

Medication adherence and knowledge of older patients with and without multidose drug dispensing

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Abstract

Objective: we compared the self-reported medication adherence and knowledge of older patients receiving their drugs via multidose drug dispensing (MDD users) with patients receiving manually dispensed drugs (non-MDD users).

Methods: MDD users (≥ 65 years, ≥ 5 oral chronic drugs) were randomly selected from eight Dutch community pharmacies. Non-MDD users (≥ 5 oral chronic drugs) were matched on age and gender. Medication adherence was assessed by using the Medication Adherence Reporting Scale (MARS) and medication knowledge by asking the indication of drugs. Cognitive function was measured with Mini-Mental State Examination (MMSE) for a sub selection of patients.

Results: the percentage of patients being adherent to all drugs was higher for MDD users ($n = 119$, 81%) compared with non-MDD users ($n = 96$, 58%, $P < 0.001$). The percentage of patients with adequate knowledge was lower for MDD users (40%) compared with non-MDD users (79%, $P < 0.001$). The differences in adherence were independent of knowledge and MMSE scores.

Conclusion: this study shows that older patients receiving their drugs via MDD reported a higher medication adherence compared with patients receiving manually dispensed drugs, despite a lower knowledge and lower cognitive function among patients receiving MDD.

Keywords: medication knowledge, adherence, multidose drug dispensing, adherence aids, older people

Introduction

Older people with polypharmacy may experience difficulties managing their medications. These difficulties could be due to complicated therapeutic regimens or practical problems (e.g. halving tablets and opening packaging) [1, 2]. Dosing aids may help patients with these practical problems to adhere to their therapeutic regimens [3, 4]. The awareness of the availability of dosing aids by older patients may vary considerably between, and even within countries [5, 6].

Multidose drug dispensing (MDD), also known as automated drug dispensing, is a sophisticated dosing aid that provides patients with robot-dispensed unit doses. All drugs intended for one dosing moment are gathered in disposable

bags and labelled with patient data, drug contents and the date and time for intake [4, 7, 8]. Most research originates from the Scandinavian countries and the Netherlands where MDD is used by community-dwelling patients and patients in nursing homes [4, 8–10]. The number of community-dwelling MDD users in The Netherlands increased strongly in recent years till 360.000 in 2011 [11]. This increase is partly due to a change in legislation which does not allow home healthcare employees to manage patient's medications anymore. Next to home health care, Dutch patients are mostly recruited for MDD by community pharmacists, general practitioners (GPs) or family when older patients experience difficulties managing their medications [4]. GPs can also refer patients for more specific reasons [e.g. decreased cognitive function, (suspected) non-

adherence or severe psychiatric problems] [4]. MDD is especially appropriate for persons who chronically use several drugs without frequent medication changes [9]. Prescription lists provided by community pharmacies for MDD users are authorized manually by GPs and other prescribers. These prescriptions are ordered through a community pharmacy, which electronically forwards the total orders to an MDD supplier. Dispensed drugs are returned to the community pharmacists who deliver MDD systems to the patients [12, 13]. It has been suggested that MDD reduces medication errors, increases medication adherence and decreases waste of unused drugs [8, 9]. However, it may be questioned whether patients still know the indication of the drugs in the MDD systems.

Previous studies showed that adequate medication knowledge differed from 60 to 72% [3, 14, 15]. Most studies reported a positive association between patients' knowledge and adherence [3, 15–18]. It is thought that patient knowledge of manually dispensed drugs is essential for competently managing their medication regimen [19]. However, as adherence is frequently determined by multiple factors, knowledge plays only a minor role [20]. Studies into the relation between adherence and cognitive function show conflicting results [3].

The aim of our study was to assess the self-reported adherence and medication knowledge of older patients receiving their drugs via MDD users compared with patients receiving only manually dispensed drugs (non-MDD users).

Methods

Study design

This was a cross-sectional study. Patients were selected and interviewed between October 2010 and January 2012. The majority of patients in the Netherlands are registered at only one community pharmacy, independently of prescriber, and patient medication records are virtually complete with regard to prescription drugs [21].

