Kidney Medicine

Optimizing Self-Management Programs in Kidney Disease: Implementation of Sick-Day Protocols

Yuenting Diana Kwong and Delphine S. Tuot

Over 50% of adults in the United States live with at least one chronic medical condition, such as hypertension, diabetes, and chronic kidney disease (CKD).[1] These illnesses often require patients to manage multiple medications, which requires a basic understanding of their roles, benefits, and potential harms to maximize health while preventing adverse events. This can be challenging, even for the most educated and health literate patients. Self-management programs, in which guidance is provided to patients to help them titrate medications in case of changes in their health, are meant to ease this process and are well established in the care of diabetes, asthma, and hypertension.[2] Insulin titration algorithms improve glycemic control among individuals with diabetes, and patients with asthma have action plans to alter inhaler use based on respiratory symptoms.[3-5] These are now cornerstones of diabetes and asthma education.[6] Similar programs have been developed to empower patients with hypertension to titrate antihypertensive medications based on home blood pressure measurements.[7] Although early studies evaluating the efficacy of such programs had mixed results, more recent ones examining refined programs incorporating digital technology to support patient decision making have been shown to improve blood pressure control.[8,9]

Related articles, ••• and •••

In this issue of *Kidney Medicine*, Fink et al[10] and Watson et al[11] explore the use of sick-day protocols, self-management programs that have been promoted in patients with CKD. Patients with CKD are often prescribed several medications (ie, renin-angiotensin system inhibitors, sodium glucose cotransporter 2 inhibitors, and diuretics) that improve long-term health outcomes. However, these medications may be harmful and induce acute kidney injury (AKI) by worsening volume status and increasing the risk of hypotension when patients are feeling unwell. Epidemiologically, AKI is most often attributed to volume depletion and hypotension and can be associated with increased morbidity and mortality.[12] As such, sick-day protocols that instruct patients with CKD to stop specific medications when they have symptoms of infection or are at risk for volume depletion (ie, diarrhea, vomiting) to prevent AKI have been recommended by several health organizations, including the National Institute for Health and Care Excellence in the United Kingdom, the Kidney Disease Improving Global Outcomes organization, and the American Society of Nephrology.[13-15] The efficacy and safety of these protocols in CKD have not been rigorously evaluated, especially when weighing the benefits of avoiding AKI risk against the potential hazards of discontinuing therapies that are known to decrease cardiovascular morbidity and mortality.

Fink et al[10] address this issue by assessing the efficacy of a sick-day protocol in a randomized control trial that included 315 patients with stage 3-5 CKD treated with medications that could contribute to AKI or cause toxicity during an AKI event: renin-angiotensin system inhibitors, diuretics, nonsteroidal anti-inflammatory drugs, or metformin.[10] Patients were randomized to usual care or an education program that consisted of 2 elements: (1) written educational materials that describe and define sick days and instruct patients to stop specific medications for up to 48 hours while sick and (2) an interactive voice response system that calls patients weekly to survey for sick-day events and assess adherence to the protocol. Although the interactive voice response system component did not deliver educational content, it served as a reminder about the recommended sick-day protocol, playing a key role in program sustainability. Both groups were instructed to complete laboratory testing after a presumed sick day. The primary outcome of the trial was change in kidney function after 6 months; secondary outcomes included AKI events defined by *International Classification of Diseases, Tenth Edition* codes, acute service utilization (ie, emergency department or urgent care visit), and reported sick days in the intervention arm only.

Although patients randomized to implement the sick-day protocol maintained an impressive high level of engagement with the interactive voice response system (~80% calls responded), no difference was found in clinical outcomes among the 2 groups. The mean change in estimated glomerular filtration rate at 6 months was -0.69 mL/min/1.73 m^2 (95% CI, -2.07 to 0.76) in those randomized to the sick-day protocol compared with -0.77 mL/min/1.73 m^2 (95% CI, -2.24 to 0.70) in those randomized to usual care ($P = 0.99$). Both groups had 4 participants with AKI events based on the *International Classification of Diseases, Tenth Edition* code. The rate of acute service utilization was 11.5/100 events per person-month in those randomized to the sick-day protocol compared with 8.4/100 events per person-month in the usual care group, with the adjusted prevalence ratio of 1.30 (95% CI, 0.96-1.76). Notably, only 23% of patients randomized to the intervention arm reported a sick-day event, which accounted for 1.6% of the calls. Of the reported events, only 50% were designated to be true sick days after follow-up and only 50% of these patients followed the instructions correctly during the event and withheld their

