



# Real-World Health Care Services Utilization Associated With the Management of Patients With Relapsed and Refractory Multiple Myeloma in Spain: The CharisMMa Study

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## Abstract

**This observational, cross-sectional, multicenter study describes the real-world utilization of health care services in relapsed/refractory multiple myeloma (RRMM) patients in Spain. We included data from 276 patients collected from medical records and during a structured interview. Utilization of health care services—mostly hospitalizations, consultations with specialists and imaging tests—was high, underscoring a significant economic burden for the health care system.**

**Background:** Most patients with multiple myeloma (MM) relapse or become refractory, resulting in high health care costs. However, real-world data regarding the utilization of health care services among the relapsed/refractory MM (RRMM) population are scarce. **Methods:** Observational, cross-sectional, multicenter study of the utilization of health care services by RRMM patients who had relapsed within the previous 6 months in Spain in a real-world setting. Data were collected from the clinical records and during a single structured interview and included sociodemographic and clinical characteristics at last relapse, the treatment and health care services nature, and were presented using descriptive statistics. **Results:** The 276 patients enrolled (53.3% males), with a mean [SD] age of 67.4 [10.5] years, had experienced their most recent relapse a median (IQR) of 1.61 (0.74, 3.14) months before entering the study. Patients lived a median (IQR) of 9.0 (3.0, 30.0) km away from the hospital and visited the hospital a median (IQR) of 3.0 (2.0, 5.0) times/month to receive treatment for their most recent relapse. They spent a median (IQR) of 15.84 (5.0, 42.0) euros/month on transportation. Since their most recent relapse, most patients had been admitted to a hospital unit (n = 155, 56.2%), had required ≥1 diagnostic tests (n = 227, 82.2%), and had consulted the hematologist (n = 270, 97.8%) a mean (SD) of 5.5 (5.4) times. In half of the visits, patients were accompanied by an actively working caregiver (n = 112, 54.4%). **Conclusions:** RRMM treatments are associated with a high utilization of health care services and pose a significant burden for patients and caregivers. **Trial registration number:** NCT03188536

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## Introduction

Multiple myeloma (MM) is a neoplasm of plasma cells that represents the second most frequent blood cancer and accounts for approximately 10% of all hematologic malignancies worldwide.<sup>1,2</sup> In Europe, its estimated incidence ranges between 4.5 and 6.0 cases per 100,000 people per year; in Spain, it had an incidence of 5.61 during the 2010 to 2016 period.<sup>1,3,4</sup> However, both the incidence and prevalence of MM are expected to increase in high-income countries, probably due to population aging and the availability of new, more effective drugs.<sup>5</sup>

In recent years, new treatment options have increased the survival rates and quality of life of MM patients, turning this disease into a chronic condition in an increasing number of cases.<sup>5,6</sup> However, MM remains incurable, with an estimated 5-year survival rate of 54%.<sup>7</sup> Most patients—even those who achieve a long-term response with the first treatment—eventually relapse or become refractory to the current therapy, requiring several lines of treatment.<sup>6,8</sup> In this regard, managing relapsed or refractory MM (RRMM) is associated with high utilization of and expenditure on health care services and progressively increased costs with each new treatment line.<sup>9-11</sup>

According to previous studies, the main direct health care costs associated with RRMM management are driven by drug treatments, although hospital admissions, visits to general practitioners and specialists, and management of MM complications or adverse events (eg, infections, neutropenia, anemia, thrombocytopenia, fatigue) also contribute to the total expenditure.<sup>10,12-15</sup> In this regard, the rising health care costs of RRMM observed in recent years (2000-2014) are increasingly due to those associated with the use of health care resources, despite the availability of new—and potentially more expensive—treatment options.<sup>16</sup> In addition, the indirect costs of RRMM management include absenteeism, transportation, and caregiving services related to medical visits.<sup>13,14</sup>

Despite the high costs associated with RRMM management, real-world evidence is scarce and, to our knowledge, studies assessing the use of health care resources for the management of RRMM in Spain are limited.<sup>16</sup> This observational cross-sectional study aimed to describe the utilization of health care services since the most recent relapse and/or refractory episode of MM requiring active treatment in the real-world clinical practice setting in Spain.

