

# Outcomes of Care Among Patients With Gout in Europe: A Cross-sectional Survey

Ritch te Kampe<sup>1</sup> , Tim L. Jansen<sup>2</sup> , Caroline van Durme<sup>3</sup>, Matthijs Janssen<sup>2</sup> , Gudula Petersen<sup>4</sup>, and Annelies Boonen<sup>5</sup> 

**ABSTRACT.** *Objective.* To assess health- and patient-centered outcomes in gout across Europe, and explore patient-, care-, and country-level characteristics associated with these outcomes.

*Methods.* Patients with self-reported physician-diagnosed gout from 14 European countries completed an online survey. Multivariable mixed-effect logistic and linear regressions were computed for health outcomes (gout flare recurrence) and patient-centered outcomes (patient satisfaction with current medication, and unaddressed goals), accounting for clustering within countries. The role of patient-, care-, and country-level factors was explored.

*Results.* Participants included 1029 patients, predominantly diagnosed by a general practitioner (GP). One or more gout flares were reported by 70% of patients and  $\geq 3$  flares by 32%. Gout patients reported  $1.1 \pm 1.2$  unaddressed goals, and 80% were satisfied with current medication. Patients with  $\geq 3$  and  $\geq 1$  flares were less likely to be treated with urate-lowering therapy (ULT) (OR 0.52, 95% CI 0.39–0.70 and OR 0.38, 95% CI 0.28–0.53, respectively), but more likely to have regular physician visits (OR 2.40, 95% CI 1.79–3.22 and OR 1.77, 95% CI 1.30–2.41). Three or more gout flares were also associated with lower satisfaction (OR 0.39, 95% CI 0.28–0.56) and more unaddressed goals ( $\beta$  0.36, 95% CI 0.19–0.53). Notwithstanding, the predicted probability of being satisfied was still between 57% and 75% among patients with  $\geq 3$  flares but who were not receiving ULT. Finally, patients from wealthier and Northern European countries more frequently had  $\geq 3$  gout flares.

*Conclusion.* Across Europe, many patients with gout remain untreated despite frequent reported flares. Remarkably, a substantial proportion of them were still satisfied with gout management. A better understanding of patients' satisfaction and its role in physicians' gout management decisions is warranted to improve quality of care and gout outcomes across Europe.

*Key Indexing Terms:* gout, healthcare surveys, multilevel analysis, patient-reported outcome measures, quality of healthcare

Gout is highly prevalent and affects 1–4% of the population within Europe.<sup>1,2</sup> Gout flares are both unpredictable and recurrent, and are characterized by severe pain and limitations in

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<sup>1</sup>R. te Kampe, MSc, Department of Internal Medicine, Maastricht University Medical Center, Maastricht, Care and Public Health Research Institute (CAPHRI), Maastricht University, Maastricht, and Department of Rheumatology, VieCuri Medical Center, Venlo, the Netherlands;

<sup>2</sup>T.L. Jansen, MD, PhD, M. Janssen, MD, PhD, Department of Rheumatology, VieCuri Medical Center, Venlo, the Netherlands;

<sup>3</sup>C. van Durme, MD, Department of Internal Medicine, Maastricht University Medical Center, Maastricht, the Netherlands, and Centre Hospitalier Chrétien, Liège, Belgium; <sup>4</sup>G. Petersen, PhD, Grünenthal GmbH, Aachen, Germany; <sup>5</sup>A. Boonen, Professor, MD, PhD, Department of Internal Medicine, Maastricht University Medical Center, and Care and Public Health Research Institute (CAPHRI), Maastricht University, Maastricht, the Netherlands.

GP is a full-time employee in the department of Governmental Affairs & Patient Centricity at Grünenthal GmbH.

Address correspondence to R. te Kampe, Department of Rheumatology, Maastricht University Medical Centre, P.O. Box 5800, 6202 AZ Maastricht, the Netherlands. Email: r.tekampe@maastrichtuniversity.nl.

