FROM THE EDITORS

The 2016 ISPD Update on Prevention and Treatment of Peritonitis—Grading the Evidence

In this issue of *Peritoneal Dialysis International (PDI)* we publish the 2016 International Society for Peritoneal Dialysis (ISPD) Update on Prevention and Treatment of Peritonitis (1). This is an important document, which differs from the 2010 peritoneal dialysis (PD)-related infection update (2) since it focuses exclusively on peritonitis, leaving exit-site and tunnel infection to a subsequent guideline. It includes a section dedicated to the prevention of peritonitis, where previously this formed a separate ISPD position statement (3).

The recommendations of the expert group are based as much as possible on existing evidence. To this end, the group reviewed the literature up to December 2015, citing 428 references. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach is used to rate both the quality of evidence and strength of clinical recommendations that are made based on that evidence (4). There are 4 levels of evidence – high (A), moderate (B), low (C), and very low (D) (definitions presented in Table 1); with the strength of the recommendation being either level 1 (“we recommend”), or level 2 (“we suggest”).

The strength of a clinical recommendation is based on the trade-off between benefits, on the one hand, and risks, costs, and potential harms on the other. To illustrate this approach, the GRADE group present scenarios on their website (5). An example that they give of a strong clinical recommendation is the use of short-term aspirin after myocardial infarction since the relative risk of death is reduced by 25% and it is likely that virtually all patients in this situation would choose to have the aspirin. A weaker recommendation would be given where risks, benefits, and burden are more finely balanced—here the GRADE group use as an example the continuation of warfarin beyond 1 year in an individual who has had a single idiopathic deep venous thrombosis. The intervention is burdensome and the reduction in risk (approximately 10% in this case) is not marked.

It is instructive to explore how this system influenced recommendations within the guideline (summarized in Table 2). There are only 2 statements within in the guideline that are accorded the 1A rating—i.e. that the practice is both recommended and that the evidence is of the highest quality. These are both in the area of prevention of peritonitis: the first relates to the use of systemic prophylactic antibiotics immediately prior to catheter insertion, and the second relates to

TABLE 1
GRADE Definitions of the Quality of Evidence (4)

Evidence level	Definition
High (A)	Further research is very unlikely to change our confidence in the estimate of effect
Moderate (B)	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low (C)	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low (D)	Any estimate of effect is very uncertain.

TABLE 2
Frequency of Levels of Grading Used in the 2016 Peritonitis Guideline

Recommendation	Evidence level	Frequency
1	A	2
1	B	4
1	C	18
1	D	0
2	A	0
2	B	1
2	C	18
2	D	8

the use of “flush before fill” disconnect systems for continuous ambulatory peritoneal dialysis (CAPD).

There are, however, several “recommendations” where the level of evidence is lower, for example 1B for topical antibiotic application to the catheter exit site as part of routine care. In this case, the evidence is robust for the prevention of exit-site infection (presumably would be assigned 1A), but for peritonitis prevention, the level of evidence is lower. The level of recommendation comes from the context—that the use of topical antibiotics to the exit site is inexpensive, easy to apply, and that resistance has not become a major issue to date. However, there are riders in the discussion, for example that *Pseudomonas* species may become relatively more common when prophylactic agents against *S. aureus* are used. Thus, it is important to read the commentary that is presented around

the supporting evidence in the guideline document in order to understand the rationale behind the classification of each statement.

The vast majority of statements (Table 2) were given evidence level C—i.e. low quality evidence, where “further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.” The use of continuous quality improvement programs to reduce peritonitis rates is graded 1C. This is an example of a common sense recommendation that one cannot imagine could be associated with harms. It is clearly logical to adopt quality improvement strategies, but there is a requirement to develop more robust evidence of impact. The impact of continuous quality improvement on peritonitis in Australia and New Zealand is explored in a commentary by Nataatmadja, Cho, and Johnson in this issue of *PDI* (6). A similar level of grading applies to the recommendations around the diagnosis of PD peritonitis and, indeed, the initiation of empirical antibiotic therapy once appropriate microbiological specimens have been obtained. These are, of course, standard approaches that have been widely adopted in the clinical practice of PD and have been of key clinical utility. Indeed, designing clinical trials in these areas seems impractical and may be unethical. However, practice should be subjected to quality improvement methodologies.

Throughout the infection guideline, the stronger “we recommend” is used for initial antibiotic therapy, route of administration, avoidance of prolonged courses of aminoglycosides, narrowing antibiotic spectrum according to sensitivity, and catheter removal for refractory peritonitis. The “we suggest” is largely reserved for the duration of antibiotic therapy.

Thus we can be fairly confident that current recommendations will change in the future as new evidence emerges—and to this point the expert group recommends themes for further research attention. These include more detailed examination of antibiotic pharmacokinetics and stability in PD solutions, techniques to identify organisms in biologic fluids more quickly, clinical trials of treatment regimens with a particular focus on automated PD (APD), as well as increasing evidence around patient training.

The 2010 PD infection guideline was translated into Spanish, Portuguese, French, and Chinese and is the most highly cited document in *PDI*, indicating its value to the clinical community. The 2016 update is essential reading for clinical teams, and the considerable effort and detailed attention that the expert group put into this work demand recognition. It is now time to incorporate these guidelines into clinical practice; to this end, the ISPD has made this document open access. I suggest that you download the document onto your portable electronic device so that you can access it when and where required. In this way, we can collaborate to reduce the second translation gap—that which exists between evidence and practice. Join the discussion through twitter (7), and be sure to tag @PDConnect so that your comments will appear on the *PDI* website, or post questions to the authors by submitting questions online via the *PDI* website (Figure 1).

Figure 1 — Submitting a response online at www.pdconnect.com

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