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# Reporting of Adverse Drug Reactions by General Practitioners

## A Questionnaire-Based Study in the Netherlands

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### Abstract

**Background:** There has been a gradual decline over the years in the number of spontaneous reports of potential adverse drug reactions (ADRs) from general practitioners (GPs) in the Netherlands.

**Objective:** To reveal aspects of knowledge, attitudes and behaviour that can stimulate GPs to submit (more) ADRs.

**Methods:** Dutch GPs were divided into the following two groups based on their reporting behaviour during the period 2004–6: (i) active reporters; and (ii) non-reporters. A random selection from each group was sent a questionnaire, based on the Ajzen and Fishbein model, focussed on their reporting behaviour. The questions were subdivided into knowledge-related questions, attitude-related questions and questions about the influence of the professional environment.

**Results:** 700 questionnaires were completed, corresponding with an overall response of 47%. GPs who actively reported ADRs differed from their non-reporting colleagues: they had more knowledge on ADR reporting, were more interested in pharmacotherapy and more often had a positive example in their professional environment. Both reporting and non-reporting GPs considered it very important to comply with their professional environment.

**Conclusion:** Specific education and training of GPs on pharmacotherapy, preferably with extra attention to ADR reporting, is expected to improve ADR reporting. Improved communication of GPs with their fellow GPs and pharmacists as well as with their patients may further stimulate ADR reporting.

### Background

Spontaneous reporting to pharmacovigilance centres is an important tool for detecting poten-

tial adverse drug reactions (ADRs).<sup>[1]</sup> Pharmacovigilance centres rely for their information on the willingness of health professionals and patients to share their experiences in daily practice.

Reporting of suspected ADRs by all healthcare professionals is strongly supported by the WHO Drug Monitoring Programme.<sup>[2]</sup>

Not all ADRs that occur in practice are reported to pharmacovigilance centres; under-reporting is a well-known phenomenon, as has been shown in previous studies.<sup>[3,4]</sup> Various attempts have been made to increase the reporting rate and ways to improve the current system is a subject of ongoing debate in Europe.<sup>[5]</sup>

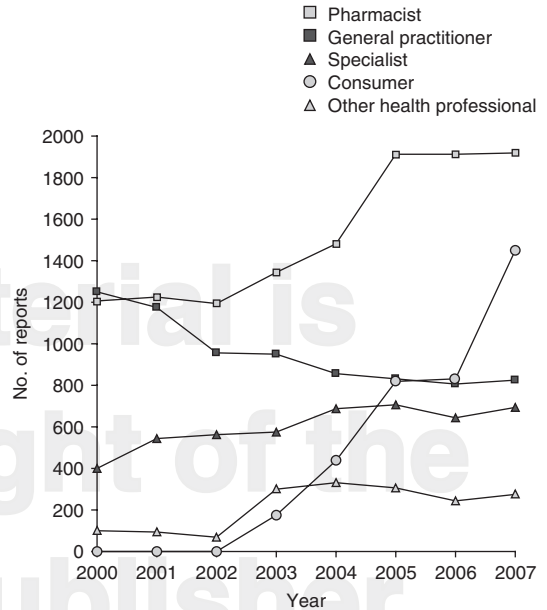
Research on the reporting behaviour of health professionals often focuses on the obstacles and reasons for not reporting.<sup>[6,7]</sup> However, in order to change the attitude towards reporting, research should also reveal the motivation to report.

#### Reporting of Adverse Drug Reactions in the Netherlands

In the Netherlands, the Pharmacovigilance Centre Lareb is responsible for collecting and analysing ADR reports on behalf of the Medicines Evaluation Board.<sup>[8]</sup> Annually, Lareb receives more than 6000 reports of ADRs from physicians, pharmacists, patients and market authorization holders, either by mail or through the Lareb website. All ADR reporters receive individual written feedback from Lareb, which is recognised as an important stimulating factor for ADR reporters.<sup>[9-11]</sup>

In recent years, the number of reports from general practitioners (GPs) has shown a small but distinct decline, as is shown in figure 1. Reporting by patients, introduced in the Netherlands in 2003, shows an opposite trend, but this cannot explain the fall in GP reports. The decline in GP reports may be due to a change in their knowledge and/or behaviour with respect to reporting ADRs. Knowledge of the reporting process is a prerequisite for reporting ADRs, whereas the attitude towards the behaviour and influence of the professional environment affects the eventual reporting behaviour, as described by Ajzen and Fishbein<sup>[12]</sup> (figure 2). This model corresponds well with the mixed theoretical model of factors that influence the reporting of ADRs by health professionals.<sup>[13]</sup>

