Atrial fibrillation and the ‘other drug problem’: reducing non-adherence with technology

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Introduction

The terms compliance, adherence, concordance, and persistence are used to characterize important aspects of medication-taking behaviour. According to the International Society for Pharmacoeconomics and Outcomes Research Medication Compliance and Persistence Work Group, medication compliance (or adherence) is defined as ‘the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen’; while medication persistence is ‘the duration of time from initiation to discontinuation of therapy’.¹

The medical profession is well aware that non-adherence to recommended medications represents a worldwide problem, encompassing a large variety of illnesses, treatments, and age groups. Non-adherence leads to worrying consequences, for patients, health professionals, and healthcare systems. According to the World Health Organization (WHO), almost 50% of patients do not take medications as prescribed,² and evidence shows that non-compliance with medications leads to an inadequate control of the illness, placing patients at a higher risk for complications and adverse outcomes.³–⁵ Expenditure on direct and indirect consequences of non-adherence to treatment (e.g. hospital admissions, underutilized drugs, and disease progression) represents a substantial burden for healthcare systems.⁶

Indeed, in 2003 the WHO called for initiatives to improve adherence in chronic conditions, claiming that ‘increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment’.³ Non-adherence is a frequent phenomenon: approximately only one-third of patients fully comply with prescribed treatment.⁶ For long-term therapies, adherence begins to decline within the first 10 days. Clinical and economic consequences are huge: in the USA 43% of the general population, 55% of the elderly, and 54% of teenagers are not compliant with their treatment causing 10–25% of hospital and nursing home admissions as well as 125 000 deaths annually. The costs for the healthcare system are as high as $100 billion annually, with almost half of them due to drug-related hospitalization.⁶ Since healthcare costs represent an ever-increasing proportion of the national budget, it remains a top-tiered issue in politics.

With a non-adherence rate of 50%, the UK has ≈£4 billion of medicines not used correctly; as a consequence, non-adherence is responsible for 11–30% of UK hospital admissions.⁷ Across Europe, the lack of compliance with prescriptions causes €1.25 billion of healthcare expenditure, as well as nearly 200 000 deaths annually.⁸

Conscious of the growing value that adherence has in current patient care, we wish to focus on this important topic, paying particular attention to the situation in the field of cardiology and exploring the characteristics of an ideal adherence monitoring programme based on technology.

Atrial fibrillation and non-adherence: the magnitude of the problem

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia with estimated prevalence in over 6 million people in Europe and up to 6.1 million in the USA, and is becoming more frequent as the population ages.⁹ It is also estimated that the prevalence of AF will more than double by 2050. The treatment of AF costs healthcare systems ≈€6.2 billion in Europe and $6.65 billion in the USA.¹⁰,¹¹ These increases when treatment for AF complications, including stroke, heart failure, and hospitalization, are taken into consideration. As the recent update of ESC guidelines for AF highlights, adherence to prescribed treatment is of the utmost importance in order to avoid these complications, particularly when considering anticoagulation therapy. Until recently vitamin K antagonists (VKAs) were the only oral anticoagulants available; their numerous limitations, such as frequent monitoring, need for dose adjustments, food–drug and drug–drug interactions, and a narrow therapeutic window, make VKAs very difficult to use; thus a good adherence rate is essential but difficult to achieve. Nowadays, with novel oral
anticoagulants (NOACs; e.g. dabigatran, rivaroxaban, and apixaban) that target factor II or X, some disadvantages of VKAs have been overcome, but new challenges have arisen. Although NOACs may be easier to use than VKAs, their pharmacology imposes some new issues: their short half-life makes the matter of medication adherence a key factor for their success, as the efficacy can be lost with just one or two missed doses. Thus, ESC guidelines strongly recommend ‘strict adherence to approved indications’.9 Data on patient adherence to antithrombotic treatment show that between 10 and 26% of patients with AF who are on warfarin therapy are non-adherent to their prescription,12 while 58% of AF patients do not monitor their international normalized ratio regularly. Furthermore, only 53.5% of warfarin users are persistent to their prescription for ≥ 1 year, whereas the discontinuation rate within 1 year is 42.6%.13 The RE-LY trial shows that twice daily dabigatran is still associated with some adherence issues: discontinuation rates are 15.5% at 1 year and 21.2% at 2 years compared with 10.2 and 16.2% of once daily warfarin, respectively.14 The issue of patients not filling their prescriptions due to high cost also contributes to patient non-adherence.6 In a US study of cost-related medication non-adherence among 14 000 elderly and disabled Medicare beneficiaries, 29% of patients either skipped doses or did not fill a prescription due to the high cost.15 Thus, we are persuaded that for optimal management of AF patients, monitoring adherence to prescribed medications is imperative.

