BCKD 2023

BC KIDNEY DAYS

Deconstructing ISPD Guidelines in the Management of Peritonitis

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Disclosure

We have nothing to disclose.

Overview

- Diagnosing peritonitis
- Measuring, monitoring and reporting peritonitis
- Fungal prophylaxis
- Antibiotic management of peritonitis

Special Series/Guidelines

PERITONEAL DIALYSIS INTERNATIONAL

Peritoneal Dialysis International
2022, Vol. 42(2) 110–153

DOI: 10.1177/08968608221080586
journals.sagepub.com/home/ptd

SAGE

ISPD peritonitis guideline recommendations: 2022 update on prevention and treatment

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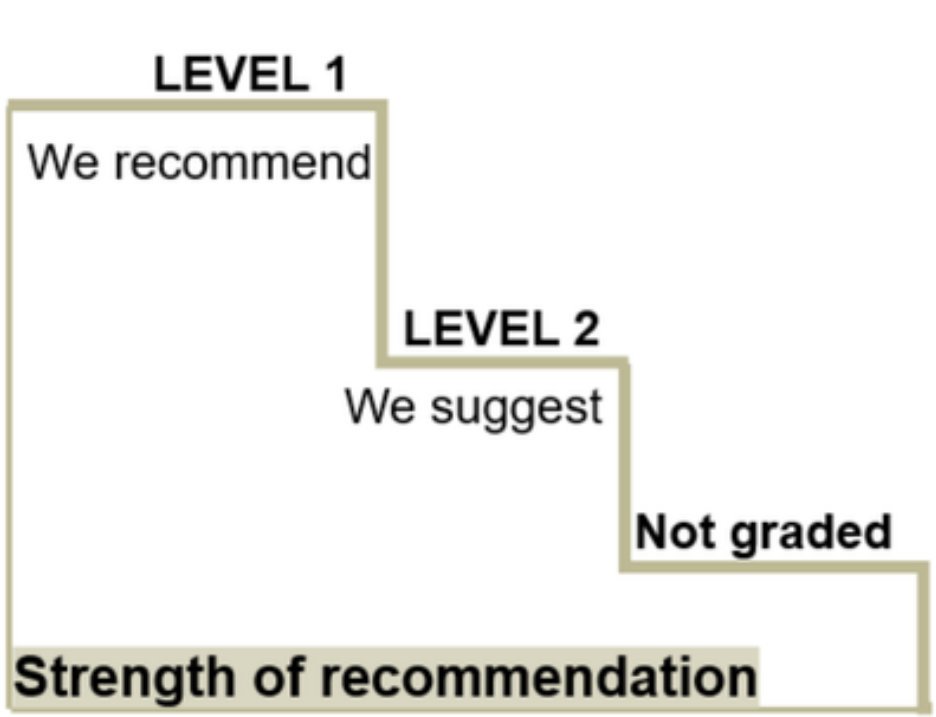
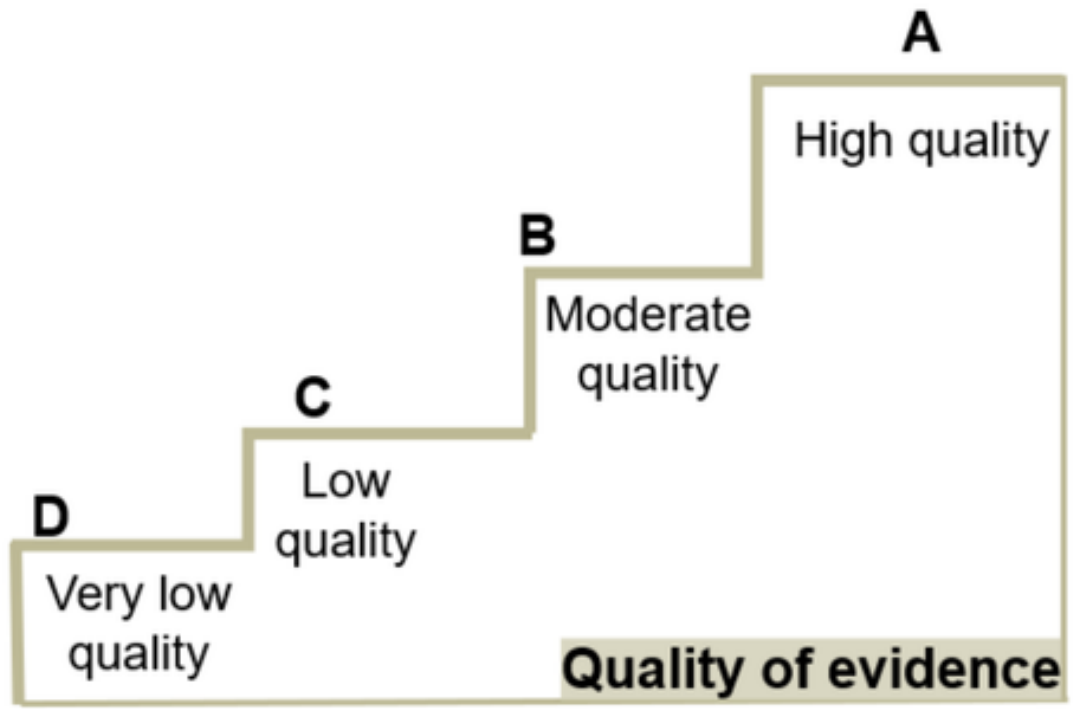
GRADE recommendations





ISPD guideline grades

Grade	Number of Recommendations
1A	1
1B	5
1C	16
1D	1
2A	1
2B	4
2C	17
2D	11
Not Graded	13

Definition of peritonitis varies

77 PD studies were included in systematic review

30% of studies do not describe definition of peritonitis

42% of studies modified ISPD peritonitis definitions

Standardizing definitions for reporting of peritonitis and associated outcomes will better enable studying peritonitis.

Standardizing definition of peritonitis [1C]

TWO of the following are present:

1) clinical features: abdominal pain and/or cloudy dialysis effluent

2) dialysis effluent white cell count > 100/mL or > 0.1 x 109/L (after a dwell time of at least 2 h), with > 50% polymorphonuclear leukocytes (PMN).

*WBC count depends on duration of dwell, especially in CCPD

3) positive dialysis effluent culture

Cause specific peritonitis

Diagnose peritonitis according to organism

- Staphylococcus aureus peritonitis
- Culture-negative peritonitis

Catheter-related peritonitis:

- Peritonitis occurring within 3 months of catheter infection (either exit-site or tunnel) with the same organism as in effluent
- Allowed to have one site sterile if antibiotic exposure

Enteric peritonitis:

- An intestinal source involving processes such as inflammation, perforation or ischemia of intraabdominal organs
- If a peritonitis episode in this context is culture negative, we suggest that it be recorded as enteric peritonitis rather than as culture-negative

Time specific peritonitis

PD catheter insertion related peritonitis

- Any peritonitis that occurs within 30 days after insertion, regardless of whether patient is established on PD or not
- Aim for less than 5% of all catheter insertions

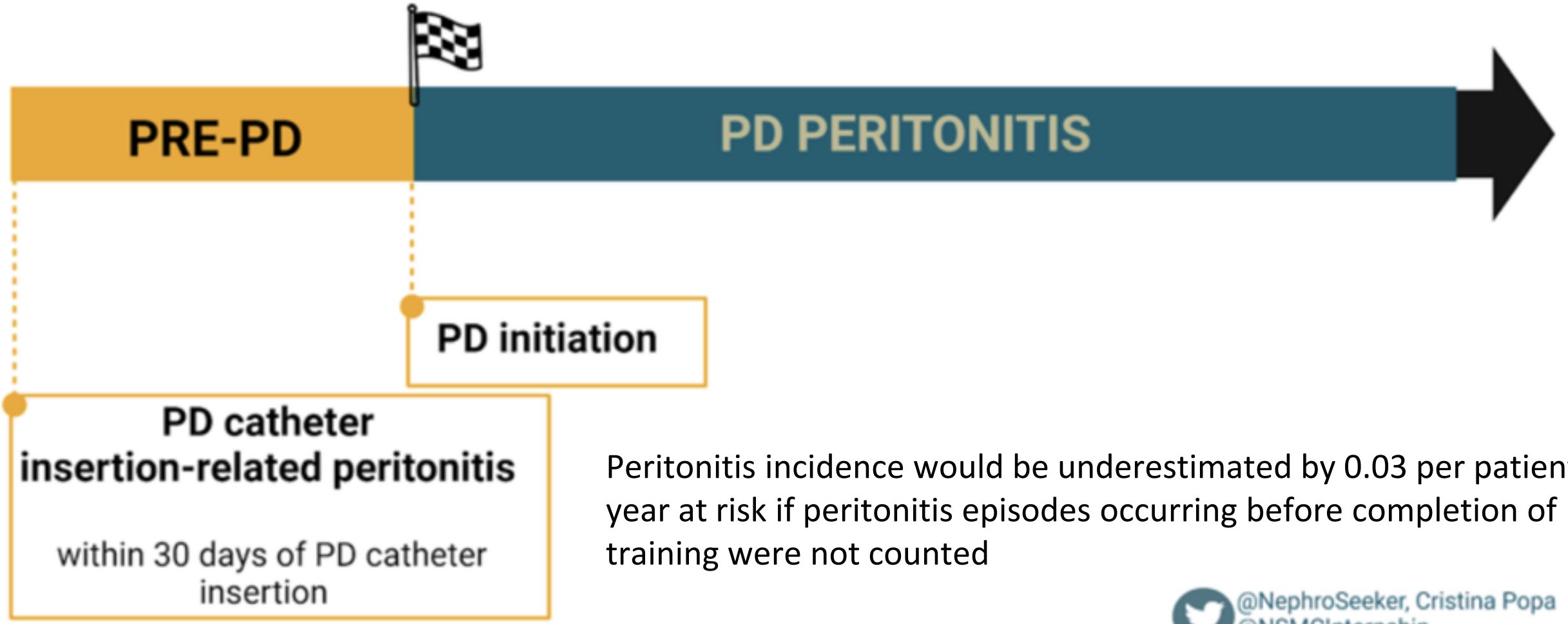
Pre-PD peritonitis

- Occurring after catheter insertion and before PD initiation, defined as first day of PD treatment with intent of long-term PD
- Flushing PD catheter does not count
- Many units only capture peritonitis after patients commence PD

