Peritoneal Dialysis International, Vol. 36, pp. 472–477
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COMMENTARIES

CONTINUOUS QUALITY IMPROVEMENT INITIATIVES TO SUSTAINABLY REDUCE PERITONEAL DIALYSIS-RELATED INFECTIONS IN AUSTRALIA AND NEW ZEALAND

BACKGROUND

Peritonitis represents a major factor limiting the uptake and retention of patients on peritoneal dialysis (PD) in Australia and New Zealand. Until recently, peritonitis was an all-too-frequent complication, with peritonitis rates static at approximately 0.6 – 0.75 episodes per patient-year for 15 years between 1994 and 2008 and 40% of Australian PD units and 60% of New Zealand PD units failing to meet the maximum acceptable peritonitis rate of 0.67 episodes per patient-year recommended by the 2005 International Society for Peritoneal Dialysis (ISPD) Guidelines (1). There was an extraordinary 10-fold variation in peritonitis rates between centers, predominantly associated with center-level characteristics (2). For every 100 patients experiencing peritonitis, 14 would experience a relapse, 22 would have their catheter removed, 18 would be permanently transferred to hemodialysis, and 3 would die (3). Peritonitis represented the second commonest cause of PD technique failure after death (4), and nearly 60% of Australian pre-dialysis patients indicated that they were concerned or very concerned about PD-related peritonitis (5).

In response to the seemingly entrenched and refractory nature of the peritonitis problem in Australia and New Zealand, a coordinated, multi-pronged approach has been undertaken by PD clinicians over the last decade to address this issue by (i) generating better evidence to inform peritonitis guidelines and clinical practice; (ii) improving translation of evidence and guidelines into clinical practice; and, (iii) improving peritonitis rates and outcomes through the establishment of continuous quality improvement (CQI) processes at local, state, and national levels. This review will outline the processes undertaken to achieve a sustained reduction in peritonitis rates in Australia and New Zealand over the last 5 years and the initiatives being put in place to ensure continued improvement.

BETTER EVIDENCE

An important maxim in quality assurance is that a problem cannot be managed if it cannot be measured. Consequently, any attempt to improve PD-related peritonitis is critically dependent on accurate collection of detailed peritonitis data. In many parts of the world, it is assumed that most PD units will assiduously undertake this task as a core clinical activity. However, a survey of Australian PD units undertaken by our group identified that one-third of units did not know their exit-site infection (ESI) rates and one-sixth did not know their peritonitis rates (6). The Australian and New Zealand Dialysis and Transplant (ANZDATA) Registry was relied upon by PD units as a major source for recording and reporting peritonitis rates, but, prior to 2003, only the dates of first peritonitis episodes and the number of peritonitis episodes during a survey period were collected.

In an attempt to address the peritonitis issue at a national level, a critical first step was establishing a comprehensive national peritonitis registry under the auspices of ANZDATA (in October 2003) to collect detailed information on all peritonitis episodes in all PD units, including information about dates, rates, microbiological causes, treatments, and outcomes. In order to ensure adequate PD unit buy-in, a compromise was struck to ensure collection of sufficient information to inform clinical practice but not so much that data collection became unduly burdensome, leading to drop-out. Consequently, data collection was limited to one A4 page (forms can be obtained at www.anzdata.org.au). Considerable groundwork was undertaken to engage units and, although contribution of data was voluntary, 100% participation was secured from the outset. Once the registry data matured over the next few years, a wealth of information was generated in relation to the predictors, treatment, and outcomes of all-cause and microorganism-specific peritonitis (7-15). Furthermore, novel risk factors were identified for peritonitis occurrence and outcomes, including living distantly from PD units (16), living in tropical climatic regions (17), seasonal periodicity (for particular organisms) (18), obesity (19), and onset of peritonitis on weekends (20). Return to PD following temporary hemodialysis transfer for severe peritonitis was not associated with inferior clinical outcomes compared with patients who had milder forms of peritonitis that remained on PD or who were transferred to hemodialysis permanently for severe peritonitis, suggesting that return to PD after peritonitis was a viable option for patients regardless of the cause or severity of their peritonitis (21). Poorer patient outcomes were observed when practices significantly deviated from evidence-based recommendations, such as use of 1 rather

