High perceived sensitivity to medicines is associated with higher medical care utilisation, increased symptom reporting and greater information-seeking about medication

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ABSTRACT

Purpose The belief that one is especially sensitive to the actions and side effects of medicines can influence treatment adherence and side-effect reporting. In this study, we investigated the prevalence of perceived medication sensitivity in the general population and its relationship to symptom complaints, information seeking about medications, use of medical care and demographic factors.

Methods A nationally representative sample of 1000 New Zealand residents completed the Perceived Sensitivity to Medicines scale and symptoms experienced during the previous 7 days. Demographic data and medical visits, medication use and information seeking about medicines were also collected.

Results Over 20% of the general population reported being very sensitive to the effects of medication (20.2%) and that small amounts of medicines can upset their body (25.3%). Participants who reported high levels of perceived sensitivity to medicines reported significantly more symptoms ($\bar{M} = 9.54$, SE = 0.47) than people with low ($\bar{M} = 5.04$, SE = 0.49) or moderate ($\bar{M} = 5.91$, SE = 0.24) levels, $p < .001$. This relationship was strongest in participants who were currently taking prescription medication. Those with high perceived sensitivity also reported being more likely to seek information about medicines, and had significantly more general practitioner visits.

Conclusions Perceived sensitivity to medicines is common in the population and associated with important clinical variables including information seeking, GP visits and symptom reporting. Identifying patients with higher perceived sensitivity to medicines may improve patient care by providing the basis for targeted and personalised interventions to reduce side effects and improve adherence to medications.

INTRODUCTION

Perceived general sensitivity to medicines is the belief that one is especially sensitive to the actions and side effects of medicines. Such beliefs are commonly reported in clinical practice.1 Higher levels of perceived sensitivity may influence the decisions patients make about treatment initiation, whether or not they take treatments as prescribed, and the number of side effects reported once treatment has been started.1,2 While a number of patients will have experienced an adverse physiological reaction to a drug or class of drugs, it would be extremely rare for someone to be sensitive to all medicines.

Evidence from randomised controlled trials of commonly prescribed medications including antihypertensive drugs and statins demonstrate similar discontinuation rates in active treatment and placebo control arms, as well as similar rates of adverse events, indicating that many reported side effects would have occurred just as frequently on placebo treatment.3–5 The experience of physical symptoms often does not reflect underlying physiological changes,6,7 and may be driven more by psychological factors including negative affect, attention and expectations.6,8–12

Patients who hold general beliefs about their high level of sensitivity to medicines are likely to have heightened expectations of experiencing side effects
following medical treatment that may influence patients’ experiences of adverse effects.\textsuperscript{8,13} The belief that one is particularly sensitive to medicines also results in patients attributing significantly more symptoms to a medical treatment.\textsuperscript{14} The belief that one is more likely to experience medication side effects may influence expectations by prompting patients to search for information about drug side effects in order to confirm this belief.\textsuperscript{15} Knowledge of potential adverse effects of a treatment can lead to heightened levels of side-effect reporting.\textsuperscript{16}

A number of other beliefs about medicines and health behaviours are associated with perceived sensitivity including more negative medication beliefs, higher levels of concern about the possible adverse effects of medications and less belief in the necessity of medical treatments. Believing that one is highly sensitive to medications is also associated with lower levels of treatment adherence.\textsuperscript{1} Importantly, perceived sensitivity to medicines and associated side effects may be on the rise in the general population.\textsuperscript{17} This is evidenced by the avoiding of modern medicines, which are seen as having toxic or harmful effects on the body, in favour of alternative medicines in order to reduce the chance of side effects.\textsuperscript{17–21}

The recently developed Perceived Sensitivity to Medicines (PSM) scale allows for the examination of beliefs about medication sensitivity.\textsuperscript{1} This scale is likely to be useful in clinical practice for identifying patients who hold such beliefs, and who may be at increased risk of medication non-adherence and heightened attribution of symptoms as drug side effects. While the PSM scale has not been used in a general medical sample to date, it has been used with patient populations, and the scale was designed for use in both general population and patient samples. The current study was conducted to provide further information about the relationship of perceived sensitivity to medicines with symptom reporting, and utilisation of medical care and drug information in the general population. It was hypothesised that higher PSM scale scores would be associated with higher rates of symptom reporting, and greater medication information seeking in comparison to respondents with lower PSM scale scores.