Patients

Patients were recruited from eight Dutch community pharmacies. MDD users were defined as patients with at least one drug dispensed by MDD. MDD users were eligible if they were aged ≥ 65 years, used at least five different oral prescription chronic drugs, lived at home or in a residential care home. MDD users had to be able to take their own drugs to explore if they had other medication management problems than patients that used only manually dispensed drugs (non-MDD users). Patients in nursing homes were therefore excluded. Even if the MDD system is used, a large share of the MDD users will still also need manually dispensed drugs, e.g. insulin, eye drops and vitamin K antagonists. MDD users were selected randomly from participating community pharmacies using computer-generated random numbers. MDD users were invited to participate in the study by one of the pharmacists or research assistants.

Non-MDD users were selected using the same inclusion criteria as for the MDD users, except no drugs were dispensed by an MDD system. For each MDD user, two non-MDD users in the same community pharmacy were invited and matched on age (plus or minus 1 year) and gender. The second patient was selected in advance in case the first patient was not willing to participate in the study.

Data collection

The interviews in both groups were conducted by the patient's own pharmacist or one of the research assistants (either C.O. or G.S.). Prior to each patient interview, drug dispensing records were collected from the community pharmacy. Besides the pharmacy list with dispensed drugs, the interviewer evaluated other drugs that the patient was using, including prescription drugs not on the list, over-the-counter drugs and complementary and alternative drugs. The drugs actually taken by the patient were used for analysis. Ninety-two per cent of patient interviews were conducted at the patient's home.

Main outcome measures

The primary outcomes were self-reported medication adherence and knowledge. Adherence was measured by the Medication Adherence Report Scale (MARS). The MARS consists of five statements concerning self-reported adherence: forgetfulness, altering the dosage, stopping taking medication, missing a dose and taking less than instructed. The statements have response categories on a five-point Likert scale where 1 = always, 2 = often, 3 = sometimes, 4 = rarely and 5 = never [22, 23]. For each drug, a sum for MARS was calculated ranging from 5 to 25. The MARS-score per patient was the mean of the different MARS scores for each of their drugs. As there is no concordance in the cut-off point for adherent and non-adherent behaviour and MARS scores generally show a very skewed distribution, a score ≤ 22 was considered as non-adherent [22, 23].

Medication knowledge was measured by asking the patient for the indication of their drugs. Medication knowledge was graded as 'knowing indication of drug' if the patient could tell the indication of the drug spontaneously or patient was able to retrieve the indication from a patient information leaflet. Patients who use patient information leaflets have access to relevant information in daily life and therefore can be regarded as having knowledge of indication. When patients could not tell the indication or mentioned a wrong indication, this was regarded as 'not knowing indication of drug'. Knowing the indication of minimal 75% of their drugs was considered as adequate knowledge.

To explore the influence of cognitive function on both adherence and knowledge, we added the assessment of Mini-Mental State Examination (MMSE) while the study was ongoing. Therefore, MMSE tests for MDD users were conducted 6–12 months after the interview on adherence and knowledge. MMSE tests for non-MDD users were

conducted simultaneously with the interview on adherence and knowledge. Patients were divided in two subgroups: MMSE score >27 and MMSE score ≤27.

Confidentiality

To protect the patient's privacy, all medical data were anonymized by the community pharmacist and research assistants using a randomly assigned unique number for each patient. Informed consent was obtained from all participants who agreed in performing MMSE tests.

Statistical analyses

Independent *t*-tests were used for continuous variables with a normal distribution and non-parametric Mann–Whitney *U* tests for other continuous variables with a skewed distribution (age, MMSE, MARS-score per patient). The Pearson chi-squared (χ^2) tests were applied for each categorical variable. A *P*-value < 0.05 was considered statistically significant.

Data were analysed using database (Microsoft Access 2010; Microsoft Corporation, Redmond, WA, USA) and statistical software (SPSS version 20.0; SPSS, Inc., Chicago, IL, USA).

