Journal of Bone Oncology 17 (2019) 100243

Contents lists available at ScienceDirect

Journal of Bone Oncology

journal homepage: www.elsevier.com/locate/jbo

Research Paper

Unplanned admissions for patients with myeloma in the UK: Low frequency but high costs

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ARTICLE INFO

Keywords:
Multiple myeloma
Unplanned admissions
Elective admissions
Costs

ABSTRACT

Background: Multiple myeloma (MM) is associated with high healthcare resource utilisation and increasing hospitalisation rates. The aim of this study was to characterise the hospital use by patients with MM in the English National Health Service (NHS).

Methods: Routinely-collected aggregate data about all NHS-funded hospital admissions of patients with MM were analysed. Data were obtained from the English Hospital Episodes Statistics on admissions between 1 April 2014 and 31 March 2018.

Results: A total of 754,345 admissions were reported over four years, equivalent to a mean of 188,586 admissions per year. Of the 41,845 patients admitted during this period, 42% were women and 58% men. From the total admissions, 90% were elective and 10% unplanned. Mean annual estimated costs over the period were £46 million for elective and £56 million for unplanned admissions. The number of elective admissions increased by 4.5% with costs increasing 1.5% per year; for unplanned admissions, these figures were 4.1% and 9.0%, respectively.

Conclusions: MM is associated with a significant number of hospital admissions and NHS costs. The majority of the hospital admissions are elective, but the highest burden in terms of costs relates to unplanned admissions, with numbers increasing over time.

1. Introduction

Multiple myeloma (MM) is a malignant plasma cell neoplasm associated with considerable morbidity and mortality. The incidence of MM has increased globally by 126% between 1990 and 2016 [1]. Population growth, the aging world population, and rising age-specific

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https://doi.org/10.1016/j.jbo.2019.100243
Received 15 March 2019; Received in revised form 31 May 2019; Accepted 4 June 2019
Available online 07 June 2019

incidence rates contributed to the increased global incidence. The highest incidence and death rates for MM are reported in Western Europe, North America, and Australasia [1]. MM is more prevalent in men compared to women, with a global incidence rate of 2.4 per 100,000 for men and 1.8 per 100,000 for women [1,2]. MM is associated with impairments in quality-of-life (QoL) of patients and was responsible for 2.1 million disability-adjusted life-years (DALYs) at a global level in 2016 [1,3,4].

MM is also related to increased healthcare utilisation and high healthcare costs [5,6]. A recent study found that 42% of MM patients reported at least one disease-driven hospital visit during the previous six months, 71% declared at least one specialty visit during the three months prior, and 9% received emergency care in the previous three months [6]. Healthcare costs per MM patient have increased steadily between 2000 and 2014 for all healthcare services including treatment-related drug costs, the main contributor being outpatient visits [7]. Hospitalisation costs account for an important proportion of healthcare cost. These were found to make up for 22% of the total healthcare costs in 2000 and for 33% in 2014, whilst during this same period hospitalisation rates per patient per month increased from 0.05 to 0.11 [7]. Both healthcare utilisation and hospitalisation rates appear to be driving the rising healthcare costs associated with MM patients.

Although MM is currently not curable, several treatment options have been introduced in this century [8]. Advances in treatment have changed the natural history of MM, and as a result the clinical management of the disease [9]. Novel therapies including proteasome inhibitors (PI) and immunomodulatory drugs (IMiDs) have resulted in substantial extension of the survival time of MM patients [5,10]. A dual-cohort study at the Mayo Clinic showed that the mean survival from the time of relapse increased from 11.8 months for patients relapsing before 2000 to 23.9 months for those relapsing after that year [10].

In the context of rising MM incidence, increasing hospitalisation rates and improved survival of patients, efficient planning of healthcare services requires detailed understanding of contemporary hospital use by patients with MM. The aim of this study was to characterise and identify the drivers of hospital admissions and costs associated with the treatment of patients with MM in the English National Health Service (NHS). To that end, we: (1) describe the total number and costs of admissions by patients with MM; (2) identify the procedures driving the number and costs of both elective and unplanned admissions; and (3) place the above findings into context by comparing the number and costs of admissions by patients with MM to the number and costs of admissions by patients with a more prevalent cancer, as well as to those of the NHS as a whole.

2. Methods

2.1. Study design and setting

We used routinely-collected aggregate hospital admission data from individuals with MM from across all 451 hospitals trusts in the English NHS [11]. Data were sourced from the Vantage platform, by Health iQ, which aggregated data taken from the English Hospital Episodes Statistics (HES) database produced by the Health and Social Care Information [12]. Hospital trusts manage NHS hospital care in England, including community care and mental health services. The data extracted reflected inpatient hospital records provided by HES Admitted Patient Care (HES APC). HES APC contains data on all hospital admissions, including elective and unplanned admissions to the NHS and admissions to independent sector providers paid for by the NHS [11]. Elective admissions are those that occur when the decision to admit and the actual hospital admission happen at different times, such as with planned admissions or those originating from a waiting list and include both day case admissions and those requiring an overnight stay. An unplanned admission is defined by admission that was not arranged in advance [13]. A hospital admission in HES APC is referred to as a 'spell' and it is defined as an uninterrupted inpatient stay at one hospital. A spell may include several finished consultant episodes if a patient is seen by various consultants during the same stay. However, a spell does not include transfers between different hospitals. In a case where the patient is transferred to another hospital, a new spell begins [11]. For our analysis, we used APC data organised by spell covering the period between 1 April 2014 and 31 March 2018, corresponding to four full financial years.

