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RESEARCH ARTICLE

THE EFFECT OF MEDICATION REVIEWS ON REDUCING MEDICATION ANTICHOLINERGIC BURDEN IN ELDERLY PATIENTS

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ABSTRACT

Anticholinergic side effects of medications often misdiagnosed as cognitive function decline in the elderly. The study aims to explore the effectiveness of home medication reviews on reducing anticholinergic burden caused by medications with anticholinergic properties in elderly patients in Australia. The study was a qualitative, prospective, observational case-control study. Interviews at baseline and six-month were performed. Medications changes were theoretically possible to reduce the Anticholinergic Cognitive Burden score, but occasionally are impractical to implement. When it was safe to implement, recommendations were in most cases dismissed by doctors. The study could not draw a clear conclusion on pharmacist ability to improve older patients' cognitive functions as the recommendations were not tested. The home medication review process is lacking the step that obligate the referring doctor to communicate the reason for not implementing the recommendations made by the pharmacist who needs to be addressed by Medicare. This will ensure that medication use is optimised.

INTRODUCTION

Many medications have anticholinergic properties that are unwanted. Recent studies demonstrate that the use of medications with anticholinergic activity increases the risk of cognitive function decline or impairment, especially in older patients (Pasina *et al*. 2013). A recent study in France in older participants (n = 544) showed that poor performance in the mini-mental state examination (MMSE) was highly associated with the use of medications with anticholinergic properties over one year than in non-users(Han, Agostini, and Allore 2008). The Personnes Agees Quid (PAQUID) population study (n = 1780) also showed a significant association between the use of anticholinergic medications and the poor performance on the MMSE and visual memory and verbal fluency (Lechevallier-Michel *et al*. 2005). In another study (n = 3075) it was demonstrated that the use of anticholinergic medications had led to accelerated decline over six years on psychomotor speed, executive functioning and attention(Bottiggi *et al*. 2006). The Health, Ageing, and Body composition study (n = 3075)reported thatthe use of medications with anticholinergic properties was associated with poorer performance using the digit symbol substitution test for cognitive performance and continuous measure for physical function (Hilmer *et al*. 2007).

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However the intensity of anticholinergic side effects depended on the individual response.Thus, theyare often missed, especially when they are mild in a patient with relatively good cognitive health. When they are misdiagnosed in the elderly or patients with a pre-existing condition like dementia, these effects can be serious and may lead to an increased risk of mortality, but can be confused with ageing or worsening of the preexisting condition (Tune 2001). Pharmacists can play a valuable role as a first point of call for over the counter medication and during dispensing. Effective pharmacist intervention can aid in reducing, managing and preventing medication-induced adverse events, including anticholinergic burden (Schnipper *et al*. 2006). A study showed that pharmacists were able to decrease the rate of preventable adverse drug reactions after discharge from hospital through patient counseling, telephone follow-up, home medication reviews (HMRs) and residential medication management reviews (RMMRs) (Schnipper *et al*. 2006). Additionally, effective collaboration between pharmacists and doctors to ensure optimization of medication use and patient self-management has been shown to improve patient health literacy and outcomes (Eijk *et al*. 2001).The aim of this research wasto explore the effect of home medication reviewson the reduction of anticholinergic burden caused by medications with anticholinergic properties in elderly patients.

MATERIALS AND METHODS

Design: A qualitative, prospective, observational, case-control study was conducted in Australia (Sydney) using data from two home medication review (HMR) sessions, 6-months apart. The HMR was unpaid and conducted for the purpose of this study. Patients were consented to participate. The HMRs were conducted by the primary researcher, female, HMR accredited registered pharmacist at patient homes. Participating doctors were informed about the project details and what will be required from them verbally and in writing. Doctors were to identify patients who are 65 years or older, who are taking five medications or more, have one or more chronic medical conditions and are able to consent. Doctors were then to discuss the HMR referral with their patients and forward the referral to the investigator if they agree. It was made clear to the doctors that neither them nor the investigator will submit MediCare claims for the HMRs conducted for the purpose of this research. The methodology of the study including the communication cycle (Figure 1) was also discussed.

