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A multicentre prospective study in the UK

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ORIGINAL ARTICLE

Can doctors identify older patients at risk of medication harm following hospital discharge? A multicentre prospective study in the UK

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Keywords geriatric medicine, medical education, patient safety, pharmacovigilance, prescribing

AIMS

Medication-related harm (MRH) is common in older adults following hospital discharge. In resource-limited health systems, interventions to reduce this risk can be targeted at high-risk patients. This study aims to determine whether (1) doctors can predict which older patients will experience MRH requiring healthcare following hospital discharge, (2) clinical experience and confidence in prediction influence the accuracy of the prediction.

METHODS

This was a multicentre observational prospective study involving five teaching hospitals in England between September 2013 and November 2015. Doctors discharging patients (aged ≥65 years) from medical wards predicted the likelihood of their patient

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experiencing MRH requiring healthcare (hospital readmission or community healthcare) in the initial 8-week period post-discharge. Patients were followed up by senior pharmacists to determine MRH occurrence.

RESULTS

Data of 1066 patients (83%) with completed predictions and follow-up, out of 1280 recruited patients, were analysed. Patients had a median age of 82 years (65–103 years), and 58% were female. Most predictions (85%) were made by junior doctors with less than 5 years' clinical experience. There was no relationship between doctors' predictions and patient MRH (OR 1.10, 95% CI 0.82–1.46, $P = 0.53$), irrespective of years of clinical experience. Doctors' predictions were more likely to be accurate when they reported higher confidence in their prediction, especially in predicting MRH-associated hospital readmissions (OR 1.58, 95% CI 1.42–1.76, $P < 0.001$).

CONCLUSIONS

Clinical judgement of doctors is not a reliable tool to predict MRH in older adults post-discharge.

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Medication-related harm is common and often preventable in older people.
- Existing risk prediction tools are poorly predictive of medication-related harm.

WHAT THIS STUDY ADDS

- Clinical judgement of doctors does not predict medication-related harm in older people.
- Years of clinical experience does not increase the predictive accuracy of medication-related harm.
- Higher levels of confidence of doctors in their predictions is associated with greater predictive accuracy.

Introduction

Medication-related harm (MRH) is an increasing public health problem in England [1]. The estimated cost per year to the National Health Service (NHS) of preventable hospital admissions associated with MRH is £530 million [2]. The older population (aged ≥65 years) is particularly vulnerable to MRH due to polypharmacy [3] and age-related changes in pharmacokinetics and pharmacodynamics [4]. A systematic review found that approximately one in ten hospital admissions in older adults are due to MRH and a similar proportion of patients experience MRH in the inpatient setting [5]. The transition period back into the community following hospital discharge is a particularly challenging time for patients [6, 7], with a high frequency of medication changes [8], hospital-related deconditioning, and ongoing recovery from acute illness [9]. Prospective studies from Europe and North America have shown between 17% and 51% of older adults experience MRH within 1 month post-discharge [10].

Reducing the burden of MRH requires identification of high-risk patients and supporting them with targeted, evidence-based intervention. Currently there are no risk prediction tools to identify high-risk patients for MRH post-discharge, and the success of pharmacist interventions to reduce MRH and hospital readmission has been inconsistent [11–14]. Risk stratification to reduce adverse events in the NHS is a national priority [15].

Doctors, particularly junior staff, are expected to play a pivotal role in planning and coordinating a safe hospital discharge for patients [16]. In this role they are required to consider the ongoing health-related needs of patients following their transition back into the community. Doctors organizing patient discharge might be well-placed to predict MRH given they have some knowledge of a patient's predisposing factors. For instance, doctors prescribing discharge medicines and writing discharge summaries to General Practitioners should be familiar with the patient's clinical state (e.g. renal function, cognition) and social environment (e.g. support with medicines). In addition, adverse drug reactions (ADR) are the most common MRH and are usually predictable from the known pharmacological action of the drug (i.e. type 'A' reactions) [17, 18].

