BMJ Open

How common are symptoms? Evidence from a national telephone survey

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2014-005374
Article Type:	Research
Date Submitted by the Author:	01-Apr-2014
Complete List of Authors:	Petrie, Keith; University of Auckland Faasse, Kate; Auckland University, Psychological Medicine Grey, Andrew; Auckland university, Medicine Crichton, Fiona; Auckland university, Psychological Medicine
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	PUBLIC HEALTH, GENERAL MEDICINE (see Internal Medicine), EPIDEMIOLOGY

How common are symptoms? Evidence from a national telephone survey

Keith J. Petrie, Kate Faasse, Fiona Crichton & Andrew Grey

Keith J. Petrie, Kate Faasse, Fiona Crichton Department of Psychological Medicine, University of Auckland, Auckland, New Zealand

Andrew Grey, Department of Medicine, University of Auckland, Auckland, New Zealand

Keywords: symptom reporting; somatic complaints; medical visits; gender differences; general population

Word count: 2080

Correspondence to: Professor Keith Petrie, Department of Psychological Medicine, University of Auckland, PO Box 92019, Auckland 1142, New Zealand. Ph +649-923-6564; Fax +649373-7013 Email: kj.petrie@auckland.ac.nz

ABSTRACT

Objective: To assess the frequency of symptoms in a general population sample over the previous week and the associations between symptom reporting and medication use, medical visits and demographic factors.

Design: A representative sample general population sample (n = 1,000) was recruited using random digit dialing. Participants were asked whether they had experienced any of 46 symptoms in the previous 7 days and if so, whether the symptom was mild, moderate or severe. Demographic data and information on medical visits and medication use were also collected.

Results: Symptom reporting was very common. The median number of symptoms reported by participants in the previous week was 5 with only 10.6% of participants reporting no symptoms. The five most common symptoms in the previous 7 days were: back pain, fatigue, headache, runny or stuffy nose and joint pain. The five most bothersome symptoms in terms of severity ratings were sexual difficulties, vomiting, tremor, suicidal thoughts and sleep problems. Symptom reporting was significantly positively associated with medical visits in the previous year and current medication taking. Females reported a significantly greater number of symptoms. We found was no significant association between age or household size and symptom reporting.

Conclusions: This population-based study, using a longer symptom checklist than previous studies, found that symptoms are more commonly experienced in the general population than previously estimated and are strongly associated with health care visits. Appreciation of the high prevalence of symptoms may help normalize the experience of symptom complaints among the general population.

Strengths and limitations of this study

- Our participants were a large representative sample that allowed us to estimate the prevalence of a wide range of symptoms in the general population.
- We used a longer symptom questionnaire than in previous research. This allowed us assess a greater range of symptoms experienced in the previous 7 days.
- The survey was conducted during the New Zealand winter period and this may mean that flu and cold symptoms are more prominent during this period.
- The survey was reliant on self-reported symptoms and it was not possible to check the veracity of participant's complaints.

INTRODUCTION

Physical symptoms are often believed to be a sign of poor health but previous research shows that symptoms are a common daily experience and, in most cases, unassociated with serious illness [1,2]. While there is considerable research activity on the psychological effects of serious illness, such as cancer and cardiovascular disease, there is less work on the burden and factors associated with more frequently occurring daily symptoms. This is despite the fact that such symptoms are the major cause of medical visits and health care costs, and are strongly related to disability [3-4].

Previous research on daily symptoms has been limited by the lack of a standard measure that adequately captures the breadth and severity of daily symptom reports. A recent review of measures used in symptom studies identified 40 different self-report symptom scales ranging in length from 5 to 78 symptoms, with 48% of scales consisting of 15 or fewer items [5]. The instruments also varied in the time frame used for symptom recall from a 7-day period up to a lifetime. Many scales were designed specifically to assess medically unexplained symptoms. Perhaps most surprising was the lack of consistency in assessing common symptoms. While 70% of the questionnaires assessed headaches, other relatively common symptoms were inconsistently assessed, with only 43% of scales assessing fatigue, 38% heart palpitations, 30% vomiting, and 23% joint pain [5].

As many of the previous studies looking at the frequency of physical symptoms have focused on medically unexplained symptoms, a large proportion of the sample of previous studies of symptoms been drawn from medically-defined samples such as individuals registered with general practices [6-8], primary care samples [9-11], hospital outpatients [2,12] or high users of hospital care [13]. Where general population samples have been used, the number and range of symptoms assessed tend to be much smaller, which makes it difficult to get an accurate picture

of the breadth and frequency of symptoms experienced in the general population [14-16].

In the current study we were interested in assessing the following questions: (1) how frequently do individuals in the general population report experiencing symptoms in the previous 7 days? (2) What symptoms are most common and which are rated as being most bothersome? (3) What are the associations between symptom reporting and medication use, medical visits and demographic factors? To examine these questions we administered a comprehensive 46-item symptom checklist to a large nationally representative general population.

METHOD

Participants

A representative sample of 1,000 members of the New Zealand population was recruited using random digit dialing. A nationally representative sample was achieved using set quotas based on the age, gender and regional distribution of New Zealand. Telephone interviews were conducted over June and July, 2013. In total, 24,068 numbers were called to achieve the final survey sample of 1,000 participants. From a total of 11, 453 calls to residential landlines that were answered, 6,354 declined to participate and 233 were excluded because of language difficulty. After eligibility was assessed, 4,899 people were deemed eligible to participate. Of these, 3,876 were excluded because the group to which they belonged – with regard to age, gender, and region – was already sufficiently represented in the sample. A small number of participants (n = 23) abandoned the interview part way though.

Measures

Symptoms

Interviewers read a list of 46 symptoms and asked respondents whether they had experienced any of the symptoms in the previous 7 days and if so, whether the symptom was mild, moderate or severe. The symptom list included 36 items from the General Assessment of Side Effects Scale,[17] a measure designed to assess

commonly reported medication side effects. The scale is a comprehensive measure of common side effects and has demonstrated good psychometric properties in a large German general population.[17] While the scale does cover drug side effects, it does not include some of the commonly reported symptoms frequently found in other symptom scales. Therefore, 10 additional common symptoms were added. These items were: cough, congested or runny nose, ear problems, ear and vision problems, upset stomach or indigestion, numbness or tingling sensations, drowsiness, memory problems, difficulty concentrating, and muscle weakness. Each of the 46 symptoms were coded from 0 (not present) to 3 (severe). Cronbach's alpha showed the scale had high internal consistency (alpha = .90). Corrected item-total correlations ranged from r = 0.60 (fatigue) to r = 0.19 (increased appetite). The total number of symptoms was created by adding dichotomized (present or not present) symptoms minus menstruation.

Demographic and clinical information

Information was collected on the participant's gender, age group, marital status, employment, education, ethnicity, residence region and the number of adults currently residing in their household. Participants were also asked to recall how many times they had visited their family doctor (for themselves) during the previous year, and whether they were taking any prescription medications for the treatment of an illness (excluding the contraceptive pill). Female participants were also asked if they were currently pregnant.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics 20. Frequency information was calculated for individual symptoms, as well as the total number of symptoms reported by each participant. An intensity score was calculated for each symptom by dividing the sum of the intensity ratings (ranging from 1 to 3) by the total number of times that symptom was reported. Chi square tests were used to assess gender differences in the percentage of participants reporting individual symptoms.

Independent samples t-tests were used to assess differences in the number of symptoms reported by participants across medication use, sex, and education level. Pearson's correlations were used to investigate the relationship between symptom reporting and age group, number of adults in the household, and the reported number of GP visits during the previous year. Analysis of variance (ANOVA) was used to further investigate differences in the number of symptoms reported by people who visited their GP zero, one, two, three to four, or five or more times during the previous year. An alpha level of .05 was used for all statistical tests.

RESULTS

We first examined the total number of symptoms reported by participants in the previous 7 days. Reports of symptoms were very common with only 10.6% of participants reporting no symptoms. The number of symptoms reported ranged from 0 to 36 with 49.6% reporting fewer than five symptoms and 23% reporting 10 or more (see Figure 1).

Insert figure1 about here

The five most common symptoms in the previous seven days were: back pain, fatigue, headache, runny or stuffy nose and joint pain. Using data from only participants who experienced the symptom, most symptoms were rated as mild, with an average intensity rating of M = 1.39 (SD = 0.10). The five most bothersome symptoms in terms of intensity ratings were in descending order: sexual difficulties, vomiting, tremor, suicidal thoughts and sleep problems (ranging from 1.62 to 1.53). The reference data for the frequency of symptoms reported in the general population and by sex is presented in Table 1.

