Rationale and design of MUSIC OS-EU: an international observational study of the treatment of postmenopausal women for osteoporosis in Europe and Canada

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Abstract

Objective

The Medication Use Patterns, Treatment Satisfaction, and Inadequate Control of Osteoporosis Study (MUSIC OS-EU) was designed to better understand the rate and burden of gastrointestinal (GI) events on clinical and health care outcomes among postmenopausal women with osteoporosis.

Methods

MUSIC OS-EU is a prospective, multinational, observational cohort study of postmenopausal women ≥50 years of age diagnosed with osteoporosis and enrolled in physician clinics in six countries: France, Italy, the Netherlands, Sweden, the United Kingdom, and Canada. The MUSIC OS-EU study has three components: (i) a physician survey to describe their management of osteoporotic patients with GI events; (ii) a retrospective chart survey to describe the receipt and type of osteoporosis medication prescribed; and (iii) a prospective cohort study including untreated and treated patients diagnosed with osteoporosis to investigate the rate of GI events and association with osteoporosis medication use patterns, health-related quality of life, treatment satisfaction and resource utilisation among postmenopausal women with osteoporosis.

Results

Physicians at 97 sites completed the physician questionnaire and data for 716 patients were abstracted for the retrospective chart review. Enrolment and the baseline data collection for the prospective cohort study were conducted between March 2012 and June 2013 for 292 untreated and 2,959 treated patients, of whom 684 were new users and 2,275 were experienced users of oral osteoporosis medications.

Conclusion

The results of MUSIC OS-EU will illuminate the association of GI events with the management of osteoporosis and with patient-reported outcomes among postmenopausal women with osteoporosis in Europe and Canada.

Key words

osteoporosis, postmenopausal, bisphosphonates, drug therapy, gastrointestinal events

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Introduction

Osteoporosis affects about 22 million women in the European Union (EU) (1). As a result of osteoporosis, women in the EU are estimated to have lost 780,000 quality-adjusted life years (QALYs) in 2010 (1). The economic value of QALYs lost for both men and women in the EU in 2010 is estimated at approximately 60 billion euros, while the total cost of osteoporosis combined with the value of QALYs lost in the EU was 98 billion euros in that same year (1).

Pharmacotherapies for osteoporosis, including bisphosphonates, which are the first-line and most commonly prescribed osteoporosis treatment for postmenopausal women (2-4), reduce the risk of fracture in clinical trials (5-9). However, some patients with osteoporosis experience gastrointestinal (GI) problems, such as heartburn, nausea, upper or lower abdominal pain, esophagitis and peptic ulcers, while on treatment with bisphosphonates or other oral osteoporosis therapies (4, 10, 11). Patients diagnosed with osteoporosis also commonly report GI problems prior to treatment initiation (3, 10-12). The consequences of GI problems include poor adherence to osteoporosis therapy and discontinuation of therapy altogether (10, 11, 13-16). Furthermore, GI problems may be significantly associated with a patient's quality of life and treatment satisfaction and lead to increased health care resource utilisation.

The burden of GI events on treatment patterns and patient-reported outcomes among osteoporotic women has not been thoroughly investigated, and there is a lack of understanding of the physician's perspective on the current treatment approach to the management of GI events in European countries and Canada. These questions are addressed by the Medication Use Patterns, Treatment Satisfaction, and Inadequate Control of Osteoporosis Study (MUSIC OS-EU). MUSIC OS-EU is an international, multicentre, prospective, observational study designed to describe the frequency of GI events in postmenopausal women with osteoporosis and to provide further insight into the association of GI events with patterns of medication use, treatment satisfaction, health-related quality of life, and resource utilisation in this patient population. The study is also designed to describe physicians' perspectives of treatment patterns for osteoporosis with regards to management of GI events. In this paper, we describe the objectives, design, and methodologies of MUSIC OS-EU. Forthcoming manuscripts will present the findings on GI events, treatment patterns, patient-reported outcomes, and physicians' treatment approaches.

