SCOPE Work Package 6
Healthcare Professional Survey

Medicines Safety Communications and their Effectiveness

2016

SCOPE

SCOPE Work Package 6 Healthcare Professional Survey

Contents

Acknowledgments

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1. Preface

1.1 Definitions and abbreviations

Terminology	Description
ADR	Adverse drug reaction
DK	Denmark
DHPC	Direct healthcare professional communication
χ^2--test	Chi-square test
EM	Educational material
EMA	European Medicines Agency
EPS/EDS	Electronic Prescribing/Dispensing Systems
ES	Spain
GP	General Practitioner
HCP	Healthcare Professional
HR	Croatia
IE	Ireland
IT	Italy
MAH	Marketing Authorisation Holder
MS	Member State
NCA	National Competent Authority
NL	Netherlands
NO	Norway
PRAC	Pharmacovigilance Risk Assessment Committee
PV	Pharmacovigilance
SE	Sweden
SmPC	Summary of Product Characteristics
UK	United Kingdom

1.2 Document revision history

Version	Revision date	Authors	Summary of Changes
Version 1	2015-10-08	J.M. van der Sar, S.T.de Vries, P.G.M. Mol	First draft
Version 2	2015-12-14	J.M. van der Sar, S.T. de Vries, P.G.M. Mol	Second draft
Version 3	2016-01-16	J.M. van der Sar, S.T. de Vries, P.G.M. Mol	Discussion added
Version 4	2016-03-11	J.M. van der Sar, S.T. de Vries, P.G.M. Mol	Report adapted based on comments provided by project members
Version 5	2016-04-19	J.M van der Sar, S.T. de Vries, P.G.M. Mol	Second adaptation based on comments provided by project members

1.3 Attachments

Ref No	Document name
Annex I	Survey

2. Executive summary

In this report we present the view of **3625 healthcare professionals** (HCPs), from nine European countries, on safety communication activities by national competent authorities (NCAs), which may be conducted in collaboration with marketing authorisation holders (MAHs). These HCPs represent three northern European countries (Norway (NO), Sweden (SE), Denmark (DK)), three western European countries (Ireland (IE), United Kingdom (UK) and the Netherlands (NL)) and three southern European countries (Spain (ES), Italy (IT) and Croatia (HR)). The HCPs targeted were general practitioners (GPs), pharmacists (except for ES and SE) and cardiologists. Of the participants, 49% were GPs, 36% pharmacists and 6% cardiologists. A sizeable group of 'other HCPs' completing the online survey, who were active across various disciplines in clinical practice, were also included (9%).

Respondents were mostly female (61%) and the majority (70%) were employed in a community setting. There was sufficient variation of HCPs over different age ranges and different durations of work experience. Electronic prescribing/dispensing systems were widely used, ranging from 93% of responding HCPs in SE using these systems to 43% in the UK. GPs were the primary professional group indicating use of electronic prescribing systems.

2.1 Three safety communication tools

We asked HCPs about their views on three safety communication tools: Direct Healthcare Professional Communications (DHPCs), national regulatory agency communications and educational materials.

2.1.1 Direct Healthcare Professional Communications (DHPCs)

The majority of respondents were very familiar (approx. 90%) with DHPCs and indicated reading them. Two-thirds indicated reading only those DHPCs that are relevant for their practice. Of the respondents who were familiar with DHPCs, 90% found them *useful* to *very useful*, and up to 80% indicated taking the recommended action stated in the DHPCs. Approximately 80% of respondents only need to receive an electronic version and not a paper-based version of this communication. The differences in views of HCPs by country and profession were, although statistically significant, often not large with respect to the perceived usefulness and action taken. Although a more sizeable proportion (approx. 40%) of HCPs from the NL, SE and IE than in the other six countries preferred to receive at least a paper-based DHPC.

2.1.2 National regulatory agency communications

There are varying types of national regulatory agency communications. These include regular (mostly monthly) newsletters summarising recent drug safety information, e.g. appearing shortly after the Pharmacovigilance Risk Assessment Committee (PRAC) meeting (most countries), individual electronic mailings about a drug safety issue and website communications highlighting a drug safety issue, sometimes also notified through a DHPC (NL, ES) or as electronic reminders (pop-ups) in electronic prescribing systems (NO). The majority (90%) of respondents were familiar with regulatory agency safety communication. Like with DHPCs, an equal number of respondents found these communications useful and take action in response to them. However, in the NL, HCPs were much less familiar (28%) with this type of safety communication. In addition, cardiologists were less aware of this type of safety communication (74%).

2.1.3 Educational materials

The level of familiarity with educational materials, although still quite high (approx. 66%), was considerably less than for the other two communication tools. Again, the majority (approx. 84%) of HCPs that were familiar with educational materials thought they were *useful* to *very useful*. HCPs slightly favoured paper-based material over online materials for use in consultation with patients, or to be read at home. HCPs were of the opinion that the following information should be incorporated into educational materials: a) information on how to correctly use/take the product (93% of respondents); b) warnings about serious ADRs and how the risk may be minimized (83%); and, to a slightly lesser extent, c) a summary of both the benefits and risks of using the product (74%). Danish, Dutch and Italian HCPs had a more negative view than respondents from other countries about incorporating this latter option into educational materials.

2.2 General preferences

Nine questions addressed the general preferences of HCPs with regard to safety communications received from NCAs. NCAs were considered the most positive as a **sender** of safety information, followed by professional bodies and the European Medicines Agency (EMA). Pharmaceutical companies and, especially, the lay press, were considered most negatively.

Two-thirds of HCPs preferred electronic communication, 20% preferred hardcopy, and 14% did not mind either way. Again, Swedish, Dutch and Irish HCPs had the largest preference for hardcopy material. Emails and point-of-care alerts are the preferred **electronic channels** through which to be kept up to date on drug safety issues. Face-to-face meetings (in person) were also seen as mostly positive to very positive. Social media (e.g. Twitter), mobile phones (text messaging or personal calls), and television/radio were all considered very negatively. From six additional communication **channels**, irrespective of electronic or hardcopy, national clinical guidelines and medicines references books were most often valued very positively by HCPs. Personalised letters, medical journals and Summaries of Product Characteristics (SmPCs) were in this order valued mostly positively, however, newspapers were considered negatively.

Almost half of the surveyed HCPs expected to **be informed immediately** of new safety issues, whereas a quarter thought this information could be grouped and communicated on a weekly or monthly basis. **Repetition** of the safety message was considered useful by the majority (90%) of respondents. Dutch, Swedish and UK respondents were more relaxed with the timing of sending safety information. They were also slightly less convinced of needing to repeat safety information, suggesting this was dependent on the issue.

A number of **factors** were highlighted that may affect when HCPs read **safety communications**. Respondents agreed most strongly with the statements that relevance of the safety information for their daily practice and trust in the sender determined if they read the safety communication. Respondents indicated that they were more likely to **take action** in cases where the *ADR is severe or causes irreversible harm*, the *safety information was relevant* for their daily practice and the *sender was trusted*. These factors were deemed more relevant than suggestions that the *safety recommendation be clearer*, that *sufficient background information be provided*, and that recommendations can easily be *implemented in daily practice*. Least important was that HCPs themselves, or their colleagues, agreed with the safety message, and finally that a *patient was requesting an action* based on their prior research.

The differences between countries were mostly modest, except for the response to the severity of a safety issue. In particular, Spanish, and to a lesser extern Norwegian and Dutch HCPs, indicated that they were more likely (strongly agree) to take action if the ADR was more severe or caused irreversible harm. GPs were more outspoken than other HCPs on this issue.

2.3 Specific drug safety issue updates

HCPs were asked if they were **aware** of **four specified recent** drug safety **updates** – combined hormonal contraceptives, diclofenac, valproate and ivabradine – and how they had learned of the particular issue. The responding HCPs were most familiar with diclofenac (cardiovascular risk) and combined oral contraceptives (thrombotic risk), and less familiar with valproate (restrictions for use in women of childbearing age) and ivabradine (cardiovascular risk/bradycardia). HCPs in southern European countries, the UK and IE, indicated greater awareness of the valproate safety issue.

The ivabradine issue was best known in IE, UK, ES and IT. GPs and pharmacists were most aware of the first three issues, whereas cardiologists were more aware of the ivabradine issue.

Across all countries, the issues were best known through the DHPC, website or newsletter, except for NL, where professional bodies and medical journals were the most often mentioned channels of information for diclofenac and the oral contraceptives.

2.4 Current practice

Twelve options were presented to HCPs on how they currently **keep themselves up-to-date with (new) medicine knowledge**. The most used option was a medicines reference book that was most often accessed on a daily basis, except by Italian HCPs, who used reference books less frequently. The SmPC, national clinical guidelines, medical journals, NCA website/newsletter, and international guidelines were used on a weekly basis. There was little use of medicines advisory committees, company representatives (although in IT 50% of HCPs receive them on a weekly basis), and the EMA website. Mobile phone apps and blogs were rarely, if ever, used.

Based on these findings, **recommendations** for good practices have been provided in Section 6.1. The most important of which being that safety communications should be sent directly by the NCA, as a trusted source. Moreover, safety information should preferably be built into point-of-care alerts. DHPCs may be disseminated using emails, with the exception of some countries. Safety communication may be repeated if care is taken to keep the message of interest and the information is not sent too frequently, in order to prevent 'alert-fatigue'. Information should be targeted to HCPs that are likely to use the implicated drug in their daily clinical practice.

3. Purpose of the document

The purpose of this document is to provide a comprehensive overview of the results of the SCOPE survey conducted among European healthcare professionals. The aim of the survey was to establish the attitudes, knowledge, preferences and behaviours of healthcare professionals in Europe, regarding methods to communicate safety issues of medicines.

4. Background

The Guideline on good pharmacovigilance practices module on safety communication (GVP Module XV) states: *"Communicating safety information to patients and healthcare professionals is essential for achieving the objectives of pharmacovigilance in terms of promoting the rational, safe and effective use of medicines, preventing harm from adverse reactions and contributing to the protection of patients' and public health"* (1). This module indicates that the views and expectations of concerned parties, including patients and healthcare professionals (HCPs) should be taken into account. HCPs play an essential role as primary target audiences and safety communications are intended to enable informed decision-making and to allow HPCs to give clear and useful information to their patients. Safety communication is considered effective when the message transmitted is received and understood by the target audience in the way it was intended, and when the target audience has taken appropriate action (1).

Safety communications such as Direct Healthcare Professional Communications (DHPCs), national competent authority (NCA) communications and educational materials (including prescriber and patient materials, such as brochures and patient alert cards) also constitute additional risk minimisation measures, which may be required to minimise the occurrence and/or the impact of adverse drug reactions (ADRs) for a particular medicinal product. The pharmacovigilance (PV) legislation requires that the effectiveness of such risk minimisation measures be evaluated during the product life cycle (2).

Previous studies investigating the impact of safety communications, including DHPCs, have questioned their effectiveness (3-5). In the current study, a survey among HCPs was conducted focusing on process-related indicators relating to the effectiveness of general safety communications. While such measures are not outcome indicators for the evaluation of risk minimisation (6, 7), GVP module XVI (Guideline on good pharmacovigilance practices module on risk minimisation measures: selection of tools and effectiveness indicators) acknowledges the contribution of process indicators in assessing the overall effectiveness of a risk minimisation programme (2).

The focus of the survey in this study was on specific methods used to communicate new or emerging safety information, which is defined in the GVP Module XV as: *"new information about a previously known or unknown risk of a medicine which has or may have an impact on a medicine´s benefit-risk balance and its condition of use"* (1). The Module gives particular consideration to DHPCs because of their generalised use in targeting HCPs. In addition to these means, however, other specific safety communication methods, such as NCA communications and educational materials, were also of interest. In the survey, country-specific examples of NCA communications were given. Educational materials are tools developed to facilitate informed decision-making to support risk minimisation when prescribing, supplying and/or using a medicinal product. Educational materials were optionally included within the scope of the HCP survey.

5. Methodology

The aim of this study was to establish the attitudes, knowledge, preferences and behaviours of HCPs in Europe regarding safety communication methods. With this information, the effectiveness of the current safety communication tools is evaluated in order to contribute to good practice recommendations for NCAs.

This study was conducted in the countries actively involved in SCOPE WP6, which focuses on risk communication (Norway (NO), Sweden (SE), Denmark (DK), Ireland (IE), the United Kingdom (UK), the Netherlands (NL), Italy (IT), Spain (ES) and Croatia (HR)).

5.1 Survey

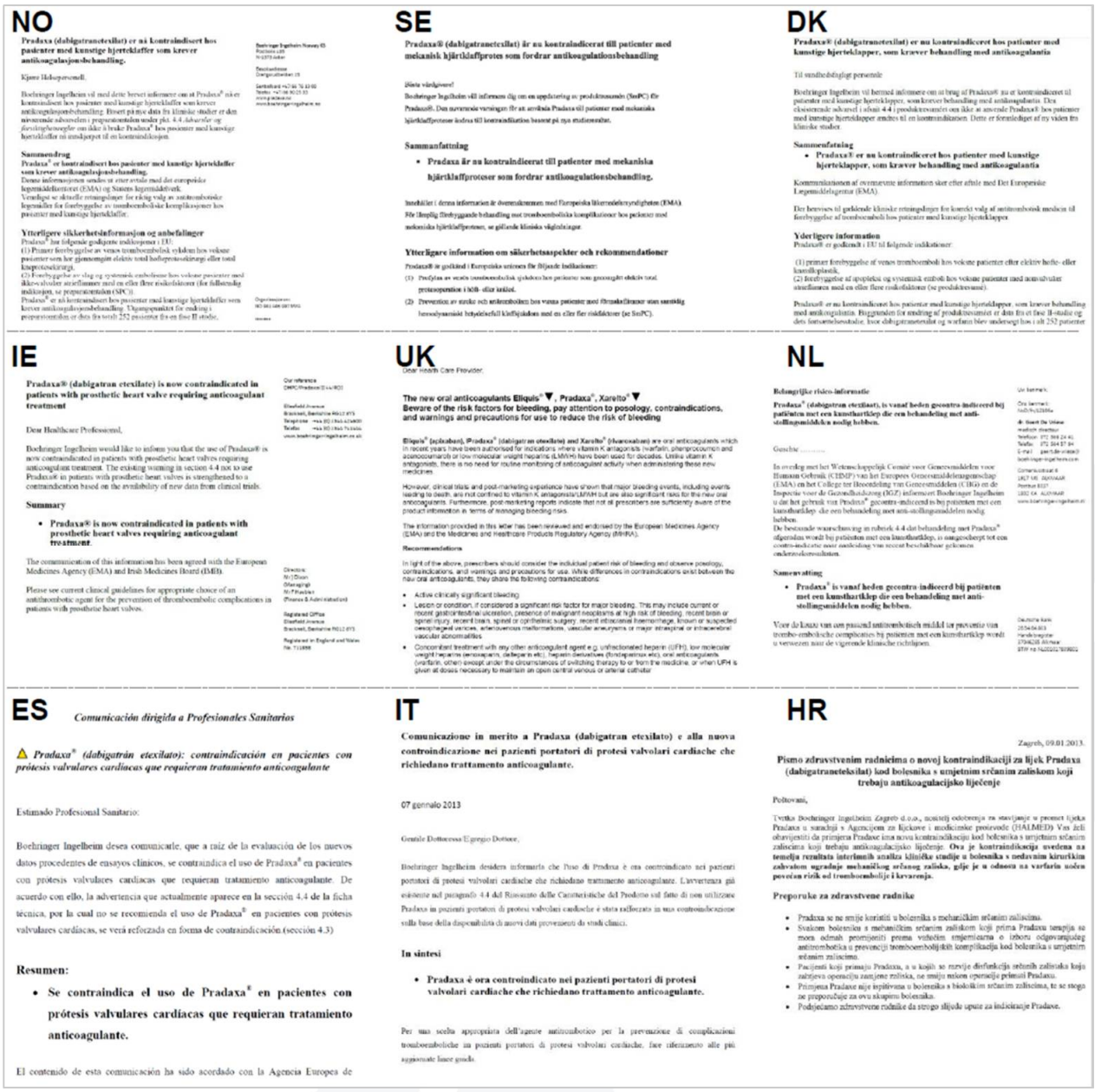
A general English web-based version of the survey was developed first by the SCOPE team, focusing on key uncertainties in the area of risk communication, as identified by the group.

The survey addressed three types of **safety communications**, namely *DHPCs*, *NCA communications* and *educational materials*. For each of these safety communications, screenshots of examples were presented to the respondents to ensure they knew what was meant by each. Selected examples were relevant to the target population of the study – that is, general practitioners (GPs), cardiologists and pharmacists. Where possible, the same examples were used across the countries.

For the DHPC section in the survey, the examples of dabigatran (all countries) (see Figure 5.1.1) and domperidone (DK, ES, IE, IT, NL, UK), diclofenac (HR and SE), or valproate (NO) were presented.

NCAs use various methods (NCA communications) to communicate the risks of medicinal products (SCOPE WP6 survey report Topic 1 – Audit of national methods of communication). Some NCAs have more experience with these communication methods than others. All authorities in the survey have a website/web-portal on which they present information about medicines. Besides this, others actively distribute these communications to HCPs through different channels. A specific example of the NCA communication was presented for each country in order to ensure HCPs understood what type of 'national regulatory agency communication' the questions pertained to (Figure 5.1.2).

The examples used in each country for *educational materials* are shown in Figure 5.1.3.



NO	SE	DK
DHPC pradaxa NO.pdf	dhpc pradaxa SE.pdf	DHPC pradaxa DK.pdf
IE	**UK**	**NL**
DHPC Pradaxa IE.pdf	DHCP Oral anticoagulant UK.pdf	1301DHPCPradaxaNL.pdf
ES	**IT**	**HR**
DHPC_Pradaxa_ES.pdf	dhpc pradaxa IT.pdf	DHPC pradaxa_HR.pdf

Figure 5.1.1. Screenshots and full text examples of DHPCs used in the survey

NO NCA communication Alerts prescriptions s	SE NCA communication valproate SE.pdf	DK newsletter domperidon DK.pdf
IE NCA communication valproate IE.pdf	UK NCA communication Drug Safety Update J	NL newsletter thyrax titel verborgen NL.pd
ES NCA_valproate_ES.p df	IT NCA communication valproate IT.pdf	HR newsletter valproate_HR.pdf

Figure 5.1.2. Screenshots and full text examples of NCA communications used in the survey

		DK Pradaxa OrdinaVejl_DK.pdf
IE Educational material Pradaxa IE.pdf	UK Educational_material _Tresiba_UK(1).pdf	NL Educational material tresiba NL poster.pdf
ES Educational material_Pradaxa_ES	IT educational material pradaxa IT.pdf	HR educational material 1_HR.pdf

Figure 5.1.3. Examples of educational material used in the survey

Participants were asked if they were familiar with each of these communication methods and, if so, follow-up questions were asked regarding how useful they were considered to be.

In a separate section, respondents were asked if they were aware of **four specific recent safety issues** concerning combined hormonal contraceptives (CHCs), diclofenac, valproate and ivabradine. These safety issues were chosen because the safety reviews were conducted relatively recently, the medicines are commonly used, and used in general practice (with the exception of ivabradine), and there were numerous types of communications used in relation to these issues. If the respondents were aware they were asked to indicate how they had heard about this drug safety issue.

The survey was built on the Protective Action Decision Model (8), which highlights that the channel and source of a message may influence the perceptions and behaviour of the receiver in response to the message. Therefore, the survey contained a **general** section focusing on the participants' **preferences** for the channel and source of safety communications.

Participants were offered the option of providing additional open-ended comments for each survey section.

The maximum number of questions participants would be asked to answer was 35 and there were some differences in the number of questions in the survey among the countries. For instance, some countries excluded questions related to educational materials (Table 5.1.1), and some questions were not included if they were not relevant to a country (e.g. ivabradine is not marketed in all countries) or were considered to result in an overly lengthy survey (NO, SE, or e.g. Dutch pharmacists association).

The survey contained different types of questions: open-ended questions, multiple-answer questions and single-answer questions. For some of the single-answer questions, respondents were asked to provide answers on a visual analogue scale or 5-point Likert scale.

If a participant was not familiar with a topic or was not willing to complete a question, the participant could skip the question(s).

A basic version of the survey was customised per country, incorporating local information and removing irrelevant questions. This local English version of the survey was translated by a translation agency into Norwegian, Swedish, Danish, Dutch, Spanish, Italian and Croatian.

Back translation was performed by local SCOPE members according to previously suggested methods (9), and changes were made to the translation if necessary. The translated versions were entered into the Unipark software (www.unipark.com/en/). These online versions were checked by local SCOPE members and pilot tested with 3-5 persons. The survey was adapted based on the comments from this pilot and a final version was created, which was again checked by the local SCOPE team before being distributed. The final version of the survey is presented in Annex 1.

5.1.1 Distribution of the survey

The survey was distributed to HCPs, who could complete it anonymously. The target group for the survey was GPs, cardiologists and pharmacists, although ES and SE did not include pharmacists. GPs were included, since they are the usual target group for DHPCs, however WP6 also included a specialist group: cardiologists. This group was chosen as a number of safety issues that had been communicated in the period prior to distribution of the survey concerned cardiovascular-related topics. In many countries, pharmacists were also included as a target group, as these also represent a common target audience for DHPCs in these countries.

The survey was sent out as a link and, in general, three different methods were used for distribution:

- In a separate email, based only on the survey, which was sent by researchers/the NCA or via a third party (such as a professional body or commercial organisation) to HCPs
- In a digital newsletter sent by a third party/the NCA
- On a website, for instance, those of NCAs and/or professional bodies.

Table 5.1.1 Overview of survey distribution methods per country

Country	Target population	Exclusion of topics	Coupon
Norway	GP, Car, Ph	Educational material	No
Sweden	GP, Car	Educational material	No
Denmark	GP, Car, Ph	NA	No
Ireland	GP, Car, Ph	NA	No
UK	GP, Car, Ph	NA	Yes
Netherlands	GP, Car, Ph	NA (educational material for pharmacists through professional body)	Yes
Spain	GP, Car	NA	No
Italy	GP, Car, Ph	NA	No
Croatia	GP, Car, Ph	NA	No

GP: general practitioner, Car: cardiologists, Ph: pharmacist

- NO used direct mailings through a commercial third party (Cegedim), a professional organisation and an in-house cardiologist. The link to the survey was also posted on the NCA website and on social media. In addition, doctors were asked to participate through a professional organisations journal (Journal of the Norwegian Medical Association) and hospitals were asked to promote the survey through their channels.
- In SE, the survey was distributed through the regional medicines advisory committees that had agreed to participate. In addition, the professional organisation for GPs posted the survey on its website.

- In DK, professional organisations were used for the distribution of the survey.
- IE distributed the survey via a professional organisation to GPs and cardiologists and sent the survey directly to pharmacists following collaboration with the relevant pharmacist regulatory body. The Health Products Regulatory Authority's Drug Safety Newsletter also encouraged participation in the survey.
- The UK distributed the survey via professional bodies and posted an article in the Drug Safety Update bulletin highlighting the survey.
- The NL used a commercial party (Cegedim) and professional organisations.
- ES recruited participants via scientific societies, some regional authorities, and via a link to the survey on the NCA and scientific societies' websites. In addition, the survey was sent to physicians collaborating with the BIFAP database (Spanish database for pharmacoepidemiological research in primary care), and two local authorities participated in the distribution.
- IT used the regional PV centres, which posted the survey on their websites.
- HR distributed the survey through professional organisations, which posted the survey on their websites and informed their members by email. In addition, the call for participation was published on the NCA website, on a popular national web-portal targeted at HCPs, as well as in monthly journals of the Medical Chamber and Pharmaceutical Society.
- As an incentive for participants, the UK and the NL included the option to win a coupon (Table 5.1.1).

For planning purposes a sample size calculator (examples Bold Educational Software Sample Size Calculator and Creative Research Systems Sample Size Calculator) was used in which a 10% margin of error and 95% confidence level were applied. An approximate number of 100 respondents per HCP group per country would provide adequate statistical power in order to draw meaningful conclusions.

5.2 Data analysis

Due to the use of a web-based survey, answers were directly entered into a single collective dataset. The dataset was fully anonymised before analysis was performed. This anonymisation involved the removal of reported email addresses, which had been entered to win a coupon or to be informed about the study results, as this was the only personal data included by respondents.

Descriptive statistics were used to explore the demographic characteristics of the respondents. In addition, descriptive statistics were used to analyse the attitudes, knowledge, preferences and behaviours of the HCPs.

Analyses were performed to assess differences in attitudes, knowledge, preferences and behaviours between countries and among GPs, cardiologists and pharmacists. For these analyses, Chi-square tests χ^2-tests) and Kruskal-Wallis tests were used, where appropriate. In view of the large number of tests performed, p-values <0.001 were considered as statistically significant.

The analyses were conducted using Stata version 13 (Stata Corp., College Station, TX).

The responses to open-ended questions were interpreted with care as quantification is challenging and in some cases contradictory comments were recorded. Therefore, the answers provided on the open-ended questions are used in this report to support – or elaborate – on the closed questions in order to enrich the interpretation of the respondents' views on specific safety communication aspects.

6. Results

6.1 Response per country

The survey was performed between the beginning of June and mid-September 2015. The responses per country were not linear over time (Figure 6.1.1). The survey was initially planned to run up until mid-July, however, due to a delayed start in some countries, due to a holiday period in many countries resulting in a relatively low response rate, it was decided to extend the survey deadline until mid-September.

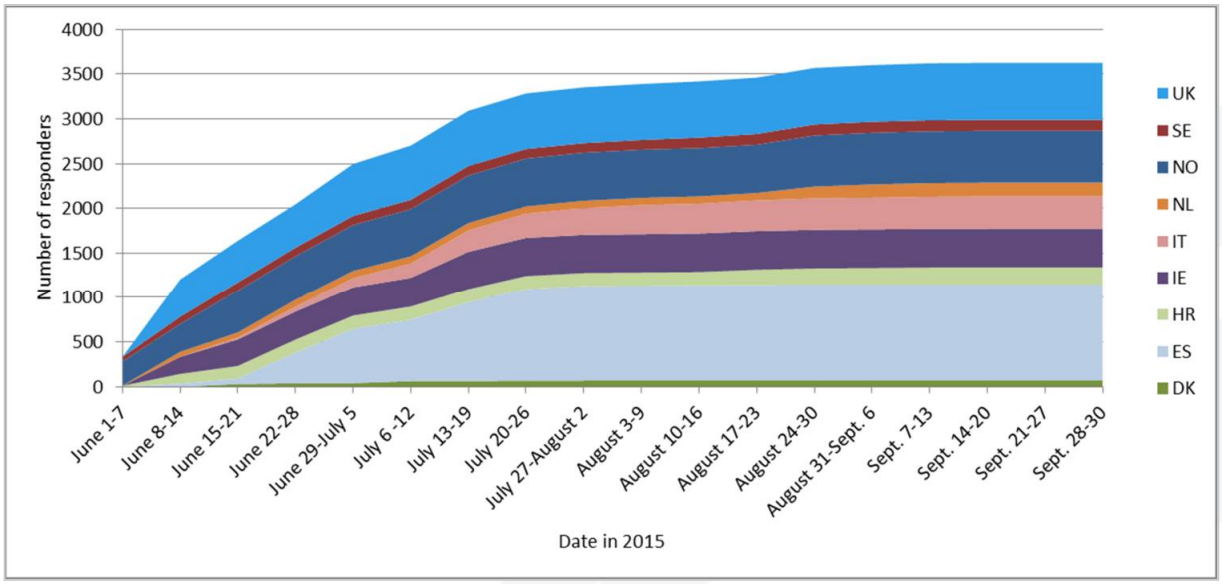


Figure 6.1.1. Response per country over time

Overall, 3685 professionals responded, of whom 60 were HCPs not active in clinical practice. These responders were excluded from further analysis. Thus, 3625 respondents are included in this report, ranging from 68 in DK to 1076 in ES. There was a good spread of responses through northern European countries (NO, SE, DK), western European countries (IE, UK, NL) and southern European countries (ES, IT and HR) (Figure 6.1.2).

An overview of the response rates per country and per target population is presented in Table 6.1.1.

