Quantifying and characterising Multi-compartment Compliance Aid provision; a national survey of community pharmacies in England

Authors: Riddhi Shenoy, Sion Scott and Debi Bhattacharya

Correspondence to:

Debi Bhattacharya
School of Pharmacy
University of East Anglia
Norwich
Norfolk
NR4 7TJ
d.bhattacharya@uea.ac.uk

Background
Medication compliance aids (MCAs) to support adherence lack evidence for cost-effectiveness yet a 2001 survey in England estimated 100,000 patients receiving an MCA whilst living in their home.

Objective(s)
To obtain a contemporary estimate of MCA provision by community pharmacies in England and describe factors influencing pharmacist decision-making regarding MCA initiation.

Methods
A stratified random sample of two community pharmacies per county (n=40) in England were surveyed by telephone and a more detailed postal survey sent to participants expressing an interest. Data were collected to determine magnitude of MCA provision and, professional and administrative factors influencing initiation were reported as percentage (95% confidence interval) respondents reporting a factor.

Results
An estimated 273,529 MCAs are filled by community pharmacies in England with a median (IQR) of 20(10, 50) MCAs per pharmacy per month provided for patients living in their home. Practitioners' judgement of appropriateness for MCA initiation was reported by 51.3 ±11% as the primary factor influencing decision-making relative to 16.3 ±8% and 20 ±8.8% reporting patient's and carer's opinion respectively. Some form of assessment tool was reported by 13 ±7.3% respondents.

Postal survey respondents (n=31) indicated that decision-making regarding MCA initiation was often or always affected by suitability of medication for dispensing in an MCA by 58% ±17% of respondents; 74.2% ±15.4% and 53.3% ±17.9% of respondents' decision-making was never or rarely affected by the risk of adverse events and reduced patient autonomy arising from an MCA respectively.

Conclusions
Provision of MCAs by pharmacies in England has more than doubled in the past decade. Beyond considering the practicalities of whether an MCA is suitable for a patient, there is limited evidence of pharmacists considering patient choice or risk of adverse events arising from sudden increased adherence prior to initiation.

Keywords
Cost, Dossett, compliance aid, pill organiser, assessment, determinants, influencers

Introduction

Adherence to prescribed medication directions is a complex health behaviour which requires the patient to have the opportunity to access their medication, capability to take it as prescribed and motivation to adhere to the prescribed directions.(1) Non-adherence may therefore be intentional with patients not having the motivation to adhere and thus choosing to deviate from prescribed directions or unintentional due to practical barriers such as forgetfulness, confusion or difficulty swallowing. Often, however, patients report an amalgam of both intentional and unintentional behaviour.(2) It is unsurprising therefore that systematic reviews and meta-analyses of adherence interventions repeatedly conclude that the most effective interventions are complex in nature.(3)

Historically, clinical practice has been dominated by simple adherence interventions such as provision of Multi-compartment Compliance Aids (MCAs) which are designed to support unintentional non-adherence. MCAs are sometimes described as pill organisers and are generally variations on a box or blister pack with compartments divided into days of the week and times of the day in which medicines are organised according to their dose timings. MCAs are intended to act as an aide memoire to prevent omission and duplication of doses. Interviews with MCA users indicate that for those who self-fill their MCA, they help people to 'bring order to chaos' in terms of taking their medication regimen as prescribed.(4) In contrast, interviews with older MCA users reported feelings of reduced autonomy arising from their medication being taken from its original packaging and dispensed into an MCA. They also reported feeling that the MCA had been imposed on them in a paternalistic manner rather than as a shared decision.(5) Questionnaire results from 96 frail older people who consented to participate in a North American trial of an electronic MCA reported that 84% would consider using the MCA beyond the trial end.(6) This positive attitude towards the MCA may be related to each trial participant actively choosing participation and therefore receipt of an MCA.

A 2018 systematic review of factors affecting medication adherencesolely in the older population reported MCAs to be ineffective at improving adherence to the medication regimen.(7) A 2011 (8)and more recent 2016 (9) systematic review of MCAs including more heterogeneous populations have reported slightly more favourable findings for MCAs but both conclude that there is insufficient evidence to confirm that they are an effective and cost-effective adherence intervention. Both systematic reviews conclude that further research is needed to improve the targeting of these devices to patients who are unintentionally non-adherent.

Whilst evidence of universal benefit from MCAs is lacking, there is a substantial body of literature indicating that MCAs introduce greater risk of error associated with the dispensing and prescribing processes. Dispensing into MCAs requires removal of medication from its original packaging. This introduces potential hazards such as increased opportunity of dispensing errors and accidental ingestion by children as they are often not child resistant packaging.(10) The integrity of the medication may also be compromised as MCAs do not always offer the level of protection afforded by the manufacturer's original packaging. A recent literature review of information sources utilised by pharmacists to determine medicine stability in an MCA outlined the need for pharmacists to access appropriate information sources to determine medication suitability for an MCA. The review concluded that pharmacists should consider the physiochemical properties of the drug, the dosage form of the drug (e.g. some chewable tablets may be unsuitable for inclusion in an MCA), the co-storage of drugs and the type of MCA including the levels of moisture permeation of the MCA material.(11) Furthermore, an Australian study aimed to produce recommendations specific to repackaging medications into MCAs. Recommendations included counselling patients to store MCAs away from light, heat and humidity as well as to monitor the integrity of the MCA to preserve the medicines inside.(12)

Additional patient confusion may also be generated by some medicines not being in the MCA such as those with hygroscopic properties or frequently changing doses being kept in original packaging.(13) A 2018 review of stability studies for repackaged medicines concluded that pharmacists should be mindful of these factors when initiating an MCA and provide counselling for patients regarding correct storage and usage.(11) Repackaging medication into an MCA by members of the pharmacy team is estimated to take seven minutes for one patient with one month's supply of only three medications. This estimate excludes the time taken to unpack medication from its original packaging and labelling(14). There is therefore a significant resource implication for community pharmacies filling MCAs. Repackaging MCAs when regimes change partway through the MCA cycle generate further costs and pharmacy teams have described the challenges of managing these changes due to poor communication between the prescriber and pharmacy team.(15)

