



# Perceived sensitivity to medicines: a study among chronic medicine users in Norway

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## Abstract

**Background** Little is known about patients' Perceived Sensitivity to Medicines (PSM), "the belief that one is especially sensitive to the actions and side effects of medicines". **Objective** (i) To explore the extent of and factors associated with high Perceived Sensitivity to Medicines in a Norwegian population of chronic medicine users; (ii) to assess the psychometric characteristics of the tool to measure PSM. **Setting** Community pharmacies in the Oslo area, Norway. **Method** A cross-sectional, questionnaire-based study was conducted between October 2015 and January 2016. Patients filling prescriptions for chronic disorders were recruited. **Main outcome measure** Perceived sensitivity to medicines. **Results** The study population included 214 patients (response rate 36.7%). In total 20.1% of the patients reported low, 61.7% moderate and 18.2% high perceived sensitivity to medicines. Factors positively associated with high perceived sensitivity were female gender (Adjusted Odds Ratio (aOR) 5.33, 95% CI 1.52 to 18.72,  $p < 0.001$ ) and having a non-native language (aOR 4.76, 95% CI 1.48 to 15.30,  $p < 0.001$ ); lower educational level (aOR 0.43, 95% CI 0.17 to 1.07,  $p < 0.001$ ) and using generic medicines (aOR 0.12, 95% CI 0.03 to 0.57,  $p < 0.001$ ) were negatively associated with high perceived sensitivity to medicines. There was no association between the perceived sensitivity and the number of prescription medicines taken. The Norwegian version of the Perceived Sensitivity to Medicines tool demonstrated good psychometric characteristics. **Conclusion** Almost one out of five patients in this study reported high sensitivity to medicines. Female gender, having a non-native language, lower educational level and using generic medicines were important factors related to the perceived sensitivity. Health care providers should be aware of the impact negative expectations about medicines can have on health behaviors and treatment outcomes, and seek to elicit and address patients' beliefs about their personal sensitivity to medicines.

**Keywords** Beliefs about medicines · Generic substitution · Nocebo · Norway · Perceived sensitivity to medicines · Side effects

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## Impacts on practice

- The PSM scale can be easily administered in a community setting, and serve as a discussion tool to elicit and address negative treatment expectations.
- Health care providers should be aware that many patients believe that they are particularly sensitive to the effects of medicines, and that this is related to treatment side effects and use of generic medicines.
- Regulatory agencies and other stakeholders should take the nocebo effect into consideration when developing counselling guidelines on generic medicine use.

## Introduction

Patients' beliefs and attitudes towards medicines are important drivers of health behaviors. Studies have consistently shown that these factors are strongly associated with patients' decisions about whether to start and/or continue a needed treatment [1–4]. Patients' beliefs about medicines may also be highly related to the expectations about the effect of a pharmacological treatment, in terms of effectiveness and/or potential side effects. In 2013 Horne et al. developed a five-item scale to measure patients' perceived sensitivity to medicines (PSM), defined as “the belief that one is especially sensitive to the actions and side effects of medicines” [2]. Despite the importance of understanding factors impacting patients' medicine taking behavior, little is known about patients' increased sensitivity to medicines. To date, only one study has explored the prevalence of PSM [5], and found it to be as high as 16% in the general population of New Zealand [5].

Side effects might be related to a known pharmacological or physiological mechanism, they can also be non-specific and driven by the nocebo effect, where negative expectations about a treatment—rather than active ingredients—cause side effects [6]. The nocebo effect is the less well known counterpart of the placebo effect [7]. The placebo-nocebo phenomenon can help to better understand a treatment and how the words affect our brain. As a consequence, the nocebo effect can reduce the potential effectiveness of and adherence to a prescribed treatment [6]. For example, Faasse et al., found a relationship between high PSM and increased symptom reporting compared with people who did not view themselves as sensitive to medicines [5]. Similarly, Horne et al. found that high PSM predicted elevated symptom reporting after vaccination ( $r=0.26$ ) [2]. Moreover, other studies have shown that cancer patients who hold negative treatment expectations are more likely to experience unpleasant side effects [8, 9]. It is not yet understood how patients using medicines for chronic disorders perceive their own sensitivity to medicines, and what correlates are associated with high PSM.

## Aim of the study

This study aimed to (i) to explore the extent of and factors associated with high PSM in a Norwegian population of chronic medicine users, (ii) and to assess the psychometric characteristics of the PSM in this population. The study focuses solely on increased perceived sensitivity to medicines.