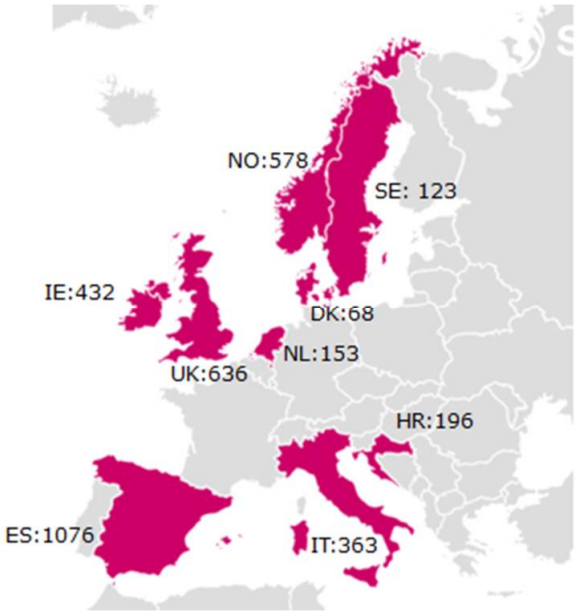


Figure 6.1.2. Response across European SCOPE WP6 countries

Table 6.1.1. Overview of response rates and number of professionals in each country

Country	Profession	Number of professionals	Response	Percentage
NO	GPs	6,000	105	1.8
	Cardiologists	800	40	5.0
	Pharmacists	~3,100	381	12.3
SE	GPs	~5,900[1]	108	1.8
	Cardiologists	~750	15	2.0
DK	GPs	3,900	25	0.6
	Cardiologists	400	7	1.8
	Pharmacists	700	35	5.0
IE	GPs	4,000	144	3.6
	Cardiologists	97	5	5.2
	Pharmacists	5,245	281	5.4
UK	GPs	60,132	197	0.3
	Cardiologists	3,207[2]	15	0.5
	Pharmacists	71,220[3]	318	0.4
NL	GPs	9,253	72	0.8
	Cardiologists	1,004	17	1.7
	Pharmacists	2,747	64	2.3
ES[4]	GPs	28,498	847	3.0
	Cardiologists	3,451	56	1.6
IT	GPs	44,900	183	0.4
	Cardiologists	12,800	63	0.5
	Pharmacists	3,740	104	2.8
HR	GPs	2,530	85	3.4
	Cardiologists	166	4	2.4
	Pharmacists	2,723	104	3.8

1. Not all are active
2. 2,254 doctors with cardiology specialty and 953 consultant cardiologists
3. 48,814 pharmacists and 22,406 pharmacy technicians
4. No formal recruitment of pharmacists

6.2 Demographic characteristics of respondents

The majority of respondents (61%) were females, half (49%) were GPs, 36% pharmacists, 6% cardiologists and 9% were 'other' HCPs that were active in clinical practice (Table 6.2.1). Examples of HCPs included in the 'other' category are nurse practitioners, anaesthetists, geriatricians, nurses, digestive pathologists, paediatricians and rheumatologists. Most of the responders (70%) work in the community and 26% in hospitals. The age range of respondents was somewhat equally distributed across the under 35 to over 55 categories, and almost 90% had been accredited as a HCP for over 5 years. Differences were seen across the countries, for example, Croatian respondents were predominantly female (89%), younger, and practiced largely in a community setting. ES and SE did not (actively) recruit pharmacists. Finally, relatively few cardiologists (1% to 17%) were recruited per country.

Table 6.2.1. Demographic characteristics of respondents

	Total	Norway[1]	Sweden	Denmark[2]	Ireland	UK[3]	Netherlands	Spain4	Italy	Croatia
N included	3625	578	123	68	432	636	153	1076	363	196
Female n (%)	2215 (61)	386 (67)	64 (52)	52 (76)	278 (64)	400 (63)	48 (31)	667 (62)	152 (42)	168 (86)
Profession n (%)										
GPs	1766 (49)	105 (18)	108 (88)	25 (37)	144 (33)	197 (31)	72 (47)	847 (79)	183 (50)	85 (43)
Cardiologists	222 (6)	40 (7)	15 (12)	7 (10)	5 (1)	15 (2)	17 (11)	56 (5)	63 (17)	4 (2)
Pharmacists	1300 (36)	381 (66)	NA	35 (51)	281 (65)	318 (50)	64 (42)	13 (1)**	104 (29)	104 (53)
Others	337 (9)	52 (9)	0 (0)	1 (1)	2 (0)	106 (17)	0 (0)	160 (15)	13 (4)	3 (2)
Primary employment setting n (%)										
Community based	2570 (70)*	400 (69)	111 (90)	25 (37)	325 (75)*	276 (43)	124 (81)	914 (85)	210 (58)	185 (94)
Hospital-based	857 (24)*	160 (28)	11 (9)	5 (7)	95 (22)*	279 (44)	28 (18)	142 (13)	131 (36)	6 (3)
Other	244 (6)*	17 (3)	1 (1)	38 (56)	59 (14)*	81 (13)	1 (1)	20 (2)	22 (6)	5 (3)
Age n (%)										
<35 year	625 (17)	137 (24)	12 (10)	14 (21)	140 (32)	74 (12)	22 (14)	118 (11)	31 (9)	77 (39)
35 – 45 year	964 (27)	172 (30)	34 (28)	24 (35)	131 (30)	181 (28)	37 (24)	263 (24)	63 (17)	59 (30)
46 – 55 year	1071 (30)	114 (20)	27 (22)	11 (16)	95 (22)	243 (38)	48 (31)	404 (38)	85 (23)	44 (22)
>55 year	964 (27)	155 (27)	50 (41)	19 (28)	66 (15)	137 (22)	46 (30)	291 (27)	184 (51)	16 (8)
Accreditation n (%)										
<5 years	370 (10)	88 (15)	12 (10)	13 (19)	55 (13)	26 (4)	16 (10)	82 (8)	21 (6)	57 (29)
5 – 20 years	1394 (38)	262 (45)	47 (38)	30 (44)	219 (51)	218 (34)	64 (42)	359 (33)	101 (28)	94 (48)
>20 years	1859 (51)	228 (39)	64 (52)	23 (34)	158 (37)	392 (62)	73 (48)	635 (59)	241 (66)	45 (23)

GPs = general practitioners

* Respondents could reveal multiple answers

** No formal recruitment of pharmacists

1. In Norway, one responder did not answer the question about primary employment setting
2. In Denmark, two responders did not fill in the question about accreditation
3. In the UK, one responder did not fill in the question about gender and one responder did not answer the question about age
4. In Spain, one responder did not fill in the question about gender

6.3 DHPCs – survey questions

The answers to the individual questions on DHPCs are presented below.

6.3.1 Q1: Are you familiar with this type of safety information?

Approximately 90% of HCPs responding to the survey were familiar with DHPCs as a safety communication tool. Some differences were noted between countries ($p < 0.001$, χ^2-test), for example, only around 80% of the responding HCPs were familiar with DHPCs in NO and SE (Figure 6.3.1). Familiarity was generally high among all types of HCPs (Table 6.3.1).

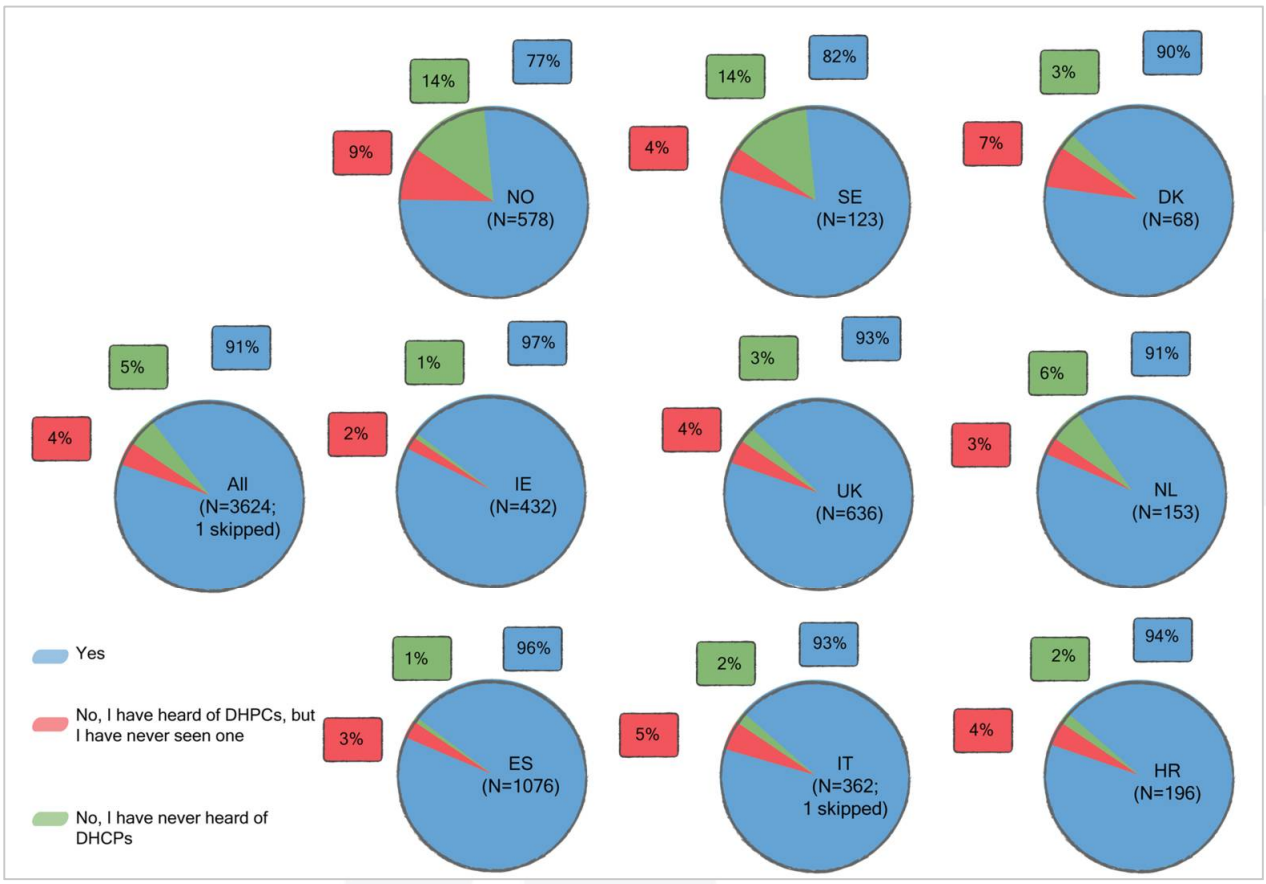


Figure 6.3.1. Results of Q1: Are you familiar with this type of safety information (DHPC)?

Presented per country. ($p < 0.001$, χ^2-test)

Table 6.3.1. Results of Q1: Are you familiar with this type of safety information (DHPC)?

Presented per professional group. ($p < 0.001$, χ^2-test)

	GP	Cardiologist	Pharmacist[1]	Other	Total1
Yes	1652 (94%)	200 (90%)	1164 (90%)	286 (85%)	3302 (91%)
No, I have heard of DHPCs, but I have never seen one	58 (3%)	11 (5%)	66 (5%)	24 (7%)	159 (4%)
No, I have never heard of DHPCs	56 (3%)	11 (5%)	69 (5%)	27 (8%)	163 (5%)
Total	1766 (100%)	222 (100%)	1299 (100%)	337 (100%)	3624 (100%)

1. One pharmacist skipped this question.

6.3.2 Q2: Do you read the DHPCs you receive?

The majority of respondents stated that they read the DHPCs that they receive. However, two-thirds indicated generally only reading those DHPCs that contained important information for their own practice. The responses to these questions varied considerably across countries ($p < 0.001$, χ^2-test), with the most noticeable finding being that higher percentages of respondents from HR, IT and IE read all letters they receive from industry (Figure 6.3.2). Pharmacists were more likely than other HCPs to read all the letters they receive from industry (Table 6.3.2; $p < 0.001$, χ^2-test).

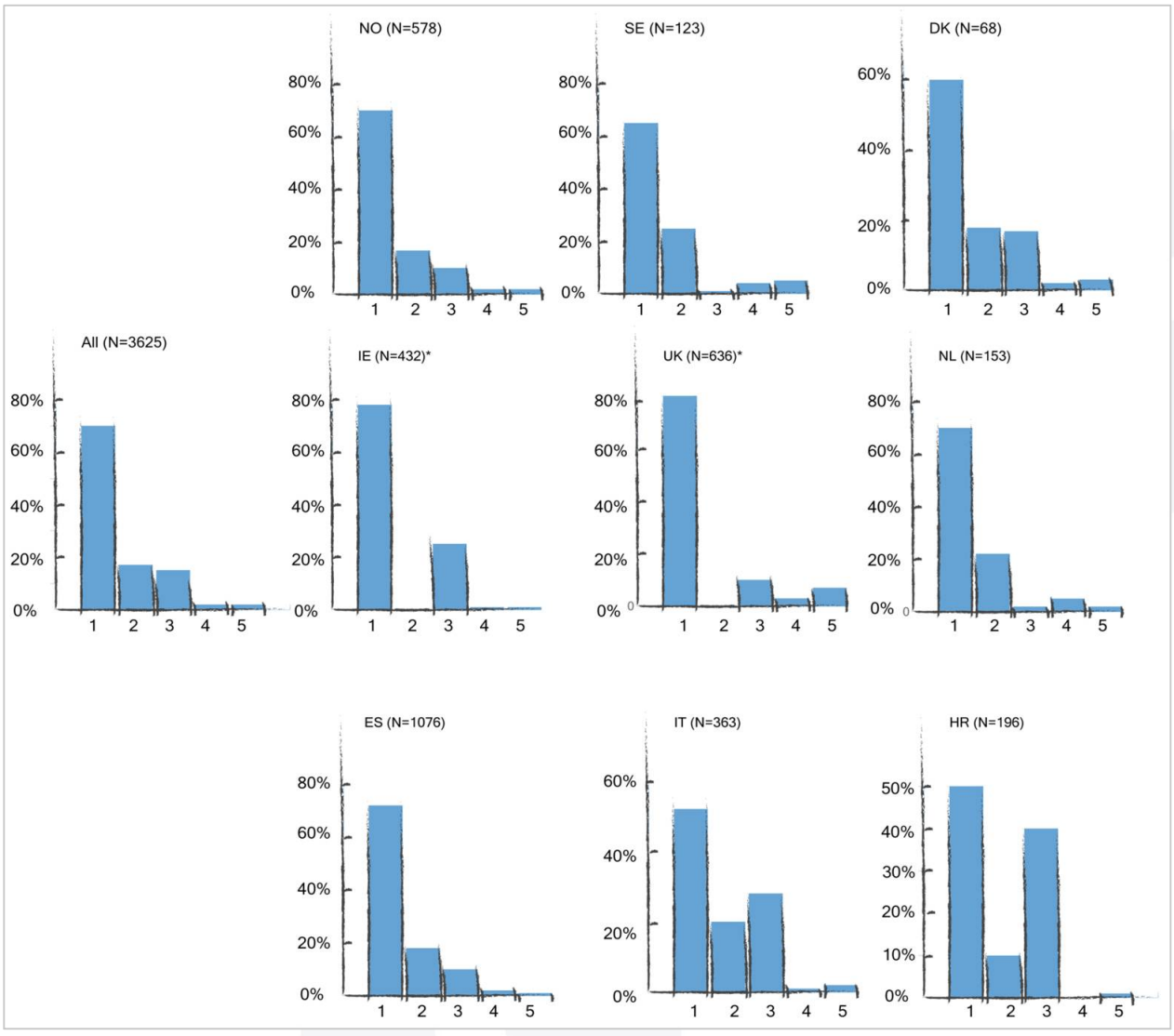


Figure 6.3.2. Results of Q2: Do you read the DHPCs you receive?

Presented per country for the following categories:
1. Yes, if they contain safety information that is important to me: $p < 0.001$ (χ^2-test)
2. Yes, only when the envelope indicates it contains important, non-commercial information: $p = 0.048$ (χ^2-test)
3. Yes, I read all letters from the pharmaceutical industry: $p < 0.001$ (χ^2-test)
4. No, I do not read any letters from the pharmaceutical industry: $p < 0.001$ (χ^2-test)
5. Not applicable: $p < 0.001$ (χ^2-test)

**IE and UK did not include option 2 "yes, only when the envelope indicates it contains important, non-commercial information" since currently the envelopes in these countries do not present this information.*

Table 6.3.2. Results of Q2: Do you read the DHPCs you receive?

Presented per professional group.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (χ^2-test)
1.	1264 (72%)	161 (73%)	873 (67%)	240 (71%)	2538 (70%)	0.046
2.	304 (21%)	37 (18%)	105 (15%)	31 (14%)	477 (19%)	0.001
3.	187 (11%)	28 (13%)	314 (24%)	44 (13%)	573 (16%)	<0.001
4.	71 (4%)	6 (3%)	40 (3%)	5 (1%)	122 (3%)	0.085
5.	32 (2%)	7 (3%)	58 (4%)	33 (10%)	130 (4%)	<0.001

1. Yes, if they contain safety information that is important to me
2. Yes, only if the envelope indicates it contains important non-commercial info
3. Yes, I read all letters from the pharmaceutical industry
4. No, I do not read any letters from the pharmaceutical industry
5. Not applicable

Of note, more than one (yes) answer could be provided per respondent. Therefore, the total numbers add up to more than the total number of respondents and the percentages add up to more than 100%.

If respondents were familiar with DHPCs, they received the following additional questions:

6.3.3 Q3: How useful do you find DHPCs in general?

2803 (85%) of 3302 HCPs responding to this question considered DHPCs useful or very useful. Country differences were statistically significant (p <0.001, Kruskal-Wallis) (Figure 6.3.3), with HCPs from NL and SE being slightly more neutral (>20%) on how useful they thought DHPCs were. Across the professional groups there were similar answers on the usefulness of DHPCs, with a slightly higher proportion of 'other HCPs' finding them very useful (p <0.001, Kruskal-Wallis) (Table 6.3.3).

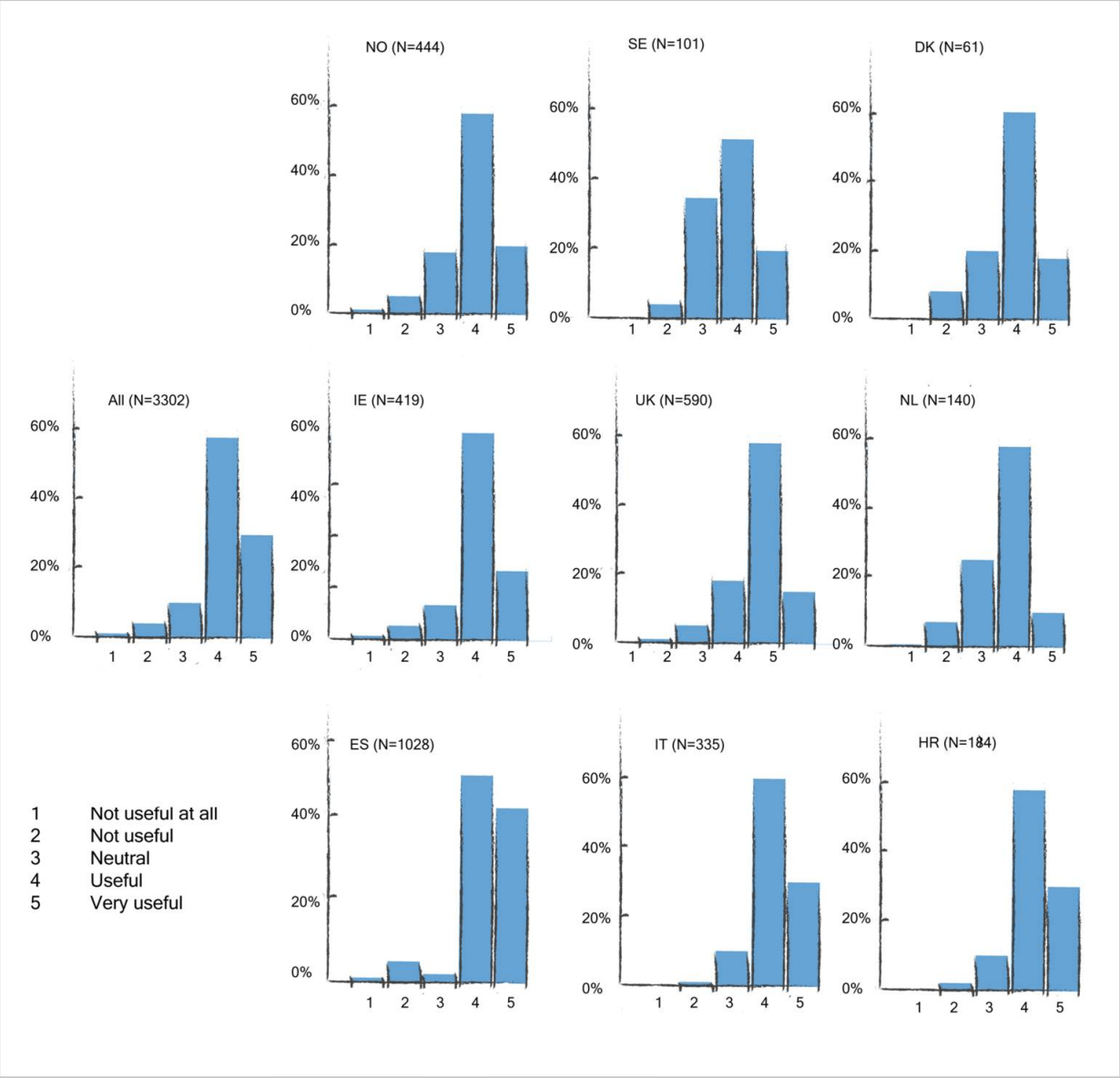


Figure 6.3.3. Results of Q3: How useful do you find DHPCs in general?
Presented per country. p <0.001 (Kruskal-Wallis)

Table 6.3.3. Results of Q3: How useful do you find DHPCs in general?

Presented per professional group. Scale from not useful at all (1) to very useful (5). p <0.001 (Kruskal-Wallis)

Profession:	GPs	Cardiologists	Pharmacists	Others	Total
Not useful at all	19 (1%)	0 (0%)	1 (0%)	2 (1%)	22 (1%)
Not useful	75 (5%)	6 (3%)	33 (3%)	6 (2%)	120 (4%)
Neutral	176 (11%)	24 (12%)	140 (12%)	17 (6%)	357 (11%)
Useful	908 (55%)	131 (66%)	705 (61%)	163 (57%)	1907 (58%)
Very useful	474 (29%)	39 (20%)	285 (24%)	98 (34%)	896 (27%)
Total	1652 (100%)	200 (100%)	1164 (100%)	286 (100%)	3302 (100%)

Open-ended answers to Q3

A large number of respondents (n=1543) provided open-ended comments on this issue. A brief overview of the most informative comments is given here. The majority of respondents gave positive comments, suggesting that the summary of safety information was appreciated, that the DHPC could be easily stored for later use, and that it was a good means for sharing safety information with colleagues or staff members (all countries). The DHPC was considered a good tool to inform of a change in a drug's benefit/risk profile and of changes to patient management (IT). Spanish respondents considered the timeliness of DHPCs an important feature, allowing them to seek further information from other sources (e.g. learned societies) if needed. Dutch HCPs stated that sometimes information was already known through the lay media and that drugs should be better evaluated before approval so that there was no need to send such warnings. Some Norwegian HCPs indicated that some DHPCs were sent for drugs used by a small selection of specialists only. A small number of respondents indicated that too many DHPCs were being sent, however, as long as numbers were kept low, the DHPC was considered a useful safety communication tool. Finally, HCPs commented that the DHPC is not available at the time of prescribing and it would be useful to build recommendations into electronic prescribing systems (EPS).

Many HCPs indicated that they felt the DHPCs should be more succinct, whereas a smaller number of HCPs saw a need for more detail in the letters, e.g. with respect to the level of evidence underpinning the safety communication (UK).

6.3.4 Q4: How often do you take the action that is recommended in this type of communications?

For this question, respondents had to use a slider to indicate how often they take the action recommended in DHPCs (from 0% to 100% of the time). Overall, HCPs take the recommended action in a median of 83% of cases with a range from 60% in NL to 89% in DK (Figure 6.3.4.1, Table 6.3.4.1). The variation was small between professional groups (82% to 88%) (Figure 6.3.4.2, Table 6.3.4.2).

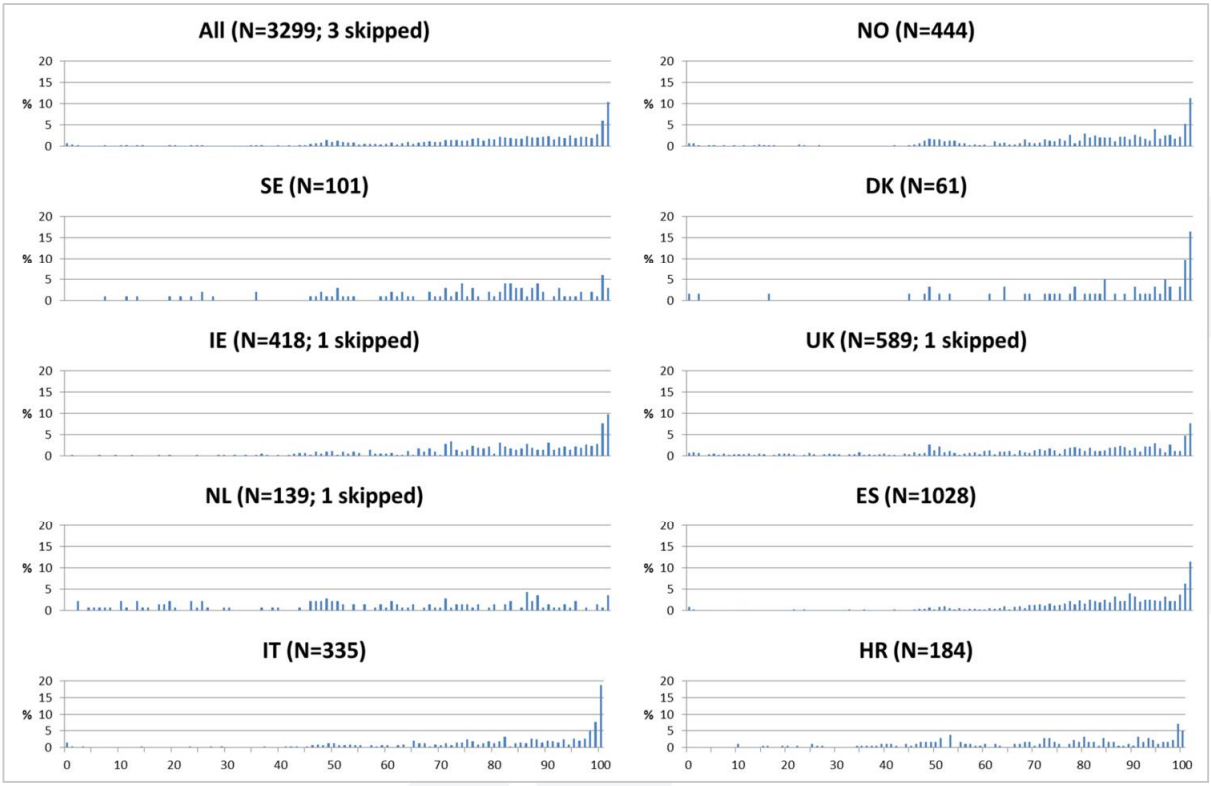


Figure 6.3.4.1 Results of Q4: How often do you take the action that is recommended in this type of communication?

Presented per country. p <0.001 (Kruskal-Wallis)

On the y-axis the percentage of responding HCPs (all/per country) is indicated with the x-axis presenting how often (never, 0% of the time – always, 100% of the time) they indicated to have taken the action recommended in a DHPC.

Table 6.3.4.1 Results of Q4: How often do you take the action that is recommended in this type of communication (never – always)?

Presented per country, where Q1 is the lower quartile and Q3 the upper quartile

	NO	SE	DK	IE	UK	NL	ES	IT	HR	Total
Q1	67	60	72	70	52	30	75	73	53	67
Median	83	76	89	83	77	60	86	88	74.5	83
Q3	95	87	99	96	92	84	96	99	91.5	95

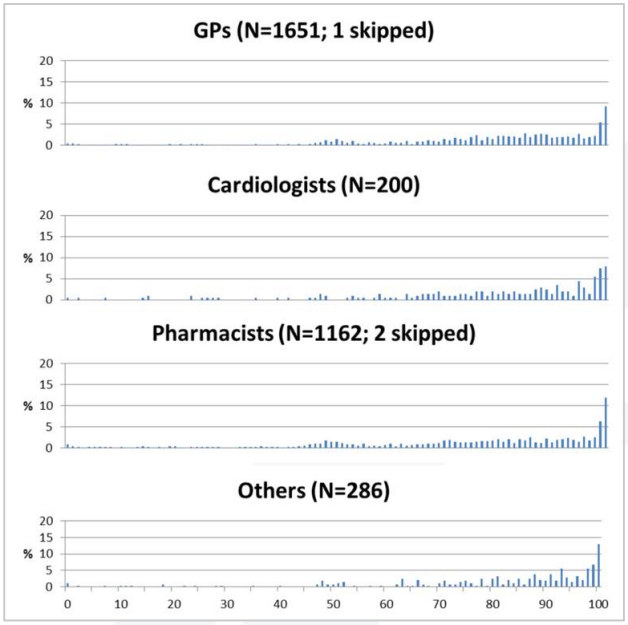


Figure 6.3.4.2. Results of Q4: How often do you take the action that is recommended in this type of communication (never, 0% of the time – always, 100% of the time)?

