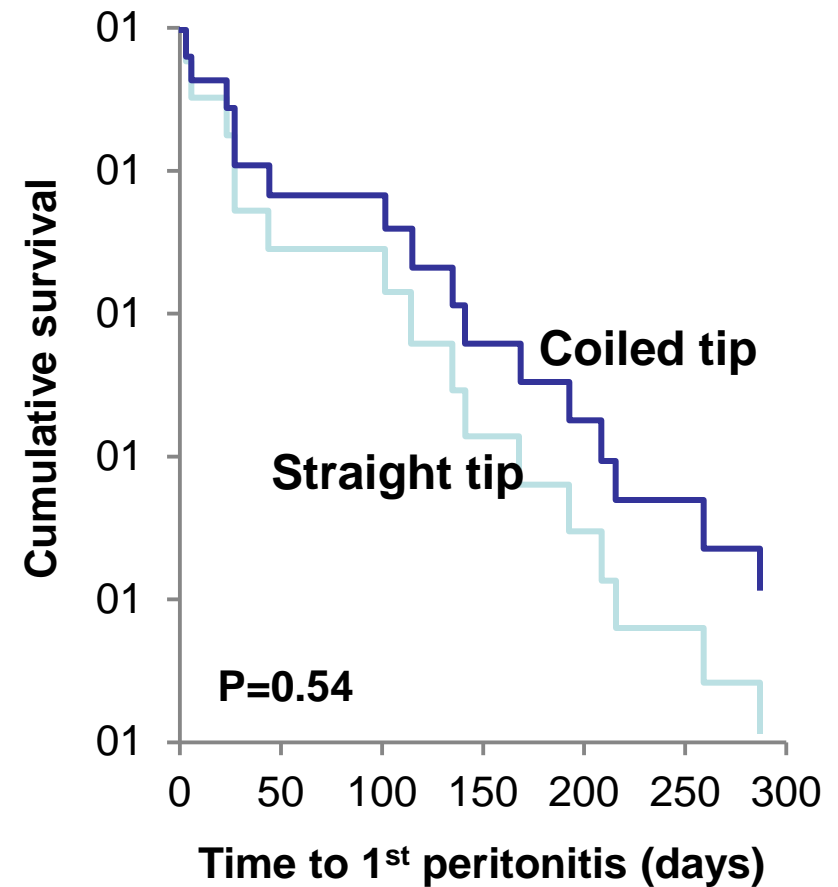
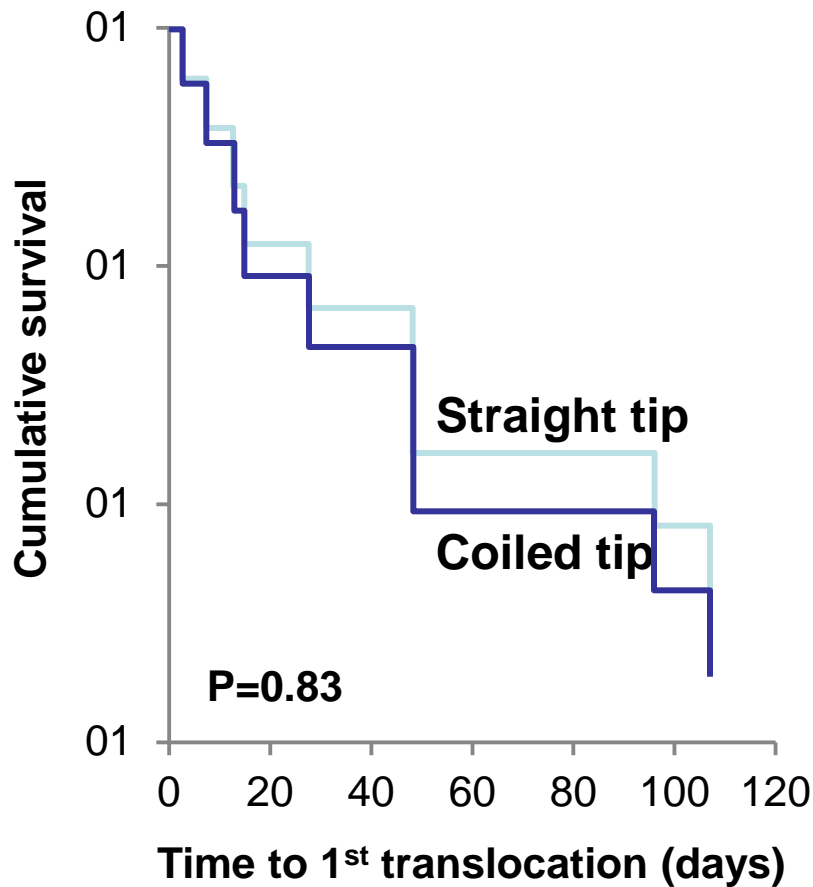