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physical function. If left untreated, a chronic course may occur, with persistent joint inflammation and development of tophi, potentially causing joint damage and disability.<sup>3,4,5,6</sup> In addition, the increased prevalence of comorbidities, such as cardiovascular and chronic kidney diseases and type 2 diabetes mellitus (T2DM), contribute to the effect of gout on overall functioning and health, healthcare costs, and even mortality.<sup>7,8,9,10</sup> Fortunately, the majority of patients with gout can be managed adequately. Different symptom-relieving drugs (colchicine, nonsteroidal antiinflammatory drugs, or prednisone) are available to control acute gout flare, and for long-term management, urate-lowering therapy (ULT) can be prescribed. The most recent European Alliance of Associations for Rheumatology (EULAR) guideline recommends consideration and discussion of starting ULT after a first gout flare.<sup>11</sup> Notwithstanding, outcomes of gout remain suboptimal,<sup>5,6,12,13</sup> and population studies show that 37–72% of patients have 1 or more gout flares.<sup>14,15,16</sup> Several factors contribute to suboptimal gout care, including low awareness of disease severity and its management among both physicians and patients, poor adherence to physicians' guidelines, poor adherence to medication, and finally the failure, intolerance, or contraindications (presence of comorbidities) of ULT.<sup>17,18,19,20</sup>

Around the turn of the 21st century, calling patients to account for their personal situation, needs, and involvement in disease management decisions gave impetus to more patient-centered healthcare.<sup>21</sup> In line with this, the Institute of Medicine emphasized the importance of patient-centeredness in addition to effectiveness, safety, timeliness, equitability, and efficiency as part of the 6 pillars of quality of care.<sup>22</sup> Patient-centered care is defined as measuring and responding to patient needs, experiences, and satisfaction with disease control.<sup>23</sup> This paradigm shift urged healthcare providers to integrate patients' needs, goals, experiences, and satisfaction with the traditional biomedical and patient-reported health outcomes.<sup>22,23,24</sup> While patient experiences of care can be pertinent outcomes by themselves, they might also provide insight into why treatments may not reach the expected health outcomes in a real-world setting. In gout, substantial research clarified the effect of gout on health outcomes.<sup>25,26</sup> However, there is little knowledge on the effect of care on patients' experiences (e.g., unaddressed goals, satisfaction),<sup>4,27</sup> nor about the relationship between these experiences and health outcomes. Finally, to fully understand the outcomes of care, it has been shown repeatedly that not only patient and care characteristics but also country characteristics play a role. For example, patients from higher-income countries had lower disease activity in rheumatoid arthritis (RA) and spondyloarthritis. This was partly explained by higher uptake of innovative (and expensive) medication. Moreover, a paradox was seen, as patients with RA living in less wealthy countries had higher disease activity but reported better well-being and lower fatigue.<sup>28,29,30</sup> Little is known about the association of country characteristics and geographic variation on gout health outcomes and experiences of care.<sup>31</sup> Knowledge about variations in these outcomes and their relationships with patient and care characteristics might help physicians across countries to understand priorities when enhancing quality of care for patients with gout.

The objective of this study was (1) to evaluate the impact of gout on gout-specific and generic health outcomes as well as on patient-centered outcomes in a real-world setting across 14 European countries; and (2) to explore which patient, care, or country characteristics contribute to variations in outcomes.

## METHODS

This study was a cross-sectional international European online survey. Data were collected between June 13 and September 30, 2018.

**Patients.** Patients aged > 18 years with self-reported physician-diagnosed gout from 14 European countries (Austria [AT], Belgium [BE], Denmark [DK], France [FR], Germany [GE], Ireland [IE], Italy [IT], Malta [MT], Netherlands [NL], Norway [NO], Portugal [PT], Spain [SP], Sweden [SE], and Switzerland [CH]) were considered eligible to participate in the study. Patients were primarily recruited from open panels of an online market research organization (Dynata and Toluna) and from patient associations, and incidentally by rheumatologists or general practitioners (GPs) who were aware of the study and could hand out a leaflet to potential participants. It was planned to include at least 1000 patients, with a sample size per country varying between 25 and 150, depending on country size. Prior to the survey's initiation, the participants received information on the objective of the study, were made aware that Grünenthal financed this study, and gave explicit consent. Following standards of market research,

ethical approval was not needed for a study with anonymous data collection (Market Research Society; www.mrs.org.uk).

**Data collection.** The content of the questionnaire has been determined by a working group comprising both patients and clinical experts in gout, to ensure that outcomes relevant to evaluating gout care were covered. The survey can be found in the Supplementary Data 1 (available with the online version of this article). The online survey took approximately 15 minutes and contained 5 parts: (1) patient sociodemographics (e.g., age, sex, country of residence, and employment status); (2) history of gout diagnoses (e.g., healthcare provider who diagnosed gout); (3) patient knowledge about gout and lifestyle; (4) current gout management, including patient perspective (e.g., gout treatment, satisfaction with current medication, number of flares in the past year, physician visits in the past year, and comorbidities); and (5) impact of gout (e.g., effect on mental and physical health, number of missed work days in the past year, treatment goals). In the absence of a validated measurement instrument for some of the domains, the working group formulated items to assess these goals. The English questionnaire was translated into 11 different languages and checked for user-friendly language.