## Ethics approval

Ethics approval was received from the Norwegian Regional Committees for Medical and Health Research Ethics. The study was reported to the Data Protection Official at the Norwegian Centre for Research Data. Patient gave written informed consent and data were anonymized. Patients could participate in a symbolic (about 100 euro) gift card drawing.

## Methods

### Study design and data collection

This was a cross-sectional study conducted between October 2015 and January 2016 in three community pharmacies located in different areas of Oslo, Norway. Inclusion criteria were age over 18 years, understanding the Norwegian language, and filling a prescription to treat a self-reported chronic disorder (e.g. asthma). All patients filling a prescription were invited to participate in the study. Recruitment took place during different opening hours. Data were collected through a self-administered structured questionnaire. One member of the research team was available at the recruitment sites to answer questions and assist patients in filling out the questionnaires in a separate information room in the pharmacy. The questionnaire was first piloted. Data from the pilot were not included in the analysis. We required a sample size of 246 patients to detect a 20% prevalence of high PSM with a precision of  $\pm 5\%$  [5].

### Measures

Our outcome variable was patients' perceived sensitivity to medicines, measured via the validated psychometric instrument PSM [2]. The PSM is a structured, self-reported sensitivity measure with a satisfactory internal consistency (Cronbach's alpha) of 0.79–0.94 [2, 4, 5]. The PSM scale consists of five items (see Box 1) [2]; patients indicated their degree of agreement with each statement on a 5-point Likert scale

#### Box 1 Individual items of the perceived sensitivity to medicines scale (PSM)

1. My body is very sensitive to medicines
2. My body overreacts to medicines
3. I usually have stronger reactions to medicines than most people
4. I have had a bad reaction to medicines in the past
5. Even very small amounts of medicines can upset my body.

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(1 = strongly disagree to 5 = strongly agree). Individual item scores were added, giving a total score of 5–25. A higher score indicates a greater increased sensitivity to medicines. The PSM score was then categorized into three groups: low (5–9), moderate (10–15) and high (16–25) PSM, based on a previous study [5]. Because previous research found no relevant differences between participants with low and moderate PSM scores, these groups were combined in some of the current analyses [5]. The translation from English (original version) to Norwegian, and the back-translation were done by two independent native speakers. Discrepancy between the two English versions was settled by discussion between the two translators. (See Supplementary Table S4 for the translated version).

Patients' beliefs about medicines were explored via the 12-item Beliefs About Medicines in General Questionnaire (BMQ-General) [10, 11], which comprises three subscales (4 items each): Harm, Overuse and Benefit. BMQ-General was used to test the psychometric characteristics of the PSM-scale [2]. Patients indicated their degree of agreement with each statement on a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree). Individual item scores were added, giving a total score of 4–20 for each subscale. Higher scores indicate stronger beliefs in the concepts represented by the subscale. The belief variables were used as continuous in the analysis. A validated Norwegian version of the BMQ-General was used [12].

Patients were asked to self-report which prescription medicine(s) they were dispensed at the pharmacy on the same day of recruitment into the study, by answering the question "Which medicine(s) have you been dispensed today"? Patients could report as free-text entry the name of each medicine, along with information whether this was a treatment for a chronic condition, and whether it was a generic (Yes/No). Based on this information, we estimated how many generics were dispensed at the pharmacy out of all prescriptions filled, and corrected this estimate by the availability of a generic option, using the Norwegian Medicine Agency as reference source [13]. The generic medicine variable was then divided into three groups: no generic use (even though there was an available generic option), using < 75% generic medicines, using  $\geq$  75% generic medicines. Patients having no generic use option were grouped separately. The cut off was pragmatically chosen to provide equal group sizes. Patients were also questioned about any other medicine use via the question "Do you use other medicines (over-the-counter (OTC), e.g. paracetamol, or other prescription medicines)?" If yes, patients could report as free-text entry the name of the other medicines, whether it was OTC or prescription, and frequency of use. All recorded medicines were coded into the corresponding Anatomical Therapeutic Chemical (ATC) codes in accordance with the

World Health Organization ATC index [14]. The number of medicines regularly taken was calculated.

