

A conceptual model of multiple myeloma symptoms and impacts and a characterization of pain among patients living with relapsed and refractory multiple myeloma (RRMM)

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BACKGROUND

- Multiple myeloma (MM) is a progressive, recurrent, incurable hematologic malignancy characterized by the accumulation of neoplastic plasma cells in which patients often experience serious organ damage that leads to deterioration in health-related quality of life (HRQoL), high morbidity, and high mortality rates^{1–9}
- MM can place a profound burden of symptoms on patients, with common symptoms including bone pain, fatigue, dyspnea, various gastrointestinal symptoms, and psychological disorders (e.g., anxiety and depression). MM also has a detrimental effect on HRQoL, including impairments in physical, cognitive, emotional, and social functioning^{8–10}
- Although previously published conceptual models have documented symptoms related to MM and its treatments,^{11,12} the patient experience of pain in MM remains understudied

OBJECTIVES

- To conduct concept elicitation interviews with patients living with relapsed and refractory multiple myeloma (RRMM) to:
 - Develop a conceptual model of RRMM symptoms and impacts
 - Characterize pain experienced by patients with RRMM and its impact on their quality of life

KEY TAKEAWAYS

- Pain and fatigue were dominant concepts; both emerged as widely experienced and highly bothersome symptoms/symptomatic adverse events (AEs), and as the driving force behind many of the impacts of RRMM on patients' HRQoL**
- Patients' experiences of pain are heterogeneous (e.g., in location and severity), with multidimensional impacts on functioning and well-being**



Scan the QR code for Supplementary material

Abbreviations

AE, adverse event; HRQoL, health-related quality of life; IRB, institutional review board; MM, multiple myeloma; RRMM, relapsed and refractory multiple myeloma.

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Table 1. Patient characteristics

	Total (N=15) n (%)
Median age (range), years	66 (49–91)
Sex	
Female	8 (53.3)
Male	7 (46.7)
Ethnicity	
Non-Hispanic/non-Latino	14 (93.3)
Hispanic/Latino	1 (6.7)
Race	
White/Caucasian	8 (53.3)
Black or African American	6 (40.0)
Native Hawaiian/other Pacific Islander	1 (6.7)
Highest education level	
High school	2 (13.3)
Some college/associate degree	4 (26.7)
Bachelor's degree	5 (33.3)
Graduate degree	4 (26.7)
History of anti-CD38 antibody therapy	13 (86.7)
R-ISS stage	
Stage 1	2 (13.3)
Stage 2	7 (46.7)
Stage 3	5 (33.3)
Unknown	1 (6.7)
Current treatment line	
Third line	12 (80.0)
Fourth line	2 (13.3)
Fifth line	1 (6.7)
Pain severity on a typical day	
No pain	1 (6.7)
Mild	6 (40.0)
Moderate	8 (53.3)
Severe/very severe	0

R-ISS, Revised International Staging System.