**Outcomes.** Outcomes for the current study included recurrence of gout flares ( $\geq 3$  gout flares and  $\geq 1$  gout flare in the past year), self-reported impact of gout on mental and physical health (mean of 8 5-point Likert scale statements dichotomized as impact higher than median (3–5) vs impact below median (< 3)), missed work (for those employed,  $\geq 1$  work day missed in past year due to gout), patient satisfaction with current medication (5-point Likert scale dichotomized as satisfied [very satisfied and satisfied] vs less satisfied [very dissatisfied, dissatisfied, and neutral]), and finally, patients' unaddressed treatment goals. The unaddressed treatment goals were calculated as the sum of the treatment goals that patients indicated were relevant to them but were not addressed by their physician (max score = 9; Supplementary Data 1, questions D3 and D4, available with the online version of this article).

**Explanatory factors.** Explanatory factors were selected a priori as relevant covariables or confounders across 3 main domains. Patient factors were as follows: sex (male vs female), age (> 55 vs  $\leq 55$  yrs), employment status (employed vs not employed), highest level of education achieved (higher education [university and postgraduate] vs other qualifications), comorbidities (sum score [0–5] of chronic kidney disease, T2DM, obesity, hypertension, and hypercholesterolemia), and knowledge about disease and lifestyle (anchors range from 1 to 5: not knowledgeable [score 1–3] vs knowledgeable [score 4–5]). Care factors were as follows: currently treated with ULT (yes vs no), number of follow-up visits in the past year (dichotomized as  $\geq 2$ ), and type of physician who diagnosed gout (GP vs other). Country factors were as follows: gross domestic product (GDP) and healthcare expenditures (HCE) per capita in international dollars (Int\$) extracted from the Organisation for Economic Co-operation and Development (2018 or latest available; www.oecd.org) and geographic regions (West [NL, BE, FR, IR], middle [GE, AT, and CH], South [IT, PT, SP, MT], and North [DK, NO, SE]).

**Statistical analysis.** The study sample, including outcomes and explanatory factors of interest, was described for the total group as well as subsamples from different geographic regions.

Multivariable mixed-effect logistic and linear (for unaddressed treatment goals) regression models were computed for each outcome of interest, accounting for clustering of patients within countries (random intercept). In a first step, all patient- and care-related explanatory factors were introduced in the model for each outcome. Of note, the number of gout flares ( $\geq 3$ ) was included as a covariate when the outcome was the impact on mental and physical health,  $\geq 1$  day of work missed, satisfaction, or unaddressed treatment goals. In a second step, country-level factors (GDP, HCE, and geographic region) were each included separately in the final models to assess their independent contribution and the confounding effect of the country factors in the model. To avoid overadjustment, the role of the geographic region was explored in the 1-level model. Statistical analyses were performed using IBM SPSS, version 25.0 (IBM Corp.).

## RESULTS

A total of 1029 patients with gout from 14 European countries (range 12–186 patients per country) participated in this survey. Overall, approximately 90% of patients were recruited by research panels, except for Malta (n = 12). Inclusion by rheumatologists or GPs was incidental. Overall, 228/1029 (22%) patients were female, 554/1029 (54%) were older than 55 years, and 398/1029 (39%) had a higher education (Table 1; Supplementary Table 1 for characteristics per country, available with the online version of this article). Patients had on average  $1.8 \pm 1.5$  comorbidities. Patients were mainly diagnosed by their GP (746/1029 [73%]); 423/1029 (41%) patients had regular follow-ups ( $\geq 2$  in the past year), and 604/1029 (59%) patients were currently being treated with ULT. Among geographic regions, patients from Southern Europe were more likely to be younger than 55 years, employed, knowledgeable about the disease, and frequently treated with ULT. Southern European countries also had a markedly lower GDP and HCE.

*Gout outcomes across Europe.* In Europe, the proportion of patients with  $\geq 3$  and  $\geq 1$  gout flare in the past year was 32% (324/1029) and 70% (724/1029), respectively (Table 1; Supplementary Table 1 for characteristics per country, available with the online version of this article). The impact of gout on mental and physical health that was higher than

median was reported by 43% (443/1029) of the patients, and 52% of the employed patients (264/512) missed at least 1 day of work due to gout in the past year. A total of 80% (818/1029) of patients were satisfied with current medication, and patients revealed on average 1.1 (SD 1.2) unaddressed treatment goals. The top 3 unaddressed goals were to “forget about gout” (24%), “manage/minimize pain” (19%), and “prevent tophi” (18%; Figure 1).