Table 1
Symptoms in previous 7-days in total sample and by sex

	Sex				Total Sample	
	Male *n* (%)		Female *n* (%)		*n* (%)	
Back or neck pain*	171	(34.8)	211	(41.5)	382	(38.2)
Fatigue or loss of energy***	139	(28.3)	216	(42.4)	355	(35.5)
Headache***	137	(27.9)	217	(42.6)	354	(35.4)
Congested or runny nose	163	(33.2)	181	(35.6)	344	(34.4)
Joint pain or stiffness	164	(33.4)	172	(33.8)	336	(33.6)
Insomnia or sleeping problems*	120	(24.4)	166	(32.6)	286	(28.6)
Cough*	125	(25.5)	158	(31.0)	283	(28.3)
Muscle pain	115	(23.4)	116	(22.8)	231	(23.1)
Low blood pressure or circulation problems***	77	(15.7)	136	(26.7)	213	(21.3)
Upset stomach or indigestion	99	(20.2)	94	(18.5)	193	(19.3)
Irritability or nervousness*	72	(14.7)	102	(20.0)	174	(17.4)
Skin Rash or itching	68	(13.8)	92	(18.1)	160	(16.0)
Difficulty concentrating*	63	(12.8)	89	(17.5)	152	(15.2)
Dry mouth	62	(12.6)	83	(16.3)	145	(14.5)
Anxiety or fearfulness	62	(12.6)	79	(15.5)	141	(14.1)
Drowsiness	67	(13.6)	73	(14.3)	140	(14.0)
Depressed mood	78	(15.9)	60	(11.8)	138	(13.8)
Breathing problems	65	(13.2)	67	(13.2)	132	(13.2)
Agitation	64	(13.0)	63	(12.4)	127	(12.7)
Numbness or tingling sensations	59	(12.0)	65	(12.8)	124	(12.4)
Memory problems***	43	(8.8)	78	(15.3)	121	(12.1)
Abdominal pain*	46	(9.4)	71	(13.9)	117	(11.7)
Ear or hearing problems	62	(12.6)	55	(10.8)	117	(11.7)
Eye or vision problems	51	(10.4)	60	(11.8)	111	(11.1)
Nightmares or abnormal dreams	47	(9.6)	62	(12.2)	109	(10.9)
Muscle weakness	54	(11.0)	55	(10.8)	109	(10.9)
Hot flushes***	16	(3.3)	76	(14.9)	92	(9.2)
Reduced appetite*	34	(6.9)	55	(10.8)	89	(8.9)
Increased appetite	46	(9.4)	42	(8.3)	88	(8.8)
Dizziness	36	(7.3)	50	(9.8)	86	(8.6)
Nausea***	27	(5.5)	57	(11.2)	84	(8.4)
Tendency to develop bruises***	14	(2.9)	66	(13.0)	80	(8.0)
Tremor or muscle spasms	45	(9.2)	35	(6.9)	80	(8.0)
Palpitations or irregular heartbeat**	22	(4.5)	49	(9.6)	71	(7.1)
Chest Pain	38	(7.7)	33	(6.5)	71	(7.1)
Fever or increased temperature**	23	(4.7)	47	(9.2)	70	(7.0)
Diarrhoea	34	(6.9)	33	(6.5)	67	(6.7)
Abnormal sweating*	20	(4.1)	36	(7.1)	56	(5.6)
Hair loss	24	(4.9)	27	(5.3)	51	(5.1)
Constipation	19	(3.9)	29	(5.7)	48	(4.8)
Sexual problems	22	(4.5)	15	(2.9)	37	(3.7)
Difficulty urinating**	22	(4.5)	6	(1.2)	28	(2.8)
Thoughts about suicide**	18	(3.7)	6	(1.2)	24	(2.4)
Vomiting	7	(1.4)	15	(2.9)	22	(2.2)
Convulsions or seizures	3	(0.6)	5	(1.0)	8	(0.8)
Painful or irregular menstruation			45	(8.8)		

Note: Sex differences * p ≤.05; ** p ≤.01; *** p ≤.001

We next examined associations between symptom reporting and medication use, medical visits and demographic factors. Current medication taking was reported by 39% of respondents. We found symptom reporting was significantly higher in those participants who also reported taking medication (M = 8.32, SE = 0.35) compared to those not taking medication (M = 4.91, SE = 0.19), $t(614.66) = -8.55$, $p < .001$. The number of reported symptoms in the previous 7-days was also strongly associated with the number of GP visits in the previous year, $r = 0.25$, $p < .001$. This effect was further investigated using Analysis of Variance, comparing the number of symptoms reported across five GP visit groups (zero visits, one visit, two visits, three or four visits, and five or more visits to the GP over the previous year). There was a significant main effect of the frequency of GP visits on the total number of symptoms reported, $F(4, 994) = 34.28$, $p < .001$, (see Figure 2). Post hoc tests using a Bonferroni correction revealed that participants who reported never seeing their GP in the previous year reported significantly fewer symptoms (M = 3.97, SE = 0.38) than those who reported one visit (M = 4.80, SE = 0.36), two visits (M = 6.22, SE = 0.39), three or four visits (M = 7.39, SE = 0.40), and five or more visits (M = 10.08, SE = 0.44), p values for all comparisons < .001. Participants who went to the GP only once reported fewer symptoms than those who went three or more times, ps < .001, and participants who reported attendance at their GP clinic five or more times during the previous year reported significantly higher numbers of symptoms than all other groups, ps < .001.

Insert Figure 2 about here

In terms of demographic differences, the overall number of symptoms reported by females (M = 6.88, SE = 0.27) was significantly higher than males (M = 5.59, SE = 0.25), $t(998) = -3.49$, $p < .001$. We found 17 of 45 symptoms were significantly more frequently reported by female respondents; two symptoms,

difficulty urinating and thoughts about suicide, were more commonly reported by males, all p values < .05 (see Table 1). Symptom reporting was lower in participants who reported a tertiary (M = 5.78, SE = 0.22) versus a secondary school level education (M = 6.69, SE = 0.32), t(771.56) = 2.35, p = .02. However we found no association between the number of symptoms reported and age, r = -0.03, p = .34, or household size, r = -.02, p = .56.

DISCUSSION

In a large nationally representative sample responding to a large comprehensive symptom questionnaire we found symptom complaints to be very common. The median number of symptoms reported by participants was five in the previous week. The most common symptoms reported by participants were fatigue, back pain and headache. Higher symptom reporting was strongly associated with previous general practitioner visits, medication taking and a female gender.

The most common symptoms in the current survey are consistent with previous UK studies using samples drawn from GP practice lists. However, the current study, which uses a larger range of symptoms than previous population surveys, suggests that the symptom burden is likely to be higher among the general population than previous studies have suggested. The study also identified that there are a significant proportion of the general population that experience a large number of symptoms each week with a fifth of the sample experiencing over 10 symptoms a week and 10% reporting 14 or more symptoms.

The five most common symptoms in this survey, back pain, complaints of fatigue, headache, congested or runny nose and joint pain or stiffness are also commonly reported in other studies. Four of the five are in the top most common symptoms reported in the McAteer survey[6] and three also appear in the top five symptoms reported by Hannay.[7] In terms of the study limitations, it should be noted that the survey was reliant on self-reported symptoms and it was not possible

to check the veracity of participant's complaints. The survey was conducted during the New Zealand winter period and this may mean that flu and cold symptoms are more prominent during this period.

Bearing in mind these limitations, our findings suggest that symptoms in the general population are more common than previously believed may be a strong driver for the use of health care. Understanding the breadth and depth of symptom reporting in the general population is important to appreciate the scope for common symptoms to be misconstrued as indicative of serious health conditions. The symptoms most commonly reported in the study, such as back pain, fatigue and headache, are not reliable indicators of underlying pathology, but are often reported in medically unexplained syndromes, associated with functional disability and high health care utilization.[18] Further, given the ease with which symptom complaints are ascribed to perceived environmental threats, which pose no genuine health risk,[19,20] insight into the extent that reported symptoms are part of the normal human experience may provide reassurance to those with health concerns and reduce symptom misattribution.[21] Ensuring that both the general public and medical professionals have access to reliable information about the prevalence of symptoms may normalize the experience of symptoms, allay distress and reduce health care seeking, as well as help to prevent unnecessary medical testing and over-diagnosis.

Contributors KP generated the initial study idea. KP, KF & AG designed the study and drafted the manuscript. KF & FC performed the data analysis. All authors assisted with the interpretation of the results and critical revision of the manuscript. KP is the guarantor of this study.

Funding This research was funded by Pharmac, the New Zealand Government's Pharmaceutical Management Agency.

Competing Interests The authors have no competing interests to report.

Data sharing statement No additional data are available

REFERENCES

[1] Pennebaker JW. *The psychology of physical symptoms*. New York: Springer-Verlag; 1982.

[2] Kroenke K, Mangelsdorff AD. Common symptoms in ambulatory care: incidence, evaluation, therapy, and outcome. *Am J Med* 1989; *86*: 62–6.

[3] Bruusgaard D, Tschudi-Madsen H, Ihlebaek C, Kamaleri Y, Natvig B. Symptom load and functional status: results from the Ullensaker population study. *BMC Public Health* 2012; *12*: 1085

[4] Barsky AJ, Orav EJ, Bates DW. Somatization increases medical utilization and costs independent of psychiatric and medical comorbidity. *Arch Gen Psychiatry* 2005; *62*: 903–10.

[5] Zijlema WL, Stolk RP, Lowe B, Rief W, Bioshare, White PD, Rosmalen JGM. How to assess common somatic symptoms in large-scale studies: A systematic review of questionnaires. *J Psychosom Res* 2013; *74*: 459-468.

[6] McAteer A, Elliott AM, Hannaford PC. Ascertaining the size of the symptom ice- berg in a UK-wide community-based survey. *Br J Gen Pract* 2011; *61*:e1-11.

[7] Hannay DR. Symptom prevalence in the community. *J R Coll Gen Pract* 1978; *28*: 492–499.

[8] Elliott AM, McAteer A, Hannaford PC. Revisiting the symptom iceberg in today's primary care: results from a UK population survey. BMC Fam Pract 2011; *12*: 16. doi:10.1186/1471-2296-12-16

[9] Kroenke K, Spitzer RL, deGruy FV, Swindle R. A symptom checklist to screen for somatoform disorders in primary care. *Psychosomatics* 1998; *39*: 263–72.

[10] Interian A, Allen LA, Gara MA, Escobar JI, Diaz-Martinez AM. Somatic complaints in primary care: further examining the validity of the Patient Health Questionnaire (PHQ-15). *Psychosomatics* 2006; *47*: 392–8.

[11] Steinbrecher N, Koerber S, Frieser D, Hiller W. The prevalence of medically

unexplained symptoms in primary care. *Psychosomatics* 2011; *52:* 263–71.

[12] Kroenke K, Arrington ME, Mangelsdorff AD. The prevalence of symptoms in medical outpatients and the adequacy of therapy. *Arch Intern Med* 1990; *150:* 1685–9.

[13] Reid S, Wessely S, Crayford T, Hotopf M. Medically unexplained symptoms in frequent attenders of secondary health care: retrospective cohort study. *BMJ* 2001; *322:* 1-4.

[14] Eriksen HR, Svendsrod R, Ursin G, Ursin H. Prevalence of subjective health complaints in the Nordic European countries in 1993. *Eur J Public Health* 1998; *8:* 294-298.

[15] Kroenke K, Price RK. Symptoms in the community: prevalence, classification, and psychiatric comorbidity. *Arch Intern Med* 1993;*153*:2474-2480.