## Material and Methods

### Study Design and Patients

This was an observational, cross-sectional, multicenter study of RRMM patients routinely treated at 27 public hospitals in Spain (ClinicalTrials.gov ID. NCT03188536). Patients were recruited between June 2017 and November 2018. This study included among its objectives the analysis of the utilization and costs of health care services, while its primary objective was to identify the profile of MM patients with symptomatic relapse and/or refractory disease in Spain.<sup>17</sup> Adult patients (aged  $\geq 18$  years) diagnosed with MM who had received 1 or more previous lines of treatment and had experienced symptomatic relapse and/or refractory disease<sup>18</sup> within the last 6 months before enrollment in the study were included.

After patients gave their written consent, information related to their diagnosis, previous courses of treatment and last relapse were retrospectively gathered from their clinical records; data regarding selection criteria, demographics, lifestyle habits, adverse events, concomitant drugs, current treatment, and treatment costs, including transportation costs, were collected during a single structured interview. Subsequently, the data were processed in accordance with General Data Protection Regulation 2016 of 679 on data protection and privacy for all individuals within the European Union, as well as in accordance with the local data protection regulatory framework. The study protocol was approved by the local independent ethics committee.

### Study Variables

The sociodemographic characteristics gathered included age, sex, area of residence, distance from the patients' home to the hospital, employment status, cohabitation status, and degree of dependence, defined with the following categories: independence (the patient does not require assistance to perform day-to-day activities), grade I (the patient requires assistance to perform day-to-day activities at least once a day), grade II (the patient requires help to perform day-to-day activities more than once a day, but not continuously), and grade III (the patient requires constant support).

Patients' clinical characteristics at the time of their most recent relapse and/or refractory episode were recorded, including the International Staging System (ISS) scores, the cytogenetic risk, determined by bone marrow fluorescence *in situ* hybridization (FISH) and stratified as high (deletion [del] 17p / translocation [t] [14; 16] / t [4; 14]) or standard risk (ie, absence of high-risk genetic abnormalities), and the presence of plasmacytomas, bone fractures, infections and comorbidities. Laboratory parameters included serum lactate dehydrogenase (LDH) levels in serum and paraprotein and heavy/light chain concentrations in serum and urine. Serum calcium levels, renal insufficiency, anemia or bone lesion (CRAB) features at diagnosis were additionally recorded. Details of the treatment recorded included the types of drugs prescribed at the last relapse (immunomodulatory drugs, proteasome inhibitors, and monoclonal antibodies) and the number of previous lines of treatment. Variables related to the utilization of health care services since the most recent relapse included the monthly number of visits to the hospital to receive treatment and their associated costs, the means of transportation used (private vehicle, public transport, or ambulance), the number of patients admitted to hospital according to the type of unit/department (intensive care unit, hospital ward, emergency department, and others), the length of the hospital stay, the number of consultations with different medical specialists (oncologist, hematologist, general practitioner, psychologist, or others), and the tests performed. These tests included magnetic resonance imaging (MRI), X-rays, positron emission tomography/computed tomography (PET/CT), single proton emission computed tomography (SPECT), multiple gate acquisition scan (MUGA), bone marrow aspirate, bone marrow biopsy, fine-needle aspiration of abdominal fat pad (FNAFP), laboratory analysis, ultrasound, echocardiogram, electrocardiogram, endoscopy, densitometry, spirometry, walking test, and dialysis. Visits attended by patients alone and visits accompanied by a patient's caregiver—either formal or informal—

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**Table 1** Employment Status and Level of Dependence of Patients With Relapsed or Refractory Multiple Myeloma. *n* (%) *N* = 276<sup>a</sup>

Employment Status, <i>n</i> = 275	
Unemployed	15 (5.5)
Active <sup>b</sup>	14 (5.1)
Temporary/permanent disability	55 (20.0)
Retired	179 (65.1)
Other	12 (4.4)
Level of dependence, <i>n</i> = 275 <sup>c</sup>	
Independent	196 (71.3)
Grade I	40 (14.5)
Grade II	35 (12.7)
Grade III	4 (1.5)

<sup>a</sup> Unless otherwise specified, the assessment corresponds to the complete study population  
<sup>b</sup> Active patients were either full-time employed (*n* = 10), part-time employed (*n* = 3) or unknown (*n* = 1).  
<sup>c</sup> Defined as: Independent, the patient does not need assistance to perform activities of daily living; Grade I, the patient needs assistance to perform activities of daily living at least once a day; Grade II, the patient needs help to perform activities of daily living more than once a day, but not in a continuous manner; and Grade III, the patient needs constant support.

and the employment status of the patient's caregiver were also recorded.