*Factors associated with gout outcomes* Patients with  $\geq 3$  gout flares in the past year were less likely to be treated with ULT (OR 0.52, 95% CI 0.39–0.70) in comparison to patients with  $< 3$  flares. Also, patients with  $\geq 3$  flares visited a physician more frequently for their gout (OR 2.40, 95% CI 1.79–3.22), were more likely to report more comorbidities (OR 1.15, 95% CI 1.04–1.27), and were more likely to consider themselves knowledgeable about gout (OR 1.53, 95% CI 1.13–2.07; Table 2; for univariate associations for all outcomes, see Supplementary Table 2, available with the online version of this article).

Patients with  $\geq 1$  gout flares in the past year were even less likely to be treated with ULT (OR 0.38, 95% CI 0.28–0.53) in comparison to those with  $\geq 3$  flares. In comparison with those with  $\geq 3$  flares, patients with  $\geq 1$  flares were more likely to visit their physician more regularly (OR 1.77, 95% CI 1.30–2.41). The reverse association between male sex and older

Table 1. Patient, care, country characteristics, and gout health outcomes and patient-experienced outcomes overall and per geographic region.

	Western Europe, n = 331	Middle Europe, n = 210	Southern Europe, n = 388	Northern Europe, n = 100	Total, n = 1029
<b>Patient characteristics</b>					
Females	70 (21)	43 (21)	88 (23)	27 (27)	228 (22)
Age > 55 yrs	221 (64)	118 (56)	166 (43)	59 (59)	554 (54)
Higher education	146 (44)	46 (22)	181 (47)	25 (25)	398 (39)
Employed	124 (38)	105 (50)	242 (62)	41 (41)	512 (50)
Comorbidities, mean (0–5)	1.5 (1.3)	1.8 (1.4)	2.0 (1.6)	1.5 (1.2)	1.8 (1.5)
Knowledgeable about disease	104 (31)	58 (28)	228 (59)	20 (20)	410 (40)
Knowledgeable about lifestyle	235 (71)	187 (89)	332 (86)	75 (75)	829 (81)
<b>Care characteristics</b>					
Treated with ULT	179 (54)	116 (55)	262 (68)	47 (47)	604 (59)
Regular follow-ups ( $\geq 2$ )	141 (43)	93 (44)	172 (44)	17 (17)	423 (41)
Diagnosed by GP	258 (78)	150 (71)	262 (68)	76 (76)	746 (73)
<b>Country characteristics<sup>a</sup>, mean (SD)</b>					
GDP (Int\$, in thousands)	53.4 (10.2)	56.6 (4.9)	41.3 (2.1)	58.2 (5.5)	49.9 (9.5)
HCE (Int\$, in thousands)	5.0 (0.1)	6.1 (0.5)	3.4 (0.1)	5.6 (0.3)	4.7 (1.1)
<b>Gout health outcomes</b>					
$\geq 3$ gout flares in past year	106 (32)	61 (29)	116 (30)	41 (41)	324 (32)
$\geq 1$ gout flare in past year	235 (71)	128 (61)	296 (76)	65 (65)	724 (70)
<b>Patient-experienced outcomes</b>					
Impact of gout on mental and physical health	131 (40)	60 (29)	218 (56)	34 (34)	443 (43)
Missed $\geq 1$ day of work <sup>b</sup>	58 (47)	51 (49)	140 (58)	15 (37)	264 (52)
Satisfaction with current medication	273 (83)	165 (79)	306 (79)	74 (74)	818 (80)
Unaddressed treatment goals (0–9), mean (SD)	1.1 (1.3)	1.1 (1.3)	1.2 (1.1)	1.2 (1.4)	1.1 (1.2)

Values are expressed as n (%) unless otherwise indicated. <sup>a</sup> International dollars (Int\$) extracted from the Organisation for Economic Co-operation and Development (2018 or latest available; www.oecd.org). <sup>b</sup> Only employed patients (512/1029 [50%]). GDP: gross domestic product; GP: general practitioner; HCE: healthcare expenditures; ULT: urate-lowering therapy.