Methods

Objectives of MUSIC OS-EU

The primary objectives of MUSIC OS-EU were to describe: (i) the frequency of GI events among postmenopausal women receiving pharmacologic treatment for osteoporosis; (ii) the association between GI events and adherence to, discontinuation of, and switching between osteoporosis medications; and (iii) the association between GI events and health-related quality of life, treatment satisfaction, and health care resource utilisation and costs. Secondary objectives were: (i) to describe the physician's approach to the management of osteoporosis patients with GI events; (ii) to estimate the rates of pharmacologic treatment and non-treatment of osteoporosis; and (iii) to determine the factors associated with the decision of whether to treat or not to treat osteoporosis with pharmacotherapy in clinical practice.

Study design

The design of MUSIC OS-EU is shown in Figure 1. MUSIC OS-EU includes three separate study components: a physician questionnaire on the management of postmenopausal osteoporosis; a retrospective chart review, also completed by physicians, to record the rate of treatment for osteoporosis; and a prospective cohort study to assess the frequency of GI events in patients treated for osteoporosis, the association of GI events with quality of life and health care resource use in treated and untreated patients, and the association of GI events with medication adherence and treatment satisfaction in treated patients (Fig. 1). Site investigators were both specialist and primary

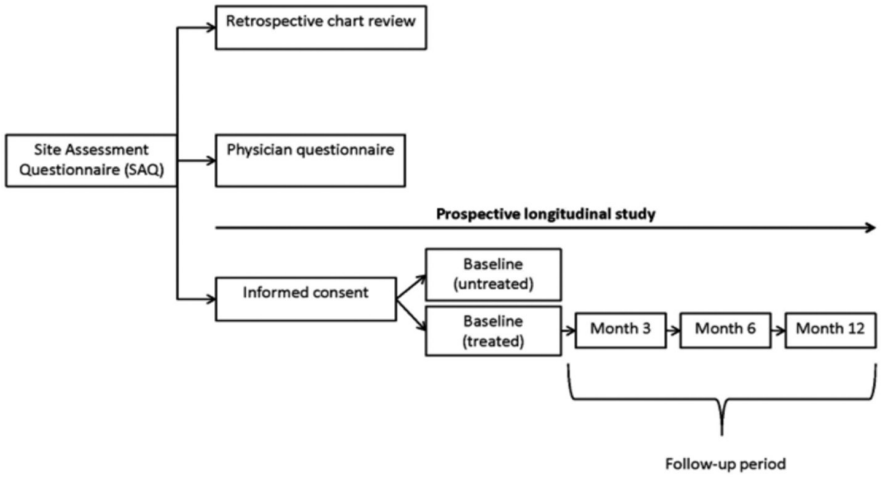

Fig. 1. MUSIC OS-EU study design.

care physicians and were invited to complete the physician questionnaire and retrospective review of patients' charts. Patients fulfilling the selection criteria while visiting the clinic for their routine care were then invited to participate and were enrolled sequentially into the prospective cohort study. Participants were allocated to either the treated or untreated patient groups depending on their current treatment status. Baseline assessments were conducted for both untreated and treated patients at the enrolment visit, while follow-up questionnaires were completed only by treated patients at 3, 6, and 12 months after enrolment (Fig. 1).

Physician and site selection

Physicians and sites were selected for participation in the study based on their ability to conduct observational trials and their access to patients with osteoporosis, derived from their responses to the Site Assessment Questionnaire (SAQ). The SAQ solicited information about the investigator's experience in conducting clinical research, interest in participating in the study, ability to dedicate time and resources to conduct the study, and whether the investigator had adequate access to the participant population being studied.

The investigators comprised both primary care physicians and specialists who could be community-based or hospital-based. Sites that met the selection criteria and were confirmed for participation in the study were asked to complete the physician questionnaire at the beginning of the study.