Transfer of medication from original packaging to an MCA also restricts a patient's ability to distinguish one medication from another. In cases of intentional non-adherence, an MCA may lead patients to take none of their medication if they are unable to identify their chosen medication(s) to avoid. Conversely, in cases of purely unintentional non-adherence, a dramatic, sudden increase in adherence arising from MCA initiation may lead to dose related adverse effects.(16) Furthermore, for the unintentionally non-adherent patient with impaired eyesight, manual dexterity or cognitive function, MCAs can present a greater challenge to the patient accessing their medication than the original manufacturer's packaging. (17) The extent to which alternative interventions to supporting adherence are being routinely used is unknown. For example, increasing regimen complexity has been consistently associated with reduced adherence thus simplifying a regimen is an evidence-based approach to supporting unintentional non-adherence arising from mild confusion or forgetfulness.(18)

A causal relationship has been identified between receipt of an MCA and provision of poorer quality medicines management.(19, 20) Patients in receipt of an MCA were significantly more likely to be prescribed a potentially inappropriate medication relative to those without an MCA.(19) The poorer medicines management was consistent even when patients were matched for age, sex and living status. Suggested causes for this disparity included MCAs being associated with prescription renewal without review and reticence to make prescription amendments due to the added inconvenience of communicating changes to the pharmacy.(20)

MCAs may be purchased by patients and self-filled or requested by other members of the healthcare team. In the latter situation, MCAs are often provided and filled by a member of the pharmacy team. Historically, many of these requests have been initiated by formal, paid carers to facilitate the medication administration process. This has been described as an inappropriate use as it deskills carers.(21) A 2001 evaluation of community pharmacies in one city in the North of England reported that 77% of the surveyed pharmacies filled one or more MCAs for use by patients in their own home. An average of 11 patients per pharmacy were reported to be provided with this service. These data were extrapolated to estimate that over 100,000 patients living in their own home in Britain, receive an MCA filled by community pharmacy staff.(22) A more recent 2015 survey of 48 pharmacies in one Scottish city, through extrapolation reported a greater than five-fold increase in MCA provision since 2001.(23) There are however, no studies sampling pharmacies from more than one area in order to generate estimates regarding the number of patients receiving MCAs for use in their own home that are filled by community pharmacy teams. The rationale for generating a contemporary estimate of the magnitude of this service provision is that there are additional costs incurred by community pharmacies, potential hazards to the MCA user and no agreed assessment criteria for MCA eligibility.

Given that there is currently no standardised tool for assessing MCA appropriateness, it is anticipated that a variety of subjective factors are influencing the decision to initiate an MCA. The present study

therefore aims to describe, at a national level, MCA provision from community pharmacies to patients living in their own home in terms of magnitude and factors influencing provision.

Method:

Ethical committee approval was obtained from the University of East Anglia Faculty of Medicine and Health Sciences research ethics committee for inviting staff of any community pharmacy in England registered to provide NHS services to complete a brief telephone survey regarding MCA provision and an optional supplementary survey inviting more detailed responses.

Participant identification and recruitment

A stratified, random sample, using a random number generator, of all 14,366 General Pharmaceutical Council registered pharmacies in England, was selected. Stratification was by the 40 health regions in England approximating to the 48 counties. Two pharmacies were randomly selected from each region in order to capture any variation in local policy and services that may influence MCA provision e.g. local arrangements for funding MCA provision by community pharmacies. The sampling strategy yields a sample size of 80 pharmacies that is proportionate for the study aims. Pharmacists, pharmacy technicians, dispensers and pharmacy managers were eligible. Temporary pharmacists, hub pharmacies (pharmacies providing dispensing services on behalf of multiple community pharmacies) and pharmacies not providing MCAs were excluded.

Each of the 80 selected community pharmacies were contacted by telephone and invited to participate in the survey. A new pharmacy was randomly selected from the area if a pharmacy declined to participate or there was no answer after two attempts to contact by telephone.

Following confirmation of not being a hub pharmacy, the brief survey was administered and participants invited to complete a further supplementary survey. Those expressing a willingness to complete the supplementary survey were provided an electronic or postal version depending upon preference.

Sample size estimation

Based on the previous estimate of 77% of pharmacies providing MCA, a variety of sample sizes were investigated.(22) A sample of one pharmacy per health region yielding a sample size of approximately 40 would provide a 95% confidence interval of 13%. Doubling to two pharmacies per region reduced the margin of error to within 9% for estimating the percentage of pharmacies providing MCAs and was therefore deemed acceptable.

Survey development and content

A 12 item survey informed by the MCA literature was developed to fulfil the study objectives.(5),(24)Face and content validity of the survey were investigated through cognitive interviews(25) with a convenience sample of community pharmacists identified from the professional network of the authors. Cognitive interviewing allows evaluation of how the target audience perceives survey instruments and their constructs. How a participant interprets a question, processes the information, applies information stored in memory and prepares a response are captured as verbal data during the cognitive interview process. Data gathered may be used to identify survey flaws and improve questions prior to administration in a study(25)

The cognitive interview participants represented persons employed by independent pharmacies, small chains and large multiples. Two community pharmacist interviews were undertaken before making any refinements to the survey. Both pharmacists advised that all 12 items were valid but that the response burden was too great. One interviewee additionally recommended that one of the items be split into two separate items. This initial 12 item survey was subsequently split into a six-item survey administered by telephone with a further seven-item survey distributed by post to telephone respondents expressing an interest in ongoing study participation. Further minor refinements were made to the surveys after a third interview; no recommendations for change were identified at the fourth interview thus this iteration of the surveys proceeded to the national survey.

The brief six-item telephone survey was designed to quantify and describe MCA provision from community pharmacies to patients living in their own home. Three items enabled characterisation of the survey respondent and a further three items were used to generate estimates for the following: 1) magnitude of weekly MCA provision; 2) factors discouraging MCA initiation; 3) criteria for determining whether an MCA may be beneficial.