**Interactive voice response system to improve adherence**

Reasons for non-adherent behaviour are multiple: there are factors related to the patient, the medication, the prescriber, the pharmacy, and the healthcare system.6 Strategies to improve patient compliance should take into account this multi-factorial scenario and involve the many players who can determine the desired outcome: from patients and caregivers, to providers and payers. Technology has been adopted in healthcare systems in many ways, most relevant here is better communication with patients with the aim of improving their adherence to treatment. There are numerous studies proving that technology in general (e.g. telecalling, text messaging, online communication, electronic forums, electronic pills dispenser)16–18 can encourage patient adherence.

For example, in the EASY-IMPACT trial, telephone support (four telephone calls from a nurse) dramatically improved adherence rates and medication persistence in patients who had received drug-eluting stents. After 1 year, over 90% of the patients who received standard of care follow-up were adherent with their prescribed medication (aspirin and clopidogrel), whereas over 99% of the patients who received telephone follow-up were adherent.6

To evaluate the utility of text messaging to help the management of malaria infection, 119 health workers in Kenya received text messages for 6 months while a control group did not. Correct management of the cases increased by 23.7% (absolute) immediately following the text messaging intervention, and by 24.5% six months after the intervention.17

In a study conducted in 4 community-based paediatric clinics in New York City involving 9213 children ages 6 months to 18 years from low income households, parents were randomized to receive text messages providing educational information regarding the seriousness of influenza, safety of the vaccine, and dates of vaccine programs or to standard care. By the end of the influenza season, vaccination rates increased significantly by ~4% absolute with intervention. However, fewer than half of the children in both groups were

![Figure 1](image-url) Flow of the Interactive Monitoring System.
vaccinated, suggesting simple text messaging alone may not be a sufficient strategy.18

The interactive voice response (IVR) system is a widespread and low-cost technology that has been shown to support patients in self-managing their condition, increasing adherence to medication regimens, or encouraging behavioural changes.19,20 Studies confirm that a programme for enhancing adherence based on an IVR system may be cost-effective, easy to use, and well accepted by patients with cardiovascular conditions as well as other chronic illnesses. The system may also be particularly useful for patients living in rural areas who have difficulty reaching the healthcare provider. Whatever the solution, for an adherence programme to be successful, it must attempt to uncover whether and why patients are or are not compliant. The IVR system is not only able to provide individualized messages for each patient, it may also help to investigate the reasons for a patient’s behaviour. For example, the interactivity feature of the phone keypad allows patients to provide immediate feedback, thus prompting the healthcare provider to intervene based on actual patient behaviour. Healthcare providers are among the top key influencers of patient adherence. It is crucial therefore to have a solution that they recognize as supportive and time saving in their daily practice.

Since the issue of adherence in AF patients is of the utmost importance, we believe an Interactive Monitoring System (IMS) offers an opportunity to leverage technology on behalf of patients, physicians, and other healthcare providers. Interactive Monitoring System is a new integrated compliance programme designed to help increase adherence among patients with chronic diseases. While it automatically reminds patients to take their medication through an IVR system, it also monitors and records patients’ responses (Figure 1). There are several additional advantages. First, real-time data coming from patients’ answers are stored in IMS databases; thus health professionals receive informative feedback and can monitor patients’ adherence at any time using a dedicated web interface. Consequently caregivers are better positioned to advise about appropriate actions to achieve treatment objectives, and interaction between healthcare providers and patients is encouraged. Secondly, caregivers have valid support in managing their patients remotely; as a result their ambulatory time is optimized without the pressure of a busy waiting room. Thirdly, the system is supported by different channels including landline, mobile phones, smart phones, tablets, and a dedicated web interface. Consequently caregivers are better positioned to advise about appropriate actions to achieve treatment objectives, and interaction between healthcare providers and patients is encouraged. Secondly, caregivers have valid support in managing their patients remotely; as a result their ambulatory time is optimized without the pressure of a busy waiting room. Thirdly, the system is supported by different channels including landline, mobile phones, smart phones, tablets, and a dedicated web interface. Consequently caregivers are better positioned to advise about appropriate actions to achieve treatment objectives, and interaction between healthcare providers and patients is encouraged. Secondly, caregivers have valid support in managing their patients remotely; as a result their ambulatory time is optimized without the pressure of a busy waiting room. Thirdly, the system is supported by different channels including landline, mobile phones, smart phones, tablets, and a dedicated web interface.

Conflict of interest: E.N. is an employee of FBCommunication. A.J.C. and R.P.G. are members of the International Multidisciplinary Scientific Board for the Interactive Monitoring Service for FBCommunication.

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