2.2. Study populations

Inclusion criteria were based on recorded primary or secondary diagnosis of multiple myeloma in the admissions record. International Classification of Diseases-10 (ICD-10) codes of either Multiple myeloma (MM, code C90.00) or osteoporosis in multiple myelomatosis (OMM, code M82.00) were applied for the study period. With data available only in aggregate form, no individual patient follow-up or characterisation beyond extracted tables by financial year, gender and age group was possible. To ensure confidentiality, small number suppression and rounding of patient and admission counts were applied to all outputs, in accordance with NHS Digital guidelines.

Data for all NHS hospital admissions in the period of analysis were also extracted to investigate what percentage of the total NHS admissions and costs were related to myeloma. In addition, we collected data on admissions and costs by patients with colon cancer diagnosis to compare our findings about myeloma against those of a more prevalent cancer. Colon cancer was chosen as a comparator as it also affects both women and men, its economic burden has been extensively investigated [14,15] and its ICD-10 codes have been validated in previous studies using HES APC [16,17]. ICD-10 codes used to extract data on colon cancer admissions were "Malignant neoplasms of the colon" (C18), of the rectosigmoid junction (C19), and of the rectum (C20).

2.3. Variables

Data were extracted by gender, age groups, admission method (i.e. elective or unplanned), procedure codes, and patient classification. Procedures are reported using the OPCS-4 classification system for interventions and procedures used by healthcare providers in England, either by the main four-character code recorded for a hospitalization spell, or by corresponding OPCS-4 chapters. Description of specific procedure codes clearly identify which intervention was performed, but in some cases the main code extracted characterizes the intervention without making clear which procedure it was (e.g. 'Z94.2 Right sided operation'). Because there are thousands of procedure codes in the classification system and these are grouped into chapters, we use the latter to describe procedures at a higher level of aggregation [18]. Patient classification is reported as day-case, ordinary, or regular. 'Day-case' is defined as an inpatient elective admission for treatment during the course of the day without overnight stay; 'ordinary' is further classified into inpatient elective or unplanned admission for treatment and staying in hospital for at least one night; and 'regular' was defined as an inpatient elective admission that is part of a planned series of admissions for an on-going regime of broadly similar treatment and the patient is discharged within 24 h [19]. For each variable level, aggregate data on number of admissions, number of patients, and costs were obtained.

Costs were directly extracted from the platform as calculated by the data provider. They are treated as estimates, as they were calculated at spell-level but extracted in aggregate form. Reported cost estimates are based on the NHS national tariff according to core Healthcare Resource Group (HRG) codes assigned to each spell, plus any additional costs associated with excess bed days (for spells with lengths of stay beyond the trim point of the respective HRG code). Unbundled HRG codes (specific elements of costs separated from core HRGs) [20] were not reported or accounted for in the calculation of costs. Reported figures

hence represent an estimate of what it costs the NHS to reimburse hospitals for the core care they provided patients admitted as per the inclusion criteria.

2.4. Data analysis

Descriptive statistics and figures were used to summarize findings and characterise the hospital admissions and total costs by patients with MM. The count of patients are reported for different age groups. Total numbers or means are reported, but given the lack of patient-level data, inter-quartile ranges or standard deviations could not be provided.

To identify the main drivers of admissions and costs for patients with MM, we categorised admissions according to the 25 clinically-relevant procedure and intervention OPCS chapters used by the NHS (e.g. “Nervous System”, “Diagnostic Imaging, Testing and Rehabilitation”, “Bones and Joints of Skull and Spine”, etc.) [18]. In addition, primary procedures related to chemotherapy were identified via a series of OPCS procedure codes either exclusively used for chemotherapy (e.g. X35.2 “Intravenous chemotherapy”) or used mainly though not exclusively for it (e.g. X28.1 “Intermittent intravenous infusion of therapeutic substance”). Similarly, OPCS procedure codes were also used to identify those admissions whose primary procedure was radiology, such as U05.1 “Computed tomography of head”. Finally, the number of patients admitted, number of admissions, and total costs for patients with MM were compared to those with colon cancer as well as all NHS patients.

3. Results

3.1. Total number and costs of admissions

For patients with MM as primary or secondary diagnosis (ICD-10 code C90.00), there were a total of 754,345 admissions reported between 1 April 2014 and 31 March 2018, equivalent to a mean of 188,586 admissions per year. Of the 41,845 patients admitted during the period, 17,555 (42%) were women and 24,290 (58%) men. For patients with OMM as primary or secondary diagnosis (ICD-10 code M82.00), only 205 admissions were reported during the four years, involving 45 patients, 25 of whom were women and 20 men. Based on these admission figures, we focused our analyses exclusively on patients with a diagnosis of MM.

