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ORIGINAL ARTICLE

Missed opportunities: unnecessary medicine use in patients with lung cancer at the end of life – an international cohort study

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Keywords deprescribing, life limiting illness, lung cancer, medication utilisation, older people, polypharmacy

AIMS

The aims of the current study were: (i) to examine the prescribing of preventative medication in a cohort of people with advanced lung cancer on hospital admission and discharge across different healthcare systems; and (ii) to explore the factors that influence preventative medication prescribing at hospital discharge.

METHODS

A retrospective cohort study was conducted across two centres in the UK and the US. The prescribing of preventative medication was examined at hospital admission and discharge for patients who died of lung cancer. A zero-inflated negative binomial regression model was used to examine the association between preventative medications at discharge and patient- and hospital-based factors. The classes of preventative medication prescribed included were: vitamins and minerals, and antidiabetic, antihypertensive, antihyperlipidaemic and antiplatelet medications.

RESULTS

In the UK site (n = 125), the mean number of preventative medications prescribed was 1.9 [standard deviation (SD) 1.7) on admission, and 1.7 (SD 1.7) on discharge, and in the US site (n = 191) the mean was 2.6 (SD 2.2) on admission and 1.9 (SD 2.2) on discharge. The model found a significant association between the number of preventative drugs prescribed on admission and the number on discharge; it also found a significant association between the total number of drugs prescribed on discharge and the number of preventative medications on discharge. Other indicators related to patient and hospital factors were not significantly associated with the number of preventative medications supplied on discharge.

CONCLUSIONS

The use of preventative medication was common in lung cancer patients, despite undergoing discharge. Patient- and hospital-based factors did not influence the prescribing of preventative medication.

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- The presence of multimorbid conditions is common in a lung cancer population.
- It is common for this patient group to have complex, costly and often inappropriate medication regimens.
- This patient group is frequently hospitalized in the last year of life.

WHAT THIS STUDY ADDS

- The use of preventative medication is common in lung cancer patients, and this is evident across different healthcare systems.
- There is no association between the receipt or not of preventative medications at discharge, and patient- (e.g. stage of cancer) and hospital-based (e.g. time spent in hospital) factors.
- Deprescribing interventions directed towards reducing preventative medication use could be implemented at the point of hospital discharge.

Introduction

Lung cancer is the most common cancer in the world, with around 1.8 million new cases diagnosed annually [1]. It is the most frequent cause of cancer-related mortality, accounting for approximately 1.5 million deaths each year – roughly equating to around one in five of all cancer-related deaths [2]. Lung cancer, like the majority of other cancers, is predominantly a disease of older people: around two in three cases are reported in people aged over 65 years, and the mean age of diagnosis is 70 years [3].

Due to age as well as common risk factors, the presence of multimorbid conditions – including cardiovascular disease, diabetes mellitus and chronic obstructive pulmonary disease (COPD) – is common in a lung cancer population [4]. The presence of these chronic conditions is accompanied by the long-term use of medications to maintain disease control or to treat the symptoms associated with these conditions, or to prevent further worsening of them. The overall effect of this paradigm is that polypharmacy is common and the pill burden is high among this patient group [5, 6]. This is challenging, particularly for medication used in the context of primary or secondary prevention. A recent systematic review showed that many preventative medications are inappropriately prescribed in the context of life-limiting illnesses, such as lung cancer; the review identified vitamins and minerals, and antidiabetic, antihypertensive, antihyperlipidaemic and antiplatelet medications as preventative medications of questionable benefit [7]. In addition, previous research has demonstrated that inappropriate medication use in a palliative setting could increase the risk of the patient developing severe drug–drug interactions, possibly resulting in hospitalization or even death [8].

Previous work has shown that lung cancer patients are frequently hospitalized in their last year of life – perhaps more so than patients with any other type of cancer [9]. For example, Mayer and colleagues showed that out of 37 760 cancer-related emergency room (ER) visits, 26.9% were attributable to lung cancer patients (compared with 6.3%, 6.0% and 7.7% of visits for breast, prostate and colorectal cancer patients, respectively) [10]. Common reasons for the hospitalization of lung cancer patients included pain, respiratory distress and gastrointestinal issues [10]. Given this observation, and the fact that lung cancer patients often have complex, costly and burdensome medication regimens, it is not clear how episodes of hospitalization – or prolonged periods of time spent in hospital – influence or change a patient's medication or, indeed, how this varies according to healthcare system. In the UK, for example, patients with advanced disease receiving cancer therapy may be cared for in a hospice for a long period before death and may still be admitted to the hospital [11]. In the US, patients are referred to hospice care late in the disease process, with a median length of hospice stay of 19 days for patients with cancer [12]. We hypothesized that a hospital stay would present an opportunity to reduce the number of prescriptions for medications of questionable benefit, and thus, through medicine optimization and hospital discharge, it would be more likely that preventative medication would be discontinued.