To the best of our knowledge, the accuracy of clinical judgement in predicting MRH has not been tested. Experts in this field have previously called for research into this [19]. This study aims to address this gap. Our primary objective was to investigate whether hospital doctors can predict MRH in patients that they discharge. Secondary objectives were to explore whether doctors' years of clinical experience influence their ability to predict MRH, and whether doctors' confidence in their predictions is associated with its accuracy.

Methods

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

Design, setting and participants

The methods for the PRIME study are described in detail in the published protocol [20]. Briefly, this was a multicentre prospective cohort study of patients aged 65 years and over, conducted between September 2013 and November 2015. Research nurses invited patients from the medical wards of five teaching hospitals in South England to participate, as near as possible to the time of hospital discharge. The nurses collected baseline data from consenting patients, including

demographic data, and clinical and social parameters. Senior, trained pharmacists subsequently followed participants for 8 weeks into the community to determine whether they experienced MRH. We excluded patients if they were terminally ill, if they lacked capacity with no nominated consultee or if they were transferred to other acute healthcare settings. Capacity, in accordance with the Mental Capacity Act 2005, was assessed by the research nurses who had all undertaken capacity and consent training.

At the point of hospital discharge, a research nurse asked the doctor that arranged the patient discharge to complete a questionnaire (see Supporting Information Appendix S1). On this questionnaire, the doctor anonymously predicted the likelihood of their patient experiencing MRH requiring healthcare utilization (hospital admission or community healthcare) in the first 8 weeks following discharge. We asked doctors to classify their prediction based on recognized categories in this field [21]: doubtful, possible, probable or definite. Predicting a likelihood for a given consequence (MRH serious enough to seek healthcare) to estimate risk is based on the National Patient Safety Agency risk model matrix [22]. We also asked doctors to assign a confidence rating to their judgements using a six-point Likert scale based on previous studies in this topic area [23]. This Likert scale consists of: (1) little or no confidence; (2) slight to moderate confidence; (3) less than 50% confidence but a close call; (4) more than 50% confidence but a close call; (5) strong confidence; (6) virtually certain. Doctors provided information on their level of training according to their medical grade (e.g. foundation year one, foundation year two, core trainee, registrar, consultant). We grouped these into the following categories of clinical experience; less than 1 year (reflecting foundation year one), 1–4 years (reflecting senior house officer) and more than 4 years (reflecting registrar or consultant). Given the regular rotation of junior doctors, we recognized the need for providing ongoing information about the study. During the induction of new doctors joining the participating medical wards, the doctors were given clear information about the specific details of their involvement in completing questionnaires and it was reiterated that they should not complete questionnaires if they were not familiar with the patient. In addition, research nurses conducting the questionnaires were trained to ensure that only doctors that confirmed knowledge of the patient's case history were asked to complete questionnaires.

Definition of medication-related harm (MRH)

Medication-related harm (MRH) included adverse drug reactions (ADR) and harm arising from a failure to receive medication owing to nonadherence. 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*. (1990) [24].

Assessment of MRH

Senior pharmacists collected data from three sources to determine whether MRH occurred, and associated healthcare utilization: (1) participant and/or carer telephone interview at 8 weeks using a structured questionnaire, (2) General Practitioner (GP) records, and (3) hospital readmissions by prospective review, in conjunction with the admitting medical consultant.

To assess ADR causality, the validated Naranjo algorithm [25] was used, with reference to the British National Formulary and Summary of Product Characteristics. For MRH suspected to be associated with nonadherence, we used a modified version of a standard questionnaire to assess patient nonadherence [26, 27]. 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 regularly held between the research pharmacists to ensure standardization of MRH assessments. We classified outcomes as 'doubtful', 'possible', 'probable' or 'definite' MRH. This is consistent with the Naranjo algorithm and prior research on MRH [17, 21, 28–30]. In cases where the MRH was unclear, or hospital readmissions when the research pharmacist and admitting medical consultant disagreed, an end-point committee consisting of one senior researcher in clinical pharmacy and therapeutics (J.G.D.) and three senior geriatricians (K.A., C.R., R.S.) reviewed the available information to reach a consensus decision. The end-point committee was independent from data collection and were provided 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.