**METHODS**

**Sample**

A nationally representative sample of the New Zealand adult population was recruited to take part in the telephone survey using random-digit dialling and set quotas based on age and gender by region of New Zealand. Numbers of participants required in each category were calculated, and recruitment continued until the quota for each category had been reached. A sample of 1000 participants allowed us to estimate the level of perceived sensitivity to medicines in the population with a precision of 1.3\% to 3.1\%, based on the underlying level in the population being between 5\% and 50\%.

UMR Research, a professional survey organisation, conducted the interviews between 24 June and 5 July 2013. Participants provided verbal informed consent.

In all, 24068 numbers were telephoned. A total of 11453 calls to residential landlines were answered. Potential participants were excluded if they had language difficulties (\(n=223\)) or were aged under 18 years, and in a large proportion of calls, the potential participants declined the invitation to participate (\(n=6354\)). After eligibility was assessed, 4899 people were deemed eligible to participate. Of these potential participants, 3876 were excluded because the group to which they belonged—with regard to age, gender and region—had already met the required quota. A small number of participants (\(n=23\)) abandoned the interview part way though. A total of 1000 participants completed the telephone survey.

**Measures**

Information was gathered verbally during a single telephone call, which took approximately 12 min to complete.

**Demographic information.** Information was collected on the geographic region of New Zealand in which participants reside, their sex and the age group to which they belong in order to gather a representative sample of the New Zealand population. Participants were also asked about marital status, employment, education, ethnicity and the number of adults living in their household.

**Health information.** Participants were 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).

**Perceived sensitivity to medicines (PSM) scale.** Participants were asked to complete the PSM scale, a short five-item questionnaire that assesses people’s...
perceptions of their personal sensitivity to medications\(^1\) (Supporting Information). Participants rated their level of agreement with each of the statements on a five-point Likert-type scale from 1 (strongly disagree) to 5 (strongly agree). Values were summed to give a total score between 5 (not at all sensitive to medicines) and 25 (extremely sensitive to medicines). Participants were categorised by their total scores as having low (5–9; \(n=218\)), moderate (10–15; \(n=557\)) or high (16–25; \(n=146\)) perceived sensitivity to medicines.

The PSM scale has demonstrated acceptable internal consistency. Cronbach’s alpha values range from 0.78 to 0.94 across a range of participants including university students, vaccination patients, and cardiac and general medical patients in the UK and New Zealand.\(^{1,14,22,23}\) The scale also demonstrates high test–retest reliability \(r=0.89, p<.001\). Good criterion-related validity with the beliefs about medicines scale has been found, as well as good predictive validity for both symptoms reported in a vaccination patient sample and non-adherence to treatment in HIV patients. In addition to this, the scale shows high acceptability, with 98 to 100% scale completion rates seen across both patient and student samples.\(^1\) The internal consistency of the PSM in the current sample was very good (Cronbach’s alpha = .85).

**Symptoms.** Participants were asked about symptoms they had experienced during the past week using a modified version of the General Assessment of Side Effects scale.\(^{24}\) This scale was designed to assess commonly reported medication side effects, and has demonstrated good internal consistency. This was the first time this scale has been used in a telephone survey. It was modified by the addition of 10 commonly reported symptoms (cough, congested or runny nose, ear or hearing problems, eye or vision problems, upset stomach or indigestion, numbness or tingling sensations, drowsiness, memory problems, difficulty concentrating and muscle weakness), and respondents, instead of side effects, were asked about all physical symptoms experienced during the previous week. Participants were asked to rate their experience of the intensity of 46 symptoms on a scale from 0 (not present) to 3 (severe). Ratings for each symptom were dichotomised (present or not present) and summed (excluding menstrual difficulties) to create a total symptom score out of 45. This is in line with previous research investigating physical symptoms.\(^{25–27}\)

**Medication information.** How likely participants were to seek out information about a newly prescribed medication was indexed using two questions. These asked how frequently respondents read the drug packet information sheet, and how frequently they looked up information about a drug on the Internet. Answers were on a five-point scale, ranging from never to always. The responses to the two questions were summed, providing a total information-seeking score between 2 and 10, with higher scores indicating greater likelihood that participants would seek out drug-related information. These questions were asked because of particular interest in Internet usage with regard to medication information, and because little information about the use of packet inserts has been collected in general population samples to date.