than 2 antimicrobial agents for the treatment of *Pseudomonas* species peritonitis (22), failure to treat fungal peritonitis with both catheter removal and antifungal therapy (15), and failure to use anti-fungal prophylaxis when treating bacterial peritonitis with antibiotics (15,23). Data were generated to support the ISPD definitions of relapsed, recurrent, and repeat peritonitis (23,24), and the increased risk of mortality due to infection, cardiovascular causes, or dialysis withdrawal in the first month following peritonitis (25) has informed definitions of peritonitis-associated death in the 2016 ISPD Peritonitis Guidelines (26). More recently, the importance of variations in center practices and outcomes has been identified and reported, in which poor outcomes appeared to be driven predominantly by "center effects" rather than case mix (2).

Identification of modifiable PD center practices that are associated with better peritonitis rates and outcomes has been somewhat impeded by the limited depth of data collection in the ANZDATA registry. This issue has been addressed by Australia's strong participation in the design and conduct of the peritonitis component of the Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS) (27). The future outcomes of PDOPPS will hopefully include identification of practices and service organizations that deliver the optimal outcomes in the real-world setting to help inform policy decisions, direct future clinical trials in PD peritonitis, and implement standardized definitions and nomenclature to be used across the globe. Important questions being examined include the roles of exit-site care, patient retraining, and optimal intraperitoneal antibiotic regimen to treat peritonitis (27).

As the data generated by ANZDATA and PDOPPS are hypothesis-generating only, it is also important to generate high-quality evidence in the field of peritonitis and infection management through randomized controlled trials (RCTs) and systematic reviews. In 2005, Kidney Health Australia and the Australian and New Zealand Society of Nephrology endorsed and seed-funded the establishment of the Australasian Kidney Trials Network (AKTN) to conduct patient-focused, high-quality, high-impact, multi-center, multinational, investigator-initiated RCTs (28). Peritonitis prevention and management have been accorded priority status within this framework, and subsequent AKTN activity has generated important evidence that neutral-pH, ultra-low glucose degradation product (GDP) PD solutions may reduce peritonitis rates (29-31) and that nasal mupirocin is superior to exit-site standardized antibacterial honey as an infection prevention strategy (32,33). In light of the poor evidence regarding the impact of PD training on peritonitis rates (34), the AKTN has also now successfully secured seed funding to pilot the **T**argeted **E**ducation **A**pproa**CH** to improve **P**eritoneal **D**ialysis outcomes (**TEACH-PD**) RCT, a multi-center, multi-country, clustered-randomized trial evaluating the effect of a standardized training curriculum and approach versus usual care on a composite infectious end-point in incident PD patients.

Evidence generated from RCTs conducted by the AKTN and other groups has subsequently been incorporated into systematic reviews and meta-analyses by the Cochrane Kidney and Transplant Group (formerly known as the Cochrane Renal Group), based in Sydney since May 2000 (http://kidneyandtransplant.cochrane.org/). These reviews have identified important practices leading to improved peritonitis outcomes, including disconnect (Y-set and twin-bag) systems (35,36), topical antibiotic prophylaxis (37), pre-operative antibiotics prior to Tenckhoff catheter insertion (37), anti-fungal prophylaxis (37), intraperitoneal (rather than intravenous) administration of antibiotics during treatment of peritonitis (38), and PD catheter removal for refractory or relapsing peritonitis (38). These findings have been incorporated into the ISPD Guidelines (1,26,39,40).

