

Medication Monitoring and Optimization: A Targeted Pharmacist Program for Effective and Cost-Effective Improvement of Chronic Therapy Adherence

Job F.M. van Boven, PharmD, MSc; Ada G.G. Stuurman-Bieze, PharmD, PhD;
Eric G. Hiddink, PharmD, MScBA; Maarten J. Postma, PhD; and Stefan Vegter, PharmD, PhD

ABSTRACT

BACKGROUND: Community pharmacies provide a promising platform for monitoring and improving therapy adherence and providing pharmaceutical care. Structured methods and appropriate software are important tools to increase pharmacist effectiveness and improve health outcomes. In 2006, the Medication Monitoring and Optimization (MeMO) program was introduced in several community pharmacies in the Netherlands. MeMO facilitates targeted and continuous patient-centered pharmaceutical care around chronic medication, such as for osteoporosis, cardiovascular disease, and asthma/chronic obstructive pulmonary disease (COPD).

OBJECTIVES: To describe the MeMO program and summarize findings from publications on its effectiveness, patient satisfaction, and cost-effectiveness.

METHODS: In the first part of this article, the MeMO program is extensively described. In the second part, a review of the evidence of effectiveness, cost-effectiveness, and patient satisfaction of the MeMO program is provided. Evidence is based on 5 previously published articles.

RESULTS: The MeMO program starts with structured counseling sessions with patients at the initiation and follow-up of chronic therapies. This process is followed by a continuous phase in which patients' therapy adherence is monitored on a monthly basis, using standardized search algorithms in the pharmacy database. When the algorithm detects a patient's discontinuation of therapy, tailored interventions are used to improve adherence and optimize pharmacotherapy. For osteoporosis patients, treatment discontinuation with bisphosphonates after 1 year dropped from 31.7% to 16.1% ($P < 0.001$). This program was shown to be cost-effective in patients initiating osteoporotic therapy. Future scenarios with lower drug prices (e.g., from generic prescribing) result in cost savings for the MeMO program. For lipid-lowering drugs, the MeMO program has been shown to lower therapy discontinuation after 1 year from 25.9% to 13.6% ($P < 0.001$). By extrapolating these results to patients' lifetimes, the intervention was estimated to be cost-effective, with gains for primary prevention of cardiovascular events, and even cost saving in secondary prevention. Results from the ongoing MeMO asthma/COPD program are promising, showing marked improvements in therapy control and quality of life for asthma and COPD patients. Almost all patients participating in MeMO programs are satisfied with the pharmacy team and have gained knowledge of the effectiveness and administration of their medications and the importance of therapy adherence.

CONCLUSION: The MeMO program is an effective and structured method to improve patients' adherence to chronic medication in the field of osteoporosis, lipid-lowering drugs, and asthma/COPD and is well received by patients. By targeting the program toward nonadherent and high-risk patients, the program showed favorable cost-effectiveness.

J Manag Care Pharm. 2014;20(8):786-92

Copyright © 2014, Academy of Managed Care Pharmacy. All rights reserved.

What is already known about this subject

- Adherence to chronic medication is often suboptimal.
- Pragmatic and structured pharmacist intervention programs can optimize pharmacotherapy and improve therapy adherence.

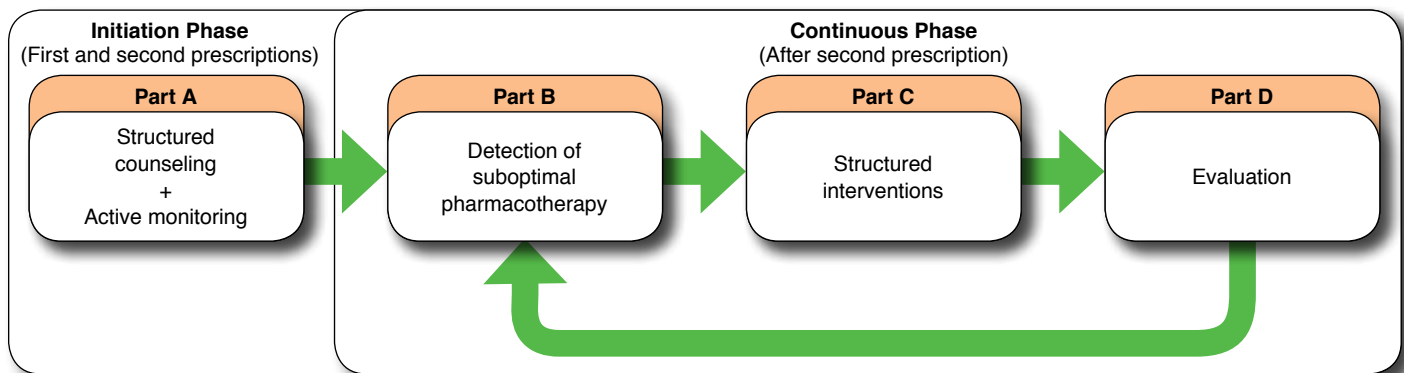
What this study adds

- Structured periodic interventions by pharmacists in the Medication Monitoring and Optimization program improved therapy adherence.
- Structured and targeted improvement of adherence is cost-effective and in some scenarios even cost saving.