PD related peritonitis

- During PD treatment

PERITONEAL DIALYSIS PERITONITIS - TIMELINE



Peritonitis incidence would be underestimated by 0.03 per patient-year at risk if peritonitis episodes occurring before completion of PD training were not counted

@NephroSeeker, Cristina Popa
@NSMCInternship

PD-PERITONITIS OUTCOMES

Medical cure

Complete resolution of peritonitis

Refractory peritonitis

Peritonitis persistently after 5 days of appropriate antibiotic therapy

Recurrent peritonitis

Peritonitis - within 4 weeks of completion of therapy of a prior episode, **different organism**

Relapsing peritonitis

Peritonitis within 4 weeks of therapy of a prior episode with the **same organism** or **one culture negative episode followed by culture negative (or specific organism)**

Repeating peritonitis

Peritonitis > 4 weeks of therapy of a prior episode with the **same organism**

Peritonitis-associated catheter removal

- as part of the treatment of peritonitis episode

Peritonitis-associated hemodialysis transfer

- as part of the treatment for a peritonitis

Peritonitis-associated hospitalization

Hospitalisation for the purpose of peritonitis treatment delivery

Peritonitis-associated death

Death within 30 days of peritonitis onset or death during hospitalisation due to peritonitis

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METHOD 2: Peritonitis Rate: Episodes per patient year[1]

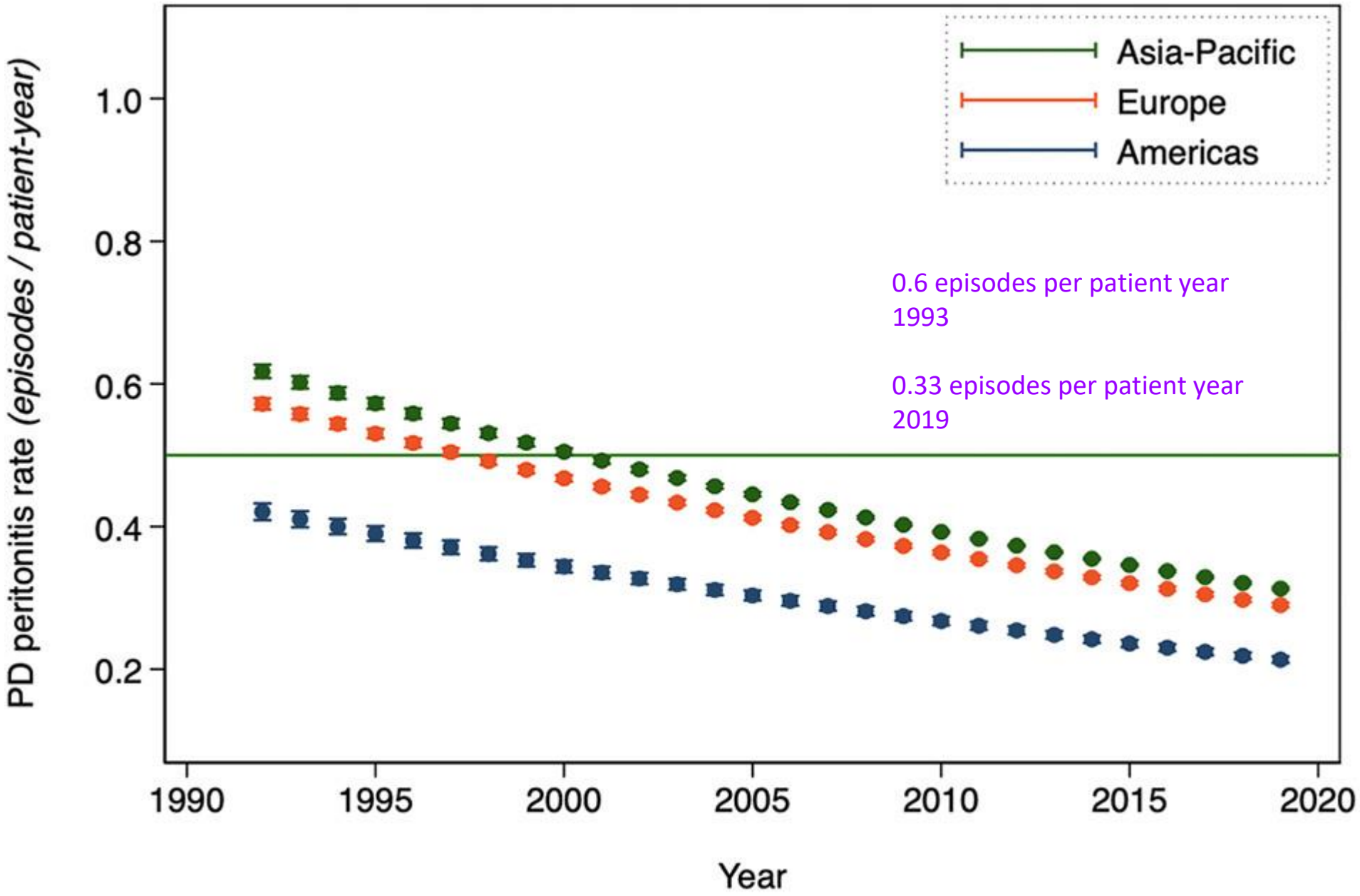
step 1	Total number CAPD/APD patient days at risk/365 days per year = patient years experience **Example:** 2,000 days/365 days per year = 5.5 years experience
step 2	Number of episodes of peritonitis/number of years experience = Episodes per patient year **Example:** 2 episodes peritonitis/5.5 patient years = 0.36 episodes per patient year

Important points:

- Include hospital days (once home therapy begins) in total days at risk
- Include hospital acquired peritonitis (once home therapy begins) in total peritonitis rate[2]
- Relapsing episodes of peritonitis are counted as a single episode of peritonitis[2]
- Recurrent peritonitis is a new episode of peritonitis and should be counted as an individual occurrence[2]
- Peritonitis rates should be no more than 0.5 episodes per year at risk (one episode per 24 patient – months) per ISPD 2016 recommendations[2]
- Programs should also be aware of the percentage of patients who are peritonitis free to include in unit's quality management programs
- Exit-site infection rates are calculated in the same manner as above

Table 2. Measurement and reporting of peritonitis.

	Unit of measure	Minimum frequency	Target
Peritonitis rates (overall and organism-specific)	Episodes per patient year	Yearly	<0.4 episodes per patient-year
Culture-negative peritonitis	% of all peritonitis episodes	Yearly	<15% of all peritonitis episodes
Time to first peritonitis episode	Mean unit time to first episode peritonitis	Quarterly (local report)	–
Proportion of patients free of peritonitis	% per unit time	Quarterly (local report)	>80% per year
Pre-PD peritonitis	% of all peritonitis episodes	Quarterly (local report)	–
PD catheter insertion-related peritonitis	% of all PD catheter insertions	Quarterly (local report)	<5%
Medical cure	% of all peritonitis episodes	Quarterly (local report)	–
Recurrent peritonitis	% of all peritonitis episodes	Quarterly (local report)	–
Relapsing peritonitis	% of all peritonitis episodes	Quarterly (local report)	–
Peritonitis-associated catheter removal	% of all peritonitis episodes	Quarterly (local report)	–
Peritonitis-associated haemodialysis transfer	% of all peritonitis episodes	Quarterly (local report)	–
Peritonitis-associated death	% of all peritonitis episodes	Quarterly (local report)	–



Marshall MR et al *Peritoneal Dialysis International*. 2022;42(1):39-47.