In the seven item supplementary survey, a five point Likert scale ranging from "strongly disagree" to "strongly disagree" was used to ascertain the factors influencing choice of MCA from a pre-determined list of eight factors and option to add additional unlisted factors. Further five point Likert scales ranging from rarely (1) to very frequently (5) were used to estimate frequency of the following during the previous year:

1. The potential for negative outcomes (from a range of six outcomes) influencing decision making regarding MCA initiation
2. Use of a range of nine adherence interventions other than MCAs
3. Nature of communication between General Practitioner (GP) and pharmacist regarding MCAs in terms of four characteristics
4. Requests to initiate MCAs from a range of seven different health and social care individuals

An open question captured the information sources used to determine the physical stability of medications in an MCA and therefore inform the appropriateness of dispensing into an MCA. Two further open questions captured respondents' experiences of any requests for an MCA that were deemed inappropriate and any further comments.

Analysis

Descriptive statistics were calculated for all data collected and 95% confidence intervals reported for estimates regarding the key objectives of the brief survey. To maintain anonymity, responses to the supplementary survey were not linked to the brief survey therefore, no inferential statistics were performed. Data were entered into SPSS for windows version 22 for statistical analysis and content analysis was performed on extended responses provided in the supplementary survey.

Results

To obtain the 80 completed telephone surveys, 132 pharmacies were identified of which nine (6.8%) could not be contacted, one (0.8%) pharmacy used a hub pharmacy service and 38 (28.8%) refused to participate. Four pharmacies (3.0%) did not provide MCAs to patients living in their home.

From the 80 pharmacies providing MCAs and four pharmacies not providing MCAs, the estimated prevalence of pharmacies in England providing MCAs for patients living in their own home is therefore 80/84 = 0.952 (95.2%, 95% confidence interval from 88% to 99%). From the 80 respondents, the

median (IQ) number of MCAs dispensed per pharmacy per month was 20 (10, 50). Based on 95.2% of 14,366 pharmacies filling a median of 20 MCAs for patients living in their own home, the projected total number of MCAs supported by community pharmacies across England is 273,529.

Of the 80 included pharmacies, 41 (51.3%) were independent and 39 (48.8%) were multiple. The median (IQ) number of MCAs dispensed per multiple pharmacy, per month was 25 (10, 50) compared with 18 (10, 31.5) per month for independent pharmacies. Figure 1 illustrates the variations in the mean number of MCAs filled per month across health regions of the UK, ranging from 2 to 90.

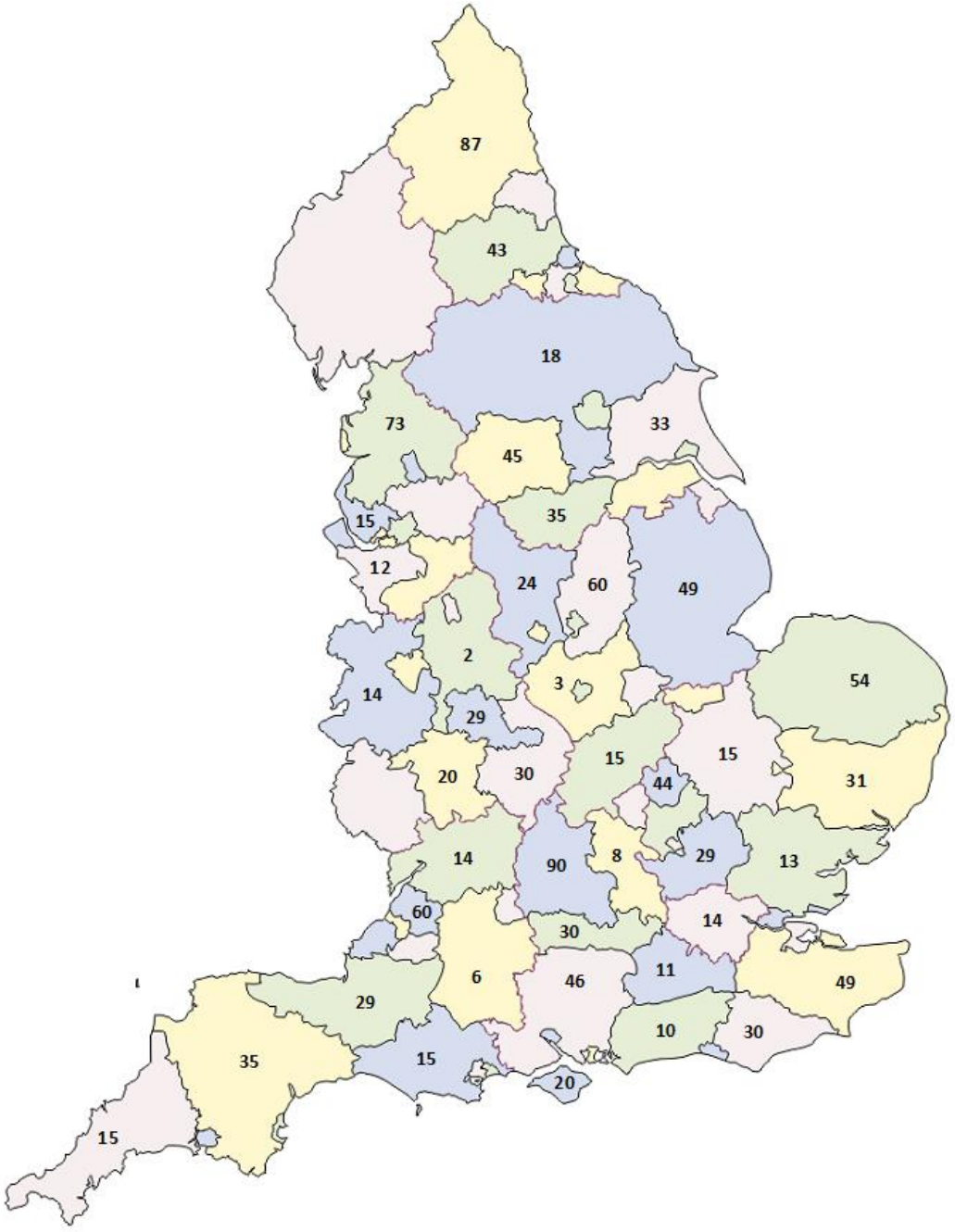

Figure 1 Illustration of the mean number of MCAs filled per pharmacy per week per health region of England

From the 80 respondents, 40 (50 %) were pharmacists, 22 (27.5%) were dispensing technicians or dispensers and 18 (22.5 %) were pharmacy managers with a median (IQR) duration in post of 6.5 years (2, 13.7). Figure 1 illustrates the percentage (95% CI) around the respondents selecting one of five potential barriers to MCA initiation. Lack of time and payment were the primary barriers, however, over a quarter of respondents perceived no factors discouraging initiation.

