



EDITORIAL COMMENT

**Patient adherence to direct oral anticoagulants:  
To take or not to take, is it a patient's choice?**



**Adesão do doente aos anticoagulantes orais diretos: tomar ou não tomar, uma escolha do doente?**

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“Drugs don’t work in patients who don’t take them.”  
C. Everett Koop, MD, US Surgeon General, 1985

Not many drugs in this century can claim to be “game changers” in disease management as is the case with direct oral anticoagulants (DOACs). Their introduction led to a true revolution in anticoagulation, reaching a greater number of patients, with a wide range of indications, safer profile, and more convenient use and dosage than that of vitamin K antagonists (VKAs). Recently, epidemiological data have suggested that atrial fibrillation (AF) related strokes are decreasing as the uptake of DOACs is increasing.<sup>1</sup> Yet, for drugs to work they must be properly prescribed by physicians and patients must be compliant, particularly in chronic diseases such as AF.

Adherence is defined as the extent to which patients can follow the recommendations for prescribed treatments. It is particularly important in a therapy that relies on full compliance and adequate dosing for efficacy and safety in preventing thromboembolic events.

In the article by Brízido et al.<sup>2</sup>, using data from AF patients followed in a specialized cardiology outpa-

tient clinic from 2016 to 2018, a concerning scenario was depicted. Half of the patients were considered non-adherent, only one in three patients were fully adherent and nearly one in five changed DOACs during the study. Likewise, treatment for secondary prevention of thromboembolic events (16% of all patients) had no impact on adherence. As expected, higher out of pocket costs, bid posology and longer treatment duration were predictors of non-compliance.

This was a cross-sectional, retrospective analysis of a cohort of 264 patients with low bleeding risk (median HAS-BLED score of 1), followed by cardiologists at a high-volume tertiary center. This is certainly a selected population, 30% of whom had vascular disease and 34% were on antiplatelet therapy. One can speculate that the setting may be more dismal outside cardiology outpatient clinics, where patients are older, have more comorbidities, with a higher bleeding risk and more irregular follow-up. Non-adherence was defined as medical refill adherence <90%, a threshold considered appropriate given the nature of the intervention. There are several ways to assess adherence, but medical refill is probably one of the simplest and can be determined by any doctor at any time, given precious information that can help

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to address barriers to compliance. Therefore, this study is an import call to action to doctors following AF patients.

Non-adherence comes at a cost. A meta-analysis of over 500 studies on medication compliance revealed an average non-adherence rate of 25%, with variations according to disease.<sup>3</sup> Good adherence has been associated with increased survival, probably also due to the “healthy adherent effect” since patients compliant with placebo also have better survival.<sup>4</sup> Adherence is, in fact, the reflection of several health-related factors, comprising behavior changes toward a healthier lifestyle.

Recently, an analysis of the Stockholm Healthcare database, including 21 028 AF patients claiming a first DOAC prescription from 2011 to 2018, showed a persistence rate of 70% after a median follow-up of two years, although 85% of the patients were under treatment at the end of the study due to re-initiation of treatment. Adherence in those that continued on medication remained stable at 90% throughout the study period. Non-persistence and poor adherence were both associated with increased stroke risk.<sup>5</sup>

Non-adherence is a complex problem and results from the interplay between patients, physicians and health care systems, and the treatment itself.<sup>6</sup>

According to the World Health Organization, there are five aspects influencing adherence: factors related to the health care system and providers (namely doctor-patient relation and costs); factors related to treatment (complexity of dosing regimen, side effects and lack of immediate results); disease-related factors (disease severity, treatment impact and comorbidities); and patient-related factors (health literacy, socioeconomic status, fear of side effects, unintentional non-adherence).<sup>7</sup>

In Portugal, a study performed in 2008 by the Portuguese Association of Pharma Industry, including a cohort of 1400 participants, representative of the mainland Portuguese population, identified the following as frequent reasons for non-compliance: forgetting to take the medication (46.7%); abandoning therapy due to clinical improvement (26.6%); and side effects (22.2%). More concerning was that of those surveyed, 31.7% were afraid of questioning their doctor, 28.1% did not pay attention when the therapeutic regimen was being explained, 20.5% did not understand the advantages of the treatment, and 12.5% did not trust their doctor.<sup>8</sup>

Understanding individual reason(s) for non-compliance is vital to establish effective interventions, which need to be tailored and frequently multifactorial. But first, we should acknowledge that non-adherence is not just a patient's choice.

There are several key interventions that can have a huge impact on results. Health care system strategies such as

reducing out of pocket costs, allowing for long-term prescription refills (finally approved in Portugal) and incentives in primary care for adequate treatment of preventable diseases, like thromboembolic events in AF, are relevant for ensuring therapy continuance. Education for patients and caregivers, especially on how to manage complications or on the consequences of therapy discontinuation or inadequate dosing must be improved, involving nurses and pharmacists in the process. Finally, making time to establish a stronger doctor-patient relationship, in a safe and open environment that allows for discussion and shared decisions, is of the utmost importance if we want our patients to make wise choices.

## Conflicts of interest

The author has no conflicts of interest to declare.

## References

1. Cowan JC, Wu J, Hall M, et al. A 10-year study of hospitalized atrial fibrillation-related stroke in England and its association with uptake of oral anticoagulation. *Eur Heart J*. 2018;39(August):2975–83.
2. Brízido C, Ferreira AM, Lopes P, et al. Adesão à terapêutica com anticoagulantes diretos em doentes com fibrilhação auricular não valvular – uma análise de mundo real. *Rev Port Cardiol*. 2021; <https://doi.org/10.1016/j.repc.2020.10.017>do artigo.
3. van Dulmen S, Sluijs E, van Dijk L, et al. Patient adherence to medical treatment: a review of reviews. *BMC Health Serv Res*. 2007;7(April):55.
4. Simpson SH, Eurich DT, Majumdar SR, et al. A meta-analysis of the association between adherence to drug therapy and mortality. *BMJ*. 2006;333(July):15.
5. Komen JJ, Heerdink ER, Klungel OH, et al. Long-term persistence and adherence with non-vitamin K oral anticoagulants in patients with atrial fibrillation and their associations with stroke risk. *Eur Heart J Cardiovasc Pharmacother*. 2021;7(April (F11)):f72–80.
6. Hugtenburg JG, Timmers L, Elders PJ, et al. Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. *Patient Prefer Adherence*. 2013;7(July):675–82.
7. De Geest S, Sabaté E. Adherence to long-term therapies: evidence for action. *Eur J Cardiovasc Nurs*. 2003;2(December):323.
8. Cabral MV, Silva PAA. adesão à terapêutica em Portugal: atitudes e comportamentos da população portuguesa perante as prescrições médicas. Lisboa: APIFARMA; 2010.