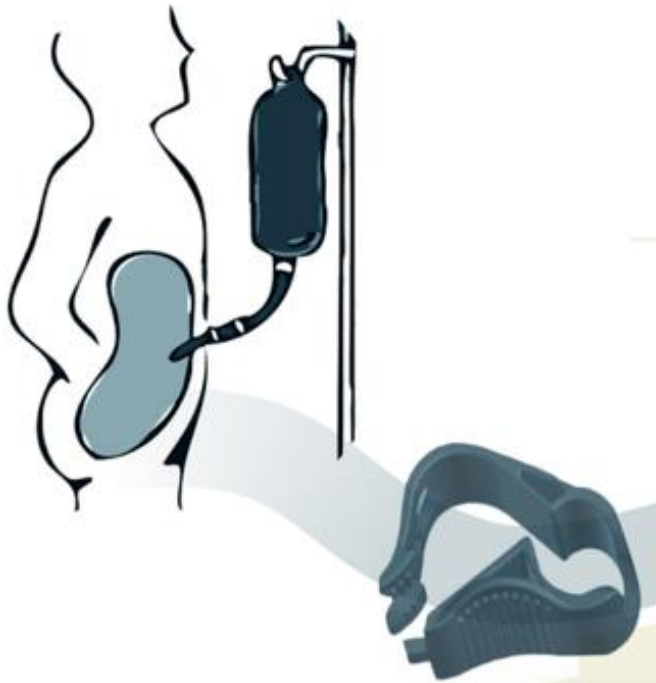
Contamination of PD system

Dry contamination: contamination of a closed PD system

Wet contamination: contamination with an open system

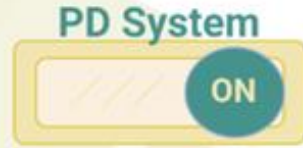
IP prophylactic antibiotics recommended for all wet contaminations

PD PERITONITIS : WET vs DRY CONTAMINATION



Dry contamination
- outside a closed PD system
- disconnection distal to a closed clamp

Wet contamination
- open system
- contaminated dialysis fluid is infused



Examples:
- leaks from dialysate bags
- leaks or breaks in tubing proximal to the tubing clamp
- catheter administration set was left open for an long period
- breach of aseptic technique

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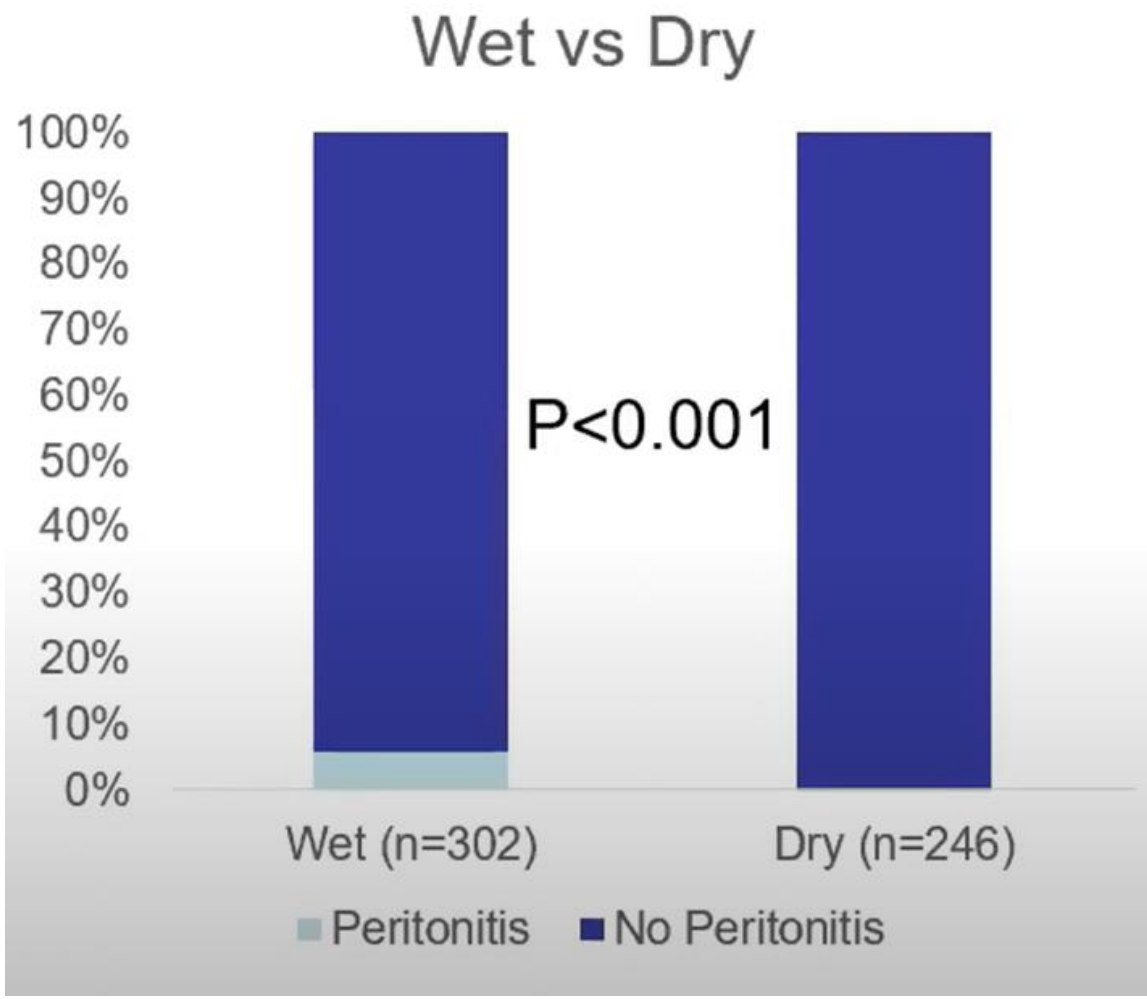
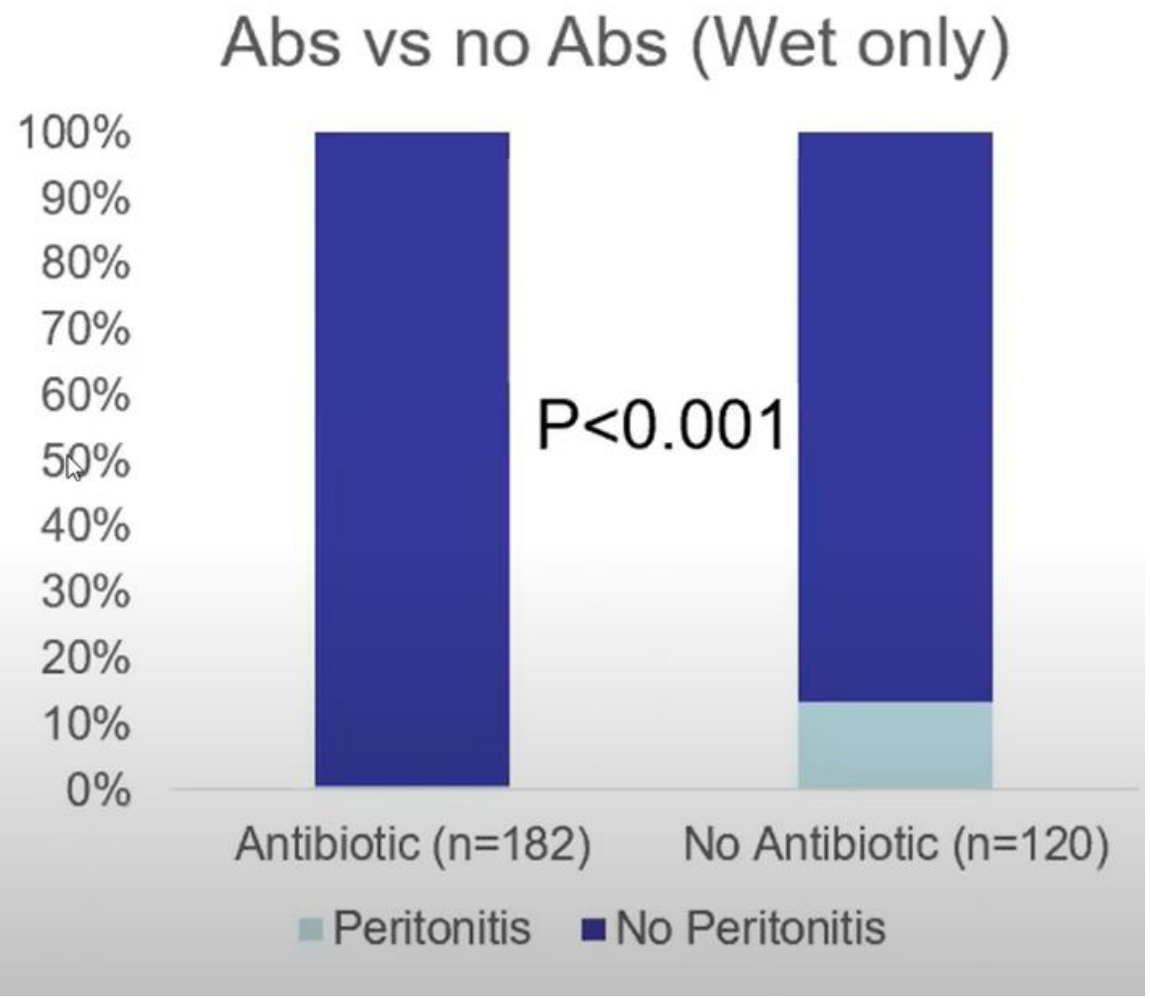




Wet contamination resulted in peritonitis 3.1% of time

Yap et al Peritoneal Dialysis 2012

Modifiable risk factors

We suggest that avoidance and treatment of hypokalemia may reduce the risk of peritonitis [2C].

We suggest that avoiding or limiting the use of histamine-2 receptor antagonists may prevent enteric peritonitis [2C].

