Arthritis Care & Research
DOI 10.1002/acr.23147

Illness Perceptions Predict Mortality in Patients with Gout: A Prospective Observational Study

Anna Serlachius PhD[1], Greg Gamble MSc[2], Meaghan House MPH[2], Zoe L Vincent PhD[2], Julie Knight BA[2], Anne Horne MBChB[2], William J. Taylor PhD FRACP[3], Keith J Petrie PhD[1], Nicola Dalbeth MD FRACP[2].

Affiliations:

1. Department of Psychological Medicine, Faculty of Medical and Health Sciences, The University of Auckland
2. Bone and Joint Research Group, Department of Medicine, Faculty of Medical and Health Sciences, The University of Auckland
3. Department of Medicine, University of Otago Wellington

Financial support: This study was funded by Arthritis New Zealand, the University of Auckland Faculty Research Development Fund, and the Henry Cotton Charitable Trust.

Conflict of interest statement: William J Taylor: consultancy, honoraria or speaker fees from Pfizer (<$10,000), educational grants from Abbvie, Roche, Pfizer (all <$10,000), all outside the submitted work. Nicola Dalbeth: consultancy, honoraria or speaker fees from Takeda (<$10,000), Teijin (<$10,000), Menarini (<$10,000), Pfizer (<$10,000), ArdeaBiosciences/AstraZeneca (<$10,000), Cymabay (<$10,000), and Crealta (<$10,000), all outside the submitted work. The other authors have no disclosures.

Received: Jul 24, 2016; Revised: Sep 27, 2016; Accepted: Nov 01, 2016

Corresponding Author: Dr Anna Serlachius, Department of Psychological Medicine, The University of Auckland, Auckland, New Zealand. Email: a.serlachius@auckland.ac.nz. Tel: +64 9 923 3073.

Word count: 2,295

References: 15

Tables: 3

Running Head: Illness Perceptions and Mortality in Gout

ABSTRACT

Objective: To examine whether illness perceptions independently predict mortality in early-onset gout.

Methods: Between December 2006-January 2014, a total of 295 participants with early-onset gout (<10 years) were recruited in Auckland and Wellington, New Zealand. The participants were followed up until February 2015 and mortality information was collected. Participants with complete data were included in the current study (n=242). Cox proportional hazards models were used to examine the association between illness perceptions and risk of mortality, after adjusting for covariates associated with disease severity and mortality in gout.

Results: In a Cox proportional hazards model adjusted for predictors of disease severity and mortality in gout (number of tophi, serum urate, flare frequency), consequence beliefs, identity beliefs, concern beliefs, and emotional response to gout were associated with all-cause mortality (Hazard Ratios: 1.29, 1.15, 1.18, 1.19 respectively, p-values <.05). In the fully-saturated model, the association between consequence beliefs and mortality remained robust after additional adjustment for ethnicity, disease duration, diuretic use, serum creatinine, and pain score (HR=1.18, CI: 1.02-1.37, p=0.029).

Conclusion: Negative beliefs regarding the impact of gout and severity of symptoms, as well as concerns about gout and emotional response to gout are independently associated with all-cause mortality. Illness perceptions present important and potentially modifiable risk factors to target in future interventions.

Key words: gout, illness perceptions, mortality

SIGNIFICANCE AND INNOVATIONS

- Illness perceptions predict mortality in several different chronic diseases, but this association has not been previously examined in gout patients.
- We found that illness perceptions (i.e. consequence beliefs, identity beliefs, concern beliefs and emotional response) are independently associated with all-cause mortality in gout, after adjusting for covariates associated with disease severity and mortality in gout.
- Negative beliefs regarding the impact of gout (i.e. consequence beliefs) remained an independent predictor of all-cause mortality after further adjustment for several important covariates associated with comorbidity and mortality in gout.
- The findings of this study underline the importance of patients' perceptions of their illness in the long-term management and outcome of their disease.