Adherence to chronic medication has been shown to be suboptimal across many therapeutic areas. Nonadherence has been linked to adverse clinical outcomes, for example, in osteoporosis, asthma/chronic obstructive pulmonary disease (COPD), and cardiovascular diseases.¹⁻⁴ Community pharmacies offer a promising platform for monitoring and improving therapy adherence and for providing medication therapy management.^{5,6} The ability of community pharmacies to monitor long-term dispensing data provides pharmacists with a tool to identify nonadherent patients and approach them for intervention.⁷ However, structured methods and appropriate software for such approaches are often lacking, thereby limiting pharmacist effectiveness and reducing the continuity of care and patients' health outcomes.⁸

In 2006, the Medication Monitoring and Optimization (MeMO) program was introduced in several community pharmacies in the Netherlands. MeMO facilitates targeted and continuous patient-centered medication therapy management for chronic, preventive medication in the field of cardiovascular diseases, asthma/COPD, and osteoporosis. Since the launch of the program, several studies have assessed clinical and economic outcomes of the MeMO program.⁹⁻¹³ In this article, we describe the concept and structure of the MeMO program, its effectiveness, cost-effectiveness, and patient satisfaction with the pharmacies participating in the program.

FIGURE 1 MeMO Initiation, Monitoring, Intervention, and Evaluation Phases



MeMO = Medication Monitoring and Optimization program.

Methods

Overview and Structure of the MeMO Program

Pharmacies participating in the MeMO program use a pharmacist information system that stores the medication history of enlisted patients. These databases can be queried using search algorithms, for example, to select nonadherent patients or patients receiving specific medications. In the Netherlands, patients show a high commitment to a single (“their”) pharmacy.¹⁴ Therefore, these searches can detect nonadherence. Several studies have used prescription data to study therapy adherence.^{15,16} Pharmacists new to the MeMO program are supervised in implementation of the program and follow courses to perform standardized database queries and to conduct patient interventions (www.pharmapartners.nl [in Dutch]).¹⁷ A schematic overview of the MeMO program is shown in Figure 1. Each part is more thoroughly explained in this section.

Initiation Phase: Structured Counseling and Active Monitoring

When patients redeem their first prescription of a newly initiated chronic medication, the pharmacy team provides verbal and written information about the medication’s clinical effectiveness and mechanism of action, the time that it will usually take to notice the drug’s effects, the dosing regimen, potential side effects, and instructions on proper administration of the medication (First Dispense Counseling [FDC]). In The Netherlands, a follow-up assessment after 2 weeks is common practice by physicians, in order to monitor effects of treatment on disease symptoms. After this follow-up assessment, a second prescription (for 3 months) is prescribed. When patients redeem their second prescription in the pharmacy (usually also after 2 weeks), drug use, in particular, is evaluated. This practice contributes to safe and responsible drug use and prevents wasting of medication. The second counseling session focuses on side effects, beliefs and expectations, and discom-

forts encountered with patients’ medication (Second Dispense Counseling [SDC]). In the Netherlands, FDC and SDC are considered usual care by the pharmacy profession guidelines, but they are not routinely performed in all pharmacies. In the MeMO program, FDC and SDC counseling are always performed and documented, using standardized protocols. When patients do not redeem their second prescription, they are contacted to discuss medication problems or administration difficulties. Similarly, patients are contacted when they do not redeem their third prescription on time (in the Netherlands, usually 3 months after the second prescription). After their third prescription, patients enter the continuous phase of MeMO.

Continuous Phase: Detection of Suboptimal Pharmacotherapy

The continuous phase of MeMO has a similar structure for all areas. The purpose of the monitoring phase is to detect suboptimal pharmacotherapy, using monthly searches to identify nonadherent patients in the pharmacists’ dispensing database. The different algorithms to detect nonadherence differ between drug classes. For osteoporosis medication and lipid-lowering drugs, nonadherent users are identified as patients who potentially discontinue their medication (nonpersistent users) or patients who continue with low adherence. Nonpersistent users are defined as those patients who did not redeem a new prescription after the theoretical end date of their previous prescription, using a margin of 30 days. Low adherence was defined as having medication coverage for less than 80% of the days from initiation of therapy to the end date of their last prescription. In the asthma/COPD program, patients also need to have an additional risk factor as specified in the section below.

Osteoporosis Medication. For patients identified as potentially nonadherent, medication profiles are inspected manually to determine possible reasons for discontinuations. Valid

reasons for discontinuations are discontinuation of oral corticosteroids, switches to a different type of osteoporotic medication, drug stockpiling, or a treatment length that exceeds the recommended duration of osteoporotic medication (5-10 years).

