BMJ Open Quality

Adherence Monitoring Package (AMoPac) in patients suspected of non-response to antihypertensive treatment: perceived usefulness by general practitioners

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To cite: Dietrich F, Zeller A, Hersberger KE, *et al*. Adherence Monitoring Package (AMoPac) in patients suspected of non-response to antihypertensive treatment: perceived usefulness by general practitioners. *BMJ Open Quality* 2024;**13**:e002451. doi:10.1136/bmjoq-2023-002451

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjoq-2023-002451).

Received 7 June 2023
Accepted 7 January 2024

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ABSTRACT

Background Non-adherence to antihypertensive agents is common, mainly because of the low perceived burden of high blood pressure. General practitioners (GPs) are unable to predict whether patients are adhering to a recommended treatment. Knowledge about adherence might be of clinical interest in patients non-responding to antihypertensive treatment.

Aim To assess the usefulness of an Adherence Monitoring Package (AMoPac) to identify non-adherence in patients non-responding to antihypertensive treatment.

Methods AMoPac consists of (1) 4 weeks of electronic adherence monitoring, (2) pharmacist's feedback on patient's intake behaviour and (3) adherence metrics including clinical-pharmaceutical recommendations to the GP. AMoPac-HYP ('**A**dherence **Mo**nitoring **Pac**kage to identify non-adherence in ambulatory **HYP**ertensive patients') is an observational study among GPs and ambulatory patients with hypertension in a real-world setting. The primary outcome was GPs' perceived usefulness of AMoPac. Secondary outcomes were (1) frequency of medication problems and prescribing errors; (2) types of pharmacist's' recommendations; (3) acceptance of the recommendations by GPs; (4) medication adherence and (5) patients' satisfaction. Outcomes are reported descriptively. Data were collected with questionnaires and electronic monitoring of medicine intake.

Results Fifteen GPs and 15 patients with hypertension participated in the AMoPac-HYP Study. Patients were on average 62 years old, and mean blood pressure was 137/83 mmHg. All GPs rated AMoPac as useful. The most frequently mentioned use was excluding non-adherence in patients with hypertension (93%). Medication problems and prescribing errors were observed in 80% of the patients. The study pharmacist recommended adherence support (N=9 patients) and treatment optimisation (N=8 patients). The recommendations were accepted and implemented in 10 of 17 cases by the GP. Patients' mean taking and timing adherence were 90% and 86%, respectively. Satisfaction with the study procedures among patients was high.

Conclusion AMoPac was rated as useful for identifying and excluding non-adherence in patients with hypertension and was highly accepted among patients. Including adherence data in clinical decision-making could contribute to optimising patient care.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Non-adherence is the most common reason for antihypertensive therapy failure. The knowledge of medication adherence might be useful to guide clinical decisions in patients non-responding to pharmacotherapy.

WHAT THIS STUDY ADDS

⇒ General practitioners rated the Adherence Monitoring Package as useful for judging medication adherence in patients with hypertension.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Including adherence data in clinical decision-making could contribute to optimising pharmacological therapies in patients with hypertension.

INTRODUCTION

Non-adherence to antihypertensive agents is a common issue. About 28% of patients with a new antihypertensive medicine do not initiate treatment.[1] In addition, half of those who started the treatment discontinued taking it within the first year.[2] Multiple factors influence non-adherent behaviour. Mainly, the perceived burden of hypertension is low because most patients are asymptomatic.[3] Pharmacotherapy with antihypertensive agents does not immediately benefit the patient but can cause unpleasant side effects such as nocturnal urination. This unfortunate combination might decrease medication adherence.[4 5]

Hypertension guidelines recommend monitoring antihypertensive treatment by measuring patients' blood pressure.[6] Blood pressure is defined as controlled under treatment when below 130/80 mmHg if tolerated. In patients older than 65 years, values below 140/90 mmHg are targeted.[6] General practitioners (GPs) are trained to adapt treatments

based on clinical values (eg, kidney function) or physical examinations (eg, blood pressure measurement). In case of non-response to pharmacotherapy, non-adherence is the most common reason.[6] GPs are unable to predict whether patients are adhering to a recommended treatment.[7] The knowledge of medication adherence might be useful to guide clinical decisions in patients non-responding to pharmacotherapy.