After the interview, and during the process of report writing, the anticholinergics burden (ACB) score was allocated to each of the medications used by the participant to calculate their baseline ACB total score which was later compared to their score at the second HMR after 6 months. The K10, WAYM and ACB scale are not usual part of the HMR process they are additional items used for the purpose of this study, with intention to test their usability by a pharmacist and their usefulness as part of the HMR process for patients above the age of 65 years. K10 uses a score system where WAYM uses a categorical dichotomous variable, no or yes answers and the ABC scale allocate final numerical score. The data was analysed categorically. Variables with high and low range were used as well as other variables such as the ACB scores, number of medications and medical conditions and were all analysed by age and gender. The baseline HMRwas followed by a report to the treating doctor with the drug optimisation recommendations as required by the HMR guidelines. Additionally, the report included the K10, WAYM results and the ACB score.

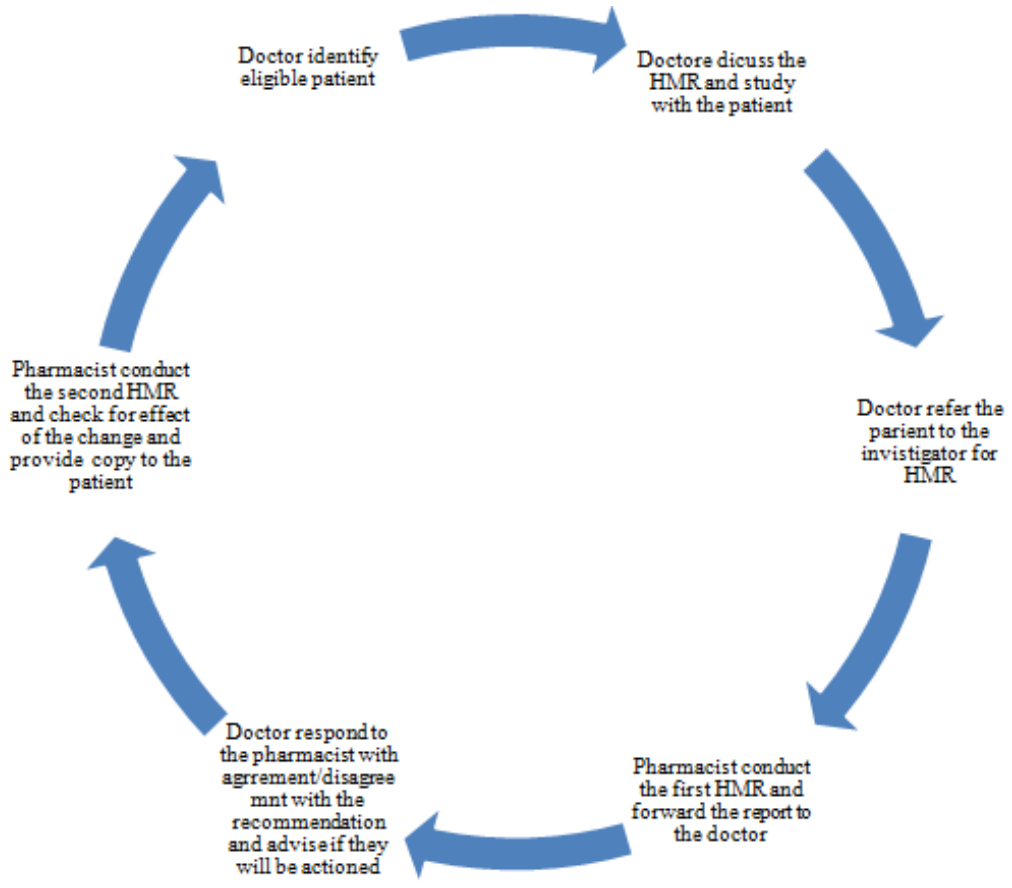


Figure 1. Communication Cycle

There were 103 patients identified by their doctors as being 65 years or older, with different medical conditions and multiple medications. Patients were then contacted by the investigator and the HMR interview was conducted at their homes at the time they elected. In addition to conducting the HMR in accordance to the Pharmaceutical Society of Australia, the Australian Association of Consultant Pharmacists and MediCare guidelines, the investigator also administered Kessler Psychological Distress Scale 10 (K10) and Worried About Your Memory (WAYM) tools. The two instruments are designed for self-administration and no training is required. All occasions where the pharmacist and doctor communication was required were registered and an entry was made if the communication took place or not, its type (by phone, in person or in writing) and the outcome; to understand if doctors were prepared for this level of close collaboration. The study results were analysed using GSEM statistical model.

Ethics

Ethicsclearance was gained from the Charles Darwin University Human Research Ethics Committee prior to the

commencement of data collection. The researcher did not receive HMR payment for the 103 patients included in this study.