**Statistical Analysis**

Categorical variables were presented as frequency and percentage of patients in each category, and quantitative variables as the mean and standard deviation (SD) or the median and interquartile range (IQR, 25th and 75th percentiles). All the analyses were descriptive and were performed using SAS software v9.4 (SAS Institute Inc., Cary, NC).

A formal sample size calculation to assess the outcomes presented in this study was not performed. This sub-analysis was part of a main study and the estimated sample size of 350 patients was calculated based on the primary objective, namely identifying the profile of MM patients with symptomatic relapse and/or refractory disease in Spain.<sup>17</sup>

**Results**

**Patients' Characteristics at Relapse**

Of 282 eligible patients, 6 were excluded: 1 declined to participate, 1 had missing data in terms of the selection criteria, and 5 had not relapsed within the previous 6 months (more than 1 reason was possible). Thus, the study included a total of 276 patients, who had experienced their most recent relapse in a median (IQR) of 1.61 (0.74, 3.14) months before entering the study. They had a mean (SD) age of 67.4 (10.5) years and were equally distributed among both sexes: 147 (53.3%) were men and 129 (46.7%) were female. Most patients (*n* = 249, 90.5%) were retired, unable to work due to a disability, or unemployed, and a small proportion had some degree of dependence (*n* = 79, 28.7%) (Table 1). In addition, they resided between 0.5 and 530 km away from the hospital (median [IQR] of 9.0 [3.0, 30.0] km), mostly in urban areas (*n* = 209, 75.7%). Most patients lived with relatives (*n* = 235, 85.8%), while 34 (12.4%) and 5 (1.8%) lived alone and alone with assistance, respectively.

**Table 2** Utilization of Health care Services by Multiple Myeloma Patients since the Most Recent Relapse and/or Refractoriness (≤6 Months), *n* (%) *N* = 276<sup>a</sup>

Patients Admitted	
Admission units <sup>b</sup> , <i>n</i> = 155	
ICU	7 (4.5)
Hospital ward	92 (59.4)
Emergency department	60 (38.7)
Other services	42 (27.1)
Specialists consulted <sup>b</sup>	
Oncologists	7 (2.5)
Hematologists	270 (97.8)
General practitioners	60 (21.7)
Psychologists	10 (3.6)
Others	88 (31.9)
Tests <sup>b</sup> , <i>n</i> = 227	
PET/CT	177 (78.0)
MRI	111 (48.9)
X-Rays	98 (43.2)
Bone marrow aspirate	43 (18.9)
Laboratory analysis	18 (7.9)
Ultrasound	15 (6.6)
Echocardiogram	14 (6.2)
Electrocardiogram	9 (4.0)
Densitometry	5 (2.2)
Endoscopy	3 (1.3)
Bone marrow biopsy	2 (0.9)
Spirometry	2 (0.9)
Walking test	2 (0.9)
FNAFP	1 (0.4)
SPECT	1 (0.4)
Dialysis	1 (0.4)
MUGA	1 (0.4)
Unspecified	3 (1.3)

Abbreviations: CT = computed tomography; FNAFP = fine-needle aspiration of abdominal fat pad; MRI = magnetic resonance imaging; MUGA = multiple gate acquisition scan; PET/CT = positron emission tomography/computed tomography; SPECT = single proton emission computed tomography.

<sup>a</sup> Unless otherwise specified, the assessment corresponds to the complete study population.  
<sup>b</sup> More than 1 possible option.

The number of patients that were receiving second, third, and fourth or subsequent lines of therapy were 118 (42.8%), 73 (26.4%), and 85 (30.8%), respectively. Table S1 and S2 summarize the main clinical characteristics of patients at the time of the most recent relapse/refractory episode and their treatments, respectively.