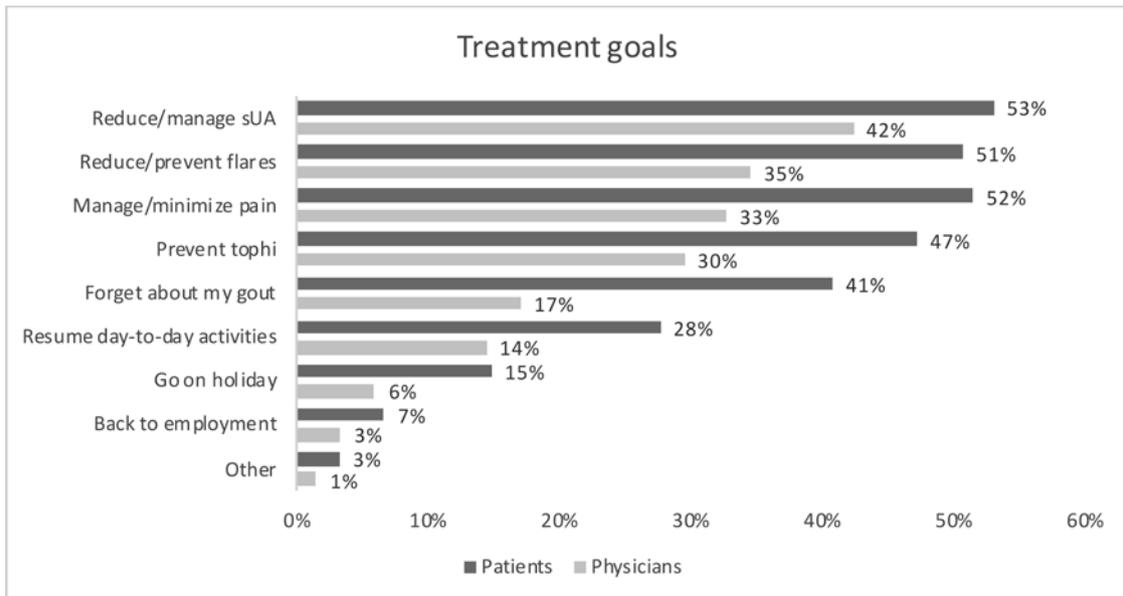


Figure 1. Treatment goals. sUA: serum uric acid.

Table 2. Results from multilevel multivariable logistic (OR and 95% CI) and linear ( $\beta$  and 95% CI) regressions for the various outcomes of interest.

	≥ 3 Gout Flares, n = 1029		≥ 1 Gout Flare, n = 1029		Impact of Gout on Mental and Physical Health, n = 1029		Missed ≥ 1 Day of Work, n = 512		Satisfaction, n = 1029		Unaddressed Goals, n = 1029	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	$\beta$	95% CI
<b>Patient factors</b>												
Sex (male vs female)	0.81	0.58–1.13	<b>0.67</b>	<b>0.46–0.99</b>	1.19	0.85–1.67	1.02	0.63–1.65	<b>2.02</b>	<b>1.39–2.93</b>	0.03	–0.16 to 0.22
Age (> 55 vs ≤ 55 yrs)	0.76	0.55–1.06	<b>0.55</b>	<b>0.39–0.78</b>	<b>0.72</b>	<b>0.52–0.99</b>	<b>0.36</b>	<b>0.23–0.58</b>	1.01	0.68–1.51	–0.03	–0.21 to 0.15
Education (high vs other)	0.75	0.55–1.02	0.76	0.56–1.04	0.86	0.64–1.16	0.78	0.51–1.20	0.86	0.59–1.24	0.08	–0.08 to 0.24
Employment (work vs nonwork)	1.04	0.75–1.45	1.15	0.82–1.61	1.22	0.89–1.69	–	–	1.01	0.68–1.50	0.05	–0.13 to 0.23
Comorbidities, mean (0–5)	<b>1.15</b>	<b>1.04–1.27</b>	1.06	0.95–1.18	<b>1.22</b>	<b>1.10–1.35</b>	<b>1.16</b>	<b>1.01–1.33</b>	1.06	0.94–1.19	–0.02	–0.08 to 0.03
Gout flares past year (≥ 3 vs < 3)	–	–	–	–	<b>2.59</b>	<b>1.91–3.50</b>	<b>2.48</b>	<b>1.59–3.87</b>	<b>0.39</b>	<b>0.28–0.56</b>	<b>0.36</b>	<b>0.19–0.53</b>
Knowledgeable about disease (yes vs no)	<b>1.53</b>	<b>1.13–2.07</b>	1.25	0.91–1.71	<b>1.35</b>	<b>1.01–1.81</b>	1.30	0.85–1.99	<b>1.68</b>	<b>1.15–2.44</b>	–0.03	–0.19 to 0.13
Knowledgeable about lifestyle (yes vs no)	0.92	0.64–1.32	1.18	0.82–1.70	<b>1.96</b>	<b>1.36–2.84</b>	1.60	0.91–2.80	<b>2.73</b>	<b>1.86–4.00</b>	0.20	–0.01 to 0.39
<b>Care factors</b>												
ULT treatment (yes vs no)	<b>0.52</b>	<b>0.39–0.70</b>	<b>0.38</b>	<b>0.28–0.53</b>	<b>0.59</b>	<b>0.44–0.80</b>	0.76	0.50–1.16	<b>2.85</b>	<b>2.00–4.06</b>	0.02	–0.14 to 0.19
Regular follow-ups (≥ 2 vs < 2)	<b>2.40</b>	<b>1.79–3.22</b>	<b>1.77</b>	<b>1.30–2.41</b>	1.02	0.76–1.36	<b>2.75</b>	<b>1.82–4.17</b>	1.04	0.73–1.48	<b>–0.17</b>	<b>–0.33 to –0.01</b>
Diagnosed by GP (yes vs no)	0.77	0.56–1.05	1.02	0.73–1.42	<b>0.69</b>	<b>0.50–0.94</b>	<b>0.48</b>	<b>0.31–0.75</b>	1.18	0.81–1.72	–0.02	–0.19 to 0.16

