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ORIGINAL REPORT

Patients' motives for participating in active post-marketing surveillance

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ABSTRACT

Purpose Web-based intensive monitoring is a method to actively collect information about adverse drug reactions (ADRs) using patients as a source of information. To date, little is known about patients' motivation to participate in this kind of active post-marketing surveillance (PMS). Increased insight in this matter can help us to better understand and interpret patient reported information, and it can be used for developing and improving patient-based pharmacovigilance tools. The aim of this study is to gain insight into patients' motives for participating in active PMS and investigate their experiences with such a system.

Method A mixed model approach combining qualitative and quantitative research methods was used. For both parts, patients participating in a web-based intensive monitoring study about the safety of anti-diabetic drugs (excluding insulins) were used. A questionnaire was developed based on the results from qualitative interviews. The data collected through the questionnaires was analysed with descriptive statistics. Relations between patient characteristics and motives were analysed using a *t*-test or a Chi-squared test.

Results 1332 (54.6%) patients responded to the questionnaire. The main motive for participation was altruism. Often experiencing ADRs or negative experiences with drugs were not important motives. The patient's gender played a role in the different motives for participation. For men, potential future personal benefit from the results was more important than for women. The overall opinion about the system was positive.

Conclusion The knowledge that patients participate in this kind of research from an altruistic point of view may strengthen patient involvement in pharmacovigilance. Copyright © 2012 John Wiley & Sons, Ltd.

KEY WORDS—pharmacovigilance; intensive monitoring; adverse drug reaction; web; patient; motivation; pharmacoepidemiology

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INTRODUCTION

Patients have become important players in pharmacovigilance. Some countries have accepted patient reports to their spontaneous reporting systems for a long time, and the experiences so far are favorable.[1–3] Recent studies show that patient reports also contribute significantly to signal detection.[4] In addition, patient reports give a new perspective on adverse drug reactions (ADRs).[5,6] The new European pharmacovigilance legislation[7,8] which will come into force mid 2012 also accentuates the growing importance of patients in pharmacovigilance. Patients will be represented in the Pharmacovigilance Risk Assessment Committee, the highest administrative body concerning pharmacovigilance issues within the European Medicines Agency. In addition, all countries will be obliged to introduce patient reporting to their spontaneous reporting systems. The reporting will be promoted by including a reference in the patient information leaflet to where patients can report ADRs.[9,10]

In 2006, the Netherlands Pharmacovigilance Centre Lareb, which is responsible for the spontaneous reporting system in the Netherlands, started its Lareb Intensive Monitoring (LIM) system as a complement to their spontaneous reporting system. LIM is a non-interventional observational cohort study using patients as a source of information. Patients are identified in their pharmacy when a drug under study is dispensed for the first time and are asked to participate with LIM. After

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online registration, the patient will receive electronic questionnaires by e-mail containing questions about patient characteristics, drug use and ADRs. The LIM methodology has been described more in depth earlier.[11–13] So far, three (groups of) drugs have been followed with LIM, namely pregabalin, duloxetine and anti-diabetic drugs (excluding insulins).

Patients' motivation to report to a spontaneous reporting system has been previously investigated.[6,14] However, to date, little is known about patients' motivation to participate in active post-marketing surveillance systems such as LIM. Increased insight into patients' motives for participation can help us to better understand and interpret patient reported information. Increased knowledge about patients' motives for participation can also be used for developing and improving patient-based pharmacovigilance tools.

The aim of this study is to gain insight into patients' motives for participating in active PMS and investigate their experiences with the system using a mixed model approach.[15]

METHOD

Questionnaire design

A mixed model approach combining qualitative and quantitave research methods was used. Qualitative interviews were used as a basis for the questionnaire to assure the internal validity.

Patients aged 18 years and older who participated in the LIM diabetes study and had completed the first questionnaire were eligible for inclusion. Participant recruitment was continued until an informational saturation point was reached,[16] which lead to an inclusion period of 3 months (between September 1st and December 4th, 2008). Eligible patients were sent an invitation letter, and if they were willing to participate, they were contacted via telephone by one of the researchers (ML) and an appointment for the interview was made. Written informed consent was obtained from all participants prior to the interview. No form of compensation was provided. The research plan was submitted to the Medical Ethics Committee for approval. No approval was needed.