Medication adherence can be assessed with different methods. Electronic monitoring is the preferred method to describe the implementation of pharmacotherapy and to identify patterns of non-adherence.[8 9] We developed the Adherence Monitoring Package (AMoPac) for monitoring, evaluating and reporting adherence. The feasibility and the acceptance of AMoPac among GPs have previously been assessed in a pilot study among patients with heart failure.[10] Although the feasibility and acceptance could be proven in the pilot study, it also revealed technical problems with the integrated transmission of the adherence report into GPs' electronic health records. Based on our experiences from the pilot study, we made two adaptations for the AMoPac-HYP ('**A**dherence **Mo**nitoring **Pac**kage to identify non-adherence in ambulatory **HYP**ertensive patients') Study. First, in the AMoPac-HYP Study, the report was sent via Health Info Net (HIN)-secured email. HIN-secured email is a standard way of communicating patient information that most healthcare professionals in Switzerland use. Second, we selected hypertension instead of heart failure. Interviews with GPs revealed that elevated clinical values in patients with heart failure demand fast action to prevent disease deterioration. However, our study design required at least 4 weeks to monitor adherence before making any changes to the treatment. This delay was considered inappropriate by some of the GPs. The preventive nature of the antihypertensive treatment allows a longer observation period before treatment adaptions become necessary. The aim of this study was to assess the usefulness of AMoPac among GPs to identify non-adherence in patients with hypertension non-responding to treatment.

METHODS

AMoPac is a tool to assess, evaluate and report patients' medication adherence to a healthcare professional. It consists of (1) electronic adherence monitoring, (2) feedback on patients' intake behaviour given by a pharmacist, (3) analysis of adherence data and (4) adherence report with adherence metrics including clinical-pharmaceutical recommendations to the GP.[10 11]

Study design

Patients with arterial hypertension non-responding to treatment (eg, with uncontrolled blood pressure) participated in the AMoPac-HYP Study. GPs were approached to participate in the study via the network of the research group and the HIN mail registry (https://www.hin.ch/). GPs recruited eligible patients during routine visits at their surgery. Patient inclusion criteria were (1) ≥18 years, (2) diagnosis of arterial hypertension, (3) treatment with ≥1 antihypertensive agent, (4) self-administering medication and (5) suspected deviant intake behaviour by the GP. The selection of patients was at the GP's discretion and could be due to uncontrolled blood pressure despite guideline-conform treatment; missed appointments with the GP or late refills at the pharmacy, among others. In addition, GPs could include any patient who in their opinion might benefit from a medication adherence assessment.

Patients used the electronic device Time4Med (Adherence Innovations, Hong Kong) to monitor daily medication intake for 4 weeks.[12] Every time a patient takes medication, the button of this small device shall be pressed until a beeping sound occurs. The device records date and time stamps on a microchip that can be downloaded via near-field communication on a tablet computer. The study pharmacist gave instructions on the use of the device during a phone call the day following the recruitment. Four weeks later, the study pharmacist visited the patient at home and gave feedback on their intake performance after downloading the data and obtaining the so-called dot chart, a graphical representation of all intake times. Patients' comments were welcome. An adherence report was created by the pharmacist and sent to the GP via HIN-secured email. HIN offers encrypted email communication to guarantee data protection. The report provides adherence metrics, a dot chart and clinical-pharmaceutical recommendations for treatment optimisation.[11] At the next visit, it was at the GPs' discretion to implement the recommendations. After study completion, GPs assessed the usefulness of AMoPac in a questionnaire. The patient's blood pressure was measured at study inclusion and study completion in the GP's office. Remuneration was SFr50 for patients and GPs. Regular study newsletters were sent to the GPs with the current recruitment status. These newsletters increased the awareness of the study and answered frequently asked questions of GPs.

In this article, the term 'medication problems and errors' is defined as any problem or error occurring in the medication use process, including non-adherence.[13] The term 'prescribing error' refers to any error leading to reduced effectiveness of a treatment or to increased risk of harm when compared with generally accepted practice.[14]

Study outcomes

The primary outcome was the usefulness assessment of AMoPac. The attribute 'useful' was granted if ≥75% of participating GPs agreed that AMoPac was useful (1) to identify medication problems and errors, (2) to identify non-adherence, (3) to exclude non-adherence or (4) for something else, please explain. Answer options were yes/no.

Secondary outcomes were as follows:

1. Description of:

- Patients' self-reported medication problems and errors.
- Prescribing errors.