**Statistical analysis**

Statistical analyses were conducted using IBM SPSS Statistics 20 (IBM, Armonk, NY, USA). Because of the large sample size, outcome variables were assessed for normality using West and colleagues’ absolute skew and kurtosis criteria.\(^{28}\) None of the outcome variables showed a substantial departure from normality, and parametric statistical tests were utilised. Independent samples \(t\)-tests, analysis of variance (ANOVA) and analysis of covariance (ANCOVA) were utilised in order to assess between-group differences in PSM scale scores. A Pearson’s correlation was used to investigate the relationship between perceived sensitivity to medicines and age. ANOVA was used to investigate differences in the total number of symptoms reported by the low, moderate and high perceived sensitivity to medicines groups, and a 3 (PSM) \(\times\) 2 (medication) ANOVA was utilised to assess differences in symptom reporting across the three PSM groups between participants who were currently taking prescription medication and those who were not. ANOVA was also used to investigate differences in information seeking between the perceived sensitivity groups. Post hoc tests for ANOVAs were conducted using a Bonferroni correction. An alpha level of .05 was used for all other tests.

**RESULTS**

**Sample characteristics**

The representative sample was comprised of 49% men and 51% women. Approximately half of the participants were aged between 30 and 49 years, almost one-third were aged 50 years and over and almost one-fifth were aged 18 to 29 years. The majority (82%) of participants were of New Zealand
European ethnicity, with 11% identifying as Maori, 3% as Pacific Island people, 7% as Asian and 3% as being of another ethnicity (participants were able to report multiple ethnicities; percentages total more than 100%). Most participants (71%) reported being in a marriage or de facto relationship, 19% were single and 9% were divorced, separated or widowed.

Most participants (61%) were not currently taking prescribed medication to treat a medical condition. One-fifth of participants had not visited their general practitioner (GP) at all over the past year. Approximately two-fifths of respondents had seen their GP once or twice, and 16% reported having attended five or more GP visits.

**Perceived sensitivity to medicines in the general population**

The total PSM scale mean score for the sample was 11.53 (Standard Error (SE)=0.14; Median (Mdn)=10, Inter-Quartile Range (IQR)=10–13). The mean score for each item can be seen in Table 1. Around 20% of participants agreed with the statement that their body is sensitive to medicines. About a quarter of participants agreed with the idea that even small amounts of medicines can upset their body. An even higher percentage (30.2%) agreed with the statement that they had had a bad reaction to medicines in the past. Twelve per cent of participants reported that their body overreacts to medicines, and almost 10% reported that they have stronger reactions to medicines than others.

Participants were categorised by their total PSM scores as having low (5–9), moderate (10–15) or high (16–25) perceived sensitivity to medicines. The mean and median PSM scores for each of these groups, as well as gender and age characteristics, can be seen in Table 2.

**Symptom reporting**

There was a significant positive correlation between the total number of symptoms reported and PSM scale scores, \( r = 0.28, n = 921, p < 0.001 \), indicating that greater perceived sensitivity was associated with increased rates of symptom reporting.

The total number of reported symptoms was compared across low, moderate and high PSM groups. There was a significant main effect of perceived sensitivity on symptom reporting, \( F(2, 918) = 30.01, p < 0.001 \). Post hoc tests revealed no significant difference in the number of symptoms reported by people with low (\( M = 5.04 \), SE=0.39) or moderate (\( M = 5.91 \), SE=0.24) levels of perceived sensitivity to medicines, \( p = 0.16 \). Participants in the high perceived sensitivity group reported significantly more symptoms (\( M = 9.54 \), SE=0.47) than their low or moderate counterparts.