Lipid-Lowering Drugs. Records of potential nonadherent users of lipid-lowering drugs are also manually inspected to determine possible reasons for discontinuation. Valid reasons for discontinuation include clear signs of drug stockpiling or switches to different medications in the same therapeutic area.

Asthma/COPD Medication. For asthma/COPD medication, only “high risk” nonadherent patients are identified for intervention. These are defined as patients having received at least 2 short courses of oral corticosteroids and having discontinued respiratory maintenance medication or showing low adherence (<80%). To increase the likelihood of identifying COPD patients (instead of older asthma patients), an age threshold of ≥ 50 years is used, preferably in combination with a recorded comorbidity of COPD (if available). Asthma patients are identified based on an age threshold of ≤ 50 years.^{18,19} The suspected diagnosis is confirmed with the prescribing physician before the intervention.

Continuous Phase: Structured Interventions

Patients with suspected suboptimal pharmacotherapy are selected for structured interventions in the MeMO program. For patients using osteoporosis and lipid-lowering drugs, those selected are mainly (intentionally or unintentionally) nonadherent patients. In the asthma/COPD program, these may also include patients with drug therapy problems (such as inhalation technique errors). The interventions are tailored to patients’ needs and can be divided into medication-related interventions and lifestyle interventions.

Medication-Related Interventions. Elements in the counseling include side effects of medication, information on the benefits and long-term effects of adherence, advice for integrating chronic drug therapy in daily routine, and motivational interviewing to improve medication adherence. In some cases, the pharmacy team also supported daily drug use with practical advice or unit-dose drug dispensing systems, especially when cognitive problems (e.g., forgetfulness) were the cause of non-adherence. For some interventions, the prescriber is involved, for example, when dose or drug changes are recommended. Note that the way these recommendations are communicated could differ per individual patient and/or pharmacy (setting) and that recommendations are not always followed. In the MeMO asthma/COPD program, additional disease-specific interventions include repeating inhalation device instructions. Disease-monitoring questionnaires are also used in this program, namely the Asthma Control Questionnaire (ACQ)²⁰ and the Clinical COPD Questionnaire (CCQ)²¹ for asthma and COPD patients, respectively.

Lifestyle Interventions. In addition to interventions focusing on optimal use of medication, lifestyle recommendations are often provided. Lifestyle interventions include smoking cessation, exercise advice, or dietary recommendations. If needed, the pharmacist suggests that patients schedule an appointment with a physiotherapist or dietician. In general, when lifestyle interventions are deemed necessary, patients are also recommended to contact their prescribing physicians to maintain continuity of care.

Continuous Phase: Evaluation

After intervention, medication use is extensively monitored and evaluated. Depending on the intervention, extra telephone calls can be made with the patient or prescriber, or reminders can be sent to the patient. In the MeMO asthma/COPD program, patients are scheduled for in-person follow-up visits (generally after 3 months) to reevaluate disease status using the ACQ or CCQ questionnaires.

Results

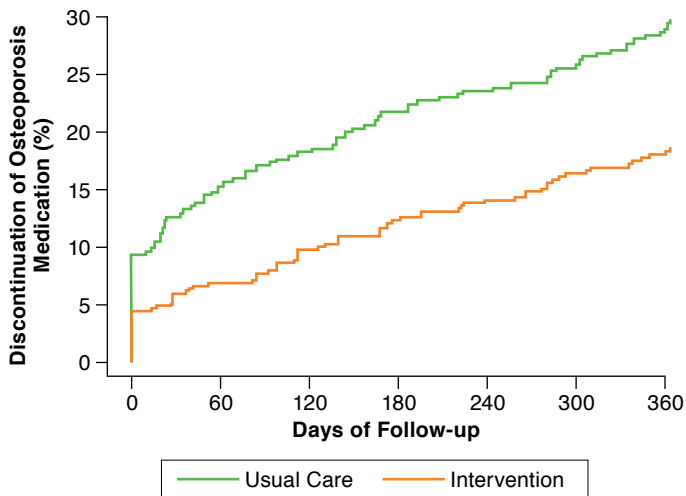
The following section provides an overview of published data on the effectiveness, cost-effectiveness, and patient satisfaction of the MeMO program. For detailed descriptions of the methods and results of the studies we refer to the literature.⁹⁻¹³

Impact on Medication Adherence and Effectiveness

Osteoporosis. A total of 227 patients, in 13 pharmacies, who initiated osteoporotic therapy, received structured FDC and SDC counseling, and their medication use was monitored in the MeMO program. The effectiveness of the program on therapy adherence was assessed and compared with a historical cohort of 408 patients from the same pharmacies who initiated osteoporotic therapy before the MeMO program was implemented, receiving usual care. Usual care included FDC and SDC but no continuous monitoring.⁹ Therapy discontinuation after 1 year was 16.1% in the MeMO patients, compared with 31.7% in the control patients ($P < 0.001$; Figure 2). In a recently completed follow-up study (495 patients in the MeMO program and 442 control patients), similar results were observed, with 32.8% discontinuing in the control group and 19.0% in the MeMO group ($P < 0.001$).²² In addition, data from follow-up studies showed that the patients in the MeMO program maintained high levels of adherence in the second year of follow-up.²²