Research on the reporting of ADRs often focuses on the obstacles and reasons for not



**Fig. 1.** Number of reports to the Netherlands Pharmacovigilance Centre Lareb over the years per type of reporter. Other health professionals include physicians in social medicine, nursing home physicians, other physicians, nurses.

reporting. Our approach was to find factors that stimulate the reporting behaviour of GPs. In order to identify these positive influences, we looked for differences between (i) active reporters; and (ii) non-reporters. Dutch GPs were divided into the two groups based on their reporting behaviour. We sent a questionnaire to investigate reporting attitudes and behaviour to a random selection from both groups. In designing the questionnaire we focused on the question: are there differences in the knowledge, attitudes and influence of the professional environment between GPs? Our aim was to investigate how this information can be used to stimulate reporting among GPs.

## Methods

We analysed the reporting behaviour of Dutch GPs between 1 January 2004 and 31 December 2006. We designed a descriptive study in which the study population comprised all practising Dutch GPs. Active reporters were defined as those GPs who reported one or more cases to the

Netherlands Pharmacovigilance Centre Lareb within the study period of 3 years. This group contained about 18% of the total number of 8400 practising GPs in the Netherlands. The non-reporters were GPs who did not report any ADRs within this period.

We selected 500 GPs randomly within the group of active reporters and, because we expected the response in the non-reporters group to be lower, 1000 GPs within this group. We designed a questionnaire, based on the Ajzen and Fishbein model,<sup>[12]</sup> to focus on the GPs' reporting behaviour. Lareb assessors and scientists evaluated the questions until consensus was reached regarding their suitability for inclusion. The questionnaire was sent out by mail to all selected active reporters and non-reporters, accompanied by a letter and a prepaid return addressed envelope. Two weeks after sending out the questionnaire, a postal reminder was sent to any GPs who had not responded.

The questions were subdivided into knowledge-related questions, attitude-related questions and questions about the influence of the professional environment. A final open-ended question invited the respondents to suggest possible ways to stimulate reporting. A full list of the questions is shown (table I). Answers containing a 5-point Likert scale of agreement (1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree) were used for some of the questions.

For statistical analyses, we used SPSS for Windows 15.0. Comparisons were made using the chi-square test for all discrete variables, re-

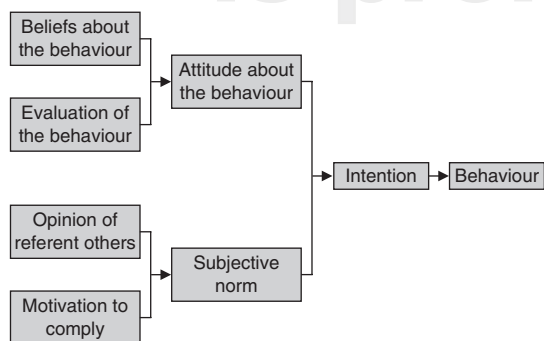


Fig. 2. The Ajzen and Fishbein model.<sup>[12]</sup>

Table I. Overview of all questions in the questionnaire

Knowledge-related questions
Are you familiar with the Netherlands Pharmacovigilance Centre Lareb? (Y/N)
Do you know how to report an adverse drug reaction to Lareb? (Y/N)
When reporting an ADR, I use (the website/a paper form)
After introduction of a new drug, the majority of ADRs are already known <sup>a</sup>
When reporting an ADR, one has to be sure of the causal relationship <sup>a</sup>
When reporting an ADR, anonymity of the reporter is guaranteed <sup>a</sup>
Attitude-related questions
I am interested in pharmacotherapy <sup>a</sup>
By reporting ADRs, I contribute to drug safety <sup>a</sup>
When I notice an ADR, I want to share this with colleagues <sup>a</sup>
Reporting an ADR is time consuming <sup>a</sup>
When reporting an ADR, it could have legal consequences for me personally <sup>a</sup>
Questions related to the influence of people in the social environment, according to the Fishbein and Ajzen model <sup>[12]</sup>
My colleagues report ADRs to Lareb (Y/N)
Patients sometimes ask me to report ADRs (Y/N)
I am willing to report an ADR at the request of a patient <sup>a</sup>
We have a clear mutual agreement on ADR reporting among regional GPs and pharmacists (Y/N)
I am willing to comply with the mutual agreement on ADR reporting among regional colleagues <sup>a</sup>
Do you have any suggestions to stimulate reporting or any general remarks?
a Indicating an answer with a 5-point Likert scale of consent (1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree).
ADR = adverse drug reaction; GPs = general practitioners; N = no; Y = yes.

jecting the null hypothesis at a value  $p < 0.05$ . In all cases, the answers to questions left blank were treated as missing. The independent variables drawn from the 5-point Likert scale were included in the analysis with all five categories, but were pooled to three categories for presentation (table II).