Statistical analysis

To describe the baseline characteristics of our population, we first examined the distribution of the variables by plotting histograms and used these in conjunction with the Kolmogorov–Smirnov test for normality. We calculated the median and interquartile range for continuous variables. For further analyses, we excluded patients that did not have a doctor's prediction or that were lost to followup, i.e. no MRH outcome information at 8 weeks. We compared the characteristics of the patient cohort included in our final analysis with those that were excluded using the Mann–Whitney U-test for continuous, nonparametric variables. To compare categorical variables, we used Fisher's Exact Test.

We examined the relationship between the discharging doctors' prediction of MRH and the observed outcome of MRH using a logistic regression model. Patients were grouped as having experienced MRH if they had a possible, probable or definite event. Consistent with this, doctors' predictions of possible, probable and definite MRH were grouped together as a prediction that MRH will occur. We also calculated the sensitivity, specificity, positive and negative predictive values, and the area under the receiver operating curve (AUROC) to quantify the discriminatory ability of the doctors' predictions.

A sensitivity analysis using a logistic regression model that only included probable and definite MRH predictions and events was conducted to investigate any impact on the main results of the inclusion of 'possible' cases in our categorization of MRH. Similarly, a sensitivity analysis was conducted including only ADRs (excluding harm only due to nonadherence and medication error) to determine any effect of definition.

Using logistic regression, we also explored whether (a) the years of clinical experience of doctors', and (b) the confidence doctors placed in their predictions, influenced the accuracy of the MRH prediction. All models were controlled for site of patient recruitment. A *P*-value of <0.05 was regarded statistically significant. Analyses were done using Stata software, version 14.2.

Results

The study recruited 1280 older patients at hospital discharge to follow-up for 8 weeks. Of this recruited cohort, 17 patients (1.3%) died with no follow-up, and 197 (15.4%) patients either did not have a prediction of MRH or did not have an 8-week follow-up. Subsequently, we analysed the data of 1066 patients. The baseline population characteristics are shown in Table 1. The median age of the patients was 82.0 years (IQR 75.6–87.0), and 58% were female. The median Charlson comorbidity index was 2 (IQR 1–3), and median number of drugs prescribed at discharge was nine (IQR 7–12).

From the cohort of 1066 patients, 315 (29.5%) experienced MRH requiring healthcare (emergency department and/or hospital readmission, outpatient consultation, GP consultation including out of hours), in the 8 weeks post-discharge.

Over half of MRH predictions (*n* = 595, 55.8%) were by doctors with less than one full year of clinical experience post-medical qualification, i.e. foundation year one, 306 (28.7%) predictions by doctors with 1–4 years clinical experience, i.e. senior house officer level, and 126 (11.8%) predictions by senior doctors of five or more year's clinical experience, i.e. registrar or consultant grade. The grade of the doctor was unknown for 39 (3.7%) predictions.

Accuracy of MRH predictions

Doctors correctly predicted the outcome (MRH or no MRH) in 469 out of 1066 patients (44%). Doctors correctly predicted