Presented per profession. p <0.001 (Kruskal-Wallis)

Table 6.3.4.2. Results of Q4: How often do you take the action that is recommended in this type of communication (never – always)?

Presented per profession, where Q1 is the lower quartile and Q3 the upper quartile

	GPs	Cardiologists	Pharmacists	Other
Q1	67,5	69	62	74
Median	82	85	82	88
Q3	94	96	96	98

Open-ended answers to Q4

Again, a large number of respondents (n= 1348) provided information in the open-ended field to indicate why they did, or did not, always take the recommended actions. Many respondents indicated **having taken** the recommended action where they considered the recommendations useful, good for patient safety and to be their duty as a HCP. Some indicated that they would take the action if they trusted the information (NL, UK, SE), and that this could be supported by professional guidelines. Spanish HCPs indicated taking the recommended action because they assumed that DHPCs were sent by the NCA who revised and authorised the safety information. A few Italian respondents cited potential legal consequences of not following recommendations.

A reason for **not taking** the appropriate action was that respondents did not use/prescribe the medicine, e.g. as it fell outside of their clinical expertise. Some also indicated that they found the measure unduly cautious, that it was not supported by sufficient evidence, or that more background information should be provided. Others indicated that they sometimes forget about the issue or that organisational constraints prevented them from taking the appropriate action. Also, a lack of clarity in the message affected their willingness to take action. Sometimes a lack of alternative treatment options was mentioned for not taking the recommended action.

Some respondents also indicated that they **take action depending** on the situation, e.g., the specific patient, weighing risks and benefits, and in some cases involving patient preferences in decision-making. The severity of the ADR, duration of use and the age of the patient were also factors that were taken into consideration when deciding to take action. The majority of comments were shared across countries.

6.3.5 Q5: Would it be sufficient for you to only receive an electronic DHPC instead of a hardcopy version?

The responses to this question were more variable, with 20% of the 3301 respondents and over a third of the respondents in SE (42%), the NL (39%) and IE (34%) indicating that it would not be sufficient for them to receive only an electronic version of a DHPC (Figure 6.3.5). Interestingly, in ES, paper versions of DHPCs are no longer sent in most cases, which did not seem to be a major concern, as 84% of respondents thought an electronic version was sufficient. There were no statistically significant differences between the professional groups (p =0.006, χ^2-test) (Table 6.3.5).

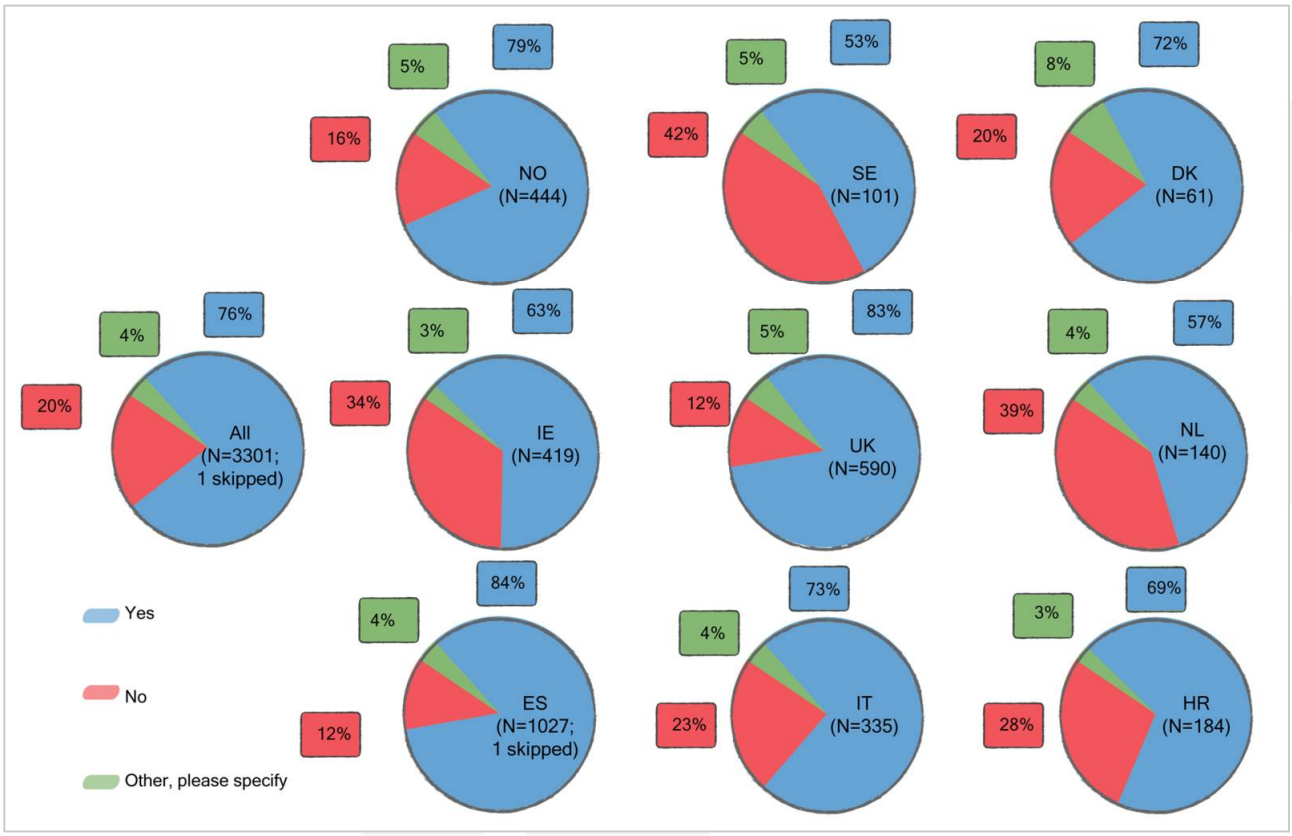


Figure 6.3.5. Results of Q5: Would it be sufficient for you to only receive an electronic DHPC instead of a hardcopy version?

Presented per country. p <0.001 (χ^2-test)

Table 6.3.5. Results of Q5: Would it be sufficient for you to only receive an electronic DHPC instead of a hardcopy version?

Presented per profession. p =0.006 (χ^2-test)

	GPs[1]	Cardiologists	Pharmacists	Others	Total[1]
Yes	1229 (74%)	155 (78%)	894 (77%)	239 (84%)	2517 (76%)
No	344 (21%)	41 (21%)	227 (20%)	33 (12%)	645 (20%)
Other	78 (5%)	4 (2%)	43 (4%)	14 (5%)	139 (4%)
Total	1651 (100%)	200 (100%)	1164 (100%)	286 (100%)	3301 (100%)

1. One GP skipped this question.

Open-ended answers to Q5

Fewer (n= 134) respondents provided open comments to this question. The main reason for preferring paper-based copies over electronic DHPCs was that HCPs received so many emails already and therefore felt that hardcopies were more distinctive. However, this was also mentioned in countries (e.g. ES) where a large proportion of respondents only need an electronic DHPC. Some highlighted trepidation about sharing email addresses with industry. A few suggested that hardcopy information would be better remembered, more easily stored, could be shared with colleagues and more effectively 'grabs your attention'. However, with regard to emails, some HCPs also suggested that these had the advantage of easy storage and retrieval and were easy to share with colleagues.

Regarding emails, HCPs highlighted that they should be clearly identifiable as containing important safety information and that other practical issues, such as the need to maintain a database/registry of valid email addresses, should be considered. Dutch HCPs suggested that email addresses should be verified annually. Nevertheless, quite a few respondents indicated a preference for both hardcopy and electronic versions, with a small group suggesting NCA websites as a good information source. If information was to be sent electronically, the sender should be clear and there should be a defined header indicating the topic and enabling HCPs to distinguish communications from spam/commercial information and avoid deletion. UK HCPs suggested mentioning 'DHPC' in the header. Spanish HCPs suggested that a monthly or quarterly overview of DHPCs could be sent round, and others suggested that DHPCs could be distributed or announced through social media rather than email.

6.3.6. General comments on DHPC section

Approximately 500 professionals made general remarks on DHPCs. These comments provided both positive and negative feedback. For example, HCPs felt that the information kept them up-to-date, and could be used for formal training and Drug and Therapeutics Committee-like meetings. DHPCs would be easier to identify if letters (or the envelope) clearly indicated that it contained new/important safety information. Unofficial documents caused confusion and some mentioned that it was not always clear what action needed to be taken and that this should be highlighted within the text, e.g. with a different, bold font. The title should highlight the safety concern and the recommendations should be clearly summarised. A repository of DHPCs could be useful.

More comments suggested that the NCA would be better as a sender, as material coming directly from industry was distrusted and therefore may not be read. DHPCs should be targeted at the relevant specialist. Others mentioned only glancing through DHPCs, or only picking up a DHPC that was specifically marked with an 'orange hand' (the Dutch symbol for DHPCs that require extra attention).

Some mentioned that emails were not effective and paper was better, while others stated that post was always late and that they identified the issue earlier from the web (NCA website).

6.4 National regulatory agency communications – survey questions

The answers to the individual questions on NCA communications are presented below.

6.4.1 Q6: Are you familiar with this type of safety information?

In general, the familiarity of HCPs with this kind of safety information was high (87%) in most countries with the exception of the NL (28%) (Figure 6.4.1). Cardiologists (74%) were less familiar with this type of safety information than GPs (89%) and pharmacists (85%) (Table 6.4.1).

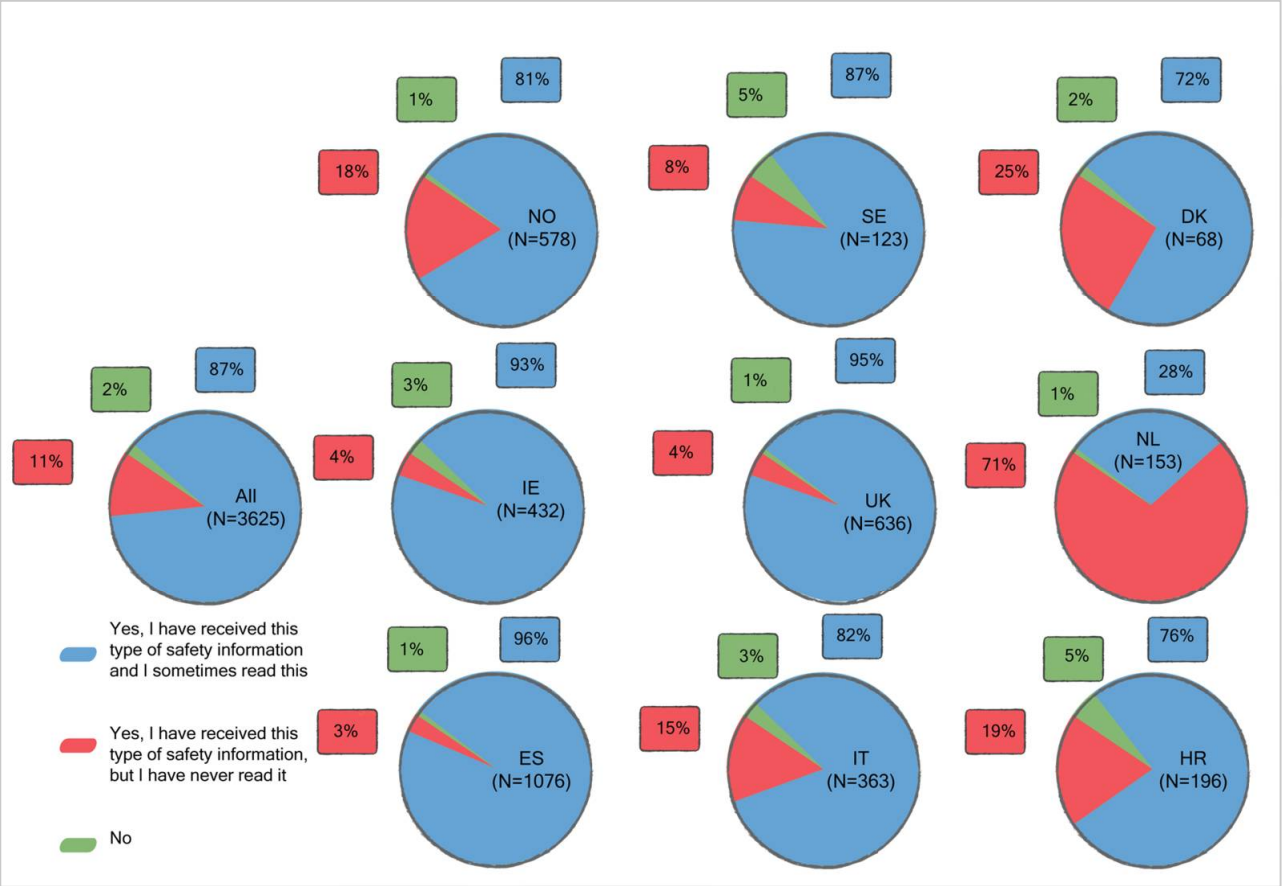


Figure 6.4.1. Results of Q6: Are you familiar with this type of safety information (NCA communications)?

Presented per country. $p < 0.001$ (χ^2-test)

Table 6.4.1. Results of Q6: Are you familiar with this type of safety information (NCA communications)?

Presented per profession. p <0.001 (χ^2-test)

	GPs	Cardiologists	Pharmacists	Others	Total
Yes, I have received this type of safety information and I sometimes read it	1571 (89%)	164 (74%)	1108 (85%)	307 (91%)	3150 (87%)
Yes, I have received this type of safety information, but I have never read it	35 (2%)	8 (4%)	23 (2%)	2 (1%)	68 (2%)
No	160 (9%)	50 (23%)	169 (13%)	28 (8%)	407 (11%)
Total	1766 (100%)	222 (100%)	1300 (100%)	337 (100%)	3625 (100%)

Open-ended answers to Q6 (n=584)

In the **UK** the Drug Safety Update is a well-established information source – at least among respondents – and received a large number of **positive** comments (n=127). The HCPs appreciated the collecting of issues together into a good summary, which aids HCPs in keeping up to date. They indicated reading the communication regularly, and that the content was, for example, reviewed and appropriate action initiated by Medicines Management Committees or Drug Therapeutic Committees. Respondents indicated that the material was also used for teaching. Some stated an appreciation for the information coming from a trusted source. Printouts could be stored for referencing. Some indicated that these Drug Safety Updates were more useful than DHPCs.

The most supported **format** was a combination of an email, with an attachment or a link to the information, and a short summary on the first page. Digital information was strongly appreciated, but sometimes difficult to locate once stored. A central repository may reduce this difficulty. Colour should be used to improve readability and some suggested that a drug name should be included in the email subject, and that too much information could dilute the message.

Some mixed comments on **access to information** were received. For UK respondents, the information should be more easily retrievable from a central repository, ideally at the.gov.uk domain. Some indicated that the current mailing list seemed incomplete, communications were not received consistently or in a timely manner, and others stated that they just receive too much mail.

Finally, it was suggested that a better way of educating HCPs and possibly certificating the way follow-up/action should be organised, and thus making HCPs accountable, was needed.

Twenty-one comments were received in **IT** on this topic, however, comments were mixed. Some suggested this was the best way for NCAs to inform HCPs. However, the frequency was considered too high by some respondents, with some suggesting that preferably no more than one message should be sent per week. Others had never received this communication and it was therefore suggested this information should be referenced on the NCA website.

Few HCPs provided comments on this in the **NL**. Some received the information from the pharmacists (KNMP) association, but not directly from the CBG-MEB (NL regulatory agency). Sometimes a time gap between DHPC and CBG email/newsletter seemed to exist.

In **NO**, alerts will be implemented in the dispensing system for pharmacies and are already available through the patient prescription systems for doctors, in addition to the medicines reference book and the NCA's website. Most responders find these alerts useful and important, keeping them up to date. The alerts are appreciated as they permit HCPs to give appropriate information to patients. The HCPs requested that messages be short, factual, easily available, quick to read, and comprehensive.

In **ES** the NCA communications were rated highly by the respondents. However, some doctors stated that, even though the information received is very useful, it was not always easy to retrieve the information at a later date. Reminders, which summarise all the NCAs communications within a certain period, were suggested as the best route to keeping HCPs up to date. It was suggested that the NCA communications and DHPCs could be sent together, or a linkage between those documents could be added. Also, it was suggested that these communications should be incorporated into the electronic prescribing tools, and combined with the NCA web-portal housing product information. It was mentioned that a subscription list should be set up. In this way, a personal email could be sent. It was suggested that it should be possible to indicate your speciality to receive more targeted information. HCPs generally liked the summary of information at the beginning of the document, including the safety problem, recommendation and target population, in addition to some information on the medicine. Moreover, the structured content of the document was found useful.

Only a few comments were received from **SE**, where respondents indicated that they recognised the information as coming from the MPA (SE regulatory agency) and considered this as a positive. A respondent suggested using both generic and brand names for medicines, as generics may not be well known.

In **HR**, half of the comments received indicated that HCPs received the NCA's newsletter. The half of the respondents who did (remember to) receive these safety communications considered them important, e.g. 'I read it carefully, even when I am on vacation.'

In **IE**, mostly positive views on the HPRA (IE regulatory agency) newsletters were received and it was indicated that these were considered independent and more objective than information received from industry. Newsletters were used as an educational tool by some. It was commented that important content was clear and well presented. Some negative responses were that information was repetitive and not timely, echoing what was said by some in relation to DHPCs. It was suggested that there should be an online searchable web-portal with this information.

The open-ended comments are quite extensively reported here, given the usefulness of assessing heterogeneous types of communication across different countries. However, in some countries, only a few comments were made and it is therefore important to realise that such comments may not be representative for all surveyed HCPs.

If respondents were familiar with NCA communications, they received the following additional questions.

6.4.2 Q7: How useful do you find national regulatory agency communications in general?

There are some differences between countries and professionals, but more than 90% of the respondents answering this question thought the communications were useful or very useful (Figure 6.4.2, Table 6.4.2). The main difference was in whether the communication was considered *useful* or *very useful*.

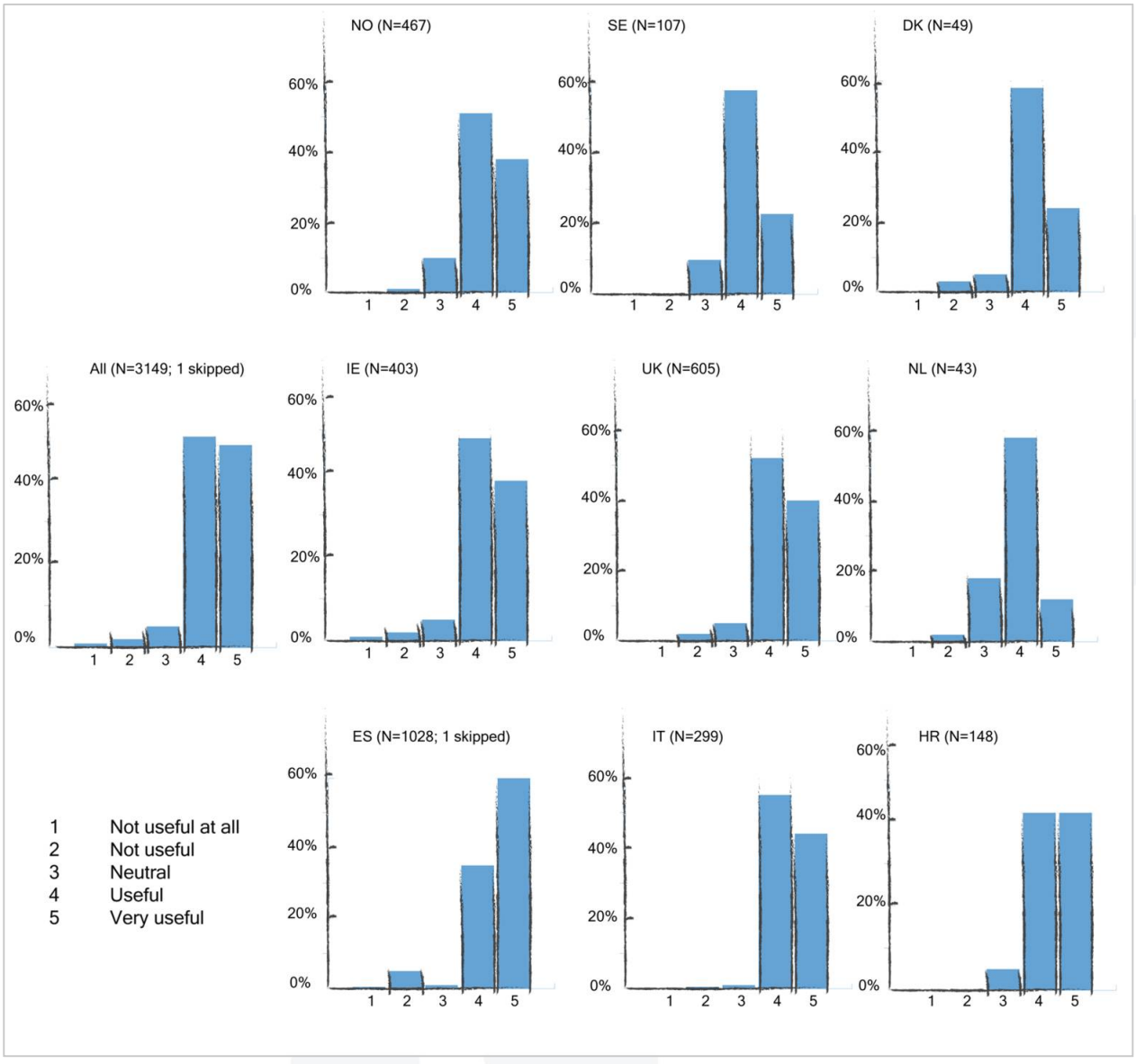


Figure 6.4.2. Results of Q7: How useful do you find national regulatory agency communications in general?

Presented per country. p <0.001 (Kruskal-Wallis)

Table 6.4.2. Results of Q7: How useful do you find national regulatory agency communications in general?

Presented per profession.
Scale from not useful at all (1) to very useful (5). p <0.001 (Kruskal-Wallis)

	GPs[1]	Cardiologists	Pharmacists	Others	Total1
Not useful at all	2 (0%)	1 (1%)	0 (0%)	0 (0%)	3 (0%)
Not useful	15 (1%)	5 (3%)	9 (1%)	2 (1%)	31 (1%)
Neutral	86 (5%)	7 (4%)	57 (5%)	13 (4%)	163 (5%)
Useful	687 (44%)	114 (70%)	561 (51%)	143 (47%)	1505 (48%)
Very useful	780 (50%)	37 (23%)	481 (43%)	149 (49%)	1447 (46%)
Total	1570 (100%)	164 (100%)	1108 (100%)	307 (100%)	3149 (100%)

1. One GP skipped this question

Open-ended answers to Q7 (n=1043)

In the **UK**, respondents supported the value of the national communication for providing updates. Communications were a standing item on the Drug and Therapeutic Committee's agenda. An interesting response suggested that these communications were also a reminder for HCPs to use the Yellow Card system to report ADRs. The way the information was presented was considered helpful, with a summary and overview for quick reading, drawing attention to important information. Background information was also appreciated. Some indicated the information was easily located, while others indicated having problems with access. Regarding the format, the writing style was considered difficult to engage with. It was considered good that an MHRA header (indicating an authoritative and reliable source) was used to increase trust in the communication, and that there was a clear link to the Department of Health for further information. Clear guidance was often, but not always, given; therefore, it was suggested that this needs attention.

Many other positive responses were received from the UK survey, including how information was often repetitive in coming from both NICE and BNF. Therefore, the MHRA as a single channel would be preferred.

In **IT**, HCPs gave generally, positive comments on the timely, reliable and rapid updates; however, they stated that too many communications are currently sent. A suggestion was to apply a means of differentiating by priority.

In the **NL**, the information was considered independent, reliable and to result in increased knowledge and improved patient care. Some argued, however, that information was provided on drugs HCPs were not using, and a suggestion was made to incorporate this information into the electronic prescribing system.

Respondents from **NO, ES, HR** and **IE** had generally positive views on NCA safety communications. They reported that clear, concise, up-to-date, clinically relevant, and useful information was provided through these NCA communications. The NCA was considered as a trustworthy sender. In IE, HPRA Drug safety newsletters were also used an educational tools. Some concerns were raised about the length (too long), repetition (from DHPC), and communications being too slow. In addition, many felt that information provided was often not relevant to their own clinical practice.

6.4.3 Q8: How often do you take the action that is recommended in this type of communication?

HCPs indicated taking action in response to 74% of these NCA communications in HR, compared to 93% in ES and DK (Figure 6.4.3.1, Table 6.4.3.1). The median response ranged from 85% of cases among pharmacists to 91% among 'other HCPs' (Figure 6.4.3.2, Table 6.4.3.2). Again, as with the response to the DHPC (6.3.4), this is considered a high level of action.

SE did not include this question in their questionnaire.

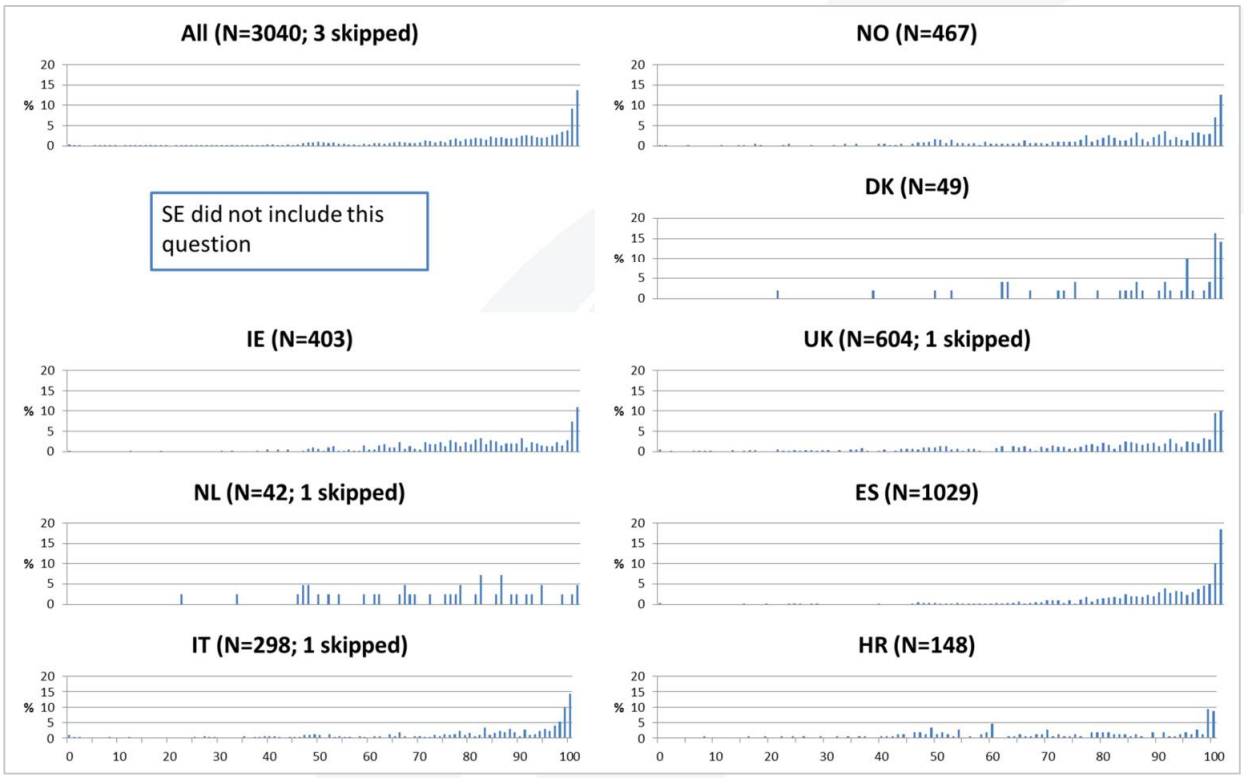


Figure 6.4.3.1. Results of Q8: How often do you take the action that is recommended in NCA communication?

Presented per country. p <0.001 (Kruskal-Wallis).

On the y-axis the percentage of responding HCPs (all/per country) is indicated with the x-axis describing how often (never, 0% of the time – always, 100% of the time) they indicated to have taken the action.

Table 6.4.3.1. Results of Q8: How often do you take the action that is recommended in this NCA communication (never – always)?

Presented per country, where Q1 is the lower quartile and Q3 the upper quartile.