INTRODUCTION

There is a growing literature that illness perceptions are predictive of mortality in multiple patient groups including patients with end-stage renal disease (1), heart disease (2), and diabetes (3). Many of these chronic conditions are comorbidities of gout, a common form of inflammatory arthritis which develops in close to 4% of the American population (4). Gout is a treatable condition in which monosodium urate crystals deposit in the joints and periarticular tissues, causing inflammation and painful flares of arthritis. In more severe cases tophaceous gout may also occur. Although treatable, the prevalence of gout is increasing and patients often struggle to successfully manage the condition (5). Advanced gout is associated with impaired mobility and reduced health-related quality of life, as well as an increased risk of all-cause mortality (5).

Illness perceptions form part of the Common Sense Model of self-regulation (CSM), a theory developed to describe how individuals come to understand their illness by constructing illness beliefs about their condition and the treatment (6). These illness beliefs help people understand, cope and manage their condition. Illness perceptions (i.e. illness beliefs) are important determinants of self-care behaviours, and positive/adaptive illness beliefs are associated with improved outcomes and improved adherence in chronic illness (7, 8). For example, studies have examined the association between illness perceptions and several clinical and behavioural outcomes including self-management behaviours, recovery (7) and survival (1-3) across different patient groups.

According to the CSM, illness beliefs are grouped into five categories: identity (how the illness is defined), timeline (beliefs regarding duration), cause (beliefs regarding cause), controllability (beliefs regarding controllability of illness), and consequences (beliefs regarding how illness will impact one's life). We have previously examined how negative or pessimistic illness beliefs about gout are associated with poorly controlled disease, lower

adherence to urate-lowering therapy, and progression of musculoskeletal disability in gout (9). We therefore wanted to expand on these findings to examine whether illness perceptions predict mortality in gout. To our knowledge, no other studies have examined this association. Our aim was thus to examine whether patients' illness perceptions independently predict mortality, controlling for important covariates associated with disease severity and mortality in gout patients (10, 11) including number of tophi, serum urate, and flare frequency.

METHODS

Setting and Participants

Participants were recruited from primary and secondary care clinics and using community advertising in Auckland and Wellington, New Zealand to participate in a prospective observational study. Inclusion criteria included: (1) a physician's diagnosis of gout as defined by the 1977 American Rheumatism Association preliminary gout classification criteria (12), (2) first onset of gout-related symptoms occurring less than ten years prior, (3) ability to complete forms in English and provide informed consent.

Recruitment began in December 2006 and was completed in January 2014, with a total of 295 participants recruited in this time-frame. The participants were followed up until the 1st of February 2015. Participants with complete data on illness perceptions and important covariates were included in the current study, resulting in a sample size of 242 participants. The study was conducted in accordance to the Helsinki Declaration and was approved by the New Zealand Multi-Regional Ethics Committee.

Illness Perceptions

Illness perceptions were measured using a gout-specific Brief Illness Perceptions Questionnaire (Brief IPQ)(13), which examines the five key illness perception dimensions as well as items measuring the patient's concern, understanding, and emotional response to

illness. The eight item questionnaire consisted of the following items measured on a 0-10 Likert scale, with higher scores indicative of stronger endorsement: consequences (how much gout affects the patient's life), timeline (how long the patient thinks gout will continue), personal control (how much control the patient has over his or her gout), treatment control (how much the patient's medication can control gout), identity (severity of gout symptoms), concern (how concerned the patient is about his or her gout), understanding (how well the patient feels he/she understand their gout), and emotional response (how much gout affects the patient emotionally.) The Brief IPQ has satisfactory reliability and validity across a range of chronic illnesses (14).

Outcome Measures

All-cause mortality was our primary outcome measure, with data censored at 1st February 2015 or date of death, whichever came first. Mortality was assessed from primary and secondary care electronic health records and/or death certificates and participants were assumed alive in the absence of evidence of recorded death (11). All-cause mortality was grouped into cardiovascular causes (myocardial infarction, aortic dissection, congestive heart failure, stroke or pulmonary embolism) and non-cardiovascular causes (accident, cancer, infection, multiple organ failure, renal disease, suicide or unknown).