There was a significant difference between the number of admissions for elective and unplanned procedures. Of the total number reported during the period of analysis, 675,400 (90%) were elective and 78,945 (10%) unplanned admissions. Some procedures, such as “Autologous peripheral blood stem cell transplant”, reported both elective (4,360) and unplanned (245) admissions during the period of analysis. For all elective admissions, 41% of the admitted patients were women and 59% men, and for unplanned admissions proportions were 43% and 57%, respectively. On average during the four years of analysis, each patient had 18 admissions recorded.

Total estimated core costs during the full period analysis were £183,389,143 (mean of £45,847,286 per year) for elective and £227,650,088 (mean of £56,912,522 per year) for unplanned admissions. From all elective admission costs, 43% corresponded to admissions of women and 57% to those of men, a nearly identical split as that of unplanned admissions (42% and 58%, respectively). From the total estimated core costs from all admissions, 65% were from day-cases, 20% from ordinary cases, and 15% from regular attenders. Despite unplanned admissions making up only 10% of all admissions, they accounted for 55% of the total estimated hospitalisation costs. Over the period of analysis, elective admissions increased in average by 4.5% per year whilst the average yearly increase in costs was 1.5%; for unplanned admissions, these figures were 4.1% and 9.0%, respectively. Fig. 1 shows the number of admissions and total estimated costs separately for elective and unplanned admissions by month for the period of analysis. Fig. 2 shows the average number of patients per year for the different age groups of patients admitted with MM. The age groups contributing most to the number of admissions for MM were those between 65 and 84 years or age (median age group = 70 - 74 years of age), accounting for 62% of admitted patients.

3.2. Main procedures driving admissions and costs

The most common procedure for elective admissions was chemotherapy, accounting for 69% of the total elective admissions. The costs from chemotherapy contributed 32% of all elective costs. The classification of all primary procedures driving the number of admissions is described in Fig. 3a and the classification of procedures driving the cost of elective admissions in Fig. 3b.

Of all unplanned admissions, the most common primary procedure code used was diagnostic radiology, accounting for 34% of the total number of such admissions and 33% of the costs. The classification of all primary procedures driving the number of unplanned admissions is described in Fig. 3c and the classification of procedures driving the cost of unplanned admissions in Fig. 3d.

3.3. Comparison with colon cancer and total NHS

Table 1 shows the number of admissions, number of patients and total costs comparing MM with all NHS admissions for the entire period of analysis. Of all patients admitted to hospital in the NHS, 0.2% had a diagnosis of MM, yet they accounted for 1% of all admissions and 0.5% of all inpatient NHS costs in the period of analysis. Whereas the average NHS patient reports 0.7 hospital admission per year, a mean cost per admission of £1,205 and average costs of £870 per patient per year, for those admitted with a diagnosis of MM the mean number of yearly admissions was 4.5, each admission costing the NHS an average of £544, and a mean yearly cost per patient of £2,455. This compares with 166,100 patients with diagnosis of colon cancer with 956,615 admissions reported and estimated total costs of £1,246,139,188 during the period of analysis. On average, patients with colon cancer had 1.4 hospital admissions per year, a hospital admission costed on average £1,302, and the mean cost per patient per year was £1,876.

4. Discussion

This study has identified that patients with MM have accounted for an average of 188,586 hospital admissions per year to the NHS between 1 April 2014 and 31 March 2018 and that 90% of those were elective admissions. We found that the mean annual core (excluding unbundled) cost of those admissions was £45,847,286 for elective admissions and £56,912,522 for unplanned admissions, indicating that despite unplanned admissions making up only 10% of all admissions, they accounted for over half (55%) of total hospitalisation costs.

We observed an increase in the number of admissions and costs for patients with MM over time. Elective and unplanned admissions are increasing at a similar rate but costs for unplanned admissions are increasing much more rapidly. This increase in the number of admissions for patients with MM is in line with published reports of the respective increase for the NHS as a whole (4.3% per year for both elective and unplanned admissions) [21]. The annual increase in costs for MM patients, especially for unplanned admissions, is also consistent with previous findings indicating that costs related to MM are increasing steadily since 2000 [5,7]. The increase in hospitalisation costs for MM patients is of particular relevance considering the shrinking of NHS funding (1.1% per year between 2015 and 2021) [21].

The number of admitted patients with MM was highest for the group aged between 65 and 84, which accounted for 62% of admitted patients. Due to the lack of patient-level data we were unable to calculate the mean age of the patients, but we identified that the median age was contained in the group of 70 to 74 years of age. Most of the admitted