In total, 21 patients were interviewed, 62% of the interviewees were male and the average age was 61 years. The interviews, except one, were carried out by two researchers. During the interviews, one researcher acted as main inquirer, the other as observer. The interviews were structured by using an interview guide. The interview guide was specifically constructed for this study. In developing the interview guide, the main research questions were divided into themes and subthemes. The themes subsequently formed the interview topics, see Table 1. The themes and subthemes were consequently translated to truly open questions.

The guide was reviewed between interviews, ensuring that topics that were not included but were relevant for the aim of the study were also discussed during the following interview. All interviews were held in the patient's home (in their mother tongue Dutch) and lasted between 25 and 45 min. The interviews were recorded, and notes were taken concurrently. The interviews were transcribed verbatim, and Nvivo 8.0.264.0 SP3 software for qualitative research (QSR international, Melbourne Australia) was used to assist with the coding, sorting and retrieval of the data.

In the interview transcripts, continuous portions of text with some apparent coherence about one clear subject were identified and given a code. Eight interviews were open coded by two researchers independently (ML and LH or EB). Coding was compared and discussed to resolve any differences. The codes were organised into three coding schemes and were thereafter categorised/grouped into a coding set. Coding of all data according to the coding set was performed by one of the researchers (ML). In order to ensure a uniform analysis of the data, four interviews were randomly selected for double coding by another researcher (LH), and the coded interviews were compared and discussed by the two researchers. From the interviews, patients' motives for participation and patients' experiences with LIM were identified. The reported motives for participating together with illustrative patient quotes are described in Table 2.

The results from the interviews were used to design a questionnaire in Dutch. In the questionnaire, statements were formulated concerning 'Motives' and 'Experiences'. The 'Motives' part consisted of possible

Table 1. Topics covered by the interview guide

Number	Topic
1	Introduction – personal information
2	Patient's explanation / perception of LIM
3	Contact with pharmacy staff during the request to participate with LIM
4	Other information sources for/on LIM
5	Attitudes towards (other) commercial and non-commercial research
6	Motives for participating with LIM
7	Experience with the LIM study
8	Experience of LIM with PC (pros and cons)
9	How to motivate other patients to participate with LIM
10	Advice to other patients who consider participating with LIM

The topics are placed in order of appearance in the interview guide

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Table 2. Quotations from interviewees concerning motives for participating

Motives	Quotations
Altruistic	
Others	It's always good for other people too. If you can help with it. You should do it. (4)
Help knowledge	To pass on my knowledge, the science to you. I think it is important to pass things on, and again, for the sake of new drug. (11)
Pharmacy's request	Just because the pharmacist handed over the folder. (15)
Fear about negative effects of drugs	To know it the new drug will cooperate with my other medicines, because I use so many other drugs I think it is important. (2)
Personal experience/ discomfort	Because I think this is pretty important. I once had penicillin, and all of a sudden I had a anaphylactic shock, that was a very intense, which resulted in a hospital admission. You do get shocked from something like that and you then wonder, about how important it is that lots of information is available on specific drugs. (12)
Egoistic motives	They cannot do enough research and it's me that will benefit, on the first place it's a bit egoistic. (6)

R = respondent, ML = interviewer

reasons which might have influenced a patient's decision to participate in LIM. The 'Experiences' part contained statements relating to the LIM questionnaire and its user-friendliness. A five-point Likert scale with the options strongly disagree, disagree, neutral, agree, strongly agree was used as answer options. To ensure that no important motive was missed, an open question was added to the questionnaire. The questionnaire also contained questions relating to patient demographics (gender and birth date) and level of education. In addition, questions relating to their LIM participation such as when they registered for LIM (year), the number of questionnaires filled in and if they had experienced any ADRs while participating in the LIM study were asked.