Disc-bead double cuff swan neck
(Missouri catheter)

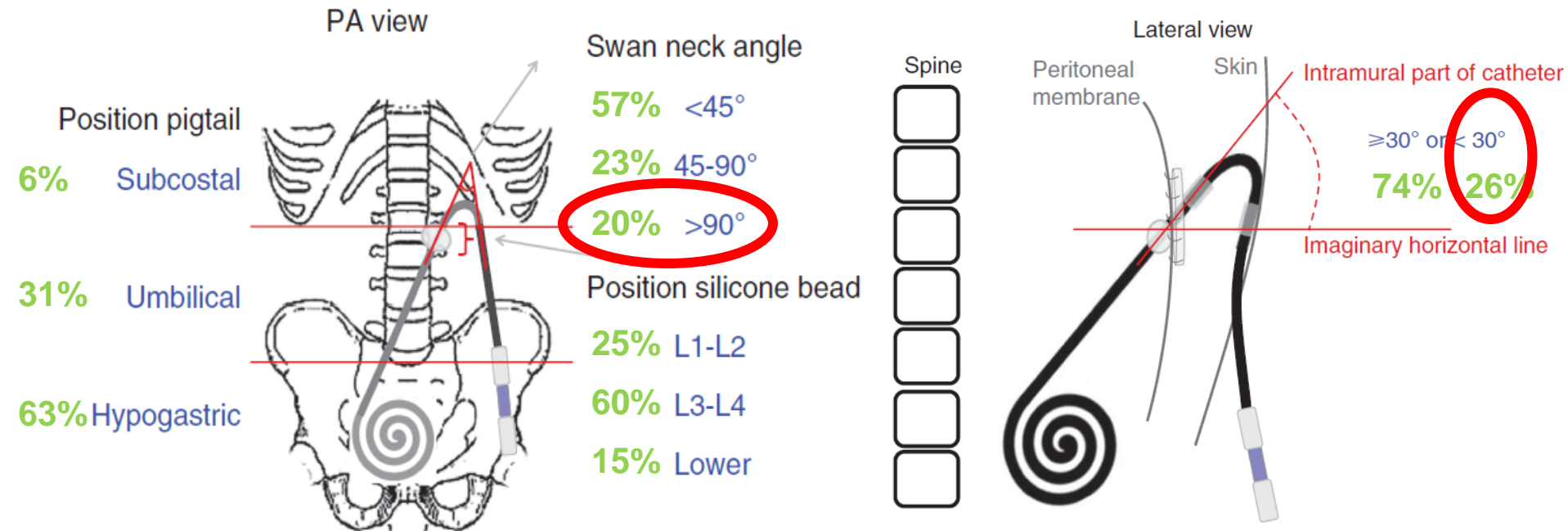
PERITONEAL ACCESS: CATHETER TYPE

- A: Straight tip – double cuff – Tenckhoff
- B: Straight tip – double cuff – Swan neck
- C: Coiled tip – double cuff – Tenckhoff
- D: Coiled tip – double cuff – Swan neck
- E: Self-locating catheter
- F: Single cuff