Patients were asked about suspected side effects that they had experienced following the use of any medicine. Patients were asked to complete a brief questionnaire consisting of a list of ten commonly reported side effects (e.g., muscle pain, nausea, dizziness), selected according to prior literature [15]. For each side effect, patients were asked whether they had every experienced it (Yes/No), and were also able to make comments via free-text entry. The number of suspected side effects was then summed.

Patients reported the number of visits they had made to their general practitioner (GP) in the previous year (0, 1–2, 3–5, > 5, cannot remember), whether they were currently using vitamins and/or supplements (Yes/No/Cannot remember) and if yes, which ones. The total number of all reported vitamins and supplements was also assessed and summed. Information about patient information leaflet (PIL) reading before starting a new medicine was collected.

Patients sociodemographics included gender, age, native language, marital status, annual household income, level of education, and health-related education or a family member with health education (categorized as in Table 1). We assessed the study's external validity by comparing the distribution of age and gender in the sample with that of the Norwegian general population filling specific prescriptions in 2015 in Oslo (via the Norwegian Prescription Database) (Supplementary Table S5).

## Statistical analyses

The Pearson Chi square and the Student's *t* test were used to compare proportions and mean scores between independent groups, respectively. The psychometric characteristics of the PSM were assessed by measuring the extent of completion (%), acceptability, the internal consistency (Cronbach's alpha), and the PSM correlation with (a) three BMQ-general subscales, (b) number of reported side effects, and (c) total number of generics [2]. The Pearson and Spearman correlation coefficients were used to relate the BMQ-general subscales with number of reported side effects and generics. This was done to test if PSM is a related, but a separate domain from the BMQ. A *p*-value of < 0.05 was considered statistically significant. To test the robustness of the correlation with PSM and number of reported side effects, item 4 was excluded.

Univariate and multivariate generalized estimation equations (GEE) with a binomial distribution (high versus moderate/low PSM) was fit to account for clustering within the reported chronic disorders [16]. The multivariate model was built after fitting the univariate model for all explanatory variables. Purposeful selection of candidate variables was done based on a univariate *p*-value < 0.20. We fitted

a reduced model by removing variables having no role ( $p$ -value  $> 0.05$ ) or yielding a change smaller than 15% in the beta coefficients of the retained variables [17]. A listwise deletion approach was applied. Data are presented as crude (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI). As a sensitivity analysis a regular multivariate logistic model was carried out. All statistical analyses were performed using SPSS 22.0 (SPSS Inc., Chicago, IL, USA).

## Results

The study included 218 chronic medicines users (response rate 36.7%) of which four were excluded, because of missing values on the PSM. This resulted in a final sample of 214 patients. The sample characteristics and the reported chronic disorders by PSM level are presented in Table 1 and Supplementary Fig S2, respectively. Overall, 60.7% of participants were women and mean age was 62.3 years (SD: 15.2; range: 23–93 years). On average the patients used 5.7 regular medicines (SD: 2.7; range: 2–16), and 1.5 supplements (SD: 1.4; range: 1–7).

Table 2 outlines the degree of agreement with each individual PSM item. In the sample, the total PSM mean score was 12.2 (SD: 3.9; median 12) (Supplementary Fig. S3). On the basis of the PSM, 20.1% of the patients presented low perceived sensitivity to medicines, 61.7% moderate and 18.2% high (Supplementary Table S6). Patients with high PSM more often reported experiencing side effects such as dizziness, headache, constipation compared to patients with low/moderate PSM (Fig. 1).

The crude and adjusted association measures are presented in Table 3. Four factors were found to be independently associated with high PSM. Specifically, women or patients with a native language other than Norwegian had about fivefold increased odds of having high PSM compared with men or native Norwegians. Acceptance of some generic substitution was associated with lower perceived sensitivity to medicines, and patients with high school education were less likely to view themselves as highly sensitive to medicines when compared to those with tertiary education. Similar association measures and overlapping confidence intervals were found in regular logistic analysis (results not shown).

The PSM was acceptable (98.2% completion), and with good internal consistency (Cronbach's alpha: 0.83). The PSM correlated negatively with the BMQ-benefit ( $r = -0.22$ ;  $p = 0.001$ ), and total numbers of generics ( $r = -0.14$ ;  $p = 0.038$ ). The PSM correlated positively with the BMQ-harm ( $r = 0.27$ ;  $p < 0.001$ ), BMQ-overuse ( $r = 0.22$ ;  $p = 0.002$ ), reported side effects ( $r = 0.46$ ;  $p < 0.001$ ; item 4 excluded:  $r = 0.39$ ;  $p < 0.001$ ). There was no significant correlation between any of the BMQ subscales and number

of reported side effects. BMQ-overuse correlated negatively with numbers of generics ( $r = -0.18$ ;  $p < 0.009$ ).