The present study therefore aimed: (i) to examine the prescribing of preventative medication in a cohort of people with advanced lung cancer on hospital admission and discharge across different healthcare systems; and (ii) to explore the factors that influence preventative medication prescribing at hospital discharge in a cohort of lung cancer patients.

Methods

Setting

To meet our study aims, two tertiary care centres were chosen as sites of data collection: the MD Anderson Cancer Centre, Houston, TX, US ('MD Anderson'); and, the Newcastle Hospitals Foundation Trust, Newcastle-upon-Tyne, UK ('Newcastle'). MD Anderson focuses solely on cancer care, and has around 1.5 million patient contacts per year, with patients who have Medicare, private insurance or other means of healthcare insurance coverage, whereas Newcastle provides all aspects of healthcare, including cancer care, and has around 1.7 million patient contacts per year, the vast majority of which are managed through the National Health Service (NHS). There are approximately 1800 inpatient beds at Newcastle, and around 600 at MD Anderson [13, 14]. Study approval and registration were obtained from each site; as this was a retrospective study on deceased patients, this work was considered 'not human subject research', as defined by the federal regulations. In view of this, full institutional review board approval was not required, and the waivers of informed consent and authorization were granted.

Design
This was a retrospective cohort study of medication use at hospital admission and hospital discharge during the hospitalization prior to death for patients who died of lung cancer.

Inclusion criteria
Patients were included in the analysis if they had primary non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC), were admitted to a hospital study site at least once within the last 6 months of life and died in 2013. A hospital admission was defined as an encounter in which a patient received continuous care at the hospital as an inpatient.

Exclusion criteria
Any patient who received care exclusively as an outpatient in a study site was excluded from the study. Patients who died in hospital were excluded. Patients were excluded if the hospital admission was unrelated to the lung cancer (e.g. due to a road traffic accident).

Data sources
Data relating to patient deaths, cancer type and staging were obtained from either the electronic medical record (MD Anderson) or from cancer registries linked to the study site (Newcastle). Patient and medication data were then extracted from each hospital computer system and included the following: medications on admission, medications on discharge, length of hospital stay, presence of hospital admissions in last 6 months of life and presence of comorbidities. Each medication was classified according to British National Formulary (BNF) category; all continuous and 'when required' medications were included in the analysis. Preventative medications of questionable benefit were defined in one of five categories: vitamins and minerals, and antidiabetic, antihypertensive, antihyperlipidaemic and antiplatelet medications, based on a previous systematic review [7]. Comorbidity was calculated according to the Charlson Comorbidity Index, although for our calculations we removed the scores related to tumour without metastases, and metastatic solid tumour for lung cancer, and included other cancers [15].

Outcome measures
The primary outcome was the number of preventative medicines prescribed on hospital discharge. We defined preventative medicines as antidiabetic, antihypertensive, antihyperlipidaemic and antiplatelet agents, and vitamins and minerals. We included clinical and demographic variables, hospitalization variables and medication use variables as possible predictors of discharge preventative medicine use.

