Managing new drug safety information in the Dutch hospitals

[1]*Peter de Vries, [2] Staijnim. T. Bakker, [3]Deminor C Francisca, [4] Elisabeth Croonemon, [5]Peteria F. Decemnig, [6]Veronica K.L Mol

Abstract:

The implementation of new drug safety information and Direct Healthcare Professional Communications (DHPCs) in hospitals is important for patient safety. The aim of this study was to gain insight into which procedures and practices are in place to handle new drug safety information and particularly DHPCs in the Dutch hospital setting. We first conducted focus groups including medical specialists and hospital pharmacists, focusing on handling of drug safety information at the individual and organisational level. A survey was then developed and distributed among hospital pharmacists in all Dutch hospitals to quantify the existence of specific procedures and committees to handle drug safety information and DHPCs. Eleven specialists and 14 pharmacists from six hospitals participated in focus groups. Drug safety information was usually considered before drugs were included in formularies or treatment protocols. Furthermore, drug safety information was consulted in response to patients experiencing adverse events. DHPCs were mostly dealt with by individual professionals. DHPCs could lead to actions but this was very uncommon. Completed surveys were received from 40 (53%) of the hospitals. In 32 (80%), the hospital pharmacy had procedures to deal with new drug safety information, whereas in 11 (28%) a hospital-wide procedure was in place. Drug safety was considered in committees concerning drug formulary decisions (69%) and antibiotic policies (63%). DHPCs were assessed by a hospital pharmacist in 50% of the hospitals. Drug safety information was used for evaluation of new treatments and in response to adverse events. Assessment of whether a DHPC requires action was primarily an individual task.

Key points:

Hospital pharmacy, Drug safety, pharmacists, high-risk medications, Healthcare Professional

1. Introduction:

Safe use of medications in Dutch hospitals is a topic of great importance and plays a key role in patient safety. Hospitalised patients are a particularly vulnerable population for medication-related harm due to their underlying illness and the interventions they undergo, including the often high-risk medications they receive. Three-quarters of Direct Healthcare Professional Communications (DHPCs) issued

between 2001 and 2016 in the Netherlands had a specialist indication, making hospital-based healthcare professionals (HCPs) a key target audience for information about newly identified drug safety issues. Many hospitals have multiple committees and procedures in place to ensure optimal use of medication, such as a drug formulary committee or an antibiotic policy committee. It is not clear whether hospitals have procedures or committees in place to deal with new drug safety information, such as that communicated in DHPCs.

Effective communication in case of newly identified drug safety issues is essential for continued safe and effective use of drugs. While DHPCs are an important instrument for regulators to communicate such issues, the awareness of drug safety issues and the impact on prescribing behaviour is shown to be suboptimal. Although most studies do not focus on hospital settings specifically, it was found that the prescribing and monitoring behaviour in these settings often does not change in line with the advice given in DHPCs or other safety communications, with the exception of communications concerning erythropoiesis products. In the Netherlands, it was found that prescribing of drugs requiring initiation of a specialist was less affected by a DHPC than other drugs. A survey conducted in the Netherlands showed that internists were less aware of communicated safety issues than hospital or community pharmacists. Actions, such as adjusting therapy or informing colleagues, would be taken by 23% of the questioned internists. Several factors that can influence the uptake of a DHPC have been identified, related to the message, the medium used, the sender and/or the recipient. The questioned Dutch internists preferred that the information was issued by professional associations and national authorities. Other studies showed that a structured message, repetition of the message as well as an additional email improved uptake of the safety issue.

2. Methods:

2.1. Study design:

We used a mixed methods approach, combining semi-structured focus group interviews with a cross-sectional survey to explore and quantify how drug safety information is handled.