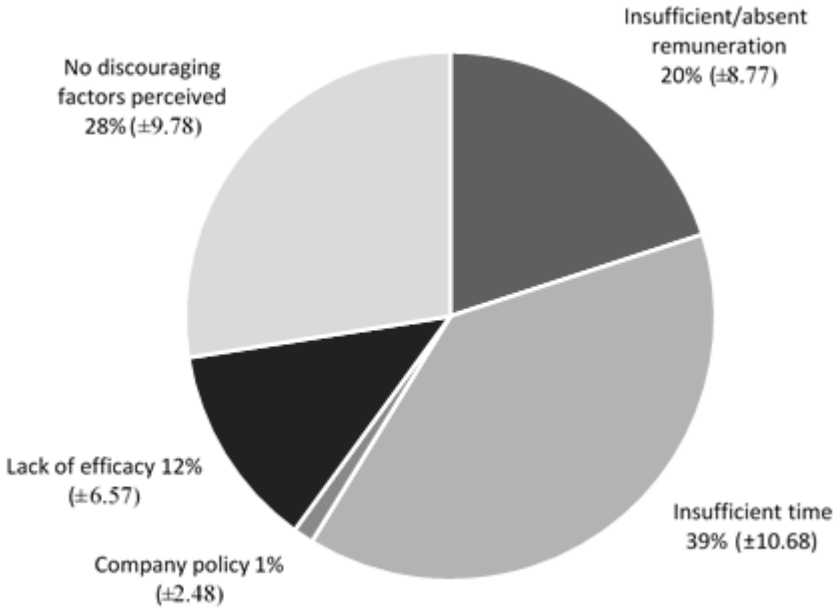

Figure 2 Factors discouraging MCA initiation by the community pharmacy team (n=80)

Figure 3 provides the percentage (95% CI) of respondents selecting one of six factors as their primary influencer of decision making regarding whether a patient may benefit from an MCA. Approximately 50% of respondents selected either the opinion of the pharmacist or the GP as the single most important factor guiding decision-making. In contrast, the two least favoured options were the patient's opinion or results of a formal assessment. For the ten respondents favouring a formal assessment, two each described them as a company standard operating procedure and local health service commissioner guidance whilst the remaining six respondents reported using the national medication use review form as their influencer of decision making regarding MCA appropriateness of MCA initiation.

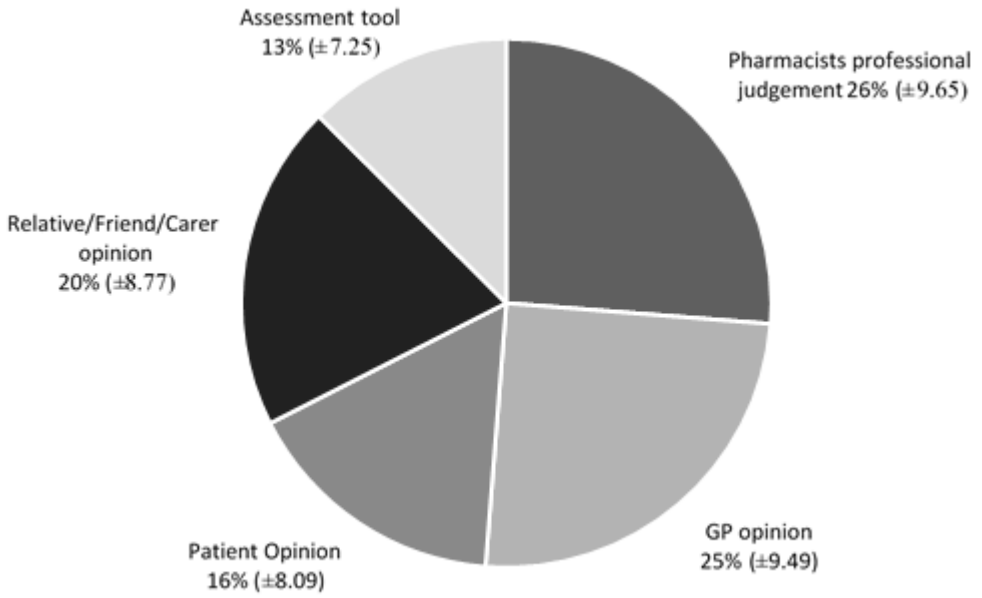

Figure 3 Factors influencing decision marking regarding initiation of an MCA (n=80)

Supplementary postal surveys were distributed to 58 pharmacies and 31 (53.4%) responses were obtained. Table 1 provides the median and spread of responses to items inviting a Likert scale response from never (1) to very frequently (5). The most frequent influencers of pharmacist opinion regarding whether to initiate an MCA were the suitability of the medications with 18 (58.1%) respondents indicating that it frequently or very frequently influenced their decision-making. This was followed by the patient's physical ability to use an MCA and ability to manage 'when required' medication which were both reported by 9 (29.1%) respondents as frequently or very frequently affecting the decision making. The potential for an MCA to reduce patient autonomy, the risk of filling errors and risk of adverse events arising from a sudden increase in adherence due to the introduction of an MCA were rarely influencers of decision-making.

Table 1: Responses to Supplementary Questionnaire.