[16] Ihlebaek C, Eriksen HR, Ursin H. Prevalence of subjective health complaints (SHC) in Norway. *Scand J Public Health* 2002; *30*: 20-29.

[17] Rief W. Barsky AJ, Glombiewski JA, Nestoriuc Y, Glaesmer H, Braehler E. Assessing general side effects in clinical trials: reference data from the general population. *Pharmacoepidemiol Drug Saf* 2011; 20: 405-15.

[18] Kroenke K. Patients presenting with somatic complaints: epidemiology, psychiatric comorbidity and management. *Int J Methods Psychiatr Res* 2003; *12:* 34-43

[19] Page L, Petrie KJ, Wessely S. Psychosocial responses to environmental incidents: A review and proposed typology. *J Psychosom Res* 2006; *60*: 413-422.

[20] Rubin GJ, Nieto-Hernandez R, Wessely S. Idiopathic environmental intolerance attributed to electromagnetic fields (formerly “electromagnetic hypersensitivity”)” An updated systematic review of provocation studies. Bioelectromagnetics 2010; *31*: 1-11.

[21] Filipkowski K, Smyth J, Rutchick A, Adya M, Santuzzi A, Petrie KJ, Kaptein AA. Do healthy people worry? Modern health worries, subjective health complaints, perceived health, and health care utilization. *Int J Behav Med* 2010; *17:*182-188.

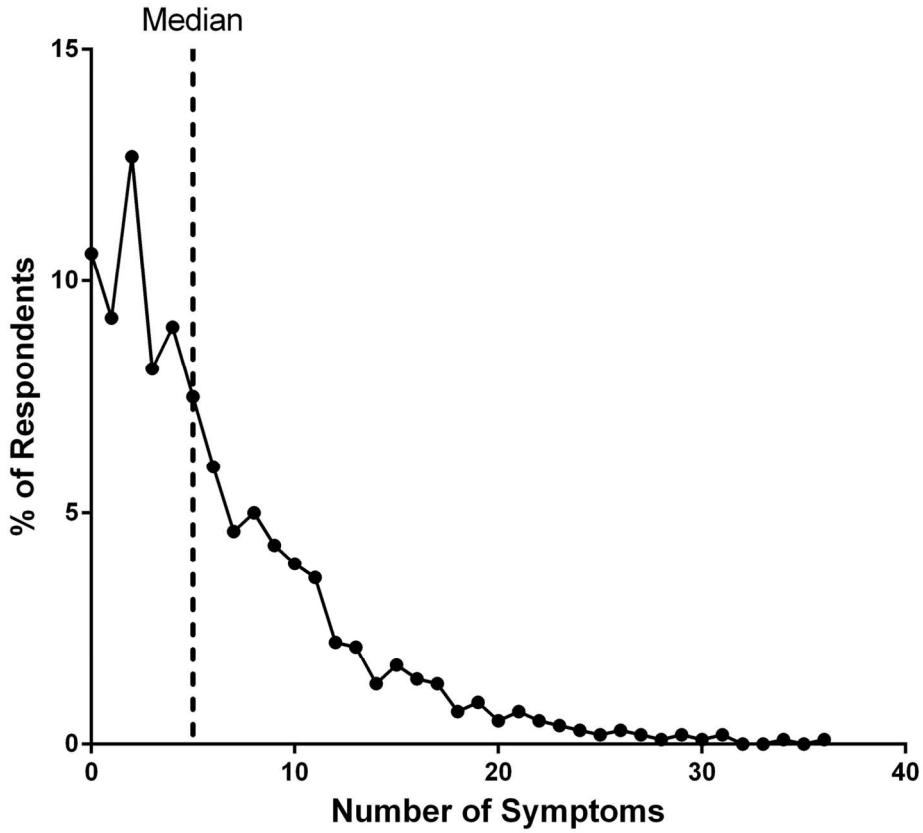
Figure Legends

Figure 1

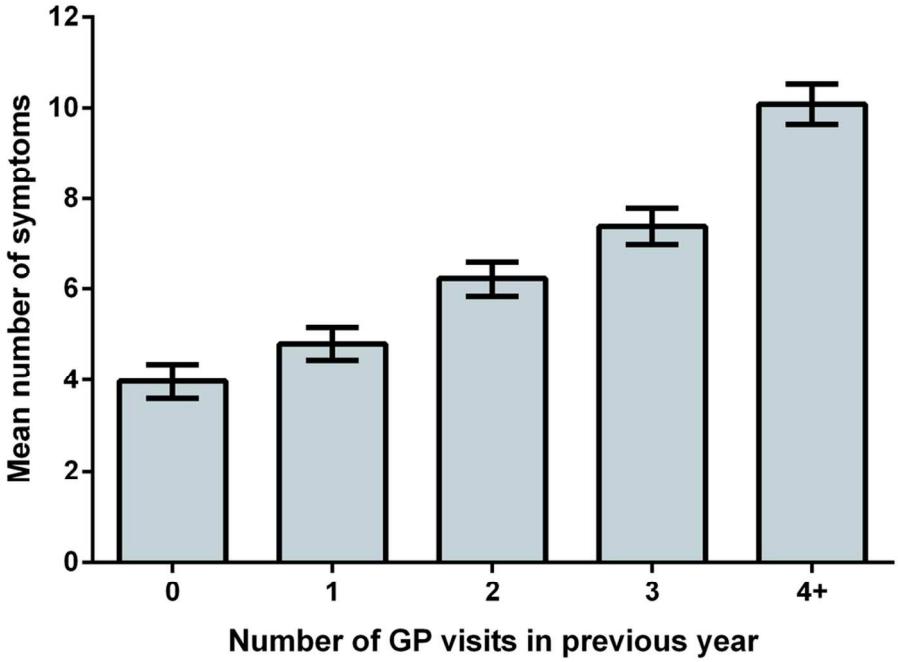
Number of symptoms reported in last 7 days

Figure 2

The mean (SE) number of symptoms reported in the previous 7-days and number of GP visits in previous year.



133x116mm (300 x 300 DPI)



99x71mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	*6-7*
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6-10
		(*c*) Explain how missing data were addressed	na
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	na
		(*e*) Describe any sensitivity analyses	na
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	na
		(b) Indicate number of participants with missing data for each variable of interest	na
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	na
		(*b*) Report category boundaries when continuous variables were categorized	na
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

How common are symptoms? Evidence from a New Zealand national telephone survey

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2014-005374.R1
Article Type:	Research
Date Submitted by the Author:	22-May-2014
Complete List of Authors:	Petrie, Keith; University of Auckland Faasse, Kate; Auckland University, Psychological Medicine Crichton, Fiona; Auckland university, Psychological Medicine Grey, Andrew; Auckland university, Medicine
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	PUBLIC HEALTH, GENERAL MEDICINE (see Internal Medicine), EPIDEMIOLOGY

How common are symptoms? Evidence from a New Zealand national telephone survey

Keith J. Petrie, Kate Faasse, Fiona Crichton & Andrew Grey

Keith J. Petrie, Kate Faasse, Fiona Crichton Department of Psychological Medicine, University of Auckland, Auckland, New Zealand

Andrew Grey, Department of Medicine, University of Auckland, Auckland, New Zealand

Keywords: symptom reporting; somatic complaints; medical visits; gender differences; general population

Word count: 2080

Correspondence to: Professor Keith Petrie, Department of Psychological Medicine, University of Auckland, PO Box 92019, Auckland 1142, New Zealand. Ph +649-923-6564; Fax +649373-7013 Email: kj.petrie@auckland.ac.nz

ABSTRACT

Objective: To assess the frequency of symptoms in a general population sample over the previous week and the associations between symptom reporting and demographic factors, medical visits and medication use.

Design: A representative sample general population sample (n = 1,000) was recruited using random digit dialing. Participants were asked whether they had experienced any of 46 symptoms in the previous 7 days and if so, whether the symptom was mild, moderate or severe. Demographic data and information on medical visits and medication use were also collected.

Results: Symptom reporting was very common. The median number of symptoms reported by participants in the previous week was 5 with only 10.6% of participants reporting no symptoms. The five most common symptoms in the previous 7 days were: back pain (38%), fatigue (36%), headache (35%), runny or stuffy nose (34%) and joint pain (34%). The five symptoms rated highest in terms of severity were sexual difficulties, vomiting, tremor, suicidal thoughts and sleep problems. Symptom reporting was significantly positively associated with medical visits in the previous year and current medication taking. Females reported a significantly greater number of symptoms. We found was no significant association between age or household size and symptom reporting.

Conclusions: This population-based study found that symptoms are more commonly experienced in the general population than previously estimated and are strongly associated with health care visits. Appreciation of the high prevalence of symptoms may help normalize the experience of symptom complaints among the general population.

Strengths and limitations of this study

- Our participants were a large representative sample that allowed us to estimate the prevalence of a wide range of symptoms in the general population.
- We used a longer symptom questionnaire than in previous research. This allowed us assess a greater range of symptoms experienced in the previous 7 days.
- The survey was conducted during the New Zealand winter period and this may mean that flu and cold symptoms are more prominent during this period.
- The survey was reliant on self-reported symptoms and it was not possible to check the veracity of participant's complaints.

INTRODUCTION

Physical symptoms are often believed to be a sign of poor health but previous research shows that symptoms are a common daily experience and, in most cases, unassociated with serious illness [1,2]. While there is considerable research activity on the psychological effects of serious illness, such as cancer and cardiovascular disease, there is less work on the burden and factors associated with more frequently occurring daily symptoms. This is despite the fact that such symptoms are the major cause of medical visits and health care costs, and are strongly related to disability [3-4]. While the vast majority of symptoms are transient and benign, doctors working in primary care frequently deal with a large number of patients who present with bodily symptoms but no medical diagnosis [5]. At the other end of the continuum, some patients with serious symptoms often delay for a lengthy time before seeking medical care, which can compromise their health [6-7].