BETTER TRANSLATION

Generating high-quality evidence and guidelines is no guarantee that PD units will incorporate these into their practice. It is currently recognized that 85% of research is avoidably wasted and only a minority of evidence is actually translated into clinical practice (41). In a recent editorial by Martin Wilkie, it was conceded that "whilst there is a clear need to improve the evidence around the delivery of peritoneal dialysis, there is an equal need to apply what is known more consistently" (42). It is important to recognize that inconsistent and generally poor adherence to guidelines will not necessarily be fixed by more research; instead, each unit must take responsibility for its own outcomes and conscientiously adopt an attitude and desire for improvement. Grol and Grimshaw discussed 3 basic issues which influence the uptake of evidence: attributes of the evidence, barriers and facilitators to changing practice, and effectiveness of dissemination and implementation strategies (43). Uptake may therefore be influenced by the strength of the evidence supporting the guidelines, but also by how the guidelines fit in with staff's own existing beliefs and values, how complex the recommendations are, and whether or not they would require further training or new skills (43).

In an attempt to better identify barriers and facilitators to antimicrobial prophylaxis in PD patients, the Kidney Health Australia Caring for Australasians with Renal Insufficiency (KHA-CARI) Steering Committee commissioned an implementation research project involving 8 PD units in Australia and New Zealand. Adherence to guideline recommendations was found to be highly variable, as were definitions used to count peritonitis and catheter-related infection episodes (44). Barriers to antimicrobial prophylaxis also varied considerably between units, leading to the need to construct process maps and customize specific implementation tools for individual units (such as prophylactic antibiotic checklists, patient wallet-sized cue cards for antifungal prophylaxis, emergency department flyers for antifungal administration, etc.).

Education has also been viewed as a key element in achieving better PD outcomes, as evidence has shown that units and clinicians with greater PD experience are associated with better PD patient outcomes (45–47). In recognition of the fact that experience with, and exposure to PD during nephrology training was highly variable and often inadequate, the

Australian and New Zealand PD Academy was established in 2009 and endorsed by the ISPD to provide an annual short-course targeted to training and newly qualified nephrologists in PD practice. In addition to this initiative, other strategies known to increase implementation of guidelines have been instituted, including reminders and feedback, educational outreach visits, multiprofessional collaboration, development of standardized peritonitis pathways, interactive small group meetings, media campaigns, use of technology, and financial incentives (Clinical Practice Improvement Payments) (43). Furthermore, a "Call to Action" paper was published in *Nephrology* in 2011 (48) in an attempt to draw clinicians' attention to the parlous state of PD practice and outcomes in Australia, including poor overall peritonitis rates and outcomes and unacceptably large between-center variations in practice and outcomes. Several recommendations were made across 5 key domains to try to improve outcomes by addressing: a) selection of appropriate patients for PD; b) prophylaxis and timely treatment of infectious complications; c) investigation of social causes of technique failure; d) provision of patient education and continuous support; and e) establishment of clinical governance and professional standards. Emphasis was also placed on the role of government and medical organizations to work together to establish minimum professional standards and key performance indicators (KPIs) for benchmarking, as well as to facilitate further PD research to improve levels of evidence.

BETTER QUALITY

Following bridging the evidence and translation gaps, the final platform of the coordinated strategy to improve PD practice and peritonitis outcomes in Australia and New Zealand has been the institution of CQI programs at local, state, and national levels. In 2011, the ISPD released a position statement on reducing risks of PD-related infections (40). This included steps to monitor peritonitis, such as mandated monitoring of infection rates and standardized reporting of peritonitis, as well as a multi-disciplinary team approach to CQI. This seminal document provided a benchmark target to achieve a peritonitis rate below 0.36 episodes per patient per year and recommended an increase in frequency of monitoring infection rates to at least quarterly (39,40). Although many of the recommendations were based on expert opinions, it provided an important stepping stone to develop structured surveillance programs and to initiate CQI processes to improve outcomes.