Results

Patient flow and characteristics

A total of 141 MDD users ≥65 years were invited to participate in the study and 127 patients (90%) accepted the invitation. Matching at age and gender resulted in 238 eligible non-MDD users of whom 96 participated (Figure 1).

Baseline characteristics of both MDD users and non-MDD users are shown in Table 1. No significant differences were seen in the total number of drugs per patient. Furthermore, there were no significant differences in the percentages of most used prescription drug classes, except for drugs used in diabetes.

Adherence and knowledge of MDD users versus non-MDD users

Self-reported adherence and medication knowledge are shown in Table 2. Self-reported adherence was higher for MDD users (median MARS score 25.0) compared with non-MDD users (median 24.7, *P* 0.001). The percentage of patients being adherent to all drugs (MARS score ≥23 for each of their drugs) was higher for MDD users compared with non-MDD users (91 versus 58%, *P* < 0.001). The mean percentage of drugs for which patient knew the indication was lower for MDD users compared with non-MDD users (63 versus 85%, *P* < 0.001). The percentage of patients with adequate knowledge was 40% for MDD users and 79% for non-MDD users (*P* < 0.001).

After stratification for medication knowledge, adherence remained higher for MDD users in both subgroups (see Supplementary data available in *Age and Ageing* online,

Appendix Table S1). No correlation was found between the mean percentage of drugs for which patients knew the indication and the MARS score per patient (Spearman's rho: -0.054, *P* = 0.4).

MDD users reported for 16 of 1,128 drugs (1.4%) non-adherence (MARS score ≤ 22) against 59 of 960 drugs (6.1%) for the non-MDD users (*P* < 0.001). Non-adherence was most often reported for drugs for peptic ulcer and GORD (12%) and high-ceiling diuretics (9%).

Comparison of MDD drugs and manually dispensed drugs in MDD users

Eighty-six per cent of MDD users (102 of 119) used also manually dispensed drugs. Medication adherence and knowledge of MDD-drugs versus manually dispensed drugs within the group of MDD users is shown in Table 3.

Sixty-seven per cent of MDD users (80 of 119) used at least one manually dispensed drug chronically. The distribution of MARS scores was different (*P* < 0.001), while the median MARS scores were similar (25.0). The percentage of patients being adherent to all drugs (MARS score ≥ 23 for each of their drugs) was lower for MDD drugs (93%) compared with manually dispensed drugs (97%, *P* < 0.001).

Within the group of MDD users, the knowledge per patient for MDD drugs was lower (50%) compared with manually dispensed drugs (95%, *P* < 0.001). The percentage of patients with adequate knowledge of MDD drugs was lower (35%) compared with the percentage of patients with adequate knowledge of manually dispensed drugs (92%, *P* < 0.001).

Cognitive function

We were able to measure cognitive function by MMSE for a selection of the included patients (58 MDD users (49%), 73 non-MDD users (76%)). Reasons for not performing MMSE for MDD users were deceased (*n* = 6), not willing to participate (*n* = 11), unable to contact (*n* = 38) and other reasons (*n* = 4). Reasons for not performing MMSE for non-MDD users were admission to hospital (*n* = 2), not willing to participate (*n* = 4) and unable to contact (*n* = 11). The median MMSE score was different for MDD users compared with non-MDD users (27 versus 28, *P* = 0.02).

After stratification for cognitive function in subgroups of MMSE scores <27 and ≥27, self-reported adherence remained higher for MDD users within both subgroups. Likewise, medication knowledge remained lower for MDD users in both subgroups (see Supplementary data available in *Age and Ageing* online, Appendix Table S2).