Statistical analysis
Patient age, gender, cancer diagnosis, cancer stage, Charlson Comorbidity Index score, length of hospital stay, length of time from discharge to death and the number of preventative medicines used in each category were stratified by the US and the UK cohorts. Means, medians, standard deviation (SD) and range for each measure were reported. The McNemar test was then used to compare preventative medicine use at admission and at discharge, to determine whether there was a significant difference in the proportion of patients taking any preventative medicine or preventative medicines in each of the five categories. In multivariable analysis, we conducted the same analyses for the UK and the US cohorts. With the outcome of number of preventative medicines on discharge, we constructed zero-inflated negative binomial regression models to account for excess zeros in the number of preventative drugs at discharge. The decision to use a zero-inflated negative binomial regression model was made *a priori* based on our understanding of the data. We first built models based on groups of variables, including clinical and demographic variables (age at death, gender, cancer type, cancer stage, comorbidity), hospital variables (length of stay, number of hospitalizations in the last 6 months of life) and medication use (total preventative medicine use at admission and preventative medicine use in each of the five categories at admission and discharge, as well as total medicine use at admission and discharge). Except for gender, cancer type, cancer stage, comorbidity and receipt of types of preventative medicines (yes/no), the remaining variables were continuous. For the US data only, we included palliative care consultation as a single, ungrouped variable in the models. We built stepwise models by adding these groups of variables, and did stepwise deletion by groups of variables and then further by individual variables, retaining variables in the model with $P < 0.1$. The likelihood ratio test was used to compare models at each step (Appendix Table A1). The final US and UK models had some important differences in significant variables, and we took a final step to investigate whether similar models were appropriate for both sets of data. A P-value of <0.05 was considered statistically significant. All analyses were conducted separately for the UK and US cohorts. The UK data were analysed using SAS software version 9.1 (SAS Institute Inc., NC, USA), and the US data were analysed using STATA version 14 (StataCorp, TX, USA). No statistical comparisons were made between the two cohorts.

Results

Participant characteristics
In 2013, there were a total of 185 deaths of lung cancer patients who had received care in the UK study site, and 349 in the US study site. From the UK data, 19 patients died 6 months after their last hospital admission, 37 patients died in hospital and four patients had missing data (cancer stage, and information relating to medications on admission and discharge). From the US data, 109 patients died in hospital, 29 were treated only in the ER or on observation status without inpatient admission, 14 had cancers other than NSCLC or SCLC, three patients had admissions unrelated to lung cancer, and three patients had missing data. In total, there were 125 patients (UK) and 191 patients (US) included in the analysis.

Characteristics
The median patient age was 73 years for the UK site (range 48–98 years), and 65 years for the US site (range 22–90 years). There were more males than females for both study sites, and the majority of people presented with stage IV lung cancer;

NSCLC was more common than SCLC. Of the UK cohort, 62.4% had a Charlson Comorbidity Index score of 1 or higher, and 52.4% of the US cohort had a score of 1 or higher (Table 1).

In the last 6 months of life, repeated hospital admissions were common at both study sites: the mean number was 2.0 (SD 1.0) for the UK site, and 1.9 (SD 1.4) for the US site. The mean length of each hospital stay was 10.9 days (SD 9.0) for the UK site, and 7.8 days (SD 7.4) for the US site, and patients at both sites lived for around 6 weeks, on average, after their last hospital admission. Polypharmacy, defined as ≥5 medications, was also common at both sites (observed in 81.6% and 93.7% of individuals admitted to hospital at the UK and US sites, respectively), with the total number of medications increasing after each hospital admission (Table 2).

Table 1

Study participant characteristics for UK and US sites

		UK (%) *n* = 125	US (%) *n* = 191
Gender	Female	48.8	46.6
	Male	51.2	53.4
Cancer type	NSCLC	85.6	86.4
	SCLC	14.4	11.5
	Other	0.0	2.1
Staging	1A	0.8	2.1
	1B	3.2	0.0
	IIA	1.6	0.0
	IIB	1.6	0.5
	IIIA	8.8	6.8
	IIIB	16.0	2.6
	IV	68.0	88.0
Charlson Comorbidity Index score	0	37.6	47.6
	1	44.8	23.6
	2	9.6	17.3
	3	6.4	6.8
	4	0.8	2.1
	5	0.0	1.6
	6	0.8	0.0
	7	0.0	0.5
	8	0.0	0.5

NSCLC, nonsmall cell lung cancer; SCLC, small cell lung cancer

Preventative medication

The mean number of preventative medications was 1.9 (SD 1.7) and 2.6 (SD 2.2) on admission, and 1.7 (SD 1.7) and 1.9 (SD 2.2) on discharge for UK and US sites, respectively. On admission, approximately 73% of patients received a preventative medication at the UK site, and approximately 80% at the US site. Overall, the number of preventative medications reduced at discharged to 63% at the UK site, and 69% at the US site; this change was significant for both sites (Table 3). The most commonly prescribed preventative medications were the antihypertensive agents at the UK site, and vitamin and minerals at the US site; the least commonly prescribed medications were the antidiabetic agents, at both sites. The number of prescribed preventative medications reduced in all categories after discharge, apart from antidiabetic agents, and vitamins and minerals, which increased in the UK, although not significantly, and antihypertensive medications, which remained constant in the US.