Covariates

Demographic data, including sex, age and ethnicity were collected at baseline. Comprehensive gout history (confirmation of diagnosis, disease duration, frequency of gout flares, gout treatments), medical history, and a physical examination including a tophus count were recorded by trained health professionals at baseline. Frequency of gout flares in the past three months ranged from 0-90, with 90 indicating that the patient was having constant flares over that time period. Questionnaires were also administered at baseline including the pain

visual analog score (100-mm scale). Lastly, laboratory tests were obtained for clinical markers including serum urate and serum creatinine.

Statistical Analyses

Univariate analyses were used to examine differences in all the predictor variables between the participants with and without missing data using t-tests for continuous variables or Chi-squared tests for categorical variables. We also examined inter-correlations between the Brief IPQ items using Pearson's correlations.

Cox proportional hazards models were performed to evaluate illness perceptions as predictors of all-cause mortality. Firstly, we used a univariate model which assessed the individual predictive ability of each of the eight items from the Brief IPQ. In the second model we added sex and age as covariates. In the third model, we added number of tophi, serum urate and flare frequency to the model; covariates associated with disease severity of which serum urate and tophi have previously been identified as independent predictors of mortality in gout patients (10). Lastly, we also conducted a fully saturated model, where we included other risk factors including ethnicity, disease duration, diuretic use, serum creatinine, and pain score. In each model, the Brief IPQ predictors were entered separately. As a sensitivity analysis, we also stratified our analyses by age (using tertiles), to account for possible confounding by age. Lastly, we repeated the analyses using the full sample to account for any possible confounding by excluding cases with missing data.

Proportionality assumptions were tested by assessing time dependent covariates together in the adjusted model using the SAS Proc PHREG Proportionality Test. Proportionality assumptions were verified ($p>.05$). We also plotted Schoenfeld residuals for all the covariates (please see Supplementary Figures 1-13). The analyses were performed using SPSS (version 22) and the proportionality tests using SAS (version 9.4).

RESULTS

A total of 295 participants were recruited of which 242 formed our analytic sample (see Table 1). There were no significant differences between patients in the analytic sample and those with missing data on any of the predictor variables.

The study sample characteristics in Table 1 shows that mean age was 58.5 years (SD 14.7) and the majority of participants were male (72.7%). The majority of patients identified as European New Zealanders/other, with 27.3% identifying as Māori or Pacific ethnicity. The average disease duration from when gout was diagnosed was 5.3 years (3.1 SD). There were significant comorbidities in our sample, with 43.4% reporting hypertension, 49.6% hypercholesterolaemia, 13.6% type 2 diabetes, and 25.2% kidney disease.

Survival Data

The mean follow-up duration was 5.1 (1.6) years (total of 1,511 patient years accrued). During this period, 33 participants (13.6%) of people in the analytic sample died. Cardiovascular deaths made up 58% of the deaths in our sample.

Illness perceptions

Pearson's correlations between the illness perception subscales demonstrated moderate inter-correlations (r=0.21-0.68), which is consistent with previous studies (14).

Predictors of mortality

In the un-adjusted Cox proportional hazards model, where we examined the individual illness perceptions as predictors of mortality (see Table 2, Model 1), consequence and identity beliefs were significant predictors of all-cause mortality (HR=1.22, 95% CI, 1.10 to 1.36, p<.001; HR=1.14, 95% CI, 1.02 to 1.14, p=.024 respectively). In Model 2 which adjusted for age and sex, consequence beliefs (HR=1.28, 95% CI, 1.15 to 1.43, p<.001), identity beliefs (HR=1.17, 95% CI, 1.04 to 1.32, p=.009) and emotional response (HR=1.16, 95% CI, 1.05 to

1.29, p=.005) were significant predictors of mortality. Lastly, after further adjustment for number of tophi, serum urate and flare frequency in Model 3, consequence beliefs, identity beliefs, concern beliefs and emotional response were all associated with higher mortality risks (HR 1.29, 1.15, 1.18, 1.19 respectively, p-values <.05).