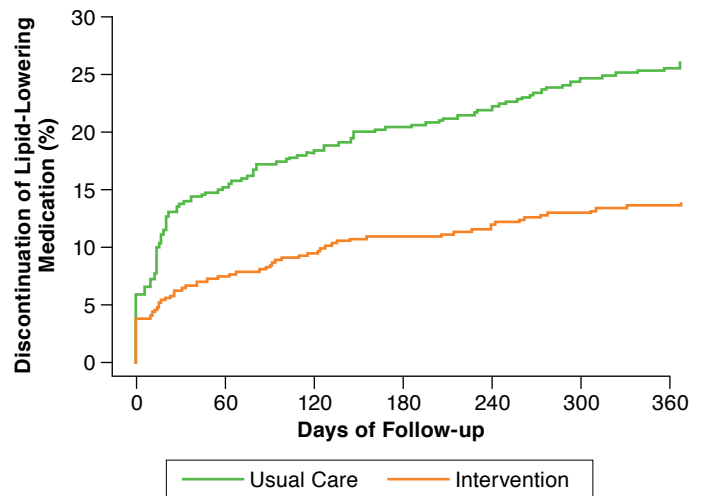
Lipid-Lowering Drugs. The impact of the MeMO lipid-lowering drugs program on adherence was assessed using a similar study design as that used in the osteoporosis program.¹² A total of 500 patients received MeMO care; these were compared with 502 historical controls. After 1 year, the therapy discontinuation rate was 13.6% in the MeMO cohort and 25.9% in the control group ($P < 0.001$; Figure 3). During a 1-year follow-up study, the discontinuation rate in the MeMO group was reduced even further to less than 5% (unpublished data).

FIGURE 2 Reduction in Percentage of Patients Discontinuing Osteoporosis Medication^a



^aFull study reports in Stuurman-Bieze AG, Hiddink EG, Pharmaceutical care interventions, initiated by computerized drug prescription monitoring, improve drug compliance,⁹ and Stuurman-Bieze AG, Hiddink EG, van Boven JF, Vegter S, Proactive pharmaceutical care interventions decrease patients' non-adherence to osteoporosis medication.²²

FIGURE 3 Reduction in Percentage of Patients Discontinuing Lipid-Lowering Drugs^a



^aFull study report in Stuurman-Bieze AG, Hiddink EG, van Boven JF, Vegter S, Proactive pharmaceutical care interventions improve patients' adherence to lipid-lowering medication.¹²

Asthma/COPD. A pilot study with 31 participants has explored the effectiveness of the asthma/COPD program.²³ In the pilot study, ACQ and CCQ questionnaires were given to patients at the start of the MeMO program and after 3 months.^{20,21} Despite the low number of participants, the results showed marked improvements in ACQ and CCQ questionnaire scores. The ACQ scores 3 months after the intervention had improved from 1.65 to 1.12 ($P < 0.05$). CCQ scores had improved nonsignificantly from 1.99 to 1.51 ($P = 0.06$), implicating a clinically relevant improvement in 44% of the asthma patients and 46% of the COPD patients. Effects of the program on adherence in the pilot program were inconclusive, likely due to the low patient numbers.

Patient Satisfaction

Osteoporosis. A satisfaction questionnaire was sent out to patients after their third prescription.²⁴ The response rate was 63%. Almost all respondents (93%) were satisfied with the information provided by their community pharmacy. The majority (69%) indicated that they had gained knowledge of the effectiveness and administration of their medication. One-third of participants had received this information only from their pharmacy, while half had also received information from their physician or nurse. Only a few participants (8%) had privacy concerns regarding counseling by the pharmacy team.

Lipid-Lowering Drugs. A patient satisfaction survey was sent to participating patients, with a response rate of 54%.¹² Almost all participants (92%) in the MeMO program were satisfied

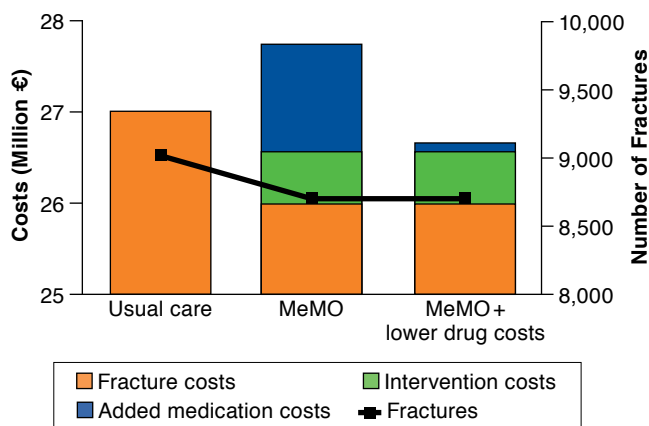
with expertise and the information provided by the pharmacy; half of the patients (52%) were more satisfied with their pharmacy after the MeMO program than before the counseling sessions. The majority of patients (74%) mentioned that their knowledge had increased on the medication effectiveness and administration and on the importance of therapy adherence. One-quarter of patients said that the pharmacy was their only source of information regarding the effectiveness and administration of their drugs.