2.2. Study Setting:

At the time of our study, there were 79 hospitals with a hospital pharmacy in the Netherlands. Some hospital organisations have multiple or specialised locations, which do not all have their own hospital pharmacy. Hospitals can have local committees or dedicated persons to maintain a drug formulary, guide rational drug use, or detect and prevent medication errors. All hospitals are obliged by law to have internal procedures to handle incidents related to patient safety. To inform HCPs about new important

drug information in The Netherlands, marketing authorisation holders send paper-based DHPCs to all or a selection of the HCPs, including specialists in training. On this letter and its envelope, an orange or white hand is printed depending on the severity and urgency of the safety issue. Besides the hand figure, the following text is included: Important, non-commercial risk information concerning a pharmaceutical product. The DHPC may include warnings, recommendations for safe use but also information about a suspension or withdrawal of marketing authorisation due to safety issues or communicate a—usually batch-specific—drug recall due to quality defects. The content of the information is developed by the marketing authorisation holder together with the European Medicines Agency and/or national authorities.

2.3. Outcomes:

The focus groups were used to explore how drug safety information and, in particular, drug safety information and DHPCs were handled at an organisational level and by individual HCPs. This could include specific hospital or department procedures (e.g. protocols, agreements, policy or organisational structure), hospital committees (e.g. working groups) handling (new) drug safety information or DHPCs, sources of drug safety information used by HCPs and practices of HCPs when confronted with (new) drug safety issues or information.

In the survey, the existence of specific procedures and committees to handle (new) drug safety information and DHPCs in the hospitals were quantified. The survey questions were designed based on the focus group results.

2.4. Focus groups:

2.4.1. Study population and recruitment:

We aimed to recruit groups of hospital pharmacists and medical specialists from different hospitals, including at least two academic, two top clinical and two general hospitals in the Netherlands. Hospitals were approached to get in contact with a HCP with knowledge about drug safety information handling in the hospital, which was often the hospital pharmacist. This HCP was asked to come up with other relevant HCPs within their hospital, including medical specialists most frequently receiving DHPCs in the Netherlands between 2016 and 2018 (i.e. oncologists, haematologists, gynaecologists, cardiologists, internists and neurologists), who were then contacted and asked to participate.

2.4.2. Topic list:

The focus groups were conducted in a semi-structured way. To explore the handling of (new) drug safety information and, particularly, DHPCs in the hospitals, several domains derived from the Theoretical Domains Framework (TDF) were used to create a topic list. The included domains were related to

knowledge acquisition, motivation and goals, social/professional role and identity and environmental context and resources (Supplementary Table 2, see electronic supplementary material [ESM]).

3. Results:

3.1. Focus groups:

Between October 2018 and July 2019, a total of eight focus groups were conducted in six hospitals: three academic, two top clinical and one general hospital. In one academic and one top clinical hospital, two separate focus groups had to be conducted due to conflicting agendas of the participants. Eleven hospital pharmacists and 14 medical specialists participated in the focus group sessions. In one academic hospital, the focus group consisted of members of the drug formulary committee.

Participants talked about handling different types of drug safety information, including general drug safety information, information related to adverse drug events or incidents and information from DHPCs. It was discussed that such information was sometimes handled at hospital organisation level and/or at individual HCP level, and sometimes led to changes in hospital-wide procedures or individual practices, as depicted in Fig. 1. For some HCPs, the hospital policies and procedures were not that clear (Supplementary Table 1; quotes 0.01–0.02, see ESM). It was noted by the interviewer that participants often looked at the hospital pharmacist to name the relevant committees present at the hospital.

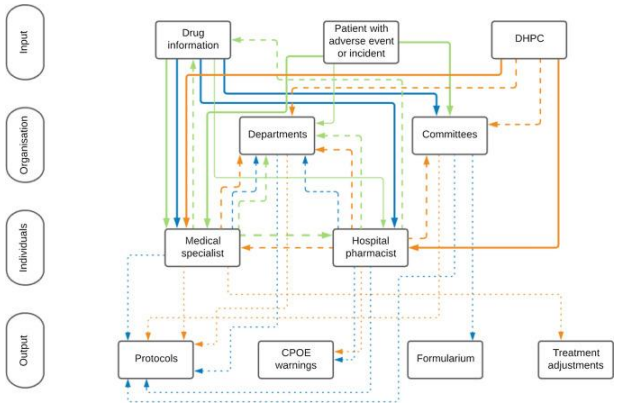


Figure. 1: Handling of drug safety information within Dutch hospitals.