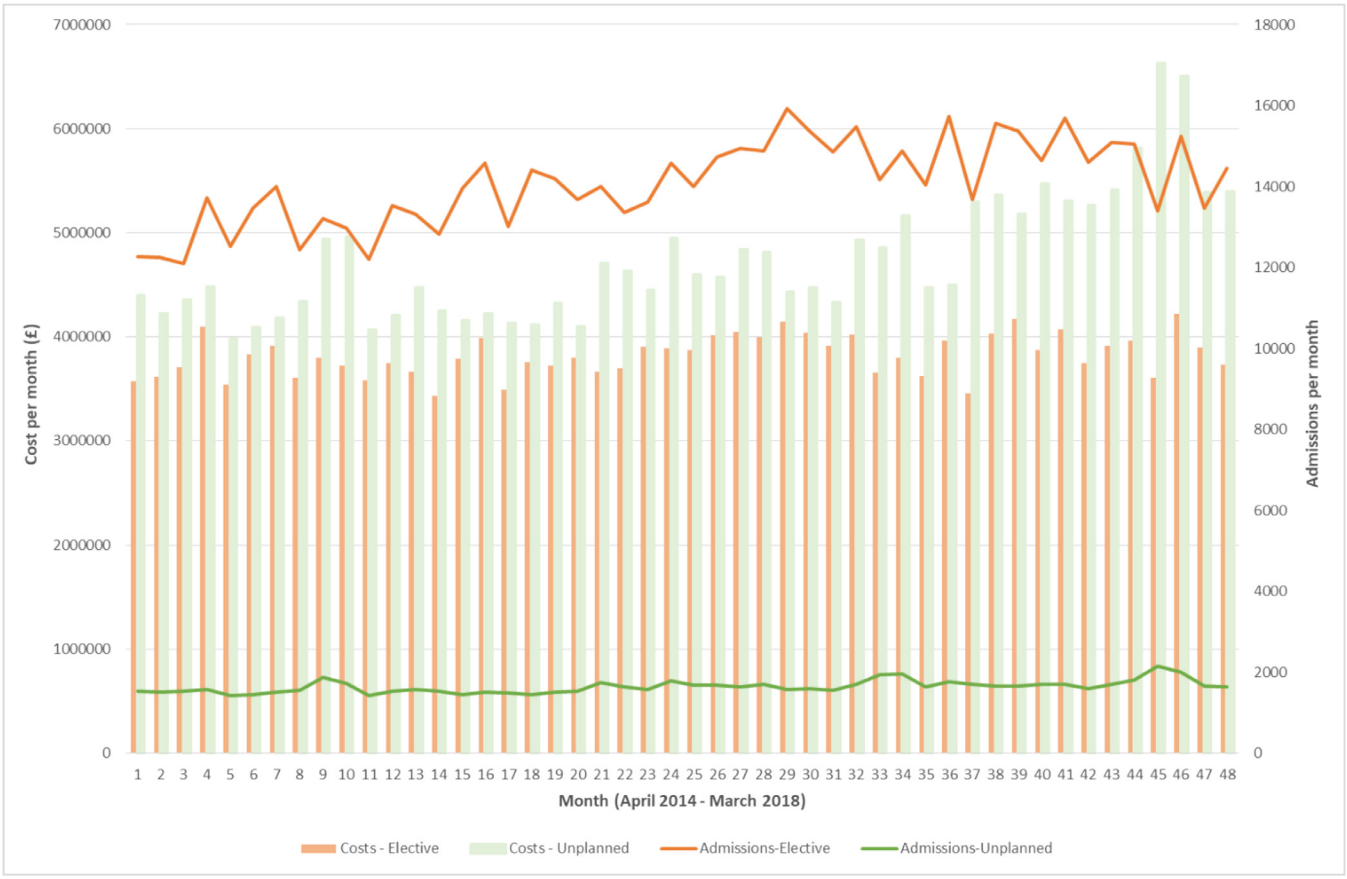


Fig. 1. Total estimated costs and number of admissions for elective and unplanned admissions of patients with MM in the NHS (April 2014–March 2018).