Physician questionnaire

The physician questionnaire collected information about the investigator's practices for the management of osteoporosis and GI events. The questionnaire addressed secondary objectives (i) and (iii). The questionnaire collected information regarding the physician's: (a) medical specialty, practice size, and setting; (b) standard practice regarding the diagnosis and treatment of patients with osteoporosis; and (c) perspective on current osteoporosis treatment approaches and medication adherence. Treatment approaches were examined specifically with regards to the management of patients with GI events.

Retrospective chart review

The retrospective chart review addressed secondary objective (ii). Physicians were asked to review the charts of the last 10 postmenopausal female patients 50 years of age or older with osteoporosis, as diagnosed by their doctor with or without a bone mineral density (BMD) evaluation, seen in the clinic at least one month prior to the start of MUSIC OS-EU. The questions were limited to whether the patient was receiving pharmacologic therapy – oral or injected, calcium and/or vitamin D, or none – for their osteoporosis. No attempt was made to enrol patients whose charts were reviewed into the prospective study.

Prospective cohort study

This longitudinal, prospective, observational study enrolled postmenopausal women in one of two arms, untreated patients or treated patients, depending on whether they were receiving pharmacotherapy for osteoporosis at the time of enrolment.

Patient inclusion / exclusion criteria.

Patients were eligible for enrolment in the prospective cohort study if they were postmenopausal women, at least 50 years of age, had osteoporosis in their physician's judgment (with or without a BMD test), were literate, were willing and able to follow the study protocol and complete all scheduled assessments, and provided informed consent. Patients were excluded if they had been diagnosed with Parkinson's disease or any other neuromuscular disease or Paget's disease; were currently treated with any injected medication for osteoporosis, including intravenous bisphosphonates, subcutaneous parathyroid hormone, or denosumab; had been switched between oral pharmacologic osteoporosis medications having different active ingredients within the 3 months prior to study entry; were considered by the investigator to be unwilling or unable to complete the study or comply with the protocol; were involved in any active litigation or compensation issues, including disability dispute cases with government; or were currently enrolled in a clinical trial or had participated in a clinical trial within the past 90 days.

The prospective component of MUSIC OS-EU included a cross-sectional analysis of the untreated group, which comprised a maximum of 300 participants who were not receiving osteoporosis treatment at the time of enrolment and completed the baseline questionnaire only. Reasons for non-treatment were documented, as were GI events in the prior 6 months. In addition, health care resource utilisation in the prior 3 months, and quality of life over the prior 2 weeks, were assessed. The information provided by untreated patients is intended to improve understanding of non-treatment of osteoporosis from a patient perspective, and to document

the rate of GI events and their association with quality of life and healthcare resource utilisation in participants who remain untreated for osteoporosis.

A maximum of 3,300 participants with osteoporosis receiving oral pharmacologic agents for the treatment of osteoporosis were targeted for enrolment in the treated group. To be considered as treated, participants must have been receiving oral pharmacologic therapy for osteoporosis, which included prescribed bisphosphonates (*e.g.* alendronate, risedronate, and ibandronate), calcitonin, strontium ranelate, and selective oestrogen-receptor modulators (raloxifene and bazedoxifene). These patients may also have been receiving calcium and/or vitamin D treatment, and oestrogen and/or hormone replacement therapy, in addition to pharmacologic therapy for osteoporosis, but these agents were not by themselves considered pharmacologic treatment for osteoporosis. Treated participants must not have been switched between oral pharmacologic medications with differing primary active ingredients within the 3 months prior to study entry.

Treated participants were further classified as new users or experienced users. New users were defined as patients who had been receiving oral pharmacologic therapy for less than 3 months, with no prior history of any pharmacologic therapy for osteoporosis. Experienced users must have been receiving the same oral pharmacologic therapy for at least 3 months and continuing that treatment at the time of enrolment. The treated participants completed the baseline evaluation and were followed for the subsequent 12 months from the date of entry into the study. Data were collected at 3, 6, and 12 months of follow-up. The treated group is intended to capture the endpoints for all of the primary research objectives of this study.

– Evaluations and outcome measures

Data collected at baseline only were: patient demographics, risk factors for osteoporosis, fracture history, medical history, osteoporosis medications, BMD test results (T-scores), vitamin D/calcium use, and, for untreated patients only, concerns about treatment.

