

# Adherence to Therapy: Burden, Complexity, and Perception



Pierre Delanaye<sup>1,2</sup> and Christophe Mariat<sup>3</sup>

<sup>1</sup>Department of Nephrology, Dialysis, and Transplantation, University of Liège (ULg CHU), Liège, Belgium; <sup>2</sup>Department of Nephrology-Dialysis-Apheresis, Hôpital Universitaire Carêmeau, Nîmes, France; and <sup>3</sup>Department of Nephrology, Dialysis and Renal Transplantation, Hôpital Nord, Centre Hospitalier Universitaire de Saint-Etienne, Jean Monnet University, Saint-Etienne, France

*Kidney Int Rep* (2021) 6, 5–6; <https://doi.org/10.1016/j.ekir.2020.11.005>

© 2020 International Society of Nephrology. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

[See Clinical Research on Page 128](#)

The lack of adherence to prescribed therapy is a major issue in patients with kidney disease. For instance, non-adherence occurs in a significant proportion of patients with resistant hypertension with or without chronic kidney disease (CKD).<sup>1,2</sup> In dialysis patients, the lack of adherence also explains an uncontrolled hyperphosphatemia and hyperparathyroidism.<sup>1,3</sup> In renal transplantation, non-adherence to immunosuppressive therapies can lead to serious complications, such as acute rejection and graft loss.<sup>4</sup> Studying and understanding non-adherence is thus of importance. Different factors are known to be associated with non-adherence. Among them, pill burden and polypharmacy are well-identified risk factors.<sup>1</sup> The issue of pill burden is well illustrated in the study by Marianne *et al.*<sup>5</sup> in this issue. Of interest, the authors studied pill burden before and until 1 year after renal transplantation. In this retrospec-

tive study, the same patients from 1 center in France were followed before and after transplantation. A comparison with the French registry of dialysis and transplantation showed that the patients included were representative of the CKD population in that country.

In addition to the pill burden, the authors also studied the complexity of the treatment, based on a recognized score, the Medication Regimen Complexity Index. This score varies with the number of drugs prescribed and is based on 3 components: dosage form or administration route, dosing frequency, and additional instructions concerning administration. The authors convincingly show that both the pill burden and the complexity of the treatment are higher after than before transplantation. Also, the authors clearly show that the class of drugs varies from dialysis to transplantation (immunosuppressive drugs becoming the first class of drug after transplantation). The study remains, however, descriptive, and we do not know whether this higher pill burden or complexity will lead to the same degree of non-adherence in

patients before and after transplantation. The perception of the patient (but also of the physician) regarding the relevance of the drug is probably important but is difficult to capture in the context of a retrospective study.<sup>1</sup>

The perception of the importance of the drug can be easily illustrated by some examples in which both the patient and the physician will be involved. Indeed, one could reasonably hypothesize that, at the same level of complexity, adherence to immunosuppressive drugs is higher in a transplant recipient than adherence to phosphate binders when the same patient was undergoing dialysis.

Immunosuppressive drugs are certainly considered essential to the patients who will keep in mind the risk of returning to dialysis, whereas phosphate binders are prescribed to control hyperphosphatemia, which will have very few direct impacts on patients' symptoms. In addition, the physician will surely explain (and insist on) the risk of non-adherence to immunosuppression to their patients, probably in a more intense manner than the risk of phosphate binding, for which a definitive evidence of efficacy on clinically relevant outcomes is still lacking. Regardless of the shared perception between physicians and patients, it remains likely that decreasing the pill burden and the complexity of treatment could certainly help to improve adherence of the patients (even if strictly speaking the impact of decreasing complexity on adherence still needs to be proven). As reminded by the authors, a strategy of "polypills" is interesting (even if not always easy to implement), as is a strategy of "deprescribing."

**Correspondence:** Pierre Delanaye, Service de Dialyse, CHU Sart Tilman, 4000 Liège, Belgium. E-mail: [pierre\\_delanaye@yahoo.fr](mailto:pierre_delanaye@yahoo.fr)

The potential role of education, social support, or both, and the intervention of pharmacists dedicated to patients with CKD are probably also of interest in all aspects of our specialty.<sup>6,7</sup> Other straightforward ideas deserved to be explored. First, the concept of medication reconciliation must not be neglected. Albeit obvious and fundamental with regard to medication safety, the notion of medication reconciliation has been well shown to be insufficient in patients with complex conditions such as CKD, especially during care transitions. Medication conciliation is always the first step to improve adherence to therapies.<sup>8</sup> Likewise, in dialysis patients, the directly observed therapy—that is, a drug given directly by the nurse during the dialysis session—should be promoted when possible. We have shown, for example, that directly observed therapy with native vitamin D (cholecalciferol, 25,000 units once a week) was associated with better vitamin D 25-OH concentrations. In the same context, therapies dedicated to the treatment of secondary hyperparathyroidism can be prescribed orally for home use or orally or intravenously during the dialysis session (calcitriol or either cinacalcet or etelcalcetide). The better results obtained in the

real life with intermittent therapies is due, at least in part, to the better adherence associated with a directly observed therapy strategy. In transplantation, simple strategies can help to improve adherence—for example, health apps on smartphones, which have been shown to reduce variability in tacrolimus trough concentrations.<sup>9</sup>

Although improving adherence to drug regimens by patients with CKD remains a true and important challenge, the mechanisms underlying adherence and the impact of specific interventions still need to be further clarified.

## DISCLOSURE

All the authors declared no competing interests.

## REFERENCES

1. Burnier M, Pruijm M, Wuerzner G, Santschi V. Drug adherence in chronic kidney diseases and dialysis. *Nephrol Dial Transplant*. 2015;30:39–44.
2. Siddiqui M, Judd EK, Dudenbostel T, et al. Antihypertensive medication adherence and confirmation of true refractory hypertension. *Hypertension*. 2020;75:510–515.
3. Karamanidou C, Clatworthy J, Weinman J, Horne R. A systematic review of the prevalence and determinants of nonadherence to phosphate binding medication in patients with end-stage renal disease. *BMC Nephrol*. 2008;9:2.
4. Gokoel SRM, Gombert-Handoko KB, Zwart TC, et al. Medication non-adherence after kidney transplantation: a critical appraisal and systematic review. *Transplant Rev (Orlando)*. 2020;34:100511.
5. Marianne J, Laville SM, Caillard P, et al. Evaluation of changes over time in the drug burden and medication regimen complexity in ESRD patients before and after renal transplantation. *Kidney Int Rep*. 2021;6:128–137.
6. Sousa H, Ribeiro O, Paúl C, et al. Social support and treatment adherence in patients with end-stage renal disease: a systematic review. *Semin Dial*. 2019;32:562–574.
7. Murali KM, Mullan J, Roodenrys S, et al. Strategies to improve dietary, fluid, dialysis or medication adherence in patients with end stage kidney disease on dialysis: a systematic review and meta-analysis of randomized intervention trials. *PLoS ONE*. 2019;14:e0211479.
8. Frament J, Hall RK, Manley HJ. Medication reconciliation: the foundation of medication safety for patients requiring dialysis. *Am J Kidney Dis*. 2020;76:868–876.
9. McGillicuddy JW, Chandler JL, Sox LR, et al. Exploratory analysis of the impact of an mhealth medication adherence intervention on tacrolimus trough concentration variability: post hoc results of a randomized controlled trial. *Ann Pharmacother*. 2020;54:1185–1193.