2. Description of pharmacists' recommendations in case of errors.
3. GPs' acceptance of the pharmacist's recommendations, for example, by adapting the treatment or offering counselling (online supplemental file A).
4. Medication adherence, measured by electronic monitoring:
   - Taking adherence (%): the proportion of doses taken in relation to doses prescribed.
   - Timing adherence (%): the proportion of doses taken within a grace interval in relation to doses prescribed.
   - Correct dosing days (%): the proportion of days with the correct amount of doses taken in relation to monitored days.
   - Drug holidays: the number of consecutive days without medicine use.
5. Patients' satisfaction: assessed with 11 questions with answer options on a 5-point Likert scale (online supplemental file B).

Sample size

This is a qualitative study using questionnaires; therefore, no sample size calculation is needed. We aim at recruiting 15 GPs who will enrol at least one patient each, in order to get at least 12 full sets of electronic patient data.

Data analysis

Study outcomes were analysed descriptively and reported as absolute numbers with percentages or means with SDs. Microsoft Word V.2016 and Microsoft Excel V.2016 were used to calculate adherence and to create adherence reports. Study newsletters were created with Adobe InDesign V.2022. A patient satisfaction score was calculated by reversing negative statements and attributing numbers to the frequency between 1 (disagree) and 5 (agree). The average of all answers was reported as patient satisfaction score. Values range between 1 and 5 (highest satisfaction).

RESULTS

Population characteristics

From 89 approached GPs, 15 agreed to participate in the AMoPac-HYP Study. From April 2022 to April 2023, they recruited 15 patients with hypertension. Five GPs recruited two patients each, five GPs recruited one patient each and five GPs did not enrol any patient. The mean (SD) working experience of GPs was 20 years (8) and 30% of GPs were women.

Patients were on average 62 years old (range: 27–85) and monitored their medication intake on average for 32 days. Sixty per cent of the patients (9 of 15) had uncontrolled blood pressure (table 1). All patients completed the study.

Primary outcome: usefulness of AMoPac

All GPs (N=10) rated AMoPac as useful. The most frequently raised use was excluding non-adherence (in 14 of 15 patients, 93%), followed by identifying critical medication problems and errors (3 of 15, 20%). One GP rated AMoPac as useful for identifying non-adherence, and one found it helpful for optimising treatment.

Secondary outcomes

Medication problems and prescribing errors

A total of 17 medication problems and prescribing errors were observed in 12 patients (80%). Four patients presented with more than one error. Seven problems and errors (41%) concerned the antihypertensive treatment (table 2). Medication problems and prescribing errors that concerned the concomitant medication are shown in online supplemental file C.

Table 1 Characteristics of patients (N=15)

Parameter	N (%)	Value	
		Mean (SD)	Min–max
Women	7 (47)		
Age, years		62 (17)	27–85
Systolic blood pressure, mmHg*		137 (12)	121–161
Diastolic blood pressure, mmHg*		83 (13)	58–114
Patients with controlled blood pressure†	6 (40)		
Number of prescribed active agents		5.6 (3.4)	2–15
Number of antihypertensive agents		2.7 (1.2)	1–4
Number of daily medicines		5.2 (3.9)	1–13

*Blood pressure was measured at the GPs' office twice for each patient (at study inclusion and study completion). For this table, the means of the two values were used.
†Below 130/80 mmHg or below 140/90 mmHg in patients older than 65 years.
GPs, general practitioners.

Table 2 Summary of medication problems and prescribing errors concerning the antihypertensive treatment in seven patients with the corresponding recommendations by the pharmacist and whether the GP accepted the recommendation

Type of error	Pharmacist's recommendation	Accepted by GP
Medication problems and errors		
► Drug holidays (no medicine intake on 3 consecutive days)	► Patient counselling on the importance of regular medicine intake	Yes
► Missed intake (N=2 patients)	► Implement a medication intake reminder (eg, a smartphone application) ► Implement a medication management system (eg, a pillbox) to remember evening intake	No No
► Intake of a reduced dose of indapamide due to side effects	► Re-evaluate the dosage of indapamide or switch to another hypertensive class	Yes
► The interval between two times per day intake was too short (risk of blood pressure spikes)	► Reschedule evening intake, for example, when watching the news	No
► Morning intake times fluctuated (shift worker)	► Reschedule morning intake to fit the work schedule	Yes
Prescribing errors		
► Ramipril intake every 48 hours	► A once daily regimen would be preferred (if tolerated) to achieve a steady-state plasma concentration	Yes

See online supplemental file C for medication problems and prescribing errors concerning the concomitant medication.
GP, general practitioner.