Table 1

Baseline characteristics

Characteristic	Included patients (*n* = 1066)	Excluded patients (*n* = 214)	*P*-value*
Age, median (IQR), years	82.0 (75.6–87.0)	80.2 (74.3–85.7)	0.008
Gender, *n* (%),			
Women	619 (58.1)	126 (58.9)	
Men	447 (41.9)	88 (41.1)	0.879
Hospital stay, median (IQR), days	7 (3–14)	7 (3–13)	0.383
Number of Charlson Index comorbidities (%)			
0–1	521 (48.9)	108 (50.5)	
≥2	545 (51.1)	106 (49.5)	0.708
Selected comorbidities, *n* (%)			
Hypertension	582 (54.6)	115 (53.7)	0.822
CLD	310 (29.1)	72 (33.6)	0.191
Atrial Fibrillation	263 (24.7)	59 (27.6)	0.388
Diabetes	255 (23.9)	45 (21.0)	0.378
IHD	212 (19.9)	50 (23.4)	0.265
CKD	146 (13.7)	28 (13.1)	0.913
CCF	143 (13.4)	27 (12.6)	0.826
Depression	92 (8.6)	15 (7.0)	0.500
Dementia	51 (4.8)	6 (2.8)	0.274
Charlson Index score, median (IQR)	2 (1–3)	2 (1–3)	0.385
Barthel Index Score, median (IQR)	17 (13–20)	18 (14–20)	0.017
Number of discharge medicines, median (IQR)	9 (7–12)	9 (7–12)	0.202
Multicompartment compliance aid, *n* (%)	351 (32.9)	63 (29.4)	0.337
Discharge to care home, *n* (%)	29 (2.7)	9 (4.2)	0.267
Living alone after discharge, *n* (%)	531 (49.8)	100 (46.7)	0.498

*Mann–Whitney U test for continuous variables and Fisher's Exact test for categorical variables

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

MRH will occur in 204 out of the 315 MRH cases (64.8%), and that MRH will not occur in 265 out of 751 patients that did not experience MRH (35.2%). Thus, the sensitivity of doctors' predictions was 0.65; specificity was 0.35, and the positive predictive value 0.30 and the negative predictive value 0.70. The AUROC was 0.50, which demonstrates no predictive discrimination between patients that did or did not experience MRH. Using logistic regression models, there was no relationship between the doctors' predictions and MRH outcome (odds ratio (OR) 1.10, 95% CI 0.82–1.46, P = 0.53) (Table 2). A sensitivity analysis to determine whether exclusion of possible cases of MRH and doctor's predictions affects this relationship demonstrated no meaningful difference (OR 0.90, 95% CI 0.53–1.52, P = 0.68). A further sensitivity analysis to determine if doctors could correctly predict ADRs, rather than the broader definition of MRH (includes harm from nonadherence and medication error), also demonstrated no significant relationship (OR 0.91, 95% CI 0.64–1.28, P = 0.57).

Influence of doctor's seniority and confidence

We found no significant difference in predictive ability between doctors with varying years of clinical experience (<1 year, 1–4 year, >4 years) (Table 2). Our results did show, however, that a higher confidence placed by doctors in their own MRH predictions ('little or no confidence' through to 'virtually certain') was associated with a more accurate prediction (see Table 3). Increasing confidence levels in doctors' predictions of MRH leading to hospital readmission was associated with 58% increased odds of a more accurate prediction (OR 1.58, 95% CI 1.42–1.76, $P < 0.001$). Similarly, increasing confidence was associated with the accuracy of doctors' predictions of MRH leading to community healthcare use (OR 1.14, 95% CI 1.03–1.26, P = 0.009).

Table 2

Relationship between discharging doctors' predictions and medication-related harm (MRH) by (a) all doctors and (b) level of clinical experience

	Odds ratio (OR)	95% Confidence interval	*P*-value
(a) Discharging doctor prediction of MRH (Yes *vs* No)[a]	1.10	0.82–1.46	0.527
(b) <1-year experience[b]	1		
1–4 years[b]	1.32	0.88–1.98	0.181
>4 years[b]	1.14	0.58–2.23	0.709

[a]Based on 1066 predictions.
[b]Based on 1028 predictions.
Possible, probable and definite classifications for predictions and outcomes grouped as affirmative of MRH occurrence.

Table 3

Relationship between discharging doctors level of confidence in their prediction of (a) hospital readmission associated with MRH, and (b) community health service use associated with MRH, and the accuracy of the prediction

	Odds ratio (OR)	95% Confidence interval	*P*-value
(a) Level of confidence in prediction of MRH readmission[a]	1.58	1.42–1.76	<0.001
(b) Level of confidence in prediction of MRH community health service use[b]	1.14	1.03–1.26	0.009

[a]Based on 1062 predictions
[b]Based on 1053 predictions

Discussion

This study's main finding is that the clinical judgement of doctors is not a reliable predictor of post-discharge MRH in older patients. This finding was not influenced by the seniority of the discharging doctor; however, predictions made with a higher confidence were more likely to be accurate. Eighty-five per cent of the doctors that participated in this study were junior doctors. This reflects the fact that junior doctors are normally the member of the medical team responsible for facilitating patient discharge in the UK.