Question	*Median (IQ)
Frequency with which potential barrier to MCA initiation influenced decision making in the previous year	
Patient ability to use compliance aid	3 (2, 4)
Adverse events if patient's adherence is suddenly increased	2 (2, 3)
Patient ability to manage 'when required' medication	3 (2, 4)
Reducing patient autonomy	2 (2, 3)
Some items being unsuitable for a compliance aid	4 (3, 4)
Risk of error when filling	2 (1, 2)
Frequency of using adherence interventions other than MCAs in the previous year	
Pictures and Symbols	2 (1, 2)
Pill press or pill punch	2 (1, 3)
Large print labels	3 (1, 3)
Different languages/ interpreter	1.(1, 2)
Simplification of regime	3 (2, 3)
Medicines Administration Record (MAR) chart	3 (2, 4)
Extra patient counselling	4 (3, 4)
Prescription ordering	5 (4, 5)
Referral for additional care support	3 (2, 3)
Frequency of monitoring processes related to MCA provision in the previous year	
Communication to GP to inform that a compliance aid has been initiated	4 (3, 4)
Communication from GP in a timely manner of prescription changes	4 (2, 4)
Record of the brand of compliance aid provided	3 (1, 4)
Review of patient's need for and ability to use their compliance aid	3 (3, 4)
Frequency with which the following sources request initiation of an MCA	
Social services carer	4 (3, 4)
Relative/friend of patient	4 (3, 4)
Hospital	3 (3, 4)
District nurse	3 (2, 3)
GP	4 (3,4)
Patient	4 (3, 4)
Yourself/other pharmacist	3 (3, 4)
Frequency with which request is inappropriate	2 (1, 2)

*Likert Scale responses from 1 to 5 where one indicates never and 5 indicates very frequently.

The supplementary postal survey also captured the factors influencing choice of MCA. The patient's physical and cognitive ability were the key drivers of MCA choice, with 25 (80.7%) and 24 (77.4%) respectively, reporting that they agreed or strongly agreed that they influenced their decision-making. These practical factors were followed by patient preference for which 22 (70.9%) respondents agreed or strongly agreed. The nature of the patient's care arrangements e.g. whether they are living with

an informal carer influenced 21 (67.7%) respondents' choice of MCA. The number and size of prescribed medication and ease of MCA transportability for the patient were statements to which 17 (54.8%) and 11 (35.5%) respectively agreed or strongly agreed. Company policy and the time taken to fill the MCA both received 8 (25.8%) respondents agreeing or strongly agreeing.

Multiple resources were reportedly used to check the stability of medications in an MCA with some respondents reporting using several. The most frequently cited resource was the product's manufacturer either through direct contact, using the summary of product characteristics or the company website; this was reported by 10 (28.6%) respondents. The national prescribing formulary was reported by 8 (22.9%) and product information leaflets by 6 (17.1%) of respondents as an information source. The use of a medicines information service was reported by 7 (20.0%) respondents. An article in a professional journal and materials produced by the UK Centre for Pharmacy Postgraduate Education were each reported by one respondent (5.7%). Two (5.7%) of respondents reported referring to their pharmacist line manager for advice.

From table 1, it can be seen that for patients known or suspected to be non-adherent, other than the use of an MCA, all respondents reported using pharmacy managed prescription ordering either frequently or very frequently during the previous year. The use of extra patient counselling was also a frequently reported adherence intervention. In contrast, simplification of medication regime and Medication Administration Records charts were reported to be used only sometimes or rarely by over 80% of participants.

No one process associated with monitoring patients using MCAs was consistently reported to be implemented frequently or very frequently. Informing the GP of the initiation of an MCA was reported to occur very frequently by 22.6% of respondents. Similarly, only 16.1% of respondents reported that communication from the GP about prescription changes was very frequently received in a timely manner and 25.8% reported that they were rarely received in a timely manner.

Social services were the main source of requests to initiate an MCA with 58.1% of respondents reporting that this occurred frequently or very frequently during the previous year. This was followed by the GP with 54.8% of respondents and patient with 48.4% of respondents reporting them to be frequently or very frequently requesting an MCA. Ten (32.3%) respondents considered that during the past year they had received requests for an MCA that they considered inappropriate.

Three themes were generated from the content analysis of responses to open questions and are provided in table 2. Respondents described a variety of strategies to address the perceived insufficient resource currently available for MCA provision under the NHS contract. These included direct remuneration for activities and managing capacity through requiring referral from a GP. The second theme was the practical challenge of accommodating some MCA requests such as situations where there are frequent medication changes, daily dispensing is requested or medication stability may be compromised. The third theme comprised situations where initiating an MCA was perceived inappropriate. These were described either in terms of the patient's physical or cognitive function being insufficiently impaired to warrant an MCA or being so impaired that they would be unable to safely use an MCA.