METHODS

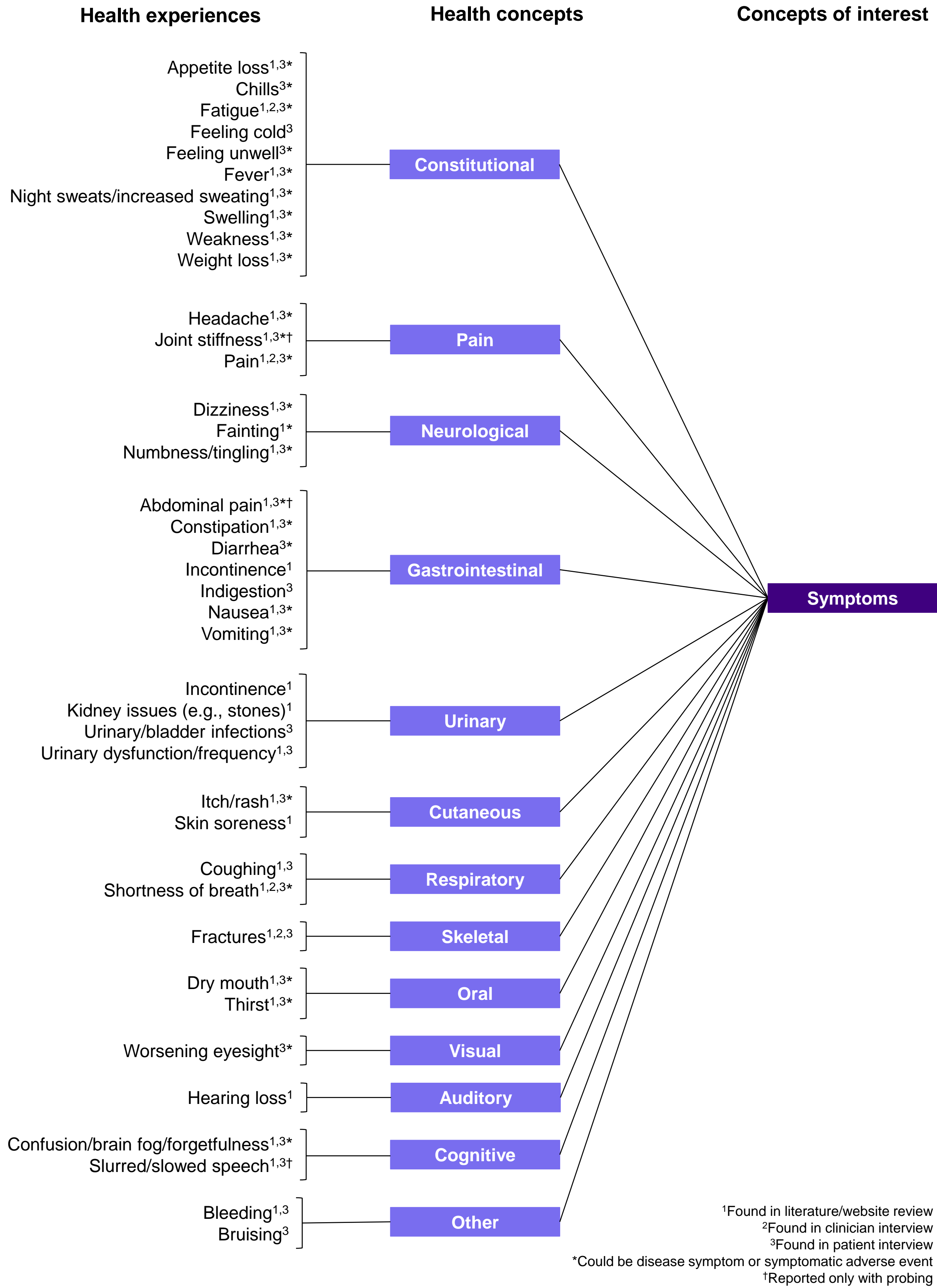
- Key inclusion criteria were age ≥18 years, living in the USA, diagnosis of RRMM, history of treatment with lenalidomide and a proteasome inhibitor, and 2–4 prior lines of MM therapy
- Patients were recruited by professional recruitment agencies and compensated for their participation. No clinical trials were associated with recruitment
- The study was approved by the WCG IRB, and patients provided written informed consent
- 90-minute cross-sectional, non-interventional, qualitative, online interviews followed an open-ended, semi-structured guide and included concept elicitation and cognitive debriefing (only concept elicitation is reported here)
- Interviews broadly explored the patient experience of symptoms, symptomatic AEs, and impacts in MM, and specifically the concept of pain, with probing for additional details about pain experiences
- Transcripts were coded, ordered and grouped chronologically to assess conceptual saturation, and thematically analyzed

“The pain that I was experiencing was just unremitting. It was just on all the time.” – CH004

“And there were days that the pain is bad that I don't even want to get up. You just feel tired all the time. You're tired and weak. I can't do much of the stuff that I used to be able to do.” – CH009