## Results

### Response

In total, 700 questionnaires were completed, corresponding to an overall response of 47%. In the group of active reporters, 302 questionnaires were returned (60%), compared with 398 in

**Table II.** Score per question: absolute numbers of respondents. For scores on a 5-point Likert scale<sup>a</sup>, the upper two scores and lower two scores were taken together

Statement from the questionnaire	Non-reporters			Active reporters		
	agree	disagree	neutral	agree	disagree	neutral
I know the ADR centre	395	2	NA	300	1	NA
I know how to report	365	19	NA	294	1	NA
I use the website to report <sup>b</sup>	65	213	NA	125	162	NA
All ADRs of new drugs are known <sup>b</sup>	8	272	12	6	277	3
Need to be sure of causality <sup>b</sup>	65	161	65	48	195	45
My anonymity is guaranteed <sup>b</sup>	132	37	115	126	35	119
Interest in pharmacotherapy	238	15	131	216	19	58
Contribution to drug safety <sup>b</sup>	259	11	22	260	12	16
Share ADRs with colleagues <sup>b</sup>	223	23	43	219	16	52
Reporting is time consuming	100	74	117	106	72	108
Legal consequences <sup>b</sup>	3	264	25	5	260	24
My colleagues report	72	18	303	81	10	203
Patients ask me to report	59	337	NA	60	240	NA
Willing to report for patients	313	11	46	251	3	32
Mutual agreement on reporting <sup>c</sup>	49	341	NA	54	241	NA
Comply with mutual agreement <sup>d</sup>	112	3	17	97	5	11

a 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree.

b This question was only put to GPs who had reported in the past (>3 years ago).

c The mutual agreement is a semi-formal arrangement between the regionally collaborating GPs and pharmacists and reached by them.

d This question was only answered by GPs with a mutual agreement on ADR reporting.

ADR = adverse drug reaction; GPs = general practitioners; NA = not applicable.

the group of non-reporters (40%). Of these non-reporters, 108 had never reported an ADR before, while 290 of them had reported, but more than 3 years ago. Reporters did not differ significantly from non-reporters in their age, sex, time since registration and type of practice.

The score per question, in absolute numbers of respondents, is shown in table II. All significant differences ( $p < 0.05$ ) between both groups are summarized in table III and an overview of the main findings in common with both groups is shown in table IV.

### Knowledge

All, except three, responding GPs knew about the Netherlands Pharmacovigilance Centre. Nineteen non-reporters compared with one active reporter responded that they lacked knowledge about how to report an ADR (4.9% vs 0.3%;  $p < 0.01$ ; table III). Non-reporters who had reported ADRs more than 3 years ago completed

a paper form, rather than using the website, significantly more frequently than active reporters (76.6% vs 56.4%;  $p < 0.01$ ). The introduction of a new drug to the market does not imply that all of its ADRs are known and, with the exception of eight non-reporters (2.7%) and six reporters (2.0%), the GPs were aware of this.

The fact that all ADRs can be reported, even if the role of the suspect drug is uncertain, was known by 67.7% of the active reporters compared with 55.3% of the non-reporters: a significant difference ( $p < 0.05$ ). Only about 45% of both groups knew that anonymity is guaranteed when reporting an ADR, while over 40% had no knowledge of this (table IV).

### Attitude

Of the active reporters, 73.7% were interested in pharmacotherapy compared with 62.0% of the non-reporters: a significant difference ( $p < 0.01$ ). Over 90% of the GPs in both groups felt that

reporting ADRs contributes to drug safety and knew that reporting an ADR does not have personal legal consequences. About 75% in both groups wished to share knowledge of an identified ADR with colleagues.