RESULTS

The identified variables of the study are highlighted in Table 1. The mean value reduction in the number of medications, ACB score, K10 score and WAYM score variables between baseline and at six months were statistically significant (Table 2).

Table 1. List of the variables and their key properties

Variable Name	Variable Description	Type of Variable	Possible Values
Age	Age of Patient (years)	Scale	Range: 65–94 years
Gender	Patient Gender	Categorical	Female (n = 49) Male (n = 54)
K10 Baseline	K10 Score at Time = Baseline	Scale	Range: 11–55 points
K10 6 Months	K10 Score at Time = 6 Months	Scale	Range: 11–55 points
WAYM Baseline	WAYM Score at Time = Baseline	Scale	Range: 0–36 points
WAYM 6 Months	WAYM Score at Time = 6 Months	Scale	Range: 0–36 points
WAYM Y/N Baseline	WAYM Yes/No at Time = Baseline	Categorical	No Yes
WAYM Y/N 6 Months	WAYM Yes/No at Time = 6 Months	Categorical	No Yes
No. Med. Conditions	Number of Medical Conditions	Scale	Range: 1–11 Conditions
No. Med. Conditions Group	Number of Medical Conditions Group	Categorical	Low: 1–4 Conditions (n = 59) High: 5–11 Conditions (n = 44)
ACB Baseline	ACB Score at Time = Baseline	Scale	Range: 0–12 points
ACB 6 Months	ACB Score at Time = 6 Months	Scale	Range: 0–10 points
ACB Baseline Group	ACB Score at Time = Baseline Group	Categorical	Low: ACB Score 0–3 (n = 59) High: ACB Score 4–12 (n = 42)
ACB 6 Months Group	ACB Score at Time = 6 Months Group	Categorical	Low: ACB Score 0–3 (n = 75) High: ACB Score 4–12 (n = 26)
No. Meds Baseline	Number of Medications at Time = Baseline	Scale	Range 1–23 Medications
No. Meds 6 Months	Number of Medications at Time = 6 Months	Scale	Range 1–21 Medications
No. Meds Baseline Group	Number of Medications at Time = Baseline Group	Categorical	Low: 1–8 Medications (n = 51) High: 9–23 Medications (n = 52)
No. Meds 6 Months Group	Number of Medications at Time = 6 Months Group	Categorical	Low: 1–8 Medications (n = 53 High: 9–23 Medications (n = 46)

Table 2. Study variables at baseline and at six months

Variable	Baseline	6 Months	Change (95% CI) over 6 months	Test for Difference[1] (p-value)
	Mean (SD)	Mean (SD)		
K10 Score	20.32 (8.9)	18.05 (8.5)	–2.27 (1.12)	< 0.001**
WAYM Score	8.34 (8.7)	7.17 (8.7)	–1.16 (0.97)	0.019*
ACB Score	3.56 (2.5)	2.76 (1.8)	–0.80 (0.23)	< 0.001**
Number of Medications	8.87 (4.6)	8.55 (4.3)	–0.32 (0.16)	< 0.001**

