British Journal of Clinical Pharmacology

ORIGINAL ARTICLE

Incidence and cost of medication harm in older adults following hospital discharge: a multicentre prospective study in the UK

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Received 13 February 2018; **Revised** 3 April 2018; **Accepted** 8 April 2018

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Keywords health economics, health service use, hospital discharge, medication harm, older adults, pharmacoepidemiology

AIMS

Polypharmacy is increasingly common in older adults, placing them at risk of medication-related harm (MRH). Patients are particularly vulnerable to problems with their medications in the period following hospital discharge due to medication changes and poor information transfer between hospital and primary care. The aim of the present study was to investigate the incidence, severity, preventability and cost of MRH in older adults in England postdischarge.

METHODS

An observational, multicentre, prospective cohort study recruited 1280 older adults (median age 82 years) from five teaching hospitals in Southern England, UK. Participants were followed up for 8 weeks by senior pharmacists, using three data sources (hospital readmission review, participant telephone interview and primary care records), to identify MRH and associated health service utilization.

DOI:10.1111/bcp.13613

RESULTS

Overall, 413 participants (37%) experienced MRH (556 MRH events per 1000 discharges), of which 336 (81%) cases were serious and 214 (52%) potentially preventable. Four participants experienced fatal MRH. The most common MRH events were gastrointestinal ($n = 158$, 25%) or neurological ($n = 111$, 18%). The medicine classes associated with the highest risk of MRH were opiates, antibiotics and benzodiazepines. A total of 328 (79%) participants with MRH sought healthcare over the 8-week follow-up. The incidence of MRH-associated hospital readmission was 78 per 1000 discharges. Postdischarge MRH in older adults is estimated to cost the National Health Service £396 million annually, of which £243 million is potentially preventable.

CONCLUSIONS

MRH is common in older adults following hospital discharge, and results in substantial use of healthcare resources.

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Polypharmacy is increasingly common in older adults in the UK.
- Older adults are vulnerable to medication-related problems during transitions of care from hospital into the community.

WHAT THIS STUDY ADDS

- Medication-related harm affects one in three older adults following hospital discharge, of which at least 10% is preventable.
- Non-adherence is implicated in one quarter of cases of medication harm.
- The cost to the NHS of postdischarge medication harm in older adults is estimated at £396 million, of which over 90% is attributable to hospital readmissions.

Introduction

Harm from medicines is a common cause of preventable morbidity and mortality in patients worldwide [1]. The European Medicines Agency describes adverse drug reactions (ADRs) as 'a response to a medicinal product that is noxious and unintended' [2]. In England, between 2008 and 2015, emergency hospital admissions due to ADRs increased by 53%, from 60 055 to 92 114 [3]. Based on data from a major UK study conducted in 2002 [4], the National Institute for Health and Care Excellence (NICE) estimated an annual cost to the National Health Service (NHS) in 2015 of £530 million from preventable ADR-related hospital admissions [5].

Older people are highly susceptible to harm from medicines, due to polypharmacy and ageing-related changes in pharmacokinetics and pharmacodynamics [6, 7]. Furthermore, non-adherence to medicines for chronic disease was found in 30% of participants (median age 67 years) in one UK study [8]. Non-adherence to medicine is strongly associated with poor health outcomes [9], including mortality [10], and high healthcare costs [11]. A systematic review found that 16% of community-dwelling older adults experience harm from their medicines at any one time, compared with 5% of younger adults [12].

The transition period from hospital to home following hospital discharge has rarely been explored, despite the vulnerability of patients to medication problems during this period. For instance, patients often experience medication changes [13] with limited involvement in these decisions [14]. Provision of information about possible side effects can be poor [15], and communication is often lacking between secondary and primary care [16]. Furthermore, this is a time of heightened physiological stress for patients, due to the lingering impact of acute illness and deconditioning from their hospital stay [17].

In England, medication-related harm (MRH) in the postdischarge period has not been studied in an older population. The aims of the present study were: (i) to determine the incidence, severity and preventability of MRH postdischarge in older adults; (ii) to describe the main types of MRH and implicated drugs; (iii) to describe health service utilization and cost associated with MRH.

Methods

The study was approved by the National Research Ethics Service, East of England (REC Reference 13/EE/0075).