3.2. Drug safety information:

Information about drugs in general is handled at organisation and individual level (Supplementary Fig. 1A, see ESM). Generally, committees consisting of hospital pharmacists and medical specialists were in place to discuss the inclusion of new drugs in the hospital formulary. Within these drug formulary committees, efficacy and safety information of new drugs is evaluated before new drugs are included in the formulary. In a few hospitals, individual HCPs sometimes presented new drugs at department

meetings. In some hospitals, treatment protocols for new drugs or protocol updates were established by certain hospital committees or departments, although these updates were, in some cases, still initiated by the individual medical specialists. It was illustrated by a medical specialist that this could occur after becoming aware of new drug safety information (quote 1.01; Supplementary Table 1, see ESM). Two pharmacists mentioned they were not always involved in drafting treatment protocols, not even for the medication section of the protocol. This was considered by them as a topic for improvement (quote 1.02–1.03; Supplementary Table 1, see ESM). Other hospital pharmacists mentioned they were usually involved in the development of treatment protocols. Here, treatment protocols were updated once every few years when new experiences from clinical practice and new drug safety information could also be taken into account (quotes 1.04–1.06; Supplementary Table 1). Furthermore, it was mentioned that hospital pharmacists could add additional warnings or make other adjustments in the CPOE system in relation to new drug safety information. All six hospitals had a safety incidents committee (Supplementary Fig. 1B, see ESM). In one top clinical hospital they cooperated with an academic hospital in case of more complex incidents.

3.3. Patients with an adverse drug event or incident:

Specialists mentioned that once they had started to prescribe a drug, new safety information was only searched for in response to patients presenting with adverse events (quotes 1.11–1.12; Supplementary Table 1; Supplementary Fig. 1B, see ESM). Hospital pharmacists were sometimes approached for advice (quotes 1.13–1.14; Supplementary Table 1, see ESM). Similar to the medical specialists, multiple hospital pharmacists also searched only reactively for (new) drug safety information (quotes 1.15–1.16, Supplementary Table 1, see ESM). Both medical specialists and hospital pharmacists mentioned that they sometimes presented a specific case or adverse event within their department or reported it to Lareb. One hospital pharmacist mentioned that a review of an adverse event had never led to updating a protocol or the drug formulary (quote 1.17; Supplementary Table 1, see ESM).