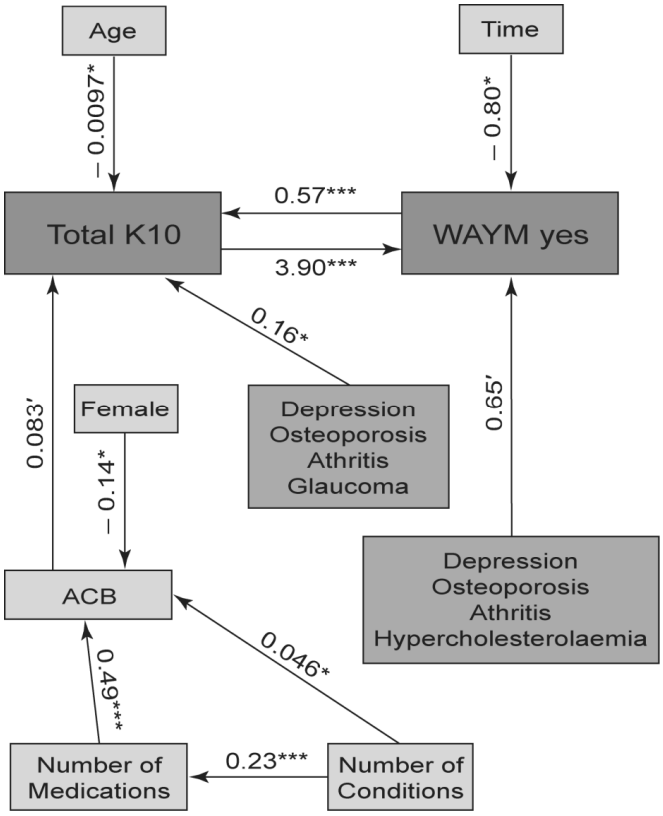
* Denotes statistical significance at the $p < 0.05$ level

** Denotes statistical significance at the $p < 0.01$ level

[1]The test used in each case was the 'Paired samples t-test'. This is a more sensitive test than the 'Independent samples t-test', used elsewhere in this report

An in-depth analysis using a generalised structural equation modelling (GSEM) statistical models, showed that the ACB score has a significant impact on the K10 score and an indirect impact on the WAYM 'yes' outcome through the total K10 score variables. Total K10 score can be used to potentially predict WAYM and vice versa. The type of medical conditions has been shown to affect both (Figure 2). The time taken to administer K10 and WAYM reduced at the six-month follow-up from that spent at baseline. The total time taken to complete the HMR report including K10, WAYM and ACB score calculation per patient was 3 hours and 50 minutes, which exceeded the time used as the basis of Medicare payment for completion of HMR (three hours) by 50 minutes at baseline and by 30 minutes at the second HMR after 6 months, which is sustainable (Table 3). Male and female participants did not differ markedly in ACB scores. Females, ACB score was lower on average than for males by 0.14.The GSEM statistical model revealed that the ACB had direct and significant impact on the K10 score (average of 6% per individual patient), which is sufficient to confirm correlation, but not the causality. It was also found that changing the ACB by 1 point results in a change to the K10 total score of 0.21. This result indicates that ACB score reduction is likely to have a positive effect on patient cognitive function (statistical significance), but the intensity will be patient specific. However, the ACB score did not have a significant direct impact on the WAYM outcome.

GSEM and confirmatory factor analysis (CFA) revealed that the gender variable appears to have a significant impact on the WAYM factor. Female participants also had a WAYM value smaller than males by 0.46 in average. Additionally, the study shown that WAYM results were affected by the type of medical conditions the participants had. If a person had; depression, hypercholesterolaemia, osteoporosis or arthritis the predicted probability for this person to have a 'yes – (positive)' WAYM outcome (i.e. memory impairment) is higher than for a person with any other medical condition. However, increasing the total K10 score resulted in a significant increase of the WAYM positive result. There was a relationship between WAYM 'yes' results and the total K10 scores, one of them was high the other was also high. Thus, either can be used to potentially predict the other.