Low Serum Potassium Levels and Clinical Outcomes in Peritoneal Dialysis (PD) - International Results from PDOPPS

STUDY POPULATION/METHODS

- 7421 PD patients
- 7 Countries
- 2014-2017
- Baseline serum potassium (K)
- Logistic Regression - Factors associated with serum K <4 mEq/l
- Cox regression - Impact of serum K levels on peritonitis and mortality

FINDINGS

38%
K< 4 mEq/l

Hypokalemia Risk Factors

- Lower urine volume
- Lower blood pressure
- Higher dialysis dose
- Greater diuretic use
- Not on renin-angiotensin system inhibitor
- Protein energy wasting factors: lower body mass index, serum albumin, phosphorus, and urea

Hypokalemia Consequences

80% higher peritonitis (K<3.5 mEq/l)

40% higher mortality (K<4.0 mEq/l)

CONCLUSION:
Hypokalemia was associated with markers of protein energy wasting, higher mortality, and peritonitis even after extensive adjustment for patient factors among patients receiving PD.

KI REPORTS
KIReports.org
Davies et al, 2021

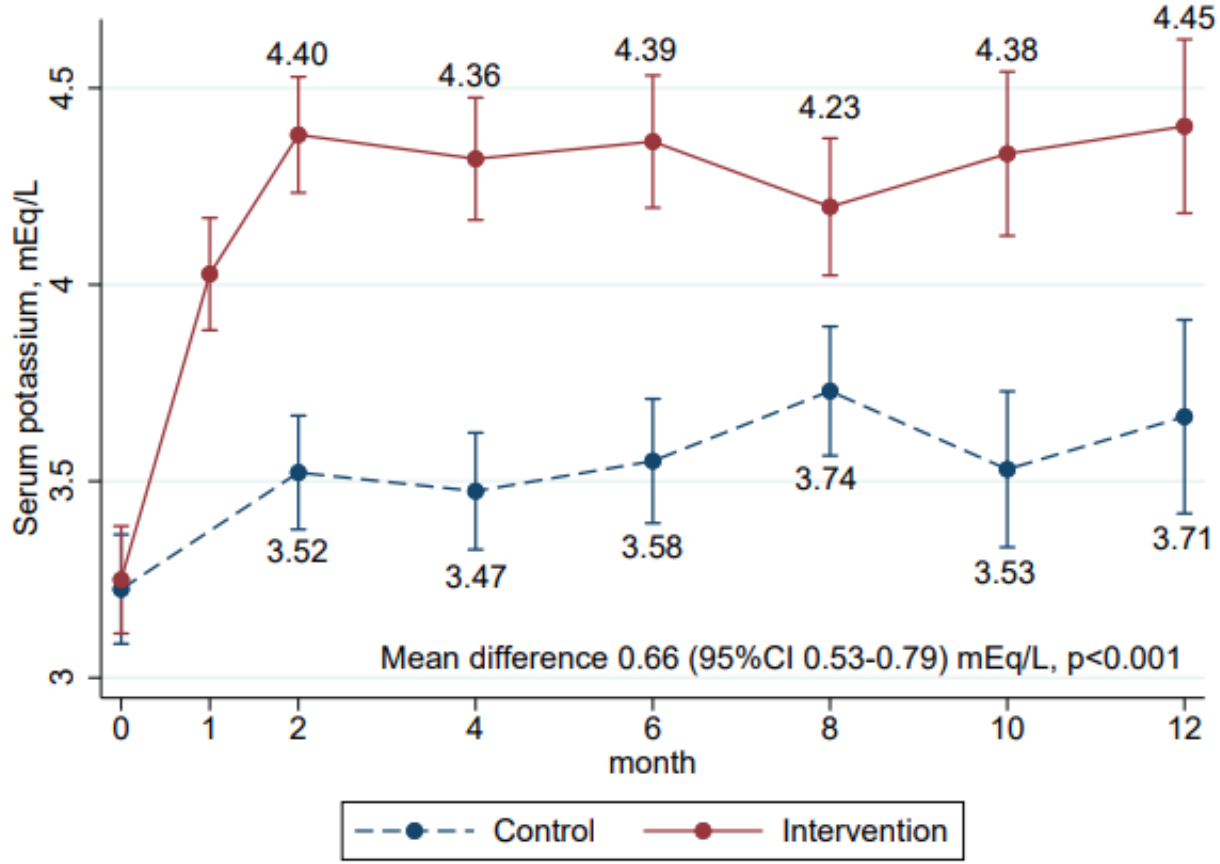
Hypokalemia and peritonitis

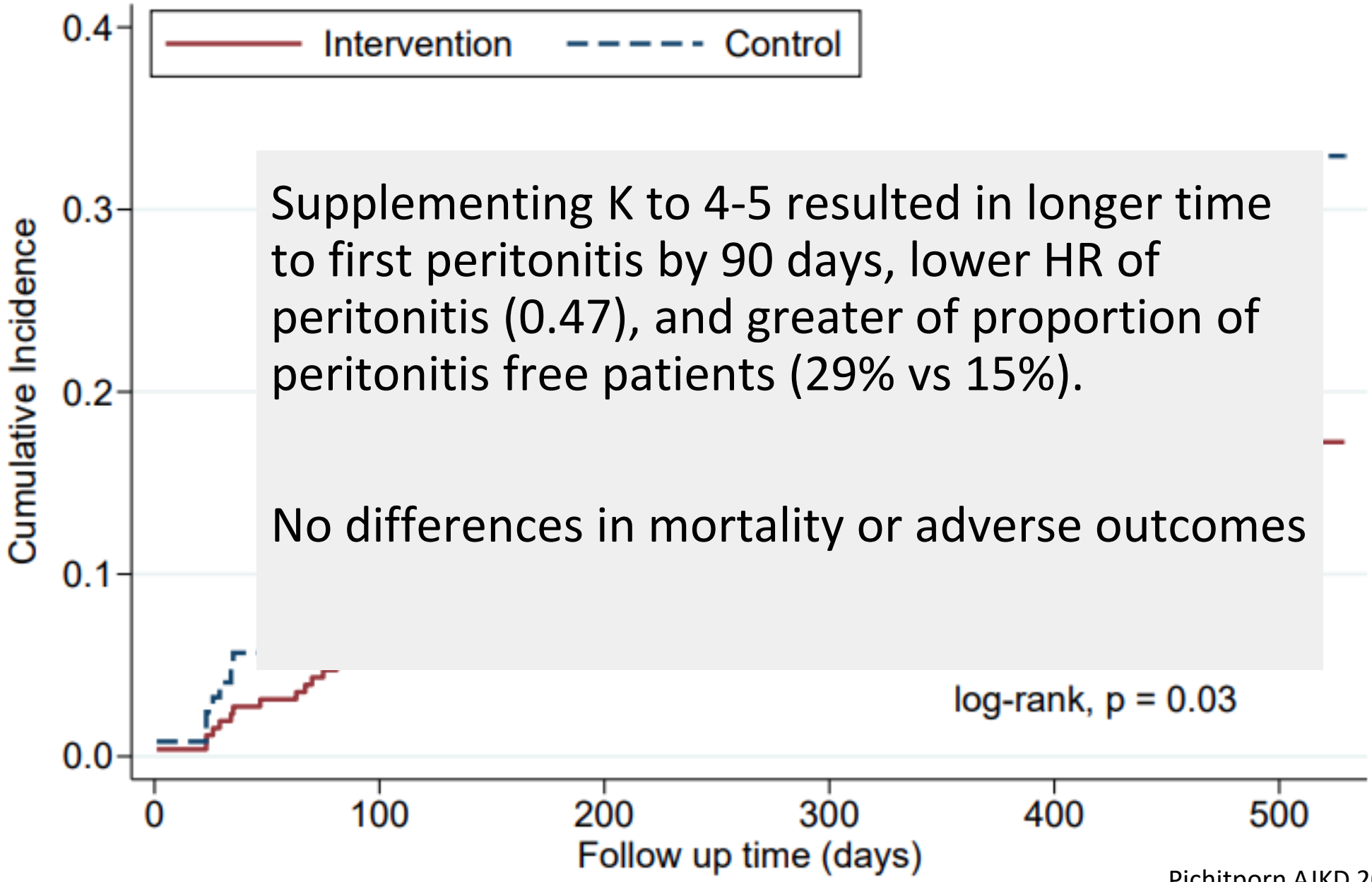
Thai study N = 167

Open RCT

Control: supplement when K <3.5

Intervention: supplementation to maintain K 4-5





Supplementing K to 4-5 resulted in longer time to first peritonitis by 90 days, lower HR of peritonitis (0.47), and greater of proportion of peritonitis free patients (29% vs 15%).

No differences in mortality or adverse outcomes

Pichitporn AJKD 2022

H2 antagonists

Meta-analysis suggested H2 blockers associated with increased risk for enteric peritonitis

Causality is questionable?