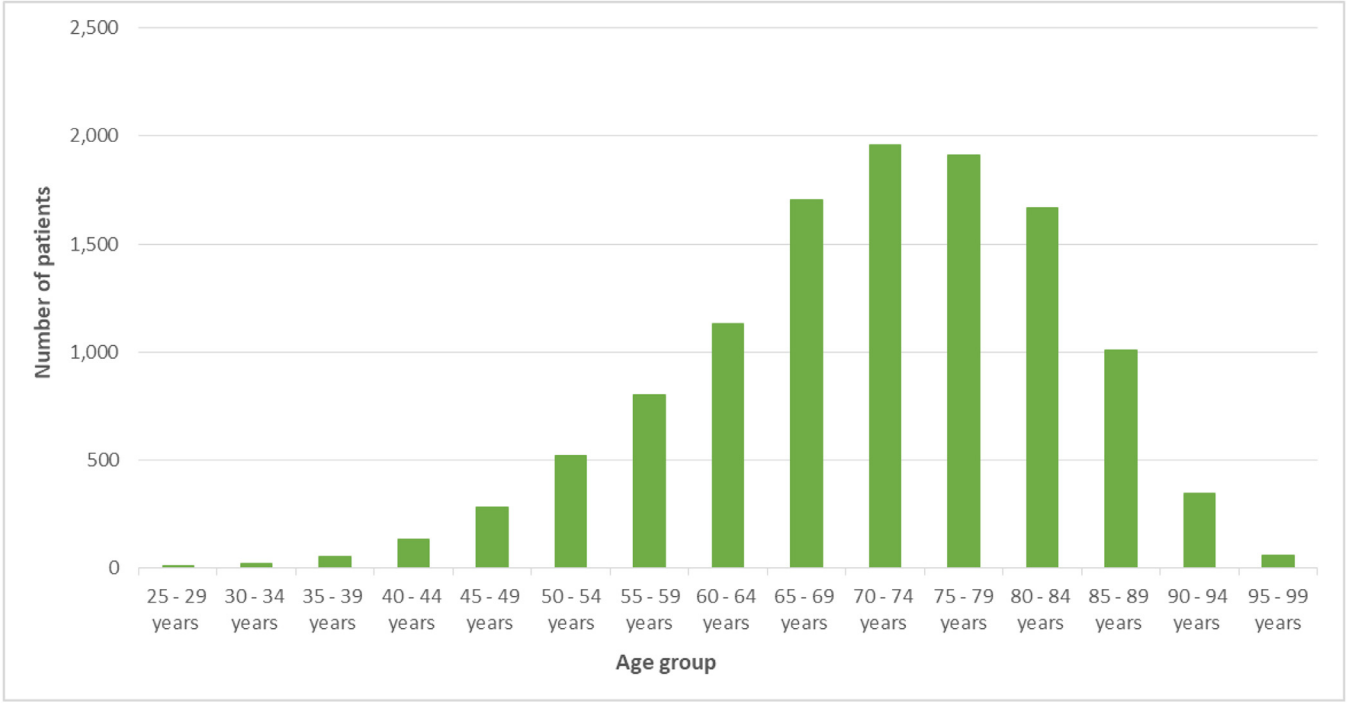
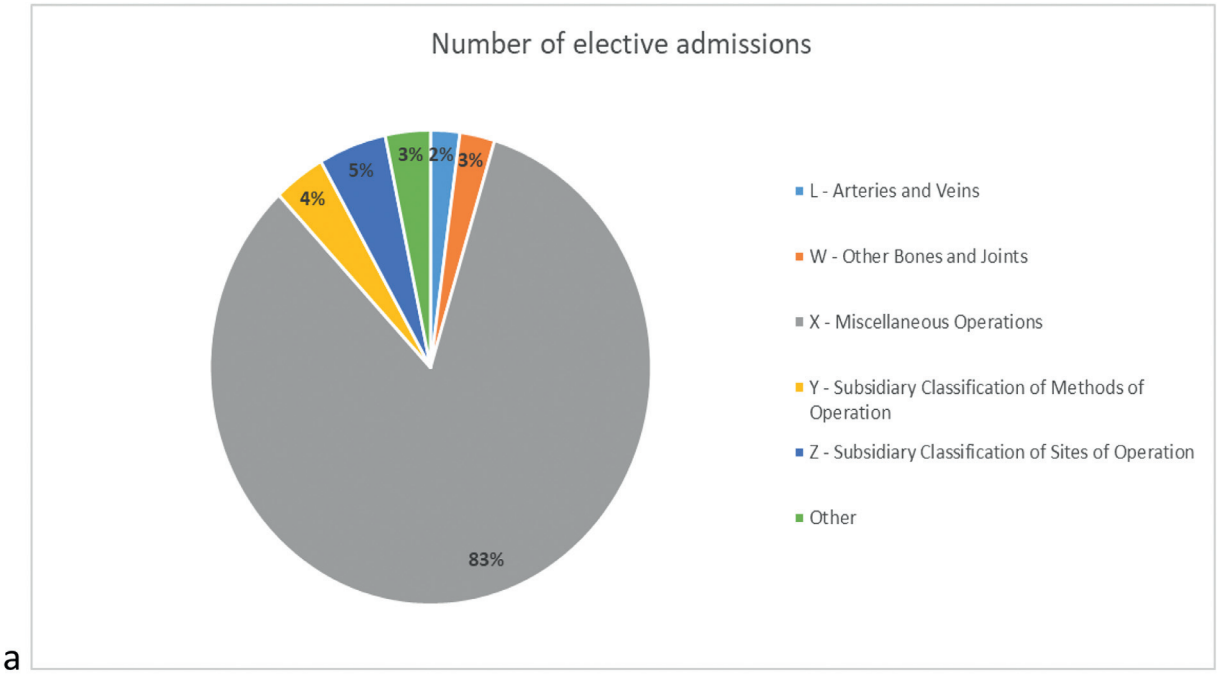


Fig. 2. Average number of patients per year for different age groups of patients admitted with MM.