Pharmacists' recommendations

The study pharmacist recommended adherence support in nine patients, such as rescheduling the intake time to fit the patients' daily routine. In addition, in eight patients, treatment adaptations unrelated to adherence were recommended, for example, discontinuation of proton-pump inhibitors due to missing indication (table 2 and online supplemental file C).

GPs' acceptance of pharmacists' recommendations

GPs accepted and implemented the recommendations made by the pharmacist in 10 of 17 cases (59%, table 2). Additional counselling on adherence behaviour based on the adherence information presented in the report was provided by GPs in 11 patients (73%). The adherence counselling included regular self-measuring of blood pressure at home (N=8), integrating the medicine intake into daily routine (N=8) and disease education (N=5).

Medication adherence (electronic monitoring)

Mean (SD) taking and timing adherence was 90% (8) and 86% (14), respectively. One patient presented with taking adherence levels below 80% (76.7%). One patient presented drug holidays of 3 days (table 3).

Patients' satisfaction

Patients reported high satisfaction with AMoPac (satisfaction score: 4.8). No difficulties in operating the monitoring device were reported. All patients stated to have a good relationship with their healthcare professionals and that they appreciate the collaborative approach of AMoPac. Half of the patients would recommend the monitoring device to others, one patient disagreed and six remained neutral (see online supplemental file B for all answers).

DISCUSSION

The AMoPac-HYP Study was an observational study that aimed to investigate the usefulness of the AMoPac to identify non-adherence in patients with hypertension non-responding to treatment.

The primary endpoint of this study was reached as all GPs rated AMoPac as useful. The most often mentioned argument was the exclusion of non-adherence in patients with hypertension who were not responding as expected to pharmacological treatment. Although treatment non-response in hypertension can have several reasons, non-adherence is the most common issue. In daily practice, it is difficult for GPs to estimate patients' adherence.[7 13] Once non-adherence is excluded, the GP can check other causes for treatment non-response, such as secondary hypertension.[6] Therefore, ruling out non-adherence is

Table 3 Medication adherence to antihypertensive medication measured by electronic monitoring during 4 weeks by study participants (N=15)

	Values	
Adherence metrics	Mean (SD)	Min–max
Taking adherence (%)	90 (8)	77–100
Timing adherence (%)	86 (14)	52–100
Correct dosing days (%)	87 (11)	68–100

an important aspect of the clinical decision process in hypertension.[14 15]

In our study, the pharmacist analysed the entire polypharmacy of patients on antihypertensive medication and observed medication problems and prescribing errors in 12 of 15 patients, with 41% concerning the antihypertensive medication. The recommendations made by the pharmacist aimed at optimising the prescribed treatment or the intake behaviour of the patient. Some of the recommended treatment adaptations were not directed at antihypertensive agents, for example, reschedule acetylsalicylic acid intake before meal and take all medicines at once. Because non-adherence increases with the number of medicines, and non-adherence may concern one, some or all agents of a polytherapy, analysing the entire polypharmacy can be seen as the optimal approach to tackle individual problems.

The GPs accepted and implemented these recommendations in most cases. Recommendations to adapt the pharmacotherapy were less frequently accepted than recommendations to optimise patients' intake behaviour. The GPs who participated in our study were seeking answers to why patients are non-responding to antihypertensive treatment. Therefore, the recommendations on other medicines might have been unexpected and were not further evaluated. However, the GPs did not document the reasons for not implementing the pharmacists' recommendations.

In our study, medication adherence was measured with electronic monitoring enriched by patient comments. Electronic adherence monitoring is the preferred method to objectively measure patients' intake behaviour because it is less prone to manipulations by the patient, among others.[8] By enriching the electronic intake data with patient comments, we gained a complete picture of the patient's intake behaviour. In our study, the GPs suspected patients to be non-adherent. However, mean taking adherence was high with 90% and non-adherence was verified only in a few cases. The final interpretation of this finding can only be made by the GPs who have the full clinical picture at disposal. Nevertheless, we suggest that the inclusion in the study with the creation of an interprofessional network through the involvement of the pharmacist, and the introduction of the measuring tool, might have increased patient performance, similar to the Hawthorne effect. Therefore, it is unsurprising that most GPs rated AMoPac as useful for excluding non-adherence in patients non-responding to hypertensive treatment. However, and in view of sustainability, it might be important for GPs to measure blood pressure in regular intervals after the observation period.