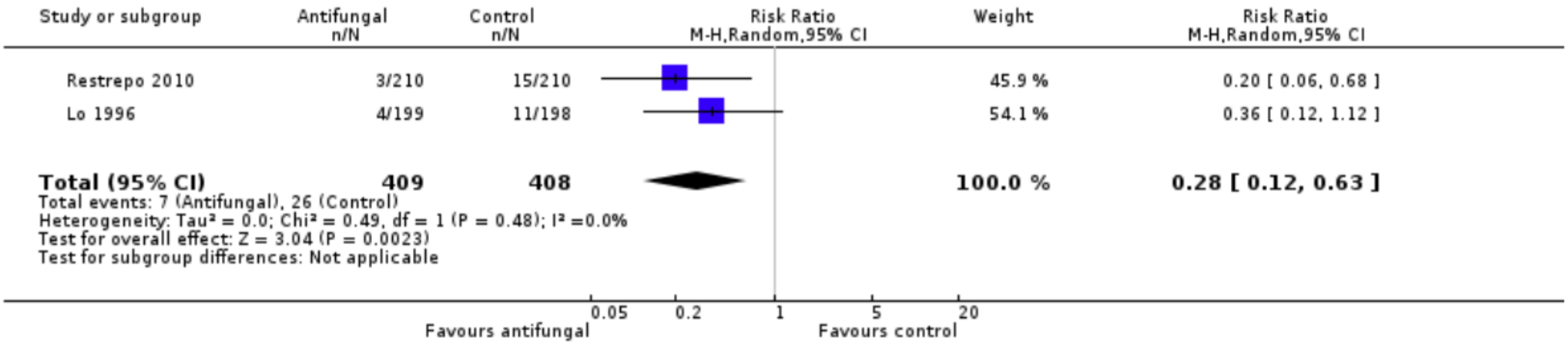
Those on PPI did not have higher risk of enteric peritonitis

Fungal prophylaxis

To prevent fungal peritonitis, we recommend that anti-fungal prophylaxis be co-prescribed whenever PD patients receive an antibiotic course, regardless of the indication for that antibiotic course [1B].

Nystatin (500,000 units PO qid) or fluconazole (200 mg PO q48h)

Review: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients
Comparison: 10 Antifungal versus placebo/no treatment
Outcome: 1 Fungal peritonitis (number of patients with one or more episodes)



Campbell et al Cochrane Database of Systematic Reviews 2017

Summary

ISPD peritonitis definition

Cause specific

- Organism
- Culture Neg
- Catheter-related
- Enteric

Time specific

- Catheter insertion
- Pre-PD
- PD

Outcome specific

Cure, refractory, recurrent, relapsing, repeat, HD transfer, catheter removal, death

New Targets

- Aim <0.4 epi/patient yr
- Culture Neg less than 15%
- % peritonitis free >80%/yr
- Cath insertion peritonitis <5%

Prevention

- Wet contamination IP Abx
- Treat hypoK
- H2 antagonists?

Antibiotic management

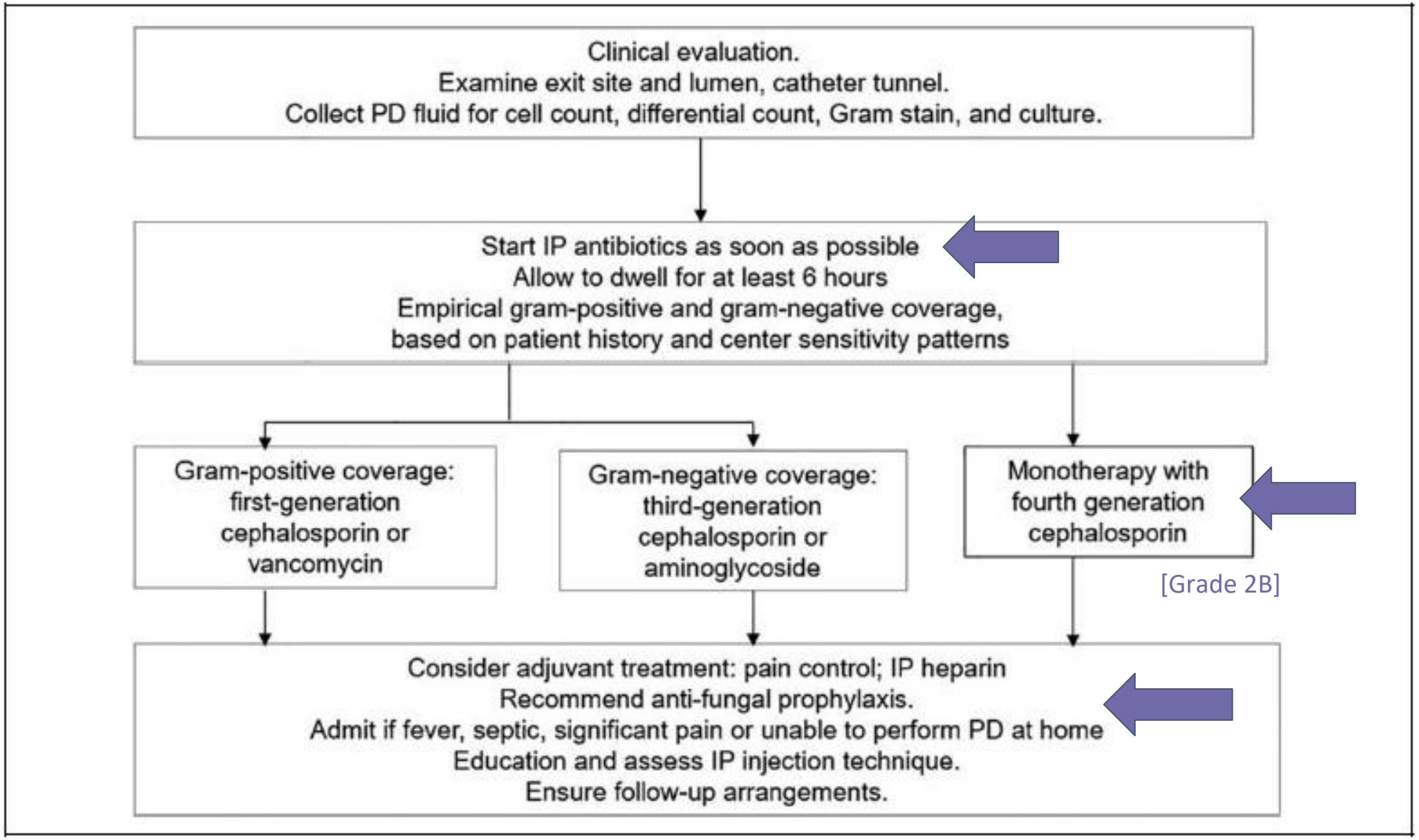


Figure 1. The algorithm of initial management for PD patients presenting with a clinical diagnosis of peritonitis. PD: peritoneal dialysis.

Prompt empiric antibiotic treatment

Prospective multicentre study (Australia) of 159 episodes

- The contact-to-treatment time was independently associated with treatment failure
- Each hour of delay in administering antibiotic therapy from the time of presentation to a hospital facility, the risk of PD failure or death was higher by 5.5%

Retrospective study of 109 episodes

- 24 h delay in administering antibiotics conferred a 3-fold risk of peritoneal catheter removal by multivariate analysis

Muthucumarana K et al. Kidney Int Rep 2016; 1(2): 65–72.
Oki R et al. Sci Rep 2021; 11(1): 6547.

Cefepime coverage

- 4th generation cephalosporin
- Broad-spectrum: Gram+, Gram- (including Pseudomonas)
  - ➢ Does not cover Coagulase negative Staph
- Less likely to induce β-lactamase producing strains

	Enterococcus	MSSA	Coag -ve Staph (S)	S. epidermidis (S)	Strep	Citrobacter/ Enterobacter	P. aeruginosa
Cefazolin	0	+	+	+	+	0	0
Ceftazidime	0	0	0	0	+	0	+
Cefepime	0	+	0	+	+	+	+

The Sanford Guide to Antimicrobial Therapy 2022; 52nd Edition.

Cefepime

- Elimination half-life
  - Adults: 2 h
  - HD: 13.5 h; PD: 19 h
- Excretion: urine (85% as unchanged drug)
- Formulary status: restricted for chemotherapy induced febrile neutropenia OR cystic fibrosis
- Daily cost
  - Hospital: $25 (cefepime 2 g vial) vs. $13.74 (total for cefaz + ceftaz)
  - Calea: $10.96 (cefepime 2 g PFS) vs. $7.84 + $11.77 (cefaz 2 g PFS + ceftaz 2 g PFS, respectively)

The Sanford Guide to Antimicrobial Therapy 2022; 52nd Edition.

Cefepime monotherapy

Wong et al. 2001	Li et al. 2000	Kitrungphaiboon et al. 2019
Prospective, open-label, RCT (Hong Kong) N = 39 (Group A) and 34 (Group B)	Prospective, noncontrolled, nonrandomized trial (Hong Kong) N = 87	Multicentre, open-label, non-inferiority RCT (Thailand) N = 70 (mono) and 74 (combo)
Grp A: cefepime 2 g IP loading dose, then 1 g IP daily x 9 days Grp B: vancomycin IV + netilmicin IP	Cefepime 2 g IP loading dose, then 250 mg per exchange. If no clinical response by day 5, review therapy.	Cefepime 1 g IP loading dose, then 250 mg IP per exchange Cefazolin + ceftazidime (same dosing)
Similar overall microbiological response rates. Failure for Pseudomonas in both groups.	Primary response: 80.5% - Gm+: 83.7% - Gm-: 64.7% (Pseudomonas 37.5%) Complete cure: 67.8%	Primary response: 82.6% vs. 81.1% Complete cure: 80% vs. 80.6% Conclusion: cefepime IP is non-inferior to cefazolin+ceftazidime
No significant ADRs reported. 1 pt reported instillation pain with cefepime requiring discontinuation.	1 pt reported epigastric pain, vomiting and vertigo requiring discontinuation. 3 pts reported GI upset.	1 pt in each group developed maculopapular rash. 5 deaths (mono) and 2 deaths (combo)

IP antibiotic doses

Table 5. IP antibiotic dosing recommendations for treatment of peritonitis.