Design, setting and participants

Detailed methods for the study have been published previously [18]. In brief, this multicentre, prospective cohort study recruited adults aged 65 years and over. Between September 2013 and November 2015, research nurses invited patients to participate from medical wards in five NHS teaching hospitals in Southern England, near to the time of hospital discharge. The nurses collected baseline information, including demographic, clinical and social data, from consenting patients. Senior, trained research pharmacists followed discharged participants for 8 weeks to determine if they experienced MRH. An 8-week observation period was chosen as previous research outside of the UK has shown that this is a reasonable time frame for capturing most postdischarge MRH events [19–21]. We excluded patients if they were terminally ill, lacked capacity and had

no nominated consultee, or were transferred to other acute healthcare units.

MRH assessment

We defined MRH as an ADR or harm arising from a failure to receive medication owing to non-adherence. Harm arising from medication error was included where reported. Intentional overdose was excluded. This is a modified version of the definition by Strand *et al*. [22]. A medicine was defined by its inclusion in the World Health Organization–Anatomical Therapeutics Coding (WHO-ATC) system [23].

We determined MRH incidence using three sources of follow-up information: (i) participant and/or carer telephone interview at 8 weeks, using a structured questionnaire; (ii) general practitioner (GP) records; and (iii) prospective review of hospital readmissions, in consultation with the admitting medical consultant.

If an ADR was suspected, the validated Naranjo algorithm [24] was used to assess causality, in conjunction with the British National Formulary and Summary of Product Characteristics. For MRH associated with non-adherence to medicine, we used a modified version of a validated questionnaire to assess participant non-adherence [25]. We classified events as 'possible', 'probable' or 'definite' MRH, or 'doubtful' when no harm occurred [26–28]. We graded severity of MRH using the approach of Morimoto *et al*. [29]: fatal, life-threatening, serious (requires therapy change and/or treatment by a health professional) and significant. The preventability of MRH was assessed using the criteria of Hallas *et al*. [30]: 'definitely preventable' (treatment inconsistent with best practice or unrealistic), 'possibly preventable' (preventable with efforts exceeding obligatory clinical demands), 'not preventable', or 'not able to evaluate'. Two senior study pharmacists provided case-based training to research pharmacists involved in data collection at all participating sites, to optimize the reliability of MRH assessments. Additionally, cross-site case discussions were held regularly between the research pharmacists to ensure the standardization of MRH assessments.

An end-point committee independent from data collection, consisting of three senior geriatricians and a senior researcher in clinical pharmacy, was provided with the structured case summaries of all cases of MRH by the research pharmacists. The role of the committee was to review, scrutinize and finally confirm or reject cases of MRH by consensus. Implicated medicines were classified according to the World Health Organization–Anatomical Therapeutic Chemical (WHO-ATC) classification system.

Healthcare utilization and cost analysis

The three sources of data collected (participant interviews, GP records, hospital readmissions) provided information on NHS use over the 8-week follow-up (including emergency department visits, hospital admission, outpatient clinics, GP visits and out-of-hours care). The date and reason for consultation were used to determine NHS utilization associated with MRH.

We used the Department of Health's 2013/14 payment by results NHS tariff data to cost episodes of healthcare utilization by linking them to Healthcare Resource Groups (HRGs) [31]. When in doubt, we took the most cautious approach, such as for emergency department visits and out-of-hours care.[1]

To estimate the annual cost in England of postdischarge MRH in older adults, we multiplied the average excess cost related to MRH per discharged participant in our study by the estimated number of unplanned admissions of older people in 2013/14 in England [33].Furthermore, we disaggregated the costs of MRH-associated healthcare use by preventability.

Statistical analysis

We examined variable distributions for normality and compared the characteristics of the cohort included in the final analysis with those of patients lost to follow-up, using the Mann–Whitney U-test. Fisher's exact test was used to compare categorical variables.

The incidence of MRH is reported as: (i) the incidence proportion (number of participants experiencing MRH/total sample) and (ii) the incidence of events per 1000 discharged participants (number of events × 1000/total sample). Other descriptive statistics are based on frequency calculations. Incidence proportions are presented with accompanying 95% confidence intervals. We analysed data using IBM SPSS Statistics, version 22 (IBM Corp., Armonk, NY).