Asthma/COPD. This study is still ongoing, so no results on patient satisfaction have yet been obtained.

Cost-Effectiveness

Osteoporosis. The cost-effectiveness of the MeMO bisphosphonates program was assessed using a modeling study.^{10,11} The model included intervention costs for the additional time spent on patient care by the pharmacy team. Because clinical parameters such as bone density could not be accessed in the pharmacies, drug adherence levels were linked to clinical outcomes using data from an observational study.²⁵ The consequences of nonadherence assessed were fractures (such as hip, wrist, and vertebral fractures), costs of these fractures, and quality of life measured in quality-adjusted life-years (QALYs). Over a modeled time-window of 3 years, MeMO osteoporosis was found to be cost-effective in 52,000 patients yearly, initiating osteoporotic therapy with an incremental cost-effectiveness ratio of €16,000 per QALY gained. Costs in the MeMO program included the additional medication costs from improved

FIGURE 4 Results of the MeMO Osteoporosis Program^a



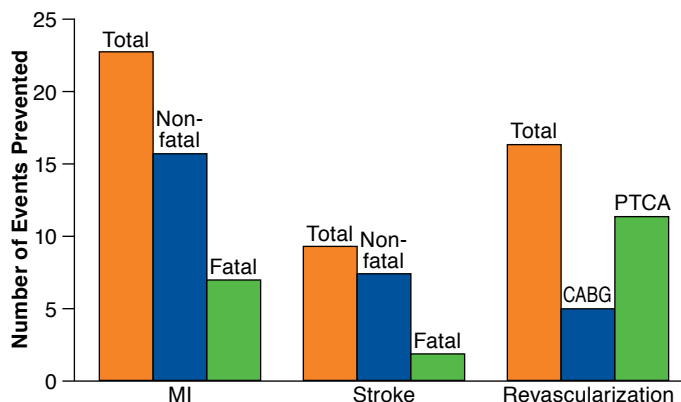
^aFull study reports in van Boven JF, Hiddink EG, Stuurman-Bieze AG, Postma MJ, Vegter S, Structured medication surveillance for improving adherence to bisphosphonate therapy offers perspectives for cost-effective pharmaceutical care,¹⁰ and van Boven JF, Oosterhof P, Hiddink EG, Stuurman-Bieze AG, Postma MJ, Vegter S. Cost-effectiveness of increasing bisphosphonates adherence for osteoporosis in community pharmacies.¹¹

MeMO = Medication Monitoring and Optimization program; € = euros.

adherence and a fee for the time investment of the pharmacy. However, these costs were partly offset by the prevention of 337 osteoporotic fractures, compared with the usual-care group. These fractures accounted for a total loss of 46.5 QALYs. When lower drug costs were assumed in the model (likely in situations of generic prescribing or therapeutic substitution), the model indicated that MeMO could be a *dominating* strategy (i.e., resulting in clinical benefits as well as cost savings). The main drivers of cost-effectiveness were a marked reduction in osteoporotic fractures, in associated health care costs, and in increased medication costs from higher adherence (Figure 4).

Lipid-Lowering Drugs. Since lipid-lowering drugs are often prescribed to be used life-long, a pharmacoeconomic model was used to estimate the life-long costs and clinical effects of increasing statin therapy adherence.¹³ This model included intervention costs for the additional time spent on patient care by the pharmacy team. Large clinical trials on the effectiveness of statins on cardiovascular events—namely, myocardial infarction (MI), stroke, and revascularization—were used, both from primary and secondary prevention populations.²⁶⁻²⁸ Efficacy data were adjusted for therapy adherence, by assuming that patients who had discontinued were “treated” with placebo. Data from Dutch observational studies were used to calibrate the model.¹³ So modeled, the MeMO program resulted in considerable clinical benefits. According to a model using 1,000 primary (40%) and secondary (60%) prevention patients, the MeMO program resulted in a reduction of 7 nonfatal strokes, 2 fatal strokes, 16 nonfatal MIs, 7 fatal MIs,

FIGURE 5 Estimated Number of Prevented Cardiovascular Events from the MeMO Lipid-Lowering Drugs Program^a



^aFull study report in Vegter S, Oosterhof P, van Boven JF, Stuurman-Bieze AG, Hiddink EG, Postma MJ, Improving adherence to lipid-lowering therapy in a community pharmacy intervention program: a cost-effectiveness analysis.¹³ CABG = coronary artery bypass grafting; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

and 16 revascularizations over patients’ lifetimes (Figure 5). Importantly, drug costs for statins are relatively low in the Netherlands because of generic substitution policies.²⁹ This low cost limited the influence of improved adherence on drug costs in the model. The cost-effective aspect was favorable for the primary prevention population (around €5,000 per QALY gained) and *dominating* for the secondary prevention population (lower costs and more health gains).