Here, WAYM 'yes' has been categorised as: (0) the number of answers 'yes' is equal to 0; (1) the number of answers 'yes' is greater than 0. The determined regression coefficients are shown next to the arrows showing the direct effects between the considered variables with the indicated levels of statistical significance: (***) $p < 0.001$; (**) $0.001 \leq p < 0.01$; (*) $0.01 \leq p < 0.05$; (') $0.05 \leq p < 0.1$; and ('') $0.2 < p \leq 0.1$. Only effects with the indicated levels of significance are shown in this GSEM scheme

Figure 2. Generalised structural equation modelling probability model for the two dependent variables: total K10 Scale and WAYM 'yes'

Table 3. Time taken to administer the tests and prepare the reports

Time taken (per patient)	Baseline	6-month
K10	15 minutes	10 minutes
WAYM	15 minutes	5 minutes
HMR interview	60 minutes	60 minutes
Sub-total	90 minutes	75 minutes
ACB score calculation after the interview	20 minutes	15 minutes
HMR/RMMR report	120 minutes	120 minutes
Total	240 minutes	210 minutes

Moreover, the number of medications and K10 scores were found to be related where a higher number of medical conditions was associated with greater K10 scores at six months. The difference in K10 scores between the female and male subgroups was small. Additionally, the study revealed that K10 was affected by the type of medical condition participants had. If a person had depression, osteoporosis, arthritis or glaucoma the predicted total K10 value for this person was larger by 0.16 than for a person with any other medical condition. This result indicates that K10 had relationship with age, gender, WAYM and medical condition.

DISCUSSION

Communication with Doctors: Communication, collaboration and teamwork between doctors and pharmacists is important for the provision of safe and effective healthcare (Rigby 2010). Poor communication between doctors and pharmacists is one of the most important common factors resulting in medication-related problems, including medication errors (Rigby 2010). This study showed that the communication between pharmacists and doctors was effective either at baseline or six-month follow-up. Beside the two written communications; referral letter (doctor to pharmacist) and the HMR report (pharmacist to doctor) there were no other communication, which may have led to their decision on whether to accept or refuse pharmacists' recommendations. It was noted that there was still a culture of 'professional importance' between doctors and pharmacists more than the other health professionals where communication regarding the HMR recommendations were not taking place after the submission of the report to the GP, this was also found to be the case in other studied (Ball, Morrissey, and Pilotto 2013). This situation my improve when more pharmacists work at GP clinic and the HMR process be tailored to allow those pharmacists to conduct HMR rather than the current process which obligate the doctor to send their referral to a community pharmacy who then conduct the One study showed that pharmacists who reviewed patient medications within medical centres and in the patient's home have a high rate of acceptability by patients (Chen and Britten 2000).

Using the K10 and WAYM: K-10 and WAYM were used in the study as tools to test the pharmacist ability to identify the association between cognitive function and anticholinergic burden and patient acceptance for the pharmacist to ask them those questions.The K10 and WAYM questionnaires have three main objectives: '*assessing the patients' mood and memory respectively; understanding the patients' medications, including adverse effects and proper use and of the drugs; and improving patients' health management and quality of life'*(Andrews and Slade 2001; Worried about your memory? 2013). The study found that through administering K10 and WAYM questionnaires, the pharmacist used less time at the six-month follow-up from that spent at baseline. This might be due to the patients having a better understanding of what is involved from their experience at the first review, or that the researcher became more confident and precise after practising at the baseline collection period, and/or that trust had been established. This result shows that the inclusion of K10, WAYM and the ABC score calculation can be sustainable if using an appropriate process and time management. The participants' feedback indicated that they did not have objection of completing the K10 and WAYM assisted by a pharmacist. A recent survey revealed that only 14% of the participants distrusted pharmacists, while 60% of the participants trusted them, and 56% trusted doctors and 51% trusted dentists (Salazar 2016). At the end of the HMR visit, the pharmacist wrote a report to the doctors advising of the K10 and WAYM results, the suggestions for reducing ACB score caused by medications, and the potential improvement in the K10 and WAYM scores that could result from a change in medications.