Previous research on daily symptoms has been limited by the lack of a standard measure that adequately captures the breadth and severity of daily symptom reports. A recent review of measures used in symptom studies identified 40 different self-report symptom scales ranging in length from 5 to 78 symptoms, with 48% of scales consisting of 15 or fewer items [8]. The instruments also varied in the time frame used for symptom recall from a 7-day period up to a lifetime. Many scales were designed specifically to assess medically unexplained symptoms. Perhaps most surprising was the lack of consistency in assessing common symptoms. While 70% of the questionnaires assessed headaches, other relatively common symptoms were inconsistently assessed, with only 43% of scales assessing fatigue, 38% heart palpitations, 30% vomiting, and 23% joint pain [8]. Unfortunately, two of the scales recommended by this review, the Symptom Checklist-90 Somatization Scale and Patient Health Questionnaire-15, only have a limited number of physical symptoms and are focused on identifying somatization.

As many of the previous studies looking at the frequency of physical symptoms have focused on medically unexplained symptoms, a large proportion of the sample of previous studies of symptoms been drawn from medically-defined samples such as individuals registered with general practices [9-11], primary care samples [12-14], hospital outpatients [2,15] or high users of hospital care [16]. Where general population samples have been used, the number and range of symptoms assessed tend to be much smaller, which makes it difficult to get an accurate picture of the breadth and frequency of symptoms experienced in the general population [17-19].

In the current study we were interested in assessing the following questions: (1) how frequently do individuals in the general population report experiencing symptoms in the previous 7 days? (2) What symptoms are most common and which are rated as being the most severe? (3) What are the associations between symptom reporting and medication use, medical visits and demographic factors? To examine these questions we administered a comprehensive 46-item symptom checklist to a large nationally representative general population.

METHOD

Participants

A representative sample of 1,000 members of the New Zealand population was recruited using random digit dialing. A nationally representative sample was achieved using set quotas based on the age, gender and regional distribution of New Zealand. Telephone interviews were conducted over June and July, 2013. In total, 24,068 numbers were called to achieve the final survey sample of 1,000 participants. From a total of 11, 453 calls to residential landlines that were answered, 6,354 declined to participate and 233 were excluded because of language difficulty. After eligibility was assessed, 4,899 people were deemed eligible to participate. Of these, 3,876 were excluded because the group to which they belonged – with regard to age, gender,

and region – was already sufficiently represented in the sample. A small number of participants (n = 23) abandoned the interview part way though.

Measures

Symptoms

Interviewers read a list of 46 symptoms and asked respondents whether they had experienced any of the symptoms in the previous 7 days and if so, whether the symptom was mild, moderate or severe. The symptom list included 36 items from the General Assessment of Side Effects Scale,[20] a measure designed to assess commonly reported medication side effects. The scale is a comprehensive measure of common side effects and has demonstrated good psychometric properties in a large German general population.[20] While the scale does cover drug side effects, it does not include some of the commonly reported symptoms frequently found in other symptom scales. Therefore, 10 additional common symptoms were added. These items were: cough, congested or runny nose, ear problems, ear and vision problems, upset stomach or indigestion, numbness or tingling sensations, drowsiness, memory problems, difficulty concentrating, and muscle weakness. Each of the 46 symptoms were coded from 0 (not present) to 3 (severe). Cronbach's alpha showed the scale had high internal consistency (alpha = .90). Corrected item-total correlations ranged from r = 0.60 (fatigue) to r = 0.19 (increased appetite). The total number of symptoms was created by adding dichotomized (present or not present) symptoms minus menstruation.

Demographic and clinical information

Information was collected on the participant's gender, age group, marital status, employment, education, ethnicity, residence region and the number of adults currently residing in their household. Participants were also asked to recall how many times they had visited their family doctor (for themselves) during the previous year, and whether they were taking any prescription medications for the treatment of

an illness (excluding the contraceptive pill). Female participants were also asked if they were currently pregnant.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics 20. Frequency information was calculated for individual symptoms, as well as the total number of symptoms reported by each participant. An intensity score was calculated for each symptom by dividing the sum of the intensity ratings (ranging from 1 to 3) by the total number of times that symptom was reported. Chi square tests were used to assess gender differences in the percentage of participants reporting individual symptoms. Independent samples t-tests were used to assess differences in the number of symptoms reported by participants across medication use, sex, and education level. Pearson's correlations were used to investigate the relationship between symptom reporting and age group, number of adults in the household, and the reported number of GP visits during the previous year. Analysis of variance (ANOVA) was used to further investigate differences in the number of symptoms reported by people who visited their GP zero (n=214), one (n = 239), two (n = 198), three to four (n = 189), or five or more times during the previous year (n = 159). An alpha level of .05 was used for all statistical tests.

RESULTS

We first examined the total number of symptoms reported by participants in the previous 7 days. Reports of symptoms were very common with only 10.6% of participants reporting no symptoms. The number of symptoms reported ranged from 0 to 36 with 49.6% reporting fewer than five symptoms and 23% reporting 10 or more (see Figure 1).

Insert figure1 about here

The five most common symptoms in the previous seven days were: back pain, fatigue, headache, runny or stuffy nose and joint pain. The reference data for the frequency of symptoms reported in the general population and by sex is presented in Table 1.

Table 1
Symptoms in previous 7-days in total sample and by sex

	Sex				Total Sample	
	Male *n* (%)		Female *n* (%)		*n* (%)	
Back or neck pain*	171	(34.8)	211	(41.5)	382	(38.2)
Fatigue or loss of energy***	139	(28.3)	216	(42.4)	355	(35.5)
Headache***	137	(27.9)	217	(42.6)	354	(35.4)
Congested or runny nose	163	(33.2)	181	(35.6)	344	(34.4)
Joint pain or stiffness	164	(33.4)	172	(33.8)	336	(33.6)
Insomnia or sleeping problems*	120	(24.4)	166	(32.6)	286	(28.6)
Cough*	125	(25.5)	158	(31.0)	283	(28.3)
Muscle pain	115	(23.4)	116	(22.8)	231	(23.1)
Low blood pressure or circulation problems***	77	(15.7)	136	(26.7)	213	(21.3)
Upset stomach or indigestion	99	(20.2)	94	(18.5)	193	(19.3)
Irritability or nervousness*	72	(14.7)	102	(20.0)	174	(17.4)
Skin Rash or itching	68	(13.8)	92	(18.1)	160	(16.0)
Difficulty concentrating*	63	(12.8)	89	(17.5)	152	(15.2)
Dry mouth	62	(12.6)	83	(16.3)	145	(14.5)
Anxiety or fearfulness	62	(12.6)	79	(15.5)	141	(14.1)
Drowsiness	67	(13.6)	73	(14.3)	140	(14.0)
Depressed mood	78	(15.9)	60	(11.8)	138	(13.8)
Breathing problems	65	(13.2)	67	(13.2)	132	(13.2)
Agitation	64	(13.0)	63	(12.4)	127	(12.7)
Numbness or tingling sensations	59	(12.0)	65	(12.8)	124	(12.4)
Memory problems***	43	(8.8)	78	(15.3)	121	(12.1)
Abdominal pain*	46	(9.4)	71	(13.9)	117	(11.7)
Ear or hearing problems	62	(12.6)	55	(10.8)	117	(11.7)
Eye or vision problems	51	(10.4)	60	(11.8)	111	(11.1)
Nightmares or abnormal dreams	47	(9.6)	62	(12.2)	109	(10.9)
Muscle weakness	54	(11.0)	55	(10.8)	109	(10.9)
Hot flushes***	16	(3.3)	76	(14.9)	92	(9.2)
Reduced appetite*	34	(6.9)	55	(10.8)	89	(8.9)
Increased appetite	46	(9.4)	42	(8.3)	88	(8.8)
Dizziness	36	(7.3)	50	(9.8)	86	(8.6)
Nausea***	27	(5.5)	57	(11.2)	84	(8.4)
Tendency to develop bruises***	14	(2.9)	66	(13.0)	80	(8.0)
Tremor or muscle spasms	45	(9.2)	35	(6.9)	80	(8.0)
Palpitations or irregular heartbeat**	22	(4.5)	49	(9.6)	71	(7.1)
Chest Pain	38	(7.7)	33	(6.5)	71	(7.1)
Fever or increased temperature**	23	(4.7)	47	(9.2)	70	(7.0)
Diarrhoea	34	(6.9)	33	(6.5)	67	(6.7)
Abnormal sweating*	20	(4.1)	36	(7.1)	56	(5.6)
Hair loss	24	(4.9)	27	(5.3)	51	(5.1)
Constipation	19	(3.9)	29	(5.7)	48	(4.8)
Sexual problems	22	(4.5)	15	(2.9)	37	(3.7)
Difficulty urinating**	22	(4.5)	6	(1.2)	28	(2.8)
Thoughts about suicide**	18	(3.7)	6	(1.2)	24	(2.4)
Vomiting	7	(1.4)	15	(2.9)	22	(2.2)
Convulsions or seizures	3	(0.6)	5	(1.0)	8	(0.8)
Painful or irregular menstruation			45	(8.8)		

Note: Sex differences * p ≤.05; ** p ≤.01; *** p ≤.001

Using data from only participants who experienced the symptom, most symptoms were rated as mild, with an average intensity rating of M = 1.39 (SD = 0.10). The highest rated symptoms in terms of intensity were sexual difficulties, vomiting, tremor or muscle spasms and thoughts about suicide. However, typically the symptoms with the highest intensity raters were infrequently reported (Table 2).

Table 2

The 10 most highly rated symptoms by intensity

	Mean Intensity /3	Symptom frequency rank
Sexual problems	1.62	41
Vomiting	1.59	44
Tremor or muscle spasms	1.55	33
Thoughts about suicide	1.54	43
Insomnia or sleeping problems	1.53	6
Nightmares or abnormal dreams	1.52	26
Abdominal pain	1.52	22
Muscle weakness	1.50	25
Convulsions or seizures	1.50	45
Back or neck pain	1.48	1

We next examined associations between symptom reporting and medication use, medical visits and demographic factors. Current medication taking was reported

by 39% of respondents. We found symptom reporting was significantly higher in those participants who also reported taking medication (M = 8.32, SE = 0.35) compared to those not taking medication (M = 4.91, SE = 0.19), t(614.66) = -8.55, p < .001.