## Discussion

In this study, almost one out of five patients had high self-reported PSM, and one out of two reported experiencing side effects to medicines in the past. High perceived sensitivity appears to be a common belief among Norwegian medicine users, and our estimate (18.2%) was similar to that observed in the general population in New Zealand (15.8%) [5]. The number of experienced side effects could explain about 20% of the PSM variance. These findings may suggest that patients with high self-reported PSM hold negative expectations about treatments, which could in turn trigger a placebo effect. Likewise, it is also possible that negative past experiences with medicines may shape perceptions of medicine sensitivity. Regardless of the direction of this relationship, both negative expectations and the experience of unpleasant side effects can make patients reluctant to start or continue an otherwise beneficial and necessary treatment, as well as contributing to poor adherence [1, 2, 5, 18]. There is growing evidence that expecting side effects, makes them significantly more likely to occur [8, 19]. Indeed, patients have been found to report similar rates of many side effects independent of being in the treatment or placebo control group, even in randomized controlled trials [5, 20, 21].

Three findings from the current study point to PSM being part of a more general network of negative beliefs about medicines, and not just a specific response to an unpleasant medicine experience. First, PSM scores were negatively correlated with beliefs about the broad benefits of medicines, and positively correlated with perceptions of medicines as being harmful and overused. Second, there was no association between perceived sensitivity and the number of prescription medicines that patients reported taking. Third, while 54.2% of respondents reported having a bad reaction to medicines in the past, only 20.6% endorsed the idea that their body was very sensitive to medicines. These findings indicate that experience of poor reactions to medicines, alone, are not sufficient to generate the perception of heightened sensitivity. We propose that the perception of high personal sensitivity to medicines may contribute to a vicious cycle, in which negative expectations (high PSM) contribute to the experience of more treatment side effects via the placebo effect, which further reinforces perceived sensitivity. This is often referred to as the concept of pharmaceutical schema: a pattern of beliefs about pharmaceuticals [10, 22, 23].

A key finding is that patients who accepted generic substitution were less likely to be categorized as having high PSM compared to users of branded drugs alone (59–88%

**Table 1** Frequency of background characteristics of the study population, according to level of perceived sensitivity to medicines (PSM)

	Low/moderate PSM (n = 175)	High PSM (n = 39)	Total (n = 214)
Gender n (%)			
Female***	97 (55.4)	33 (84.6)	130 (60.7)
Age (years) mean; SD	63.1; 15.3	58.7; 14.3	62.3; 15.2
Native language n (%)			
Norwegian	147 (84.0)	29 (74.4)	176 (82.2)
Other	26 (14.9)	10 (25.6)	36 (16.8)
Marital status n (%)			
Married or cohabiting	100 (57.1)	22 (56.4)	122 (57.0)
Other <sup>a</sup>	75 (42.9)	17 (43.6)	92 (43.0)
Annual income for the household (€) <sup>b*</sup> n (%)			
Low	47 (29.9)	11 (28.2)	58 (27.1)
Medium	59 (33.7)	16 (41.0)	75 (35.0)
High	51 (29.1)	8 (20.5)	59 (27.6)
Educational level <sup>c*</sup> n (%)			
High school	81 (46.3)	16 (41.0)	97 (45.3)
University/College	63 (36.0)	21 (53.8)	84 (39.3)
Other education	30 (17.1)	2 (5.1)	32 (15.0)
Health-related education* n (%)			
Yes	39 (22.3)	14 (35.9)	53 (24.8)
No	132 (75.4)	22 (56.4)	154 (72.0)
I do not know	4 (2.3)	3 (7.7)	7 (3.3)
Family member with health-related education n (%)			
Yes	62 (35.4)	21 (53.8)	83 (38.8)
No	111 (63.4)	18 (46.2)	129 (60.3)
I do not know	2 (1.1)		2 (0.1)
Number of regular medicines taken mean; SD	5.9; 2.7	5.3; 2.8	5.7; 2.7
Use of OTC n (%)			
No	99 (56.6)	24 (61.5)	123 (57.5)
Yes	76 (43.4)	15 (38.5)	91 (42.5)
Number of supplements taken mean; SD	1.4; 1.4	1.7; 1.6	1.5; 1.4
Generic substitution <sup>d</sup> n (%)			
No	52 (29.7)	17 (43.6)	69 (32.2)
< 75%	49 (28.0)	5 (12.8)	54 (25.2)
≥ 75%	49 (28.0)	11 (28.2)	60 (28.0)
Patient information leaflet reading n (%)**			
Never/sometimes	86 (49.1)	10 (25.6)	96 (44.9)
Always	89 (50.9)	29 (74.4)	118 (55.1)
GP visits in a year n (%)			
0–2	49 (28.0)	10 (25.6)	59 (27.6)
3–5	68 (38.9)	15 (38.5)	83 (38.8)
> 5	51 (29.1)	12 (30.8)	63 (29.4)
Cannot remember	7 (4.0)	2 (5.1)	9 (4.2)