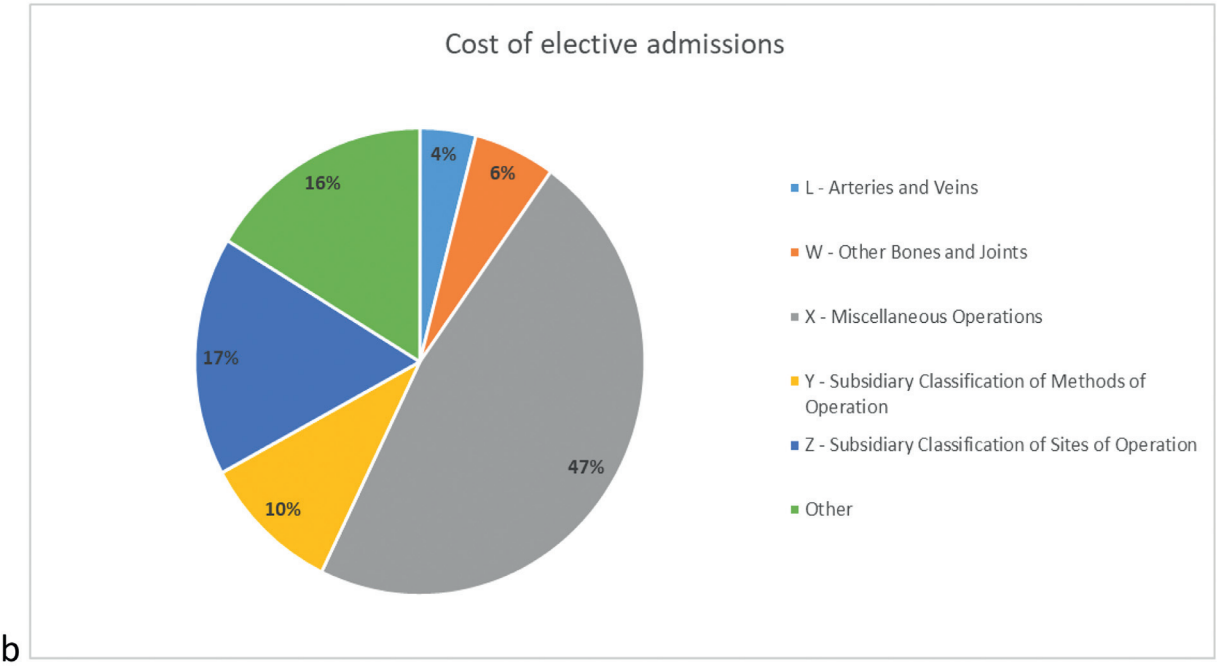
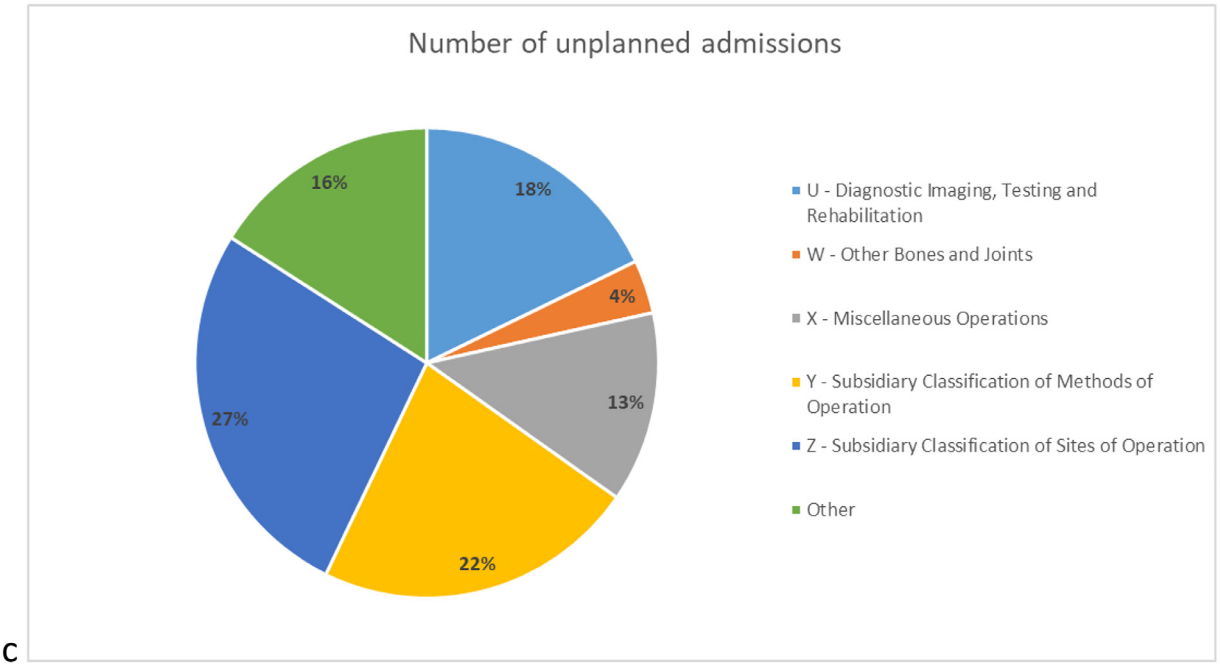


Fig. 3. Admitted patient care admissions for patients with MM, April 2014 through March 2018 - Main procedures classification by NHS OPCS code chapter for: (a) number of elective admissions, (b) costs of elective admissions, c) number of unplanned admissions, (d) costs of unplanned admissions.

patients were men (58%), and this gender difference remained the same for the number of admissions and costs. These characteristics are consistent with the findings of a study reporting incidence cases of MM in the UK based on patients identified via a primary care dataset, which found men to account for 55% of the sample with median age being 73 years, which falls within the median age group identified in our analysis [22]. A clinical trial currently assessing the benefit of antibiotic prophylaxis and its effect on associated infection has recruited nearly 1000 patients with MM with median age of 67 in both arms [23].