This is the first study that we are aware of which examines whether clinical judgement can predict MRH in older adults. The study focused on the judgement of doctors given their primary role in planning and coordinating discharge, prescribing medicine at hospital discharge, and communication with patient's GPs through discharge summaries. Discharging doctors are well-situated to intervene by highlighting medication concerns on a discharge summary or altering medicine lists in high-risk individuals. Accurate MRH risk prediction would help to better target interventions, and reduce the burden of MRH. It is surprising that much effort has been invested in the development of statistically generated risk prediction models, and yet the basic question of whether clinical judgement might suffice has remained unanswered. Indeed, experts have called for a study to investigate the accuracy of clinical judgement in predicting MRH risk, and to compare this with statistically generated risk prediction models [19]. A recent systematic review of risk prediction models to predict MRH in hospitals found that none of the tools were suitable for routine clinical implementation [31]. The tools range in their performance from poor to moderate predictive discrimination (AUROC ranges from 0.62 to 0.73) and require further prospective external validation [31, 32]. Such statistical tools are derived entirely from variables measured quantitatively. However, some risk factors for MRH have important qualitative characteristics [33] that may better lend themselves to risk prediction using clinical judgement. For example, a patient's health literacy is an important factor to consider when weighing up the risk of

MRH [34], but is challenging to comprehensively quantify [35]. Nonetheless, our results show that the clinical judgement of doctors is not a reliable tool to predict which patients are likely to experience MRH.

Whilst there are no previous studies that our findings can be directly compared with, there have been studies investigating risk prediction by doctors in related areas. A US study by Allaudeen *et al*. evaluated the ability of doctors to predict 30-day hospital readmission in a sample of 164 older adults at the point of discharge [36]. The study showed similar results to ours, demonstrating a poor ability of doctors, irrespective of seniority, to discriminate between patients that were readmitted and those that were not (AUROC 0.59 for junior doctors, and AUROC 0.58 for senior doctors). The investigators postulated that the heterogeneity of the older population in conjunction with the complex interplay between clinical and social factors that drive hospital readmission may explain their findings [36]. The drivers of MRH are comparably complex, with a multitude of recognized risk factors across biological, psychological and social domains [5, 37], and is one potential explanation for doctors being unable to predict MRH. However, an important contrast from predicting all-cause readmission, as in the study Allaudeen *et al*., is that many MRH episodes are predictable from a good understanding of clinical pharmacology (i.e. 'type A' ADRs) [17]. Therefore, another potential explanation for our findings is poor clinical pharmacology and therapeutics (CPT) knowledge amongst junior doctors [38]. Compared with diagnostic-related teaching, CPT has been a relatively neglected area of the medical curriculum in the UK and more widely (2–3% of medical education) [39, 40]. Yet, a core feature of the day-to-day work of a junior doctor is the prescribing and monitoring of medicines. A recent systematic review and large European survey of final year medical students have both shown that junior doctors are underprepared for their prescribing responsibilities, and pharmacovigilance is an area in particular need of improvement [41]. A national prescribing safety assessment for medical students in the UK, within which ADR is a key section, was rolled out in 2014 and is expected to increase the visibility of CPT within the curriculums of medical schools [42]. Increased education in CPT may support future doctors to better predict MRH, and therefore target high-risk patients for additional medicines support and monitoring in the community post-discharge. Even so, ADRs in the very old population can present atypically and be mistaken as manifestation of frailty, such as falls and chronic constipation. Therefore, doctors must remain vigilant to this, alongside increased CPT knowledge [43].