Modelling variables

Overall, the mean number of preventative medications was lower on hospital discharge compared with admission. When we examined how the number of preventative medications at discharge was related to other factors, the zero-inflated negative binomial regression model found a significant positive association between the number of preventative drugs on

Table 2

Hospital admission and discharge characteristics for study participants

	UK (*n* = 125)			US (*n* = 191)		
Indicator	**Mean, SD**	**Median**	**Range**	**Mean, SD**	**Median**	**Range**
Age (years)	72.8 ± 10.5	73	48–98	63.8 ± 10.9	65	22–90
Length of hospital stay (days)	10.9 ± 9.0	8	1–37	7.8 ± 7.4	6	1–49
Number of hospital admissions within 6 months of life	2.0 ± 1.0	2	1–5	1.9 ± 1.4	1	1–10
Number of days discharged before death	43.3 ± 46.0	28	1–178	38.4 ± 40.7	22	1–190
Total number of preventative drugs at admission	1.9 ± 1.7	2	0–7	2.6 ± 2.2	2	0–10
Total number of preventative drugs at discharge	1.7 ± 1.7	2	0–7	1.9 ± 2.0	1	0–8
Total number of medications at admission	8.8 ± 3.8	9	1–18	11.6 ± 5.0	11	0–26
Total number of medications at discharge	10.3 ± 4.3	11	1–20	12.1 ± 4.7	12	2–28

SD, standard deviation

Table 3

Number of patients prescribed preventive medication at admission and at discharge

Preventive medicine type	UK (*n* = 125)			US (*n* = 191)		
	N (%) at admission	*N* (%) at discharge	*P*-value[a]	*N* (%) at admission	*N* (%) at discharge	*P*-value[a]
Antidiabetic	8 (6.4)	11 (8.8)	0.375	23 (12.0)	21 (11.0)	0.75
Antihypertensives	59 (47.2)	44 (35.2)	0.001	97 (50.8)	97 (50.8)	1.000
Antihyperlipidaemic	57 (45.6)	40 (32.0)	<0.001	61 (31.9)	44 (23.0)	0.032
Antiplatelet	38 (30.4)	30 (24.0)	0.057	39 (20.4)	33 (17.3)	0.307
Multivitamins and minerals	30 (24.0)	36 (28.8)	0.286	106 (55.5)	73 (38.2)	<0.001
Any preventive medicine	91 (72.8)	79 (63.2)	0.017	152 (79.6)	132 (69.1)	0.002

[a]Difference between number at admission and number at discharge, using the McNemar test

admission and the number of preventative medications on discharge; for example, in the UK model, for every one preventative medication at admission, the number of preventative medications at discharge will increase by 1.27, expressed as the incidence rate ratio (IRR) [95% confidence interval (CI) 1.17, 1.39]; similarly, in the US model, for every one preventative medication at admission, the number of preventative medications at discharge will increase by 1.13 IRR (95% CI 1.06, 1.20). There was also a significant positive association between the total number of medications on discharge, and the number of preventative medications on discharge, at both the UK and US study sites (Table 4). In the US model only, there were significant associations between the total number of prescribed medications on admission [IRR 0.95 (95% CI 0.92, 0.97)], having a palliative care consultation [IRR 0.73 (95% CI 0.58, 0.92)] and the total number of prescribed medications at discharge [IRR 1.10 (95% CI 1.08, 1.13)]. None of the other indicators (age, cancer stage, cancer type, comorbidity score, length of hospital stay, number of hospitalizations) were significantly associated with the number of preventative medications prescribed on discharge, and their addition/removal did not significantly affect our models (Appendix Table A2). Multicollinearity was assessed using variation inflation factor (VIF), which showed that, although some of the variables were correlated, there was no problems associated with multicollinearity in the models (Appendix Table A3).