3.4. Direct healthcare professional communications (DHPCs):

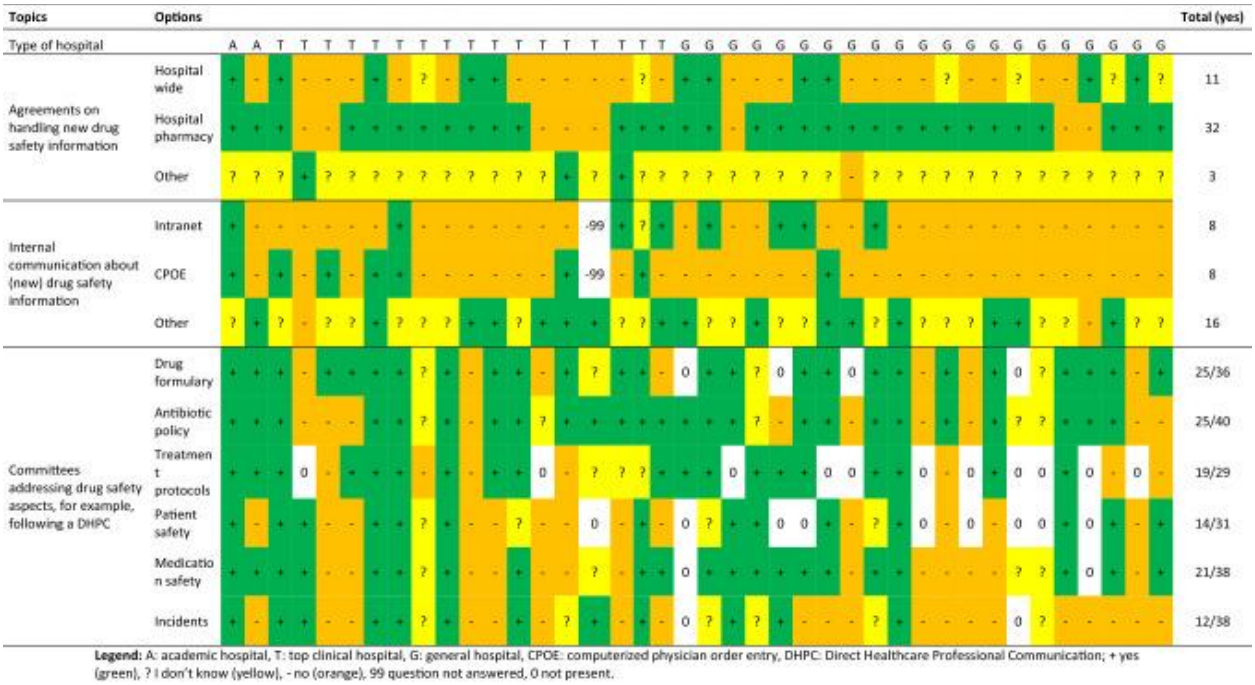
DHPCs are mainly handled at the individual or hospital pharmacy level within the hospitals (Supplementary Fig. 1C, see ESM). Both hospital pharmacists and specialists mentioned that an explicit hospital-wide procedure to handle DHPCs did not exist within their hospital, which could be seen as an omission (quotes 2.01–2.03; Supplementary Table 1, see ESM). Furthermore, it seemed that there were no systems in place in the hospitals in which one could see what decisions were made or actions were taken in response to a DHPC (quotes 2.01 and 2.04; Supplementary Table 1, see ESM). One pharmacist mentioned DHPCs were a formal item on the agenda in their pharmacy department meeting. In another hospital, DHPCs were always discussed in the drug formulary committee. The hospital pharmacist on

call would check with the drug formulary committee on who would take action when deemed necessary (quote 2.05–2.06; Supplementary Table 1, see ESM). When it came to drug recalls communicated by the DHPC, action was exclusively taken by the pharmacy (quotes 2.06–2.07; Supplementary Table 1, see ESM). One hospital pharmacist mentioned that DHPCs concerning antibiotics could be addressed in the antibiotic policy committee (quote 2.08; Supplementary Table 1, see ESM). Others mentioned that DHPCs were sometimes discussed when an individual deemed it necessary.

3.5. Survey:

In the survey study, we aimed to quantify the presence of certain procedures for handling new drug safety information within the hospital organisation as identified from the focus group analyses. This included procedures or agreements within the hospital and/or the hospital pharmacy on how to deal with new drug safety information, ways of communicating such safety information within the hospital and committees that may evaluate new safety information and adapt protocols or policies accordingly.

Table. 1: Procedures on handling new drug safety information and committees addressing drug safety aspects in 40 Dutch hospitals



Legend: A: academic hospital, T: top clinical hospital, G: general hospital, CPOE: computerized physician order entry, DHPC: Direct Healthcare Professional Communication; + yes (green), ? I don't know (yellow), - no (orange), 99 question not answered, 0 not present.

Procedures on how to deal with new drug safety information existed in 11 (28%) of the included hospitals on a hospital-wide level, and in 32 (80%) within the hospital pharmacy. In response to the open-ended question on how the DHPC was handled in their hospital, 20 (50%) of the respondents stated that DHPCs were routinely handled by the hospital pharmacist on call to assess whether action was needed, of which seven (18%) stated that DHPCs were also addressed at the department meetings of the hospital pharmacy.