Results

Participant characteristics

The study recruited 1280 older adults at hospital discharge and followed up participants for 8 weeks. Research pharmacists completed a telephone interview with 873 participants (68.2%) and retrieved the GP records of 922 participants (72.0%). From the 1280 recruited participants, 17 (1.3%) died without follow-up, and 147 participants (11.5%) were lost to follow-up because they were not readmitted, their GP records were unavailable or they could not be contacted. Therefore, our final cohort included 1116 (87.2%) participants (see Table 1).

The median age of the cohort was 82 years [interquartile range (IQR) 76–87], 58% were female and the median number of discharge medicines was nine (IQR 7–12).

Incidence of MRH

Overall, 413 participants [37.0% (95% CI 34.2–39.9%)] experienced MRH in the 8-week follow-up period, with 856 medicines implicated in 621 events. This represents an MRH incidence of 556 events per 1000 participants over an 8-week time frame. A total of 460 MRH events (74%) were attributable to medicines prescribed at hospital discharge, with the remainder prescribed in the community during the

[1]With no investigations and no treatment in the emergency department, costing £58 per episode [31]. Out-of-hours medical visits associated with MRH were costed at £53.60 using data from the National Audit Office [32], which reports that 50% of visits cost £53.60 to £86.30. This cautious approach avoided false assumptions about the extent of investigation and treatment.

Table 1

Baseline participant characteristics

Characteristic	Included participants[a] (*n* = 1116)	Excluded participants (*n* = 164)	*P* value[b]
Age, median (IQR), years	81.9 (75.5–86.9)	80.5 (74.7–86.2)	0.123
Gender, *n* (%)			
Women	652 (58.4)	93 (56.7)	0.673
Men	464 (41.6)	71 (43.3)	
Hospital stay, median (IQR), days	7 (3–14)	7 (3–13)	0.595
Number of Charlson Index comorbidities (%)			
0–1	541 (48.5)	88 (53.7)	
≥2	575 (51.5)	76 (46.3)	0.242
Selected comorbidities, *n* (%)			
Hypertension	611 (54.7)	86 (52.4)	0.615
CLD	326 (29.2)	56 (34.1)	0.202
Atrial fibrillation	279 (25.0)	43 (26.2)	0.773
Diabetes	269 (24.1)	31 (18.9)	0.167
IHD	224 (20.1)	38 (23.2)	0.352
CKD	153 (13.7)	21 (12.8)	0.808
CCF	150 (13.4)	20 (12.2)	0.713
Depression	95 (8.5)	12 (7.3)	0.762
Dementia	51 (4.6)	6 (3.7)	0.839
Charlson index, median (IQR)	2 (1–3)	1 (1–3)	0.087
Barthel score, median (IQR)	17 (13–20)	18 (14–20)	0.035
Number of discharge medicines, median (IQR)	9 (7–12)	9 (6–12)	0.393
Multicompartment compliance aid, *n* (%)	371 (33.2)	43 (26.2)	0.074
Discharge to care home, *n* (%)	30 (2.7)	8 (4.9)	0.136
Living alone after discharge, *n* (%)	551 (49.4)	80 (48.8)	>0.999

CCF, congestive cardiac failure; CLD, chronic lung disease; CKD, chronic kidney disease; IHD, ischaemic heart disease; IQR, interquartile range

[a]Ten participants were included following readmission which was not associated with medication-related harm, for whom general practitioner records were not available and were uncontactable at 8 weeks (median follow-up 29 days after recruitment)

[b]Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables

8-week observation period. Of the 413 participants whom we classified as having MRH, 246 (60%) experienced at least one MRH event considered 'probable' (*n* = 110) or 'definite' (*n* = 136). The remaining cases were 'possible' (*n* = 167). The prevalence of non-adherence in our cohort was 29.1% at follow-up (325 out of 1112 participants with adherence data).

ADRs were solely responsible for MRH in 301 out of 413 cases (72.9%), non-adherence in 45 cases (10.9%) and a medication error in 14 cases (3.4%). In five cases (1.2%), the patient experienced harm from both an ADR and a medication error. The underlying medication error was at the stage of prescribing in 11 cases, dispensing in four cases, administration by a carer in three cases and patient error in the use of a medicine administration device in one case. In 48 cases (11.6%), harm was due to both an ADR and non-adherence. For example, a participant who experienced a gastric bleed associated with antiplatelet therapy was non-adherent to their proton-pump inhibitor. One quarter of ADRs occurred in the first week postdischarge, and 68% within 30 days of discharge.