Table I. MUSIC OS-EU schedule of assessments.

Assessment	Baseline (Office visit)	Follow-up assessments[a]		
		3 months	6 months	12 months
Physician questionnaire	√			
Retrospective chart survey	√[b]			
Informed consent and eligibility	√			
Demographics and risk factors for osteoporosis	√			
Osteoporosis disease assessment	√			
Bone mineral density test/T-score	√[c]	√[c]	√[c]	√[c]
Medical history	√			
Medications (osteoporosis, GI, vitamin D and calcium)[d]	√	√	√	√
Participant treatment concerns[e]	√			
New falls and fractures		√	√	√
Adverse events		√[c]	√[c]	√[c]
Gastrointestinal events	√	√	√	√
ADEOS adherence scale [a,f]	√	√	√	√
Healthcare resource utilisation questionnaire	√	√	√	√
Health-related quality of life (EQ-5D-3L)	√		√	√
Health-related quality of life (OPAQ-SV)	√		√	√
Treatment satisfaction questionnaire for medications (OPSAT-Q) [a,f]	√		√	√

ADEOS: Adherence Evaluation of Osteoporosis Treatment; GI: gastrointestinal; OPAQ-SV: Osteoporosis Assessment Questionnaire; OPSAT-Q: Osteoporosis Patient Satisfaction Questionnaire.
[a]Not collected for untreated participants.
[b]Completed only by selected sites.
[c]Collected by the physician during any clinical office visits only if applicable.
[d]Note that at baseline, all applicable medications will be recorded, while during follow-up only those medications that had been changed ("New medications case report form") or those that had been discontinued ("Discontinued medications case report form") will be collected.
[e]Collected only for untreated participants.
[f]Treated patients classified as new users were not required to complete the ADEOS questionnaire and the OPSAT-Q at baseline if they felt they had not been receiving treatment long enough to answer the questions.

Patient-reported outcomes collected at baseline for both treated and untreated patients included GI events, health care resource use, and health-related quality of life. The same outcomes, as well as medication adherence and treatment satisfaction, were assessed in treated patients at follow-up visits according to the schedule shown in Table I. GI events were defined as the following clinical symptoms: heartburn/acid reflux, upset stomach/indigestion, nausea/vomiting, pain behind the breastbone, pain on swallowing or food sticking, stomach pain above or below the navel, diarrhoea or constipation, and bloating. Medication adherence was measured by the Adherence Evaluation of Osteoporosis treatment (ADEOS) questionnaire (17), general health-related quality of life by the European Quality of Life-5 Dimensions (EQ-5D-3L) questionnaire (18), osteoporosis-specific quality of life by the Osteoporosis Assessment Questionnaire (OPAQ-SV) (19), and treatment satisfaction by the Osteoporosis Patient Satisfaction Questionnaire (OPSAT-Q) (20). Treated patients classified as new users were not required to complete the ADEOS questionnaire and the OPSAT-Q at baseline if they felt they had not been receiving treatment long enough to answer the questions. Untreated participants did not complete the ADEOS or OPSAT-Q questionnaires at all. Health care resource use was determined by patient report and included visits in the prior 3–6 months to a general practitioner, specialist, or emergency department; and hospitalisations, fractures, or surgeries in the same time period. Changes in osteoporosis medications (new medications and medication discontinuations), occurrences of new falls, fractures, and adverse events were also recorded at the follow-up evaluations.

Study procedures

Patient recruitment occurred between March 2012 and June 2013. All sites

Table II. MUSIC OS-EU site distribution by country.