Additional quotes provided in **Supplementary material**

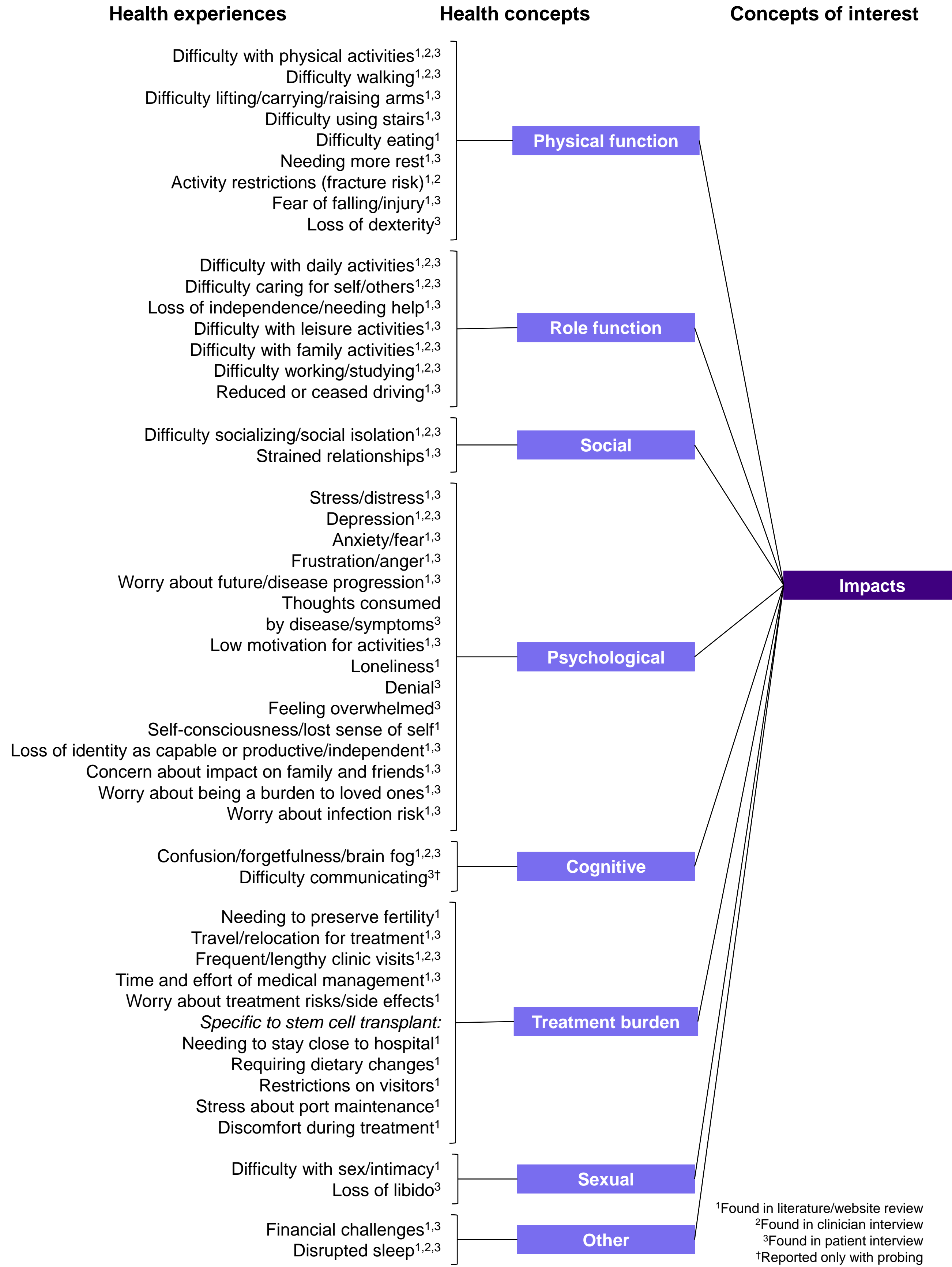
Figure 1. Conceptual model of symptoms



RESULTS

- The sample consisted of 15 patients, with a median age of 66 years (**Table 1**)
- Patients reported symptoms, symptomatic AEs, and impacts categorized into several domains in a conceptual model (**Figure 1**, **Supplementary Figure 1**, and **Figure 2**) that also integrated concepts from a literature review, website review, and clinician interview
- Findings from patient interviews generally confirmed findings from the literature review, website review, and clinician interview, with some new concepts identified
- All 15 patients spontaneously reported some form of pain as part of their RRMM experience (**Supplementary Table 1**). Most (73%) reported pain that first occurred prior to starting treatment. Fatigue was also widely reported (**Supplementary Table 2**)
- Pain and fatigue were commonly identified as the most bothersome symptoms/symptomatic AEs (**Supplementary Tables 1 and 2**)
- Patients reported numerous ways in which pain and fatigue impact their lives (quotes provided in **Supplementary Table 3**)

Figure 2. Conceptual model of impacts



RESULTS (CONT.)