**Utilization of Health Care Services since the Most Recent Relapse**

To receive treatment for their most recent relapse, patients visited the hospital a median (IQR) of 3.0 (2.0, 5.0) times per month, most of them using a private vehicle (*n* = 183, 67.8%), followed by public transportation (*n* = 68, 25.2%), with 19 (7.0%) using

**Table 3** Number of Hospitalizations and Consultations per Patient since the Most Recent Relapse ( $\leq 6$  Months)

	Mean (SD)	Median (IQR)
<b>Hospitalizations</b>		
Hospital ward, n = 77	1.6 (1.1)	1.0 (1.0, 2.0)
Emergency department, n = 52	1.4 (0.9)	1.0 (1.0, 2.0)
ICU, n = 2	1.0 (0.0)	1.0 (1.0, 1.0)
<b>Consultations</b>		
Oncologist, n = 7	1.9 (1.1)	2.0 (1.0, 2.0)
Hematologist, n = 270	5.5 (5.4)	4.0 (2.0, 6.0)
Primary care physician, n = 60	3.1 (3.0)	2.0 (1.0, 4.0)
Psychologist, n = 10	2.0 (1.2)	2.0 (1.0, 2.0)
Others, n = 88	2.9 (2.9)	2.0 (1.0, 3.0)

Abbreviations: ICU = intensive care unit; IQR = interquartile range; SD = standard deviation.

an ambulance. The monthly cost of transportation to the hospital ranged from 0.0 to 1,160 euros (median [IQR] of 15.84 [5.0, 42.0] euros). Table 2 summarizes the utilization of health care services. Since their most recent relapse ( $\leq 6$  months before entering the study), most patients had been admitted to receive some kind of health care service (n = 155, 56.2%), with treatment in a hospital ward being the most frequent (n = 92 of 276, 33.3%). In addition, most patients had required some form of testing since their most recent relapse (n = 227, 82.2%), with PET/CT being the most frequent, followed by MRI, and X-rays.

The analysis of the utilization of health care services per patient is summarized in Table 3 and, overall, showed a low number of hospitalizations per patient. The mean (SD) length of stay in hospital wards, emergency departments and ICUs was 15.9 (17.0), 1.7 (1.5), and 1.0 (0.0) days, respectively. Regarding consultations, patients who were seen by hematologists needed a mean (SD) of 5.5 (5.4) consultations, whereas the lower number of patients who were seen by general practitioners, oncologists, psychologists, and other specialists needed fewer consultations. Overall, the specialists who were visited more frequently received more visits from patients who were accompanied than from patients attending alone, and a substantial proportion of the accompanying caregivers were actively working, albeit at variable frequencies depending on the specialist consulted (Table 4).

## Discussion

In this observational, cross-sectional, multicentric study, we describe the real-world utilization of health care services and the associated costs incurred by patients with RRMM who had experienced their most recent relapse or refractory illness within the previous 6 months and had received previous lines of treatment. Most RRMM patients in this study were receiving some treatment (mostly a second and third line) for their last relapse and visited the hospital or health care center to receive treatment and to see their hematologist. In addition, since their most recent relapse, over half of the study patients were admitted to receive some kind of health care service and required imaging tests.

The results from this study show that RRMM is associated with frequent utilization of health care services. Due to their most recent relapse, most patients were admitted to health care facilities, including hospital wards, emergency rooms, and ICUs and they required imaging tests. Furthermore, since their most recent relapse, patients consulted with specialists, mostly with a hematologist (ie, 270 of the 276 patients assessed were seen by a hematologist), and visited health care centers to receive treatment (mean [SD] of 4.1 [4.8] visits per month). These results reveal a high RRMM burden for the Spanish health care system, similar to that reported in other European countries.<sup>11</sup> The previous study assessed costs across courses of treatment and phases of sickness (ie, active treatment, off-treatment and progression), as well as according to treatment response and country, precluding direct comparisons with this study. However, in this study, more patients were hospitalized and more frequently, with 92 of 276 (33%) patients admitted to hospital wards at least once, with a mean (SD) of 1.6 (1.1) hospitalizations. In contrast, in the previous study, 16% to 18% and 3% to 6% of patients needed 1 and 2 or more hospitalizations, respectively, and the mean (SD) number of hospitalizations was 1.2 (0.6) to 1.8 (1.1) (in patients receiving courses of treatment requiring the highest number of hospitalizations).<sup>11</sup> Moreover, we found considerably longer stays in hospital wards (mean [SD] of 15.9 [17.0] days), compared to the length of stay during hospitalizations reported for other European countries (mean [SD] range of 4.2 [4.9] to 9.7 [7.0] days). This difference in hospital stays could be explained by the high proportion of patients undergoing later lines of treatment and with comorbidities in our study population.<sup>17</sup>