	France	Italy	Netherlands[a]	Sweden	UK	Canada	Total
Specialty centre	8	22	6	3	0	1	40
Primary care clinic	19	0	1	0	22	14	56
Total	27	22	7	3	22	15	96

[a]After the completion of the physician questionnaire and chart review, one site in the Netherlands declined to participate in the prospective portion of the study.

completed ethics reviews according to their local ethics board requirements. Depending on the country requirements, local or centralised ethics committees were utilised. The selection of sites and physicians attempted to mimic the manner in which osteoporosis is treated in each of the participating countries. Study staff enrolled patients at routine office visits, obtained informed consent, and administered the baseline evaluation. Treated patients were provided with the month 3 follow-up questionnaire before leaving the office. Months 6 and 12 questionnaires were mailed to treated patients prior to their respective follow-up dates, and sites called participants to remind them when their questionnaires were due. Patients returned completed questionnaires by mail. Data were collected at each study site and entered into a secure, internet-based Electronic Data Capture (EDC) system (ClinStream™).

Data analysis

The anticipated analyses are descriptive and no *a priori* hypothesis is proposed. The proposed sample size of 3,300 treated participants was calculated to permit a final evaluable population of 2,700 subjects assuming an attrition rate of 15%–20%. This was expected to be sufficient for the descriptive and exploratory analyses anticipated and to permit comparisons between subgroups. The primary comparisons of interest are of patients with and without GI events.

Results

Physician questionnaire and retrospective chart review

A total of 106 sites in the 6 countries were invited to participate in the study. Of these, 97 sites agreed and were enrolled. Physicians at all sites completed the physician questionnaire. Physicians at 71 sites abstracted data from 716 patient charts to complete the retrospective chart review questionnaire.

Prospective cohort study

After the completion of the physician questionnaire and chart review, one site in the Netherlands declined to participate in the prospective portion of the study. Thus, a total of 96 sites participated in the prospective cohort study: 27 in France, 22 in Italy, 7 in the

Table III. Baseline characteristics of patients in the MUSIC OS-EU prospective cohort study.

Characteristic	Untreated patients (n=292)	Treated patients		
		New users (n=684)	Experienced users (n=2,275)	All patients (n=2,959)
Age, mean (SD) years	66.6 (9.46)	66.9 (8.85)	70.2 (9.02)	69.4 (9.08)
Age at menopause, mean (SD) years[a]	47.7 (6.23)	48.7 (5.25)	48.3 (5.46)	48.4 (5.42)
Race (%)[b]				
Asian	1 (0.4%)	5 (0.9%)	33 (1.8%)	38 (1.6%)
Black	1 (0.4%)	7 (1.2%)	13 (0.7%)	20 (0.8%)
White	221 (99.1%)	566 (96.3%)	1,722 (95.7%)	2,288 (95.9%)
Other	0 (0.0%)	10 (1.7%)	31 (1.7%)	41 (1.7%)
Height, mean (SD) cm	159.6 (6.51)	160.3 (7.17)	158.6 (6.83)	159 (6.95)
Weight, mean (SD) kg	63.2 (13.04)	63.1 (11.93)	63.4 (12.31)	63.4 (12.22)
Education (%)				
High school or less	132 (45.2%)	340 (49.7%)	1,093 (48%)	1,433 (48.4%)
At least some college	105 (36%)	198 (28.9%)	955 (42%)	1,153 (39.0%)
Prefer not to answer	55 (18.8%)	146 (21.4%)	227 (10.0%)	373 (12.6%)
Physical exercise, mean (SD) hours/week	4.6 (5.1)	5.1 (5.9)	5.8 (6.9)	5.6 (6.7)
Hypothyroidism	44 (15.1%)	76 (11.1%)	325 (14.3%)	401 (13.6%)
Mean total hip BMD T-score (SD)[c]	-1.17 (0.88)	-1.88 (0.82)	-1.85 (0.84)	-1.86 (0.84)
OP risk factors				
Alcohol use (≥3 units per day)	7 (2.4%)	7 (1.0%)	67 (2.9%)	74 (2.5%)
Current smoking	36 (12.3%)	94 (13.7%)	179 (7.9%)	273 (9.2%)
Glucocorticoid use	22 (7.5%)	36 (5.3%)	155 (6.8%)	191 (6.5%)
Parental hip fracture	47 (16.1%)	109 (15.9%)	298 (13.1%)	407 (13.8%)
Prior OP fractures	92 (31.5%)	337 (49.3%)	1126 (49.5%)	1463 (49.4%)
Rheumatoid arthritis	5 (1.7%)	18 (2.6%)	123 (5.4%)	141 (4.8%)
Secondary osteoporosis	17 (5.8%)	40 (5.8%)	138 (6.1%)	178 (6.0%)