Asthma/COPD. A larger follow-up of the program is currently ongoing, targeted specifically toward COPD patients. Economic consequences, for example, from exacerbations, will be measured in order to perform a pharmacoeconomic evaluation.³ Quality of life will be included by mapping the CCQ to EQ-5D utilities (EuroQol Group, Rotterdam, The Netherlands) suitable for economic analyses. A mapping study set up for this purpose is currently ongoing, with preliminary results presented.³⁰

Discussion

The MeMO program facilitates structured and continuous medication therapy management across different chronic therapy areas. The effectiveness, patient satisfaction, and cost-effectiveness of MeMO have been studied extensively. The intensive counseling at the initiation of chronic therapies plays an integral role in the patients’ adherence levels. Using periodic monitoring of drug use, interventions can be targeted at patients actually requiring counseling. Targeted pharmacy interventions are time-efficient and therefore are likely to improve the cost-effectiveness of the program.³¹ Pharmacists

using the MeMO program were able to improve medication adherence in patient populations with different types of chronic medications. Internal personal communications indicated that the participating pharmacists were enthusiastic about the program, the patient involvement, the multidisciplinary approach, and the results of the program.

An advantage of the Dutch health care system to pharmaceutical projects such as MeMO is that patients' loyalty to a single pharmacy is high.¹⁴ Moreover, many pharmacies exchange medication histories and even clinical parameters between hospitals, general practitioners, and other pharmacies, using local networks. This exchange ensures complete medication histories to assess therapy use, such as adherence.

Limitations

Intensive collaborations are not always in place and exist only on regional levels. Although a national electronic health record system has been a discussion point for the last few years, it has not been implemented in the Netherlands, mainly because of ongoing privacy and security issues. In countries without a national electronic health records system, such as the United States, the MeMO program can be valuable, but a couple of preconditions need to be met. While structured first- and second-dispense counseling could be relatively easily implemented, for the continuous phase of MeMO, access to a complete overview of patients' medication records is essential. Encouraging patients to sign up for and obtain their medications from only a single pharmacy (or pharmacy chain) could enable this access. Alternatively, collaborations and data exchange on regional levels could be established in order to obtain patients' complete medication records. In addition, the correct use of medication therapy management programs such as MeMO depends on appropriate pharmacist software systems.¹⁷ With adequate software systems and standardized search algorithms, the pharmacist can automatically and efficiently identify patients with suboptimal drug use. Besides these regulatory issues, personal assessment by the pharmacy team remains necessary to optimize patients' medication use, as well as to exclude factors that could justify discontinuation of therapy, such as relocation of patients, holidays, clinical reasons, or death. Signing up for a single pharmacy establishes a better relationship between pharmacist and patient and improves mutual acceptance, which forms the basis for providing optimal pharmaceutical care and medication therapy management.

Lastly, community pharmacists are often limited in their ability to evaluate the medication use of patients because they do not always possess information about the physicians' diagnoses. Instead, they often have to derive a "suspected" diagnosis based on current prescriptions and prescription history. Having access to the actual diagnosis would greatly increase the ability of pharmacists to optimize tailored patient-centered interventions.

Implications for Pharmacy Practice, Policy, and Future Research

In the Netherlands, the pharmacist's role has shifted from a compounder, dispenser, and specialist of medication toward a patient-oriented health care professional. Together with this role change, a shift in reimbursement systems is inevitable. In the future, the primary source of income of pharmacists may be earned by providing continuous medication therapy management. Recently, the Dutch health care authorities have defined several pharmacy services for which the pharmacist can be reimbursed separately from the dispense fees. Currently, the Dutch pharmacists association and health insurance companies are discussing appropriate structures and prices. However, because of the large diversity in types of services offered, more research is warranted, including cost-effectiveness and the role of the pharmacist in multidisciplinary patient-centered care. The MeMO program shows that such roles are possible and may lead to more effective and cost-effective health care. New MeMO programs, including diabetes mellitus care and antithrombotic drugs, are planned for future research. Implementation of community pharmacy-led medication therapy management programs targeting other chronic medications, such as those for human immunodeficiency virus or Crohn's disease, are also likely to contribute to increased therapy adherence.³²

Conclusion

The MeMO program is an effective method of improving patients' adherence to chronic medication in the areas of osteoporosis, lipid-lowering drugs, and asthma/COPD. By specific targeting of patients demonstrating nonadherence, the program showed favorable cost-effectiveness. Because of their potential to improve therapy adherence, pharmacists can play a valuable role in chronic patient-centered care.