Table 2: Categories arising from content analysis of extended responses

Category	Examples quote
Solutions to perceived insufficient resource for MCA provision	"Pharmacies should be reimbursed for their time and cost involved in providing (buying) compliance aid. One solution is to provide weekly prescriptions to cover the cost."
	"If we have numerous compliance aids to fill, we sometimes refer patients back to surgery to be signposted to a pharmacy that has more time or not so many patients, speaking to the patient first"
	"Because we are in a health centre most requests come from the GP. We also have some from the local medicine management group and they will clear the home of unwanted drugs first and also request a MAR chart. For this service we get paid £10 for MARs and £40 for CDS".
Insufficient patient ability preventing MCA initiation	"The patient must be physically able to receive the compliance aid upon delivery. They must be able to hear the door - this can prove challenging for the delivery driver"
	"I knew patient would have difficulties opening the blister pack"
Insufficient patient disability preventing MCA initiation	"Yes we had a couple of patients who requested a Dossett box weekly, but the pharmacist spoke to the Gp and he explained that the patients is young and can manage without it."
	"I think patients should only [be] given compliance aids if they are old and they can't look after themselves and…they need help with taking their medication. Patients who have physical ability or mental problem and not because are lazy to take their tablets. Aids are a life saver for patient [and] carer in the right context"
	"The request was made by a care company even though the patient was perfectly able to look after their own medication."
Requesting process for MCA initiation	"Patient normally likes to have a compliance aid for medication but it has to be approved by GP as they need to issue weekly prescription for Dossett patients which involves a lot of time to get them ready for collection"
	"We often get asked by carers who work for agencies to issue compliance aids, quite often it is because carers are not permitted to issue medications to patients (as their company policy). We refer all requests for compliance aids to the patients GP's who is better suited to assess the patient's needs, so all out requests for compliance aids comes via the GP"
	"With CDS trays it's a balance between the stability of the drugs and the patients taking them. Some patients are very confused and the trays are the only way for them to take their medicines on a regular basis…There has been quite a sudden decline in compliance aids as of late. We used to have approx. 85 people using them but is has dropped to 65"
Communication between health care workers	"Most communication between primary and secondary care is in regards to changes, not initiation. There is little contact with social services and district nurses."
	"GPs very poor in informing"
Inappropriate medications for MODs	"Several patients with unstable medications liable to need dose adjustments constantly [and] patients prescribed 4 weeks at a time who are not capable of leaving the others aside end up taking random days from random blister packs rather than one at a time"
	"We had one request for compliance aid to be done daily (we usually do weekly boxes). Getting the prescriptions done and doing a daily box just was not practical"

Discussion

This survey capturing any regional differences across the 40 counties in England estimates that over 270,000 MCAs are filled by community pharmacies for patients living in their own home which is more than double the 2001 estimate.(22) Insufficient time and remuneration for MCA provision were the most discouraging factors for initiation, however time was also the factor least influencing the choice of MCA. Frequent requests for initiation by social services was consistently reported by respondents and the use of either the pharmacist's or GP's professional judgement for determining the appropriateness of initiation took precedence over the patient's own opinion or the use of an assessment tool.

Assessment of face and content validity of the survey using cognitive interviews enabled identification of flaws prior to the definitive study. Based on feedback during the cognitive interviews, the survey structure was amended in order to reduce the item burden. Previous qualitative work with pharmacists regarding the potential factors influencing MCA provision offered a strong grounding for development of the quantitative survey. .(5),(24) The pre-testing phase with cognitive interviews provided further methodological rigour (25). Notable limitations of cognitive interviews are self-selecting participants most commonly characterised by higher educational levels than average survey respondents. However, given the target population for the definitive study was qualified pharmacy professionals, this limitation is unlikely to have significant implications for the present study. Moreover, these motivated participants are unlikely to accurately capture motivational barriers to survey completion. However, the objective of the cognitive interviews in the present study was to assess face and content validity only, and the high survey completion rate in the main survey suggests motivation was not a barrier to completion.

A survey response rate of nearly two thirds of the targeted pharmacies affords some confidence in the likely generalisability of the findings. Furthermore, any regional variations in MCA supply and remuneration procedures have been captured by the purposive sampling. Relative to the 2001 evaluation of MCA provision in one UK city, the current national picture suggests that MCA supply is both more widespread and that the average number filled per pharmacy has also doubled.

In England there have been no national policy changes to explain these increases which is endorsed by the main reported barriers to MCA supply still being a perception that there is insufficient workforce capacity and lack of proportionate remuneration for the service.(15, 22, 26) Ageing increases the risks of some factors associated with unintentional non-adherence such as impaired manual dexterity, eye sight and cognitive function, thus the ageing population may provide some explanation for the increased estimate.(27) Alternatively, greater precision in the estimate provided by the present national survey relative to the 2001 survey of one city may be responsible for the observed increase in MCA provision.

Despite limited evidence supporting the use of MCAs,(9) few respondents were discouraged from initiation due to a perceived lack of efficacy. With approximately one-third of community pharmacy staff perceiving no barrier to MCA use, this may reflect positive attitudes and experiences of MCAs, which accords with the existing literature.(28) Given that insufficient time was a key barrier to MCA initiation, it may be expected that MCAs which require less time to fill are favoured. Incongruously however, time taken to fill was the factor considered least likely to influence the choice of MCA. Similar to a previous review of pharmacy services across England for supporting adherence in the domiciliary setting,(29) extended survey responses indicated that there are regional variations in funding models for MCA filling by community pharmacies; some are formally remunerated for filling whilst others are reliant upon the funds within the community pharmacy contract for routine dispensing of prescriptions. This may therefore generate inequity of access with some patients receiving the MCA filling service from their local community pharmacy whilst others are refused or redirected to a different pharmacy as indicated by one respondent.

The use of an assessment tool to inform the decision regarding MCA initiation was the least influential driver, which is unsurprising as there is no validated, widely accepted tool for assessing patient need for an MCA. To reduce disparity in service provision there is clearly a need for such a tool, (15, 26, 28) however, limited research in this area is a key challenge to its development. A cross-sectional study of 26 community pharmacy staff in Scotland reported that pharmacists did not feel confident in assessing patients' needs for an MCA, nor whether they are capable of using it correctly.(24) The pharmacists' opinions taking precedence over the patient in determining the need for an MCA does therefore generate some concern, not only because pharmacists do not feel equipped to undertake this process, but also because patients should be central to decision making(30). Given that older patients in receipt of MCAs have reported negative experiences associated with this paternalistic approach to MCA initiation,(5) practitioners should attempt to engage patients with the decision-making. This devolvement of responsibility from patients to health practitioners may be a reflection of the population being considered for an MCA also being likely to have some level of cognitive impairment(31) However, if the patient has the capacity to self-manage their medication using an MCA, they are likely to also have the capacity to engage with the decision making process regarding whether an MCA is acceptable and likely to be beneficial. (32)

The criteria used to inform the pharmacist's opinion regarding appropriateness of MCA initiation are focussed on the practicalities of whether the prescribed medications are suitable and whether the medication from the MCA can be accessed by the patient. A similar picture is observed regarding the criteria informing the choice of MCA. This absence of a patient focus may be appropriate given that a study of fifty older patients reported that patient preference for an MCA is dominated by its size rather than ability to access medication, with patients selecting the smallest MCA as most preferred regardless of their inability to access medication from the MCA.(17)