OP: osteoporosis; SD: standard deviation.
[a] The patient no. for age at menopause was 285, 668, 2,237, and 2,905 for the respective patient sets.
[b] Race was not recorded in France, in compliance with French law.
[c] The patient no. for total hip BMD was 127, 456, 974 and 1,430 for the respective patient sets.

Netherlands, 3 in Sweden, 22 in the UK and 15 sites in Canada. The distribution of clinics is presented in Table II. The study site sample comprised 56 primary care clinics and 40 specialty centres, with 11 private clinics, 43 private practices, 30 university hospitals, and 12 community hospitals represented. Specialties included rheumatology, obstetrics/gynaecology, geriatrics, endocrinology, orthopaedics, or a combination of specialties.

Characteristics of untreated patients. The characteristics of the 292 untreated patients are presented in Table III. Untreated patients were, on average, 66.6 years of age. The majority of untreated patients (99.1%) were White while the remaining patients were Asian (0.4%) or Black (0.4%). Just under one third (31.5%) of untreated patients reported having prior osteoporotic fractures. The next most frequently reported risk factors for osteoporosis included parental hip fracture (16.1%) and current smoking (12.3%).

Characteristics of treated patients. The 2,959 treated patients included 684 new users and 2,275 experienced users (Table III). Treated patients were, on average, 69.4 years of age. Similar to the untreated patients, the majority of treated patients (95.9%) were White while the remaining patients classified themselves as Asian (1.6%), Black (0.8%), or other (1.7%). Nearly half (49.4%) of treated patients reported having prior osteoporotic fractures. The next most frequently reported risk factors for osteoporosis were parental hip fracture (13.8%) and current smoking (9.2%).

Discussion

Oral bisphosphonates are the most commonly prescribed treatment for osteoporosis in Europe (4). Since their introduction, oral bisphosphonates have been investigated for their association with GI events in populations of primarily or exclusively postmenopausal women (21, 22). Reported rates of discontinuation of bisphosphonates due to GI events in postmenopausal women are 2.7%–9.9% (23-25). However, the nature of the relationship between bisphosphonate use and GI events remains unclear. There is no evidence in pooled analyses of double-blind placebo-controlled clinical trials that bisphosphonates as a class are associated with GI events (9, 26-29). A possible interpretation of this is that GI side effects occur when patients outside the context of clinical trials do not adhere to the correct dosing procedure for oral bisphosphonates (22). However, GI problems commonly occur in postmenopausal women, regardless of whether they are taking an anti-osteoporosis medication. For example, in a survey of 497 women from the New York City area, 47% of postmenopausal women reported having upper GI symptoms (compared to 42% of perimenopausal women and 26% of premenopausal women) (30). Thus, GI problems in osteoporotic women may be related to confounding factors – possibly the underlying conditions of menopause or osteoporosis, or co-medications, such as non-steroidal anti-inflammatory agents, known to be a cause of GI side effects (31, 32). A perception that bisphosphonates cause GI events nevertheless persists, and guidelines for the treatment of osteoporosis continue to caution against upper GI side effects of oral bisphosphonates (33-36). The MUSIC OS-EU study will take the perspective that, regardless of the cause of the GI events, the events themselves will likely have an effect on patient-reported outcomes. These effects will be compared between patients with and without GI events in the prospective study of treated patients. The consequences of a perception that GI events in postmenopausal women are side effects of bisphosphonates might include avoidance of bisphosphonates. The rates of pharmacologic treatment and non-treatment of osteoporosis, which will be measured in MUSIC for the period 2012–2013, have been reported in several earlier large studies of treatment patterns. In a retrospective claims analysis of 65,433 women aged ≥55 years and diagnosed with osteoporosis in the United States in the period 2001–2010, 64.3% of women received no osteoporosis medication, 30.9% were treated with bisphosphonates, and 4.8% with non-bisphosphonates (12). In the baseline findings of the Global Longitudinal Study of Osteoporosis in Women (GLOW) cohort study conducted in 2006-2008 in several Western European and Anglophone countries, 48% of the cohort of 58,009 women aged ≥55 years at high risk of fracture reported by questionnaire that they had never used an osteoporosis medication, while 39% were current users (37). Only a few studies, all conducted in the United States, have addressed factors predictive of treatment of osteoporosis, with inconsistent results. In a 2007 chart review of women with osteoporosis, a GI diagnosis was the most frequent reason for not being on bisphosphonate treatment (38). Conversely, GI disease was not significantly predictive of treatment (either osteoporosis medication or a BMD scan) in a 2000-2007 analysis of electronic health records of 14,979 postmenopausal women after hip or wrist fracture (39). The MUSIC OS-EU study will add to these findings by determining the factors associated with treatment of osteoporosis from the physician's perspective. The physician and untreated patient questionnaires will also provide insight into the reasons for non-treatment of osteoporosis.