In addition to the utilization of health care services, this study investigated the burden associated with visits for treatment and consultations for both patients and caregivers. Regarding the costs of transportation to receive treatment, ambulance was the least frequently used means of transportation (7%). However, patients incurred variable expenses for public and private transportation (median [IQR] 15.8 [5.0, 42.0] euros/month), most likely based on commuting distances, which also varied (median [IQR] 9.0 [3.0, 30.0] km). In this regard, a previous study reported higher indirect costs due to productivity loss, travel, and caregiving in patients living a long distance away from hospitals.<sup>14</sup> Furthermore, patients who consulted with specialists since the most recent relapse did so an average of 2 to 5.5 times, depending on the specialist, and attended most visits accompanied by a caregiver, who was frequently actively working. These results show an additional burden of RRMM for patients and caregivers due to consultation visits, which may have resulted in missed time at work (ie, absenteeism) and daily activities. Even though we did not assess these variables, caregivers' absenteeism to accompany RRMM patients may have also contributed to increased RRMM indirect costs.

In this study, hospital admissions—with associated mean lengths of stay of  $>2$  weeks—as well as imaging tests and hematologist consultations were identified as the main drivers for the utilization of health care services. The few studies assessing the costs and use of health care services outside clinical trials in RRMM have used varying methods and criteria to estimate costs and utilization of health care services, and differing populations in terms of lines of treatment and drugs, precluding direct comparisons between

**Table 4** Consultations Alone and Accompanied According to Specialist

	Oncologist n = 7 <sup>a</sup>	Hematologist n = 270 <sup>a</sup>	General Practitioner n = 60 <sup>a</sup>	Psychologist n = 10 <sup>a</sup>	Others n = 88 <sup>a</sup>
Consultations <sup>b</sup> , n (%)	n=7	n=267	n=57	n=10	n=85
Alone	2 (28.6)	55 (20.6)	13 (22.8)	6 (60.0)	14 (16.5)
Accompanied	7 (100)	238 (89.1)	45 (78.9)	4 (40.0)	72 (84.7)
Number of consultations, median (IQR)					
Alone	1.5 (1.0, 2.0)	2.0 (2.0, 4.0)	1.0 (1.0, 2.5)	2.0 (1.0, 3.0)	2.0 (1.0, 2.0)
Accompanied	1.0 (1.0, 2.0)	4.0 (2.0, 6.0)	2.0 (1.0, 4.0)	1.5 (1.0, 2.0)	2.0 (1.0, 3.0)
Caregivers' employment status, n (%)	n = 5	n = 206	n = 40	n = 4	n = 60
Employed	1 (20.0)	112 (54.4)	19 (47.5)	1 (25.0)	32 (53.3)

Abbreviation: IQR = interquartile range.

<sup>a</sup> Total number of patients with consultations. The number of patients with available data is indicated below.

<sup>b</sup> The 2 options were possible.

studies.<sup>9,19,20</sup> Nevertheless, in line with this study, previous studies using real-world data from the UK, France, and Italy identified hospitalization as 1 of the main drivers of direct costs, while another study in the UK identified physicians' visits and admissions as the main contributors to the use of medical resources and associated costs.<sup>11,15,21</sup> Also, other studies reported high annual hospitalization and monthly office and outpatient visit rates, while another study reported hospital stays, diagnostic procedures and hospital visits as the main contributors to monthly costs, after drugs, concomitant treatments and laboratory tests.<sup>21-24</sup> Moreover, in a previous study conducted in the USA, physicians' consultations and hospitalizations ranked second and fourth among the health care services used.<sup>12</sup> Thus, regardless of the design of the study and the populations assessed, both this and previous studies concluded that the management of RRMM patients is associated with high direct costs, mainly due to hospitalizations and consultations with specialists.