Values in bold are statistically significant. GP: general practitioner; ULT: urate-lowering therapy.

age (> 55 yrs) for ≥ 1 gout flares was significant (OR for men: 0.67, 95% CI 0.46–0.99, and OR for > 55 yrs: 0.55, 95% CI 0.39–0.78; Table 2).

Patients experiencing a higher-than-median impact of gout on their mental and physical health were less frequently treated with ULT (OR 0.59, 95% CI 0.44–0.80) in comparison to patients with a below-median impact on their mental and physical health

(Table 2). Moreover, patients who experienced ≥ 3 gout flares (OR 2.59, 95% CI 1.91–3.50) were more likely to report more comorbidities (OR 1.22, 95% CI 1.10–1.35). Nevertheless, these patients considered themselves knowledgeable about lifestyle (OR 1.96, 95% CI 1.36–2.84) and gout (OR 1.35, 95% CI 1.01–1.81). Of note, patients diagnosed by a GP (OR 0.69, 95% CI 0.50–0.94) or who were older than 55 years (OR 0.72,

95% CI 0.52–0.99) experienced less impact from gout on their mental and physical health (Table 2).

Patients missing  $\geq 1$  working days due to gout in the past year were more likely to have experienced frequent gout flares (OR 2.48, 95% CI 1.59–3.87), visited a physician more frequently (OR 2.75, 95% CI 1.82–4.17), and had a 1.16 (95% CI 1.01–1.33) increased risk of having comorbidities. On the other hand, patients diagnosed by a GP (OR 0.48, 95% CI 0.31–0.75), or who were older than 55 years (OR 0.36, 95% CI 0.23–0.58) were less likely to have missed working days (Table 2).

Patients satisfied with their current medication were less likely to experience frequent gout flares (OR 0.39, 95% CI 0.28–0.56) and were more likely to be in treatment with ULT (OR 2.85, 95% CI 2.00–4.06). These patients scored themselves as being knowledgeable about lifestyle (OR 2.73, 95% CI 1.86–4.00) and gout (OR 1.68, 95% CI 1.15–2.44), and were more likely male (OR 2.02, 95% CI 1.39–2.93; Table 2).

While frequent gout flares ( $\beta$  0.36, 95% CI 0.19–0.53) were independently associated with a higher number of unaddressed treatment goals, more regular visits to their physician ( $\beta$  –0.17, 95% CI –0.33 to –0.01) were associated with fewer unaddressed treatment goals (Table 2).

*Role of country characteristics.* Country of residence ( $n = 14$ ) as a second level did not contribute significantly to variance in any of the gout outcomes explored (random intercept covariance  $P > 0.05$ ). Further exploration of specific country characteristics revealed that per thousand Int\$ GDP and HCE, there was a 1.02 (95% CI 1.00–1.05) and 1.27 (95% CI 1.01–1.61) increased risk of having  $\geq 3$  gout flares, and a negative association with higher impact on mental and physical health (significant only for HCE; Table 3). No associations were seen for GDP and HCE on patient-centered outcomes. In comparison with patients from Western European countries, patients from Northern Europe more frequently reported having  $\geq 3$  gout flares (OR 1.77, 95% CI 1.08–2.90), and those residing in Middle Europe less frequently had  $\geq 1$  flare (OR 0.51, 95% CI 0.34–0.77) and

less impact on mental and physical health (OR 0.45, 95% CI 0.30–0.68). Also, patients from Southern and Middle Europe were less satisfied (OR 0.44, 95% CI 0.28–0.68 and OR 0.56, 95% CI 0.34–0.92, respectively), in comparison with patients in Western European countries. Of note, there was no relevant confounding of country characteristic factors on covariates of the final model.