Adherence to bisphosphonates is poor, with only 24–50% of patients initiating bisphosphonates still taking them after one year (40-42). GI events may be a contributing factor to the low rates of adherence. GI events while taking osteoporosis medications – largely or exclusively bisphosphonates – have been identified as an independent risk factor for discontinuation in several observational studies (10, 13, 15). Lack of treatment satisfaction may also contribute to non-adherence (43). One consequence of poor adherence is an increased risk of fracture (40, 44-46). Fractures, in turn, require health care resource use, causing patients to incur additional costs (46-48). There is little information about the relationship between GI events while on osteoporosis medication and health care resource use (other than hospitalisation for a severe GI event) and costs. These outcomes will be studied in MUSIC OS-EU.

MUSIC OS-EU is broadly similar in design to the Prospective Observational

Scientific Study Investigating Bone Loss Experience (POSSIBLE) in Europe (4) and the US (49). All three studies enrolled postmenopausal women and used or will use patient surveys to obtain information on patient-reported outcomes. Distinctive features of MUSIC OS-EU are its focus on the link between GI events and patient-reported outcomes, its use of a physician survey to assess factors predictive of osteoporosis treatment, and the inclusion of an untreated group in the prospective cohort component of the study. Specific strengths of MUSIC OS-EU are that the study sample includes women from different regions of Europe and Canada and is large enough to detect the true rate of GI events and the impact of GI events on persistence with treatment. MUSIC OS-EU will acquire data on several rarely addressed patient-reported outcomes, including the relationship between GI events while on osteoporosis medication and health care resource use, satisfaction with treatment, and quality of life. In addition, MUSIC OS-EU will measure GI events as reported by patients, which may provide a more relevant depiction of the rate of GI events among osteoporosis patients than can be gleaned solely from chart reviews or claims database analyses. Patient-reported measures, however, may be subject to a reporting bias and to variations in patient compliance with study procedures. For example, at-home completion of the questionnaires may not occur exactly during the time frame specified in the study. One limitation of the study design is that patients were not required to report the severity of the GI events; in fact, severe GI events (*e.g.* those involving bleeding or perforation) were not included in the patient questionnaire. Another limitation is that the retrospective chart review will reflect the percentage of patients prescribed medication, not necessarily the percentage of patients who fill and subsequently take their medications.

Conclusions

It is expected that the results of MUSIC OS-EU will illuminate the association of GI events with the management of osteoporosis and with patient-reported outcomes. MUSIC will enable determination of the rates of a broad range of GI events among both treated and untreated patients, and provide a clearer understanding of the association of GI events with persistence with treatment, quality of life, treatment satisfaction, and osteoporosis- and GI-related rates of health care utilisation. Forthcoming manuscripts will present our findings on these associations.

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