Severity and preventability of MRH

Four participants (1.0%) experienced a fatal event associated with the MRH; one died following a fall and fractured neck of femur associated with lorazepam use, one from a major gastrointestinal bleed associated with use of apixaban, one from a stroke associated with non-adherence to warfarin and one from a lower respiratory tract infection associated with prednisolone-induced immunosuppression. Nine participants (2.2%) had a life-threatening event, and MRH was serious in a further 323 participants (78.2%). We classified medication harm as 'definitely' preventable in 44 cases

[(95% CI 7.8–14.0%)] and 'possibly' preventable in 170 MRH cases [(36.4–46.1%); see Appendix 1].

Types of MRH and implicated medicines

The body systems affected by MRH are shown in Table 2. The main body systems affected by MRH were gastrointestinal (25.4%) or neurological (17.9%). The most common events were diarrhoea (n = 55; 8.9%), constipation (n = 52; 8.4%), falls (n = 35; 5.6%) and bleeding (n = 31; 5.0%).

Antihypertensives and opiates were implicated in the highest proportion of MRH events (22.4% and 17.2%, respectively). However, MRH risk (incidence per 1000 prescriptions) was greatest for opiates (399), followed by antibiotics (189). The risk of MRH by medicine class is shown in Table 3.

Of the 413 participants with MRH, 85 (20.6%), who experienced 105 MRH events, managed their adverse event(s) without seeking healthcare input. The most common events were diarrhoea (n = 13; 12.4%), constipation (n = 11; 10.5%), dizziness (n = 8; 7.6%) and peripheral oedema (n = 8; 7.6%).

Health service utilization and cost

Out of the 413 MRH cases, 328 [95% CI (75.2–83.2%)] had at least one NHS service use associated with MRH, and 87 participants [95% CI (6.3–9.5%)] had an MRH-associated hospital readmission. A total of 328 participants received 441 NHS consults [GP consultation (n = 316; 71.7%), hospital readmission (n = 96; 21.8%], outpatient clinic attendance (n = 12; 2.7%], emergency department attendance (n = 9; 2.0%), out-of-hours visit (n = 8; 1.8%)]. The cumulative NHS cost, over the 8-week period after hospital discharge, was £225 747, an average cost per participant with MRH of £546.60. Hospital readmissions accounted for 93% of total costs. The estimated annual cost to the NHS of MRH postdischarge in older adults is £395.5 million. The cost of preventable MRH lies between

Table 2

Medication-related harm by body system and implicated medicine

Body system	Total events (n = 612), n (%)	Medication-related harm (n)	Commonly implicated medicines[a] (n)
Gastrointestinal	158 (25.4)	Diarrhoea, 54; constipation, 52; nausea, 21; vomiting, 13; acid reflux, 12; abdominal pain, 5; acute liver injury, 1	Opiates, 49; senna, 16; iron, 10; macrogol, 9; alendronate, 8; clopidogrel, 8
Neurological	111 (17.9)	Dizziness, 25; confusion, 19; fatigue, 19; drowsiness, 14; headache, 14; sleep disturbance, 11; involuntary movements, 4; paraesthesia, 4; seizure, 1	Opiates, 23; amlodipine, 10; bisoprolol, 9; ramipril, 6; amitriptyline, 5
Cardiovascular	68 (11.0)	Peripheral oedema, 26; postural hypotension, 17; syncope, 9; exacerbation of cardiac failure, 7; arrhythmia, 5; thrombotic event, 4	Amlodipine, 15; furosemide, 10; bisoprolol, 8; bumetanide, 7; ramipril, 6
Musculoskeletal	65 (10.5)	Fall, 35; musculoskeletal pain, 27; gout, 2; fracture, 1	Opiates, 18; bisoprolol, 10; furosemide, 8; ramipril, 7; simvastatin, 5
Dermatology	47 (7.6)	Rashes and skin lesions, 20; pruritus, 13; candidiasis, 9; alopecia, 3; facial swelling, 1; unresolving infection, 1	Clarithromycin, 4; amoxicillin, 3; flucloxacillin, 3; rivaroxaban, 3; furosemide, 3
Haematology	45 (7.2)	Bleeding, 31; bruising, 9; anaemia, 4; immunosuppression, 1	Clopidogrel, 12; rivaroxaban, 10; warfarin, 8; aspirin, 8; dalteparin, 4
Respiratory	31 (5.0)	Dyspnoea, 19; cough, 11; unresolving infection, 1;	Ramipril, 9; salbutamol, 7; tiotropium, 7; seretide, 5; symbicort, 3
Renal	26 (4.2)	Acute kidney injury, 15; electrolyte disturbance, 11	Furosemide, 11; spironolactone, 6; ramipril, 6; bumetanide, 5; omeprazole, 2
Endocrine	25 (4.0)	Hypoglycaemia, 12; hyperglycaemia, 11; gynaecomastia, 1, hot flushes, 1	Insulin, 15; gliclazide, 6; metformin, 3; prednisolone, 3; liraglutide, 2
Psychiatric	16 (2.6)	Mood or behavioural disturbance, 16	Opiates, 6; prednisolone, 3; zopiclone, 2; gabapentin, 2;
Ear nose & throat	14 (2.3)	Dry mouth, 8; taste disturbance, 4; hoarseness, 1; oral ulceration, 1	Omeprazole, 2; tiotropium, 2
Genitourinary	9 (1.4)	Incontinence, 4; urinary retention, 4; urine discolouration, 1	Furosemide, 3
Ophthalmology	6 (1.0)	Dry or sore eyes, 3; visual disturbance, 3	Prednisolone, 2