A considerable proportion of MRH is attributable to poor adherence (23% of MRH in the PRIME study) and medication errors (5% in the PRIME study) [44]. Qualitative work has shown that GPs value pharmacists' expertise on adherence-related and medication management issues, particularly in older patients [45]. Shared learning initiatives between doctors and pharmacists might enhance knowledge amongst doctors of adherence and medication management problems, and increase their ability to predict these issues in their patients.

Alternative educational approaches may also be valuable for doctors to develop a broader knowledge of the determinants of MRH and reducing its burden; a study of third year medical students in the United States found that experiential learning methods through direct involvement in patient care at the point of discharge and subsequent community follow-up improves awareness of medication-related problems in the post-discharge period [46].

Another finding from our study is the positive relationship between the confidence a doctor placed in their MRH prediction and its accuracy. There is little published research with which we can compare this finding. One US study used hypothetical medical cases, ranging in degree of clinical complexity, to examine the relationship between diagnostic confidence and accuracy in a cohort of doctors [47]. The results showed a poor calibration between doctors' confidence and accuracy in diagnosing disease, specifically finding a misplaced confidence when diagnosing the more complex cases.

An interesting direction for future research may be to explore multidisciplinary predictions of MRH. Combining the doctor's clinical knowledge with pharmacist expertise on medication safety and management including drug interactions, contraindications, adherence and monitoring, and insight from nurses on the patient's social environment, could lead to more accurate identification of high-risk patients. This form of multidisciplinary approach has shown increased accuracy in survival prediction in palliative care patients [48].

Strengths and limitations

This is the first study that we are aware of which addresses whether clinical judgement can predict MRH in older adults. A major strength of this study is the large cohort of patients recruited from multiple hospitals, which supports the external validity of our findings within the UK. In addition, we used three data sources to identify MRH and multidisciplinary expert judgement in conjunction with a validated algorithm to ascribe causality.

There are some important limitations to our findings. A sample size calculation was not specifically performed for the hypothesis tested in this study and the precision of our results should be interpreted in view of this. Whilst we analysed 1066 predictions, doctors are commonly discharging multiple patients over a given time and thus a doctor may have contributed more than one prediction to our results. This could have introduced bias through a clustering effect. However, the four-monthly rotation of junior doctors in combination with a two-year study period on multiple wards of five hospitals ensured a wide breadth of participation.

Although our results show that the years of clinical experience of the discharging doctor did not influence the accuracy of predictions, only 126 (12%) predictions were by doctors of very senior grade (registrar or consultant) and therefore this finding should be interpreted with caution.

Prompting doctors to consider the potential medication risk for each patient may have led to changes in behaviour influencing the discharge process, such as modifying discharge medicines or post-discharge support, known as the Hawthorne effect [49]. To minimize opportunity for this, we obtained the doctor's prediction as close as possible to the patient's discharge or soon thereafter. Similarly, the behaviour of discharged patients may have been influenced by

study participation. A heightened awareness of potential adverse effects of medicines might have prompted increased attention to medicines-related information and usage instructions, or higher likelihood of seeking healthcare if MRH was suspected. However, this increased knowledge may have enabled participants to report MRH more accurately when interviewed.

Conclusions

In conclusion, this study shows that doctors (predominantly junior doctors) cannot identify older patients at high risk of MRH following hospital discharge. This may reflect a combination of insufficient CPT knowledge amongst junior doctors, and the challenges in discerning complex biopsychosocial risk factors associated with poor adherence. Efforts to improve MRH risk prediction might benefit from the development of a predictive tool using statistical methods, increased CPT education for doctors and interdisciplinary collaboration with pharmacists.

Competing Interests

There are no competing interests to declare.

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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 data analysis. J.M.S., N.P. and J.H. were involved in data collection. J.G.D., K.A., R.S. and C.R. verified endpoints. N.P., J.G.D., J.M.S., K.A., S.B. 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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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

http://onlinelibrary.wiley.com/doi/10.1111/bcp.13690/suppinfo

Appendix S1 Questionnaire completed by discharging doctors to predict MRH