The question regarding the time involved in reporting an ADR could only be answered by GPs with reporting experience. In both groups of GPs, 35% found that reporting was (very) time consuming, while about 40% in both groups chose the neutral answer in the middle of the 5-point scale.

#### Influence of the Professional Environment

A higher percentage of active reporters (27.6%) than non-reporters (18.3%) believed that their fellow GPs reported ADRs ( $p < 0.05$ ). However, the majority of both groups had no knowledge about the reporting behaviour of their colleagues. Twenty percent of the reporting GPs and 14.9% of the non-reporters (no significant difference) were confronted with requests from patients to report ADRs. Both reporters and non-reporters were willing to grant such requests; fewer than 3% were not prepared to report on request of their patients.

Of active reporters, 18.3% had a mutual agreement on ADR reporting among regional GPs and pharmacists, participating together in a pharmacotherapeutic discussion group. The mutual agreement is a semi-formal arrangement between the regionally collaborating GPs and

pharmacists and reached by them. For non-reporters, this percentage was significantly lower (12.6%;  $p < 0.05$ ). About 4% in both groups were not motivated to comply with a mutual agreement on ADR reporting.

#### Suggestions/General Remarks From Participants

Various remarks and suggestions were made by participating reporters. The advice most frequently given was to continue drawing attention to the national centre and the importance of reporting. The second most frequent remark was that it was not clear which ADRs to report and that it would be impossible to report all ADRs. A direct link between the GP computer system and the reporting module of the Dutch national centre was also suggested by some GPs, as was the possibility of introducing the reporting of ADRs as a regular item on the agenda of pharmacotherapeutic discussion groups. In these groups, regionally collaborating GPs and pharmacists discuss, on a regular basis, issues concerning their patients that relate to pharmacovigilance. Several GPs commented that they did not know about the possibility of reporting via the website.

#### Discussion

In many studies on the reporting behaviour of health professionals, the negative factors influencing ADR reporting, based on the 'seven

**Table III.** Significant differences between reporters and non-reporters

Statement from the questionnaire	Percentage of GPs supporting the statement (and percentage neutral if relevant)		p-Value
	non-reporters	active reporters	
I don't know how to report an ADR	4.9	0.3	<0.01
I use the website to report an ADR <sup>a</sup>	23.4	43.6	<0.01
A causal relationship between drug and ADR is not required for reporting <sup>a</sup>	55.3 (22.3 neutral)	67.7 (15.6 neutral)	<0.05
I am interested in pharmacotherapy	62.0 (34.1 neutral)	73.7 (19.8 neutral)	<0.01
My colleagues report ADRs to Lareb	18.3 (77.1 unknown)	27.6 (69.0 unknown)	<0.05
We have a clear mutual agreement on ADR reporting among regional GPs and pharmacists <sup>b</sup>	12.6	18.3	<0.05

a This question was only put to GPs who had reported in the past.

b The mutual agreement is a semi-formal arrangement between the regionally collaborating GPs and pharmacists and reached by them.

**ADR** = adverse drug reaction; **GPs** = general practitioners.

**Table IV.** Findings in common with both groups of general practitioners (GPs)

Statement from the questionnaire	Percentage of GPs supporting the statement (and percentage neutral if relevant)	
	non-reporters	active reporters
Anonymity of reporter is guaranteed <sup>a</sup>	46.4 (40.5 neutral)	45.0 (42.5 neutral)
Reporting an ADR is (very) time consuming <sup>a</sup>	34.3 (40.2 neutral)	37.0 (37.8 neutral)
I am willing to report at the request of a patient	84.6 (12.4 neutral)	87.8 (11.2 neutral)
I am willing to comply with the mutual agreement on ADR reporting among regional colleagues <sup>b</sup>	84.8 (12.9 neutral)	85.9 (9.7 neutral)

a This question was only put to GPs who had reported in the past.

b This question was only answered by GPs with a mutual agreement on ADR reporting. The mutual agreement is a semi-formal arrangement between the regionally collaborating GPs and pharmacists and reached by them.

ADR = adverse drug reaction.

deadly sins' as proposed by Inman,<sup>[6]</sup> were described.<sup>[7,14-16]</sup> In our study, while investigating the motivation of GPs to report, some of these negative factors were also identified.

The response rate of 60% for reporters and 40% for non-reporters was comparable with the studies by Ekman<sup>[10]</sup> and Hasford et al.,<sup>[14]</sup> or somewhat lower than the response rate in similar studies,<sup>[7,15,16]</sup> but was satisfactory for this type of study.