## DISCUSSION

Among patients from different European countries, this study observed a substantial impact of gout on a broad range of health outcomes, whereas the effect on patient-centered outcomes was less striking. Overall, 70% of the patients reported at least 1 gout flare in a 12-month period, and 32% at least 3 flares. In addition, 43% of patients reported an effect on mental and physical health, and 52% of those employed missed at least 1 working day due to gout in the past year. Nevertheless, 80% of the patients were satisfied with their current medication, and patients experienced on average 1.1 unaddressed treatment goal. Multivariable exploration revealed that gout flares contributed substantially to worse health and patient-centered outcomes. As expected, current ULT was consistently associated with better health and patient-centered outcomes, except for unaddressed treatment goals. Contrary to our hypothesis, patients from wealthier countries reported more frequent gout flares.

Findings on the frequency of gout flares in this study are comparable to other European studies within population settings, where the frequency of patients diagnosed with gout with at least 1 gout flare within a 12-month period varied between 37% to 72%.<sup>14,15,16</sup> Similarly, the ULT prescription rate of 59% in our study was within the reported range of 25–73% in other GP and population settings.<sup>14,15,32–36</sup> Importantly, our study pointed to an inverse relationship between low ULT use and gout flares.<sup>15,32</sup> This raises the important question of why patients were not treated adequately despite recurrent flares. Strikingly, these patients also visited their physician more frequently. While

Table 3. Results from multilevel multivariable logistic (OR and 95% CI) and linear ( $\beta$  and 95% CI) regressions for the various outcomes of interest.

	$\geq 3$ Gout Flares, n = 1029		$\geq 1$ Gout Flare, n = 1029		Impact of Gout on Mental and Physical Health, n = 1029		Missed $\geq 1$ Day of Work, n = 512		Satisfaction, n = 1029		Unaddressed Goals, n = 1029	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	$\beta$	95% CI
Country factors <sup>a</sup>												
GDP (Int\$, in thousands)	<b>1.02</b>	<b>1.00–1.05</b>	1.01	0.98–1.03	0.98	0.96–1.01	1.01	0.99–1.04	1.01	0.98–1.04	0.00	–0.01 to 0.01
HCE (Int\$, in thousands)	<b>1.27</b>	<b>1.01–1.61</b>	0.93	0.74–1.17	<b>0.70</b>	<b>0.56–0.87</b>	1.16	0.92–1.45	1.16	0.88–1.52	–0.01	–0.09 to 0.06
European geographic region												
Western Europe	Ref		Ref		Ref		Ref		Ref		Ref	
Middle Europe	0.77	0.51–1.15	<b>0.51</b>	<b>0.34–0.77</b>	<b>0.45</b>	<b>0.30–0.68</b>	1.01	0.56–1.84	<b>0.56</b>	<b>0.34–0.92</b>	0.06	–0.22 to 0.23
Southern Europe	0.71	0.50–1.02	1.16	0.80–1.68	<b>1.55</b>	<b>1.10–2.17</b>	1.27	0.76–2.13	<b>0.44</b>	<b>0.28–0.68</b>	0.05	–0.15 to 0.24
Northern Europe	<b>1.77</b>	<b>1.08–2.90</b>	0.74	0.44–1.23	0.64	0.38–1.06	0.63	0.28–1.43	0.66	0.37–1.19	0.02	–0.26 to 0.30

GDP and HCE are derived from separate models; only minor differences were observed in individual covariates between the separate models. The European geographic region was derived from a separate 1-level model. Values in bold are statistically significant. <sup>a</sup>International dollars (Int\$) extracted from the Organisation for Economic Co-operation and Development (2018 or latest available; www.oecd.org). GDP: gross domestic product; HCE: healthcare expenditures.

we adjusted for comorbidities, including obesity, there might be residual confounding, as the severity (not the number) of comorbidities might play a role in either causing more severe gout and/or being a contraindication for a more aggressive disease, thus leading to suboptimal care (undertreatment). Unfortunately, we had no data on contraindications, past failure, or intolerance of ULT. Of note, Harrold, *et al* reported that only 9.6% of the GPs were aware of the guidelines and adhered to recommended treatment for gout flares in only 47% of the cases.<sup>37,38</sup> Somewhat counterintuitively, patients with more flares considered themselves more knowledgeable about gout. This seems to indicate that knowledge is not always a barrier to optimal treatment, as suggested by Rai *et al*.<sup>13</sup> It remains difficult to know whether patients experiencing frequent gout flares had truly difficult gout to treat or whether physicians were insufficiently aware of treatment options.<sup>39</sup> Gout flares were not benign but had large impact on mental and physical health and on work participation. Literature affirms that patients who reported  $\geq 3$  gout flares within a 12-month period had nearly a 3-fold increase in the odds of reporting symptoms of depression.<sup>40</sup> In addition, a 1-year prospective observational study showed loss of working days due to flares in 78% of patients.<sup>41</sup>