The web-based questionnaire was designed using the software Survey Monkey,[17] adding logic to the questions. A person was only asked questions relevant to his or her situation. If the patient had not filled in any LIM questionnaires the questions regarding experiences with the questionnaires were not asked. All questions were made mandatory, except for the open question, to enhance data completeness. Before sending, the questionnaire was tested by a panel consisting of 10 persons of different age and education level. The comments made resulted in adjustments of the final questionnaire. The letter type was increased for more easy reading, explanatory text were highlighted and made red so it would be more visible and the questionnaire was divided into more pages so that each page would contain less information and be easier to read.

Study setting

All patients who registered for the LIM diabetes study between February 1st, 2008 and October 22nd, 2010 were eligible for participating in the quantitative study.

Sending the questionnaire

The questionnaire was sent on October 28th, 2010 by e-mail. The link in the invitation e-mail was uniquely tied to the survey and the respondent's e-mail address, making sure each questionnaire could only be filled in once. After 10 days, a reminder was sent to the patients who had not yet responded. Four weeks after sending the initial questionnaire, the collection of responses was finished.

Data analysis

Descriptive statistics were used to get an overview of the patient's characteristics, the additional information asked about their LIM participation and the experiences and motives. The age was categorised in age categories which the Dutch National Institute for Public Health and the Environment uses for categorising type II diabetes mellitus patients.[18] A Pearson's Chi-square test was performed to detect statistical significant differences in patients' motives for participating in LIM between men and women and between motives and the year in which the participants registered for LIM. If a statistically significant difference was found, the frequencies of the distribution were calculated to give an understanding of the difference. Differences between responders and non-responders to this questionnaire were investigated. Differences in patient characteristics such as age, gender and having experienced an ADR were addressed using additional data from the LIM database. To test if there was a statistically significant difference between continuous variables, a *t*-test was performed; for differences between nominal variables, a Chi-square test was used. The responses to the open question were independently categorised by two researchers (LB and LH) independently and later combined and compared to see if new motives were mentioned.

MS Access 2000 was used for data retrieval. Statistical analyses were performed using SPSS for Windows version 17.0. P-values below 0.05 were considered statistically significant.

RESULTS

Response

For the study, a list of 2688 eligible patients was derived from the LIM database of whom 2437

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received a questionnaire. 1332 patients responded to the questionnaire yielding a response rate of 54.6%. For further details, see Figure 1.

Descriptive statistics

The patient characteristics are listed in Table 3. An overview of the motives for participating in LIM are given in Table 4. The main motives for participating with LIM ('agreed' or 'strongly agreed' are presented together) were: '*Other patients can be treated better*' (89%) and '*I want to help health care workers* (84%).

113 patients responded to the open question. The motive for participating which was most frequently mentioned (18 times) was '*To help gain more (scientific) information about ADRs*'. Apparently, this subject was not completely covered by the statement '*There is not enough knowledge about adverse drug reactions*' which was in the questionnaire. New motives/statements mentioned were '*I have become diabetic*' (4 times), '*I am using a medicine which is new on the market*' (4 times) and '*I am a health care worker*' (3 times). Motives which were already in the questionnaire or modification thereof were also mentioned. Patients also used the open text field to give comments on the questionnaire or health care in general (17 times).

For an overview of the experiences with LIM, see Table 5.

According to the responders to the questionnaire, the questions which were asked were understandable (83%), the majority, (78%) thought it was easy to participate. Only 10.5% of the patients found it time consuming to complete the questionnaires and less than 5% of the participants were concerned about the confidentiality after providing their information.