The number of reported symptoms in the previous 7-days was also associated with the number of GP visits in the previous year, r = 0.25, p < .001. This effect was further investigated using Analysis of Variance, comparing the number of symptoms reported across five GP visit groups (zero visits, one visit, two visits, three or four visits, and five or more visits to the GP over the previous year). There was a significant main effect of the frequency of GP visits on the total number of symptoms reported, F(4, 994) = 34.28, p < .001, (see Figure 2). Post hoc tests using a Bonferroni correction revealed that participants who reported never seeing their GP in the previous year reported significantly fewer symptoms (M = 3.97, SE = 0.38) than those who reported one visit (M = 4.80, SE = 0.36), two visits (M = 6.22, SE = 0.39), three or four visits (M = 7.39, SE = 0.40), and five or more visits (M = 10.08, SE = 0.44), p values for all comparisons < .001. Participants who went to the GP only once reported fewer symptoms than those who went three or more times, ps < .001, and participants who reported attendance at their GP clinic five or more times during the previous year reported significantly higher numbers of symptoms than all other groups, ps < .001.

Insert Figure 2 about here

In terms of demographic differences, the overall number of symptoms reported by females (M = 6.88, SE = 0.27) was significantly higher than males (M = 5.59, SE = 0.25), t(998) = -3.49, p < .001. We found 17 of 45 symptoms were significantly more frequently reported by female respondents; two symptoms, difficulty urinating and thoughts about suicide, were more commonly reported by

males, all p values < .05 (see Table 1). Symptom reporting was lower in participants who reported a tertiary (M = 5.78, SE = 0.22) versus a secondary school level education (M = 6.69, SE = 0.32), t(771.56) = 2.35, p = .02. However we found no association between the number of symptoms reported and age, r = -0.03, p = .34, or household size, r = -.02, p = .56.

We also looked at sex differences in medication use and GP visits. There was no significant difference between males (38.5%) and females (39.7%) in medication use, $\mathbf{X}^2$ (1, N = 1000) = 0.149, p = .699. However, there was a significant difference between males and females in reported GP visits ($\mathbf{X}^2$ (4, N = 999) = 23.707, p < .001. Males (27.3%) were more likely to report no GP visits in the previous year, compared to females (15.7%). Consistent with this, more females (18.9%) reported 5 or more GP visits during the previous year than males (12.9%).

DISCUSSION

In a large nationally representative sample responding to a large comprehensive symptom questionnaire we found symptom complaints to be very common. The median number of symptoms reported by participants was five in the previous week. The most common symptoms reported by participants were fatigue, back pain and headache. Higher symptom reporting was strongly associated with previous general practitioner visits, medication taking and a female gender.

The most common symptoms in the current survey are consistent with previous UK studies using samples drawn from GP practice lists. However, the current study, which uses a larger range of symptoms than previous population surveys, suggests that the symptom burden is likely to be higher among the general population than previous studies have suggested. The study also identified that there are a significant proportion of the general population that experience a large number of symptoms each week with a fifth of the sample experiencing over 10 symptoms a week and 10% reporting 14 or more symptoms.

The five most common symptoms in this survey, back pain, complaints of fatigue, headache, congested or runny nose and joint pain or stiffness are also commonly reported in other studies. Four of the five are in the top most common symptoms reported in the McAteer survey [9] and three also appear in the top five symptoms reported by Hannay.[10] In terms of the study limitations, it should be noted that the survey was reliant on self-reported symptoms and it was not possible to check the veracity of participant's complaints. Also, the survey was mostly focused on physical complaints rather than mental health problems. It should also be noted that the survey was conducted during the New Zealand winter period and this may mean that flu and cold symptoms are more prominent during this period.

Bearing in mind these limitations, our findings suggest that symptoms in the general population are more common than previously believed may be a strong driver for the use of health care. Previous studies have also found that high symptom reporting was associated with an increased number of reported bodily pain sites,[21] as well as more use of health care and mortality, even after controlling for relevant confounders.[22] Interestingly, a recent study in general practice patients also found that as symptom reports increased, so did the patient's belief that they were suffering from an unexplained condition such as amalgam poisoning, electromagnetic sensitivity or chronic fatigue syndrome.[23]

Understanding the breadth and depth of symptom reporting in the general population is important to appreciate the scope for common symptoms to be misconstrued as indicative of serious health conditions. The symptoms most commonly reported in the study, such as back pain, fatigue and headache, are not reliable indicators of underlying pathology, but are often reported in medically unexplained syndromes, associated with functional disability and high health care utilization.[24] Further, given the ease with which symptom complaints are ascribed to perceived environmental threats, which pose no genuine health risk,[25,26] insight into the extent that reported symptoms are part of the normal human experience may

provide reassurance to those with health concerns and reduce symptom misattribution.[27] Ensuring that both the general public and medical professionals have access to reliable information about the prevalence of symptoms may normalize the experience of symptoms, allay distress and reduce health care seeking, as well as help to prevent unnecessary medical testing and over-diagnosis.

Contributors KP generated the initial study idea. KP, KF & AG designed the study and drafted the manuscript. KF & FC performed the data analysis. All authors assisted with the interpretation of the results and critical revision of the manuscript. KP is the guarantor of this study.

Funding This research was funded by Pharmac, the New Zealand Government's Pharmaceutical Management Agency.

Competing Interests The authors have no competing interests to report.

Data sharing statement No additional data are available

REFERENCES

[1] Pennebaker JW. *The psychology of physical symptoms*. New York: Springer-Verlag; 1982.

[2] Kroenke K, Mangelsdorff AD. Common symptoms in ambulatory care: incidence, evaluation, therapy, and outcome. *Am J Med* 1989; *86*: 62–6.

[3] Bruusgaard D, Tschudi-Madsen H, Ihlebaek C, et al. Symptom load and functional status: results from the Ullensaker population study. *BMC Public Health* 2012; *12*: 1085

[4] Barsky AJ, Orav EJ, Bates DW. Somatization increases medical utilization and costs independent of psychiatric and medical comorbidity. *Arch Gen Psychiatry* 2005; *62*: 903–10.

[5] Kroenke K. Patients presenting with somatic complaints: Epidemiology, psychiatric comorbidity and management. Int J Methods Psychiatr Res 2003;1113:774-9.

[6] Perry K, Petrie KJ, Ellis CJ, et al. Symptom expectations and delay in acute myocardial infarction patients. Heart 2001;86:91 – 2.

[7] Meechan G, Collins J, Petrie KJ. The relationship of symptoms and psychological factors to delay in seeking medical care for breast symptoms. Prev Med 2003;36: 374-378.

[8] Zijlema WL, Stolk RP, Lowe B, et al. How to assess common somatic symptoms in large-scale studies: A systematic review of questionnaires. *J Psychosom Res* 2013; *74*: 459-468.

[9] McAteer A, Elliott AM, Hannaford PC. Ascertaining the size of the symptom ice- berg in a UK-wide community-based survey. *Br J Gen Pract* 2011; *61*:e1-11.

[10] Hannay DR. Symptom prevalence in the community. *J R Coll Gen Pract* 1978; *28*: 492–499.

[11] Elliott AM, McAteer A, Hannaford PC. Revisiting the symptom iceberg in

today's primary care: results from a UK population survey. BMC Fam Pract 2011; *12*: 16. doi:10.1186/1471-2296-12-16

[12] Kroenke K, Spitzer RL, deGruy FV, et al. A symptom checklist to screen for somatoform disorders in primary care. *Psychosomatics* 1998; *39*: 263–72.

[13] Interian A, Allen LA, Gara MA, et al. Somatic complaints in primary care: further examining the validity of the Patient Health Questionnaire (PHQ-15). *Psychosomatics* 2006; *47*: 392–8.

[14] Steinbrecher N, Koerber S, Frieser D, et al. The prevalence of medically unexplained symptoms in primary care. *Psychosomatics* 2011; *52:* 263–71.

[15] Kroenke K, Arrington ME, Mangelsdorff AD. The prevalence of symptoms in medical outpatients and the adequacy of therapy. *Arch Intern Med* 1990; *150:* 1685–9.

[16] Reid S, Wessely S, Crayford T, et al. Medically unexplained symptoms in frequent attenders of secondary health care: retrospective cohort study. *BMJ* 2001; *322:* 1-4.

[17] Eriksen HR, Svendsrod R, Ursin G, et al. Prevalence of subjective health complaints in the Nordic European countries in 1993. *Eur J Public Health* 1998; *8:* 294-298.

[18] Kroenke K, Price RK. Symptoms in the community: prevalence, classification, and psychiatric comorbidity. *Arch Intern Med* 1993;*153*:2474-2480.

[19] Ihlebaek C, Eriksen HR, Ursin H. Prevalence of subjective health complaints (SHC) in Norway. *Scand J Public Health* 2002; *30*: 20-29.

[20] Rief W. Barsky AJ, Glombiewski JA, et al. Assessing general side effects in clinical trials: reference data from the general population. *Pharmacoepidemiol Drug Saf* 2011; 20: 405-15.

[21] Tschudi-Madsen H, Kjeldsberg M, Natvig B, et al. A strong association between non-musculoskeletal pain symptoms: results from a population study. BMC Musculoskelet Disord 2011;12:258.

[22] Ladwig KH, Marten-Mittag B, Lacruz ME, et al. Screening for multiple somatic complaints in a population-based survey: Does excessive symptom reporting capture the concept of somatic symptom disorders? Findings from the MONICA-KORA Cohort Study. J Psychosom Res 2010;68:427-437.

[23] Tschudi-Madsen H, Kjeldsberg M, Natvig B, et al. Medically unexplained conditions considered by patients in general practice. Fam Pract 2014;31:156-163.

[24] Kroenke K. Patients presenting with somatic complaints: epidemiology, psychiatric comorbidity and management. *Int J Methods Psychiatr Res* 2003; *12:* 34-43

[25] Page L, Petrie KJ, Wessely S. Psychosocial responses to environmental incidents: A review and proposed typology. *J Psychosom Res* 2006; *60*: 413-422.