The commonest procedures of the number of admissions and costs were the same: for elective admissions the main driver was chemotherapy, whilst for unplanned admissions it was diagnostic radiology. Most of the procedures of elective admissions were classified under the chapter 'X – Miscellaneous Operations', and of unplanned admissions under chapter 'Z - Subsidiary Classification of Sites of Operation'. It appears that this classification is not very detailed and the included OPCS procedures are often not specific enough, for instance procedures were recorded as "Unspecified" or "Not elsewhere classified". Since the treatment and course of MM include many complications, such as bone pain, infections, peripheral neuropathy, asthenia and renal inefficiency, it would be useful to examine the association of these pathologies with the number and costs of elective and unplanned admissions [24,25]. We were not able to conduct this analysis with the available data, but this should be explored from future studies.

MM-related admissions are only a small part of the total inpatient stays treated in NHS (1%). However, the average cost per patient per



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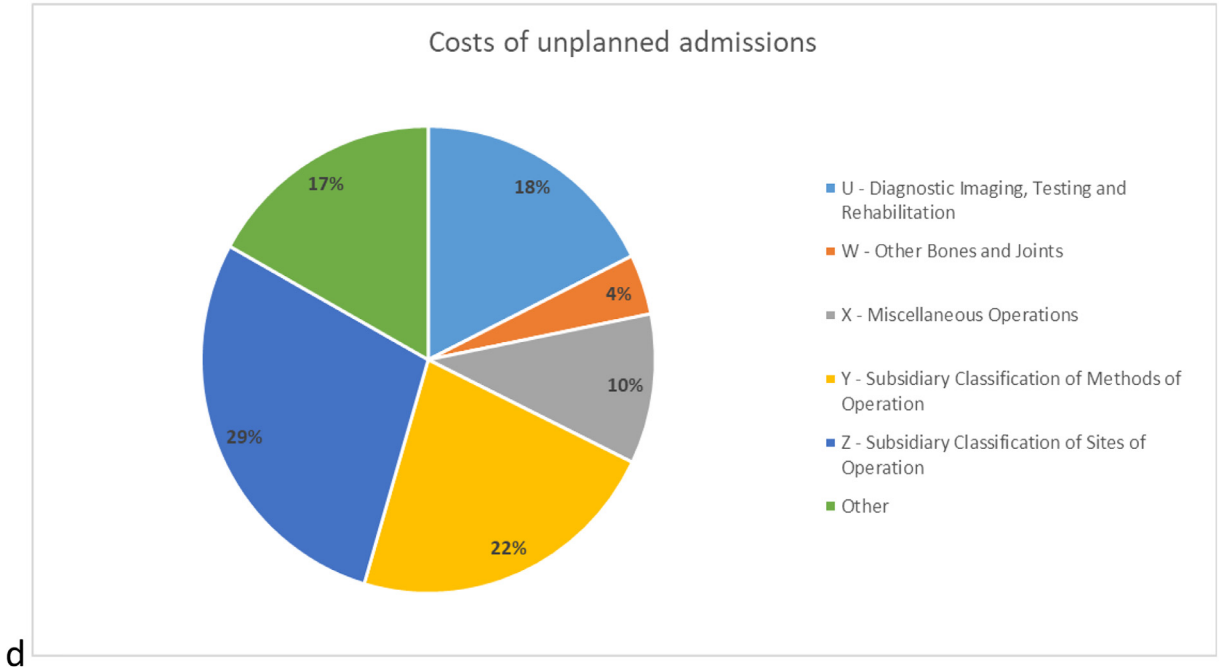

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Fig. 3. (*continued*)

year for MM-related admissions is nearly three times that of the average patient in the NHS (£2,455 vs £870). This is driven by the significantly higher average number of admissions per year for MM patients compared to the average NHS patient. Considering that cost estimates exclude unbundled HRGs (which add to the cost of chemotherapy) as they were not available from the data provider, costs of MM-related admissions are more than likely higher than estimated in this analysis. As a result, the relative cost of the inpatient care of patients with MM compared to the average patient in the NHS can be expected to be higher than three-fold.

Admission rates and costs per patient can reasonably be expected to be higher for patients with cancer than for all patients admitted to hospital, as confirmed in our analysis in the case of patients with MM. To place the characterisation of hospital admission of patients with MM into context accounting for this, we compared our findings about MM with those of colon cancer. Colon cancer admissions were found to be more costly, in average, than MM-related admissions (£1,302 vs £544), which can be expected to be equally affected by the exclusion of unbundled HRGs if chemotherapy accounts for similar shares of admissions. The difference in mean cost of admission may be explained by the different therapeutic strategy more focused on surgery. However, the average number of MM-related admissions per patient was much higher than those of colon cancer (4.5 vs 1.4, respectively), thus leading to a higher economic burden per patient for those being admitted to hospital with MM (£2,455 compared to £1,876 for colon cancer). Therefore, even though MM is not prevalent, it is related to high healthcare costs. Further investigation of clinical and cost-effective treatments that can reduce the economic burden related to the disease

Table 1
Number of admissions, number of patients, and total costs for multiple myeloma (MM) and all the NHS for the entire period of analysis (four years).

		NHS[1]	MM	% MM
Patients	Women	13,914,785	17,555	0.13
	Men	11,157,950	24,290	0.22
	Total	**25,083,320**	**41,845**	**0.17**
Admissions	Women	39,719,370	319,770	0.81
	Men	32,646,475	434,575	1.33
	Total	**72,376,430**	**754,345**	**1.04**
Costs (£)	Women	45,120,504 778	174,452,366	0.39
	Men	42,131,019 046	223,418,395	0.53
	Total	**87,256,644 580**	**410,974,873**	**0.47**

[1] The small discrepancy between the sum of female and male values and the total for NHS is due to some values labelled as unknown gender.

is warranted.