The philosophy of CQI has been described as a continuous cycle, with repeated planning, doing, checking, and acting, that is, the "PDCA cycle" (49). This approach places emphasis on the fact that improving practices is an ongoing process with no clear finishing point; instead, continuous efforts to identify opportunities for further improvements should be sought. These programs have generally included use of a multidisciplinary team to develop a culture of continuous learning, as well as implementing specific changes in clinical practice to address problem areas. Implementation of such CQI programs has been reported to be highly successful in a number of centers (49,50).

In an attempt to replicate this success at a national level, a National PD Peritonitis KPI project was established in 2010, in which identified and unit-specific peritonitis rate data were fed back to every PD unit on a quarterly basis by the ANZDATA Registry. This required the development of real-time data entry to allow timely feedback of performance data. Each unit could benchmark its performance against every other unit and, if necessary, approach units that were performing well to ascertain and adopt practices associated with peritonitis success. The success or otherwise of such practice changes could be assessed in successive iterations of the audit and feedback cycles.

At a state level, a number of statewide renal clinical networks have developed more detailed peritonitis-specific KPIs. In Victoria, the Renal Health Clinical Network developed a KPI Working Group in 2011, which facilitated the establishment of a data collection and benchmarking program. The implementation of a statewide CQI process for peritonitis resulted in a rapid improvement in peritonitis rates (51). This process was taken a step further in Queensland with the introduction in 2009 of a Government Clinical Practice Improvement Payment Scheme, which provided a financial incentive to PD units meeting KPIs for mupirocin prophylaxis of PD catheter-related infections. Over the 2-year duration of the scheme, significant improvements were seen in mupirocin use and peritonitis rates.

Finally, individual units were strongly encouraged to introduce CQI processes that addressed local clinical issues. A PD unit based in Hobart, Australia, found that they were failing to achieve their own ESI benchmark of 0.48 episodes per patient-year (52). As a result, they investigated practices and implemented a CQI process within their unit that addressed pre-catheter insertion issues, such as assessment of the home environment and fitness to support safe PD practice, as well as routine 6-monthly swabbing for nasal *Staphylococcus aureus* carriage for both the patient and their primary carer, with subsequent eradication treatment for positive cases. In addition, formal hand hygiene education was given to all patients, and chlorhexidine-based skin cleansers and standardized exit-site care were introduced. These measures, together with input from an infectious diseases consultant and regular reviews of infection rates, resulted in a fall in ESI rates from 0.58 episodes per patient-year at baseline to 0.06 episodes per patient-year 5 years later. Additionally, peritonitis rates also decreased from 0.8 episodes per patient-year to 0.15 episodes per patient-year. The success following this CQI initiative prompted the unit to develop their own clinical guideline for the prevention of ESI.

BETTER OUTCOMES

Following the abovementioned interventions, Australia and New Zealand have experienced significant reductions in peritonitis rates (Figure 1) by approximately one-third (53)