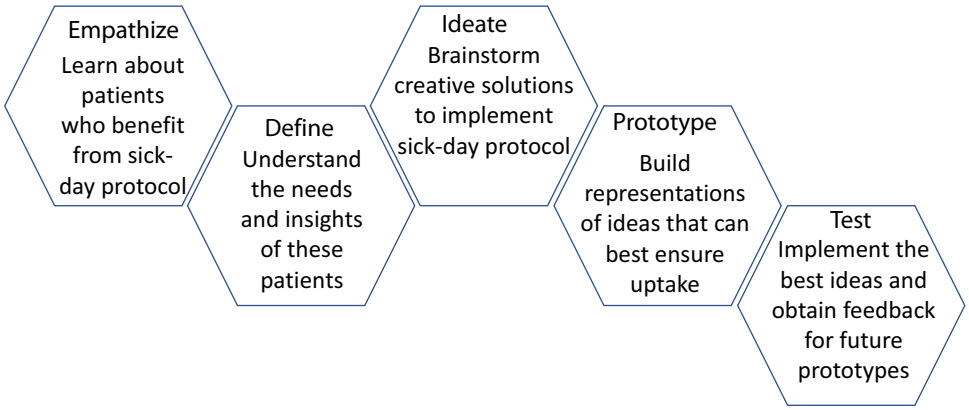

Figure 1. Applying the design thinking process to sick-day protocols.

medications. Importantly, of those who received the intervention, a majority wanted to continue using the sick-day protocol and reported confidence using the protocol even if at least 1 error was made in protocol execution.

In an accompanying systematic scoping review, Watson et al[11] characterize the literature available about sick-day protocols for patients with chronic diseases including those with CKD. The review identified 10 primary studies (including 2 usability studies and 3 randomized controlled trials) that examined the impact of sick-day protocols on clinical outcomes (n=4 studies), patient knowledge (n=9), and patient and provider experience (n=6). The study by Fink et al[10] was the only one that assessed clinical outcomes among individuals with CKD; the other 3 focused on patients with diabetes. None of the studies demonstrated significant clinical improvement among patients randomized to self-management programs. However, the interventions did meaningfully change patient and provider knowledge of sick-day protocols, an important process outcome when considering the potential for future opportunities to apply sick-day protocols during patients' lifetimes for managing their chronic illness.

Together, these 2 manuscripts highlight the limited evidence regarding the efficacy of existing sick-day protocols on health outcomes despite their high acceptability among patients and clinicians. This lack of evidence, however, must be interpreted in the context of patient adherence to the designed interventions, which can be influenced by patient literacy and whether the protocols are easy or challenging to implement in real-world settings. Fink et al[10] conducted usability testing of their intervention and found that patients assigned to the sick-day protocol reported a high frequency of errors. With a high prevalence of low health literacy among patients with CKD,[16] the errors were likely due to patient misunderstanding of the protocol, which asked them to modify pill intake in response to vague symptoms suggestive of volume depletion. A more concrete protocol identifying quantifiable targets before action (ie, blood pressure, weight, urinalysis dipstick results) may have been easier for patients to follow. It is striking that this probable confusion was present despite the research team leveraging patient input when developing the sick-day protocol before study initiation.

This trial may also have been underpowered to evaluate the effectiveness of a sick-day protocol, given the relatively low incidence of sick-day events. A statistical signal of an effective intervention may be hidden if the protocol is only effective during brief periods of time or if it is only helpful for a subgroup of the study population (ie, those with adequate health literacy). It is also possible that participating patients received conflicting information from their providers, representing an unmeasured cointervention. The Watson et al[11] review highlights the lack of consensus among providers and researchers with respect to sick-day protocols, specifically which medications to withhold and when to stop them (ie, by symptoms/circumstances vs quantifiable measures such as blood glucose level). This lack of consensus may have translated to increased confusion for patients when executing the sick-day protocol to prevent AKI.

Physiologically, sick-day protocols are likely to be effective in preventing severe AKI episodes in at-risk populations. Watson et al[11] illustrate that similar medications are recommended to be withheld when patients are suspected of intravascular hypovolemia regardless of whether the patient has underlying diabetes, kidney disease, or heart disease. A thorough evaluation of the system, provider, and patient-related facilitators and barriers to the accurate execution of sick-day protocols is a necessary next step to increase their usability, effectiveness, and generalizability. Human-centered design, a methodology that seeks to understand natural patient behaviors and preferences through active user participation and feedback, may be an attractive strategy to refine existing sick-day protocols such as the one developed by Fink et al.[10] Figure 1 displays an adapted conceptual model of applying the design thinking process to create desirable, feasible, and viable sick-day protocols that could be rapidly adopted by patients.[17] Enhancing diverse patient understanding of

sick-day protocols and ensuring accurate implementation will allow the nephrology community to build the necessary evidence base for the effectiveness of sick-day protocols in real-world settings so that medication self-management support programs to preserve kidney function can move beyond expert opinion and be codified as an evidence-based standard of care.