Antibiotic	Intermittent (1 exchange daily for at least 6 h)	Continuous (all exchanges)
Aminoglycosides		
Amikacin	2 mg/kg daily[173]	Not advised
Gentamicin	0.6 mg/kg daily[174,175]	Not advised
Netilmicin	0.6 mg/kg daily[165]	Not advised
Tobramycin	0.6 mg/kg daily	Not advised
Cephalosporins		
Cefazolin	15 mg/kg daily (for long dwell)[176,177] 20 mg/kg daily (for short dwell)[178,176]	LD 500 mg/L, MD 125 mg/L[d] [168,179]
Cefepime	1000 mg daily	LD 500 mg/L, MD 125 mg/L[d] [168]
Cefoperazone	No data	LD 500 mg/L, MD 62.5–125 mg/L[180]
Cefotaxime	500–1000 mg daily[181]	no data
Ceftazidime	1000–1500 mg daily (for long dwell) 20 mg/kg daily (for short dwell)[178]	LD 500 mg/L, MD 125 mg/L[d] [168,182]
Ceftriaxone	1000 mg daily[183]	No data
Penicillins		
Penicillin G	No data	LD 50,000 unit/L, MD 25,000 unit/L[13]
Amoxicillin	No data	MD 150 mg/L[184]
Ampicillin[a]	4 gm daily[185]	MD 125 mg/L[186]
Ampicillin/sulbactam		LD 1000 mg/500 mg, MD 133.3 mg/66.7 mg[187,188]
Piperacillin/tazobactam	No data	LD 4 gm/0.5 gm, MD 1 gm/0.125 gm[189]
Ticarcillin/clavulanic acid	No data	LD 3 gm/0.2 gm, MD 300 mg/20 mg/L[190]
Others		
Aztreonam	2 gm daily[191]	LD 500 mg/L[192], MD 250 mg/L[192,193]
Ciprofloxacin	No data	MD 50 mg/L[194]
Clindamycin	No data	MD 600 mg/bag[195]
Daptomycin	300 mg daily[196]	LD 100 mg/L[197,198,199], MD 20 mg/L[197,200]
Fosfomycin	4 g daily[201,202]	No data
Imipenem/cilastatin	500 mg in alternate exchange[203]	LD 250 mg/L, MD 50 mg/L[182]
Ofloxacin	No data	LD 200 mg, MD 25 mg/L[204]
Polymyxin B	No data	MD 300,000 unit (30 mg)/bag[188]
Quinupristin/dalfopristin	25 mg/L in alternate exchanges[b205]	No data
Meropenem	500 mg daily (for long dwell in APD)[207] 1000 mg daily (for short dwell in CAPD)[208,209]	MD 125 mg/L[206]
Teicoplanin	15 mg/kg every 5 days[210]	LD 400 mg/bag, MD 20 mg/L[211,140]
Vancomycin	15–30 mg/kg every 5–7 days[c141,212] for CAPD 15 mg/kg every 4 days[213] for APD	LD 20–25 mg/kg, MD 25 mg/L[214]

IP antibiotic doses

Cefazolin

- 15 mg/kg daily (for long dwell): CAPD; 6 h minimum
- 20 mg/kg daily (for short dwell): APD 10 h, no last dwell; added to 1st 5L bag

Ceftazidime

- 1000-1500 mg daily (for long dwell): CAPD; 6 h minimum
- 20 mg/kg daily (for short dwell): APD 10 h, no last dwell; added to 1st 5L bag

Meropenem

- 500 mg daily (for long dwell in APD): daytime dwell 15 h followed by APD
- 1000 mg daily (for short dwell in CAPD): CAPD; 6 h minimum

Vancomycin

- 15-30 mg/kg q5-7d for CAPD and 15 mg/kg q4d for APD
- Dosing will vary by site practices

Systemic antibiotic doses

Table 6. Systemic antibiotic dosing recommendations for treatment of peritonitis.

Drug	Dosing
Antibacterial	
Amoxicillin	Oral 500 mg thrice daily[219]
Ciprofloxacin	Oral 500–750 mg daily[220]
	Oral 750 mg BD for CCPD[221]
Clarithromycin	Oral 250 mg BD[222,223]
Colistin	IV 300 mg loading (for critically ill patients), then 60–200 mg daily[b224-226]
Dalbavancin	IV 1500 mg over 30 min single dose[227]
Daptomycin	IV 4–6 mg/kg every 48 h[228]
Ertapenem[a]	IV 500 mg daily[229]
Levofloxacin	Oral 250 mg daily[230] or 500 mg every 48 h
Linezolid	IV or oral 600 mg BD[231,232] for 48 h, then 300 mg BD[233]
Moxifloxacin	Oral 400 mg daily[234,235]
Rifampicin	Oral or IV 450 mg daily for BW <50 kg; 600 mg daily for BW ≥50 kg
Ticarcillin/clavulanic acid	IV 3 gm/0.2 gm every 12 h
Tigecycline	IV 100 mg loading, then 50 mg every 12 h[236,237]
Trimethoprim/sulfamethoxazole	Oral 160 mg/800 mg BD[238,239]
Anti-fungal	
Amphotericin B desoxycholate	IV 0.75–1.0 mg/kg/day over 4–6 h[240]
Amphotericin B (liposomal)	IV 3–5 mg/kg/day[241,242]
Anidulafungin	IV 200 mg loading, then 100 mg daily[243,244]
Caspofungin	IV 70 mg loading, then 50 mg daily[243]
Fluconazole	Oral 200 mg loading, then 100 mg daily[240]
Flucytosine	Oral 1 gm daily[240]
Isavuconazole	Oral or IV 200 mg every 8 h for 6 doses (48 h) loading, then 200 mg daily
Micafungin	IV 100 mg daily[243,245]
Posaconazole	Oral tablet 300 mg every 12 h loading for two doses, then 300 mg daily[246]
Voriconazole	Oral 200 mg every 12 h

BD: twice a day; IV: intravenous; BW: body weight.

[a]Ertapenem is not active against *Pseudomonas* or *Acinetobacter* species.

[b]Expressed as colistin base activity in mg.

IP antibiotic stability

Table 7. Summary of IP antibiotics stability.

Antibiotics	PD solutions: Dextrose-based	PD solutions: Icodextrin- based	Stability	Storage conditions: Room temperature	Storage conditions: Under refrigeration	Remarks[a]: Tested for	Remarks[a]: Stable for
Gentamicin	✓		14 days	✓	✓	14 days	
		✓	14 days	✓	✓	14 days	
Cefazolin	✓		8 days	✓			8 days
	✓		14 days		✓	14 days	
		✓	7 days	✓			7 days
		✓	14 days		✓	14 days	
Ceftazidime	✓		4 days	✓			4 days
	✓		7 days		✓		7 days
		✓	2 days	✓			2 days
		✓	14 days		✓	14 days	
Cefepime	✓		14 days		✓	14 days	
Vancomycin	✓		28 days	✓		N/A	
		✓	14 days	✓	✓	14 days	
Piperacillin/ tazobactam + Heparin	✓	✓	7 days		✓	7 days	

PD: peritoneal dialysis.
[a]'Stable for X days' indicates that the antibiotic concentration retained at least 90% of its initial concentration up to day X. 'Tested for X days' indicates the antibiotic concentration retained at least 90% of its initial concentration up to the study duration set for X days only.
Stability (Stable for X days) is interpreted according to the type of PD solutions and storage conditions specified.

Clinical Kidney Journal

Stability and compatibility of antibiotics in peritoneal dialysis solutions

Comprehensive review of stability and compatibility studies relating to intraperitoneal (IP) antibiotic administration in different peritoneal dialysis (PD) solutions under various storage conditions

Methods

Literature review
2016–2021

Use of IP antibiotics in different solutions:

- Dextrose
- Icodextrin
- pH neutral

Results

Stability of antibiotics in various PD solutions

	PD solution	Room temperature	Refrigerated
Gentamicin	Icodextrin	14 days	14 days
Cefazolin	Icodextrin	7 days	14 days
Ceftazidime	Icodextrin	2 days	14 days
Cefepime	pH-neutral (bicarbonate component)	4 days	7 days
Vancomycin	Icodextrin	14 days	14 days

Compatibility of antibiotics for IP administration

	Gentamicin	Ceftazidime	Cefazolin	Vancomycin
Gentamicin		N/A	✓	✓
Ceftazidime	N/A		✓	✓
Cefazolin	✓	✓		N/A
Vancomycin	✓	✓	N/A	

The stability data of other antibiotics, including amoxicillin, ampicillin, piperacillin/tazobactam, meropenem, imipenem and ciprofloxacin, were also reviewed.

Conclusion: The review provides an extended scope of antibiotic stability data for common antibiotics in PD solutions. Future research is required regarding the impact of administration of antibiotics in different compartments of dual-chamber bags, the stability data of antifungal agents and narrow-spectrum antibiotics in PD solutions.

So, SWY., et al.
Clinical Kidney Journal (2022)
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N-acetylcysteine

Adjunctive oral N-acetylcysteine (NAC) therapy may help to prevent aminoglycoside (AMG) ototoxicity [2B].