The World Health Organisation patient safety challenge "Medication without harm" launched in 2017 identifies that "health care professionals sometimes prescribe and administer medicines in ways and circumstances that increase the risk of harm to patients".(33) Inappropriate initiation of MCAs is one such example. Prior to initiating any adherence intervention, a medication review to determine the appropriateness of prescribed medicines including dosage and formulation should be undertaken.(16) The rationale for this review is twofold. Firstly, dose titrations arising from perceived inadequate response to the medication can lead to doses not tolerated by the patient if they become suddenly adherent. Secondly, between one to two thirds of older people are prescribed a potentially inappropriate medicine,(34) thus enforcing adherence before establishing whether all are appropriate may be introducing potential for further iatrogenic harm. In contrast, pharmacy managed regular prescription ordering and medication counselling were the dominant adherence interventions. This may be due to pharmacies in the UK not having access to full medical records to facilitate medication review. Moreover, the limited concern expressed by respondents regarding risk of a sudden improvement in adherence leading to dose related adverse events or the potential for MCAs to reduce patient autonomy despite evidence to the contrary may indicate a need for generating greater awareness of these risks. (35)

The use of product manufacturers' provided information being the preferred resource for checking medication stability may indicate a lack of awareness of the availability of open access databases for medication stability. This supports the conclusions of a recent review of medication stability which highlighted the need for an evidence-based source of stability and storage information for medications in MCAs.(11) Improving sources of medication stability information could increase standardisation of MCA provision and reduce the risk of using unsuitable medications for MCAs. Repackaging error rates of 11.5% were reported in a large audit of MCAs in Australian care homes, with the majority of errors relating to medications being dispensed into MCAs which are unsuitable for repackaging.(36) Associated quality improvement strategies informed by focus groups with

healthcare professionals in Australia included improving the communication between prescribers, those dispensing MCAs and care home staff, and increasing knowledge and awareness of the guidelines for repackaging medicines into MCAs.

The limited use of reminder charts is also surprising given that there is significant overlap between the functions of reminder charts and MCAs for patients where mild confusion and/or forgetfulness are the barriers to adherence.(37) This may be indicative of MCAs being initiated before other lower intensity interventions have been tried. Given that MCAs compared with lower intensity interventions are significantly more resource demanding for pharmacies to prepare and, are associated with reduced patient autonomy, research specifically capturing the interventions considered and/or tried before MCA initiation is required to enable a definitive conclusion to me made.
The sporadic nature of communication between practitioners regarding MCA initiation and medication changes is of concern. The limited communication emulates a 2005 survey investigating communication regarding MCA initiation from hospitals to community pharmacies with only 66 (49.2%) reporting that this information is transferred to the community pharmacy.(26) The present study adds to the existing literature through identifying similarly poor communication from GP surgeries to community pharmacies. This was reported in the context of less than a quarter of pharmacies receiving information regarding medication changes from GPs. Communication to the GP from the pharmacy regarding MCA initiation was marginally better.

Consistent with the literature from a decade past, social services and GPs were the most frequent source of MCA requests and pharmacists the least likely.(22) Notably, in the 2001 review of MCA provision patients were not cited as a source of MCA requests which contrasts the present findings and those reported from a recent Scottish survey.(24)

The precision around the estimate of the prevalence of pharmacies in England providing MCAs should be interpreted in the context of a third of the targeted pharmacies not providing data regarding MCA provision. However, given that 95% of the purposively sampled 80 pharmacies were comparable, it is unlikely that the true proportion differs significantly. The data were generated from respondents self-reporting procedures relating to MCAs. Whilst this may have resulted in social desirability bias, the findings are consistent with historic and contemporary research on this topic.(24, 38)

Conclusions

Provision of MCAs in England for patients living in their own home has more than doubled in the past decade. Beyond considering the practicalities of whether an MCA is suitable for a patient, there is limited evidence of appropriate safety checks prior to initiation. There is therefore an urgent need to develop and validate an assessment tool to guide safe and appropriate MCA initiation.

Acknowledgements

We would like to thank Kate Legg and Tom Wild who supported the data collection, the pharmacy staff for participating in the survey and Dr Allan Clark for providing statistical advice.

References

1. Easthall C, Taylor N, Bhattacharya D. Barriers to medication adherence in patients prescribed medicines for the prevention of cardiovascular disease: a conceptual framework. International Journal of Pharmacy Practice.0(0).