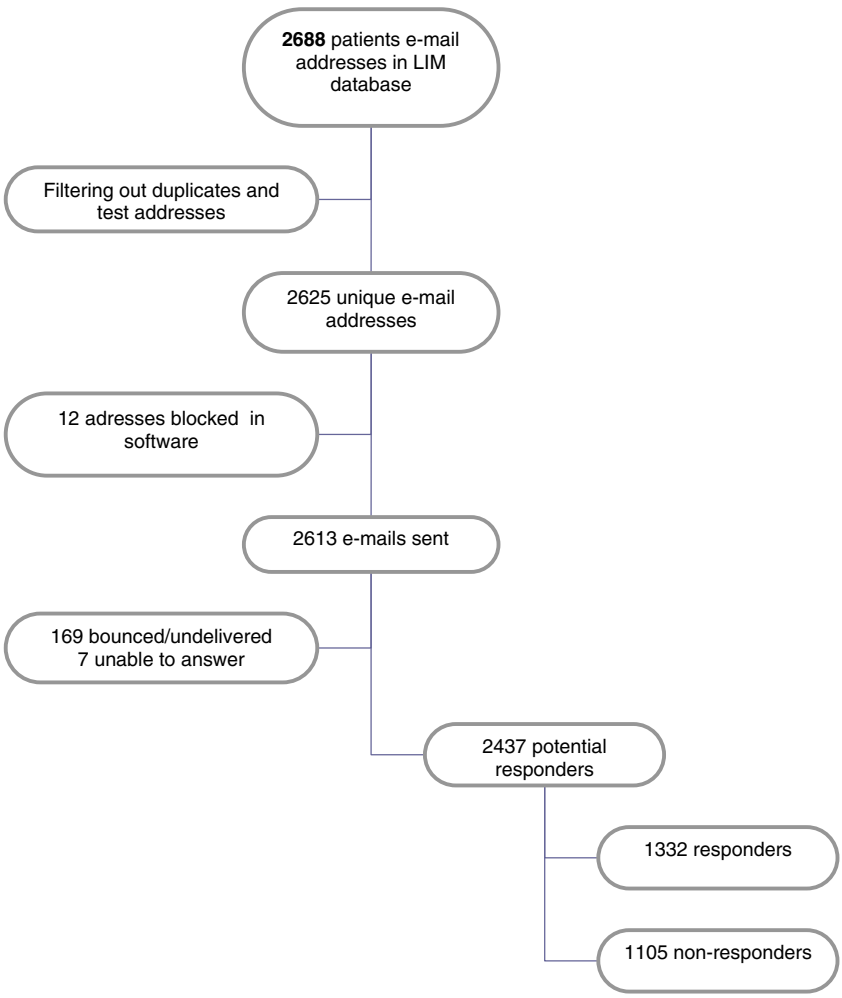

Figure 1. Response rate questionnaire

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Table 3. Patient characteristics and information about their LIM participation, the most frequently given answer is bold

Variable	Percentage % (*n*)
Gender	
Female	40.5 (545)
Male	**59.5 (787)**
Education level	
Primary school	6.8 (90)
Secondary school	23.7 (316)
Vocational education	**39.6 (527)**
Higher professional education	23.8 (317)
Academic	6.2 (82)
*Start year LIM**	
2008	21.6 (285)
2009	29.7 (392)
2010	**32.0 (423)**
Unknown	16.7 (221)
** 1321 responses, 11 missing*	
Number of questionnaires completed	
0	3.0 (40)
1	8.6 (114)
2	15.6 (208)
3	19.7 (263)
4	11.6 (155)
5	5.6 (74)
6	6.1 (81)
Unknown	**29.8 (397)**
*Reported an ADR**	
Yes	37.6 (486)
No	**62.4 (807)**
*1293 responses, 39 skipped	
*Age**	
0–14	0.2 (2)
15–24	0.1 (1)
25–44	7.7 (101)
45–64	**60.6 (804)**
65–75	26.5 (373)
75+	4.9 (50)
**1331 responses, 1 invalid*	

Differences in motives

In seven of the motives for participating in LIM, there were differences between men and women. The motives '*I often experience adverse drug reactions*', '*I am worried about drug interactions*', '*The pharmacist (assistant) asked me to participate*' and '*Other patients can be treated better*' were more important motives for participation for women than men. For men, potential future personal benefit from the results was more important than for women. On two items, '*There is not enough knowledge about adverse drug reactions*' and '*I am worried about the safety of new drugs*' there were differences between men and women.