In Table 3, we employed a fully-saturated model which adjusted for additional risk factors. In this model, the only Brief IPQ item which remained associated with mortality was consequence beliefs (HR=1.18, CI: 1.02-1.37, p=0.029). These last results suggest that keeping the other covariates constant, a 1-point increase in consequence beliefs (measured on a 0-10 Likert scale) is associated with an 18% increase in the hazard of death.

To account for possible confounding by age, we conducted a sensitivity analysis where we compared our results to a stratified analysis (please see Supplementary Table 1). In the stratified Cox proportional hazards model the results were similar in direction and magnitude to the non-stratified analysis. For example, in the stratified analysis (by tertiles), emotional response to gout was a statistically significant predictor of mortality after adjusting for sex, number of tophi, serum urate and flare frequency (HR=1.19, 95% CI, 1.06 to 1.33, p=.004), comparable to Model 3 in Table 2. Lastly, we also repeated our analyses with the full sample and found that the results were consistent with the results obtained from the analytic sample with no missing data.

DISCUSSION

Our study provides evidence that illness beliefs are associated with increased risk of mortality in gout patients, independent of other important clinical and demographic variables. In particular, we found beliefs regarding the negative consequences of having gout, beliefs regarding severity of gout symptoms, concerns about having the illness, and an increased emotional response to gout predicted mortality. In our analyses, these four Brief IPQ beliefs remained significant predictors of all-cause mortality after adjusting for multiple factors associated with disease severity and mortality in gout patients (10). Furthermore, in our fully saturated model, although over-specified, consequences remained a significant predictor of mortality, indicating the robust association between the perceived impact of gout and higher mortality risk.

The findings of this study underline the importance of patients' perceptions of their illness in the long-term management and outcome of their disease. A negative view of the consequences of gout is likely to impact on the way patients monitor and self-manage their illness. Importantly, a person's view of the consequences of gout is subjective, and may have little to no association with objective clinical markers or prognosis (15). Yet, negative or pessimistic perceptions of outcome are likely to affect patients' motivation to adhere to recommended treatments and health behaviours. In a previous study from the same cohort of patients, we found illness perceptions predicted lower adherence, as well as progression of musculoskeletal disability in gout (9). Similar to the current study, consequence beliefs and higher emotional response were associated with negative disease outcomes.

An important aspect of the findings is that, unlike many of the demographic and clinical co-morbidities present in gout, illness perceptions can be modified and, based on previous studies (7, 8), this may be a promising intervention to improve both clinical and psychological outcomes for patients with gout. The findings of this study suggest that

targeting negative beliefs regarding the impact of gout and severity of symptoms, as well as concerns about gout and emotional response to gout, have the potential to impact on self-management practices and future mortality. Developing individualised interventions for gout patients, which target in particular maladaptive beliefs regarding the negative consequences of having gout remains an important area for future research.

The strengths of our study include the detailed clinical assessments at baseline as well as the comprehensive and systematic collection of death data, allowing for thorough reporting of the cohort for death status and cause of death. Limitations include a modest sample size with a small number of reported events (n=33) for the survival analysis, indicating the need for our results to be replicated in larger samples. Secondly, our cohort included different ethnic groups prevalent in New Zealand, which may limit the generalisability of the findings. A further limitation includes our selection criteria which excluded those with longer disease duration (>10 years), thus results may not apply to all gout patients. However, despite the relatively short disease duration, a significant proportion of patients had comorbidities and presence of tophi at baseline.