Our analysis benefited from using routinely-collected real world data from the most recent four financial years from HES, which group all NHS funded hospital admissions in England. However, we only had access to data on admitted patient care. Hospital outpatient and emergency contacts are also an important part of the clinical pathway of patients with MM and of the associated costs to the healthcare system [8,9]. This is particularly relevant for patients with MM because outpatient appointments can be used for oral chemotherapy. Furthermore without access to individual level data or clinical information, we were unable to ascertain the date of diagnosis and so unable to distinguish admissions that were the presentation of myeloma vs. admissions following diagnosis. We did not have access to age breakdown within elective and unplanned admissions. This would have been important to identify their hospitalisation reason, such as possibly non-intensive treatment for the older, frail patients, or intensive therapy with transplant for younger ones. Finally, we could only access the primary OPCS procedure, and not additional procedures that may be related to each admission.

Costs were estimated based only on 'core' HRGs and excess length of stay. Although these normally capture the bulk of regular hospital admission costs in England, the exclusion of 'unbundled' HRGs is unquestionably relevant for cancer admissions. Whereas the medical and surgical care provided during hospitalisation are included in 'core' HRGs, the procurement (regimen) and delivery of chemotherapy and radiotherapy are placed into 'unbundled' HRGs, as are pharmacy costs [20,26]. This means that the total inpatient cost of MM-related admissions will be more accurately represented by the sum of the costs identified in this study plus those regularly grouped into unbundled HRGs but such analysis requires patient-level data.

Given the high admission frequency and the considerable burden of unplanned admissions, further work is needed to explore the reasons for these admissions, and to assess the cost-effectiveness of those interventions to inform planning of health services. Using patient-level data from hospital admissions including outpatient visits and considering unbundled HRGs is necessary to provide a more accurate characterisation of the economic burden of MM in the UK.

5. Conclusion

Multiple myeloma is associated with a large number of hospital admissions in the English NHS. The majority of the hospital admissions are elective, but the highest burden in terms of costs comes from unplanned admissions, where numbers are increasing over time. Elective admissions and costs are mainly driven by chemotherapy, whilst for unplanned admissions diagnostic radiotherapy is the main driver. The yearly hospitalisation cost for patients with multiple myeloma is at least 3 times that of the average patient in NHS and it is also higher than that of patients with a more prevalent cancer, such as colon cancer.

Author contributions

All authors made substantial contributions to the conception or design of the work. SK, RPV, and MKJ performed the data analysis and wrote the manuscript. All authors have contributed to the drafting and revising critically the manuscript for important intellectual content. All authors approved the submitted version of the manuscript.

Conflict of interest

Guido Nador has received research support form Amgen. Bhuvan Kishore has received travel grants and honorarium from Takeda, Celgene and Jazz. Neil K. Rabin has received consultancy, travel support and/or speakers bureau from Janssen Cilaf, Takeda, Celgene, and Novartis. Kwee Yong received honoraria, unrestricted research grants, travel and/or subsistence expenses from Amgen, Janssen, Celgene, Takeda, Sanofi. Her research has been funded from National Institute of Health Research Oxford Biomedical Research Centre supports funding for Amgen: unrestricted educational grant with no input on study design, collection, analysis, interpretation of data, writing of manuscript and decision to submit. John Ashcroft has received honoraria, unrestricted research grants, travel and /or substinence expenses from Amgen, Celgene, Janssen-Cilag, and Takeda. Karthik Ramasamy has received research grants, speaker fees, honoraria, and is in the advisory board of Amgen. Daniel Prieto-Alhambra's institution has received research grants from UCB Biopharma, Amgen and Les Laboratoires Servier; speaker fees from AMGEN; and consultancy fees from UCB Biopharma. Janssen, on behalf of IMI-funded EHDEN and EMIF consortiums, and Synapse Management Partners have supported training programmes organised by Daniel Prieto-Alhambra's department and open for external participants. Cyrus Cooper has received lecture fees and honoraria from Amgen, Danone, Eli Lilly, GSK, Kyowa Kirin, Medtronic, Merck, Nestlé, Novartis, Pfizer, Roche, Servier, Shire, Takeda and UCB outside of the submitted work. M. Kassim Javaid received honoraria, unrestricted research grants, travel and/or subsistence expenses from Amgen, Lilly UK, Shire, Internis, Consilient Health, Mereo Biopharma, Optasia Medical, Zebra Medical Vision, Kyowa Kirin Hakin, and UCB. His research has been funded from National Institute of Health Research Oxford Biomedical Research Centre. Amgen Ltd provided an unrestricted educational grant. Andrew D Chantry, Mark T. Drayson, Matthew Streetly, Rafael Pinedo-Villanueva, Stella Bowcock, and Spyros Kolovos declare no conflict of interest for this work.

Acknowledgements

The research was supported by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. The research was co-funded by an investigator initiated study award by Amgen Ltd. The funder had no input in the analysis plan, analyses, reporting or decision to submit for this publication.

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