[26] Rubin GJ, Nieto-Hernandez R, Wessely S. Idiopathic environmental intolerance attributed to electromagnetic fields (formerly “electromagnetic hypersensitivity”)” An updated systematic review of provocation studies. Bioelectromagnetics 2010; *31*: 1-11.

[27] Filipkowski K, Smyth J, Rutchick A, et al. Do healthy people worry? Modern health worries, subjective health complaints, perceived health, and health care utilization. *Int J Behav Med* 2010; *17:*182-188.

Figure Legends

Figure 1

Number of symptoms reported in last 7 days

Figure 2

The mean (SE) number of symptoms reported in the previous 7-days and number of GP visits in previous year.

How common are symptoms? Evidence from a New Zealand national telephone survey

Keith J. Petrie, Kate Faasse, Fiona Crichton & Andrew Grey

Keith J. Petrie, Kate Faasse, Fiona Crichton Department of Psychological Medicine, University of Auckland, Auckland, New Zealand

Andrew Grey, Department of Medicine, University of Auckland, Auckland, New Zealand

Keywords: symptom reporting; somatic complaints; medical visits; gender differences; general population

Word count: 2080

Correspondence to: Professor Keith Petrie, Department of Psychological Medicine, University of Auckland, PO Box 92019, Auckland 1142, New Zealand. Ph +649-923-6564; Fax +649373-7013 Email: kj.petrie@auckland.ac.nz

ABSTRACT

Objective: To assess the frequency of symptoms in a general population sample over the previous week and the associations between symptom reporting and demographic factors, medical visits and medication use.

Design: A representative sample general population sample (n = 1,000) was recruited using random digit dialing. Participants were asked whether they had experienced any of 46 symptoms in the previous 7 days and if so, whether the symptom was mild, moderate or severe. Demographic data and information on medical visits and medication use were also collected.

Results: Symptom reporting was very common. The median number of symptoms reported by participants in the previous week was 5 with only 10.6% of participants reporting no symptoms. The five most common symptoms in the previous 7 days were: back pain (38%), fatigue (36%), headache (35%), runny or stuffy nose (34%) and joint pain (34%). The five symptoms rated highest in terms of severity were sexual difficulties, vomiting, tremor, suicidal thoughts and sleep problems. Symptom reporting was significantly positively associated with medical visits in the previous year and current medication taking. Females reported a significantly greater number of symptoms. We found was no significant association between age or household size and symptom reporting.

Conclusions: This population-based study found that symptoms are more commonly experienced in the general population than previously estimated and are strongly associated with health care visits. Appreciation of the high prevalence of symptoms may help normalize the experience of symptom complaints among the general population.

Strengths and limitations of this study

- Our participants were a large representative sample that allowed us to estimate the prevalence of a wide range of symptoms in the general population.
- We used a longer symptom questionnaire than in previous research. This allowed us assess a greater range of symptoms experienced in the previous 7 days.
- The survey was conducted during the New Zealand winter period and this may mean that flu and cold symptoms are more prominent during this period.
- The survey was reliant on self-reported symptoms and it was not possible to check the veracity of participant's complaints.

INTRODUCTION

Physical symptoms are often believed to be a sign of poor health but previous research shows that symptoms are a common daily experience and, in most cases, unassociated with serious illness [1,2]. While there is considerable research activity on the psychological effects of serious illness, such as cancer and cardiovascular disease, there is less work on the burden and factors associated with more frequently occurring daily symptoms. This is despite the fact that such symptoms are the major cause of medical visits and health care costs, and are strongly related to disability [3-4]. While the vast majority of symptoms are transient and benign, doctors working in primary care frequently deal with a large number of patients who present with bodily symptoms but no medical diagnosis [5]. At the other end of the continuum, some patients with serious symptoms often delay for a lengthy time before seeking medical care, which can compromise their health [6-7].

Previous research on daily symptoms has been limited by the lack of a standard measure that adequately captures the breadth and severity of daily symptom reports. A recent review of measures used in symptom studies identified 40 different self-report symptom scales ranging in length from 5 to 78 symptoms, with 48% of scales consisting of 15 or fewer items [8]. The instruments also varied in the time frame used for symptom recall from a 7-day period up to a lifetime. Many scales were designed specifically to assess medically unexplained symptoms. Perhaps most surprising was the lack of consistency in assessing common symptoms. While 70% of the questionnaires assessed headaches, other relatively common symptoms were inconsistently assessed, with only 43% of scales assessing fatigue, 38% heart palpitations, 30% vomiting, and 23% joint pain [8]. Unfortunately, two of the scales recommended by this review, the Symptom Checklist-90 Somatization Scale and Patient Health Questionnaire-15, only have a limited number of physical symptoms and are focused on identifying somatization.

As many of the previous studies looking at the frequency of physical symptoms have focused on medically unexplained symptoms, a large proportion of the sample of previous studies of symptoms been drawn from medically-defined samples such as individuals registered with general practices [9-11], primary care samples [12-14], hospital outpatients [2,15] or high users of hospital care [16]. Where general population samples have been used, the number and range of symptoms assessed tend to be much smaller, which makes it difficult to get an accurate picture of the breadth and frequency of symptoms experienced in the general population [17-19].

In the current study we were interested in assessing the following questions: (1) how frequently do individuals in the general population report experiencing symptoms in the previous 7 days? (2) What symptoms are most common and which are rated as being the most severe? (3) What are the associations between symptom reporting and medication use, medical visits and demographic factors? To examine these questions we administered a comprehensive 46-item symptom checklist to a large nationally representative general population.

METHOD

Participants

A representative sample of 1,000 members of the New Zealand population was recruited using random digit dialing. A nationally representative sample was achieved using set quotas based on the age, gender and regional distribution of New Zealand. Telephone interviews were conducted over June and July, 2013. In total, 24,068 numbers were called to achieve the final survey sample of 1,000 participants. From a total of 11, 453 calls to residential landlines that were answered, 6,354 declined to participate and 233 were excluded because of language difficulty. After eligibility was assessed, 4,899 people were deemed eligible to participate. Of these, 3,876 were excluded because the group to which they belonged – with regard to age, gender,

and region – was already sufficiently represented in the sample. A small number of participants (n = 23) abandoned the interview part way though.

Measures

Symptoms

Interviewers read a list of 46 symptoms and asked respondents whether they had experienced any of the symptoms in the previous 7 days and if so, whether the symptom was mild, moderate or severe. The symptom list included 36 items from the General Assessment of Side Effects Scale,[20] a measure designed to assess commonly reported medication side effects. The scale is a comprehensive measure of common side effects and has demonstrated good psychometric properties in a large German general population.[20] While the scale does cover drug side effects, it does not include some of the commonly reported symptoms frequently found in other symptom scales. Therefore, 10 additional common symptoms were added. These items were: cough, congested or runny nose, ear problems, ear and vision problems, upset stomach or indigestion, numbness or tingling sensations, drowsiness, memory problems, difficulty concentrating, and muscle weakness. Each of the 46 symptoms were coded from 0 (not present) to 3 (severe). Cronbach's alpha showed the scale had high internal consistency (alpha = .90). Corrected item-total correlations ranged from r = 0.60 (fatigue) to r = 0.19 (increased appetite). The total number of symptoms was created by adding dichotomized (present or not present) symptoms minus menstruation.

Demographic and clinical information

Information was collected on the participant's gender, age group, marital status, employment, education, ethnicity, residence region and the number of adults currently residing in their household. Participants were also asked to recall how many times they had visited their family doctor (for themselves) during the previous year, and whether they were taking any prescription medications for the treatment of

an illness (excluding the contraceptive pill). Female participants were also asked if they were currently pregnant.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics 20. Frequency information was calculated for individual symptoms, as well as the total number of symptoms reported by each participant. An intensity score was calculated for each symptom by dividing the sum of the intensity ratings (ranging from 1 to 3) by the total number of times that symptom was reported. Chi square tests were used to assess gender differences in the percentage of participants reporting individual symptoms. Independent samples t-tests were used to assess differences in the number of symptoms reported by participants across medication use, sex, and education level. Pearson's correlations were used to investigate the relationship between symptom reporting and age group, number of adults in the household, and the reported number of GP visits during the previous year. Analysis of variance (ANOVA) was used to further investigate differences in the number of symptoms reported by people who visited their GP zero (n=214), one (n = 239), two (n = 198), three to four (n = 189), or five or more times during the previous year (n = 159). An alpha level of .05 was used for all statistical tests.

RESULTS

We first examined the total number of symptoms reported by participants in the previous 7 days. Reports of symptoms were very common with only 10.6% of participants reporting no symptoms. The number of symptoms reported ranged from 0 to 36 with 49.6% reporting fewer than five symptoms and 23% reporting 10 or more (see Figure 1).

Insert figure1 about here

The five most common symptoms in the previous seven days were: back pain, fatigue, headache, runny or stuffy nose and joint pain. The reference data for the frequency of symptoms reported in the general population and by sex is presented in Table 1.