Numbers do not add up due to missing numbers. Missing values were < 4% for all variables, except annual income (n = 22; 10.3%)

\* < 0.05; \*\* ≤ 0.01 \*\*\* ≤ 0.001

<sup>a</sup>Single, divorced or other

<sup>b</sup>If you was married or registered partnership and had total income: < 43,057 or 43,057–64,478€, was categorized as low income; 64,586–86,006 € you were categorized as medium income; > 86,114€ you were categorized as high income. If you were divorced/widow/widower/not married or other and had total income: < 43,057€ you were categorized as medium income; > 43,057€ you were categorized as high income. 1 Euro = 9.29 NOK, annual exchange rate for 2016 [10]

<sup>c</sup>High school education indicates secondary education with 9–12 years of education, and also education other than tertiary

<sup>d</sup>The generic variable was divided into three groups: no generic use (even though there was an available generic brand), using < 75% generic medicines, using ≥ 75% generic medicines. Patients with no choice of a generic substitution n = 34 (14.2%)

**Table 2** Mean ( $\pm$ SD) and median for the perceived sensitivity to medicines (PSM) scale of individual items and numbers and percentages of patients with different level of agreement with the PSM items (n = 214)

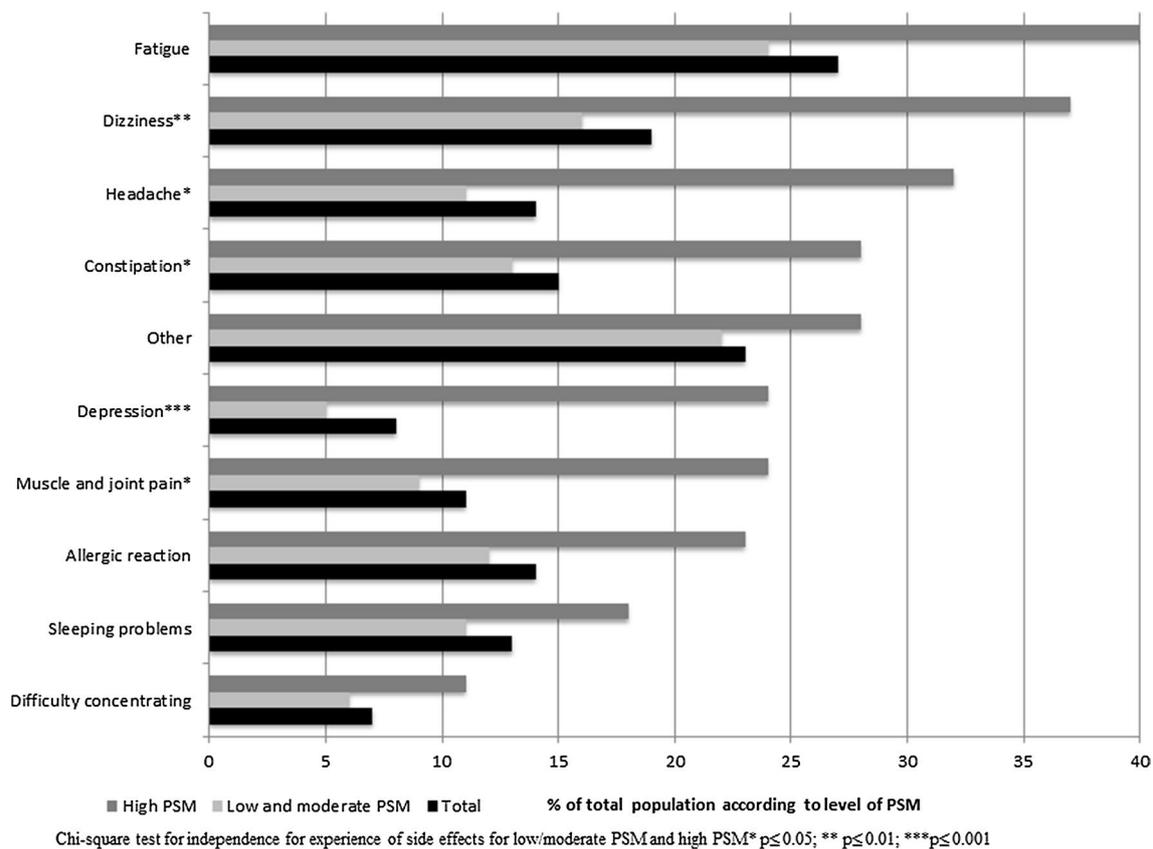
Item	Mean (SD)	Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
		n (%)	n (%)	n (%)	n (%)	n (%)
My body is very sensitive to medicines	2.5 (1.1)	25 (11.7)	107 (50.0)	38 (17.8)	31 (14.5)	13 (6.1)
My body overacts to medicines	2.2 (0.9)	34 (15.9)	129 (60.3)	32 (15.0)	15 (7.0)	4 (1.9)
I usually have a stronger reaction to medicines than most people I know	2.0 (0.9)	55 (25.7)	115 (53.7)	30 (14.0)	9 (4.2)	5 (2.3)
I have had a bad reaction to medicines in the past	3.2 (1.2)	21 (9.8)	51 (23.8)	26 (12.1)	101 (47.2)	15 (7.0)
Even small amounts of medicine can upset my body	2.2 (1.0)	46 (21.5)	108 (50.5)	34 (15.9)	20 (9.3)	6 (2.8)