[a]Top five medicines listed, except when the number of events caused by a medicine was <2. Given multiple formulations of codeine and morphine-related medicines, these are grouped into opiates

Table 3

Incidence of harm by medicine class

Medicine class[a]	Prescriptions (*n*)	MRH events (*n*)	Proportion of MRH by medicine class (%)	Risk of MRH by medicine class (events per 1000 prescriptions)
Opiates	268	107	17.2	399.3
Antibiotics	344	65	10.5	189.0
Benzodiazepines	81	15	2.4	185.2
Diuretics	496	76	12.2	153.2
Antiepileptic agents	147	21	3.4	142.9
Corticosteroids	158	21	3.4	132.9
Anticoagulants	311	41	6.6	131.8
Antidepressants	269	34	5.5	126.4
Antihypertensive agents	1163	139	22.4	119.5
Hypoglycaemic agents	314	34	5.5	108.3
Anticholinergic agents	173	12	1.9	69.4
Laxatives	616	41	6.6	66.6
Antiplatelet agents	582	38	6.1	65.3

MRH, medication-related harm

[a]Benzodiazepines include benzodiazepine-related drugs; World Health Organization–Anatomical Therapeutics Coding codes C03A and C03B are under both antihypertensive agents and diuretics

£51.6 million per year (only MRH classified as 'definitely preventable') and £243.4 million per year (MRH 'definitely' or 'possibly' preventable).

Discussion

This was the first UK study to investigate medication harm in older adults following hospital discharge. Our key findings were that MRH affects one in three older adults, and that 80% of cases were serious, and at least 10% preventable. Four out of five participants with MRH consulted an NHS service within 8 weeks postdischarge. We estimated that postdischarge MRH to the older population incurs an annual cost in the region of £400 million to the NHS, and that most of this cost is attributable to hospital readmissions.

ADRs are the main form of MRH, and 25% manifest in the first week postdischarge. A large proportion of older adults (29%) are non-adherent in the postdischarge period, and the present study clearly demonstrated the harms associated with this; non-adherence was implicated in 23% of MRH cases, including one death. While the study did not seek to identify medication errors, harm attributable to a medication error was recorded and represented a very small proportion of the overall MRH burden (<5%). In the majority of these cases, the medication error was made at the prescribing stage.

Strengths and limitations

The main strengths of the study were the comprehensive data collection (participant interview, primary care records and readmission review) and the fact that we recruited a large, multicentre cohort of older adults (average age >80 years). Our definition of MRH reflects 'real-life' for patients by including harm from non-adherence (as opposed to only ADRs), and, we employed a robust approach to ascribe MRH causality using a validated algorithm [24] and the clinical expertise of senior pharmacists and geriatricians.