In addition to health outcomes, we demonstrated a negative association between frequent flares and patient-centered outcomes. The overall satisfaction rate of 80% was comparable to Khanna, *et al*, where satisfaction with current ULT ranged from 75% to 95% in a managed care setting.<sup>42</sup> Of interest, knowledge about gout and about lifestyle were both associated with higher satisfaction, supporting the relevance of patient-centered care. Gout flares were also related to unaddressed goals. While 54% (164/305) of patients without gout flares had at least 1 unaddressed treatment goal, this increased to 73% (235/324) in those with  $\geq 3$  gout flares. Interestingly, “forget about my gout” was the most frequent unaddressed treatment goal. It is likely that this domain integrates the worries gout causes for patients, such as the unexpected nature of gout flares, the need to adhere to lifestyle changes and medication intake, and anxiety about the long-term effects of gout. The unaddressed treatment goals highlight the importance of actively addressing goals, needs, and expectations in the patient–physician relationship.

The high satisfaction rate, in contrast to the high proportion of patients with untreated gout flares, was striking. Further analyses indicated that the predicted probability of patients with  $\geq 3$  gout flares, but who are not being treated with ULT, and were nevertheless satisfied, was as high as 57–75%; this was independent of frequency of physician visits (but dependent on the remaining explanatory factors of satisfaction). In other words, “suboptimal” gout treatment does not result in a dissatisfied patient, and more insight into the role of satisfaction with quality of care and health outcomes is needed. Currently, it remains difficult to answer the question of what an acceptable pain level or frequency of gout flares is for patients without increasing medication.<sup>43</sup> In particular, the ongoing debate of a “treat to uric acid” target opposed to a “treat to avoid symptoms” target requires attention on the relation between patient satisfaction and flares.<sup>44</sup> In line with this, regular longitudinal assessments

of satisfaction with gout management in a daily practice cohort can provide more insight into factors contributing to satisfaction and its causal relation with health outcomes.

This study specifically aimed to understand similarities and differences in health and patient-centered outcomes across European countries. Results were interesting but challenging. While it was expected that patients from wealthier countries had better health outcomes, patients from countries with a higher HCE and GDP more frequently had  $\geq 3$  gout flares. It is possible that lifestyle, specifically alcohol use and obesity (partially adjusted for), is a strong risk factor for gout. In addition, it might be that in wealthier countries, patients have more difficult gout to treat in view of more severe comorbidities, as patients with heart or kidney failure might survive longer in those countries. Another striking finding was the lower satisfaction rate among patients from Southern and Middle Europe. We can only speculate about potential causes such as communication, accessibility, and out-of-pocket costs for treatments. Insight into population health and satisfaction with healthcare in the different countries would have been useful as a benchmark for interpreting our data.<sup>45,46</sup>

Limitations that are inherent to cross-sectional and survey-based studies should be discussed. First, enrolled gout patients might not be fully representative of the average gout patients in each of the participating European countries. Moreover, included patients had self-reported gout, further contributing to potential selection bias. However, self-reported physician-diagnosed gout has acceptable reliability and sensitivity, and seems more appropriate for epidemiologic studies.<sup>47,48</sup> Third, as this was an online self-reported survey, misclassification (information bias) and recall bias might have affected the findings of this study. While proposals have been made to improve assessment of self-reported gout flares, consensus on the most accurate approach has not been reached.<sup>49,50</sup> Further, stigma may influence health beliefs and coping plans, and may affect people seeking health services. Importantly, in order to assess largely unexplored domains, specifically for patient-centered outcomes, several of the survey questions were self-composed. Nevertheless, care was taken that questions were unambiguous, unidimensional, and tested among patients. Last but not least, in view of the cross-sectional nature of our study, conclusions about causality related to confounding by indication cannot be made.

In Europe, a substantial proportion of patients with gout experience gout flares but receive no ULT. Patients with frequent flares were more likely to visit their physician regularly. Interestingly, a substantial proportion of these patients were not dissatisfied with their gout management. Findings suggest that more stringent control of gout flares by physicians, even if patients seem satisfied, would contribute to improved gout outcomes, leading to eventually fewer unaddressed treatment goals and even higher satisfaction.

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## ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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