Discussion

To our knowledge, this is the first study that showed that self-reported medication adherence is higher for patients using MDD compared with patients using manually dispensed

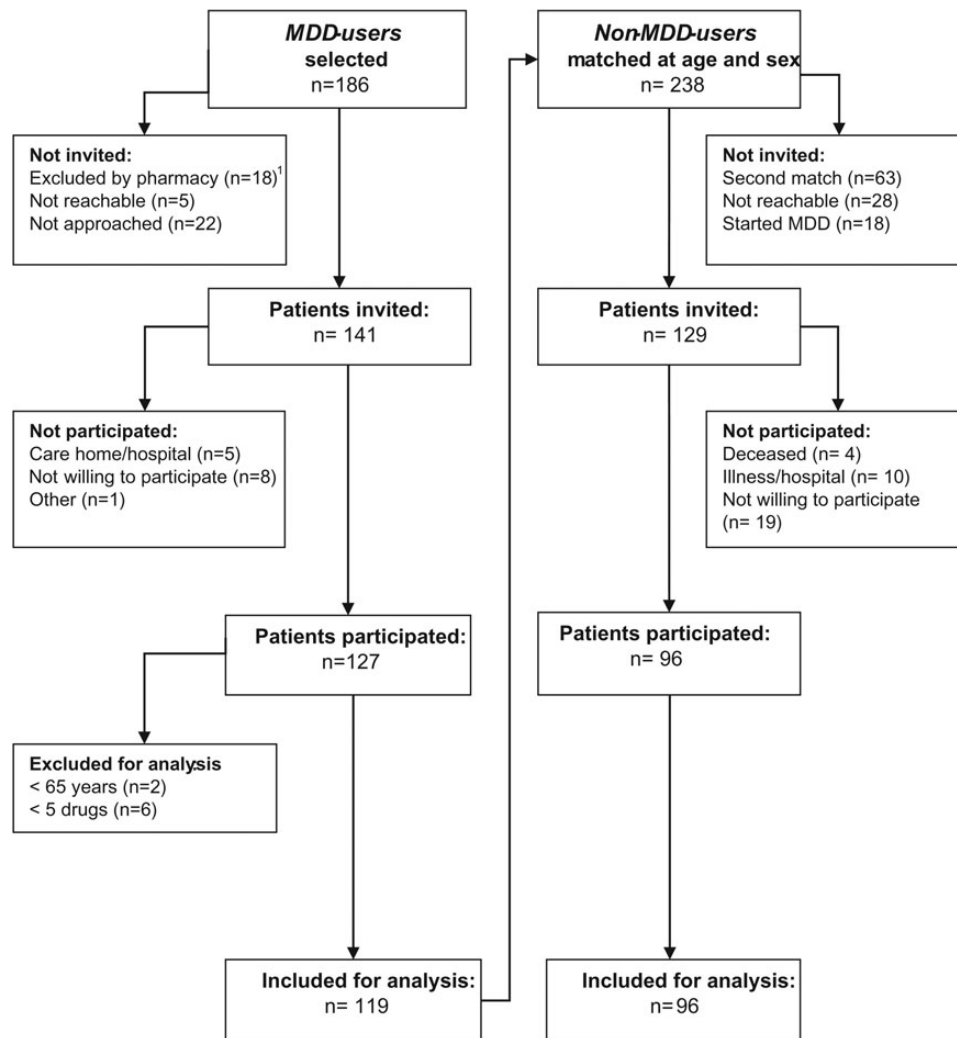


Figure 1. Study flow chart. ¹Admission to nursing home, hospital, deceased, not able to take own drugs.

drugs. This difference was independent of medication knowledge and cognitive function. There is limited evidence that dosing aids in general can increase medication adherence [24]. However, there was no specific evidence for MDD which is expected to increase medication adherence [8, 9].

Our study showed a low medication knowledge and a high adherence for MDD users and no correlation between them. At first sight, this absence of an association between knowledge and adherence for MDD users seems contradictory to earlier studies which report a positive association between knowledge and adherence [3, 15–18]. However, it could also indicate that the appropriate group of patients received MDD. Without MDD, their medication adherence probably would have been lower [15]. Moreover, knowledge is only one of the many factors that could influence adherence. Forgetfulness and practical difficulties with medication management (e.g. removing medication from its primary packaging) might be more important barriers to adequate adherence in this specific group of older patients.