The results of this study should be interpreted in the context of the limitations associated with its design. Unlike other studies assessing all types of disease-associated costs,<sup>14,25</sup> this study focused on direct costs (ie, the provision of care). For this reason, RRMM-associated indirect costs (those linked to production losses of patients and caregivers) remained unassessed, similar to previous studies based on database claims data and retrospective collection of data from medical records.<sup>9,19,20</sup> Furthermore, this study failed to distinguish between planned (ie, hospitalizations and events considered part of the treatment or the normal monitoring process) and unscheduled resource use, with the latter accounting for over half of total hospitalization costs in previous studies despite a low frequency.<sup>26</sup> In addition, no assessment was performed comparing the use of health care services between subgroups of patients according to their type or line of treatment, due to the relatively small size of this study, which may have resulted in insufficient statistical power for an analysis of those categories with few patients. However, the results on health care service utilization presented in this study were obtained in the context of a study whose primary objective was to describe the profile of patients with RRMM in Spain for which larger sample sizes were not required.<sup>17</sup> Moreover, the variability in the time elapsed between patients' most recent relapse and their inclusion in the study may have altered the probability of

them requiring health care services (eg, hospital admissions, tests, or visits to the specialists), with higher chances for those patients who relapsed earlier. Finally, the small proportion of patients with some degree of dependence may indicate a potential bias in the study population due to the consecutive recruitment of patients.

Despite these limitations, this study captured real-world data during the most recent relapse in a population of RRMM patients. High utilization of health care services was due to hospitalizations, consultations with specialists and imaging tests. In the context of the increasingly growing incidence of MM, the results of this study show that new and more effective treatments are needed in order to improve outcomes and provide a clinical benefit to RRMM patients, as well as to increase the time until relapse, which would potentially decrease the costs associated with the care and management of RRMM patients.

## Conclusions

This study shows that RRMM is associated with a significant use of health care services and reflects the burden of the course of the disease for patients and caregivers due to several circumstances, including treatment regimens, clinical assistance during hospital visits, consultations and hospitalizations. However, further real-world studies analyzing how these factors influence the utilization of health care services are needed to help in clinical decision-making and in optimizing the management of RRMM disease.

### Clinical Practice Points

- Despite new treatment options resulting in improved survival and quality of life outcomes for MM patients, most eventually relapse or become refractory to current therapy. Relapsed or refractory multiple myeloma (RRMM) management is associated with high utilization of health care services and progressively increased costs with each new line of treatment. In this context, information regarding the burden of RRMM for the health care system is essential in order to understand the impact of the disease.
- However, real-world evidence is still scarce, and studies focused on the use of health care resources for RRMM management are limited in the context of Spain.

- We found that most RRMM patients in this real-world context in Spain were on the second and third line of treatment for their most recent relapse and had a significant utilization of health care services, revealing a high RRMM burden for the Spanish health care system.
- The most frequently used services were admissions, including hospital wards, emergency rooms and intensive care units, imaging tests, and consultations, especially with hematologists. Visits to the health care center to receive treatment posed a variable burden for patients due to transportation costs, depending on commuting distances. Patients who consulted with specialists attended most visits accompanied by a caregiver, who was frequently actively working.
- Our findings capturing real-world data during the most recent relapse among a population of RRMM patients provide useful information for helping to understand patterns in the utilization of health care services among this population. This information may be useful for optimizing RRMM patient management and for guiding treatment decisions.

## Disclosure

EMO has received research support from GSK; honoraria from BMS/Celgene, Janssen, Sanofi, GSK, Oncopeptides, Amgen, MSD, and Takeda; and consultancy fees from BMS/Celgene, Janssen, GSK, Pfizer, Amgen, Sanofi, Secura-Bio, Oncopeptides, Karyopharm, and Takeda. EP-P has received fees as consultant from Celgene, Amgen, Takeda, and Janssen; and fees as speaker from Roche, Celgene, Amgen, Janssen, Abbvie, and Jazz Pharmaceutical. MS has received financial support from Celgene, Janssen, and Takeda. JMA has received consultancy fees from BMS, Amgen, Janssen, Abbvie, GSK, and Sanofi; and honoraria from Novartis, Takeda, Janssen, BMS, Roche, Sanofi, Abbvie, GSK, and Amgen. RR has received consultancy fees from Becton-Dickinson, Sanofi, and The Binding Site. LR has received honoraria from Janssen, Celgene, Amgen, and Takeda. MG, AF, and AN are employees of Takeda. CM-G, GB, SG, EG, VG-C, YG, and DM declare no conflicts of interest.