- Ototoxicity occurs with IP AMGs similar to systemic administration. The mechanism is incompletely understood.
  - Genetic predisposition (mitochondrial DNA mutations)
  - Production of free radicals causing cochlear hair cell damage
- Proposed NAC mechanism: thiol-containing antioxidant
- Oral NAC ADRs: abdominal pain, nausea, diarrhea, arthralgia

Fu, X et al. Front Cell Neurosci. 2021;15:692762.

Table 1 Studies investigating the effect of NAC in preventing aminoglycoside-induced ototoxicity

Author, year	Condition	AG	N	N (NAC)	N (P)	NAC dose	Duration of NAC	Duration of AG	Cumulative dose, g	N hearing loss (NAC)	N hearing loss (P)	Risk ratio hearing loss (95% CI)	Mean hearing loss, dB (NAC), early	Mean hearing loss, dB (P), early	Mean hearing loss, dB (NAC), late	Mean hearing loss, dB (P), late
Feldman, 2007[14]	Haemodialysis, sepsis	Gentamicin	53*	20	20	600 mg twice daily	For the duration of gentamicin therapy until 1 week after completing therapy	14.8±3.8 (NAC) 14.3 ±5.8 (P)	0.68 (NAC) 0.69 (P)	2†	11†	0.26 (0.06 to 1.04)	2.0±3.8‡	5.8±5.1‡	2.1±5.2§	7.0±8.2§
Tokgoz, 2011[16]	CAPD peritonitis	Amikacin	60	30	30	600 mg twice daily	For the duration of amikacin therapy		1.5 (NAC) 1.25 (P)	1¶	21¶	0.08 (0.01 to 0.55)	−4.7±7.4**	5.4±8.6**	-6.0±8.9††	16.9±8.1††
Kocyigit, 2014‡‡[17]	CAPD peritonitis	Amikacin	50§§	23	23	600 mg twice daily	2 weeks	9 (4–20) (NAC) 8 (4–21) (P)	1.5 (NAC) 1.2 (P)							

*In the NAC group, 1 died, 3 had airborne discrepancies, 2 were unable to cooperate; in the placebo group, 2 died, 3 had airborne discrepancies, 1 was unable to cooperate, 1 withdrew consent.
†6 weeks after completing gentamicin therapy.
‡1 week after completing gentamicin therapy, at frequencies 6000, 8000, 12 000 Hz.
§6 weeks after completing gentamicin therapy, at frequencies 6000, 8000, 12 000 Hz.
¶4 weeks after starting amikacin therapy.
**1 week after starting amikacin therapy, at frequency 10 000, 12 000, 14 000, 16 000 Hz.
††4 weeks after starting amikacin therapy, at frequency 10 000, 12 000, 14 000, 16 000 Hz.
‡‡No measurement of pure-tone average hearing threshold, but measurement of transient-evoked otoacoustic emissions and distortion-product otoacoustic emissions.
§§In the NAC group, 1 withdrew consent, 1 dropped out; in the placebo group, 1 died, 1 withdrew consent.
AG, aminoglycoside; CAPD, continuous ambulatory peritoneal dialysis; NAC, *N*-acetylcysteine; P, placebo.

- Studies assessed high-frequency hearing function
- None of the trials assessed vestibular function
- Pooled relative risk for otoprotection at 4 to 6 weeks was 0.14 (95% CI 0.05 to 0.45)
- Overall quality of evidence rated as low/very low (risk of bias and heterogeneity)

Kranzer et al. Thorax 2015;70(11):1070-77.

N-acetylcysteine

- Data based on small studies, high risk of potential bias
- Reasonable to consider co-administration of NAC 600 mg PO BID for duration of AMG in select patients
  - ➢ ? prolonged duration of therapy (e.g., TB therapy)
  - ➢ ? multiple courses of AMGs
  - ➢ ? history of hearing loss

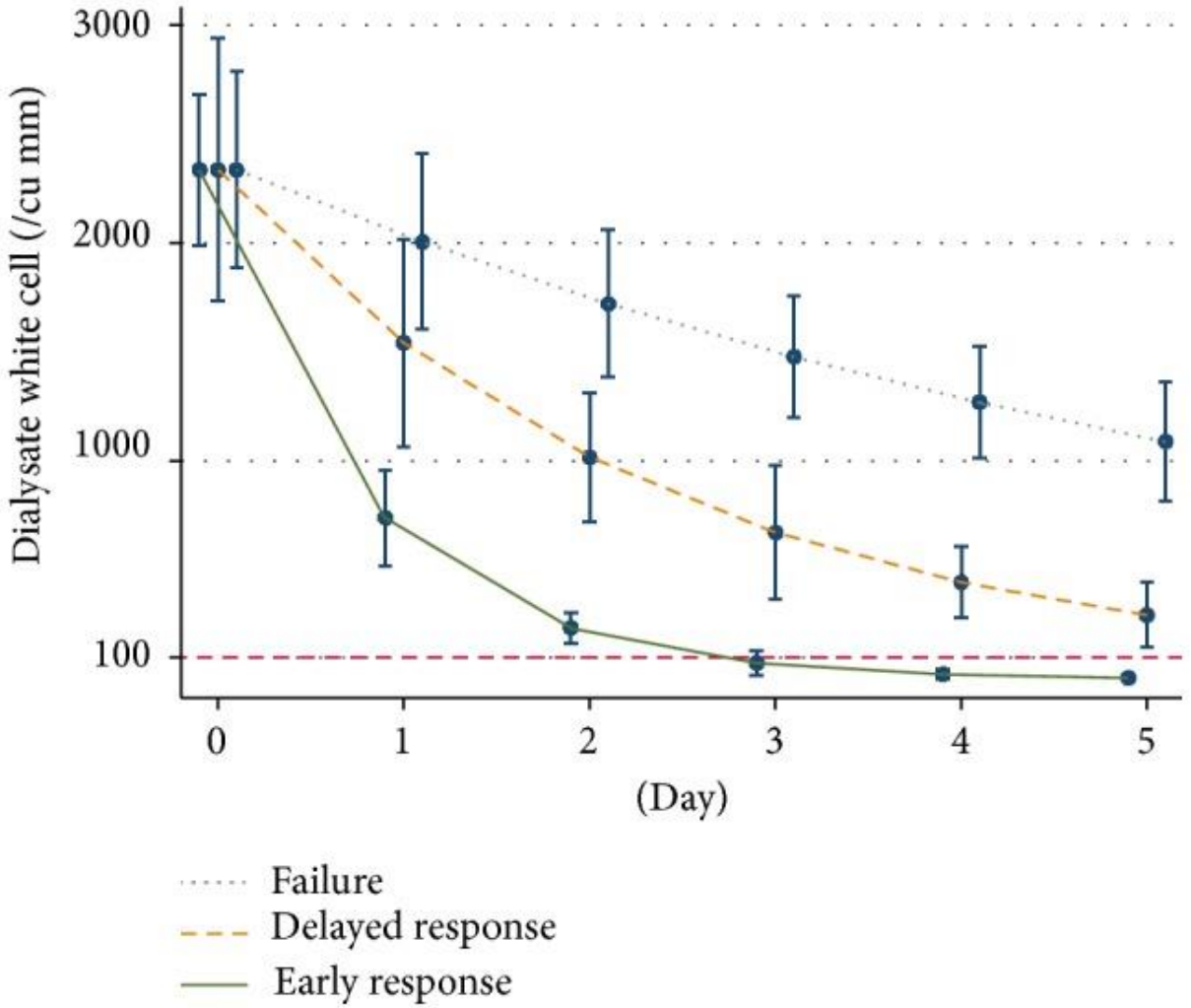
Bottom-line: avoid prolonged use of AMGs; intermittent daily dosing preferred over continuous dosing

Kranzer et al. Thorax 2015;70(11):1070-77.

Refractory peritonitis

- We recommend that PD catheter be removed in refractory peritonitis episodes, defined as failure of the PD effluent to clear after 5 days of appropriate antibiotics [1D].
- We suggest that observation for antibiotic effect longer than 5 days is appropriate if PD effluent white cell count is decreasing towards normal, instead of mandatory PD catheter removal if effluent does not clear up by day 5 [2C].