Table 4

Zero-inflated negative binomial regression models examining the association between the total number of prescribed preventative drugs at discharge and related factors

Indicator	UK (*n* = 125) IRR, 95% CI
Number of days admitted	0.99 (0.97, 1.01)
Total number of drugs at admission	0.95 (0.90, 1.01)
Total number of drugs at discharge	1.08 (1.03, 1.14)
Total number of preventative drugs at admission	1.27 (1.17, 1.39)
Indicator	**US (*n* = 191) IRR, 95% CI**
Palliative care consultation	0.73 (0.58, 0.92)
Total number of drugs at admission	0.95 (0.92, 0.97)
Hypertensive drugs at admission	1.33 (1.18, 1.50)
Total number of drugs at discharge	1.10 (1.08, 1.13)
Total number of preventative drugs at admission	1.13 (1.06, 1.20)
Antiplatelet drugs at admission	1.25 (1.00, 1.54)

CI, confidence interval; IRR, incidence rate ratio

Discussion

The present study was the first to investigate the prescribing of preventative medication in a cohort of lung cancer patients at hospital admission and discharge across different healthcare systems. We identified a number of key findings that might be of importance to healthcare practitioners and policy makers: (i) polypharmacy is common for lung cancer patients who are admitted to hospital; (ii) the mean number of medications prescribed for a hospitalized lung cancer patient increases after hospital admission; (iii) the prescribing of preventative medications is common among hospitalized lung cancer patients; and (iv) patient factors (such as age, cancer stage, cancer type, and comorbidity score) and hospital factors (such as length of hospital stay and number of hospitalizations) were not associated with the prescribing of preventative medication.

Although this was the first study specifically to assess the prescribing of preventative medication in lung cancer patients, other studies have explored prescribing and medicines use for patients who are at the end of life. For example, Currow and colleagues showed that, in a cohort of palliative care patients, as death approached, the average number of medications prescribed increased from 4.9 to 6.4 – primarily as a result of people using more symptom-specific medications [16]. Of note, the same study also showed that the number of potentially

inappropriate medications, as assessed using the Beers criteria, also increased as death approached [16]. Other studies have explored the prescribing of specific classes of medication in the context of limited life expectancy. For example, Stavrou and colleagues showed that more than 30% of cancer patients were dispensed statins within 30 days of death [17], and Bayliss and colleagues revealed that, in a cohort of cancer patients, more than 60% of individuals continued with statin therapy for 2 years after their diagnosis [18]. Our findings lend support to the literature, and show that lung cancer patients who are admitted to hospital are commonly discharged with preventative medication; this appears to have been the continuation of current medication, as opposed to initiating new preventative medication.

In terms of developing an intervention to reduce polypharmacy and rationalize medications in lung cancer patients – or possibly other life-limiting illnesses – this work is important. Indeed, our work shows that the point at which a patient is discharged from hospital might be an appropriate time to develop an intervention to reduce – or to start the process of reducing – burdensome preventative medication that is no longer appropriate, given a patient's reduced life expectancy. Further work should explore the nature of the intervention, but it is encouraging that, at the US site, a consultation with a palliative care clinician did appear to be associated with the prescription of fewer preventative medications on discharge. This is consistent with a previous study from an inpatient palliative care unit that found that, among 100 consecutive patients admitted to the unit, the number of prescribed medications increased from a mean of 9.2 to 10.1, with an increase in the number of symptomatic medications and a reduction in medications for comorbid conditions [19].

Previous literature has also shown that a pharmacist intervention at the point of discharge reduced the level of inappropriate prescribing in a general older population [20, 21]. Given the important role of clinical pharmacists in both UK and US discharge processes, they should play a key role in delivering any intervention aimed at reducing the number of inappropriate medications prescribed to this patient population. It is clear, however, that any such intervention should embrace the principles of deprescribing. Indeed, the term 'deprescribing', recently defined by Reeve and colleagues, as *the process of withdrawal of an inappropriate medication, supervised by a healthcare professional with the goal of managing polypharmacy and improving outcome* [22], has received a great deal of recent attention in the literature. The process of deprescribing has recently been reviewed [23], and the literature suggests that, in order to achieve a successful outcome, many factors need to be considered, including those that are patient based (e.g. patient misalignment with goals of care) [24] and those involving the caregiver [25]. Another issue toward deprescribing is the lack of robust evidence demonstrating the effectiveness of deprescribing preventative medication in patients with a life-limiting illness. Page and colleagues have shown that deprescribing in older adults appears to be safe and feasible [26], although, to date, Kutner and colleagues are the only group to have published a randomized clinical trial specifically addressing the issue of deprescribing medication in people with life limiting illness [27]. The trial, which discontinued statin therapy in a cohort of patients with advanced life-limiting illness, showed that stopping statin therapy is safe, and is associated with reduced costs and improved quality of life [27]. Given the high prevalence of other preventative medication identified in our cohort of patients, other trials, exploring the cessation of antihypertensive and antidiabetic agents, appear to be warranted. However, a small-scale study showed that many palliative care patients with previously diagnosed hypertension were still using antihypertensive medication, despite having low blood pressure and, in some cases, symptoms of postural hypotension [28].