	NO	SE	DK	IE	UK	NL	ES	IT	HR	Total
Q1	70	-	74	70	65	58	83	72	52	73
Median	85	-	93	82	84	75.5	93	88	73.5	88
Q3	97	-	99	95	97	85	99	98	95	98

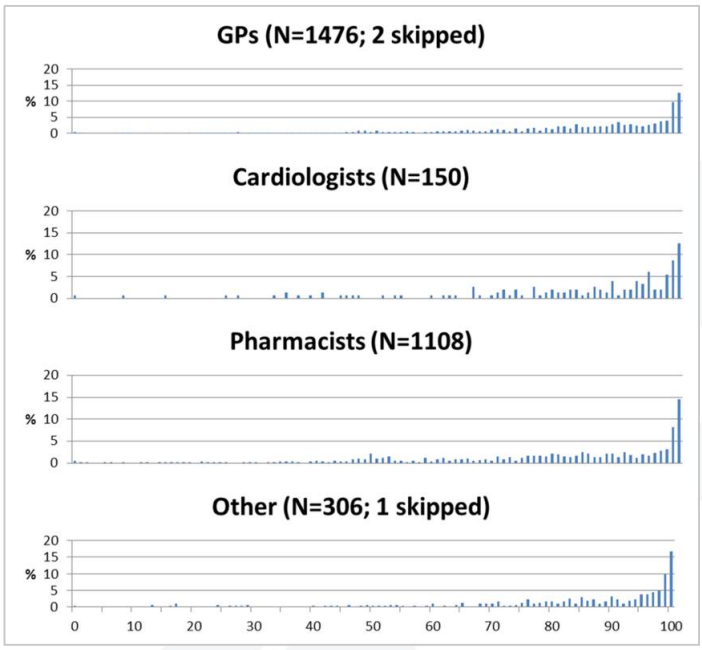


Figure 6.4.3.2. Results of Q8: How often do you take the action that is recommended in NCA communication (never, 0% of the time – always, 100% of the time)?

Presented per profession. P <0.001 (Kruskal-Wallis).

On the y-axis the percentage of responding HCPs is indicated with the x-axis describing how often (never, 0% of the time – always, 100% of the time).

Table 6.4.3.2. Results of Q8: How often do you take the action that is recommended in this type of communication (NCA communication)? (never – always).

Presented per profession, where Q1 is the lower quartile and Q3 the upper quartile.

	GP	Cardiologist	Pharmacist	Other
Q1	76	73	67	78
Median	89	89	85	91
Q3	98	98	98	99

Open-ended answers to Q8 (n= 834)

The reasons for taking action were either that HCPs considered it their duty or, because it was sent by the regulator (MHRA, **UK**), some thought it compulsory **(IE**). Trust (**ES**) in the NCA was also mentioned as an important reason to follow the recommendation. HCPs highlighted the need to access independent drug information and that NCAs could provide this.

It was also mentioned that an individual benefit-risk assessment was made only if action was needed for an individual patient. However, in a number of responses it was suggested that it would be difficult to ignore a (new) contra-indication (legal/litigation concerns).

The majority of respondents indicated (as in 6.3.4) that they would only not take action if the message was not relevant for them, either because it fell outside of their scope of medical practice, or because no patient had (yet) presented with the mentioned concern. Some also indicated that they had forgotten about the specific issue. Very few mentioned a lack of time for not following these recommendations.

6.4.4 Q9: Would it be sufficient for you to only receive an electronic version of national regulatory agency communications, instead of a hardcopy version?

This question was only included in the survey conducted in SE. A small majority of HCPs indicated they would prefer to receive a hardcopy version of NCA communications (Figure 6.4.4). This seems in line with the considerable proportion of Swedish HCPs that also had a preference for a hardcopy DHPC.

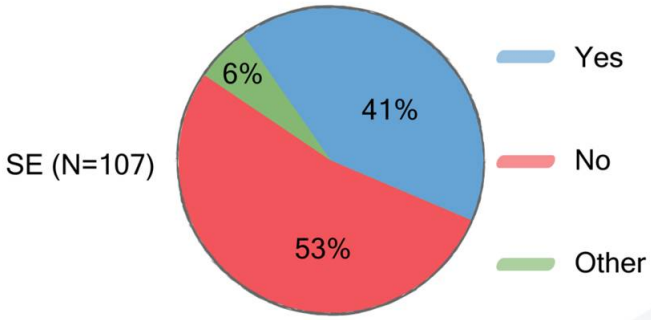


Figure 6.4.4. Results of Q9: Would it be sufficient for you to only receive an electronic version of national regulatory agency communications, instead of a hardcopy version?
(Only included in SE)

Open-ended answers (n=6)

A respondent indicated that it was appreciated that a particular paper-based news bulletin appeared regularly and could be read at home after work. More respondents indicated that it was difficult to retrieve information from the constant flow of emails, which was why the paper-based bulletin was appreciated.

6.4.5 General comments on NCA communication section

There were 170 additional general comments on NCA communications. Most overlapped with comments given on the specific questions above.

In the **UK**, there were some additional comments with regard to difficulties encountered in navigating the MHRA website after it moved to the.gov.uk domain. In IT, comments suggested that information could be more HCP-oriented. **Norwegian** HCPs preferred information to pop up on computer systems (GPs and pharmacists) and that the alerts also be addressed to dentists and nurses. In **ES**, few responses were received, but an interesting remark was made that drug consumption data could be added to contextualise safety information. In **SE**, HCPs liked the paper bulletin from the MPA and stated that it was less easily missed in the large flow of emails. Most of these issues were already raised above.

6.5 Educational materials – survey questions

The answers to the questions regarding educational materials are presented below.

6.5.1 Q10: Are you familiar with this type of safety information?

Just over a quarter (27%) of respondents indicated that they were not familiar with educational materials (Figure 6.5.1). Irish, Croatian and Dutch respondents seemed most familiar. Pharmacists (74%) were the type of HCP that showed most awareness, followed by two-thirds of GPs and cardiologists, with 'other' HCPs (45%) being the least aware (Table 6.5.1). The level of familiarity, although still quite high, was considerably lower than for the other two communication tools.

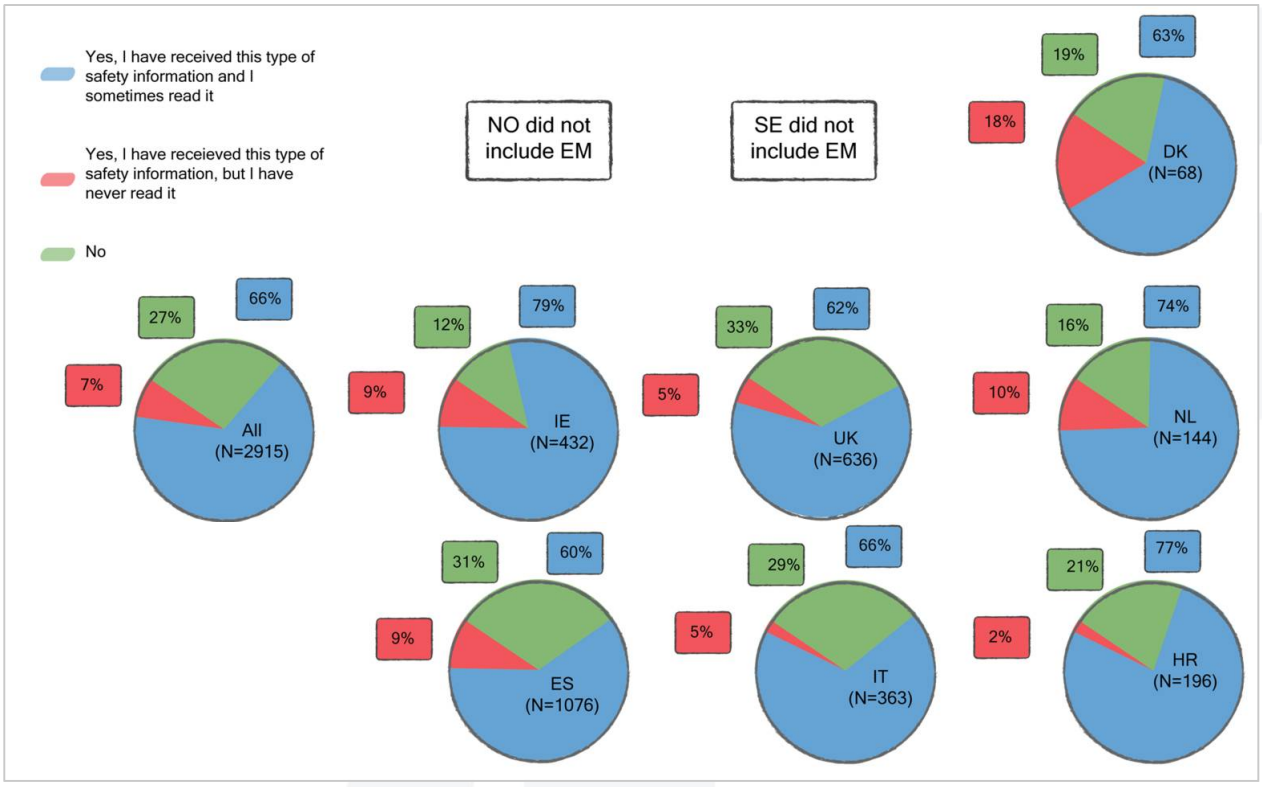


Figure 6.5.1. Results of Q10: Are you familiar with this type of safety information (educational material)?

Presented per country. p <0.001 (χ^2-test)

Table 6.5.1. Results of Q10: Are you familiar with this type of safety information (educational material)?

Presented per profession. p <0.001 χ^2(-test)

	GPs	Cardiologists	Pharmacists	Others	Total
Yes, I have received this type of safety information and I sometimes read it	995 (64%)	113 (68%)	675 (74%)	128 (45%)	1911 (66%)
Yes, I have received this type of safety information, but I have never read it	158 (10%)	16 (10%)	34 (4%)	11 (4%)	219 (8%)
No	400 (26%)	38 (23%)	201 (22%)	146 (51%)	785 (27%)
Total	1553 (100%)	167 (100%)	910 (100%)	285 (100%)	2915 (100%)

Open-ended answers (n= 445)

HCPs from the **UK** were mostly positive about these materials, but they indicated having problems locating them. They would prefer a repository on the MHRA website, and clarification as to where information is coming from. Educational materials were sometimes hard to differentiate from advertisements from pharmaceutical companies. Materials should use generic names, as brand names were not generally used in the NHS. Some **IT** HCPs indicated that they also valued scientific information from sales representatives. The materials might be confusing for some patients (e.g. elderly). Also, **Dutch** and **Irish** HCPs considered the materials difficult to differentiate from advertising materials, and stated that they had difficulties in retrieving the materials at a later date. In **ES**, many HCPs indicated a distrust in information sent by industry and do not read it.

If respondents were familiar with educational materials, they received follow-up questions related to educational materials.

6.5.2 Q11: How useful do you find educational materials in general?

The large majority of HCPs that were familiar with educational materials thought they were *useful* (59%) to *very useful* (25%) (Figure 6.5.2). There were no significant differences in appreciation of the usefulness of educational materials between the professional groups (Table 6.5.2) (p=0.071, Kruskal-Wallis).

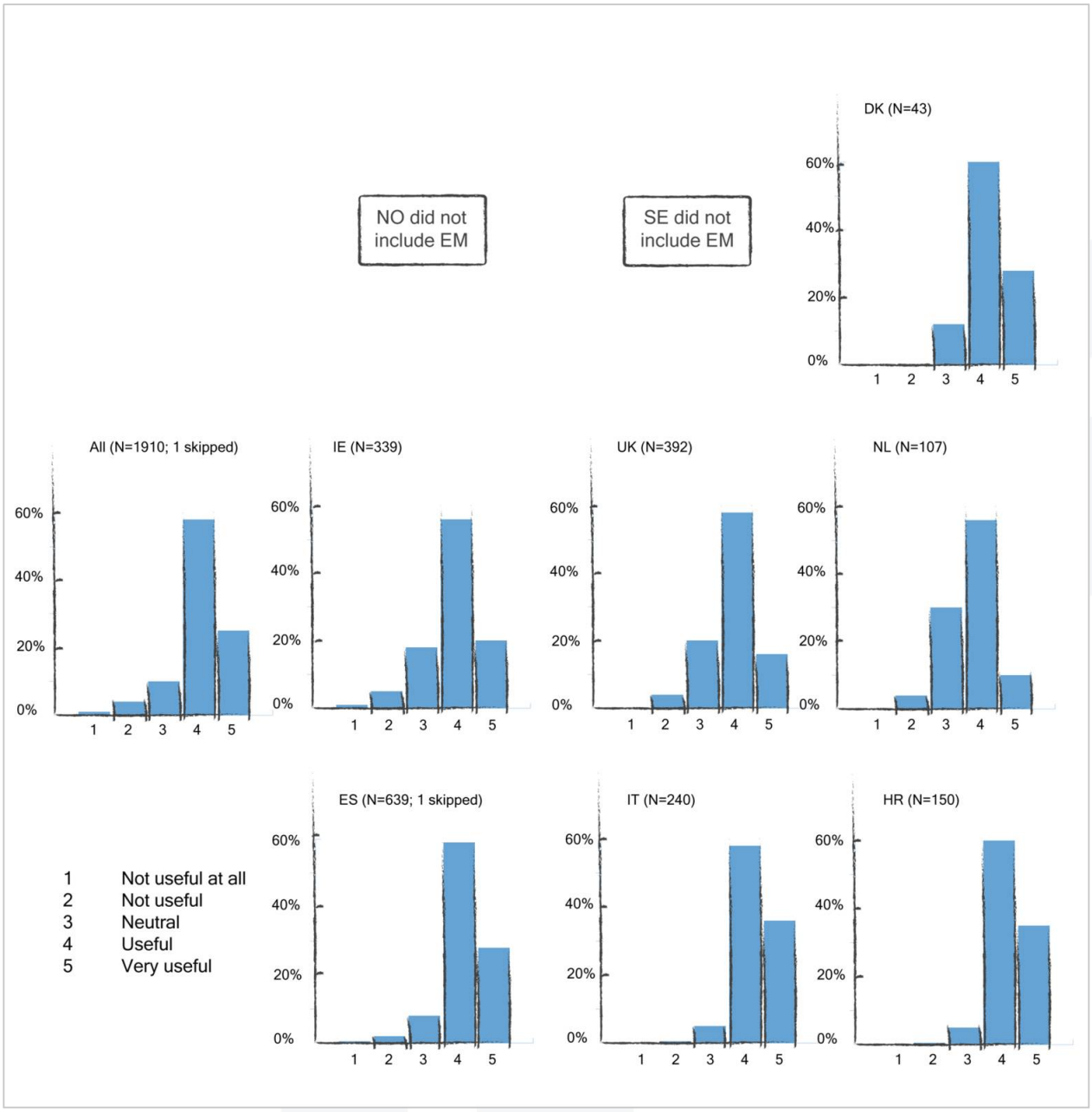


Figure 6.5.2. Results of Q11: How useful do you find educational materials in general?
Presented per country. p <0.001 (Kruskal-Wallis)

Table 6.5.2. Results of Q11: How useful do you find educational materials in general?

Presented per profession. This question was not included in NO and SE.
Scale from not useful at all (1) to very useful (5). P = 0.071 (Kruskal-Wallis)

	GPs[1]	Cardiologists	Pharmacists	Others	Total1
Not useful at all	6 (1%)	0 (0%)	1 (0%)	0 (0%)	7 (0%)
Not useful	35 (4%)	0 (0%)	15 (2%)	3 (2%)	53 (3%)
Neutral	139 (14%)	12 (11%)	88 (13%)	12 (9%)	251 (13%)
Useful	578 (58%)	69 (61%)	398 (59%)	77 (60%)	1122 (59%)
Very useful	236 (24%)	32 (28%)	173 (26%)	36 (28%)	477 (25%)
Total	994 (100%)	113 (100%)	675 (100%)	128 (100%)	1910 (100%)

1. One GP skipped this question.

Open-ended answers to Q11 (n=473)

The reason why HCPs thought educational materials were useful was mainly that these methods could reinforce information presented during consultation with patients. Visual aids were also mentioned as being very helpful. Educational materials could be used to increase adherence and appropriate drug use. It was mentioned that content and format should be clear, and plain language should be used.

Similar concerns were raised in relation to a general distrust of information coming directly from industry, i.e. concerns about potential misinformation or skewed information. Practical issues were also raised around how to access additional copies, and a need for a repository – preferably on an NCA website/portal.

6.5.3 Q12: If educational material for the patient is available, either for explanation during a consult or to be read at home, how do you value the following delivery methods?

Slightly more respondents had a neutral view with regards to online or web-based tools compared to hardcopy versions for use in patient consultation or to be used at home by patients (Figure 6.5.3). Any differences between professionals were marginal. Although a significantly lower appreciation of hardcopy material was observed for GPs ($p < 0.001$) (Table 6.5.3), the median appreciation was similar (4: positive) to the other professional groups.

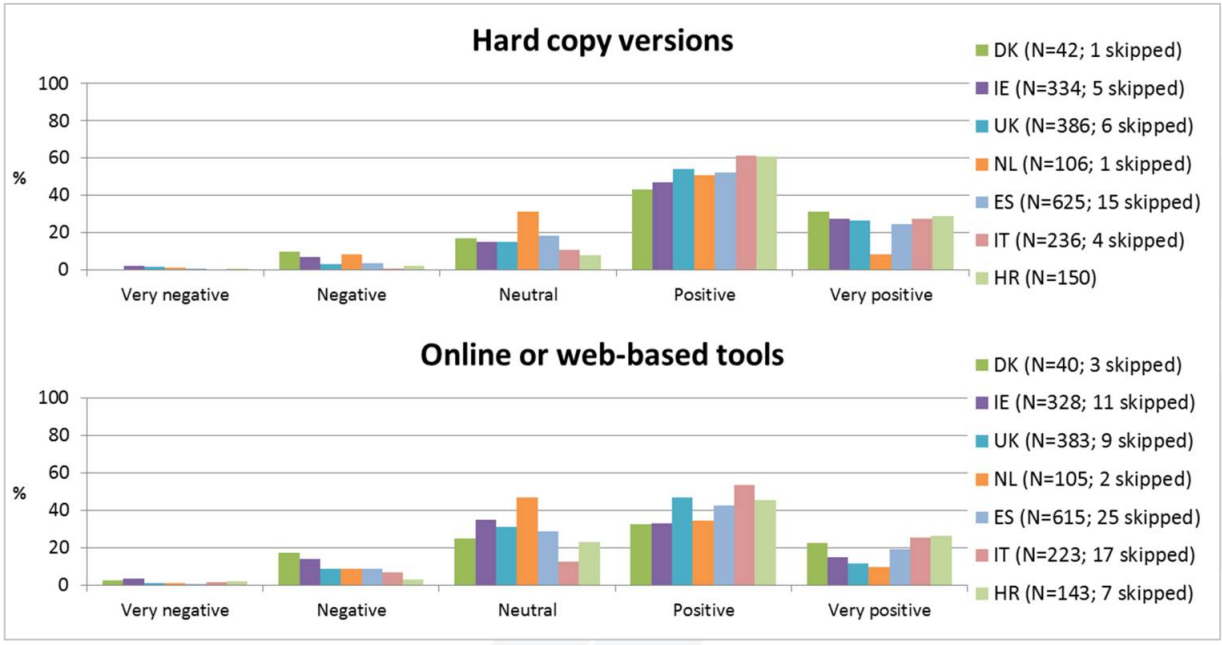


Figure 6.5.3. Results of Q12: If educational material for the patient is available, either for explanation during a consult or to be read at home, how do you value the following delivery methods?

Presented per country. Hardcopy: $p < 0.001$ (Kruskal-Wallis); Online or web-based tools: $p < 0.001$ (Kruskal-Wallis)

Table 6.5.3. Results of Q12: If educational material for the patient is available, either for explanation during a consult or to be read at home, how do you value the following delivery methods?

Presented per profession. Scale from very negative (1) to very positive (5). Q1 is the lower quartile and Q3 the upper quartile. Medians are presented (Q1; Q3).

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (Kruskal-Wallis)
Hardcopy	4 (3;4)	4 (4;4)	4 (4;5)	4 (4;5)	4 (4;5)	<0.001
Online or web-based tools	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	0.129

6.5.4 Q13: Please tick all the following contents that you think should be included in educational materials for patients.

Overall, the information that should be included according to most of the respondents was: 1) information on how to correctly use/take the product (93% of respondents); 2) warnings about serious ADRs and how the risk may be minimized (83%); and 3) a summary of both the benefits and risks of using the product (74%) (Figure 6.5.4). Although, all options were significantly different between the countries, a more outspoken or relevant difference was observed with regard presenting the benefits and risks. Danish, Dutch, Croatian and Italian respondents were significantly less in favour of this. There were few differences between the professional groups (Table 6.5.4).

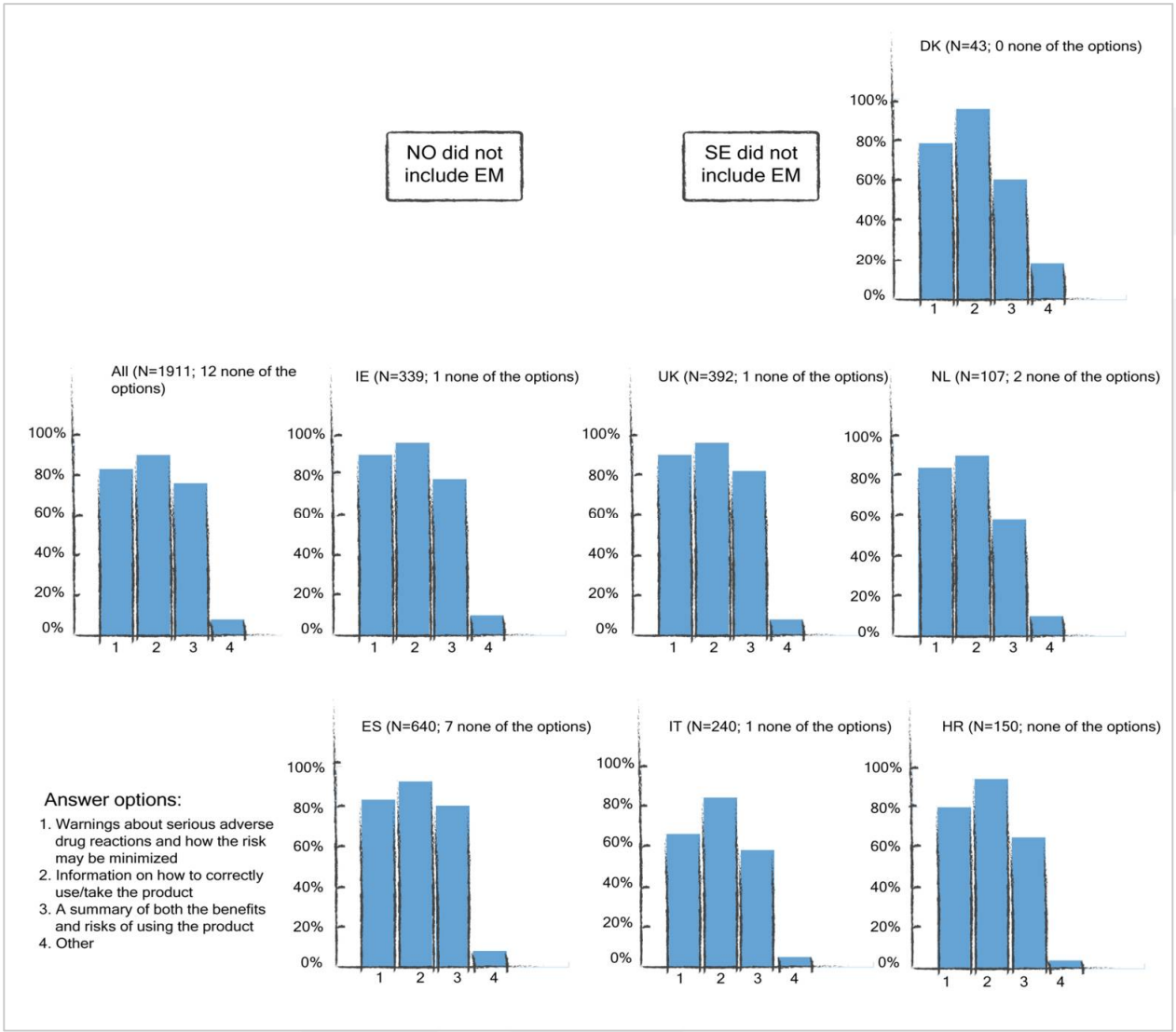


Figure 6.5.4. Results of Q13: Please tick all the following contents that you think should be included in educational materials for patients.

Presented per country. The number of respondents that ticked the box for "none of the above" is mentioned in the title of the graphs.

p-value (χ2-test)
1. <0.001
2. <0.001
3. <0.001
4. 0.009

Table 6.5.4. Results of Q13: Please tick all the following contents that you think should be included in educational materials for patients.

Presented per profession.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (-χ^2test)
1. Warnings	799 (80%)	87 (77%)	591 (88%)	113 (88%)	1590 (83%)	<0.001
2. Information	906 (91%)	102 (90%)	639 (95%)	123 (96%)	1770 (93%)	0.012
3. Summary	728 (73%)	74 (65%)	505 (75%)	102 (80%)	1409 (74%)	0.076
4. Other	70 (7%)	10 (9%)	84 (12%)	11 (9%)	175 (9%)	0.003
None of the above	4 (0%)	2 (2%)	3 (0%)	3 (2%)	12 (1%)	0.023

1. Warnings about serious adverse drug reactions and how the risk may be minimised
2. Information on how to correctly use/take the product
3. A summary of both the benefits and risks of using the product
4. Other

Open-ended answers to Q13 (n = 172)

The suggestions as to information that should be given in educational materials included placing the warnings in context of likelihood, what to do in lay terms, giving a realistic explanation of risks and not to include all risks. It was suggested that there was a need for communications to clearly indicate what action should be taken, whom to contact and when. In addition, some basic drug information should be given, as well as what patients should do if they miss a dose, interactions (drugs and food), contra-indications and how effective the drug is in treating the intended disease, to encourage adherence. There was also support for the incorporation of instructions for HCPs on how to monitor patients (e.g. organ function) and how to report ADRs.

6.5.5 Q14: Have you ever used educational materials as part of a discussion about a medicine with a patient? Multiple responses possible.

In total, 1336 (70%) of 1911 HCPs familiar with educational material had used these materials in a consultation with their patient (Figure 6.5.5). HCPs from IE, ES and HR had done this most, while Danish and Dutch HCPs had done this the least. The use of these materials in consultation with patients was similar across all HCP groups (Table 6.5.5).

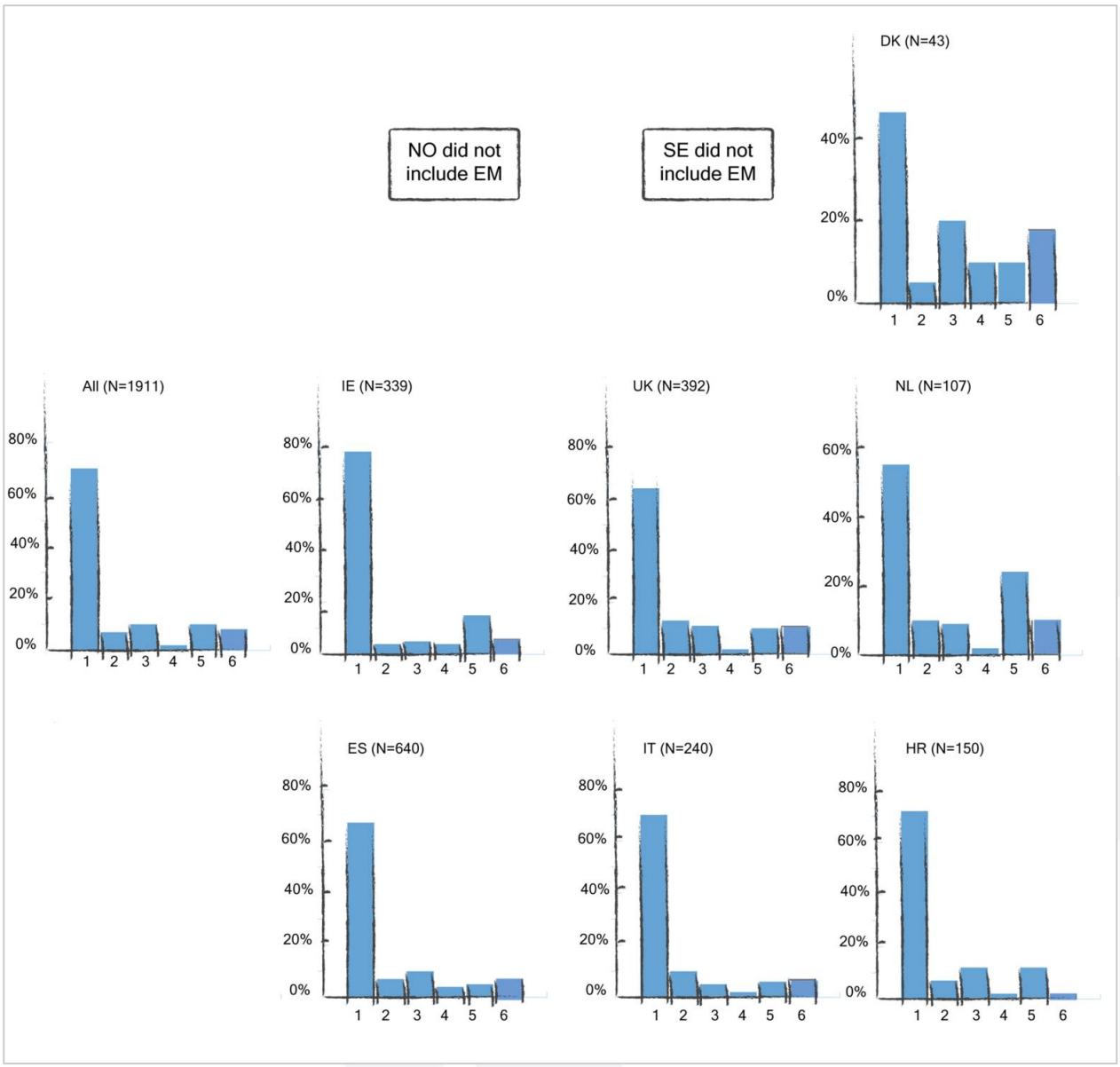


Figure 6.5.5. Results of Q14: Have you ever used educational materials as part of a discussion about a medicine with a patient?