When asked about internal communication concerning the new drug safety information, eight (20%) respondents indicated that new drug safety information was communicated through the intranet in their hospital. Eight (20%) respondents indicated the safety information was communicated through the CPOE system. In two cases, both intranet and CPOE system were used. Sixteen respondents indicated that other communication channels were used, with email or internal hospital (paper-based) mail mentioned by most (14 responders). In six responses, the receiver of these other communications was unspecified, and in eight hospitals the communication targeted the prescriber of the drug in question. In one hospital, it was specified that the drug formulary committee sends these internal mail messages.

4. Discussion:

Our mixed methods study shows that few hospitals have a hospital-wide procedure for handling new drug safety information in general and DHPCs in particular. At an organisational level, drug safety information was considered in hospital drug formulary or antibiotic policy committees, within hospital pharmacies and when drafting treatment protocols. Once a drug has been introduced into the formulary or adopted in the hospital, medical specialists mainly evaluated safety information in response to patients with adverse events. In these cases, they might consult the hospital pharmacists but also use a range of other information sources. The majority of the hospital pharmacies did have some procedures on how to handle new drug safety information, and in half of them this would include handling of DHPCs by the hospital pharmacist on call. In exceptional cases this could lead to a hospital-wide communication or a warning in the CPOE system. In addition, there were hospital pharmacy-led procedures for the recall of drugs communicated through DHPCs.Medication safety is important in the hospital setting and it seems obvious that drug safety information needs to be considered when decisions are made about including a new drug in the hospital drug formulary or drafting new treatment protocols. A previous study showed that almost all hospitals had a drug formulary and antibiotics committee, and that the involvement of hospital pharmacists in the establishment of treatment protocols varied, as was seen in our study. When new drug safety information becomes available, this might require hospital-wide changes or updates. Our study indicates that the need for adapting protocols or prescribing practices is not regulated by hospital-wide procedures, but is dependent on actions taken within committees or by individual HCPs.

5. Implications:

Although drug safety information is considered in drug formulary committees and for treatment protocols, new drug safety information such as communicated in DHPCs generally did not result in any

updates of drug formularies or treatment protocols. This may be a missed opportunity as adaptations in hospital drug formularies can have impact on both in- and outpatient drug prescribing.

Even though new drug safety information could reach the HCPs through multiple sources, DHPCs remain an important tool for regulators to inform HCPs of new drug safety issues. The current handling of the DHPC at a hospital level offers opportunities for improvement. A lack of explicit procedures for handling DHPCs in hospitals may lead to individual HCPs missing important issues or recommendations. Our findings re-emphasise the need to adapt to local (hospital) practices and have local medication committees to support optimal drug use in organisations, as well as to provide actionable recommendations when regulatory authorities and industry design risk minimisation measures or communication strategies.

6. Strengths and limitations:

We used a mixed methods approach that allowed us to gain a broad understanding of, as well as a quantification of how drug safety information is handled within hospitals at the organisational and individual HCP level. With the assumption that all survey respondents were from different hospitals, the survey had a good response with hospital pharmacists from half of all hospitals in the Netherlands responding. The focus groups and the survey included responses from academic, top clinical and general hospitals. The number of participants in the focus groups was limited. We were only able to include one general hospital in the focus groups; however, over half of the surveys were received from general hospitals. In addition, due to time limitations, not all topics were discussed to the same extent in all focus groups and therefore information could have been missed, which may have affected the survey content. Finally, it became apparent that knowledge of individual participants concerning hospital procedures was sometimes limited.

7. Conclusion:

In general, drug safety information was used at the individual level or in specific committees when evaluating new treatments, for updates of treatment protocols and in response to patients presenting with adverse events. In Dutch hospitals, there seem to be no hospital-wide procedures on how to handle drug safety information or DHPCs. Within many hospital pharmacies, procedures were in place to assess whether new drug safety information required further action, including DHPCs concerning drug recalls. The assessment of whether other actions are required following a DHPC was mostly an individual task for prescribers in hospitals.

8. References:

(1) Van der Veen W, Taxis K, van den Bemt PMLA. Veilig toedienen van geneesmiddelen in ziekenhuizen. Ned Tijdschr Geneeskd. 2017; 161:D2183.