There were no statistically significant differences in motives between patients who registered for the LIM study in different years, except for '*The pharmacist (assistant) asked me to participate*' ($p < 0.001$). For patients who recently started with LIM, this was a more important motive than for patients who started with LIM earlier.

Non-response

In total, there were 1105 non-responders (including 135 partial responders). Twelve e-mail addresses which were blocked in Survey Monkey were unknown and could not be excluded from the non-responders and were counted as non-responders, resulting in 1117 non-responders.

Differences between responders and non-responders to this questionnaire were investigated using data from the LIM database. There were no statistical significant difference in gender distribution (χ^2 test, $p = 0.393$) or age (*t*-test, $p = 0.402$). There was a statistically significant difference in reporting an ADR between responders and non-responders (χ^2 test, $p < 0.001$). Responders to the questionnaire reported more ADRs compared to non-responders.

DISCUSSION

In this study, patients' motives for participating in a web-based intensive monitoring system as well as their

Table 4. Motives for participating with LIM (1332 responses), answer which was given most frequently is marked bold

Motive	Strongly disagree % (n)	Disagree % (n)	Neutral % (n)	Agree % (n)	Strongly agree (%) n
I want to help health care workers.	1.1 (15)	1.5 (20)	13.0 (173)	**70.8 (943)**	13.6 (181)
I often experience adverse drug reactions.	8.9 (119)	**47.7 (635)**	23.3 (310)	17.9 (238)	2.3 (30)
There is not enough knowledge about adverse drug reactions.	1.8 (24)	11.3 (150)	**44.4 (591)**	38.0 (506)	4.6 (61)
The pharmacist (assistant) asked me to participate.	5.2 (69)	17.0 (227)	12.5 (166)	**54.4 (725)**	10.9 (145)
I am worried about the safety of new drugs.	2.9 (39)	25.4 (338)	**42.1 (561)**	26.2 (349)	3.4 (45)
I find it interesting to learn more about adverse drug reactions.	1.0 (13)	5.6 (75)	23.9 (318)	**58.6 (780)**	11.0 (146)
Other patients can be treated better.	0.7 (9)	0.8 (10)	9.2 (122)	**68.2 (908)**	21.2 (283)
I am worried about drug interactions.	2.1 (28)	21.2 (283)	**38.4 (511)**	32.8 (437)	5.5 (73)
I will benefit from it myself later	0.6 (8)	2.3 (30)	22.1 (295)	**63.5 (846)**	11.5 (153)
I have had bad experiences with previous drug use.	10.5 (140)	**44.6 (594)**	22.5 (300)	17.5 (233)	4.9 (65)
I want to learn more about the drug I am using.	1.1 (15)	5.6 (75)	33.4 (445)	**51.1 (680)**	8.8 (117)
Lareb Monitor directly contributes to the safety of the drugs I use.	0.6 (8)	2.0 (26)	32.5 (433)	**54.7 (728)**	10.3 (137)

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Table 5. Experiences with LIM, answer which was given most frequently is bold

Experience	Strongly disagree % (n)	Disagree % (n)	Neutral % (n)	Agree % (n)	Strongly agree (%) n
Completing the questionnaires takes too much time.	9.5 (123)	**46.3 (599)**	33.6 (435)	9.0 (117)	1.5 (19)
The asked questions are understandable.	2.2 (29)	2.6 (33)	12.3 (159)	**70.8 (915)**	12.1 (157)
I had trouble finding the drug's RVG number.	6.7 (86)	**37.4 (484)**	22.6 (292)	26.8 (346)	6.6 (85)
The questions could be formulated better.	4.8 (62)	40.8 (528)	**44.7 (578)**	8.6 (111)	1.1 (14)
After completing a LIM questionnaire, I would like to receive a copy.	6.7 (86)	25.2 (326)	26.6 (344)	**33.1 (428)**	8.4 (109)
I am convinced that the privacy of the information I send is guaranteed.	2.1 (27)	2.6 (34)	30.5 (395)	**55.1 (712)**	9.7 (125)
I find it difficult to fill in online questionnaires.	19.5 (252)	**58.7 (759)**	15.2 (197)	5.2 (67)	1.4 (18)
LIM participation is easy.	2.0 (26)	2.3 (30)	17.7 (229)	**66.2 (856)**	11.8 (152)