<table>
<thead>
<tr>
<th>Item</th>
<th>Mean (SE)</th>
<th>Median (IQR)</th>
<th>Strongly disagree (%)</th>
<th>Disagree (%)</th>
<th>Neither agree nor disagree (%)</th>
<th>Agree (%)</th>
<th>Strongly agree (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>My body is very sensitive to medicines</td>
<td>2.38 (0.04)</td>
<td>2 (2–3)</td>
<td>15.8</td>
<td>55.6</td>
<td>6.6</td>
<td>14.3</td>
<td>5.9</td>
</tr>
<tr>
<td>My body overreacts to medicines</td>
<td>2.18 (0.03)</td>
<td>2 (2–2)</td>
<td>16.5</td>
<td>61.8</td>
<td>6.8</td>
<td>8.8</td>
<td>3.2</td>
</tr>
<tr>
<td>I usually have a stronger reaction to medicines than most people I know</td>
<td>2.11 (0.03)</td>
<td>2 (2–2)</td>
<td>19.3</td>
<td>59.6</td>
<td>6.6</td>
<td>6.2</td>
<td>3.7</td>
</tr>
<tr>
<td>I have had a bad reaction to medicines in the past</td>
<td>2.54 (0.04)</td>
<td>2 (2–4)</td>
<td>19.5</td>
<td>46.9</td>
<td>2.5</td>
<td>19.8</td>
<td>10.4</td>
</tr>
<tr>
<td>Even small amounts of medicine can upset my body</td>
<td>2.44 (0.04)</td>
<td>2 (2–4)</td>
<td>17.9</td>
<td>50.5</td>
<td>4.2</td>
<td>19.3</td>
<td>6.0</td>
</tr>
</tbody>
</table>

PSM, Perceived Sensitivity to Medicine.

<table>
<thead>
<tr>
<th>Item</th>
<th>N</th>
<th>Median PSM score (IQR)</th>
<th>Mean PSM score (SE)</th>
<th>Gender (% women)</th>
<th>Age (% ≥40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low perceived sensitivity to medicines</td>
<td>218</td>
<td>7 (5–8)</td>
<td>6.83 (0.11)</td>
<td>47.7</td>
<td>53.7</td>
</tr>
<tr>
<td>Moderate perceived sensitivity to medicines</td>
<td>557</td>
<td>11 (10–12)</td>
<td>11.34 (0.07)</td>
<td>49.6</td>
<td>55.1</td>
</tr>
<tr>
<td>High perceived sensitivity to medicines</td>
<td>146</td>
<td>18.5 (17–21)</td>
<td>19.28 (0.25)</td>
<td>64.4</td>
<td>63.7</td>
</tr>
</tbody>
</table>

PSM, Perceived Sensitivity to Medicine.
moderate perceived sensitivity counterparts, \( p_s < .001 \). High perceived sensitivity to medicines was associated with almost double the number of symptoms reported when compared with lower levels of sensitivity.

We also investigated whether increased symptom reporting in people with higher perceived sensitivity to medicines occurred primarily in participants who were currently taking prescription medicines. Participants who were taking prescription medicines reported significantly more symptoms (\( M=8.70, \ SE=0.32 \)) than those not currently taking any prescribed medications (\( M=5.35, \ SE=0.28 \)), \( F(1, \ 915)=60.83, \ p<.001 \). There was a significant interaction effect between the level of perceived sensitivity to medicines and prescription medication use, \( F(2, \ 915)=4.50, \ p=0.01 \). The impact of having high perceived sensitivity on reported symptoms was greater in participants who were currently taking prescription medication. Participants with low PSM scores who were not taking medications reported a mean of 2.17 (SE=0.77) fewer symptoms than those who were taking medications, while participants with high PSM scores who were not currently taking medications reported a mean of 5.38 (SE=0.91) fewer symptoms than those who were taking prescription medicines (Figure 1).