Presented per country. Multiple responses possible.

	p-value (χ^2-test)
1. Yes	<0.001
2. No, I do not routinely prescribe medicines for which educational materials are available	<0.001
3. No, I do not know if educational materials are available for the medicines I prescribe	0.003
4. No, I do not find these materials helpful for patients	0.332
5. No, I think the Patient Information Leaflet already provides sufficient information	<0.001
6. No, because…	0.003

Table 6.5.5. Results of Q14: Have you ever used educational material as part of a discussion about a medicine with a patient?

Presented per profession. Multiple responses possible.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (χ^2-test)
1. Yes	689 (69%)	81 (72%)	476 (71%)	90 (70%)	1336 (70%)	0.918
2. No, don't prescribe	49 (5%)	5 (4%)	62 (9%)	13 (10%)	129 (7%)	0.002
3. No, don't know	99 (10%)	10 (9%)	35 (5%)	12 (9%)	156 (8%)	0.006
4. No, not helpful	43 (4%)	3 (3%)	7 (1%)	1 (1%)	54 (3%)	<0.001
5. No, PIL	92 (9%)	10 (9%)	38 (6%)	4 (3%)	144 (8%)	0.009
6. No, because…	47 (5%)	5 (4%)	71 (11%)	11 (9%)	134 (7%)	<0.001

1. Yes
2. No, I do not routinely prescribe medicines for which educational materials are available
3. No, I do not know if educational materials are available for the medicines I prescribe
4. No, I do not find these materials helpful for patients
5. No, I think the Patient Information Leaflet already provides sufficient information
6. No, because…

Open-ended answers to Q14 (n=126)

A commonly raised concern regarding educational materials was their impartiality, considering they were supplied by industry. Another concern was difficulties regarding inaccessibility. Another reason given for not using educational materials was that these materials are not patient-friendly, or that educational materials were not relevant for the respondent's professional group.

An important positive characteristic of educational materials is that visual aids can facilitate communication, or reinforce information shared, with patients. The materials may be given to patients, but should have a sufficiently large font so that the elderly can read them as well. Additional formats, such as YouTube videos, were suggested as a tool. In order to facilitate retrieval, and to not be dependent on sales reps, it was suggested that there should be a central repository (NCA, pharmaceutical reference book) that allows printing. Alternatively, it could be embedded into the electronic prescribing system.

6.5.6 General comments on educational materials

Over a quarter of all respondents, mainly pharmacists, across different countries, indicated that they had rarely seen educational materials. In general, the major concern of HCPs who had experience with these educational materials was that they were mostly (seen as) coming from industry. This was seen to be less of an issue in IT and was also not mentioned in HR. It was suggested that materials were often only available from sales representatives and were not easy to distinguish from promotional/commercial materials. Still, a number of positive comments were that these materials were considered educational and could be valuable for helping patients understand the benefits and risks of drugs.

Some of the visual aids provided were considered especially useful. In order to promote the use/uptake of educational materials, it was suggested that these materials be independently produced and available from the NCAs' websites or available from the HCPs' own IT systems. The information should be kept concise. Electronic format, e.g. availability on websites or development of mobile apps, was suggested to improve uptake and an awareness campaign was suggested to improve awareness. In ES, it was suggested to roll out an awareness campaign on the availability of these kinds of materials. A reference could be made in the Patient Information Leaflet to specify if/where educational materials could be located.

6.6 General preferences and behaviour towards medicines safety information – survey questions

In this section of the document, general issues of safety communication are discussed that are not specific to the main three regulatory communication tools: DHPCs, NCA communications and educational material.

6.6.1 Q15: How do you value the following sources as senders of safety messages?

The respondents were asked to indicate how they valued seven potential sources (NCAs; European Medicines Agency (EMA); professional bodies; pharmaceutical companies; colleagues; public press; and independent researchers) as the senders of safety messages. The NCA was considered most positive as a sender of the safety information (Figure 6.6.1.1), followed by professional bodies (Figure 6.6.1.3) and the EMA (Figure 6.6.1.2). Pharmaceutical companies (Figure 6.6.1.4) and, in particular, the lay press (Figure 6.6.1.6) were considered most negatively. Differences between countries were visible, but modest. Similarly, no important differences in preference between professionals were noted (Table 6.6.1).

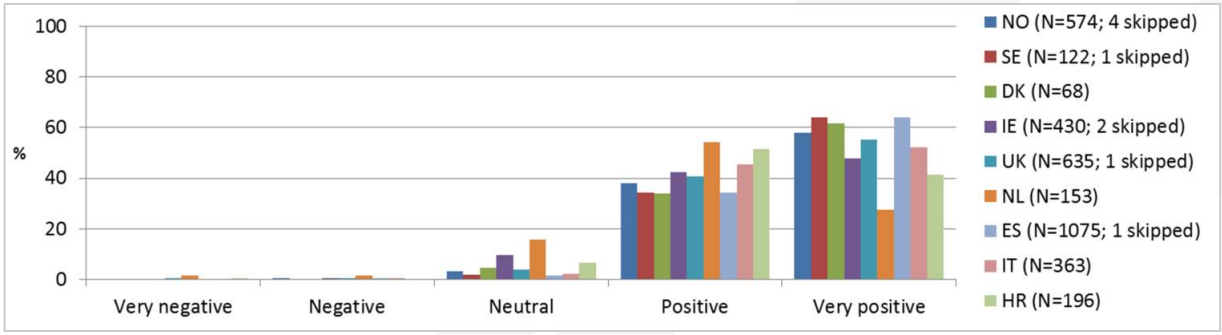


Figure 6.6.1.1. NCA. p <0.001 (Kruskal-Wallis)

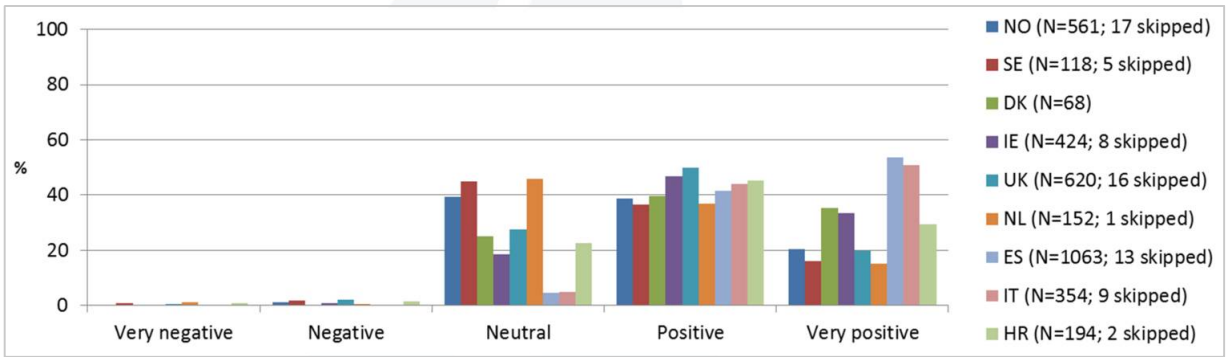


Figure 6.6.1.2. European Medicines Agency (EMA). p <0.001 (Kruskal-Wallis)

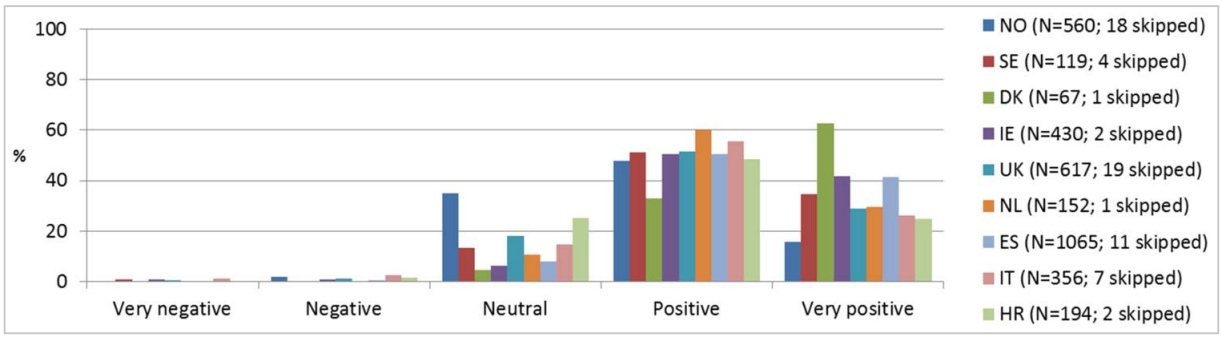


Figure 6.6.1.3. Professional body. p <0.001 (Kruskal-Wallis)

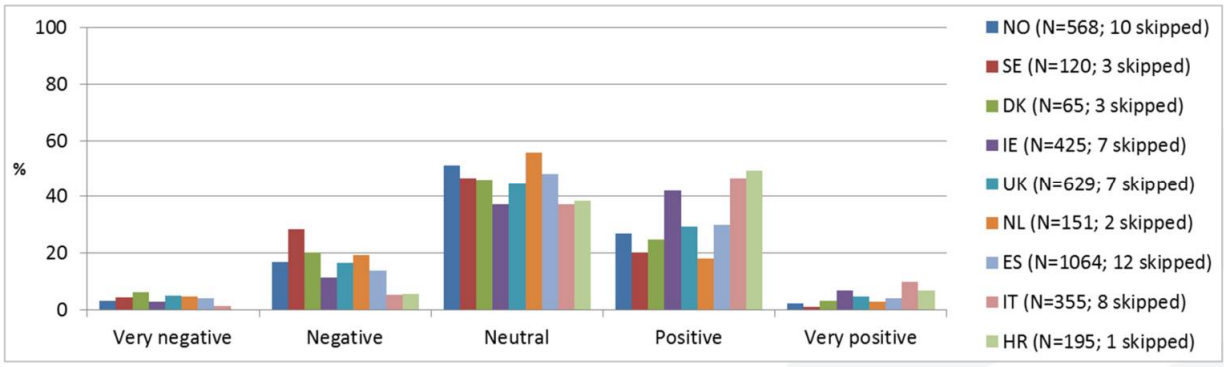


Figure 6.6.1.4. Pharmaceutical companies. p <0.001 (Kruskal-Wallis)

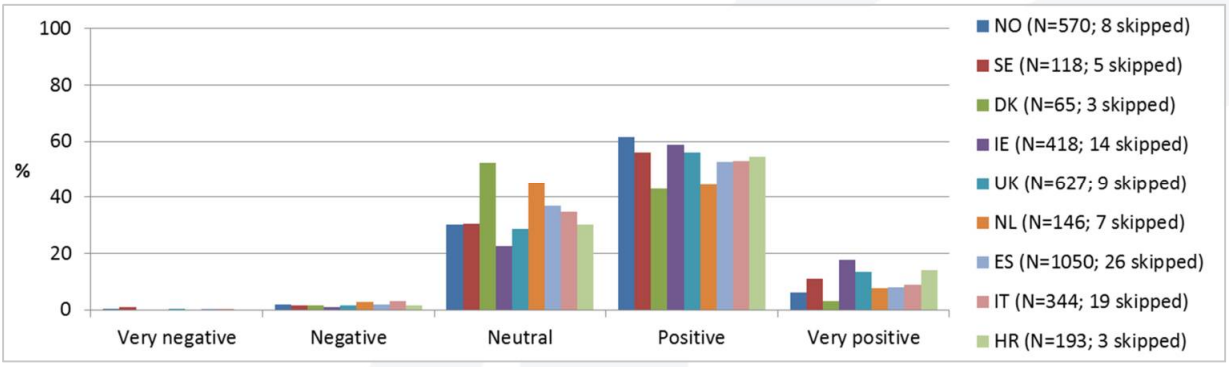


Figure 6.6.1.5. Colleague. p <0.001 (Kruskal-Wallis)

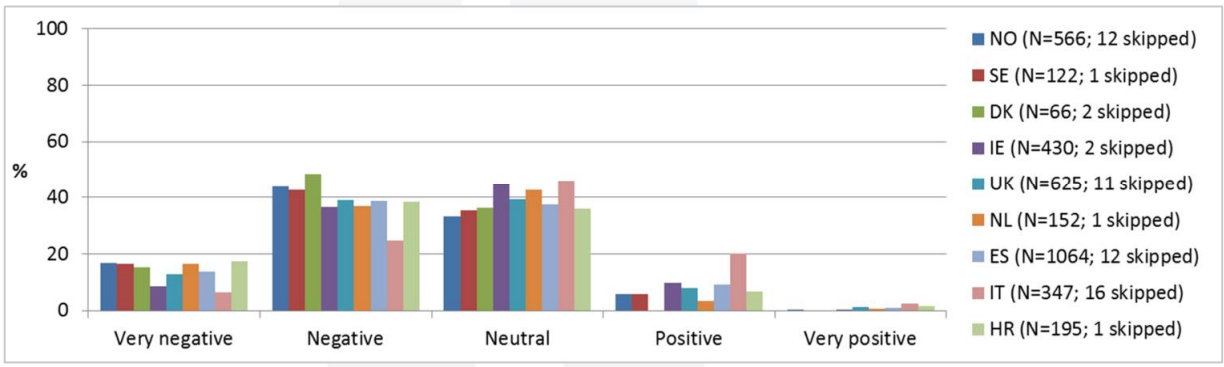


Figure 6.6.1.6. Public press
(e.g. local newspaper or news programme on television). p <0.001 (Kruskal-Wallis)

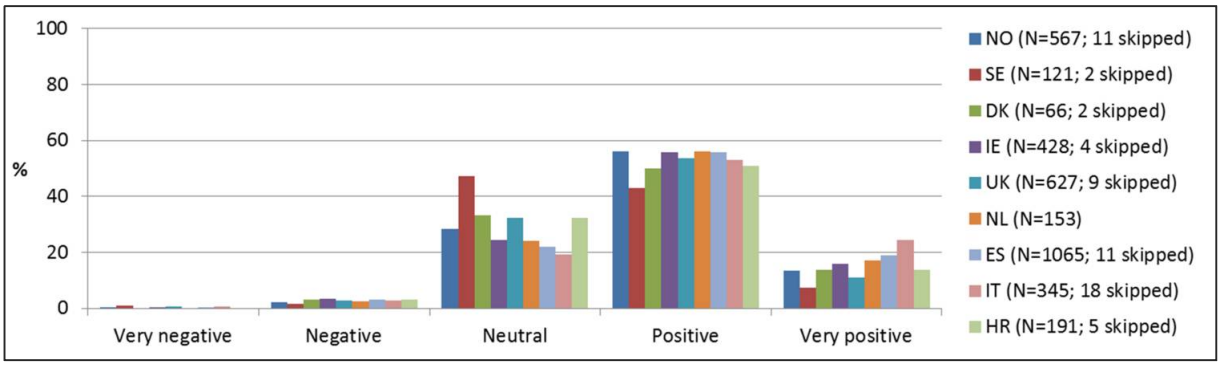


Figure 6.6.1.7. Independent researchers. p <0.001 (Kruskal-Wallis)

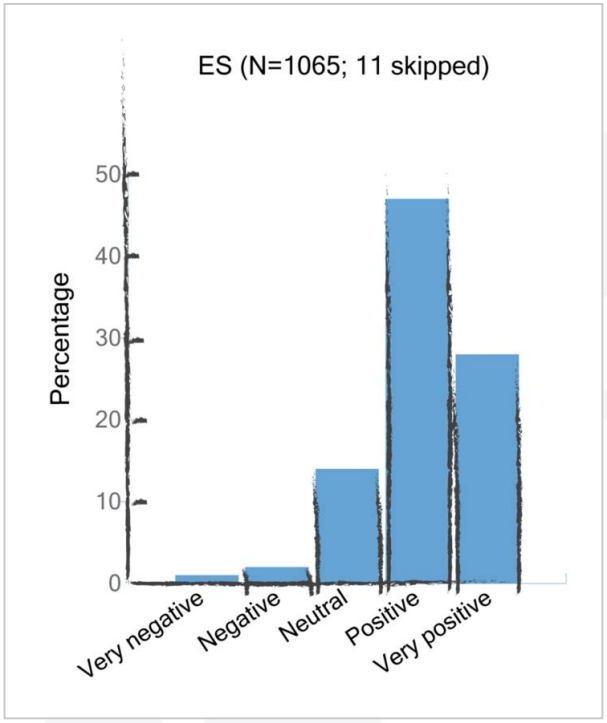


Figure 6.6.1.8. Health agencies of your autonomous region

(e.g. health service in your autonomous region, regional pharmacovigilance centres, etc.). Option was only available in ES.

The added question on the autonomous (local) health centres in ES (Figure 6.6.1.8) indicated that these were considered almost as positive as the NCA, professional bodies and the EMA.

Table 6.6.1 Results of Q15: How do you value the following sources as senders of safety messages?

Presented per profession. Scale from very negative (1) to very positive (5). Medians are presented (Q1; Q3). Q1 is the lower quartile and Q3 the upper quartile.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (Kruskal-Wallis)
NCA	5 (4;5)	4 (4;5)	5 (4;5)	5 (4;5)	5 (4;5)	<0.001
EMA	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	0.026
Professional body	4 (4;5)	4 (4;4)	4 (3;4)	4 (4;5)	4 (4;5)	<0.001
Pharmaceutical companies	3 (3;4)	3 (3;4)	3 (3;4)	3 (3;4)	3 (3;4)	<0.001
Colleague	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	0.002
Public press	2 (2;3)	2 (2;3)	2 (2;3)	3 (2;3)	2 (2;3)	0.290
Independent researchers	4 (3;4)	4 (4;5)	4 (3;4)	4 (4;4)	4 (3;4)	<0.001

Open-ended answers to Q15

In the open-ended answers to other potential sources, relatively few respondents suggested common sources (n=174). The most noteworthy were the Cochrane library, Health Technology Assessment agencies (e.g. NICE), ministry of health, medical/pharmacists associations, Drug Bulletins, World Health Organisation, medical newsletters (e.g. Medscape), and social media, with blogs and Twitter specifically mentioned.

6.62 Q16: In general, do you prefer to receive safety information in hardcopy (paper) or electronically?

This answer was consistent with the preference of receiving the DHPC (6.3.5), as a hardcopy version; the largest percentages of HCPs preferring hardcopy material were found in SE, NL and IE (Figure 6.6.2). The differences between groups of HCPs were not significant (p =0.002) (Table 6.6.2).

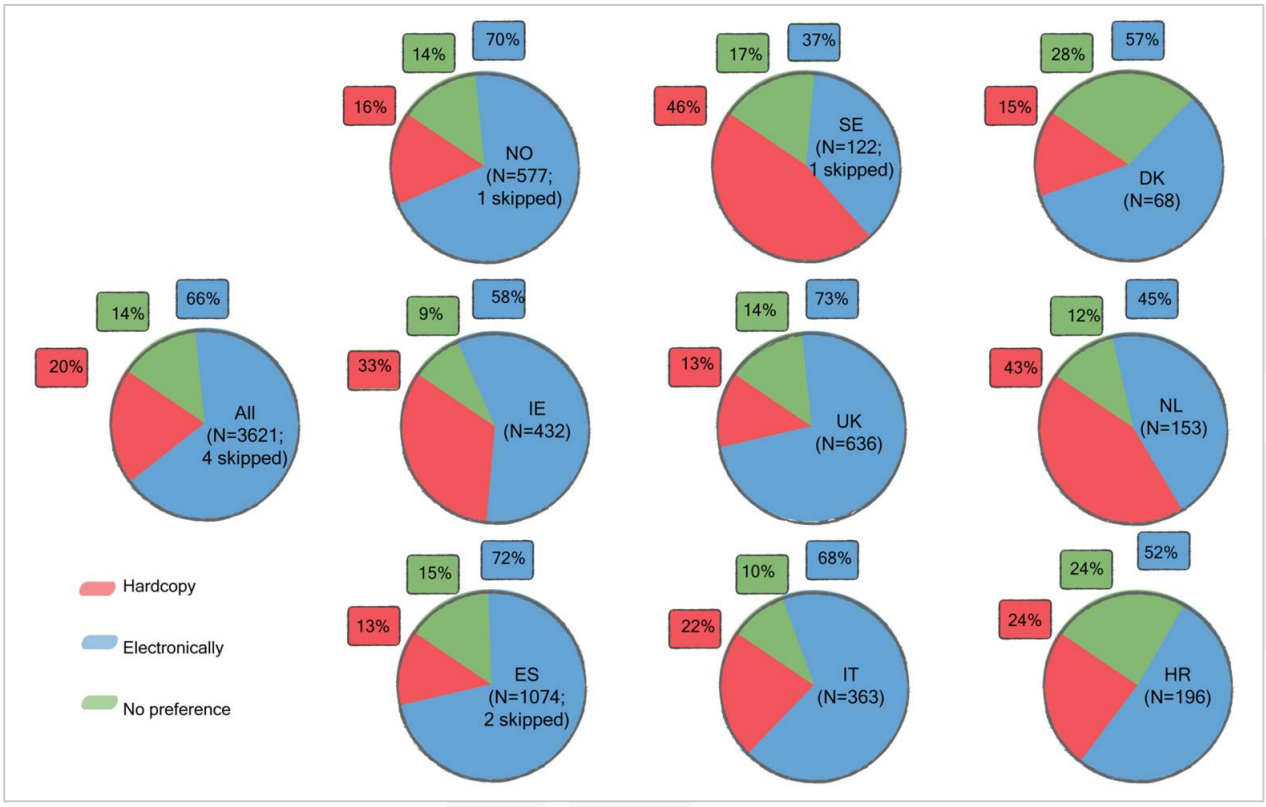


Figure 6.6.2. Results of Q16: In general, do you prefer to receive safety information in hardcopy (paper) or electronically?

Presented per country. p <0.001 (χ^2-test)

Table 6.6.2. Results of Q16: In general, do you prefer to receive safety information in hardcopy (paper) or electronically?

Presented per profession. p =0.002 (χ^2-test)

	GPs[1]	Cardiologists	Pharmacists[2]	Others	Total1,2
Hardcopy	389 (22%)	53 (24%)	231 (18%)	48 (14%)	721 (20%)
Electronically	1116 (63%)	145 (65%)	887 (68%)	243 (72%)	2391 (66%)
No preference	258 (15%)	24 (11%)	181 (14%)	46 (14%)	509 (14%)
Total	1763 (100%)	222 (100%)	1299 (100%)	337 (100%)	3621 (100%)

1. Three GPs skipped this question
2. One pharmacist skipped this question

6.6.3 Q17: Below you can find some channels, which can be both in a hardcopy and electronic format. Independent of the format, how do you value each channel to keep up to date on the safety of medicines?

Six alternative channels were presented to the respondents. They were asked to indicate how they valued each channel as a means by which to be informed of new risks about medicines. National clinical guidelines (Figure 6.6.3.6) and medicines references books (Figure 6.6.3.4) were most often valued very positively. Personalised letters (Figure 6.6.3.1), medical journals (Figure 6.6.3.2) and SmPCs (Figure 6.6.3.3) were valued next most positively, in this order. Newspapers (Figure 6.6.3.5) were considered more negatively.

Variation across countries was not large, possibly with the exception of the SmPC, where appreciation across the range from neutral to very positive was quite different for the different countries, though responses were still mostly positive.

Professional groups had significant differences in appreciation of the various channels, except for the personalised letters and national clinical guidelines. However, the same median score was given by all professional groups (Table 6.6.3).