### Knowledge

Clear information on how and what to report is essential. Improving ADR reporting rates is primarily about improving awareness of the need to report and the reporting methods.<sup>[11]</sup> The comment, by a number of GPs, that the possibility of reporting via the website was unknown to them, emphasizes the importance of GPs being more / better informed about this subject. It is especially important, as was found in similar studies,<sup>[7,10,14-16]</sup> to clarify that reports with an uncertain relationship between drug and ADR are welcome, and that not all ADRs need to be reported.<sup>[7,10,14,15]</sup> Furthermore, the fact that the anonymity of the reporter is guaranteed should be emphasized in information directed towards GPs.

### Attitude

Active reporters were more interested in pharmacotherapy than non-reporters. Arousing the interest of GPs in pharmacotherapy may

therefore result in increased reporting. This can be achieved by specific education and training, preferably with extra attention about ADR reporting.<sup>[7,11,13,15,17]</sup> For existing GPs, this effect may be achieved by publications in medical journals and by postgraduate programmes. For medical students, improved and more consistent undergraduate teaching in this area is a valuable tool<sup>[18]</sup> and is recommended.

Many GPs find reporting of ADRs time-consuming. However, the score on this question was similar for reporters and non-reporters. Apparently, the interpretation by the GPs on the amount of time they have to invest in the reporting process is not critical for the decision on whether or not to report. However, in the general remarks, some GPs did indicate that ADR reporting is considered an additional action for which little time is available in daily practice. The frequent suggestion to introduce a direct link between the GP computer system and the reporting module of the national centre may reduce the extra workload of ADR reporting for GPs.

### Influence of the Professional Environment

Amongst both reporters and non-reporters there was a desire to comply with their professional environment. The great majority of GPs indicated that they found it very important to follow the example of reporting colleagues and meet requests from patients to report ADRs. The GPs also found it very important to follow rules, set between regional GPs and pharmacists, following

a mutual agreement on ADR reporting. However, these stimulating factors are not available in most cases. More intensive contact between colleagues in healthcare professions may be an effective tool for stimulating reporting behaviour. When regionally collaborating GPs and pharmacists discuss their experiences in a pharmacotherapeutic discussion group, ADR reporting could be introduced as an item on the agenda. A clear agreement on the selection of ADRs to be reported and who reports the ADR may reduce the workload and thus improve reporting rates. Furthermore, improved communication between GPs and patients<sup>[1]</sup> may also make a considerable contribution to enhancing ADR reporting by GPs, either spontaneously or on the request of their patient.

#### Strengths and Limitations of this Study

A limitation of this type of study is the low response rate and, more specifically, the lower response rate of non-reporters compared with active reporters. This may have influenced the results of our study. However, it could be argued that a greater number of less motivated non-reporters may have chosen not to participate in the investigation. Therefore, more responses from this group may have resulted in even more pronounced differences between active reporters and non-reporters.

One of the strengths of our study is the final open-ended question that invited the respondents to suggest possible ways to stimulate reporting. This is an important tool to overcome possible omissions in the questionnaire and opens the door to new ideas.

#### Conclusions

GPs who actively report ADRs differ from their non-reporting colleagues in the following ways: they have more knowledge on ADR reporting, are more interested in pharmacotherapy and more often have a positive example in their professional environment. Both reporting and non-reporting GPs consider it very important to comply with their professional environment.

Therefore, specific education and training of GPs on pharmacotherapy, preferably with extra attention on ADR reporting, is expected to improve ADR reporting. Improved communication of GPs with their fellow GPs, colleagues in medical specialities, nurses and pharmacists, as well as with their patients may also further stimulate ADR reporting.

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Contribution of the individual authors: all authors contributed in preparing the knowledge-attitude-behaviour-based questionnaire. Eugène van Puijenbroek and Kees van Grootheest have experience with this kind of questionnaire-based research from former studies. Marije ten Napel was responsible for formulating and mailing the questionnaires and the accompanying letters, contacting the participating GPs, processing the data and performing the initial interpretation of the data. Anneke Passier was responsible for further analysis and statistical procedures, and writing and revising the paper. Eugène van Puijenbroek supervised the analysis and interpretation of the data and the writing of the paper and took overall responsibility for the study. Kees van Grootheest contributed to the design of the study and analysis of the data and critically reviewed the manuscript. All authors approved the final version of the manuscript.

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