## Author Contributions

EMO, LR, and MG conceived and designed the study; EMO, CM-G, GB, SG, EG, EP, VG, MS, JMA, YG, RR, DM, and LR participated in data collection; MG and AF-N participated in data analysis, and EMO, LR, MG, AF-N, and AN participated in manuscript drafting. All authors performed a critical review of the manuscript and its important intellectual content, gave their final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Data Sharing Statement

The datasets, including the redacted study protocol, redacted statistical analysis plan, and individual participants data supporting the results reported in this article, will be made available within 3 months from initial request, to researchers who provide a methodologically sound proposal. The data will be provided after its de-

identification, in compliance with applicable privacy laws, data protection and requirements for consent and anonymization.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.cml.2023.07.006](https://doi.org/10.1016/j.cml.2023.07.006).

## References

1. Dimopoulos MA, Moreau P, Terpos E, et al. Multiple myeloma: EHA-ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *HemaSphere*. 2021;5(2):e528. doi:[10.1097/HS9.0000000000000528](https://doi.org/10.1097/HS9.0000000000000528).
2. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin*. 2005;55(2):74–108. doi:[10.3322/canjclin.55.2.74](https://doi.org/10.3322/canjclin.55.2.74).
3. Chang-Chan D-Y-L, Ríos-Tamayo R, Rodríguez Barranco M, et al. Trends of incidence, mortality and survival of multiple myeloma in Spain. A twenty-three-year population-based study. *Clin Transl Oncol*. 2021;23(7):1429–1439. doi:[10.1007/s12094-020-02541-1](https://doi.org/10.1007/s12094-020-02541-1).
4. Galceran J, Ameijide A, Carulla M, et al. Cancer incidence in Spain, 2015. *Clin Transl Oncol*. 2017;19(7):799–825. doi:[10.1007/s12094-016-1607-9](https://doi.org/10.1007/s12094-016-1607-9).
5. Turesson I, Björkholm M, Blimark CH, Kristinsson S, Velez R, Landgren O. Rapidly changing myeloma epidemiology in the general population: Increased incidence, older patients, and longer survival. *Eur J Haematol*. 2018;101(2):237–244. doi:[10.1111/ejh.13083](https://doi.org/10.1111/ejh.13083).
6. Bobin A, Liuu E, Moya N, et al. Multiple myeloma: an overview of the current and novel therapeutic approaches in 2020. *Cancers*. 2020;12(10):1–17. doi:[10.3390/cancers12102885](https://doi.org/10.3390/cancers12102885).
7. American Cancer Society. Cancer facts and figures 2021.
8. Laubach J, Garderet L, Mahindra A, et al. Management of relapsed multiple myeloma: recommendations of the international myeloma working group. *Leukemia*. 2016;30(5):1005–1017. doi:[10.1038/leu.2015.356](https://doi.org/10.1038/leu.2015.356).
9. MacEwan JP, Batt K, Yin W, et al. Economic burden of multiple myeloma among patients in successive lines of therapy in the United States. *Leuk Lymphoma*. 2018;59(4):941–949. doi:[10.1080/10428194.2017.1361035](https://doi.org/10.1080/10428194.2017.1361035).
10. Steinmetz TH, Singh M, Lebioda A, et al. Healthcare resource utilization and costs among patients with relapsed and/or refractory multiple myeloma treated with proteasome inhibitors in real-world clinical practice in Germany. *J Med Econ*. 2021;24(1):114–122. doi:[10.1080/13696998.2020.1867469](https://doi.org/10.1080/13696998.2020.1867469).
11. Gonzalez-McQuire S, Yong K, Leleu H, et al. Healthcare resource utilization among patients with relapsed multiple myeloma in the UK, France, and Italy. *J Med Econ*. 2018;21(5):450–467. doi:[10.1080/13696998.2017.1421546](https://doi.org/10.1080/13696998.2017.1421546).
12. Madduri D, Hagiwara M, Parikh K, et al. Real-world treatment patterns, healthcare use and costs in triple-class exposed relapsed and refractory multiple myeloma patients in the USA. *Futur Oncol*. 2021;17(5):503–515. doi:[10.2217/fon-2020-1003](https://doi.org/10.2217/fon-2020-1003).
13. Robinson D, Orłowski RZ, Stokes M, et al. Economic burden of relapsed or refractory multiple myeloma: results from an international trial. *Eur J Haematol*. 2017;99(2):119–132. doi:[10.1111/ejh.12876](https://doi.org/10.1111/ejh.12876).