During the home visit, the pharmacist provided feedback on adherence and encouraged the patients to comment on any deviating behaviours. Thus, the home visit of the pharmacist was essential for the individual interpretation of patients' intake behaviour and completeness of adherence data. In order to scale up the deployment of AMoPac and implement it into practice, the resources to carry out home visits might be lacking. However, the conversation with the pharmacist can easily be performed at the community pharmacy or via phone. We used a holistic approach to evaluate medication adherence. This means we calculated various adherence metrics and interpreted them according to the pharmacological properties of the medicine, comorbidities and the patient's current situation. We claim that this approach is superior compared with judging adherence with one aggregated value and arbitrary thresholds.[16] In addition, clinical experience and data analysis training are required, in order to perform advanced adherence interpretations.

AMoPac achieved high satisfaction among patients in this study. However, any intervention aiming at improving someone's behaviour such as medication adherence should be tailored to the individual. Other options to objectively measure medication intake (eg, with smartphone applications) should be considered.

AMoPac-HYP was an observational study that was not powered to investigate the impact of medication intake behaviours on blood pressure levels. A correlation between adherence and blood pressure control has been shown in a meta-analysis.[17] Patients with hypertension who presented with higher adherence levels had more often controlled blood pressure. AMoPac is an objective method to assess and evaluate adherence. It could be used to accompany the optimisation of adherence by choosing tailored adherence-enhancing interventions and monitoring their effect on medication intake behaviour and, ultimately, on blood pressure control.

Strengths and limitations

This study has several strengths. First, AMoPac-HYP was based on a previously performed pilot study where we demonstrated the feasibility of the study procedures. Second, we included GPs in the planning of the study and used patient experiences from similar studies.[12 18] This approach added valuable insights and helped to design the study close to the real-world setting. We also want to acknowledge some limitations. First, all adherence reports were created by one study pharmacist. However, each adherence report was reviewed by a second pharmacist to reduce bias. Second, community pharmacies were not included in this study due to limited resources. We would need to recruit several community pharmacies because patients can choose their pharmacy. Therefore, we decided to substitute the community pharmacy by one study pharmacist. Third, only half of the study participants would recommend the monitoring device to others. This non-acceptance of monitoring should be interpreted with caution, as the use of Time4Med has been criticised by some patients as needing a high level of dexterity.[12 18] With the rapid evolution of devices and their diversity, it is likely that a further study will have several devices at disposal and that patients will select the more convenient for them. Finally, our study sample was small and might be prone to selection bias. Only 17% of the approached

GPs participated in our study. Those GPs are likely to be more interested in interprofessional work and medication adherence.

Outlook

In this study, we observed that pharmacists' recommendations to adapt intake behaviour and treatment were mainly implemented by GPs. However, if these adaptations have an effect on clinical outcomes, such as lowering elevated blood pressure, patient-relevant outcomes need to be analysed in future studies. Furthermore, the service needs to be implemented into primary care. This process might reveal new challenges, such as involving community pharmacies and identifying non-adherent patients. AMoPac was tested in patients with hypertension. However, the usefulness of the tool should also be assessed in patients with other diseases requiring chronic pharmacotherapy, for example, with non-forgiving medication such as antiepileptic agents or direct oral anticoagulants.

CONCLUSION

All GPs assessed the AMoPac tool as useful. The most common use was excluding non-adherence as a cause for treatment failure, followed by identifying medication problems and errors, and adapting the pharmacological treatment. The inclusion of adherence data in clinical decision-making could improve patient care.

Acknowledgements The authors thank all GPs and patients for their valuable input and participation in the study.

Contributors FD, IA and AZ were responsible for study design. FD was responsible for data analysis and manuscript writing. IA and KEH were responsible for supervision. All authors have reviewed and approved the submitted manuscript version. Guarantor: FD

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. The opinions of patients and healthcare professionals were collected during a previously conducted pilot trial and incorporated into the design of this study. Refer to the Introduction and Methods section for further details.

Patient consent for publication Not required.

Ethics approval This study involves human participants and was approved by the Ethics Committee of Northwestern Switzerland (EKNZ 2021-02392). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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