Patient Attitude as observed by the investigator: At first, during the first HMR, participants were not comfortable answering the questions based on their condition, but rather were more focused on providing the best answer. At the six-month follow up HMR, the researcher observed that

participants' attitude was different and they appeared to answer the questions with a higher level of truthfulness as they became more familiar with the pharmacist communicating this type of issue with them. Consideration may be given by GPs to including the ACB, K-10 and WAYM in the GPs referral letter in the future for patients aged 65 years older, to better prepare the patient.

Pharmacist Workload: The third issue is sustainability. The time required to administer the K10 and WAYM questionnaires was dependent on the individuals' conditions (between 15 and 20 minutes). This suggests that HMR time would increase by 20 minutes to administer K10 and WAYM questionnaires and another ten minutes to calculate the ACB score. The additional 30 minutes might concern some pharmacists, as 'unpaid service', accordingly there might be low uptake by pharmacists; however, as it would only be for a certain group of patients, Medicare may be open to the idea of increasing the pharmacist payment for patients over 65 years of age.

Additional Findings: The study revealed that in some occasions, medication change may be identified but due to patient age, patient agreement to change their long-standing medications or other social comorbidities affecting the change may become impractical. The elderly have particular issues with drug change, due to unfamiliarity with colour, shape, name and the regimen of the new drug compared to the one they are familiar with. Some participants mistakenly believed that their medical problems had *been 'adequately treated and drug changes could not improve their cognitionincluding memory problem'* (ACB03). Other patients found changing their medications to be '*inconvenient, as they frequently forgot to take new medications'*(ACB22), another did not understand the instructions and believed that '*the new medication side effects always worse than the old one'* one: (ACB43). Additionally, some patients denied the possibility of experiencing memory problems or encountered obstacles (e.g. having a problem swallowing capsules or tablets, difficulty opening bottles). Further problems included being '*afraid of dependence on the medications* (C49)', 'being *apathetic about becoming better without treatment* (C30)'or '*upsetting distrusting the doctor if they accept the changes* (ACB6)'.

Patient Adherence: Compared to the current literature, adherence in this study was found to be affected by numerous factors that are common amongst older people, but it was not affected by age itself (J. Mark Ruscin). Factors include polypharmacy, which is associated with a high risk of side effects, drug–drug interactions and problems in remembering when to administer each medication, and mental or physical impairment (J. Mark Ruscin). Moreover, older patients normally experience a high rate of adverse drug reactions due to their high sensitivity to medications resulting from pharmacokinetic and pharmacodynamics changes (J. Mark Ruscin). Older patients tend to use medications at a high rate due to suffering various chronic medical conditions, including arthritis, diabetes or Cardiovascular disease (CVD), which can be deteriorated by medications (J. Mark Ruscin). This study found that most medications taken by participants for chronic medical conditions had been used for years. One doctor (D01) did not think it worthwhile to change a medication to reduce an individual's ACB score as their medical condition was stable and the new plan could have the potential to confuse patients and worsen the condition. This is also agree with the finding from previous study which found that effective pharmacist–doctor collaboration in hospital setting substantially improve patient care (Tahaineh *et al*.2008). The same study highlighted that 48.2% of the participating doctors were uncomfortable with pharmacists suggesting the use of prescription medications to patients (Tahaineh *et al*., 2008).

Conclusion

This study found that reduction in the number of medications, improvement in the K10 score, improvement in the WAYM score and reduction in the ACB score were possible. The study could not draw a clear conclusion on pharmacist ability to improve older patients' cognitive functions as the recommendations were not implemented by the treating doctors. due to unavoidable factors that should be the HMR process is lacking the step that obligate the referring doctor to communicate the reason for not implementing the recommendations made by the pharmacist which needs to be addressed by Medicare to finalise the payment for both pharmacist and doctors. This will ensure that medication use is optimised.

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