Especially within the group of MDD users, the knowledge of MDD drugs was low while the knowledge of non-MDD drugs was very high. This may partly be

explained by patients not recognizing the different tablets within the disposable plastic bags. The majority of tablets was white and can only be identified by form and inscriptions. Furthermore, most MDD users seemed not to bother about the indications of their drugs. This patients' remoteness of their drugs has been reported earlier as a possible disadvantage of dosing aids [25]. In contrast, MDD users had a high knowledge of drugs not dispensed by MDD. Chronic drugs not suitable for MDD were especially non-oral dosage forms such as insulin, inhalation drugs and eye drops. Furthermore, laxatives (sachets or syrup) and vitamin K antagonists that often require a special dosing scheme were not dispensed in MDD. These dosage forms were generally well recognized by patients.

As expected, the median MMSE score was lower for MDD users compared with the non-MDD users. This lower cognitive function may be expected to give difficulties with medication management [26]. However, the differences in adherence and knowledge between the two groups were not influenced by the cognitive function within the two groups. This suggests that these differences could be mainly attributed to the differences in dispensing systems.

Table 1. Baseline characteristics of MDD users and non-MDD users.

	MDD users (<i>n</i> = 119)		Non-MDD users (<i>n</i> = 96)		<i>P</i> -value
Female [<i>n</i> (%)]	74	62%	63	66%	0.6 ^a
Age (y, median, IQR)	80	76–83	81	77–84	0.2 ^b
Number of drugs per patient (mean ± SD)	9.7	±3.0	10.0	±3.2	0.6 ^c
Number of manually dispensed drugs per patient (mean ± SD)	2.8	±2.1	10.0	±3.2	<0.001 ^c
Number of drugs in MDD (mean ± SD)	7.0	±2.2	–	–	–
Most prescribed drug classes (ATC) [<i>n</i> (%)]					
Antithrombotic agents (B01A)	114	98%	89	92%	0.6 ^a
Agents acting on the renin–angiotensin system (C09)	95	82%	75	78%	0.7 ^a
Lipid-modifying agents (C10A)	82	71%	55	57%	0.2 ^a
Drugs for obstructive airway diseases (R03)	41	35%	41	43%	0.4 ^a
Drugs used in diabetes (A10)	101	87%	38	39%	<0.001 ^a
Beta blocking agents (C07A)	69	60%	56	58%	0.9 ^a
Drugs for peptic ulcer and GORD (A02B)	82	71%	60	62%	0.4 ^a
Calcium channel blockers (C08C)	30	26%	33	34%	0.3 ^a
Benzodiazepine derivatives (N05BA, N05CD)	26	22%	29	30%	0.3 ^a
High-ceiling diuretics (C03C)	41	35%	23	24%	0.1 ^a
Low-ceiling diuretics (C03A, C03B, C03E)	27	23%	23	24%	0.9 ^a

MDD users, patients with at least one drug dispensed by multidose drug dispensing; non-MDD users, patients that used only manually dispensed drugs; IQR, inter-quartile range.

^aPearson Chi-squared test.

^bMann–Whitney *U* test.

^cStudent's *t* test.

Table 2. Self-reported medication adherence and knowledge at patient level of MDD users and non-MDD users

	MDD users (<i>n</i> = 119)	Non-MDD users (<i>n</i> = 96)	<i>P</i> -value
Medication adherence			
MARS score per patient (median, IQR)	25.0 (24.8;25.0)	24.7 (24.0; 25.0)	<0.001 ^a
Patients with MARS score ≥23 for each of their drugs [<i>n</i> (%)]	108 (91%)	56 (58%)	<0.001 ^b
Medication knowledge			
Percentage of drugs for which patient knew indication (mean ± SD)	62.8 ± 30.5	85.0 ± 23.2	<0.001 ^c
Patients with adequate knowledge ^d [<i>n</i> (%)]	47 (40%)	76 (79%)	<0.001 ^b

MDD users, patients with at least one drug dispensed by multidose drug dispensing; non-MDD users, patients that used only manually dispensed drugs; MARS, Medication Adherence Reporting Scale; IQR, inter-quartile range.

^aMann–Whitney *U* test.

^bPearson Chi-squared test.

^cStudent's *t*-test.

^dAdequate medication knowledge: knowing indication >75% of drugs.