ARTICLE INFORMATION

Authors' Full Names and Academic Degrees: Yuenting Diana Kwong, MD, MAS and Delphine S. Tuot, MDCM, MAS

Authors' Affiliations: UCSF Division of Nephrology, University of California, San Francisco, San Francisco, California (YDK); Center for Vulnerable Populations at Zuckerberg San Francisco General Hospital, San Francisco, California (DST); and UCSF Division of Nephrology at Zuckerberg San Francisco General Hospital, San Francisco, California (DST).

Address for Correspondence: Delphine S. Tuot, 1001 Potrero Ave, Bldg 100, Rm 342, San Francisco, CA 94110. Email: Delphine.tuot@ucsf.edu

Support: None.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Peer Review: Received August 1, 2022 in response to an invitation from the journal. Accepted August 1, 2022 after editorial review by the Editor-in-Chief.

REFERENCES

1. Boersma P, Black LI, Ward BW. Prevalence of multiple chronic conditions among US adults, 2018. *Prev Chronic Dis*. 2020;17:E106. doi:10.5888/pcd17.200130
2. Warsi A, Wang PS, LaValley MP, Avorn J, Solomon DH. Self-management education programs in chronic disease: a systematic review and methodological critique of the literature. *Arch Intern Med*. 2004;164(15):1641-1649. doi:10.1001/archinte.164.15.1641
3. Sherifali D, Bai JW, Kenny M, Warren R, Ali MU. Diabetes self-management programmes in older adults: a systematic review and meta-analysis. *Diabet Med*. 2015;32(11):1404-1414. doi:10.1111/dme.12780
4. Hou C, Carter B, Hewitt J, Francisa T, Mayor S. Do mobile phone applications improve glycemic control (HbA1c) in the self-management of diabetes? A systematic review, meta-analysis, and GRADE of 14 randomized trials. *Diabetes Care*. 2016;39(11):2089-2095. doi:10.2337/dc16-0346
5. Powell H, Gibson PG. Options for self-management education for adults with asthma. *Cochrane Database Syst Rev*. 2003;2002(1):CD004107. doi:10.1002/14651858.CD004107
6. Centers for Disease Control and Prevention. Self-management education (SME) programs for chronic health conditions. Accessed July 20, 2022. https://www.cdc.gov/learnmorefeelbetter/programs/index.htm
7. Ogedegbe G. Self-titration for treatment of uncomplicated hypertension. *Lancet*. 2010;376(9736):144-146. doi:10.1016/s0140-6736(10)61050-1
8. Tucker KL, Sheppard JP, Stevens R, et al. Self-monitoring of blood pressure in hypertension: A systematic review and individual patient data meta-analysis. *PLOS Med*. 2017;14(9):e1002389. doi:10.1371/journal.pmed.1002389
9. Li R, Liang N, Bu F, Hesketh T. The effectiveness of self-management of hypertension in adults using mobile health: systematic review and meta-analysis. *JMIR MHealth UHealth*. 2020;8(3):e17776. doi:10.2196/17776
10. Fink JC, Doerfler RM, Blakeman T, et al. Medication holds in CKD during acute volume depleting illnesses: a randomized controlled trial of a 'sick day' protocol. *Kidney Med*. Published online July 31, 2022. https://doi.org/10.1016/j.xkme.2022.100527
11. Watson KE, Dhaliwal K, McMurtry E, et al. Sick day medication guidance for people with diabetes, kidney disease, or cardiovascular disease: a systematic scoping review. *Kidney Med*. Published online May 27, 2022. doi: 10.1016/j.xkme.2022.100491
12. Mehta RL, Burdmann EA, Cerdá J, et al. Recognition and management of acute kidney injury in the International Society of Nephrology 0by25 Global Snapshot: a multinational cross-sectional study. *Lancet*. 2016;387(10032):2017-2025. doi:10.1016/s0140-6736(16)30240-9
13. Think Kidneys UK NHS. "Sick day" guidance in patients at risk of acute kidney injury: a position statement from the Think Kidneys board. January 2018. https://www.thinkkidneys.nhs.uk/aki/wp-content/uploads/sites/2/2018/01/Think-Kidneys-Sick-Day-Guidance-2018.pdf
14. Liu KD, Goldstein SL, Vijayan A, et al. AKI!Now initiative: recommendations for awareness, recognition, and management of AKI. *Clin J Am Soc Nephrol*. 2020;15(12):1838-1847. doi:10.2215/cjn.15611219
15. Kidney Disease Improving Global Outcomes. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. March 2022. https://kdigo.org/wp-content/uploads/2022/03/KDIGO-2022-Diabetes-Management-GL_Public-Review-draft_1Mar2022.pdf
16. Taylor DM, Fraser S, Dudley C, et al. Health literacy and patient outcomes in chronic kidney disease: a systematic review. *Nephrol Dial Transplant*. 2018;33(9):1545-1558. doi:10.1093/ndt/gfx293
17. Hasso Plattner Institute of Design at Stanford University. Get started with design thinking. https://dschool.stanford.edu/resources/getting-started-with-design-thinking