**Associations with demographic variables**

Perceived sensitivity to medicines was assessed across demographic variables. We found a significant difference in PSM scale scores between men and women, with women reporting higher scores (\( M=12.06, \ SE=0.22 \)) than men (\( M=10.97, \ SE=0.17 \)), \( t(888.41)=-3.93, \ p<.001 \). PSM scale scores were also significantly higher in participants who were unemployed (\( M=12.73, \ SE=0.38 \)) compared with those who were employed (\( M=11.28, \ SE=0.15 \)), \( t(206.80)=-3.58, \ p<.001 \). There was a small but significant positive correlation between age group and PSM score, \( r=0.09, \ p=0.005 \). Because of concerns that younger people may have had less experience with medicines than older participants, and that responses to the question ‘I have had a bad reaction to medicines in the past’ may be driving this relationship between total PSM score and age, correlations between individual PSM scale items and age group were assessed. Four of the five PSM scale items (my body is very sensitive to medicines; my body overreacts to medicines; I have had a bad reaction to medicines in the past; even small amounts of medicine can upset my body) demonstrated small but significant correlations with age group (\( rs=0.07-.10, \ ps=.001-.020 \)). The item ‘I usually have a stronger reaction to medicines than most people I know’ did not correlate with age group (\( r=0.04, \ p=.234 \)). There was a more general tendency for older people to report higher levels of perceived sensitivity to medicines, and this relationship was not solely driven by the past experiences with bad reactions to medicines. There were no significant differences found in PSM scale scores with regard to education level, ethnicity or relationship status. Because gender had a particularly large effect on PSM scores, all following analyses were run controlling for the effect of gender.

**Medication information seeking**

There was a significant positive correlation between participants’ reported information seeking about medicines and PSM scale scores, \( r=.16, \ n=915, \ p<.001 \), indicating that greater perceived sensitivity to medicines was associated with increased desire for information about medications.

Information seeking scores were compared across low, moderate and high PSM groups, controlling for gender. The test revealed a significant main effect of perceived sensitivity on information seeking, \( F(2, \ 911)=8.20, \ p<.001 \). Post hoc tests revealed no significant difference in medication information seeking by people who reported low (\( M=6.77, \ SE=0.15 \)) or moderate (\( M=6.85, \ SE=0.10 \)) levels of perceived sensitivity to medicines, \( p>0.99 \). However, participants in the high perceived sensitivity group reported significantly greater information seeking (\( M=7.65, \ SE=0.19 \)) than their low or moderate perceived sensitivity counterparts, \( ps<.001 \). Because of concerns about the impact of age group on reported medication information seeking, this analysis was rerun as an
GP visits
The number of GP visits was compared across low, moderate and high perceived sensitivity to medicines groups, controlling for gender. There was a significant main effect of perceived sensitivity on reported GP visits over the previous year, $F(2, 916) = 5.47, p = .004$. Post hoc tests revealed no significant differences in reported GP visits during the past year between participants with low ($M = 2.37, SE = 0.42$) and moderate ($M = 2.94, SE = 0.27$) perceived sensitivity to medicines, $p = .75$. Participants with high perceived sensitivity reported significantly more GP visits ($M = 4.54, SE = 0.52$) than either the moderate, $p = .019$, or low, $p = .004$, perceived sensitivity groups.

Prescription medication
Differences in PSM scores were investigated between participants who reported taking prescription medications to treat a medical condition (39.1% of the sample), and those who were not taking any prescription medications, controlling for gender. The PSM scores of participants who were currently taking prescription medication showed a small but statistically significant elevation ($M = 11.95, SE = 0.22$) above the PSM scores of those not taking any prescription medicines ($M = 11.26, SE = 0.18$), $F(1, 918) = 5.88, p = .016$.

DISCUSSION
This study found that over 20% of the general population believe that they are very sensitive to the effects of medication and that even small amounts of medicines can upset their body. High perceived sensitivity to medicines was associated with higher symptom reporting, particularly among participants who were taking prescribed medicines.

While it is unsurprising that people who were taking prescription medication reported more symptoms than those who were not, the combination of having high perceived sensitivity to medicines and prescription medication use resulted in a disproportionately high number of reported symptoms. High perceived sensitivity was also related to increased information seeking about medicines and having more GP visits in the previous year. Demographic differences associated with higher perceived sensitivity include female sex, unemployment and an older age.