Table 1
Symptoms in previous 7-days in total sample and by sex

	Sex				Total Sample	
	Male *n* (%)		Female *n* (%)		*n* (%)	
Back or neck pain*	171	(34.8)	211	(41.5)	382	(38.2)
Fatigue or loss of energy***	139	(28.3)	216	(42.4)	355	(35.5)
Headache***	137	(27.9)	217	(42.6)	354	(35.4)
Congested or runny nose	163	(33.2)	181	(35.6)	344	(34.4)
Joint pain or stiffness	164	(33.4)	172	(33.8)	336	(33.6)
Insomnia or sleeping problems*	120	(24.4)	166	(32.6)	286	(28.6)
Cough*	125	(25.5)	158	(31.0)	283	(28.3)
Muscle pain	115	(23.4)	116	(22.8)	231	(23.1)
Low blood pressure or circulation problems***	77	(15.7)	136	(26.7)	213	(21.3)
Upset stomach or indigestion	99	(20.2)	94	(18.5)	193	(19.3)
Irritability or nervousness*	72	(14.7)	102	(20.0)	174	(17.4)
Skin Rash or itching	68	(13.8)	92	(18.1)	160	(16.0)
Difficulty concentrating*	63	(12.8)	89	(17.5)	152	(15.2)
Dry mouth	62	(12.6)	83	(16.3)	145	(14.5)
Anxiety or fearfulness	62	(12.6)	79	(15.5)	141	(14.1)
Drowsiness	67	(13.6)	73	(14.3)	140	(14.0)
Depressed mood	78	(15.9)	60	(11.8)	138	(13.8)
Breathing problems	65	(13.2)	67	(13.2)	132	(13.2)
Agitation	64	(13.0)	63	(12.4)	127	(12.7)
Numbness or tingling sensations	59	(12.0)	65	(12.8)	124	(12.4)
Memory problems***	43	(8.8)	78	(15.3)	121	(12.1)
Abdominal pain*	46	(9.4)	71	(13.9)	117	(11.7)
Ear or hearing problems	62	(12.6)	55	(10.8)	117	(11.7)
Eye or vision problems	51	(10.4)	60	(11.8)	111	(11.1)
Nightmares or abnormal dreams	47	(9.6)	62	(12.2)	109	(10.9)
Muscle weakness	54	(11.0)	55	(10.8)	109	(10.9)
Hot flushes***	16	(3.3)	76	(14.9)	92	(9.2)
Reduced appetite*	34	(6.9)	55	(10.8)	89	(8.9)
Increased appetite	46	(9.4)	42	(8.3)	88	(8.8)
Dizziness	36	(7.3)	50	(9.8)	86	(8.6)
Nausea***	27	(5.5)	57	(11.2)	84	(8.4)
Tendency to develop bruises***	14	(2.9)	66	(13.0)	80	(8.0)
Tremor or muscle spasms	45	(9.2)	35	(6.9)	80	(8.0)
Palpitations or irregular heartbeat**	22	(4.5)	49	(9.6)	71	(7.1)
Chest Pain	38	(7.7)	33	(6.5)	71	(7.1)
Fever or increased temperature**	23	(4.7)	47	(9.2)	70	(7.0)
Diarrhoea	34	(6.9)	33	(6.5)	67	(6.7)
Abnormal sweating*	20	(4.1)	36	(7.1)	56	(5.6)
Hair loss	24	(4.9)	27	(5.3)	51	(5.1)
Constipation	19	(3.9)	29	(5.7)	48	(4.8)
Sexual problems	22	(4.5)	15	(2.9)	37	(3.7)
Difficulty urinating**	22	(4.5)	6	(1.2)	28	(2.8)
Thoughts about suicide**	18	(3.7)	6	(1.2)	24	(2.4)
Vomiting	7	(1.4)	15	(2.9)	22	(2.2)
Convulsions or seizures	3	(0.6)	5	(1.0)	8	(0.8)
Painful or irregular menstruation			45	(8.8)		

Note: Sex differences * p ≤.05; ** p ≤.01; *** p ≤.001

Using data from only participants who experienced the symptom, most symptoms were rated as mild, with an average intensity rating of M = 1.39 (SD = 0.10). The highest rated symptoms in terms of intensity were sexual difficulties, vomiting, tremor or muscle spasms and thoughts about suicide. However, typically the symptoms with the highest intensity raters were infrequently reported (Table 2).

Table 2

The 10 most highly rated symptoms by intensity

	Mean Intensity /3	Symptom frequency rank
Sexual problems	1.62	41
Vomiting	1.59	44
Tremor or muscle spasms	1.55	33
Thoughts about suicide	1.54	43
Insomnia or sleeping problems	1.53	6
Nightmares or abnormal dreams	1.52	26
Abdominal pain	1.52	22
Muscle weakness	1.50	25
Convulsions or seizures	1.50	45
Back or neck pain	1.48	1

We next examined associations between symptom reporting and medication use, medical visits and demographic factors. Current medication taking was reported

by 39% of respondents. We found symptom reporting was significantly higher in those participants who also reported taking medication (M = 8.32, SE = 0.35) compared to those not taking medication (M = 4.91, SE = 0.19), t(614.66) = -8.55, p < .001.

The number of reported symptoms in the previous 7-days was also associated with the number of GP visits in the previous year, r = 0.25, p < .001. This effect was further investigated using Analysis of Variance, comparing the number of symptoms reported across five GP visit groups (zero visits, one visit, two visits, three or four visits, and five or more visits to the GP over the previous year). There was a significant main effect of the frequency of GP visits on the total number of symptoms reported, F(4, 994) = 34.28, p < .001, (see Figure 2). Post hoc tests using a Bonferroni correction revealed that participants who reported never seeing their GP in the previous year reported significantly fewer symptoms (M = 3.97, SE = 0.38) than those who reported one visit (M = 4.80, SE = 0.36), two visits (M = 6.22, SE = 0.39), three or four visits (M = 7.39, SE = 0.40), and five or more visits (M = 10.08, SE = 0.44), p values for all comparisons < .001. Participants who went to the GP only once reported fewer symptoms than those who went three or more times, ps < .001, and participants who reported attendance at their GP clinic five or more times during the previous year reported significantly higher numbers of symptoms than all other groups, ps < .001.

Insert Figure 2 about here

In terms of demographic differences, the overall number of symptoms reported by females (M = 6.88, SE = 0.27) was significantly higher than males (M = 5.59, SE = 0.25), t(998) = -3.49, p < .001. We found 17 of 45 symptoms were significantly more frequently reported by female respondents; two symptoms, difficulty urinating and thoughts about suicide, were more commonly reported by

males, all p values < .05 (see Table 1). Symptom reporting was lower in participants who reported a tertiary (M = 5.78, SE = 0.22) versus a secondary school level education (M = 6.69, SE = 0.32), t(771.56) = 2.35, p = .02. However we found no association between the number of symptoms reported and age, r = -0.03, p = .34, or household size, r = -.02, p = .56.

We also looked at sex differences in medication use and GP visits. There was no significant difference between males (38.5%) and females (39.7%) in medication use, $\mathbf{X}^2$ (1, N = 1000) = 0.149, p = .699. However, there was a significant difference between males and females in reported GP visits ($\mathbf{X}^2$ (4, N = 999) = 23.707, p < .001. Males (27.3%) were more likely to report no GP visits in the previous year, compared to females (15.7%). Consistent with this, more females (18.9%) reported 5 or more GP visits during the previous year than males (12.9%).

DISCUSSION

In a large nationally representative sample responding to a large comprehensive symptom questionnaire we found symptom complaints to be very common. The median number of symptoms reported by participants was five in the previous week. The most common symptoms reported by participants were fatigue, back pain and headache. Higher symptom reporting was strongly associated with previous general practitioner visits, medication taking and a female gender.

The most common symptoms in the current survey are consistent with previous UK studies using samples drawn from GP practice lists. However, the current study, which uses a larger range of symptoms than previous population surveys, suggests that the symptom burden is likely to be higher among the general population than previous studies have suggested. The study also identified that there are a significant proportion of the general population that experience a large number of symptoms each week with a fifth of the sample experiencing over 10 symptoms a week and 10% reporting 14 or more symptoms.

The five most common symptoms in this survey, back pain, complaints of fatigue, headache, congested or runny nose and joint pain or stiffness are also commonly reported in other studies. Four of the five are in the top most common symptoms reported in the McAteer survey [9] and three also appear in the top five symptoms reported by Hannay.[10] In terms of the study limitations, it should be noted that the survey was reliant on self-reported symptoms and it was not possible to check the veracity of participant's complaints. Also, the survey was mostly focused on physical complaints rather than mental health problems. It should also be noted that the survey was conducted during the New Zealand winter period and this may mean that flu and cold symptoms are more prominent during this period.

Bearing in mind these limitations, our findings suggest that symptoms in the general population are more common than previously believed may be a strong driver for the use of health care. Previous studies have also found that high symptom reporting was associated with an increased number of reported bodily pain sites,[21] as well as more use of health care and mortality, even after controlling for relevant confounders.[22] Interestingly, a recent study in general practice patients also found that as symptom reports increased, so did the patient's belief that they were suffering from an unexplained condition such as amalgam poisoning, electromagnetic sensitivity or chronic fatigue syndrome.[23]

Understanding the breadth and depth of symptom reporting in the general population is important to appreciate the scope for common symptoms to be misconstrued as indicative of serious health conditions. The symptoms most commonly reported in the study, such as back pain, fatigue and headache, are not reliable indicators of underlying pathology, but are often reported in medically unexplained syndromes, associated with functional disability and high health care utilization.[24] Further, given the ease with which symptom complaints are ascribed to perceived environmental threats, which pose no genuine health risk,[25,26] insight into the extent that reported symptoms are part of the normal human experience may

provide reassurance to those with health concerns and reduce symptom misattribution.[27] Ensuring that both the general public and medical professionals have access to reliable information about the prevalence of symptoms may normalize the experience of symptoms, allay distress and reduce health care seeking, as well as help to prevent unnecessary medical testing and over-diagnosis.

Contributors KP generated the initial study idea. KP, KF & AG designed the study and drafted the manuscript. KF & FC performed the data analysis. All authors assisted with the interpretation of the results and critical revision of the manuscript. KP is the guarantor of this study.

Funding This research was funded by Pharmac, the New Zealand Government's Pharmaceutical Management Agency.

Competing Interests The authors have no competing interests to report.

Data sharing statement No additional data are available

REFERENCES

[1] Pennebaker JW. *The psychology of physical symptoms*. New York: Springer-Verlag; 1982.

[2] Kroenke K, Mangelsdorff AD. Common symptoms in ambulatory care: incidence, evaluation, therapy, and outcome. *Am J Med* 1989; *86*: 62–6.

[3] Bruusgaard D, Tschudi-Madsen H, Ihlebaek C, Kamaleri Y, Natvig B. Symptom load and functional status: results from the Ullensaker population study. *BMC Public Health* 2012; *12*: 1085

[4] Barsky AJ, Orav EJ, Bates DW. Somatization increases medical utilization and costs independent of psychiatric and medical comorbidity. *Arch Gen Psychiatry* 2005; *62*: 903–10.

[5] Kroenke K. Patients presenting with somatic complaints: Epidemiology, psychiatric comorbidity and management. Int J Methods Psychiatr Res 2003;1113:774-9.