experiences with this system were investigated using a mixed model research approach. The main motives for participation could be classified as altruistic reasons and because the pharmacist asked them to register. Often experiencing ADRs or other negative experiences with drugs were not important as motivation; however, among the responders to the questionnaire, a bigger proportion of the patients had experienced an ADR as compared to the non-responders (38% vs 27%). The patient's gender played a role in the motivation for participation. These findings are in line with other studies where patients' motivation for reporting an ADRs to a spontaneous reporting system has been investigated.[6,14]

The overall opinion about the LIM system was very positive; completing the questionnaires with the computer seemed to be easy. The only negative feedback about LIM was the question about the drug identification number (RVG-number). Patients found it difficult to identify this number on the medicine boxes.

The statements in the questionnaire were based on the results from the qualitative interviews in order to increase the internal validity of the questionnaire.[15] The open question at the end identified three new motives/statments; however, these were only mentioned by less than five patients per motive/statement and were probably no main motives, indicating a high internal validity.

On three of the statements relating to the motives for participation, the highest frequency was in the neutral group. These motives might not have been relevant for patients or the formulation of the motive was too abstract to make a distinction between 'agree' and 'disagree'. Statements formulated in a negative way also yielded a high proportion of neutral responses.

The questionnaire was sent to all patients who had registered for the LIM study in the inclusion period which meant that some patients had already finished their LIM participation when they received the questionnaire and other patients had just started. Patients who had decided to participate years earlier might not remember their motives for participation, leading to recall bias. Analysis showed that only one motive for participation was influenced by the start year, namely '*The pharmacist (assistant) asked me to participate*'. This was a more important motive for patients who had recently registered for LIM compared to patients who registered earlier.

The characteristics of the patients who responded to the questionnaire did not differ from the non-responders. In addition, they were similar to the Dutch diabetes population concerning gender and age[18] and similar to the Dutch population concerning education level.[19] There was a difference in reporting an ADR between responders and non-responders. Patients who reported an ADR were probably more willing to complete an additional questionnaire because they might have felt more involved in LIM. This might have influenced the results of the motive '*I often experience ADRs*'; however, only about 20% of the respondents agreed this was a motive. Even though the responders and the non-responders did not differ in age and gender, it is possible that they had different experiences and opinions about LIM. Difficulties to answer web-based questionnaires or a negative attitude to LIM might be the reason for non-response, leading to a bias towards the positive.

The main limitation of this study is that patients' motives for participation have only been investigated in a cohort of patients who have registered for a study about anti-diabetic medication. However, it is not to be expected that the motives would be different for patients participating in studies where other kinds of drugs are investigated. For all drugs, the information about the study, the aim and possible gain from the study is identical.

In the past, there has been a debate in pharmacovigilance whether patients can provide reliable information about their drug use and possible ADRs. Critical voices issued their concerns that patient would use their role in pharmacovigilance to represent the views of special interest groups and become strong lobbies

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easily manipulated by interested parties.[20,21] If this would be the case, one would get a very biased view of drugs and its ADRs when using patients as a source of information. This study indicates that patients do not participate in an active pharmacovigilance system because of these reasons. Patients have an honest interest in participating in this kind of research, where the feeling of doing something good for others (altruism) is the most important motive. Patients are prepared to give their time in order to contribute to additional information about the safety of drugs.

CONCLUSION

Active and independent PMS is important, and patients will play an even bigger role herein in the near future. The knowledge that patients participate in this kind of research from an altruistic point of view may strengthen patient involvement in pharmacovigilance.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

KEY POINTS
- Patients are willing to participate in active post-marketing surveillance
- The main motive for participation is the feeling of doing something good for others (altruism)
- Men and women have different motives for participation in active post-marketing surveillance

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