14. Ailawadhi S, DerSarkissian M, Duh MS, et al. Cost offsets in the treatment journeys of patients with relapsed/refractory multiple myeloma. *Clin Ther.* 2019;41(3):477–493.e7. doi:10.1016/j.clinthera.2019.01.009.
15. Gaultney JG, Franken MG, Tan SS, et al. Real-world health care costs of relapsed/refractory multiple myeloma during the era of novel cancer agents. *J Clin Pharm Ther.* 2013;38(1):41–47. doi:10.1111/jcpt.12020.
16. Fonseca R, Abouzaid S, Bonafede M, et al. Trends in overall survival and costs of multiple myeloma, 2000–2014. *Leukemia.* 2017;31(9):1915–1921. doi:10.1038/leu.2016.380.
17. Ocio EM, Montes-Gaisán C, Bustamante G, et al. Clinical and sociodemographic characteristics of patients with relapsed and/or refractory multiple myeloma and their influence on treatment in the real-world setting in Spain: the CharisMMa study. *Clin Lymphoma Myeloma Leuk.* 2021;S2152-2650(21):02369 -7. doi:10.1016/j.CLML.2021.10.001.
18. Rajkumar SV, Harousseau JL, Durie B, et al. Consensus recommendations for the uniform reporting of clinical trials: report of the international myeloma workshop consensus panel 1. *Blood.* 2011;117(18):4691–4695. doi:10.1182/blood-2010-10-299487.
19. Maiese EM, Evans KA, Chu B-C, Irwin DE. Temporal trends in survival and healthcare costs in patients with multiple myeloma in the United States. *Am Heal drug benefits.* 2018;11(1):39–46.
20. Chen C-C, Parikh K, Abouzaid S, et al. Real-world treatment patterns, time to next treatment, and economic outcomes in relapsed or refractory multiple myeloma patients treated with pomalidomide or carfilzomib. *J Manag Care Spec Pharm.* 2017;23(2):236–246. doi:10.18553/jmcp.2017.23.2.236.
21. Gooding S, Lau IJ, Sheikh M, et al. Double relapsed and/or refractory multiple myeloma: clinical outcomes and real world healthcare costs. *PLoS One.* 2015;10(9) eCollection 2015. doi:10.1371/journal.pone.0136207.
22. Hagiwara M, Panjabi S, Sharma A, Delea TE. Healthcare utilization and costs among relapsed or refractory multiple myeloma patients on carfilzomib or pomalidomide as monotherapy or in combination with dexamethasone. *J Med Econ.* 2019;22(8):818–829. doi:10.1080/13696998.2019.1614932.
23. Lin HM, Davis KL, Kaye JA, Luptakova K, Nagar SP, Mohty M. Real-world treatment patterns, outcomes, and healthcare resource utilization in relapsed or refractory multiple myeloma: Evidence from a medical record review in France. *Adv Hematol.* 2019. doi:10.1155/2019/4625787.
24. Zhou X, Xia J, Mao J, Cheng F, Qian X, Guo H. Real-world outcome and healthcare costs of relapsed or refractory multiple myeloma: a retrospective analysis from the chinese experience. *Hematology.* 2016;21(5):280–286. doi:10.1080/10245332.2015.1122259.
25. Mankinen P, Vihervaara V, Torvinen S, Martikainen J, Soini E. Costs of administration, travelling, and productivity losses associated with hospital administration of multiple myeloma drugs in Finland. *J Med Econ.* 2019;22(4):328–335. doi:10.1080/13696998.2019.1569457.
26. Kolovos S, Nador G, Kishore B, et al. Unplanned admissions for patients with myeloma in the UK: low frequency but high costs. *J Bone Oncol.* 2019;17 eCollection 2019 Aug. doi:10.1016/j.jbo.2019.100243.