2. Salter C, McDaid L, Bhattacharya D, Holland R, Marshall T, Howe A. Abandoned Acid? Understanding Adherence to Bisphosphonate Medications for the Prevention of Osteoporosis among Older Women: A Qualitative Longitudinal Study. PLoS ONE. 2014;9(1):e83552.
3. Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, et al. Interventions for enhancing medication adherence. The Cochrane database of systematic reviews. 2014(11):CD000011.
4. Lecouturier J, Cunningham B, Campbell D, Copeland R. Medication compliance aids: a qualitative study of users' views. The British journal of general practice : the journal of the Royal College of General Practitioners. 2011;61(583):93-100.
5. Nunney J. How do the attitudes and beliefs of healthcare professionals and older people impact on the appropriate use of multi-compartment compliance aids by older people living at home. Leeds: University of Leeds; 2011.
6. Reeder B, Demiris G, Marek KD. Older adults' satisfaction with a medication dispensing device in home care. Informatics for health & social care. 2013;38(3):211-22.
7. Smaje A, Weston-Clark M, Raj R, Orlu M, Davis D, Rawle M. Factors associated with medication adherence in older patients: A systematic review. 2018;1(3):254-66.
8. Mahtani KR, Heneghan CJ, Glasziou PP, Perera R. Reminder packaging for improving adherence to self-administered long-term medications. Cochrane Database Syst Rev. 2011(9):Cd005025.
9. Watson SJ, Aldus CF, Bond C, Bhattacharya D. Systematic review of the health and societal effects of medication organisation devices. BMC Health Serv Res. 2016;16(1):202.
10. Bhattacharya D. Literature Review of Indications for Monitored Dosage System Provision. http://www.primarycarecontracting.nhs.uk/98.php 2005 [Available from: http://www.primarycarecontracting.nhs.uk/98.php.
11. García ER, Thalhauser S, Loscertales HR, Modamio P, Lastra CF, Mariño EL. Current evidence in the stability of medicines in dose administration aids: implications for patient safety. Expert Opinion on Drug Delivery. 2018;15(6):577-87.
12. Haaywood A, Llewelyn V, Robertson S, Mylrea M, Glass B. Dose administration aids: Pharmacists' role in improving patient care. The Australasian medical journal. 2011;4(4):183-9.
13. Hall J, Bond C, Kinnear M, McKinstry B. Views of patients and professionals about electronic multicompartment medication devices: a qualitative study. BMJ Open. 2016;6(10).
14. McElnay J, Thompson J. Dispensing of medicines in compliance packs. International Pharmacy Journal. 1992;6(1):10-5.
15. MacLure K, MacLeod J, Forbes-McKay K, Paudyal V, Cunningham S, Strath A, et al. A Case Study Investigation into the Use of Multi-compartment Compliance Aids in Older People Resident in Very Sheltered Housing. The patient. 2016;9(6):583-90.
16. Bhattacharya D, Aldus, C.F, Barton, G, Bond, C.M, Charles, I.S, Fleetcroft, R, Holland, R, Jerosch-herold, C, Salter, C, Shepstone, L, Walton, C, Wright. D.J. Do not initiate medication organisation devices without prior detailed medication review and vigilant monitoring. BMJ: British Medical Journal. 2005;330:293.
17. Adams R, May H, Swift L, Bhattacharya D. Do older patients find multi-compartment medication devices easy to use and which are the easiest? Age Ageing. 2013.
18. Pantuzza LL, Ceccato M, Silveira MR, Junqueira LMR, Reis AMM. Association between medication regimen complexity and pharmacotherapy adherence: a systematic review. European journal of clinical pharmacology. 2017;73(11):1475-89.
19. Belfrage B, Koldestam A, Sjoberg C, Wallerstedt SM. Prevalence of suboptimal drug treatment in patients with and without multidose drug dispensing--a cross-sectional study. European journal of clinical pharmacology. 2014;70(7):867-72.
20. Sjoberg C, Edward C, Fastbom J, Johnell K, Landahl S, Narbro K, et al. Association between multi-dose drug dispensing and quality of drug treatment--a register-based study. PLoS One. 2011;6(10):e26574.

21. Wang L-N. Multi-compartment compliance aids: do you need to review what you do? The Pharmaceutical Journal [Internet]. 2013 13.04.2019 [cited 2019 13.04.2019]; 291:[120 p.].
22. Nunney JM, Raynor, D.K.T. How are multi-compartment compliance aids used in primary care? . Pharmaceutical Journal. 2001; 267(7176):784-9.
23. Counter D, Stewart D, MacLeod J, McLay JS. Multicompartment compliance aids in the community: the prevalence of potentially inappropriate medications. British Journal of Clinical Pharmacology. 2017;83(7):1515-20.
24. Stewart D, McDonald C, MacLeod J, MacLure K, Gray G, McIntosh T. The behaviors and experiences of the community pharmacy team on the provision of multi-compartment compliance aids. Res Social Adm Pharm. 2018;14(4):347-55.
25. Willis GB. Cognitive interviewing: a tool for improving questionnaire design: Sage Productions Ltd; 2005.
26. Green C, McCloskey, S. UK survey of the provision of multicompartment compliance aids and reminder charts on discharge from hospital. International Journal of Pharmacy Practice. 2005;13(1):85-90.
27. Jankowska-Polańska B, Uchmanowicz I, Dudek K, Mazur G. Relationship between patients' knowledge and medication adherence among patients with hypertension. Patient preference and adherence. 2016;10:2437-47.
28. Nunney JM, Raynor DKT. How are multi-compartment compliance aids used in primary care? Pharmaceutical Journal. 2001;267(7176):784-9.
29. Bhattacharya D, Wright, D.J, Purvis, J.R. Pharmacist domiciliary visiting in England: identifying the characteristics associated with continuation. 10.1007/s11096-007-9133-z. Pharmacy World & Science. 2007.
30. Royal Pharmaceutical Society. Medicines Optimisation: Helping patients to make the most of medicines. 2013.
31. Wrede-Sach J, Voigt I, Diederichs-Egidi H, Hummers-Pradier E, Dierks ML, Junius-Walker U. Decision-making of older patients in context of the doctor-patient relationship: a typology ranging from "self-determined" to "doctor-trusting" patients. International journal of family medicine. 2013;2013:478498.
32. National Institute for Health and Clinical Excellence. Dementia management. London; 2018.
33. World Health Organization. Medication Without Harm - Global Patient Safety Challenge on Medication Safety. Geneva: Licence: CCBY-NC-SA3.0IGO; 2017.
34. Gallagher P, Lang PO, Cherubini A, Topinková E, Cruz-Jentoft A, Montero Errasquín B, et al. Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals. European journal of clinical pharmacology. 2011;67(11):1175-88.
35. Bhattacharya D, Aldus CF, Barton G, Bond CM, Charles IS, Fleetcroft R, et al. Do not initiate medication organisation devices without prior detailed medication review and vigilant monitoring. BMJ2014.
36. Gilmartin JF, Hussainy SY, Marriott JL. Medicines in Australian nursing homes: a cross-sectional observational study of the accuracy and suitability of re-packing medicines into pharmacy-supplied dose administration aids. Res Social Adm Pharm. 2013;9(6):876-83.
37. Raynor DK, Booth TG, Blenkinsopp A. Effects of computer generated reminder charts on patients' compliance with drug regimens. Bmj. 1993;306(6886):1158-61.
38. Nunney J, Raynor D. Multi-compartment compliance aids in primary care: building an evidence base. Pharmaceutical Journal. 1999;263((Supp)):R34-5.