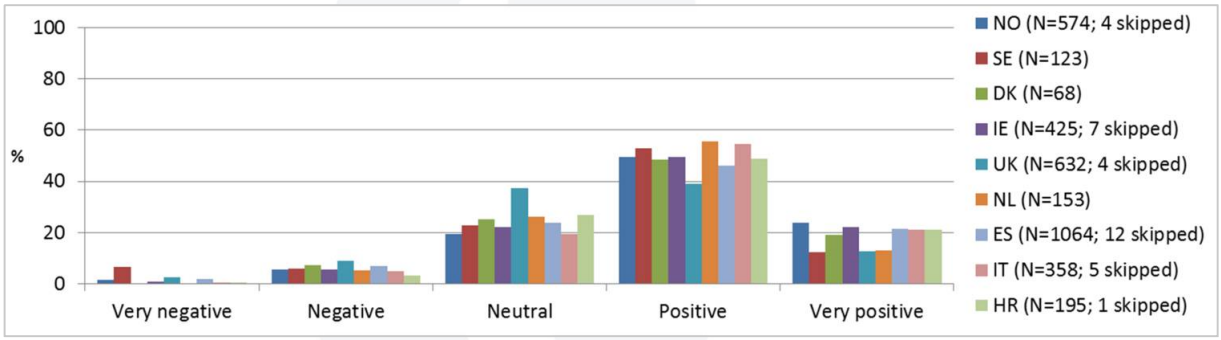


Figure 6.6.3.1. Personalised letter. p <0.001 (Kruskal-Wallis)

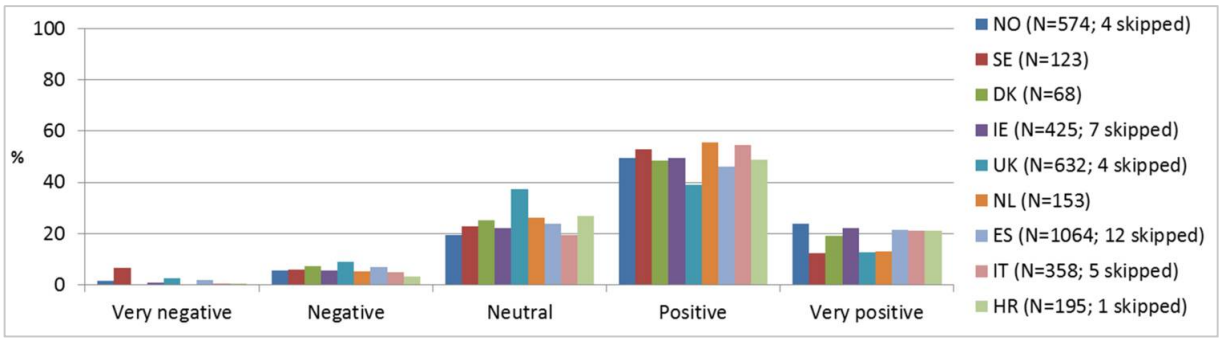


Figure 6.6.3.2. Medical journal. p <0.001 (Kruskal-Wallis)

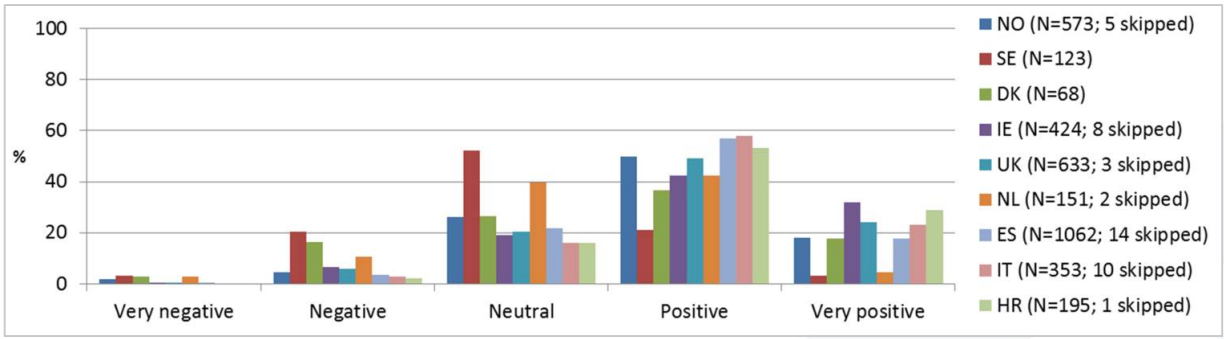


Figure 6.6.3.3. Summary of Product Characteristics / Patient information leaflet. p <0.001 (Kruskal-Wallis)

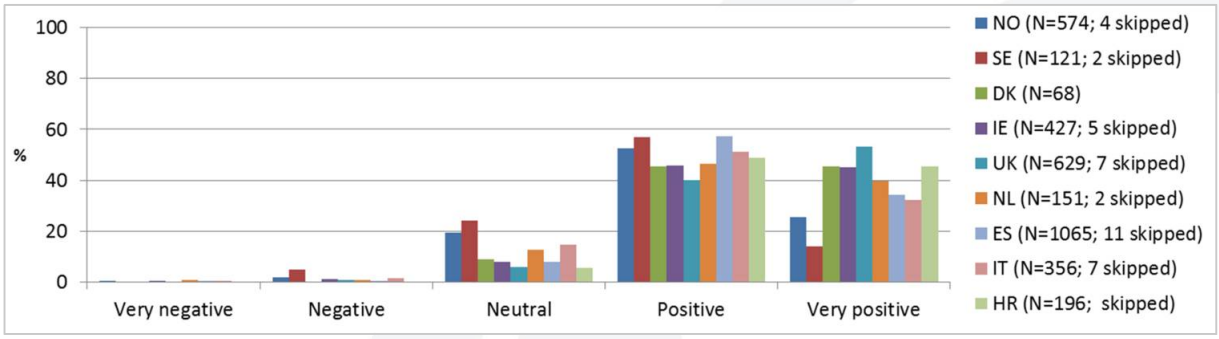


Figure 6.6.3.4. Medicines reference book. p <0.001 (Kruskal-Wallis)

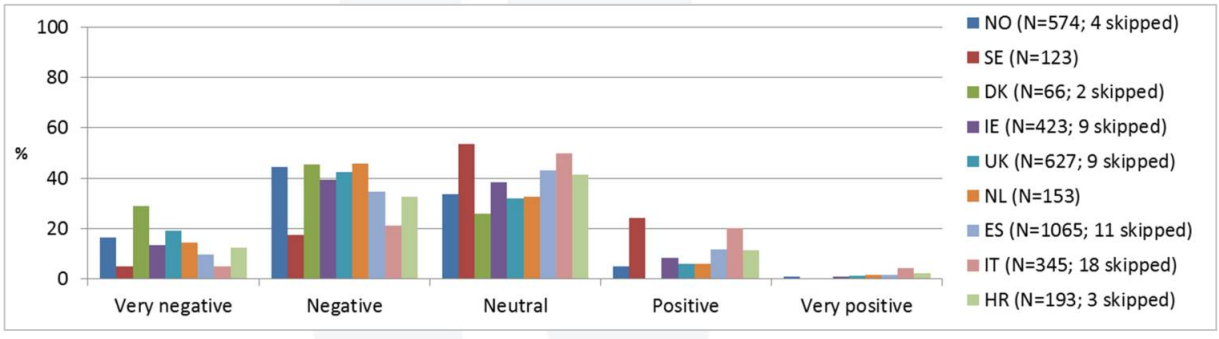


Figure 6.6.3.5. Newspaper. p <0.001 (Kruskal-Wallis)

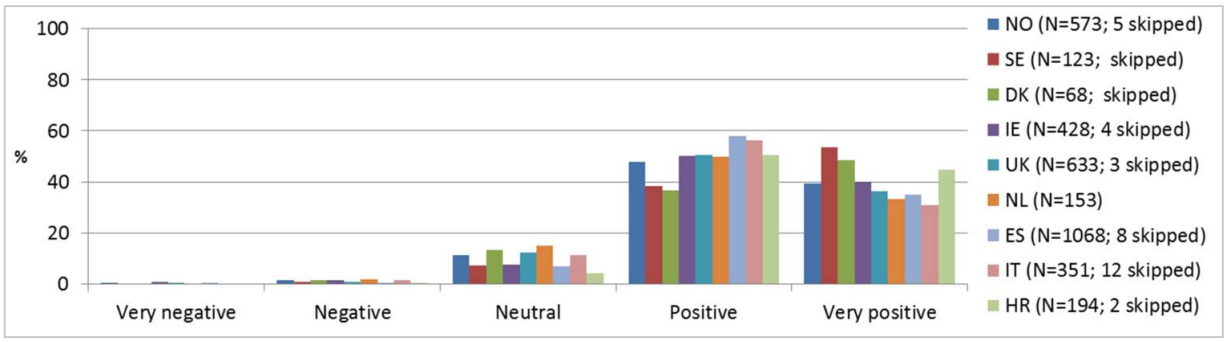


Figure 6.6.3.6. National clinical guidelines. p <0.001 (Kruskal-Wallis)

Table 6.6.3 Results of Q17: Below you can find some channels, which can be both in a hardcopy and electronic format. Independent of the format, how do you value each channel as a means by which to keep up to date on the safety of medicines?

Presented per profession. Scale from very negative (1) to very positive (5). Medians are presented (Q1; Q3). Q1 is the lower quartile and Q3 the upper quartile.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (Kruskal-Wallis)
Personalised letter	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	0.012
Medical journal	4 (4;4)	4 (4;4)	4 (4;4)	4 (4;4)	4 (4;4)	<0.001
Summary of Product Characteristics / Patient information leaflet	4 (3;4)	4 (3;4)	4 (4;5)	4 (4;4)	4 (3;4)	<0.001
Medicines reference book (e.g. BNF, BNFc)	4 (4;5)	4 (4;4)	4 (4;5)	4 (4;5)	4 (4;5)	<0.001
Newspaper	3 (2;3)	3 (2;3)	2 (2;3)	3 (2;3)	3 (2;3)	<0.001
National clinical guidelines	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	0.032

6.6.4 Q18: How do you value the following alternative channels to keep up to date on the safety of medicines?

Emails (Figure 6.6.4.1) and point-of-care alerts (Figure 6.6.4.4) were the preferred alternative electronic channels by which to be kept up to date on drug safety issues. Information provided during face-to-face meetings (in person) (Figure 6.6.4.8) also scored mostly positive or very positive. Websites (Figure 6.6.4.5) and mobile apps (Figure 6.6.4.7) were generally valued more neutrally. Social media (e.g. Twitter) (Figure 6.6.4.2), mobile phones (text messaging (Figure 6.6.4.3) or personal calls (Figure 6.6.4.9)), and television/radio (Figure 6.6.4.6) were all considered to be of negative value. Differences between professional groups were again marginal (but still significantly different); for example, GPs were slightly less negative regarding social media (Table 6.6.4).

No other important alternative channels were suggested.

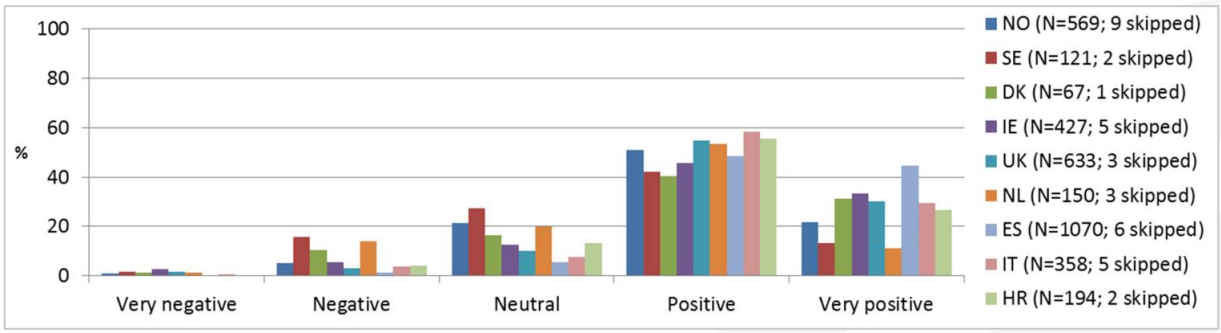


Figure 6.6.4.1. Email. p <0.001 (Kruskal-Wallis)

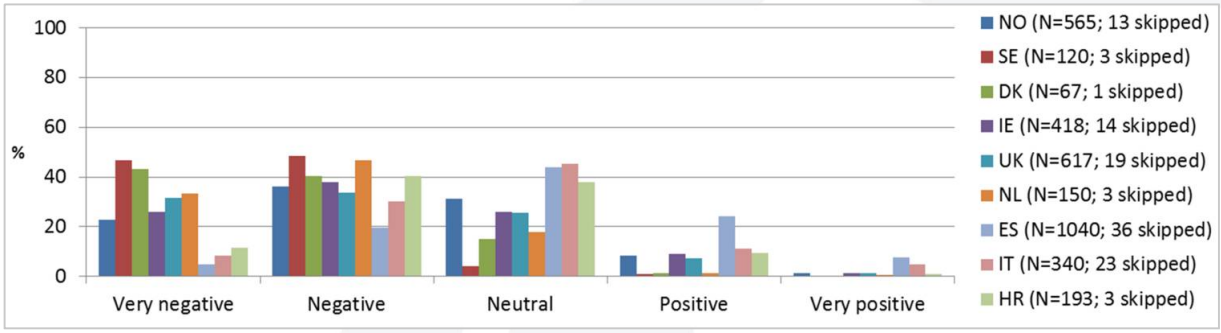


Figure 6.6.4.2. Social media (e.g. Twitter). p <0.001 (Kruskal-Wallis)

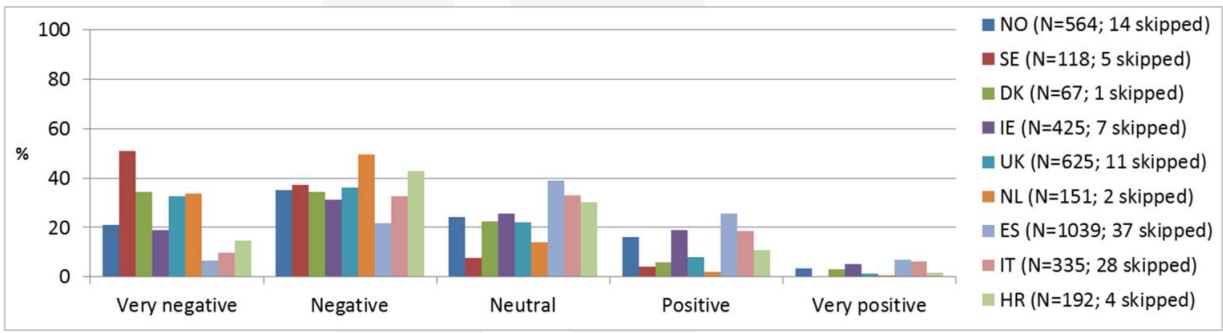


Figure 6.6.4.3. Mobile phone text (e.g. SMS). p <0.001 (Kruskal-Wallis)

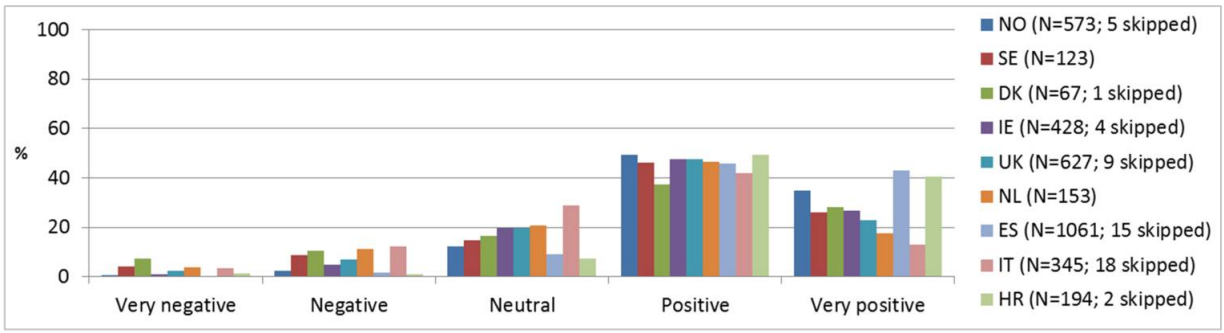


Figure 6.6.4.4. Point-of-care-alerts. p <0.001 (Kruskal-Wallis)

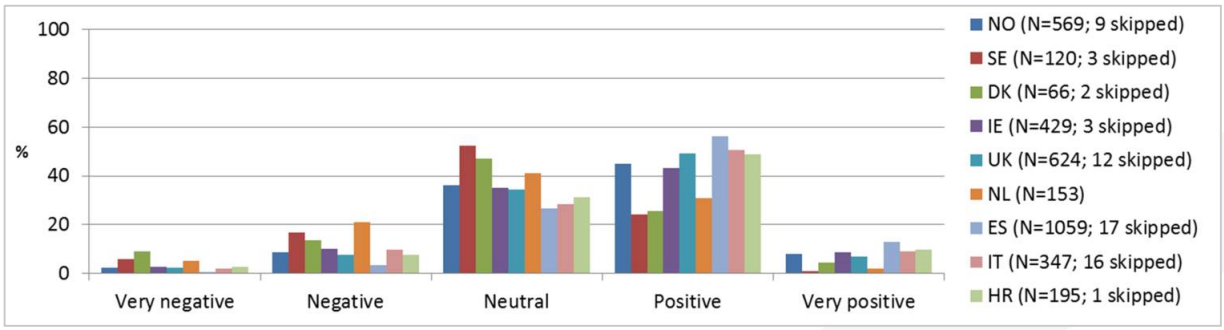


Figure 6.6.4.5. Website. p <0.001 (Kruskal-Wallis)

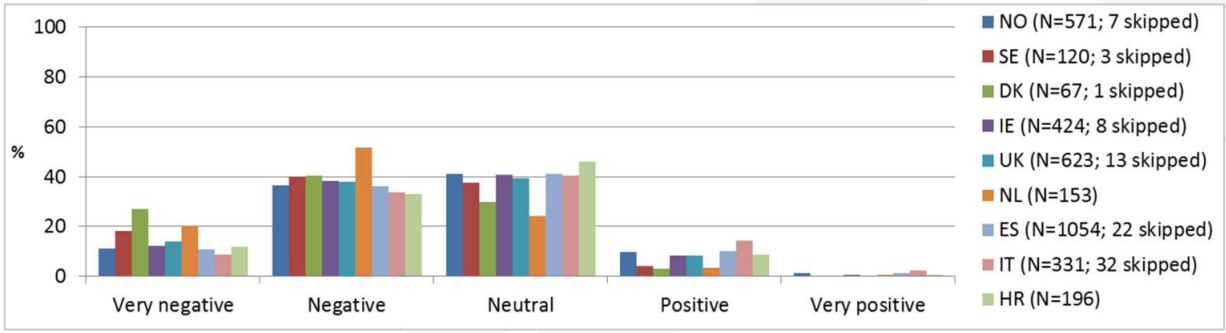


Figure 6.6.4.6. Television or radio. p <0.001 (Kruskal-Wallis)

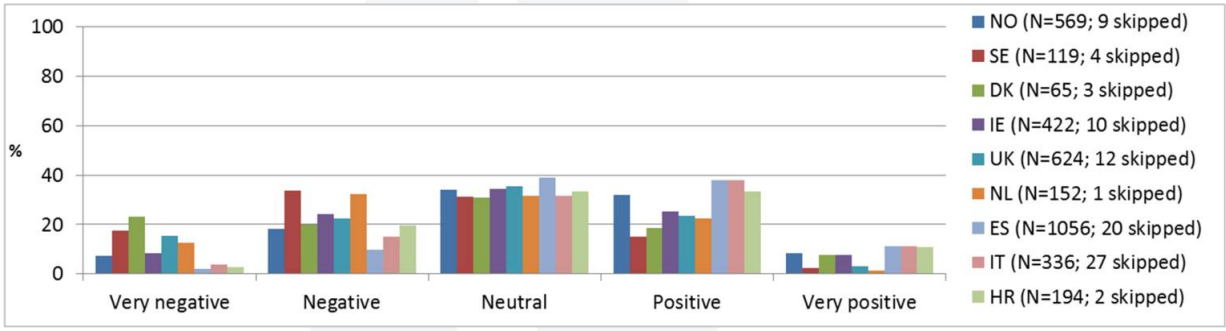


Figure 6.6.4.7. Mobile app. p <0.001 (Kruskal-Wallis)

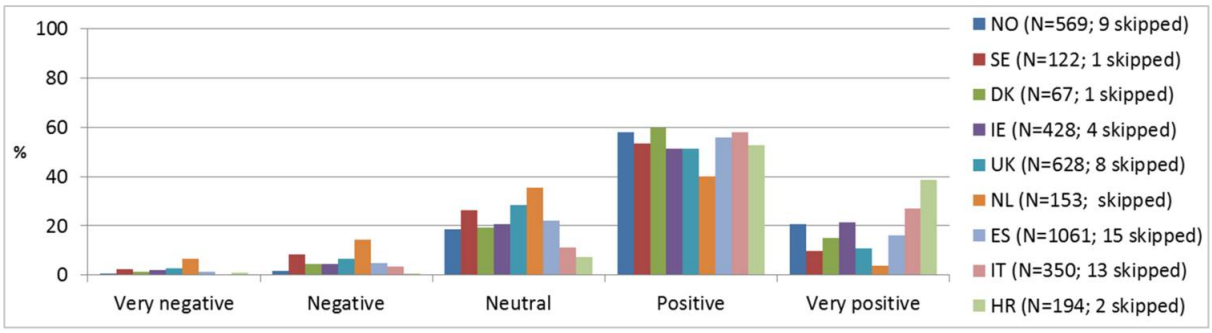


Figure 6.6.4.8. In person

(e.g. face-to-face meeting, course, medical congress or seminar). p <0.001 (Kruskal-Wallis)

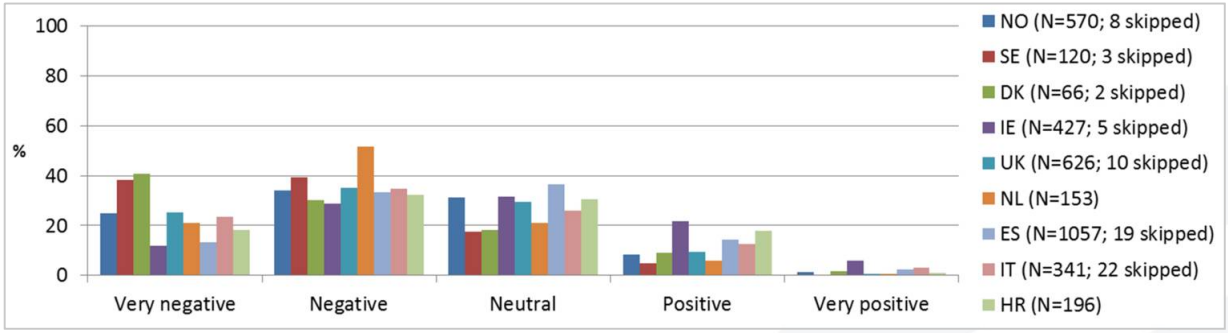


Figure 6.6.4.9. Phone call. p <0.001 (Kruskal-Wallis)

Table 6.6.4. Results of Q18. How do you value the following alternative channels to keep up to date on the safety of medicines?

Presented per profession. Scale from very negative (1) to very positive (5). Medians are presented (Q1; Q3). Q1 is the lower quartile and Q3 the upper quartile.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (Kruskal-Wallis)
Email	4 (4;5)	4 (4;4)	4 (4;5)	4 (4;5)	4 (4;5)	<0.001
Social media	3 (2;3)	2 (2;3)	2 (2;3)	2 (2;3)	2 (2;3)	<0.001
Mobile phone text	3 (2;3)	2 (2;3)	2 (2;3)	3 (2;3)	2 (2;3)	0.056
Point-of-care alerts	4 (4;5)	4 (3;4)	4 (4;5)	4 (4;5)	4 (4;5)	<0.001
Website	4 (3;4)	3 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	<0.001
Television or radio	2 (2;3)	2.5 (2;3)	3 (2;3)	3 (2;3)	3 (2;3)	0.0348
Mobile app	3 (2;4)	3 (2;4)	3 (2;4)	3 (3;4)	3 (2;4)	0.219
In person	4 (3;4)	4 (4;4)	4 (3;4)	4 (3;4)	4 (3;4)	0.009
Phone call	2 (2;3)	2 (1;3)	3 (2;3)	2 (2;3)	2 (2;3)	<0.001

6.6.5 Q19: In general, how often do you prefer to receive safety-related information?

Slightly less than half (45%) of all respondents prefer an immediate update of individual safety information, 26% suggested a weekly update and 25% a monthly update. A longer period was only preferred by a few respondents. Respondents from the NL, UK, SE and IE were more in favour of receiving less frequent safety updates (Figure 6.6.5). The differences between HCP groups were again small, but more cardiologists were satisfied with a less frequent update (Table 6.6.5).

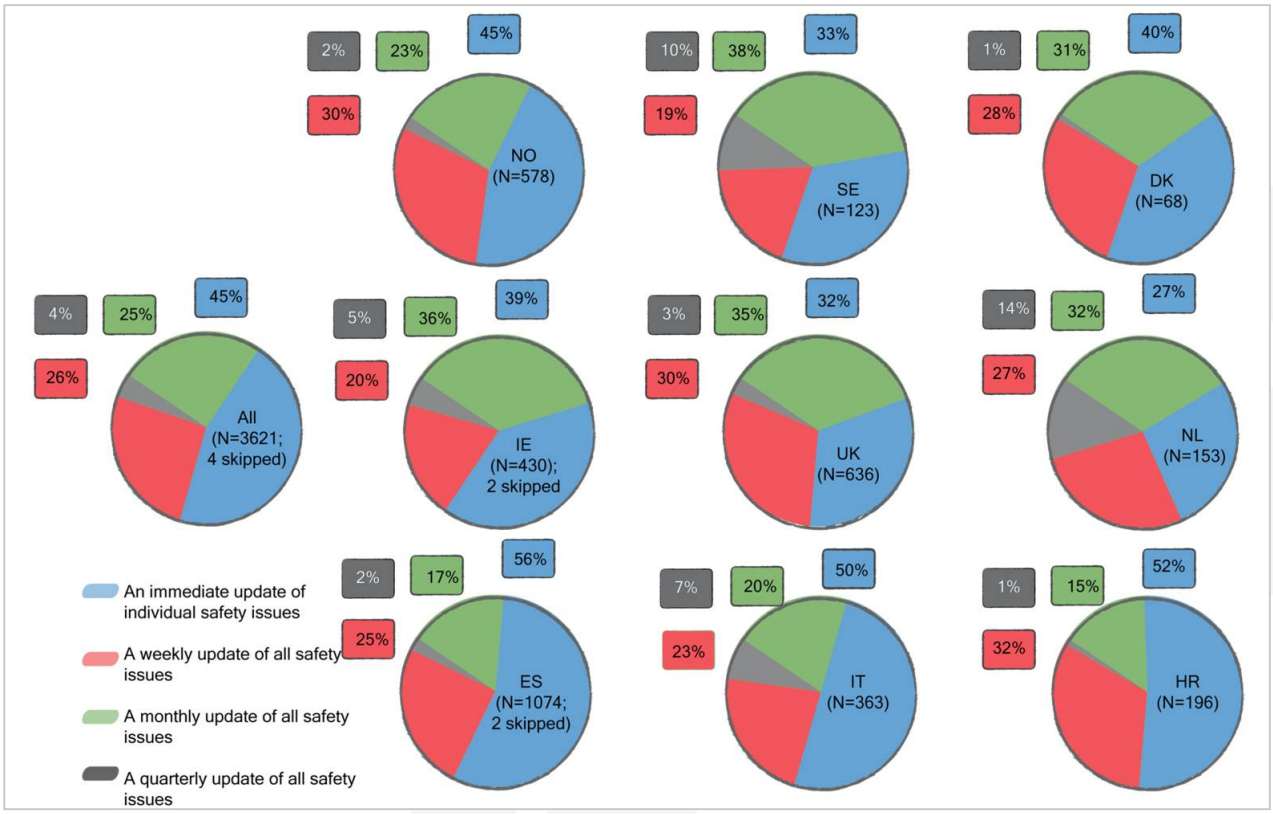


Figure 6.6.5. Results of Q19: In general, how often do you prefer to receive safety-related information?

Presented per country. P <0.001 χ^2-test

Table 6.6.5. Results of Q19: In general, how often do you prefer to receive safety-related information?

Presented per profession. p <0.001 (χ^2-test)

	GPs	Cardiologists	Pharmacists	Others	Total
An immediate update of individual safety issues	794 (45%)	90 (41%)	594 (46%)	146 (43%)	1624 (45%)
A weekly update of all safety issues	418 (24%)	43 (19%)	399 (31%)	89 (26%)	949 (26%)
A monthly update of all safety issues	461 (26%)	68 (31%)	288 (22%)	87 (26%)	904 (25%)
A quarterly update of all safety issues	91 (5%)	20 (9%)	18 (1%)	15 (4%)	144 (4%)
Total	1764 (100%)	221 (100%)	1299 (100%)	337 (100%)	3621 (100%)

6.6.6 Q20: Do you think it is useful when a safety message is repeated after a certain period of time?

The large majority (88%) of all respondents thought repeating a safety message was useful. Least convinced were Dutch, Swedish, Danish and UK respondents (Figure 6.6.6). A slightly larger proportion (13%) of cardiologists compared to other professionals saw no need for a repeated communication (Table 6.6.6).

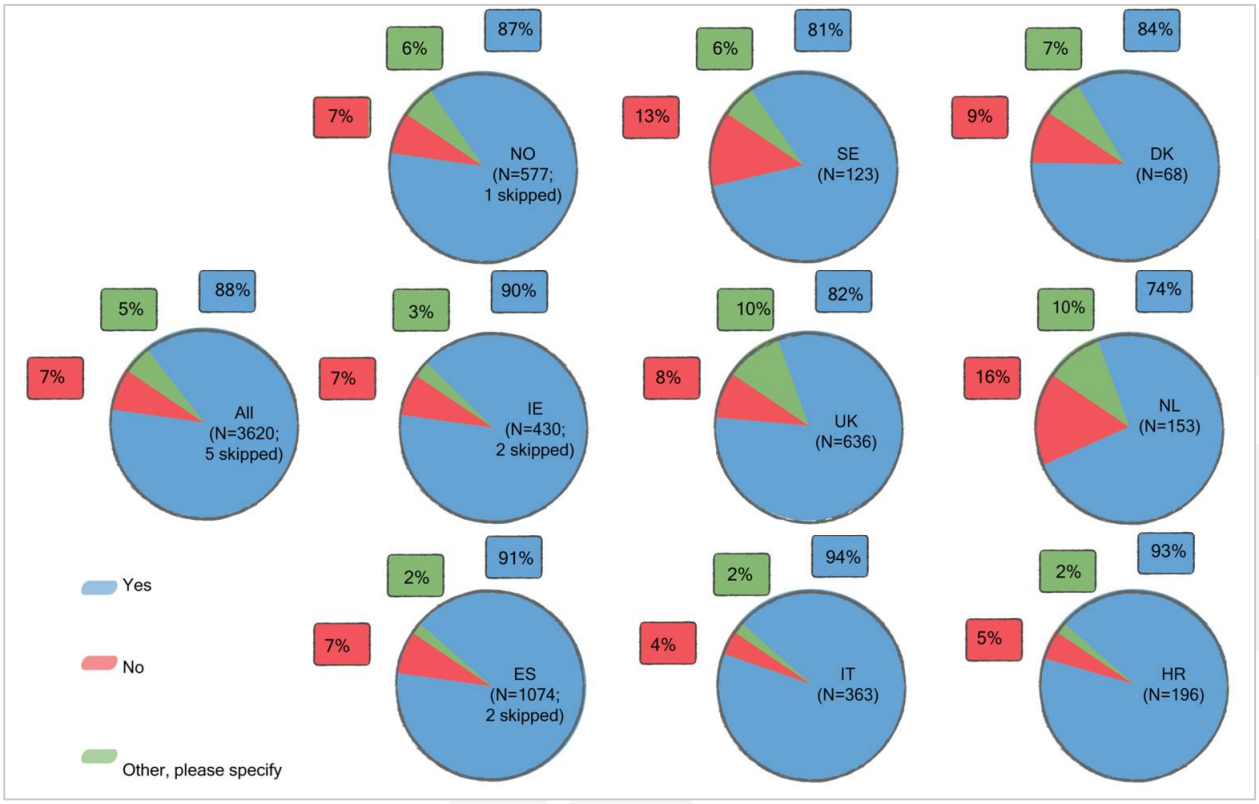


Figure 6.6.6. Results of Q20: Do you think it is useful when a safety message is repeated after a certain period of time?