Characterizing pain

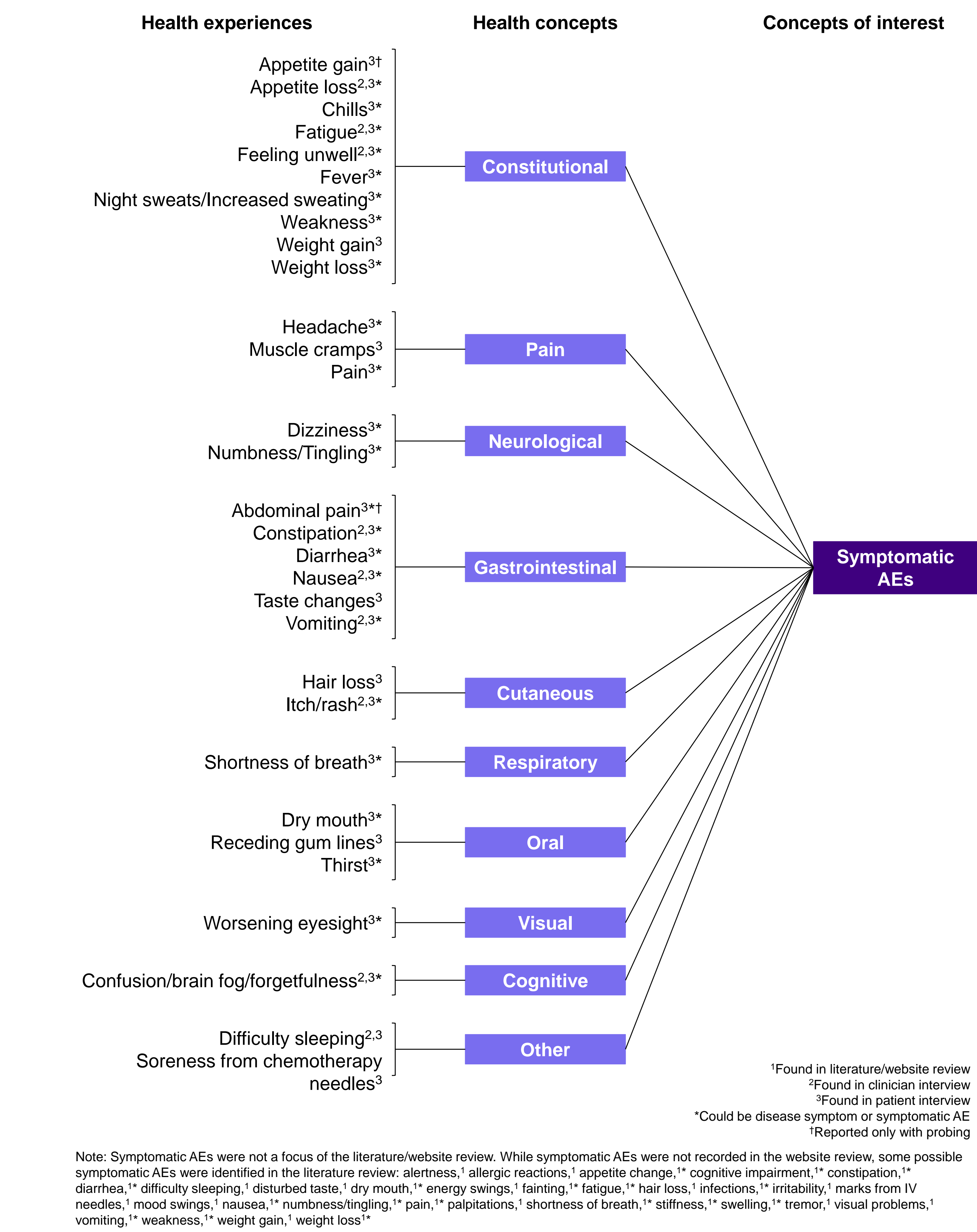
- When probed about pain symptoms, patients described their pain in many different ways
- Patients used various terms to name their pain, including bone pain, muscle pain, and body aches
- Patients reported pain throughout their body or limited to specific areas (e.g., spine, hips, knees)
- Patients offered a range of descriptors for their pain (e.g., crushing, heavy, tender, tingling, achy, uncomfortable, throbbing, stabbing, sore, arthritic, weakness)
- Pain was constant for some patients and intermittent for others
- Reported pain severity varied both within and between patients
- Some patients noted that their pain improved over the course of their RRMM, whereas others reported that it had not changed or had become worse over time
- Patients reported some types of pain that were associated with their treatment (e.g., leg cramps and neuropathy)

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Supplementary Figure 1. Conceptual model of symptomatic AEs



AE, adverse event.