However, there were also several limitations. Participants' involvement in the study might have heightened their awareness of potential ADRs. They might therefore have been more attentive to medicines-related information and usage instructions, or more likely to seek healthcare when MRH was suspected. However, this increased knowledge might also have enabled participants to attribute and report MRH more accurately.

Retrospective participant interviews may have resulted in under-reporting of MRH due to poor recall, and GPs may not have recorded all MRH encountered owing to time pressures or a perceived lack of severity [34]. Harm arising from medication errors might have been underestimated as we did not look actively for postdischarge medication reconciliation errors and assess their impact. It is possible, therefore, that some MRH was misclassified as an ADR, rather than a harm due to medication error. Nonetheless, a very small proportion of medication errors actually lead to patient harm [35].

The NHS costs we report are an approximation based on the incidence and types of MRH in the present study. We recorded NHS utilization associated with MRH, and could not infer causality. Nonetheless, hospital readmissions accounted for 93% of overall cost, and in these cases the MRH was verified as a principal driver for admission by the medical consultant in charge.

Comparison with other studies

The proportion of participants experiencing MRH (37%) in our study was higher than previously reported [36]. This was probably due to methodological differences as opposed to any peculiarities in our study population or the healthcare system. A retrospective analysis of 1000 older patients in the United States found that 18.7% experienced MRH over a 45-day period following hospital discharge [21]. This study identified events through review of medical notes, contrasting with our prospective methods, which additionally included participant interviews. Retrospective studies and studies that exclude participant interviews tend to report a lower incidence of MRH [12, 37]. A prospective European study of 209 patients (average age 74 years) found that 30% of their cohort experienced an ADR over a 30-day postdischarge period [38]. This finding was comparable to our results, although our slightly higher incidence of 37% probably reflected the inclusion of MRH from non-adherence.

We found that 11% of participants experiencing MRH had an event that was definitely preventable. Nevertheless, we believe that the true proportion is likely to be higher as 41% of MRH cases were possibly preventable. A systematic review published in 2011 by Taché *et al*. reported that 16.5% of MRH events in the community were preventable, based on all age groups [12]. The high proportion of preventable events in our study reflected the particularly challenging period (i.e. postdischarge) we investigated in an older population, and our inclusion of harm from non-adherence to medicines.

The systematic review by Taché *et al*. [12] found cardiovascular medicines to be most implicated in MRH in the community setting, reflecting the high prevalence of their use. Our study found that 22% of MRH was associated with antihypertensive medicines. However, the highest risk of MRH was associated with opiates. Concerns have been raised about the potential harm related to overuse of opiates in noncancer patients in the UK [39], and our study demonstrated the actual harm associated with opiate use in older adults.

Implications for practitioners and policy makers

Given the high proportion of preventable MRH in our study, there is considerable scope for improving patient safety. The lack of prescriber knowledge of harms is a key driver of medicines overuse [40], and, clinicians are more likely to overestimate the benefits of treatment and underestimate the harms [41]. The present study highlights the extent of MRH during a critical juncture of healthcare provision, and supports the need for increased pharmacovigilance among clinicians in secondary and primary care. While most MRH in the postdischarge period was attributable to medicines prescribed in the hospital setting, one-quarter of implicated medicines were prescribed in the community. It is crucial to reconcile the medicines that patients receive on discharge from hospital, with those already listed on the repeat prescription from the GP, and any additional medicines which the patient takes at home. Prescribers in the community must be wary of the heightened vulnerability of patients to harm in the immediate postdischarge period, as physiological systems remain impaired during recovery from acute illness and the stressors associated with hospitalization (e.g. poor nourishment, deconditioning, sleep disturbance, delirium) [17].

There are numerous lists of potentially inappropriate medicines for older adults [42] [e.g. Screening Tool of Older Persons' Potentially inappropriate Prescriptions (STOPP), Beers, (European Union Potentially Inappropriate Medications (EU-PIM)]. While these have merit, a 'hard and fast' rules-based approach does not account for the biopsychosocial complexity of patients [43, 44]. Simple guiding principles that support clinical judgement for the safe initiation of medicine [e.g. the BEGIN (1. Basis for therapy; 2. Evaluate risk of interactions; 3. Given agreement; 4. Intended benefit likely; 5. No better alternative) algorithm [45] or the Medication Appropriateness Index [46]] may be more practical and effective [47]. When prescribers initiate new medicines, a tentative stop or review date should always be specified. While it remains unclear from randomized trials if medication review on its own reduces MRH in older adults, multicomponent interventions incorporating patient education have demonstrated success during transitions of care [13, 48].