Authors

JOB F.M. VAN BOVEN, PharmD, MSc, is PhD Researcher; MAARTEN J. POSTMA, PhD, is Professor of Pharmacoeconomics; STEFAN VEGTER, PharmD, PhD, is Postdoctoral Researcher, Unit of PharmacoEpidemiology & PharmacoEconomics, Department of Pharmacy, University of Groningen, Netherlands. ERIC G. HIDDINK, PharmD, MScBA, is Researcher, Unit of PharmacoEpidemiology & Pharmacoeconomics, Department of Pharmacy, University of Groningen, and Scientific Advisor and Pharmacist, Health Base Foundation, Houten, Netherlands, and PharmaPartners, Oosterhout, Netherlands. ADA G.G. STUURMAN-BIEZE, PharmD, PhD, is Scientific Advisor and Pharmacist, Westpharmacy, Emmeloord, and Health Base Foundation, Houten, Netherlands.

AUTHOR CORRESPONDENCE: Job F.M. van Boven, PharmD, MSc, University of Groningen, Department of Pharmacy, Unit of PharmacoEpidemiology & PharmacoEconomics (PE2), Antonius Deusinglaan 1, 9713 AV, Groningen, The Netherlands. Tel.: 31(0)50.363.8204; Fax: 31(0)50.363.2772; E-mail: j.f.m.van.boven@rug.nl.

Medication Monitoring and Optimization: A Targeted Pharmacist Program for Effective and Cost-Effective Improvement of Chronic Therapy Adherence

DISCLOSURES

No funding was received for this study. Vegter has received grants from the Royal Dutch Association for the Advancement of Pharmacy (KNMP), and Postma is on several pharmacy advisory boards. Stuurman-Bieze and Hiddink are employees of the Health Base Foundation, which developed the MeMO intervention program.

All authors contributed to the concept and design of this study, with data collection primarily performed by Stuurman-Bieze, in collaboration with the other authors. All authors participated in data interpretation. The manuscript was written mostly by van Boven and Vegter, with input from other authors, and most of the revision was done by van Boven.

