Kidney Medicine

Deprescribing in Dialysis: Operationalizing "Less is More" Through a Multimodal Deprescribing Intervention

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"Less is more", a quote attributed to Ludwig Mies van der Rohe, is now finding increased relevance across several fields, including medicine. Deprescribing is an exemplar of this proverb and describes the process of deliberately withdrawing medications, with the aim of reducing pill burden and improving health and quality of life.[1] Deprescribing may mitigate multiple adverse events associated with polypharmacy, including falls, cognitive disturbances, hospitalizations and mortality risk.[2]

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Polypharmacy is common among individuals with advanced kidney disease, with an estimated prevalence of nearly 86% among individuals with Stage 3b chronic kidney disease.[3] The potential harms of polypharmacy are also substantial, including higher mortality risk with ≥5 drugs (relative risk [RR], 1.28; 95% CI, 1.19-1.39) among adults over 65 years old[4] and poorer health-related quality of life among individuals receiving dialysis.[5] Efforts to enhance judicious deprescribing in kidney care are urgently needed. These efforts must incorporate contextual factors unique to people living with kidney disease, including a rapidly evolving pharmaceutical armamentarium, dosing adjustments as eGFR declines, emerging multidisciplinary kidney care models, and frequent health care engagement and associated cascading prescribing patterns.[1,6,7]

Addressing polypharmacy also requires clinical equipoise and shared decision making tailored to the medical complexity and substantial pill burden facing individuals with kidney disease.[8] A critical area of focus for deprescribing interventions has been on potentially inappropriate medications (PIMs), which are medications, such as benzodiazepines and proton pump inhibitors, that have been identified as having limited benefit and increased potential for adverse drug reactions. However, multiple barriers to PIM have been described, including clinician time constraints, fragmented medical records and unintegrated health information technology systems,[9] poorly defined roles for deprescribing (eg, nephrologist versus primary care physician), limited knowledge about PIMs among patients and clinicians, and symptom management priorities.[10] Although studies have demonstrated that electronic clinical decision support for acutely hospitalized older adults may improve deprescribing in some specific contexts, including inpatient settings,[11-13] less has been known about the efficacy of decision support tools on PIM deprescribing among individuals with kidney failure undergoing routine outpatient hemodialysis.

In this issue of *Kidney Medicine*, Bortolussi-Courval et al[14] report their findings from a prospective, nonrandomized controlled quality improvement study conducted across 2 dialysis centers in Montreal, Canada, conducted between September and December 2022, with one facility serving as the intervention site and the other as a control site. The authors compared the impact of MedSafer (n=68) versus traditional biannual medication reconciliation (n=127) on PIM deprescribing among outpatient dialysis patients who were prescribed a median of 4 PIMs on both the control and intervention units and >14 medications overall.[14] MedSafer is evidence-based, algorithm-driven intervention for effective deprescribing whereby patients' electronic health record data are extracted and cross-referenced against evidence-based guidelines to generate stratified reports listing PIMs based on their risk level (high, intermediate, and low) of developing an adverse drug event (ADE). Notably, in this study patients in the intervention group also received EMPOWER reports, which provided direct tailored feedback regarding select PIMs identified for deprescribing from their own medical record.

The authors report that 40% of intervention unit patients achieved the primary outcome of having 1 or more PIMs deprescribed (eg, stopped, reduced, or vs 3% of control unit patients), corresponding to a 37% absolute increase in deprescription (number needed to treat, 3), with similar results in older as compared with younger patients. Of 45 total PIMs deprescribed, 89% were from patients from the intervention dialysis facility. Although ADEs were not assessed, authors report no deaths after medication reconciliation were related to deprescribing and did not identify adverse outcomes, such as a gastrointestinal bleed, among individuals who had specific PIMs, such as proton pump inhibitors, deprescribed. Notably, authors also report that 29% of deprescribing in the intervention unit resulted from newer clinical algorithm rules specified for dialysis that were incorporated into the MedSafer intervention, adapted from a prior dialysis-specific deprescribing guidelines developed by Lefebvre et al[15] that leverage widely accepted PIM-guidelines including STOPP-STARRT (Screening Tool of Older Persons' Prescriptions and Screening Tool to Alert to Right Treatment) and BEERS criteria.[1]

To our knowledge, this is among the first studies to describe an effective multimodal intervention deployed in outpatient dialysis units designed to enhance PIM deprescribing. Notably, MedSafer was initially tested by the same

study group in a nonrandomized study of 1,066 hospitalized patients aged 65 and older years that found an 8% increase in deprescribing at the time of discharge (55% in the intervention group vs 47% in control)[11] across several classes of deprescribed medications including antipsychotics, antidiabetic drugs, proton pump inhibitors, anticholinergic antihistamines, and sedative hypnotics. The MedSafer team subsequently conducted a cluster randomized controlled trial of 5,698 hospitalized patients aged 65 and older years across 11 acute care hospitals in Canada and noted an adjusted risk difference increase of 22% (95 CI, 17%-27%) in deprescribing (55% in the intervention group vs 30 % in the control group).[12] An exploratory post hoc analysis performed for that study focused on 70 hospitalized dialysis patients in each arm and noted a 9% increase in deprescribing with MedSafer (29% among intervention group vs 19% among the control group), demonstrating that the promise of the intervention described in this *Kidney Medicine* issue was possibly enhanced dialysis-specific algorithms.[13]