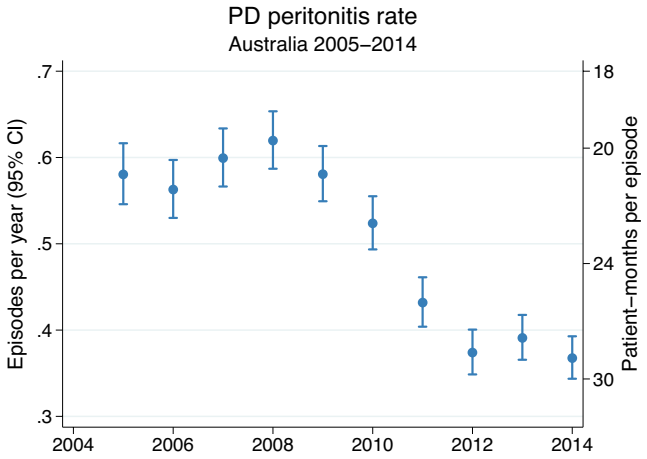
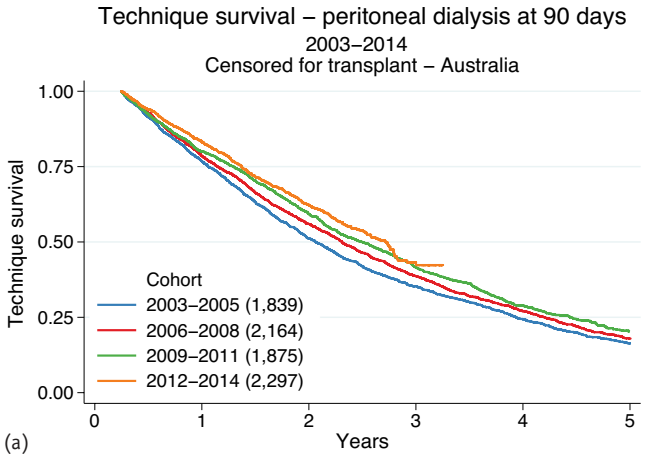


Figure 1 — PD peritonitis rates in Australia 2004–2014. From ANZDATA Registry (53). PD = peritoneal dialysis; CI = confidence interval.



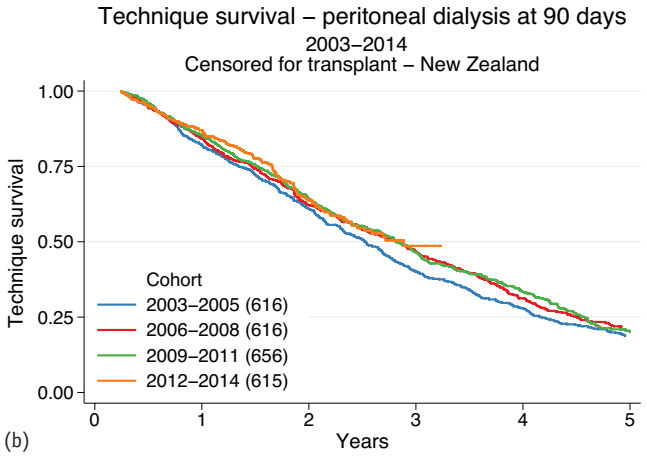
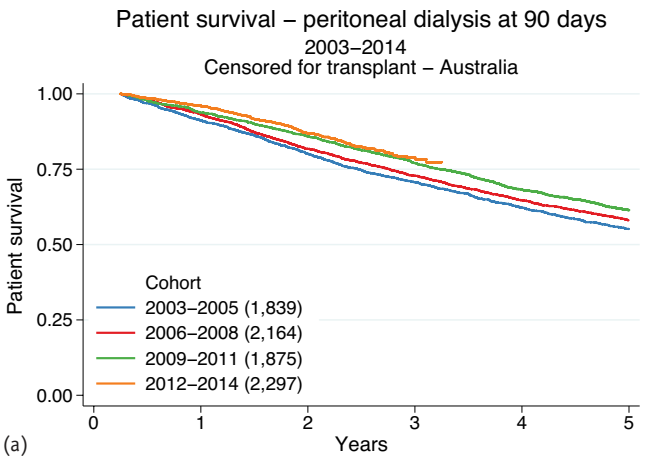


Figure 2 — Peritoneal dialysis technique survival in (a) Australia and (b) New Zealand 2002–2014. From ANZDATA Registry (53).

and reductions in between-center variations in peritonitis rates by approximately one-half (54) over the last 5 years of ANZDATA Registry reports. These improvements have been accompanied by significant improvements in PD technique survival (Figure 2) and patient survival (Figure 3).