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odds reduction). This association supports a link between a belief (PSM), and an objectively assessed behavioral outcome (use of generic medicines). Patients often state that generics are not an equal alternative to branded drugs [24]. Brand name medicines may offer a sense of reassurance and a promise of efficacy and safety to already concerned patients [25]. Patients’ trust in and willingness to use generic medicines varies, and depends on both sociodemographic factors as well as attitudes, beliefs, and experiences [26].

Thus, the PSM presents a useful indicator of general side effect expectations, which is conceptually related to both nocebo effects and generic medicine use [2, 26].

Gender, immigrant status, and educational level, were the sole patients’ characteristics independently associated with high PSM. This battery of correlates can however aid health care providers in the identification of patients at risk of high sensitivity to medicines. Women viewed themselves as more sensitive to medicines compared to men, as identified in



**Fig. 1** Distribution of reported side effects among the study population by high and low/moderate perceived sensitivity to medicines (PSM) (n = 214)

**Table 3** Prediction model of factors associated with high perceived sensitivity to medicines PSM (n = 214)

	Model 1 <sup>a</sup>		Model 2 <sup>b</sup>	
	Crude OR	95% CI	Adjusted OR	95% CI
<b>Gender</b>				
Male	1		1	
Female	4.42	1.76–11.09	5.33	1.52–18.72
Age (years) <sup>c</sup>	0.98	0.96–1.00		
<b>Native language</b>				
Norwegian	1		1	
Other	1.95	0.85–4.48	4.76	1.48–15.30
<b>Marital status</b>				
Married/registered partnership	1			
Other	1.03	0.51–2.08		
<b>Household income<sup>d</sup></b>				
Medium	1			
Low	0.86	0.37–2.04		
High	0.58	0.23–1.46		
<b>Educational level<sup>e</sup></b>				
University/college	1		1	
High school	0.49	0.24–0.98	0.43	0.17–1.07
<b>Health-related education</b>				
No	1			
Yes	2.15	1.01–4.60		
<b>Family member with health-related education</b>				
No	1			
Yes	2.09	1.04–4.22		
<b>Number of regular medicines taken</b>	0.92	0.80–1.07		
<b>Use of OTC</b>				
No	1			
Yes	0.81	0.40–1.66		
<b>Number of supplements taken</b>	1.15	0.93–1.43		
<b>Generic substitution<sup>f</sup></b>				
No	1		1	
< 75%	0.31	0.11–0.91	0.12	0.03–0.57
≥ 75%	0.69	0.29–1.61	0.41	0.15–1.13
<b>Patient information leaflet reading</b>				
Never/sometimes	1			
Always	2.80	1.29–6.10		
<b>GP visits in a year</b>				
0–2	1			
3–5	1.08	0.45–2.61		
> 5	1.15	0.46–2.91		
Cannot remember	1.40	0.25–7.78		