[6] Perry K, Petrie KJ, Ellis CJ, Horne R, Moss-Morris R. Symptom expectations and delay in acute myocardial infarction patients. Heart 2001;86:91 – 2.

[7] Meechan G, Collins J, Petrie KJ. The relationship of symptoms and psychological factors to delay in seeking medical care for breast symptoms. Prev Med 2003;36: 374-378.

[8] Zijlema WL, Stolk RP, Lowe B, Rief W, Bioshare, White PD, Rosmalen JGM. How to assess common somatic symptoms in large-scale studies: A systematic review of questionnaires. *J Psychosom Res* 2013; *74*: 459-468.

[9] McAteer A, Elliott AM, Hannaford PC. Ascertaining the size of the symptom ice- berg in a UK-wide community-based survey. *Br J Gen Pract* 2011; *61*:e1-11.

[10] Hannay DR. Symptom prevalence in the community. *J R Coll Gen Pract* 1978; *28*: 492–499.

[11] Elliott AM, McAteer A, Hannaford PC. Revisiting the symptom iceberg in

today's primary care: results from a UK population survey. BMC Fam Pract 2011; *12*: 16. doi:10.1186/1471-2296-12-16

[12] Kroenke K, Spitzer RL, deGruy FV, Swindle R. A symptom checklist to screen for somatoform disorders in primary care. *Psychosomatics* 1998; *39*: 263–72.

[13] Interian A, Allen LA, Gara MA, Escobar JI, Diaz-Martinez AM. Somatic complaints in primary care: further examining the validity of the Patient Health Questionnaire (PHQ-15). *Psychosomatics* 2006; *47*: 392–8.

[14] Steinbrecher N, Koerber S, Frieser D, Hiller W. The prevalence of medically unexplained symptoms in primary care. *Psychosomatics* 2011; *52:* 263–71.

[15] Kroenke K, Arrington ME, Mangelsdorff AD. The prevalence of symptoms in medical outpatients and the adequacy of therapy. *Arch Intern Med* 1990; *150:* 1685–9.

[16] Reid S, Wessely S, Crayford T, Hotopf M. Medically unexplained symptoms in frequent attenders of secondary health care: retrospective cohort study. *BMJ* 2001; *322:* 1-4.

[17] Eriksen HR, Svendsrod R, Ursin G, Ursin H. Prevalence of subjective health complaints in the Nordic European countries in 1993. *Eur J Public Health* 1998; *8:* 294-298.

[18] Kroenke K, Price RK. Symptoms in the community: prevalence, classification, and psychiatric comorbidity. *Arch Intern Med* 1993;*153*:2474-2480.

[19] Ihlebaek C, Eriksen HR, Ursin H. Prevalence of subjective health complaints (SHC) in Norway. *Scand J Public Health* 2002; *30*: 20-29.

[20] Rief W. Barsky AJ, Glombiewski JA, Nestoriuc Y, Glaesmer H, Braehler E. Assessing general side effects in clinical trials: reference data from the general population. *Pharmacoepidemiol Drug Saf* 2011; 20: 405-15.

[21] Tschudi-Madsen H, Kjeldsberg M, Natvig B, Ihlebaek C, Dalen I, Kamaleri Y, Straand J, Bruusgaard D. A strong association between non-musculoskeletal pain symptoms: results from a population study. BMC Musculoskelet Disord

2011;12:258.

[22] Ladwig KH, Marten-Mittag B, Lacruz ME, Henningsen P, Creed F. Screening for multiple somatic complaints in a population-based survey: Does excessive symptom reporting capture the concept of somatic symptom disorders? Findings from the MONICA-KORA Cohort Study. J Psychosom Res 2010;68:427-437.

[23] Tschudi-Madsen H, Kjeldsberg M, Natvig B, Ihlebaek C, Straand J, Bruusgaard D. Medically unexplained conditions considered by patients in general practice. Fam Pract 2014;31:156-163.

[24] Kroenke K. Patients presenting with somatic complaints: epidemiology, psychiatric comorbidity and management. *Int J Methods Psychiatr Res* 2003; *12:* 34-43

[25] Page L, Petrie KJ, Wessely S. Psychosocial responses to environmental incidents: A review and proposed typology. *J Psychosom Res* 2006; *60*: 413-422.

[26] Rubin GJ, Nieto-Hernandez R, Wessely S. Idiopathic environmental intolerance attributed to electromagnetic fields (formerly “electromagnetic hypersensitivity”)” An updated systematic review of provocation studies. Bioelectromagnetics 2010; *31*: 1-11.

[27] Filipkowski K, Smyth J, Rutchick A, Adya M, Santuzzi A, Petrie KJ, Kaptein AA. Do healthy people worry? Modern health worries, subjective health complaints, perceived health, and health care utilization. *Int J Behav Med* 2010; *17:*182-188.

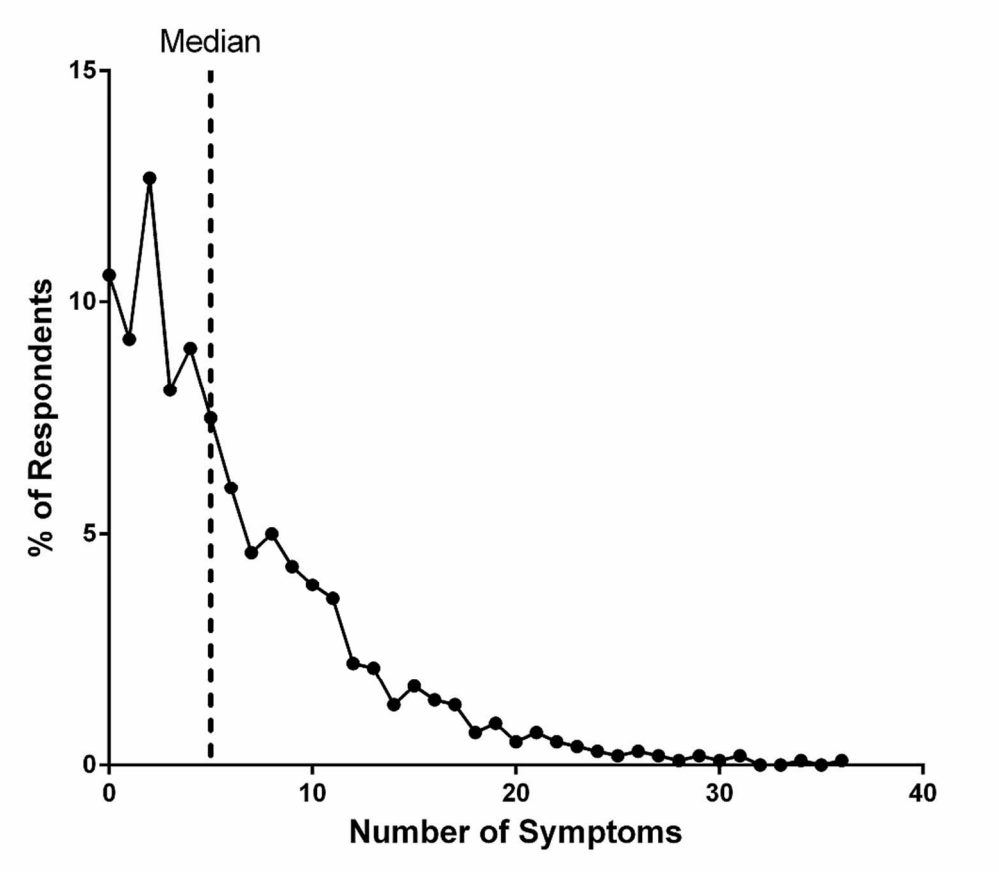
Figure Legends

Figure 1

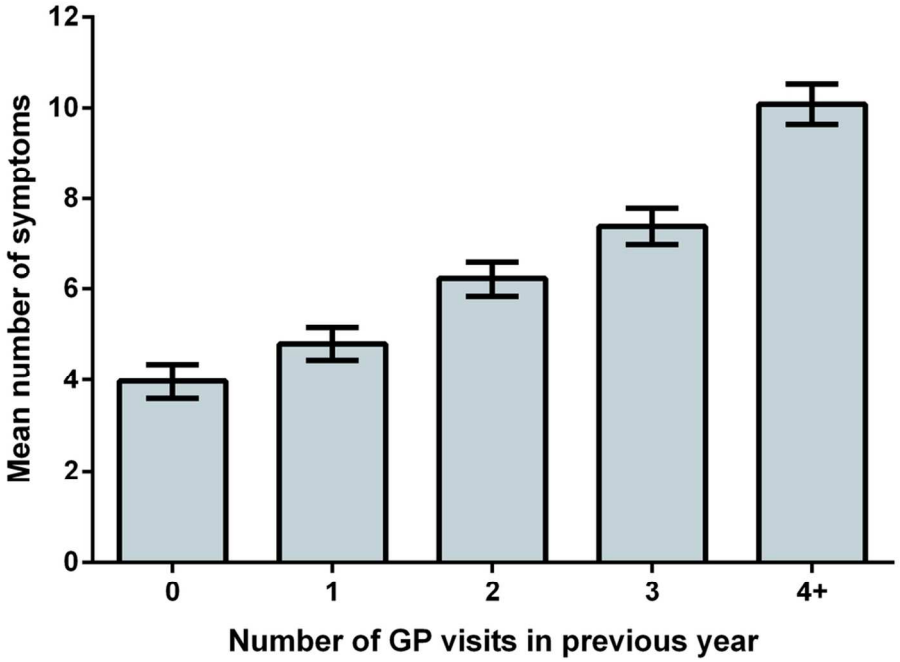
Number of symptoms reported in last 7 days

Figure 2

The mean (SE) number of symptoms reported in the previous 7-days and number of GP visits in previous year.



90x78mm (300 x 300 DPI)



99x71mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	*6-7*
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6-10
		(*c*) Explain how missing data were addressed	na
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	na
		(*e*) Describe any sensitivity analyses	na
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	na
		(b) Indicate number of participants with missing data for each variable of interest	na
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	na
		(*b*) Report category boundaries when continuous variables were categorized	na
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.