Presented per country. $p < 0.001$ (χ^2--test)

Table 6.6.6. Results of Q20: Do you think it is useful when a safety message is repeated after a certain period of time?

Presented per profession. p <0.001 (χ^2--test)

	GPs	Cardiologists	Pharmacists	Others	Total
Yes	1565 (89%)	185 (83%)	1137 (88%)	291 (86%)	3178 (88%)
No	138 (8%)	29 (13%)	79 (6%)	22 (7%)	268 (7%)
Other, please specify	60 (3%)	8 (4%)	82 (6%)	24 (7%)	174 (5%)
Total	1763 (100%)	222 (100%)	1298 (100%)	337 (100%)	3620 (100%)

Open-ended answers to Q20 (n=163)

The responses received here were mostly positive regarding repeated messages, but suggested a repeat message was conditional on the fact that HCPs had not sufficiently changed their prescribing practice, if it was considered that earlier communications had not reached all target groups, and if the safety message was of sufficient clinical relevance (with regard to level of risk to the population). Some requested a better system where earlier messages could be retrieved. It was also suggested to send reminders at regular intervals.

6.6.7 Q21: In general, how much do you agree with the following statements? I only read the safety information if, …

The respondents agreed most strongly with the statements that the relevance of the safety information for their daily practice (Figure 6.6.7.6) and trust in the sender (Figure 6.6.7.2) determined if they read the safety communication. Layout, in particular, seemed to be less relevant (Figure 6.6.7.3). The other statements showed a more mixed response (Figure 6.6.7.1, Figure 6.6.7.4, Figure 6.6.7.5, Figure 6.6.7.7). There were small, but statistically significant, differences between professionals (Table 6.6.7).

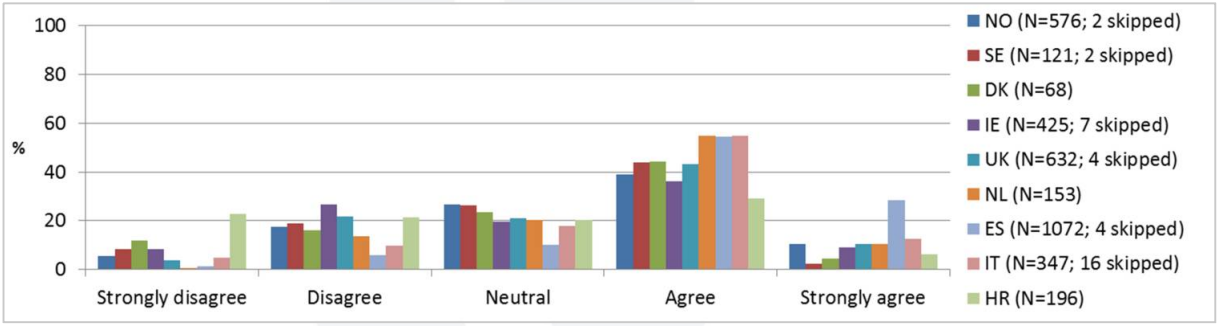


Figure 6.6.7.1. I like the channel through which the information is sent (e.g. email, hardcopy letter). p <0.001 (Kruskal-Wallis)

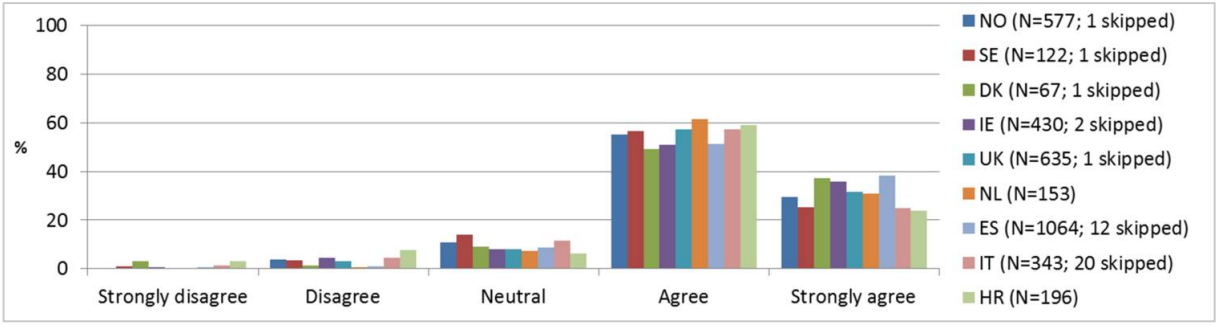


Figure 6.6.7.2. I trust the sender of the safety message. p <0.001 (Kruskal-Wallis)

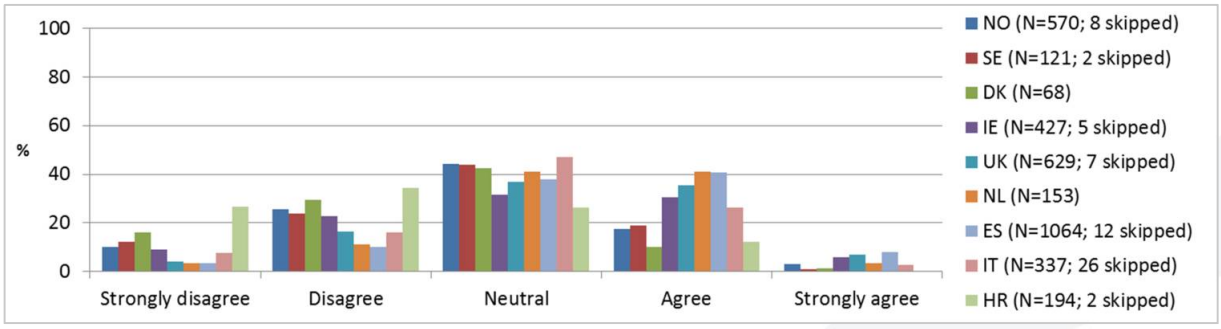


Figure 6.6.7.3. I like the layout of the document. p <0.001 (Kruskal-Wallis)

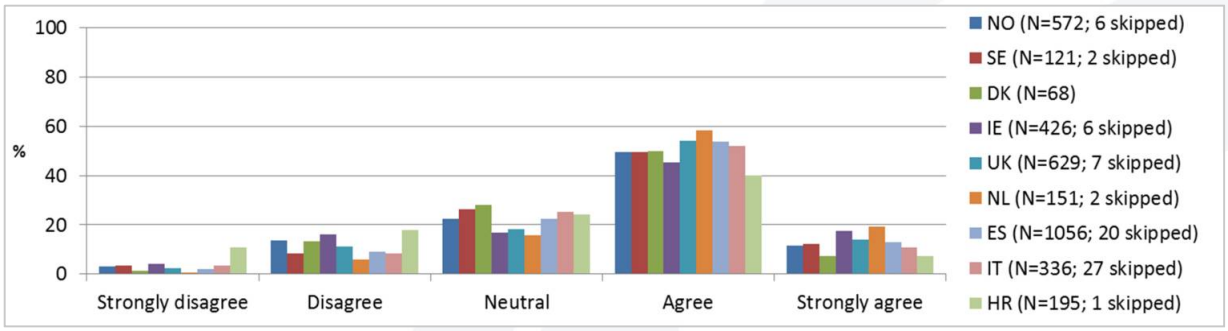


Figure 6.6.7.4. The document is not too lengthy. p <0.001 (Kruskal-Wallis)

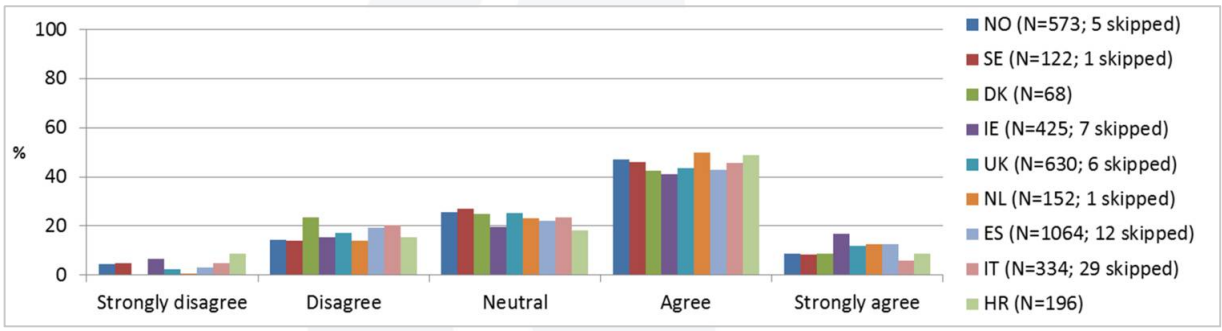


Figure 6.6.7.5. I have enough time to read the information. p =0.093 (Kruskal-Wallis)

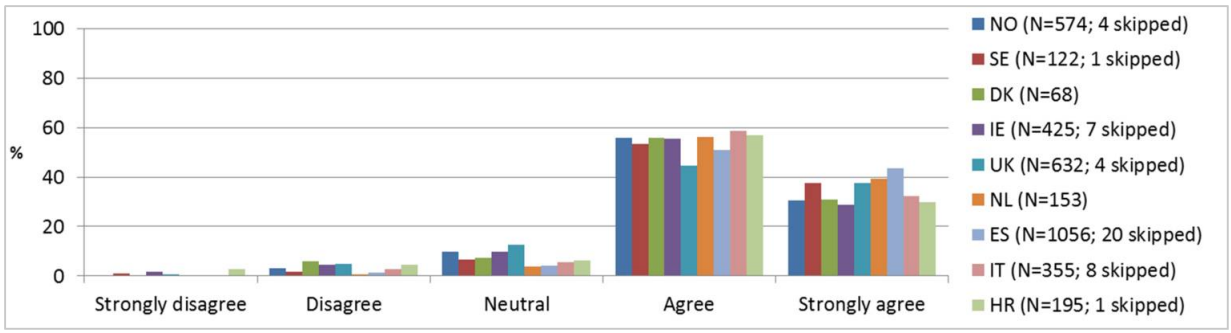


Figure 6.6.7.6. The safety information is relevant for my daily practice. p <0.001 (Kruskal-Wallis)

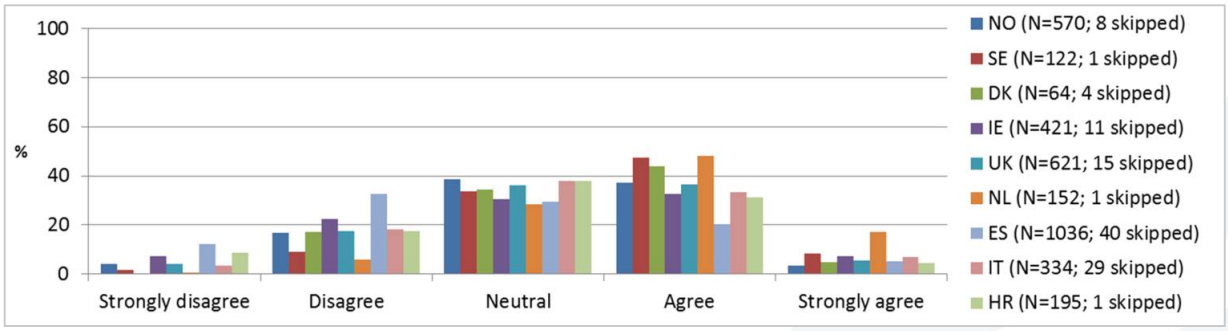


Figure 6.6.7.7. I do not receive a new safety message too often. p <0.001 (Kruskal-Wallis)

Table 6.6.7. Results of Q21: In general, how much do you agree with the following statements? I only read the safety information if…

Presented per profession. Scale from strongly disagree (1) to strongly agree (5). Medians are presented (Q1; Q3). Q1 is the lower quartile and Q3 the upper quartile.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (Kruskal-Wallis)
I like the channel through which the information is sent	4 (3;4)	4 (3;4)	3 (2;4)	4 (3;4)	4 (3;4)	<0.001
I trust the sender of the safety message	4 (4;5)	4 (4;4)	4 (4;5)	4 (4;5)	4 (4;5)	0.003
I like the layout…	3 (3;4)	3 (3;4)	3 (2;4)	3 (3;4)	3 (2;4)	<0.001
The document is not too lengthy – median	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	<0.001
I have enough time to read the information	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	<0.001
The safety information is relevant for my daily practice	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	<0.001
I do not receive a new safety messages too often	3 (2;4)	3 (3;4)	3 (2;4)	3 (2;4)	3 (2;4)	0.002

Open-ended answers to Q21

A large number of Irish respondents flagged that a summary box or key messages section outlining the key safety messages is desirable. No other important factors were volunteered.

6.6.8 Q22: In general, how much do you agree with the following statements about safety information? I only take action in response to a safety warning if, …

Respondents indicated that severity/reversibility of the risk (Figure 6.6.8.1), relevance to their practice (Figure 6.6.8.10), and trust in the sender (Figure 6.6.8.2) were the factors most likely to influence whether action was taken. These statements were considered more important than whether the recommendation was clear (Figure 6.6.8.8), sufficient background information was provided (Figure 6.6.8.3), the message was incorporated into clinical or professional society guidelines (Figure 6.6.8.6) and the recommendations could be easily implemented (Figure 6.6.8.9). Least important was that HCPs themselves (Figure 6.6.8.4), or their colleagues (Figure 6.6.8.5), agreed with the safety recommendations and where patients were requesting an action based on information he/she had found (Figure 6.6.8.7).

Therefore, trust in the sender remains an important determinant of taking action, which is considered as important as the severity of the ADR, and more important than agreeing with the recommendation. Obviously, the action here is only an intended action and it is impossible to ascertain in this survey if this translates into a real change in behaviour. The differences (all p <0.001) between countries were quite modest for most questions, except for the response to the question on the severity of the safety issue. Spanish and, to a lesser extent, Norwegian and Dutch HCPs indicated that they were more likely (strongly agree) to take action if the ADR was more severe or caused irreversible harm.

The differences between HCPs were statistically significant (all p <0.001), with the only notable difference being that, in more cases, GPs indicated that the severity of the ADR determined their action (Table 6.6.8).

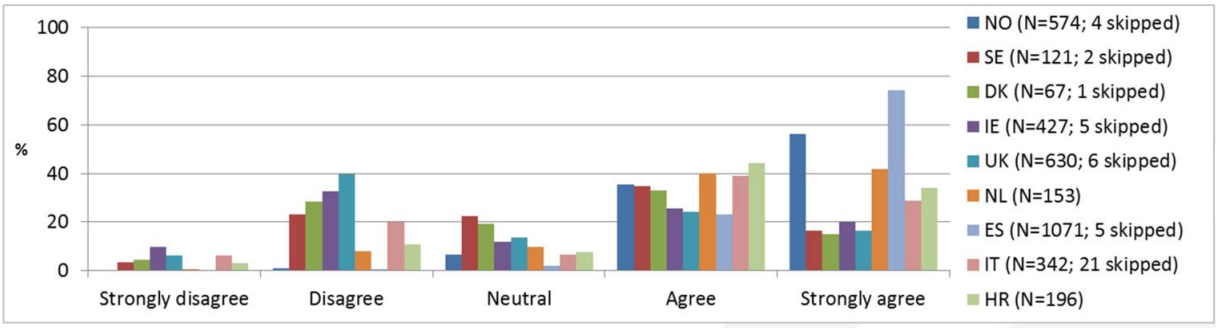


Figure 6.6.8.1. The adverse drug reaction is severe or causes irreversible harm. p <0.001 (Kruskal-Wallis)

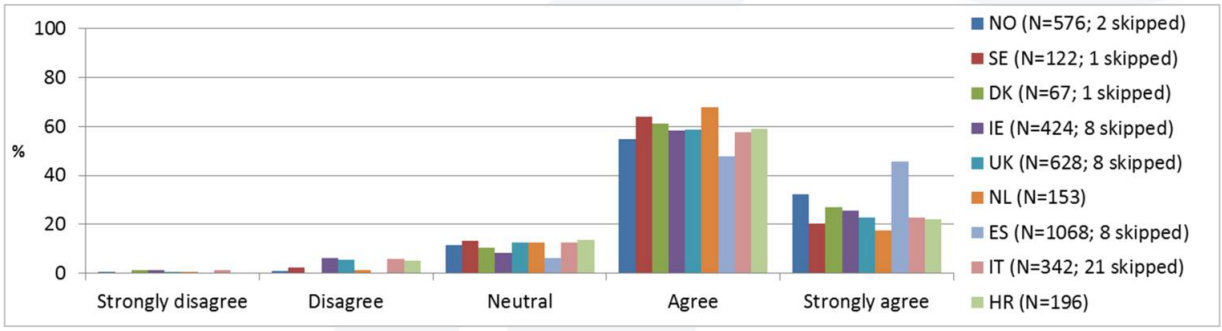


Figure 6.6.8.2. I trust the sender of the safety message. p <0.001 (Kruskal-Wallis)

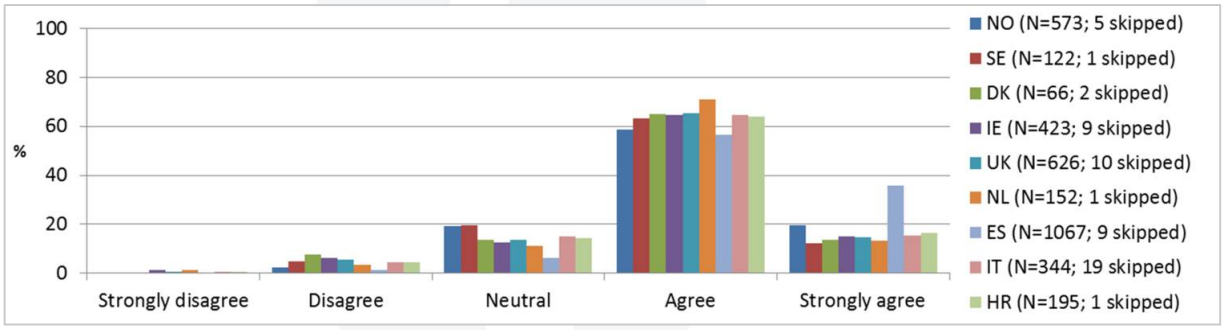


Figure 6.6.8.3. I receive sufficient background information on the basis for the safety message. p <0.001 (Kruskal-Wallis)

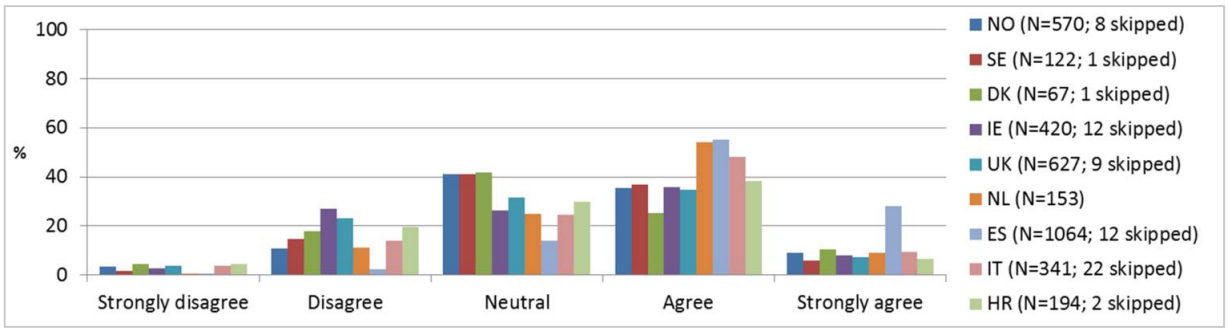


Figure 6.6.8.4. I agree with the recommendation in the safety information. p <0.001 (Kruskal-Wallis)

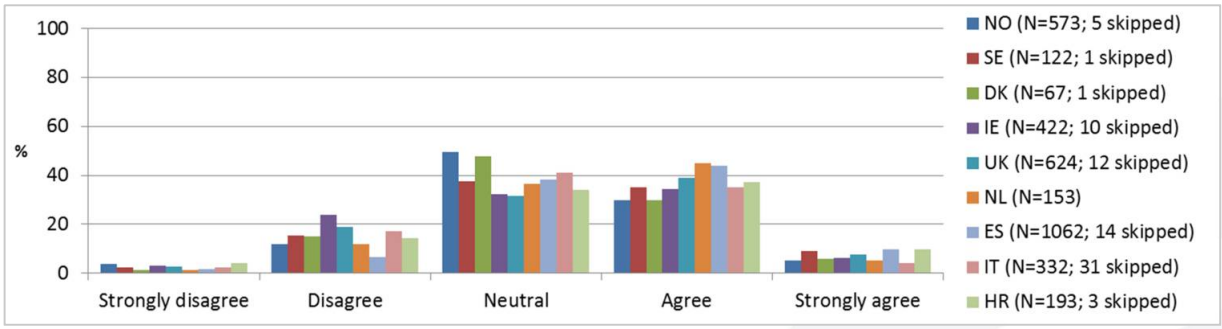


Figure 6.6.8.5. My colleagues or multidisciplinary team agree with the safety message. p <0.001 (Kruskal-Wallis)

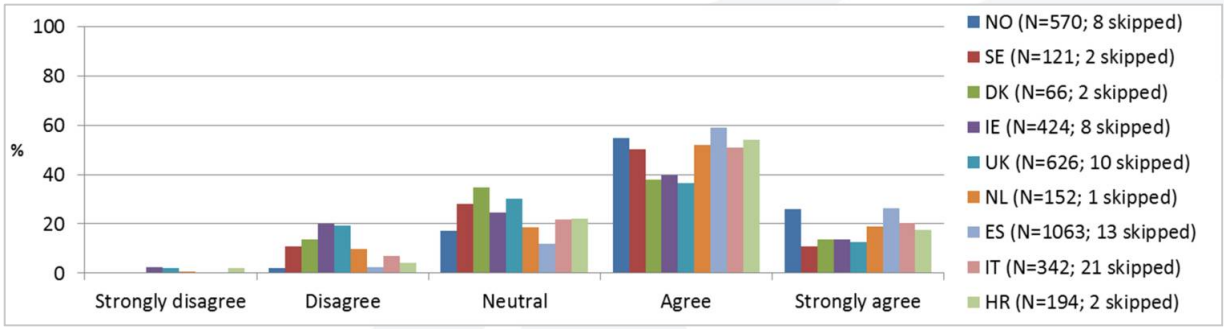


Figure 6.6.8.6. The message is incorporated in clinical or professional society guidelines. p <0.001 (Kruskal-Wallis)

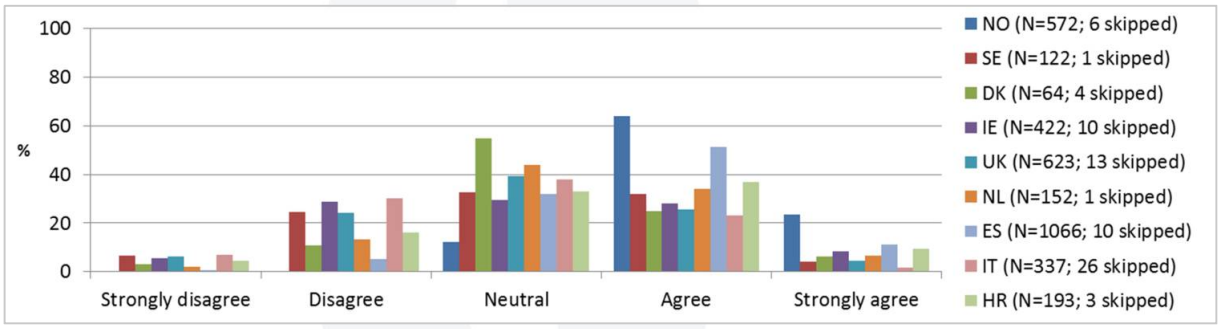


Figure 6.6.8.7. A patient requests an action in response to safety information she/he has found. p <0.001 (Kruskal-Wallis)

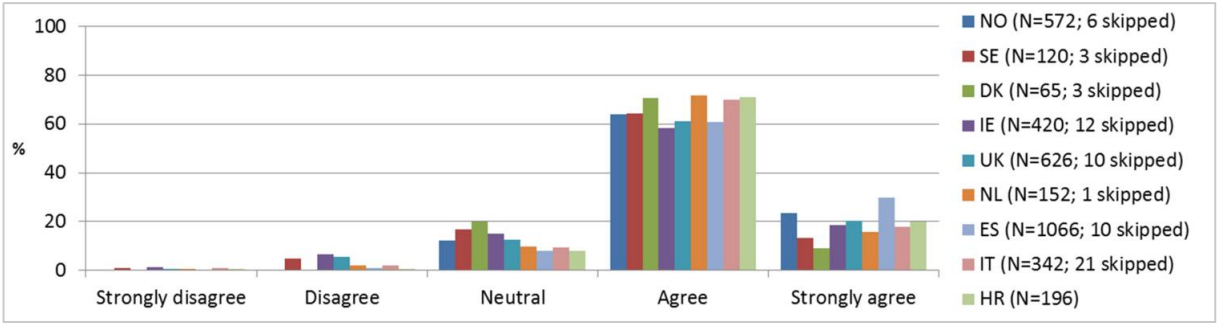


Figure 6.6.8.8. Recommendations are clear. p <0.001 (Kruskal-Wallis)

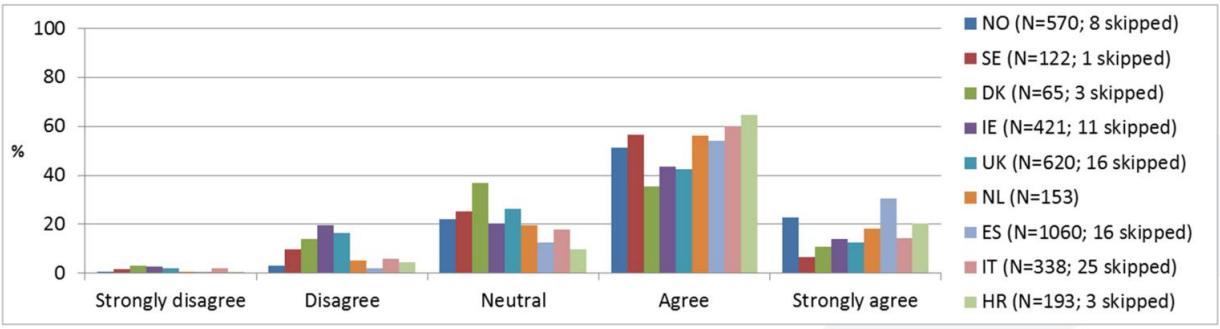


Figure 6.6.8.9. A recommendation can easily be implemented in routine daily practice. p <0.001 (Kruskal-Wallis)

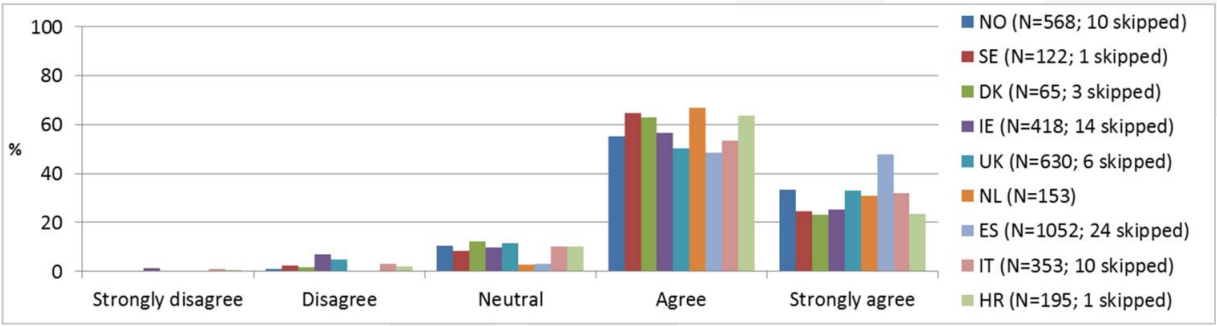


Figure 6.6.8.10. The safety information is relevant for my daily practice. p <0.001 (Kruskal-Wallis)

Table 6.6.8. Results of Q22: In general, to what extent do you agree with the following statements about safety information? I only take action in response to a safety warning if…

Presented per profession. Scale from strongly disagree (1) to strongly agree (5). Medians are presented (Q1; Q3). Q1 is the lower quartile and Q3 the upper quartile.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (Kruskal-Wallis)
The adverse drug reaction is severe or causes irreversible harm	5 (4;5)	4 (4;5)	4 (2;5)	5 (4;5)	4 (3;5)	<0.001
I trust the sender of the safety message	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	<0.001
I receive sufficient background information on the basis for the safety message	4 (4;5)	4 (4;4)	4 (4;4)	4 (4;5)	4 (4;4)	<0.001
I agree with the recommendation in the safety information	4 (3;4)	4 (3;4)	3 (2;4)	4 (3;4)	4 (3;4)	<0.001
My colleagues or multidisciplinary team agree with the safety message	4 (3;4)	3.5 (3;4)	3 (3;4)	3 (3;4)	3 (3;4)	<0.001
The message is incorporated in clinical or professional society guidelines	4 (4;4)	4 (4;4)	4 (3;4)	4 (4;5)	4 (3;4)	<0.001
A patient requests an action in response to safety information she/he has found	4 (3;4)	3 (2;4)	3 (2;4)	3 (3;4)	3 (3;4)	<0.001
Recommendations are clear	4 (4;4)	4 (4;4)	4 (4;4)	4 (4;4)	4 (4;4)	<0.001
A recommendation can easily be implemented in routine daily practice	4 (4;4)	4 (3;4)	4 (3;4)	4 (3;4)	4 (3;4)	<0.001
The safety information is relevant for my daily practice	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	4 (4;5)	<0.001

Open-ended answers to Q22 (n=63)

A few respondents highlighted other factors that affected them when deciding whether to take action in response to a safety warning. A few also mentioned that this question was not well phrased, which possibly resulted in some confusion about what was being asked.