Supplementary Table 1. Example quotes: Pain symptoms/symptomatic AEs

Theme	Example quotes
Location of pain: Throughout the body or limited to specific areas	My bones just felt – everything just felt really achy, just general – just unwell. I just kept saying everything hurts. – CH005 It's a dull pain in various parts of my body. In the spine, in the hips and... all over my body, there was bone pain. – CH009 Once in a while, it's in my hips, at the bottom of my spine, but usually, the pain is from my knees down to my ankles. – CH008
Naming of pain: Bone pain, muscle pain, body aches	Thinking back, I'd say the first sign that I experienced that something was kind of off is that I just found myself feeling unusual pain over time that I had not experienced before... It felt deep – kind of a deeper type of discomfort and pain, almost like it was in my – like deep in my muscles or maybe my bones. – CH002 I just felt like it was my bones, and it wasn't my muscles or anything. I just knew it was something that was really off. – CH005 I would probably move a certain way, and I would feel a... ooh, that hurts or that's tender. And I probably would go to move my arm, and I feel a little slight ache or tenderness or aching, and I'm like, wow, my muscles are not – something's going on. Having aches in my muscles or something has been strained. But again, since I hadn't been doing any exercise or any difficult housework, I'm saying these are minor body aches or moderate body aches. – US106
Description of pain: Crushing, heavy, tender, tingling, achy, uncomfortable, throbbing, stabbing, sore, arthritic, weak	[The spine pain] felt like crushing pain, like someone was pressed against me and pushing pressure on me, and it would help if I would sit up in my chair or wherever I was and try to stretch it out a little bit to give it some breathing room. It just felt smashed, crushed... Just if you've ever had a backache or thrown your back out, it just feels like just – it's heavy. It's pressure. It feels tender. – US103 I have bone pain a little bit up in my shoulders and in my hips and my legs. And that feels like it is a tingling sensation. It's just an achy pain. I guess pain is where you're hurting. I'm not really like hurting, like I'm in misery, but I am uncomfortable, and I'm kind of squirrely and want to move around, because it's like throbbing, maybe. – US105 I would feel like a stabbing – I'd say like a stabbing pain, just boom, boom, like a bump, and a consistent soreness, sore feeling [in back and hips]. – CH010 Almost arthritic, I'd say... I don't know how arthritis feels, but it was maybe like a stiffness... a dull aching pain. – CH003 I would almost have to say like an arthritic with a bone-on-bone type pain, where it's just really sharp pain and really hard to – you're trying to shake it off, trying to rub it off, but it's a more unrelenting type of pain. – CH004 I don't lift anything, but even five pounds, when I lift something, I can feel my arms just so weak that it hurt to my bones. I'm very weak. Everything that I do, it hurts. Body aches everywhere. – US104
Severity of pain: Varied between and within patients	It would cycle between maybe – when it did come, it was about a three to four, which wasn't that bad, to sometimes all the way up to like a seven or an eight when it was really bad on a day. – CH002 Some days it's better than others, maybe a three and a four. It all depends. – US104
Timing of pain: Constant or intermittent; dependent on time of day, activities, or weather	The pain that I was experiencing was just unremitting. It was just on all the time. – CH004 Depends on what I take with it or if I ignore it. If I ignore it and it doesn't get any worse, it's not throbbing, then it could take maybe four hours [to go away]. – CH003 [Hip pain] comes and it goes. I have good days and bad days. Some days, I have it, and some days, I don't. – CH006 The worst pain for me I always think is the morning period of time, anywhere from the time I get up until – at least for two, three hours afterwards. That's probably the toughest time. As the day goes on, it seems to subside a little bit. – CH004 When I walk a lot, that's when my back is really – when I'm really in pain. – CH001 I noticed if it was really cold, [the pain] was more bothersome. – CH005
Pain related to treatment	That [drug] gave me severe leg cramps, and they would come in the middle of the night and different times... It was a very sharp, sharp pain. – CH007 I have some neuropathy in my feet on occasion... It's more like a pain [than tingling and numbness]. – CH008
Pain as a most bothersome symptom/symptomatic AE	Pain, because sometimes it's so uncomfortable and intense, and I just think it's not going to go away. I would say pain, because I always have some sort of underlying pain. – CH005 The pain. The pain in my hips and my back...Because it debilitates me. It makes me not want to do anything else. I just want to sit and not move. – CH010

AE, adverse event.