OR odds ratio, CI confidence interval

<sup>a</sup>Univariate analysis adjusted only for clustering by patients' chronic disorder

<sup>b</sup>Adjustment was done for clustering by patients' chronic disorder, health-related education, having family member with health-related

**Table 3** (continued)

education, age and number of vitamins/supplements (as continuous variables), and frequency of SPC reading

<sup>c</sup>Age was used as a continuous variable

<sup>d</sup>If one was married or registered partnership and had total income: <43,057 or 43,057–64,478€, was categorized as low income; 64,586–86,006 € you were categorized as medium income; > 86,114€ you were categorized as high income. If you were divorced/widow/widower/not married or other and had total income: <43,057€ you were categorized as medium income; > 43,057€ you were categorized as high income. 1 Euro = 9.29 NOK, annual exchange rate for 2016 [10]

<sup>e</sup>High school education indicates secondary education with 9–12 years of education, and also education other than tertiary

<sup>f</sup>The generic variable was divided into three groups: no generic use (even though there was an available generic brand), using <75% generic medicines, using ≥75% generic medicines. Patients with no choice of a generic substitution n = 34 (14.2%)

earlier studies [5, 18]. The established gender differences in pharmacokinetics and pharmacodynamics, health behavior and physical symptom reporting, may not entirely explain the association between PSM and gender [27–29]. It is possible that females are more inclined to information seeking [30–32], including information about possible treatment side effects [33]. Patients with high school education were less likely to report sensitivity to medicines. Less educated people appear to be less likely to seek health information [34] or ask questions during medical encounters [35]. It might be that that less information about side effects may have a 'protective' effect on some patients. The results of the current study parallel the finding that parents with lower levels of education held more positive views of vaccination [36].

One strength of this study is the focus on patients taking medicines for chronic disorders, an important group of the population in relation to perceived sensitivity to medicines and the reporting of adjusted measures of association with PSM. The PSM scale has been previously validated although this study was the first utilizing the Norwegian version of the PSM [2]. Yet, this PSM version demonstrated good psychometric characteristics, and a criterion-related validity in the range and similar direction as previously described [2, 4, 5]. The PSM cut-off scores are not validated, instead based on a previous study [5]. Further, all items on the PSM scale are negatively worded, which can influence participant responding. One notable limitation is the low response rate (36.7%). The main reason given for declining was lack of time to complete the questionnaire, which was estimated to take about 15–20 min. The proportion of patients within some subgroups, such as non-Norwegian native language, was low. Another limitation is the cross-sectional nature of the study: we cannot establish whether high perceived sensitivity resulted in more side effects, or the converse. Patients filling a prescription were randomly asked to participate in the

study, however we cannot rule out the possibility of selection bias. The study did not measure medication adherence and its association to PSM, as done in prior research [2]. The research team member could solely provide technical supports to patients, i.e. where to fill out; thus, the risk of bias due to the team member influence on patients' responses is likely to be minimal. In Norway patients are aware that they are being dispensed a generic medicine, which may not be the case in other countries. Thus, our observed negative association between taking generics and high PSM may not be of relevance in countries where patients are unaware of the dispensed medicine type (i.e., whether it is a generic medicine, a branded generic, or a branded medicine). Recruitment took place only in the capital of Norway; thus extrapolation of our finding to the general Norwegian population of medicine users should be done keeping these limitations in mind. Nevertheless, the characteristics of the sample were similar to those of the general prescription fillers in Oslo as regards age and gender. The precision of detecting high PSM in our sample is  $\pm 6.0\%$ . Still, our findings must be interpreted with these limitations in mind.

## Conclusion

In this Norwegian population of patients using medicines for chronic disorders, almost one out of five patients had a high self-reported perceived sensitivity to medicines, and the Norwegian PSM version presented good validity. The factors positively associated with high PSM were female gender and having a non-native language; lower educational level and using generic medicines were negatively associated with high PSM. These findings points to the need for greater awareness about patient perceptions of their personal sensitivity to medicines among health care providers.

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