(2) Hospital admissions related to medication (HARM)-Een prospectief, multicente onderzoek naar geneesmiddel gerelateerde ziekehuispnames. Division of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences; 2006.

(3) de Vries E, Denig P, de Vries ST, Monster TBM, Hugtenburg JG, Mol PGM. Drug safety issues covered by lay media: a cohort study of direct healthcare provider communications sent between 2001 and 2015 in the Netherlands. Drug Saf. 2020; 43(7):677–690. doi: 10.1007/s40264-020-00922-7.

(4) Fijn R, de Jong-van den Berg LTW, Brouwers JRBJ. Rational pharmacotherapy in the Netherlands: formulary management in Dutch hospitals. Pharm World Sci. 1999; 21(2):74–79. doi: 10.1023/A:1008654609916.

(5) Guideline on good pharmacovigilance practices (GVP)—module XVI—Risk minimisation measures: selection of tools and effectiveness indicators (Rev 2), (2017).

(6) Mollebaek M, Kaae S, De Bruin ML, Callreus T, Jossan S, Hallgreen CE. The effectiveness of direct to healthcare professional communication—a systematic review of communication factor studies. Res Social Adm Pharm. 2019; 15(5):475–482. doi: 10.1016/j.sapharm.2018.06.015.

(7) Georgi U, Lammel J, Datzmann T, Schmitt J, Deckert S. Do drug-related safety warnings have the expected impact on drug therapy? A systematic review. Pharmacoepidemiol Drug Saf. 2020; 29(3):229–251. doi: 10.1002/pds.4968.

(8) Piening S, Reber KC, Wieringa JE, Straus SM, de Graeff PA, Haaijer-Ruskamp FM, et al. Impact of safety-related regulatory action on drug use in ambulatory care in the Netherlands. Clin Pharmacol Ther. 2012; 91(5):838–845. doi: 10.1038/clpt.2011.308.

(9) de Vries ST, van der Sar MJM, Cupelli A, Baldelli I, Coleman AM, Montero D, et al. Communication on safety of medicines in Europe: current practices and general practitioners' awareness and preferences. Drug Saf. 2017; 40(8):729–742. doi: 10.1007/s40264-017-0535-0.

(10) Weatherburn CJ, Guthrie B, Dreischulte T, Morales DR. Impact of medicines regulatory risk communications in the UK on prescribing and clinical outcomes: systematic review, time series analysis and meta-analysis. Br J Clin Pharmacol. 2020; 86:698–710. doi: 10.1111/bcp.14104.

(11) Thomas SK, Hodson J, McIlroy G, Dhami A, Coleman JJ. The impact of direct healthcare professional communication on prescribing practice in the UK hospital setting: an interrupted time series analysis. Drug Saf. 2013; 36(7):557–564. doi: 10.1007/s40264-013-0057-3.

(12) Arif SA, Drury R, Ader P. Impact of Food and Drug Administration hepatotoxicity warning on prescribing and monitoring of dronedarone in a tertiary teaching hospital. Int J Pharm Pract. 2015; 23(6):456–460. doi: 10.1111/ijpp.12217.

(13) Heaton PC, Schuchter J, Lannon CM, Kemper AR. Impact of drug label changes on propofol use in pediatrics for moderate conscious sedation. Clin Ther. 2011; 33(7):886–895. doi: 10.1016/j.clinthera.2011.05.090.

(14) Kim SC, Kim DH, Mogun H, Eddigns W, Polinski JM, Franklin JM, et al. Impact of the US Food and Drug Administration's safety-related announcements on the use of bisphosphonates after hip fracture. J Bone Miner Res. 2016; 31(8):1536–1540. doi: 10.1002/jbmr.2832.

(15) Dunker A, Kolanczyk DM, Maendel CM, Patel AR, Pettit NN. Impact of the FDA warning for azithromycin and risk for QT prolongation on utilization at an academic medical center. Hosp Pharm. 2016; 51(10):830–833. doi: 10.1310/hpj5110-830.