RCT: Influence of the Intra-peritoneal Segment on Catheter Performance



RESPECTING THE SHAPE MEMORY OF THE CATHETER

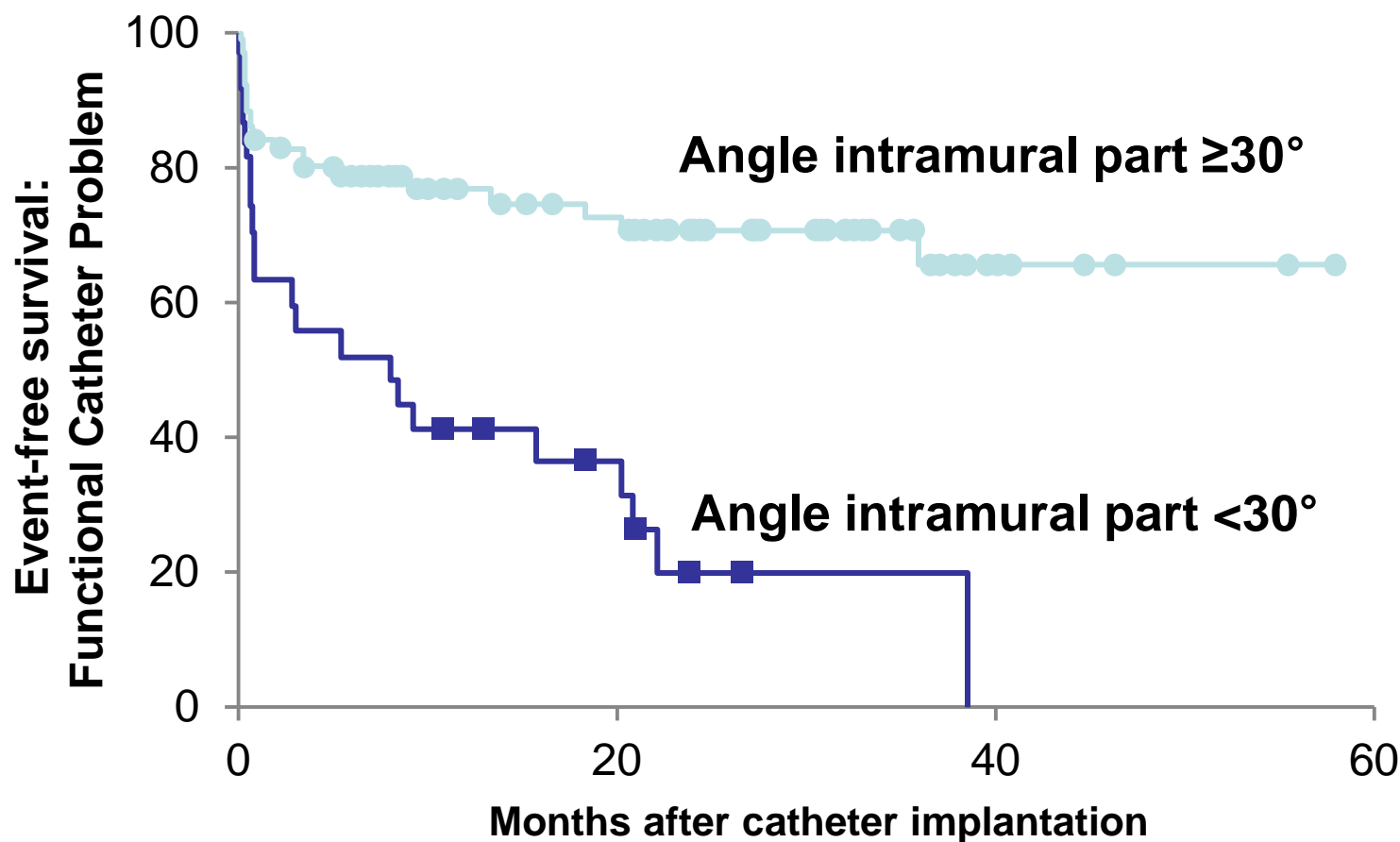


Predictors of Catheter Survival

Mean follow-up 36±17 months:

38% experienced at least one clinically overt functional catheter problem

19% required surgical intervention



PERITONEAL ACCESS: TAKE-HOME MESSAGE

- Catheter design is not an important determinant of mechanical and infectious complications
- Skills and experience of the physician/team
- Respecting shape memory reduces tip migration and catheter dysfunction
- Postimplantation radiology to confirm the preservation of swan neck and inclination angle

List of References

1. *Li et al. Perit Dial Int 2016; 36: 481*
2. *Chen et al. Perit Dial Int 2018; 38: 266*
3. *De Vriese et al. Perit Dial Int 2014; 34: 154*
4. *Whitty et al. Clin J Am Soc Nephrol 2017; 12: 2016*
5. *Szeto et al. Kidney Blood Press Res 2017; 42: 837*
6. *Cardone et al. Antimicrob Agents Chemother 2014, 58: 19*
7. *Mortier, De Vriese et al. JASN 2003; 14: 1296*
8. *Abahams et al. Perit Dial Int 2017; 37: 298*
9. *Figueiredo et al. Perit Dial Int 2010, 30: 424*
10. *van Laanen et al. Perit Dial Int 2018*
11. *Shrestha et al. Perit Dial Int 2018, 38: 163*
12. *Banin et al. Clin Exp Nephrol 2018*
13. *Bammens et al. Kidney Int 2014, 86: 1001*

List of Abbreviations

- CAPD=continuous ambulatory peritoneal dialysis
- CCPD=continuous cyclic peritoneal dialysis
- EM=enteric microorganism
- IP=intraperitoneal
- ISPD=International Society Peritoneal Dialysis
- MRCoNS=methicillin resistant Coagulase Negative Staphylococcus
- MScNS=methicillin sensitive Coagulase Negative Staphylococcus
- MRSA=methicillin resistant Staphylococcus aureus
- MSSA=methicillin sensitive Staphylococcus aureus
- VISA=Vancomycin intermediary Staphylococcus aureus
- VRSA=Vancomycin resistant Staphylococcus aureus