Given the cross-sectional nature of the research, the direction of the relationships cannot be determined, and it is possible that all the people reporting high sensitivity to medicines were actually physiologically highly sensitive to medicines in general. Gender and age are both associated with physiological and pharmacokinetic differences that may alter physiological sensitivity to medicines.29–36 However, evidence from Randomised Controlled Trials (RCTs) indicates that when people are blind to treatment group, reported side effects from common medicines are exceptionally similar across active and placebo treatment arms.3–5 It seems more likely that dispositional and psychological traits including negative affect, attention, and expectations7,8,10,11,13 are related to both perceived sensitivity to medicines and symptom reporting. This is evidenced by current findings that people with high perceived sensitivity to medicines report more symptoms whether they are currently taking medication or not.

In clinical practice, patients with higher perceived sensitivity to medicines are likely to be reluctant to start new medication, attribute more symptoms to the treatment and be more likely to discontinue with the drug because of side effects.1,2,14 The PSM scale may be useful in research and clinical practice for identifying negative expectations about a proposed treatment3 and for identifying patients who may struggle to start or persist with a new treatment. The scale contains only five items, making it quick and easy to administer in a clinical practice setting.

Patients with a perceived sensitivity to medicines may be more likely to seek out information about medicines, particularly medication side effects, which may in turn strengthen their belief that they are likely to experience adverse effects of prescription drug use.15 Previous research has shown that negative expectations do predict side effects in patients commencing a new medical treatment.37,38 It is probable that this occurs because negative expectations about the medication set up a cognitive schema that makes the noticing and attributing of normal symptom experiences to the new treatment more likely.7,39 This may lead to non-adherence, medication switching or the addition of further drugs to manage these symptoms.

The fact that individuals with higher PSM scores visit their GPs more often may on the surface seem counterintuitive. However, this could be due to the fact that these individuals also report higher numbers of symptoms, and the GP visits may be initiated more for reassurance than medication seeking. It may be that
if a medication is then prescribed during a GP visit, the higher rates of reported side effects in people with higher perceived sensitivity to medicines would also prompt further medical visits.

Our study had important strengths particularly in the recruitment of a large, representative general population sample, which allowed for the assessment of the rate of medication sensitivity beliefs across a diverse group of participants. The study also had some limitations. Recruitment for the study required that participants had an active telephone landline, which may have biased the selection of participants, and people who agreed to participate may have been systematically different from those who declined. It should also be noted that the study was cross-sectional and further longitudinal research is needed to determine direction of the relationship between PSM, information seeking and symptoms. Furthermore, the survey was reliant on self-reported symptom complaints and medical visits, and it was therefore not possible to check the veracity of participants’ responses.

The results may also be limited by the reliance on only two questions about medication information-seeking behaviour, assessing only information leaflet insert use and Internet search for information. It is likely that people also use other means of finding information about prescription medicines, and that this may differ by age. The results may also be limited by the reliance on only one question about prescription medication use, rather than including questions about use of over-the-counter medications and complementary therapies as well. Future research may benefit from investigating people’s use and perceptions of sensitivity to over-the-counter medicines and complementary therapies, as these were not assessed in the current study.

It is clear that peoples’ beliefs about their personal sensitivity to medicines are associated with important clinical variables including GP visits, desire for medication information and symptom reporting. The brief PSM scale could be of use in improving patient care and medication use. The scale is quick to administer and could be of use in medical appointments and as part of pharmacy care programmes by identifying patients who may be at higher risk of increased symptom reporting or treatment non-adherence, as well as providing the basis for targeted and personalised interventions to reduce side effects and improve adherence to medications.40

CONFLICT OF INTEREST
The authors declare no conflict of interest.

KEY POINTS
• Perceived sensitivity to medicines is relatively common in the general population.
• High perceived sensitivity to medicines (PSM) is related to increased symptom reporting and a greater number of medical visits.
• Targeted interventions to address sensitivity beliefs could be useful to increase treatment adherence and decrease medication side effects.

ETHICS STATEMENT
Participants provided verbal informed consent. The research was approved by the University of Auckland Human Participants Ethics Committee (reference number 9294).

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SUPPORTING INFORMATION

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