Although we believe that our results are robust, and have important implications for the way in which medications are prescribed to lung cancer patients, we acknowledge that our work had several limitations. Firstly, we did not assess the appropriateness of preventative medication, as we just reported on the prescribing. It is possible that some of the preventative medication was prescribed appropriately (for example, angiotensin-converting enzyme inhibitors in the case of advanced heart failure). Secondly, we only included lung cancer patients who were admitted to hospital, which may not have given a true account of the medication histories for all lung cancer patients, given that it is possible that those admitted to hospital had more complex medication regimens. We do not know if patients were discharged with a plan for medication reduction after discharge. In addition, we were not able to collect information on site about discharge home or discharge to hospice care, which might have been particularly important in the US cohort. We would therefore urge that our results are interpreted in view of these limitations. In terms of study strengths, we believe that collecting data across two healthcare systems (the UK and US) was a key strength of the study, adding international context to our work.

Conclusion

Polypharmacy is common in hospitalized lung cancer patients. The use of preventative medication remained high among such patients, despite undergoing hospital discharge. Patient- and hospital-based factors did not influence the prescribing of preventative medication. There may be scope to develop an intervention that embraces the principles of deprescribing at the point of hospital discharge, to reduce inappropriate prescribing in lung cancer patients.

Competing Interests

There are no competing interests to declare.

We would like to thank Mr Andrew Heed, Lead Clinical Informatics Pharmacist at Department of Pharmacy, The Newcastle upon Tyne Hospitals NHS Foundation Trust, who assisted with the collection of data at the UK site.

Appendix

Table A1

Likelihood ratio test comparing the saturated model and final model, to ensure that there is no substantial loss of information between the saturated model and the final, most parsimonious model

Country	Models	–2 Log likelihood (–2LL)	Number of parameters	df	Difference in –2LL	*P*-value
UK	Saturated model	303.580	22	18	8.579	0.968
	Final model	312.159	4			
US	Saturated model	592.561	24	19	-40.441	1.000
	Final model	552.012	5			

Table A2A

Type 3 test from zero-inflated negative binomial regression models for variables not included in the final model for UK data

	UK data		
Indicators	**df**	**Chi-square**	***P*-value**
Gender	1	0.07	0.785
Age	1	0.49	0.486
Cancer type	1	0.01	0.931
Cancer stage	7	2.14	0.952
Comorbidity	1	0.04	0.849
Length of hospital stay	1	3.18	0.075
Number of hospitalizations	1	0.20	0.657

Table A2B

Negative binomial regression results for variables not included in the final model for US data

Indicators	Chi-square	*P*-value
Gender	1.40	0.163
Age	–0.19	0.848
Cancer type		
Small cell lung cancer	1.28	0.202
Other	–0.83	0.406
Cancer stage		
IIB	0.80	0.422
III	1.31	0.189
IIIB	1.17	0.241
IV	0.71	0.480

(continues)

Table A2B

(Continued)

Indicators	Chi-square	*P*-value
Comorbidity score (Charlson Comorbidity Index score)		
1	1.35	0.175
2	0.53	0.596
3	1.55	0.121
4	0.88	0.380
5	1.26	0.207
7	–0.11	0.908
8	0.67	0.505
Length of hospital stay	0.42	0.673
Number of hospitalizations	0.57	0.569
Number of antidiabetic medications at admission	–1.50	0.133
Number of antihyperlipidaemic drugs at admission	–2.07	0.038

Table A3

Variance inflation factor to check for multicollinearity between the variables included in the final model. Values between 1 and 10 are considered acceptable [29]

	Variance inflation factor	
Variables	**UK data**	**US data**
Length of stay (days)	1.027	–
Number of drugs on admission	2.091	1.86
Total number of preventative drugs (admission)	1.321	2.41
Number of drugs on discharge	1.766	1.53
Number of palliative care consultations	–	1.11
Number of antihypertensive drugs (admission)	–	1.63
Number of antiplatelet drugs (admission)	–	1.29

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