In addition, there are several risk prediction tools to identify patients at high risk for MRH, although these have been largely developed for a hospitalized population [49]. In the present study, we showed that the risk of MRH is highest in the community setting following hospital discharge. Future work should focus on developing a tool to identify high-risk patients during this particularly vulnerable period.

Our national cost estimate of almost £400 million per year is a conservative estimate. It excludes the indirect costs from wasted medicines (non-adherence and poor therapeutic value, or medicines that must be stopped owing to adverse effects) and the social costs of additional formal and informal care (e.g. time taken away from work by relatives to support participants). The bulk of the cost arises from hospital readmissions. Therefore, early recognition of medication-related problems and community management as far as possible could generate large savings.

In conclusion, medication harm in older adults is a common and costly phenomenon following hospital discharge. Increased vigilance to high-risk prescribing, and supporting the appropriate use of medicines in the community, might reduce this problem.

Competing Interests

There are no competing interests to declare.

We are grateful to Dr Stephen Bremner, senior lecturer in medical statistics, Brighton and Sussex Medical School, UK, for statistical support. This study was funded by the National Institute for Health Research (NIHR) – Research for Patients Benefit Scheme (PB-PG-0711-25094). The sponsor was Brighton and Sussex University Hospitals NHS Trust. The funder and sponsor had no role in the study design; data collection, analysis or interpretation; the writing of the report; or the decision to submit the article for publication. The views expressed are those of the authors and not those of the funder, or the organizations they represent.

Contributors

J.G.D., J.M.S., K.A., J.H., R.S. and C.R. conceived the study. J.G.D., J.M.S., N.P., K.A., J.H., R.S. and C.R. designed the

study and analysed the data. J.M.S., N.P. and J.H. were involved in data collection. J.G.D., K.A., R.S. and C.R. verified end-points. N.P., J.G.D., J.M.S., K.A., J.H. and C.R. analysed and interpreted the data. T.C. provided expert guidance. All authors contributed to the preparation of the manuscript and approved the final manuscript for submission. C.R. and K.A. are guarantors.

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Appendix 1

Case examples of medication-related harm (MRH)

Case 1: Adverse drug reactions
Likelihood MRH: definite; severity: serious; preventable: definitely
Past history of MI, severe aortic stenosis, angina, COPD, diabetes. Participant sitting in chair and began to shake, and with central chest pain and shortness of breath. Felt dizzy with pain, and thought she was going to collapse. Readmitted 15 days postdischarge with negative troponin. Participant experienced a similar presyncopal episode after morning medicines as inpatient, with BP dropping to 76/35 mmHg. Impression: participant suffered a hypotensive episode secondary to a combination of medicines which lower blood pressure: losartan, ISMN, nicorandil and diltiazem.
Case 2: Medication error
Likelihood MRH: definite; severity: serious; preventable: definitely
Past history of heart failure, COPD and dementia. Participant experienced increased shortness of breath and bilateral leg swelling. Discharged 7 days previously with increased bumetanide dose. At home, carer administered medicines from old dosette box containing lower dose of bumetanide. Symptoms responded well to increased diuretics. Impression: exacerbation of heart failure due to administration of incorrect bumetanide dose.
Case 3: Adverse drug reaction and non-adherence
Likelihood MRH: definite; severity: serious; preventable: possibly
Past history of AF, diabetes, PVD, reduced mobility, grade 3 pressure sore. Daughter requested GP visit for participant 6 days post-discharge. Participant experienced nausea and constipation. No urinary symptoms, negative MSU. Had been prescribed buprenorphine patch and dihydrocodeine from hospital following fractured neck of femur. Has laxido but does not take it. Impression: constipation secondary to opioids and non-adherence to laxatives.

AF, atrial fibrillation; BP, blood pressure; COPD: chronic obstructive pulmonary disease; GP, general practitioner; ISMN, isosorbide mononitrate; MI, myocardial infarction; MSU, midstream urine; PVD, peripheral vascular disease