Refractory peritonitis

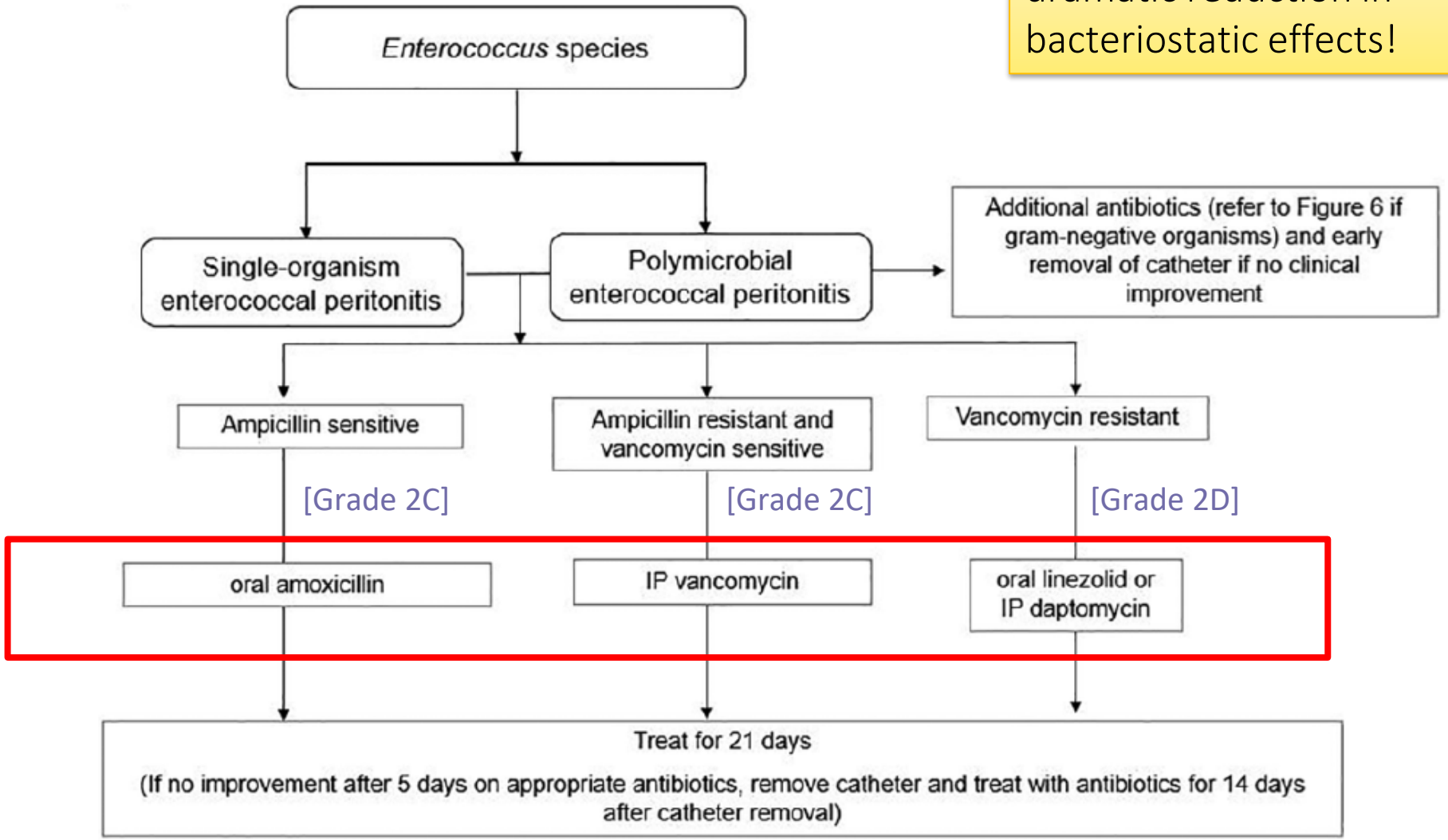


In one-fifth of the cases, patients showed delayed response with 34% reduction of effluent white cell count by day 5, without the need for PD catheter removal.

Tantiyavarong et al. Int J Nephrol. 2016; 2016: 6217135.

Enterococcus peritonitis

Do <u>not</u> use **intraperitoneal ampicillin** or **linezolid** → dramatic reduction in bacteriostatic effects!



Oral amoxicillin

105 episodes of Enterococci peritonitis; 67 mixed bacterial growth; 38 single organism.

The overall primary response rate to PO amoxicillin and IP vancomycin was 76.4% and 85.5%, respectively (p = 0.3).

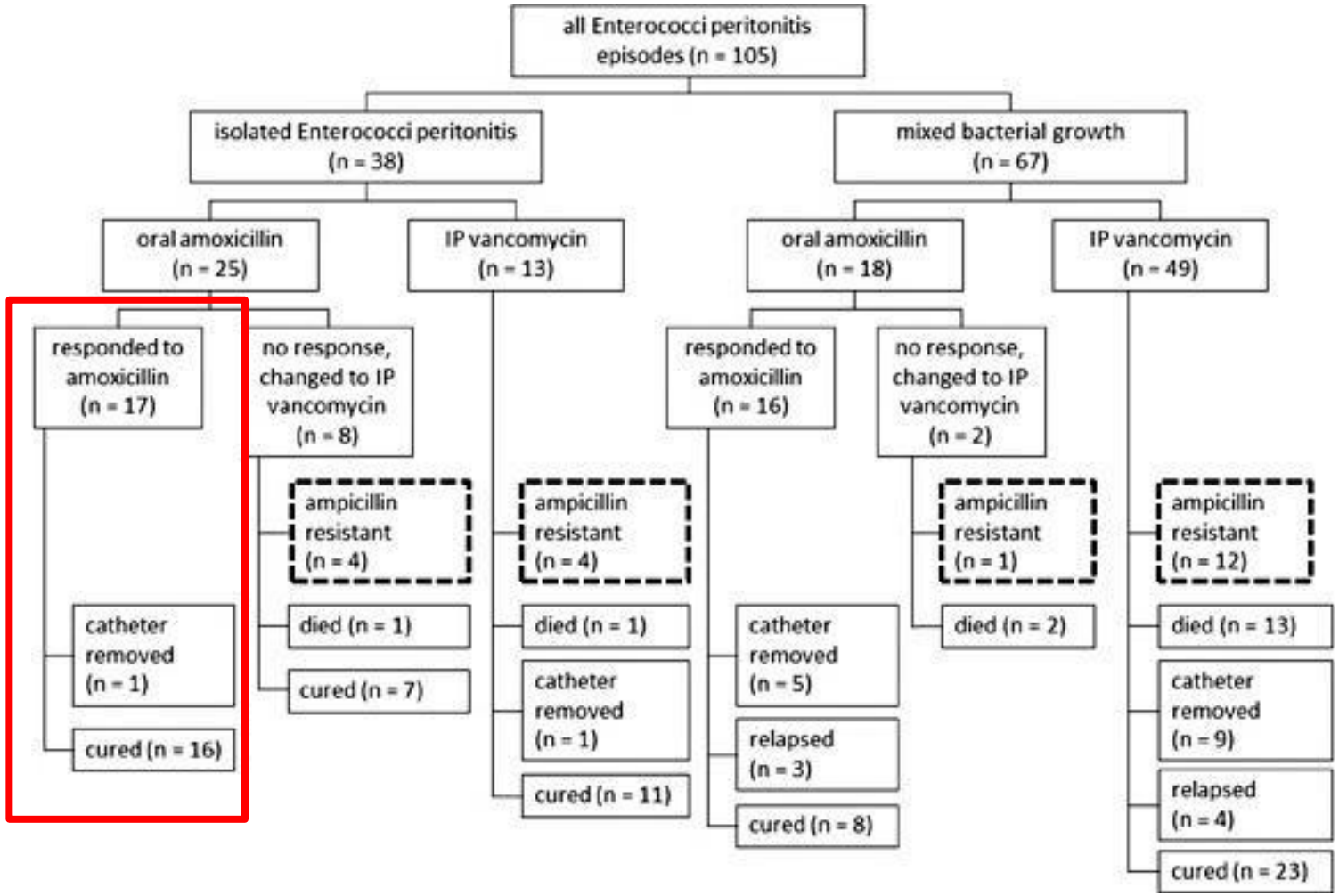
- Primary response: resolution of abdominal pain, clearing of dialysate, and PDE neutrophil <100/ml on day-10 with antibiotics alone.

The complete cure rate of PO amoxicillin and IP vancomycin was 55.8% and 54.8%, respectively (p = 0.8).

- Complete cure: complete resolution of peritonitis by antibiotics alone without relapse or recurrence within 4 weeks of completion of therapy.

Szeto CC et al. Kidney Blood Press Res (2018) 42 (5): 837–843.

Oral amoxicillin



Szeto CC et al. Kidney Blood Press Res (2018) 42 (5): 837–843.

Pseudomonas peritonitis

- We suggest that Pseudomonas peritonitis be treated with 2 antibiotics with different mechanisms of action and to which the organism is sensitive for 3 weeks [2C].
- We suggest that Pseudomonas peritonitis with concomitant exit-site and tunnel infection be treated with catheter removal [2D].
- If there is no clinical response after 5 days of effective antibiotic treatment, we suggest that Pseudomonas peritonitis be treated with early catheter removal instead of using three antibiotics as an attempt to salvage [2D].

Pseudomonas dual coverage?

Retrospective study of 191 Pseudomonas peritonitis episodes (Australia)

- Episodes treated with 2 anti-Pseudomonal agents were significantly less likely to require permanent HD vs monotherapy (10 vs. 38%; P = 0.03)
  - Majority of single agent used was ciprofloxacin; dosing not reported
  - Resistance rates not reported
- No difference in rates of relapse, hospitalization, catheter removal or death

Retrospective study of 153 Pseudomonas peritonitis episodes (HK)

- No difference in complete cure rate between episodes treated with 3 and 2 antibiotics (47.06 vs. 51.58%; P = 0.4)
- Dual antibiotic therapy used was ceftazidime + gentamicin in 83.7% of cases
  - Resistance in study: 20.9% to ceftazidime, 11.8% to gentamicin and 3.3% to both
  - FH resistance: 10% to ceftazidime and 3-4% to gentamicin

Siva, B et al. Clin J Am Soc Nephrol 2009;4(5):957-64.
Lu, W et al. PLoS ONE 13(5):e0196499.

Other notable updates

- New sections on management of Acinetobacter, Stenotrophomonas maltophilia and other Enteric gram-negative bacteria peritonitis
- Updates to management of Mycobacterium tuberculosis peritonitis, as well as updated recommendations for anti-TB antibiotic dosing
- Updates to management of non-tuberculous mycobacterial peritonitis

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Questions?