REFERENCES

- Hilgsmann M, Rabenda V, Bruyère O, Reginster JY. The clinical and economic burden of non-adherence with oral bisphosphonates in osteoporotic patients. *Health Policy*. 2010;96(2):170-77.
- Murphy AC, Proeschal A, Brightling CE, et al. The relationship between clinical outcomes and medication adherence in difficult-to-control asthma. *Thorax*. 2012;67(8):751-53.
- van Boven JF, Chavannes NH, van der Molen T, Rutten-van Molken MP, Postma MJ, Vegter S. Clinical and economic impact of non-adherence in COPD: a systematic review. *Respir Med*. 2014;108(1):103-13.
- Mayor S. Non-adherence to medication increases stroke risk in patients with high blood pressure. *BMJ*. 2013;347:f4586.
- García-Cárdenas V, Sabater-Hernández D, Kenny P, Martínez-Martínez F, Faus MJ, Benrimoj SI. Effect of a pharmacist intervention on asthma control: a cluster randomised trial. *Respir Med*. 2013;107(9):1346-55.
- Tommelein E, Mehuys E, van Hees T, et al. Effectiveness of pharmaceutical care for patients with chronic obstructive pulmonary disease (PHARMACOP): a randomized controlled trial. *Br J Clin Pharmacol*. 2014;77(5):756-66.
- van Boven JF, Hiddink EG, Stuurman-Bieze AG, Schuiling-Veninga CC, Postma MJ, Vegter S. The pharmacists' potential to provide targets for interventions to optimize pharmacotherapy in patients with asthma. *Int J Clin Pharm*. 2013;35(6):1075-82.
- Stuurman-Bieze AG, van den Berg PB, Tromp TF, de Jong-van den Berg LT. Computer-assisted medication review for asthmatic patients as a basis for intervention: constructing and validating an algorithmic computer instrument in pharmacy practice. *Pharm World Sci*. 2004;26(5):289-96.
- Stuurman-Bieze AG, Hiddink EG. Pharmaceutical care interventions, initiated by computerized drug prescription monitoring, improve drug compliance [article in Dutch]. *Pharmaceutisch Weekblad–Wetenschappelijk Platform*. 2010;4(7):128-35.
- van Boven JF, Hiddink EG, Stuurman-Bieze AG, Postma MJ, Vegter S. Structured medication surveillance for improving adherence to bisphosphonate therapy offers perspectives for cost-effective pharmaceutical care [article in Dutch]. *Pharmaceutisch Weekblad–Wetenschappelijk Platform*. 2011;5(9):147-53.
- van Boven JF, Oosterhof P, Hiddink EG, Stuurman-Bieze AG, Postma MJ, Vegter S. Cost-effectiveness of increasing bisphosphonates adherence for osteoporosis in community pharmacies. *Value Health*. 2011;14(7):A310/PMS42.
- Stuurman-Bieze AG, Hiddink EG, van Boven JF, Vegter S. Proactive pharmaceutical care interventions improve patients' adherence to lipid-lowering medication. *Ann Pharmacother*. 2013;47(11):1448-56.
- Vegter S, Oosterhof P, van Boven JF, Stuurman-Bieze AG, Hiddink EG, Postma MJ. Improving adherence to lipid-lowering therapy in a community pharmacy intervention program: a cost-effectiveness analysis. *J Manag Care Pharm*. 2014;20(7):722-32. Available at: <http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=18261>.
- Leufkens HGM, Urquhart J. Automated pharmacy record linkage in the Netherlands. In: Strom BL, ed. *Pharmacoepidemiology*. Chichester, UK: John Wiley & Sons; 2008:347-60.
- van Boven JF, de Boer PT, Postma MJ, Vegter S. Persistence with osteoporosis medication among newly-treated osteoporotic patients. *J Bone Miner Metab*. 2013;31(5):562-70.
- Vegter S, Nguyen NH, Visser ST, de Jong-van den Berg LT, Postma MJ, Boersma C. Compliance, persistence, and switching patterns for ACE inhibitors and ARBs. *Am J Manag Care*. 2011;17(9):609-16.
- de Gier JJ. The Electronic Pharmaceutical Dossier: an effective aid to documenting pharmaceutical care data. *Pharm World Sci*. 1996;18(6):241-43.
- Osborne ML, Vollmer WM, Johnson RE, Buist AS. Use of an automated prescription database to identify individuals with asthma. *J Clin Epidemiol*. 1995;48(11):1393-97.
- Pont LG, van der Werf GT, Denig P, Haaijer-Ruskamp FM. Identifying general practice patients diagnosed with asthma and their exacerbation episodes from prescribing data. *Eur J Clin Pharmacol*. 2002;57(11):819-25.
- Juniper EF, Bousquet J, Abetz L, Bateman ED, and the GOAL Committee. Identifying 'well-controlled' and 'not well-controlled' asthma using the Asthma Control Questionnaire. *Respir Med*. 2006;100(4):616-21.
- van der Molen T, Willemse BW, Schokker S, ten Hacken NH, Postma DS, Juniper EF. Development, validity and responsiveness of the Clinical COPD Questionnaire. *Health Qual Life Outcomes*. 2003;1:13.
- Stuurman-Bieze AG, Hiddink EG, van Boven JF, Vegter S. Proactive pharmaceutical care interventions decrease patients' non-adherence to osteoporosis medication. *Osteoporos Int*. 2014;25(6):1807-12.
- van Boven JF, Stuurman-Bieze AG, Hiddink EG, Postma MJ, Vegter S. Effects of targeted pharmaceutical care in patients with asthma and COPD: results of a pilot study [article in Dutch]. *Pharmaceutisch Weekblad–Wetenschappelijk Platform*. 2014(8):a1413.
- Stuurman-Bieze AG, Kokenberg ME, Tobi H, et al. Complex pharmaceutical care intervention in pulmonary care: part B. Patient opinion and process survey. *Pharm World Sci*. 2005;27(5):385-92.
- van den Boogaard CH, Breekveldt-Postma NS, Borggreve SE, Goettsch WG, Herings RM. Persistent bisphosphonate use and the risk of osteoporotic fractures in clinical practice: a database analysis study. *Curr Med Res Opin*. 2006;22(9):1757-64.
- Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. *N Engl J Med*. 1995;333(20):1301-07.
- Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet*. 2002;360(9326):7-22.
- Amarenco P, Bogousslavsky J, Callahan A 3rd, et al. High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J Med*. 2006;355(6):549-59.
- Boonen LH, van der Geest SA, Schut FT, Varkevisser M. Pharmaceutical policy in the Netherlands: from price regulation towards managed competition. *Adv Health Econ Health Serv Res*. 2010;22:53-76.
- Boland MR, van Boven JF, Rutten-van Molken MP. Mapping the CCQ onto EQ-5D scores (im)possible? *Value Health*. 2013;16(7):A329-30.
- Vegter S, van Boven JF, Hiddink EG, Postma MJ. [Health economic evaluation of pharmaceutical patient care interventions]. In: Gier H, Bouvy M, De Smet P, eds. *Handboek farmaceutische patiëntenzorg [Pharmaceutical Patient Care]*. Houten, Netherlands: Prelum Uitgevers; 2013.
- de Bruin M, Hospers HJ, van Breukelen GJ, Kok G, Koevoets WM, Prins JM. Electronic monitoring-based counseling to enhance adherence among HIV-infected patients: a randomized controlled trial. *Health Psychol*. 2010;29(4):421-28.