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Supplementary Table 2. Example quotes: Fatigue symptoms/symptomatic AEs

Theme	Example quotes
Descriptions of fatigue	<p>Tiredness in my words has been – it’s been every level from minor to major and where I just need to relax to must take a nap, where I just can’t even keep my eyes open. I’ve even had it where I’m so exhausted and tired, I’m eating and I fall asleep. – US103</p> <p>I would say the tiredness – you work a little bit, you do a little bit of work, and I would get kind of tired and exhausted. I would fall asleep much earlier in the evening and then find that I would be tired all through the day. It’s more like a lack of energy, almost. Like it was a – not wanting to do different things. I just didn’t feel up to doing things. – CH007</p> <p>I’d say that the fatigue feels almost like – kind of like I was mentioning, like a weight on my chest or an anvil on my head, just feeling weighed down. Probably more effective would be like an anvil on my head. I feel like heavier. Gravity is doubled. (laughter) Just walking down the street or just going up a flight of stairs or – yeah, sometimes even just lifting my hands to wash dishes and so on – hand-wash dishes can feel like I have lead weights in my bones. – CH002</p>
Fatigue as a most bothersome symptom/symptomatic AE	<p>Probably the constant fatigue, because that gave me the awareness that I was never back to 100%. Your being fatigued is a way of your body sending you a message, everything is not complete or there’s something wrong or something’s going on. I think your body is meant to revive itself, especially after a good night, a good night’s sleep... but when you never get back to that state, you’re always feeling sick emotionally and you know things aren’t right. – US106</p> <p>I’m going to say the fatigue, because the pain can be addressed, but there’s nothing for the fatigue and this is what is keeping me from sometimes being able to do things, to take advantage of the time that I have. – CH003</p>

AE, adverse event.

Supplementary Table 3. Example quotes: Impacts of pain and fatigue

Domain	Example quotes
Physical function	<p>Yeah, I really can’t walk that much. And I should say it’s more than before, but for a while there, I was actually in a wheelchair. Then I graduated to a walker. And I can walk now without the walker, but I can’t walk a lot. When I walk a lot, that’s when my back is really – when I’m really in pain. – CH001</p> <p>Because I was at the grocery store yesterday, and I just had to take Uber back, because I just had a hard time. Lifting and carrying – just felt impossibly tired. – CH005</p> <p>And there were days that the pain is bad that I don’t even want to get up. You just feel tired all the time. You’re tired and weak. I can’t do much of the stuff that I used to be able to do. I just can’t do it. – CH009</p> <p>Yeah, when it would come on – if you were writing with a pen or a pencil, I’d have a hard time gripping the pen or pencil, because it would be either painful – and I lost some dexterity in holding things. I’m not able to – you know, sometimes I was not able to grip the pencil or pen. – CH007</p>
Role function	<p>Well, since my back pain is the biggest problem right now, if my back pain wasn’t as severe – because once in a while, like if I do have a good day, I can go shopping with my husband, because I can lean on the cart. So, it starts out – if my back is killing me, then I can’t do anything. Then your whole day’s ruined. – CH001</p> <p>Well, I have to push myself sometimes if I’m physically having a really bad day – physically and mentally – it’s just I know I need to get up and take that shower. I know I need to get up and do things. – CH005</p> <p>Yeah, far as my family, like I don’t cook as much. I’m not on my feet as much. We hired a cleaner. So, I can’t do the same stuff that I’m used to doing and really like to do myself because I’m particular about certain things. – CH010</p> <p>And being tired, it’s just not enjoyable. I wish I had the energy to go out or do things with my kids, and I’m – prefer to decline. – US103</p> <p>[Fatigue] was severe enough for me to need to file for disability. I couldn’t work anymore. I spent most of the day in bed. – CH003</p>
Psychological	<p>The pain that I was experiencing was just unremitting. It was just on all the time. I couldn’t get enough – it was disrupting my sleep. I was just worried all the time – I become – had become very depressed, very angry... – CH004</p> <p>As a husband, as a son, as a parent, you have to be able to do the best you can because I don’t want them to notice that I’m weak, that I’m tired, that I’m in pain. – US104</p>

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Disclosures

Timothy J. Inocencio, James Harnett, Glenn S. Kroog, Qiufei Ma, and Diana Rofail are full-time employees of Regeneron Pharmaceuticals, Inc. Allison Baker, Jessica Baldasaro, and Gerrit Vandenberg are full-time employees of Modus Outcomes. Julia Choi was a full-time employee of Modus Outcomes at the time of her involvement. Regeneron provided funding for Allison Baker’s travel and expenses associated with participation in ISPOR 2025. Allison Baker served as an investigator in this study, and Modus Outcomes received funding from Regeneron to conduct this study. Diana Rofail is a stockholder of Roche.