The Practical Robust Implementation and Sustainability Model framework accounts for the multilevel factors required for implementation success including diverse and variable user characteristics (eg, patient and clinician characteristics), and the external environment (eg, shifting clinical practice guidelines).[16] Bortolussi-Courval et al[14] provide multiple examples of how to enhance intervention success through careful implementation that addresses several elements of the Practical Robust Implementation and Sustainability Model. For instance, MedSafer's success in this context may have been enhanced through the adaption a deployed evidence-based intervention,[12,13] which directly address barriers known to affect dialysis deprescribing (eg, nephrologist time to collect and reconcile medications manually, EMPOWER brochures delivered to patients with accessible language regarding PIM risks and benefits). Provision of introductory emails regarding the intervention, as well as delivery of MedSafer deprescribing clinician report examples to intervention group nephrologists, may have also enhanced intervention uptake and perceptions of usability. Finally, MedSafer incorporates several components of a recently described decision-making framework, List Evaluate Shared Decision Making and Support,[1] by leveraging the electronic health record to create an accurate medication list, providing a clear review of medications for deprescribing with risk-stratified categories, and through delivery of patient-facing EMPOWER brochures, which prompt patients to consider their need for specific PIMs and their associated risks.

The study is notable for several strengths, including the presence of a control facility, elaborately described methodology to ensure internal validity, and noncrossover of nephrologists. The authors also assessed key process and implementation factors by conducting semistructured interviews with nephrologists, which could aid in the development of future randomized clinical trials to test an adapted version of this intervention. In addition to deploying clinical algorithms to determine PIMs specific to individuals requiring dialysis, this intervention also engaged patients through provision of educational brochures describing select PIMs relevant to their care. However, several limitations of this study also deserve mention. This intervention is multimodal and includes both patient-facing reports and clinician facing reports, making it challenging to quantify which component of the intervention arm (eg, EMPOWER pamphlet distribution vs clinician reports) contributed to effective PIM deprescribing. Additionally, this study does not assess long-term intervention durability or patient outcomes and was not powered to affect ADEs. Future studies could examine long-term outcomes, including ADEs, hospitalizations, and patient-reported symptoms and outcomes associated with deprescribing, including medication complexity, which can be assessed using the Medication Regimen Complexity Index.[1] Further information regarding operationalization of nephrology champions is also essential to understand the role of these individuals in intervention arm success. Finally, the generalizability of these findings to settings lacking interoperable and unified electronic health systems (eg, the United States) is also unclear and warrants further investigation in future studies.[9,17] Regardless, the authors present a compelling example of a multimodel intervention that directly addresses key barriers to dialysis prescribing.

Over the past decade, multiple randomized controlled trials have tested interventions for deprescribing, including physician–pharmacist collaborative drug therapy management, mailing of educational brochure to patients and providers, and training sessions and family conferences for prescribers tailored for deprescribing.[18-20] Although some of these approaches have successfully reduced pill counts, further studies are needed to explore the effectiveness of these interventions in kidney care settings and on long-term outcomes (eg, hospitalizations, withdrawal events after deprescribing, ADE reduction, and patient-reported outcomes). As robust electronic platforms for deprescribing support are further developed, attention should also remain on tools that support effective shared decision making and patient-centered communication. For instance, a novel electronic deprescribing tool "Mediquit," which is in early stages of development in Germany,[21] offers verbal prompts and phrases to aid deprescribing while providing tapering information and monitoring guidance for patients. Future tool development also ideally considers patients' social contexts – or financial, physical, social, psychologic, and clinical factors that impede deprescribing (eg, ability to pay, insurance status etc., patient health literacy). Finally, expansion of these electronic deprescribing tools to (1) identify opportunities for prospective medication management/deprescribing at multiple advancing stages of CKD, (2) robustly monitor (eg, via telehealth) adverse drug withdrawal events and other outcomes, and (3) leverage pharmacist expertise warrants further consideration.

Evidence regarding the multifactorial benefits of PIM deprescribing is substantial. Findings from this study provide a compelling example of how deprescribing tools

that use technology and evidence-driven algorithms coupled with patient-facing informational brochures may reduce deprescribing barriers (eg, manual medication reconciliation and patient knowledge regarding PIM harms). As the US and other health systems strive to improve kidney care and patient outcomes through deprescribing, we must invest in promising solutions such as those presented by the MedSafer developers. By addressing foundational barriers that have impaired wider deprescribing success including dialysis care system fragmentation and her interoperability, we can move closer to this critical goal of enhancing kidney care delivery.[17]

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