In summary, our findings contribute to the growing literature on the association between illness perceptions and mortality in patients with chronic illness. In our study, negative beliefs regarding the impact of gout, the severity of gout symptoms, as well as being more concerned about gout and increased emotional response to gout predicted increased risk of all-cause mortality, independent of covariates associated with disease severity and mortality in gout.

AUTHOR CONTRIBUTION STATEMENT:

Anna Serlachius: 1a, 1c, 2, 3

Greg Gamble: 1a, 1c, 2, 3

Illness Perceptions and Mortality in Gout

Meaghan House: 1b, 2, 3

Zoe L Vincent: 1b, 2, 3

Julie Knight: 1b, 2, 3

Anne Horne: 1b, 2, 3

William J Taylor: 1b, 2, 3

Keith J Petrie: 1a, 1b, 1c, 2, 3

Nicola Dalbeth: 1a, 1b, 1c, 2, 3

REFERENCES

1. Chilcot J, Wellsted D, Farrington K. Illness perceptions predict survival in haemodialysis patients. American journal of nephrology. 2011;33(4):358-63.
2. Crawshaw J, Rimington H, Weinman J, Chilcot J. Illness perception profiles and their association with 10-year survival following cardiac valve replacement. Annals of Behavioral Medicine. 2015;49(5):769-75.
3. Vedhara K, Dawe K, Miles JNV, Wetherell MA, Cullum N, Dayan C, et al. Illness beliefs predict mortality in patients with diabetic foot ulcers. PloS one. 2016;11(4):e0153315.
4. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007–2008. Arthritis & Rheumatism. 2011;63(10):3136-41.
5. Dalbeth N, Merriman TR, Stamp LK. Gout. The Lancet. 2016.
6. Leventhal H, Diefenbach M, Leventhal EA. Illness cognition: using common sense to understand treatment adherence and affect cognition interactions. Cognitive therapy and research. 1992;16(2):143-63.
7. Broadbent E, Ellis CJ, Thomas J, Gamble G, Petrie KJ. Further development of an illness perception intervention for myocardial infarction patients: a randomized controlled trial. Journal of psychosomatic research. 2009;67(1):17-23.
8. Petrie KJ, Cameron LD, Ellis CJ, Buick D, Weinman J. Changing illness perceptions after myocardial infarction: an early intervention randomized controlled trial. Psychosomatic medicine. 2002;64(4):580-6.
9. Dalbeth N, Petrie KJ, House M, Chong J, Leung W, Chegudi R, et al. Illness perceptions in patients with gout and the relationship with progression of musculoskeletal disability. Arthritis care & research. 2011;63(11):1605-12.
10. Perez-Ruiz F, Martínez-Indart L, Carmona L, Herrero-Beites AM, Pijoan JI, Krishnan E. Tophaceous gout and high level of hyperuricaemia are both associated with increased risk of mortality in patients with gout. Annals of the rheumatic diseases. 2014;73(1):177-82.
11. Vincent ZL, Gamble G, House M, Knight J, Horne A, Taylor WJ, et al. Predictors of mortality in people with recent onset of gout: a prospective observational study. Journal of Rheumatology. in press.
12. Wallace SL, Robinson H, Masi AT, Decker JL, McCarty DJ. Preliminary criteria for the classification of the acute arthritis of primary gout. Arthritis & Rheumatism. 1977;20(3):895-900.
13. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. Journal of psychosomatic research. 2006;60(6):631-7.
14. Broadbent E, Wilkes C, Koschwanez H, Weinman J, Norton S, Petrie KJ. A systematic review and meta-analysis of the Brief Illness Perception Questionnaire. Psychology & health. 2015;30(11):1361-85.
15. Petrie K, Weinman J. Why illness perceptions matter. Clinical Medicine. 2006;6(6):536-9.