This study had several strengths. First of all, non-MDD users were matched at age and sex and were selected within the same pharmacy. Secondly, we stratified for cognition by MMSE scores.

The choice to measure adherence by self-reporting could be seen as a limitation because it could overestimate adherence. There is no gold standard for the assessment of adherence. Different measurement instruments may result in different adherence estimates for the same patient and medication group [27]. Measuring the refill rate is not possible for MDD users, because they automatically receive a

new MDD system. Although programmable MDD dispensers that can monitor adherence have recently become available, these cannot be applied for non-MDD users [5]. However, for comparing adherence in groups with different dispensing systems, self-reporting seemed the most appropriate method. Recent studies have shown that self-reported methods like MARS are concordant with direct methods [18, 23]. Another limitation of our study was that MARS has not been validated for use among people with cognitive impairment. Furthermore, especially for the MDD users, the response rate to perform an MMSE test was low. This could be due to the fact that this was not performed simultaneously with the interview on knowledge and adherence for MDD users. This might result in an underestimation of MMSE for MDD users, but does not influence adherence and knowledge outcomes. Finally, the design of the study was cross-sectional. This means that we could find a high adherence and low knowledge for MDD users, but we cannot assume a causal relationship.

Our findings may have implications for practice. The low knowledge of drugs in the MDD system may raise problems when medication has to be changed in the MDD system. For example, when a GP advises to (temporarily) stop taking a certain drug, patients may not recognise which tablet to stop. Otherwise, more readable drug information should be available to the patient while the information on the bags of the MDD systems is too limited. Furthermore, the patient's remoteness of their drugs may also lead to continuous use of drugs that otherwise would be stopped by the patient after a certain time (for example, analgesics, antihistamines). This leaves a high responsibility for the GP and, in particular, the community pharmacist to monitor the use of MDD drugs of older patients in combination with regular patient contact.

Table 3. Medication adherence and knowledge at patient level of MDD users for MDD drugs and manually dispensed drugs

	MDD users (<i>n</i> = 119)		<i>P</i> -value
	MDD drugs	Manually dispensed drugs	
Adherence	(<i>n</i> = 119)	(<i>n</i> = 80)	
MARS score per patient (median, IQR)	25.0 [24.7–25.0]	25.0 [25.0;25.0]	<0.001 ^a
Patients with MARS score ≥ 23 for each of their drugs [<i>n</i> (%)]	111 (93%)	77 (97%)	<0.001 ^b
Medication knowledge	(<i>n</i> = 119)	(<i>n</i> = 102)	
Percentage of drugs for which patient knew indication (mean ± SD)	50.4 ± 38.5	95.1 ± 17.9	<0.001 ^c
Patients with adequate knowledge ^d [<i>n</i> (%)]	41 (35%)	94 (92%)	<0.001 ^b

MDD users, patients with at least one drug dispensed by multidose drug dispensing; non-MDD users, patients that used only manually-dispensed drugs; MARS, Medication Adherence Reporting Scale; IQR, inter-quartile range.

^aMann–Whitney *U*-test.

^bPearson Chi-squared test.

^cStudent's *t*-test.

^dAdequate medication knowledge: knowing indication >75% of drugs.

In conclusion, our study showed that older patients using MDD users report higher medication adherence and have a lower medication knowledge compared with patients using manually dispensed drugs (non-MDD users). The differences in adherence were independent of medication knowledge and cognitive function. These finding suggests that the higher adherence of MDD users could be attributed mainly to the MDD system. Future intervention studies are needed to determine whether older patients who are non-adherent on manually dispensed drugs become more adherent when they start with a MDD system.

Key points

- MDD users reported a higher drug adherence and a lower medication knowledge compared with patients using manually dispensed drugs.
- The higher medication adherence was independent of medication knowledge and cognitive function.
- MDD users reported a higher knowledge of their manually dispensed drugs compared with their multidose dispensed drugs.

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Conflicts of interest

None declared.

Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

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'It could be worse ... lot's worse!' Why health-related quality of life is better in older compared with younger individuals with heart failure

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