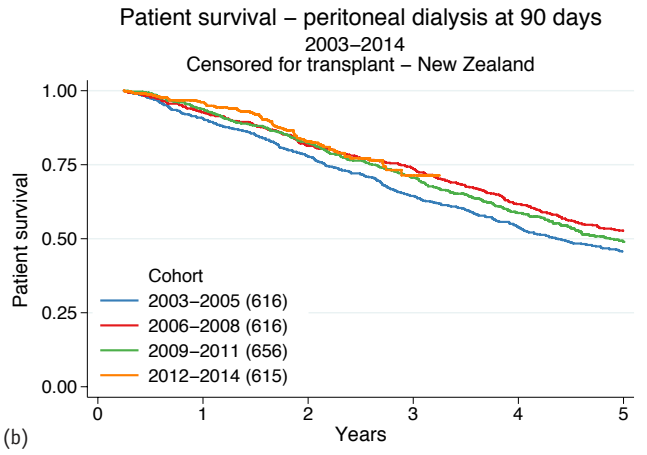


Figure 3 — Peritoneal dialysis patient survival in (a) Australia and (b) New Zealand 2002–2014. From ANZDATA Registry (53).

FUTURE STRATEGIES

Although the improvements observed in peritonitis rates in Australia and New Zealand to date are obviously very pleasing and a vindication of recent collaborative efforts, the majority of units still perform below the 2011 ISPD-recommended peritonitis target of 0.36 episodes per patient-year (40). In response to this, a follow-up "call to sustain the action" paper was published in 2016 to evaluate progress made to date (54). Variable peritonitis rates between PD units and between geographical locations were noted to be an ongoing issue and, again, deviation from recommended guidelines was thought to be a recurring problem, as variations were not explained by center size or case-mix (3). Though surveillance and recording of peritonitis rates had been identified as a key goal in the first "call to action" paper, this updated study noted that there remained inconsistencies with definitions of peritonitis and methods of reporting, thereby limiting the usefulness of the data for benchmarking and trend evaluation. Recommendations across the same 5 domains as the first paper were suggested by the authors; however, increased emphasis was placed on developing a culture of CQI within

units, with regular review of KPIs and benchmarking against other units, as well as developing coordinated approaches to clinical governance, including refinement of clinical practice guidelines and minimizing unnecessary deviations from current best practice.

In order to further consolidate quality improvement efforts to more effectively combat PD peritonitis and other pressing issues facing patients with chronic kidney disease, the Better Evidence and Translation in Chronic Kidney Disease (BEAT-CKD) program was established in 2016 (www.beatckd.org). This collaborative research and clinical translation program represents a strategic alliance between the ANZDATA Registry (hypothesis generation and CQI), AKTN (RCT design and conduct), Cochrane Kidney and Transplant Group (systematic evidence reviews), and KHA-CARI (guideline development and implementation) in order to provide a complete discovery-to-implementation pathway across the entire spectrum of chronic kidney disease. Its key objectives are to a) identify promising interventions for existing high-priority outcomes (e.g. PD peritonitis); b) identify new priority outcomes that are patient-centered, including the ISPD-funded Standardised Outcomes in Nephrology Group – PD (SONG-PD) initiative (http://songinitiative.org/); c) identify potential interventions to improve these outcomes; d) provide robust evidence about these interventions; e) identify which patients might achieve the most benefit from these interventions; and, f) identify and evaluate strategies to more effectively deliver these interventions in diverse clinical settings.

Whilst the output of this program will help to generate high-quality research evidence to inform healthcare decisions made by patients, health professionals, and policy makers, PD units will ultimately need to pursue CQI initiatives to ensure high-quality PD patient care. Whilst well-governed PD units with motivated PD clinicians will likely already be doing this, the real challenge moving forward is ensuring that poorly performing units are helped to achieve improved outcomes for their patients as well. Fostering a quality assurance culture amongst all PD units, not just select units manned by PD enthusiasts, with establishment of robust CQI process by multidisciplinary teams, is the key to achieving this.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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http://dx.doi.org/10.3747/pdi.2016.00114