Table 1: Participant Characteristics (N=242)

	n (%)	Mean (± SD)	Median (Range)
Clinical Characteristics			
Age (years)		58.5 (14.7)	
Sex (Female)	66 (27.3%)		
Ethnicity			
European/other	176 (72.7%)		
Māori/Pacific	66 (27.3%)		
Disease duration (years)		5.3 (3.1)	
No. of flares in past 3 months		2.4 (8.3)	1 (0-90)
Total number of tophi		0.50 (1.7)	0 (0-13)
Diuretic use (yes)	44 (18.2%)		
Serum urate (mmol/L)		0.41 (0.12)	
Serum creatinine (μmol/L)		105.4 (69.7)	
Pain visual analog score (mm)		18.5 (25.4)	5.1 (0-100)
Comorbidities			
Hypertension	105 (43.4%)		
Hypercholesterolaemia	120 (49.6%)		
Type 2 diabetes	33 (13.6%)		
Kidney disease	61 (25.2%)		
Brief IPQ Items			
Consequences beliefs		4.1 (3.2)	
Timeline beliefs		7.4 (3.3)	
Personal control beliefs		5.9 (3.0)	
Treatment control beliefs		7.8 (2.6)	
Identity beliefs		4.9 (3.1)	
Concern beliefs		6.6 (3.1)	
Understanding beliefs		6.9 (2.6)	
Emotional response beliefs		4.1 (3.5)	

Table 2: Univariate and multivariate cox proportional hazard models evaluating illness perceptions as predictors of all-cause mortality (n=242)

Brief IPQ item[†]	Model 1			Model 2[‡]			Model 3[§]		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Consequence beliefs	1.22	1.10 to 1.36	<.001*	1.28	1.15 to 1.43	<.001*	1.29	1.15 to 1.46	<.001*
Timeline beliefs	1.10	0.98 to 1.25	.114	1.08	0.96 to 1.22	.187	1.05	0.93 to 1.19	.438
Personal control beliefs	0.92	0.83 to 1.03	.167	0.91	0.82 to 1.02	.115	0.90	0.80 to 1.01	.084
Treatment control beliefs	0.95	0.85 to 1.08	.445	0.97	0.86 to 1.10	.638	0.98	0.86 to 1.12	.795
Identity beliefs	1.14	1.02 to 1.14	.024*	1.17	1.04 to 1.32	.009*	1.15	1.01 to 1.31	.033*
Concern beliefs	1.04	0.93 to 1.17	.477	1.12	0.98 to 1.27	.088	1.18	1.02 to 1.36	.024*
Understanding	1.05	0.92 to 1.21	.484	1.04	0.91 to 1.20	.546	1.05	0.90 to 1.21	.553
Emotional response	1.09	0.99 to 1.21	.076	1.16	1.05 to 1.29	.005*	1.19	1.06 to 1.33	.003*

[†]Brief IPQ items are entered separately as predictors in each model.

[‡]Adjusted for age and sex only.

[§]Adjusted for age, sex, number of tophi, serum urate, and flare frequency at baseline.

Events = 33

*p<.05

Table 3: Fully-saturated cox proportional hazard model evaluating illness perceptions as predictors of all-cause mortality (n=242)

Brief IPQ item[†]	Fully-Saturated Model[‡]		
	HR	95% CI	P-value
Consequence beliefs	1.18	1.02 to 1.37	.029*
Timeline beliefs	0.97	0.85 to 1.11	.669
Personal control beliefs	0.97	0.85 to 1.11	.670
Treatment control beliefs	1.14	0.98 to 1.33	.092
Identity beliefs	1.11	0.93 to 1.31	.240
Concern beliefs	1.09	0.92 to 1.29	.308
Understanding	1.01	0.88 to 1.16	.909
Emotional response	1.03	0.90 to 1.17	.691

[†]Brief IPQ items are entered separately as predictors in each model.

[‡] Adjusted for age, sex, ethnicity, number of tophi, serum urate, flare frequency, disease duration, pain score, diuretic use, and serum creatinine at baseline.

Events = 33

*p<.05