6.6.9 Q23: Are you aware of updates to the safety profiles of the following medicines? If yes, how did you hear about them?

In this section respondents were asked if they were aware of four specific recent safety issues concerning: combined hormonal contraceptives (CHCs), diclofenac, valproate and ivabradine. If the respondents were aware, they were asked to indicate how they had heard about this drug safety issue. Multiple answers were possible.

Of note, an answer option that was only included in NO was: *"Yes, via SLV (Statens legemiddelverk; Norwegian Medicines Agency)"*. In the analyses, this option is included in the "other" category. This specific information is presented only in the annex with country-specific information for NO.

The safety concerns with the use of diclofenac were best known (overall, only 9% were unaware of the issue), followed by the CHCs (16% unaware), valproate (27% unaware) and ivabradine (34% unaware).

6.6.9.1 Combined Hormonal Contraceptives (CHCs)

Overall, only 16% of respondents were not aware of the recent safety update of CHCs (Figure 6.6.9.1). Respondents had heard of the drug safety issue through many different channels that were more or less equally mentioned as the most important source of information. In some countries, however, certain channels were more dominant. In a number of countries the most important channels were the 'official channels': DK: DHPC and newsletter, ES: DHPC and specific (single topic) newsletter, IE and IT: the DHPC, and HR: DHPC, website, and educational materials. The NL was different, with most HCPs having mentioned professional bodies and medical journals as the most important sources. Almost 40% of Swedish HCPs were not aware of the recent update on the venous thromboembolism (VTE) risk of CHCs. Cardiologists (37%) were much less aware than GPs (12%) and pharmacists (11%) of this safety issue ($p < 0.001$) (Table 6.6.9.1).

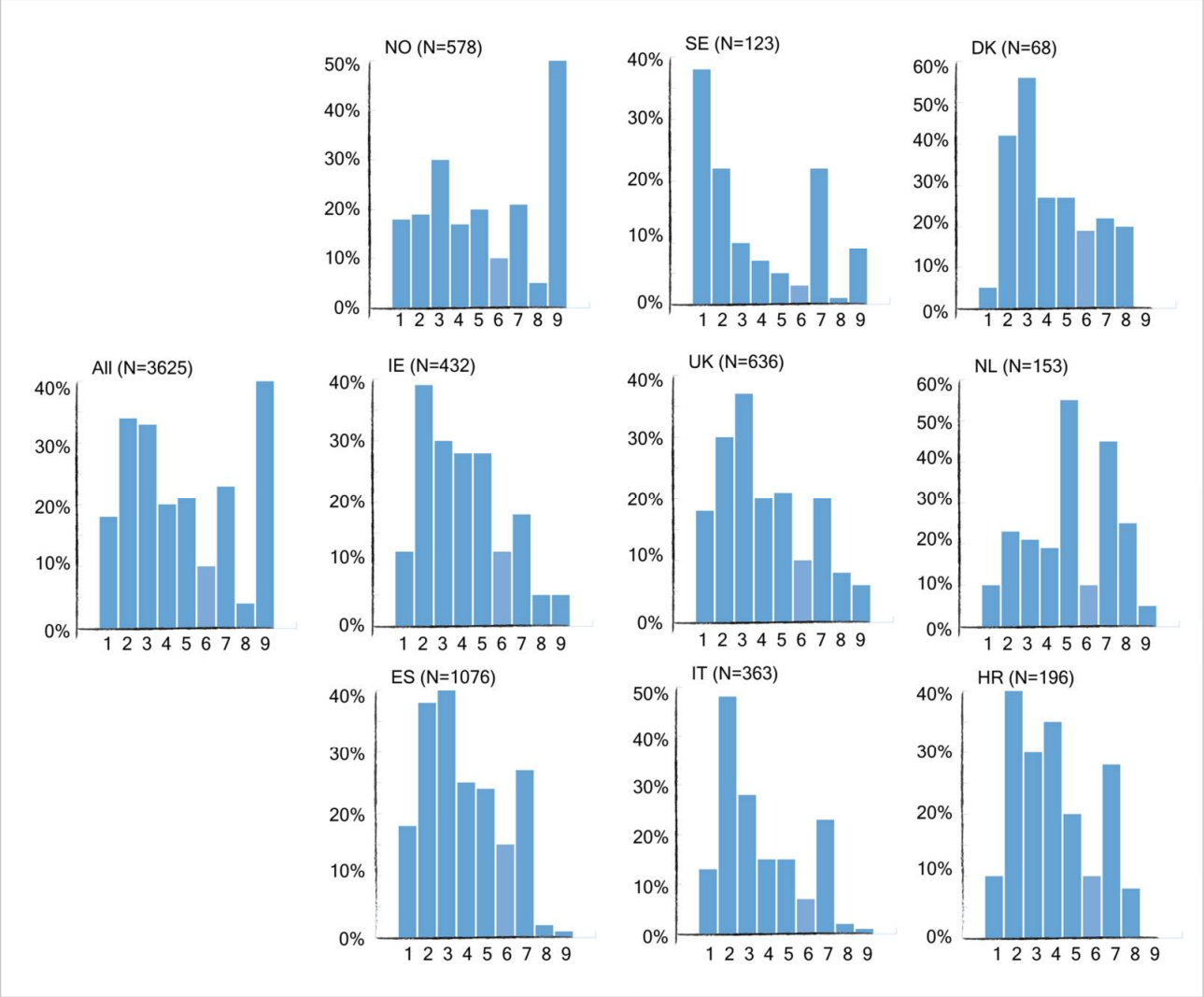


Figure 6.6.9.1. Are you aware of updates to the safety profiles of Combined Hormonal Contraceptives (update on the risk of venous thromboembolism)?

Presented per country

	p-value (χ^2-test)
1. No	<0.001
2. Yes, via DHPC	<0.001
3. Yes, via website or newsletter	<0.001
4. Yes, via educational materials	<0.001
5. Yes, via professional body	<0.001
6. Yes, via a colleague	<0.001
7. Yes, via medical journal	<0.001
8. Yes, via lay media (newspaper/television)	<0.001
9. Other, please specify*	<0.001

*For Norway this includes the option 'Yes, via SLV (Statens legemiddelverk; Norwegian Medicines Agency'

Table 6.6.9.1. Results of Q23: Are you aware of updates to the safety profiles of the following medicines? If yes, how did you hear about them?

Combined Hormonal Contraceptives – update on the risk of venous thromboembolism
Presented per profession.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (2-test)
1. No	219 (12%)	86 (39%)	141 (11%)	125 (37%)	571 (16%)	<0.001
2. Yes, via DHPC	667 (38%)	40 (18%)	430 (33%)	70 (21%)	1207 (33%)	<0.001
3. Yes, via website or newsletter	588 (33%)	25 (11%)	473 (36%)	66 (20%)	1152 (32%)	<0.001
4. Yes, via educational materials	414 (23%)	20 (9%)	261 (20%)	39 (12%)	734 (20%)	<0.001
5. Yes, via professional body	413 (23%)	25 (11%)	293 (23%)	33 (10%)	764 (21%)	<0.001
6. Yes, via a colleague	225 (13%)	10 (5%)	113 (9%)	33 (10%)	381 (11%)	<0.001
7. Yes, via medical journal	473 (27%)	63 (28%)	210 (16%)	50 (15%)	796 (22%)	<0.001
8. Yes, via lay media (newspaper/television)	77 (4%)	8 (4%)	80 (6%)	12 (4%)	177 (5%)	0.055
9. Other, please specify	44 (2%)	3 (1%)	48 (4%)	12 (4%)	107 (3%)	0.102

6.6.9.2 Diclofenac

With only 9% of respondents being unaware of the safety issue related to diclofenac, this was the best known drug safety problem in our survey (Figure 6.6.9.2). Across all countries the issue was again best known through the 'official' channels of DHPC, NCA websites or newsletters, except for the NL, where professional bodies and medical journals were the most often mentioned channels of information. None of the countries had distinctly different levels of knowledge; GPs were most aware (4% unaware), then pharmacists (10% unaware) and finally cardiologists (21% unaware) and 'other HCPs' (22%) (Table 6.6.9.2).

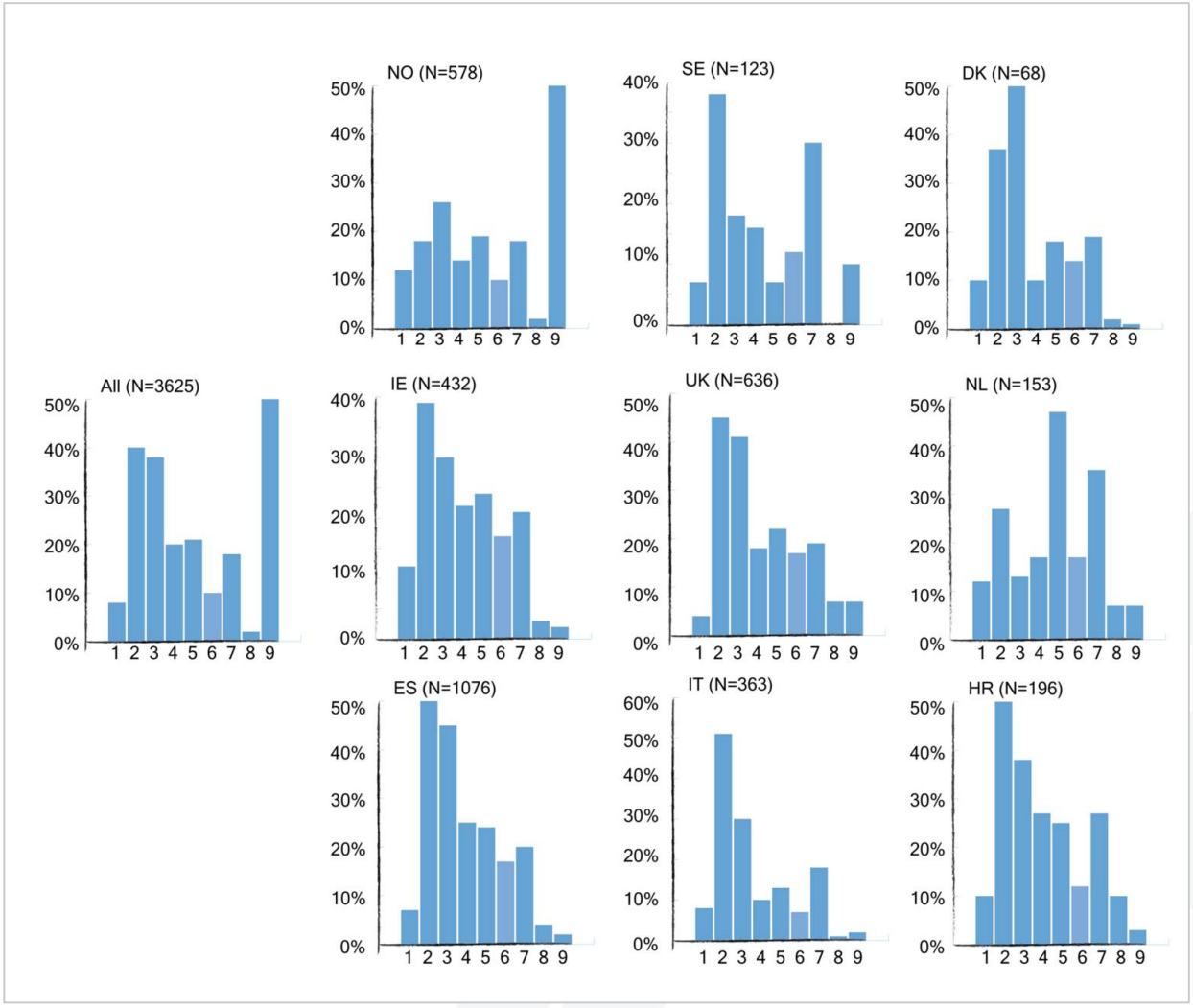


Figure 6.6.9.2. Are you aware of updates to the safety profiles of Diclofenac – new cardiovascular precautions?

Presented per country

	p-value (χ^2-test)
1. No	<0.001
2. Yes, via DHPC	<0.001
3. Yes, via website or newsletter	<0.001
4. Yes, via educational materials	<0.001
5. Yes, via professional body	<0.001
6. Yes, via a colleague	<0.001
7. Yes, via medical journal	<0.001
8. Yes, via lay media (newspaper/television)	<0.001
9. Other, please specify*	<0.001

*For Norway this includes the option 'Yes, via SLV (Statens legemiddelverk; Norwegian Medicines Agency'

Table 6.6.9.2. Results of Q23: Are you aware of updates to the safety profiles of the following medicines? If yes, how did you hear about them?

Diclofenac – new cardiovascular precautions. Presented per profession.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (χ^2-test)
1. No	78 (4%)	47 (21%)	124 (10%)	75 (22%)	324 (9%)	<0.001
2. Yes, via DHPC	846 (48%)	66 (30%)	449 (35%)	109 (32%)	1470 (41%)	<0.001
3. Yes, via website or newsletter	641 (36%)	45 (20%)	526 (40%)	89 (26%)	1301 (36%)	<0.001
4. Yes, via educational materials	394 (22%)	23 (10%)	214 (16%)	44 (13%)	675 (19%)	<0.001
5. Yes, via professional body	397 (22%)	33 (15%)	323 (25%)	32 (10%)	785 (22%)	<0.001
6. Yes, via a colleague	253 (14%)	17 (8%)	157 (12%)	32 (10%)	459 (13%)	0.005
7. Yes, via medical journal	397 (22%)	59 (27%)	213 (16%)	44 (13%)	713 (20%)	<0.001
8. Yes, via lay media (newspaper/ television)	59 (3%)	11 (5%)	57 (4%)	12 (4%)	139 (4%)	0.383
9. Other, please specify	64 (4%)	5 (2%)	60 (5%)	10 (3%)	139 (4%)	0.207

6.6.9.3 Valproate

The safety concern with valproate was not known to approximately a quarter (27%) of all respondents (Figure 6.6.9.3). Notably, approximately half of the respondents from both the Scandinavian countries and the NL indicated that they were unaware of this particular safety issue. In Southern Europe, the UK and IE, the issue seemed best known, with the most important information channels cited again as the 'official' sources, including DHPC and websites/newsletters. Again cardiologists were least aware (65%) of this issue (Table 6.6.9.3).

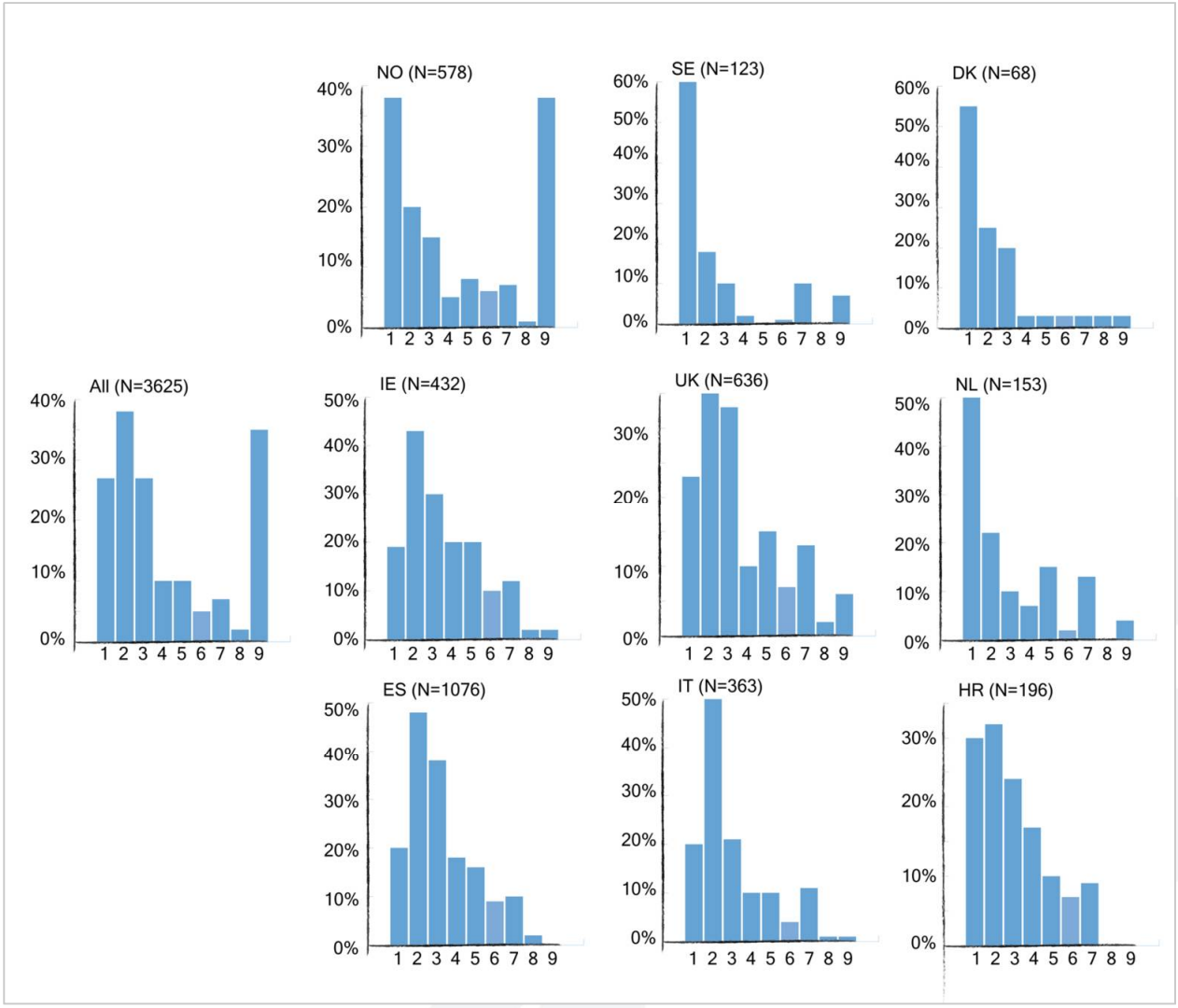


Figure 6.6.9.3. Are you aware of updates to the safety profile of Valproate (further restrictions for use in women and girls)?

Presented per country

	p-value (χ^2-test)
1. No	<0.001
2. Yes, via DHPC	<0.001
3. Yes, via website or newsletter	<0.001
4. Yes, via educational materials	<0.001
5. Yes, via professional body	<0.001
6. Yes, via a colleague	<0.001
7. Yes, via medical journal	0.245
8. Yes, via lay media (newspaper/television)	0.062
9. Other, please specify*	<0.001

*For Norway this includes the option 'Yes, via SLV (Statens legemiddelverk; Norwegian Medicines Agency'

Table 6.6.9.3. Results of Q23: Are you aware of updates to the safety profiles of the following medicines? If yes, how did you hear about them?

Valproate – further restrictions for use in women and girls. Presented per profession.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (χ^2-test)
1. No	445 (25%)	145 (65%)	283 (22%)	122 (36%)	995 (27%)	<0.001
2. Yes, via DHPC	759 (43%)	40 (18%)	465 (36%)	102 (30%)	1366 (38%)	<0.001
3. Yes, via website or newsletter	470 (27%)	21 (9%)	415 (32%)	81 (24%)	987 (27%)	<0.001
4. Yes, via educational materials	272 (15%)	7 (3%)	140 (11%)	30 (9%)	449 (12%)	<0.001
5. Yes, via professional body	191 (11%)	11 (5%)	216 (17%)	29 (9%)	447 (12%)	<0.001
6. Yes, via a colleague	104 (6%)	5 (2%)	87 (7%)	15 (4%)	211 (6%)	0.043
7. Yes, via medical journal	170 (10%)	11 (5%)	129 (10%)	22 (7%)	332 (9%)	0.031
8. Yes, via lay media (newspaper/ television)	20 (1%)	1 (0%)	16 (1%)	5 (1%)	42 (1%)	0.717
9. Other, please specify	29 (2%)	4 (2%)	41 (3%)	8 (2%)	82 (2%)	0.046

6.6.9.4 Ivabradine

Overall, 34% of respondents were unaware of this safety issue (Figure 6.6.9.4). The issue was least known in SE, DK, NL and HR, with more than 50% of HCPs being unaware. In countries where the issue was best known, the most referenced channels were the DHPC and web-site/newsletters, and in some countries (IE, UK, ES and IT) through educational materials. Cardiologists were most aware of this issue (9% unaware) (Table 6.6.9.4).

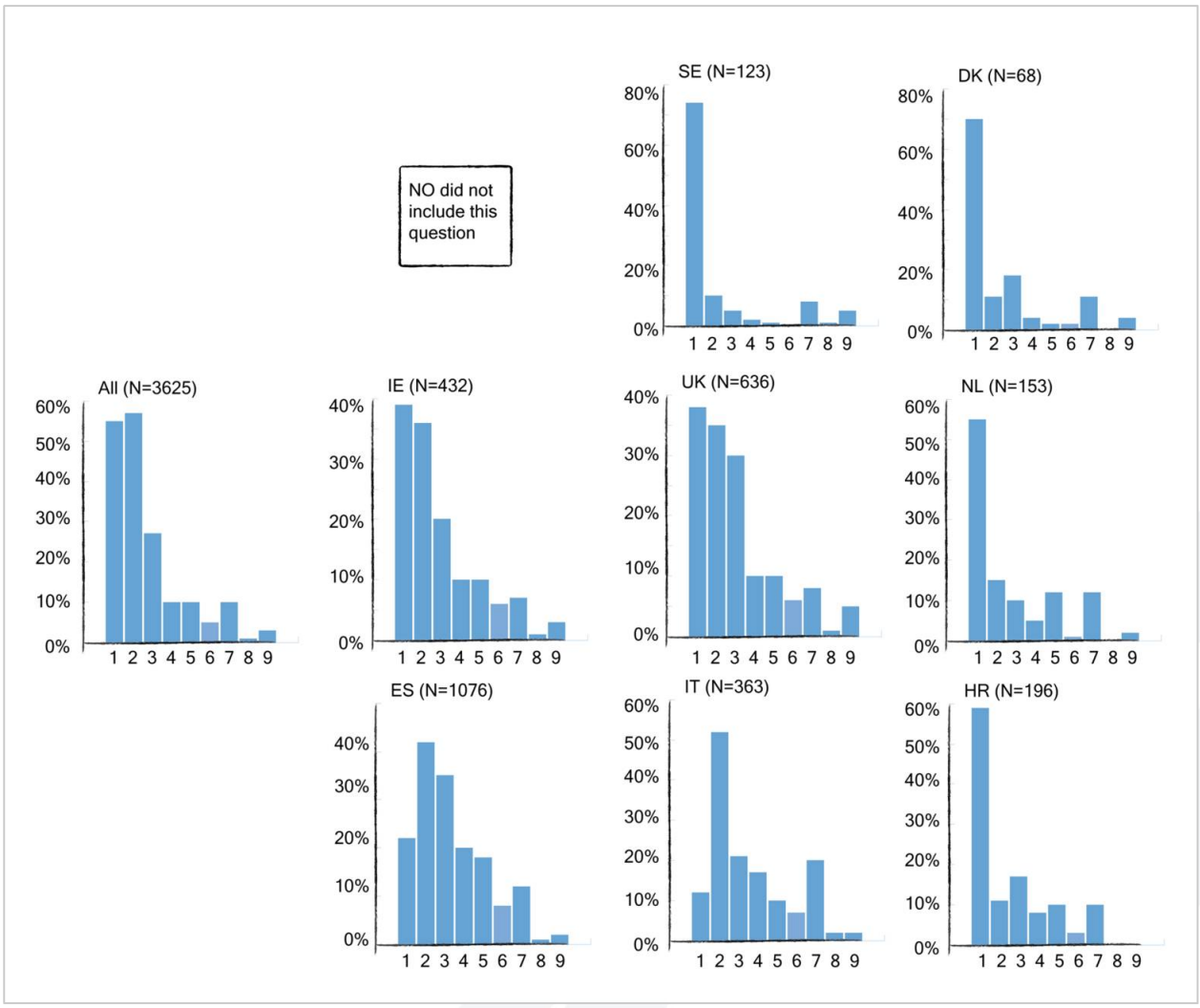


Figure 6.6.9.4. Are you aware of updates to the safety profile of ivabradine – the need to take additional measures to minimise the risk of cardiovascular events and severe bradycardia?

Presented per country

	p-value χ^2-(test)
1. No	<0.001
2. Yes, via DHPC	<0.001
3. Yes, via website or newsletter	<0.001
4. Yes, via educational materials	<0.001
5. Yes, via professional body	<0.001
6. Yes, via a colleague	0.001
7. Yes, via medical journal	<0.001
8. Yes, via lay media (newspaper/television)	0.468
9. Other, please specify*	<0.001

*For Norway this includes the option 'Yes, via SLV (Statens legemiddelverk; Norwegian Medicines Agency'

Table 6.6.9.4. Results of Q23: Are you aware of updates to the safety profiles of the following medicines? If yes, how did you hear about them?

Ivabradine – the need to take additional measures to minimise the risk of cardiovascular events and severe bradycardia Presented per profession.

	GPs	Cardiologists	Pharmacists	Others	Total	p-value χ^2-(test)
1. No	503 (30%)	16 (9%)	318 (35%)	189 (66%)	1026 (34%)	<0.001
2. Yes, via DHPC	642 (39%)	74 (41%)	299 (33%)	40 (14%)	1055 (35%)	<0.001
3. Yes, via website or newsletter	440 (26%)	34 (19%)	272 (30%)	33 (12%)	779 (26%)	<0.001
4. Yes, via educational materials	230 (14%)	45 (25%)	71 (8%)	13 (5%)	359 (12%)	<0.001
5. Yes, via professional body	184 (11%)	47 (26%)	98 (11%)	6 (2%)	335 (11%)	<0.001
6. Yes, via a colleague	87 (5%)	19 (10%)	49 (5%)	8 (3%)	163 (5%)	0.005
7. Yes, via medical journal	169 (10%)	69 (38%)	67 (7%)	7 (2%)	312 (10%)	<0.001
8. Yes, via lay media (newspaper/television)	11 (1%)	2 (1%)	1 (0%)	1 (0%)	15 (0%)	0.156
9. Other, please specify	31 (2%)	11 (6%)	26 (3%)	7 (2%)	75 (2%)	0.005

6.6.10 General comments

A total of 301 HCPs gave additional comments. These comments were in relation to additional communication channels, like social media (Twitter, radio, YouTube or a mobile app), although some expressed concerns around taking ownership for controlling the content. Local hospitals or universities could also be an acceptable source of information. Trust in the sender (not commercial), relevance to their area of clinical practice and point-of-care alerts were again highlighted as key requirements of tools for communicating safety information. Repetition could be acceptable for cases of high severity and where response to initial communication had been insufficient. A monthly update on information could be a sensible approach. Safety information should also be incorporated into text books and SmPCs (which is the case already). Keep the information short and realise that safety information also comes from other sources. In some countries, a more direct teaching role (e.g. MPA in SE) would be well received.

6.7 General survey questions

At the end of the questionnaire some general questions (Q24 to 29) were asked about the background of the professionals (see demographics Section 6.2). Two general questions are further described below: whether HCPs used an electronic prescribing or dispensing system (6.7.1) and how they kept their medicines knowledge up to date (6.7.2).

6.7.1 Q30: Do you use an electronic system to prescribe or dispense medicines?

Overall, 71% of the respondents used an electronic system, ranging from 93% in SE to 43% in the UK (Figure 6.7.1). GPs were the professional group who most commonly use electronic prescribing systems (Table 6.7.1).

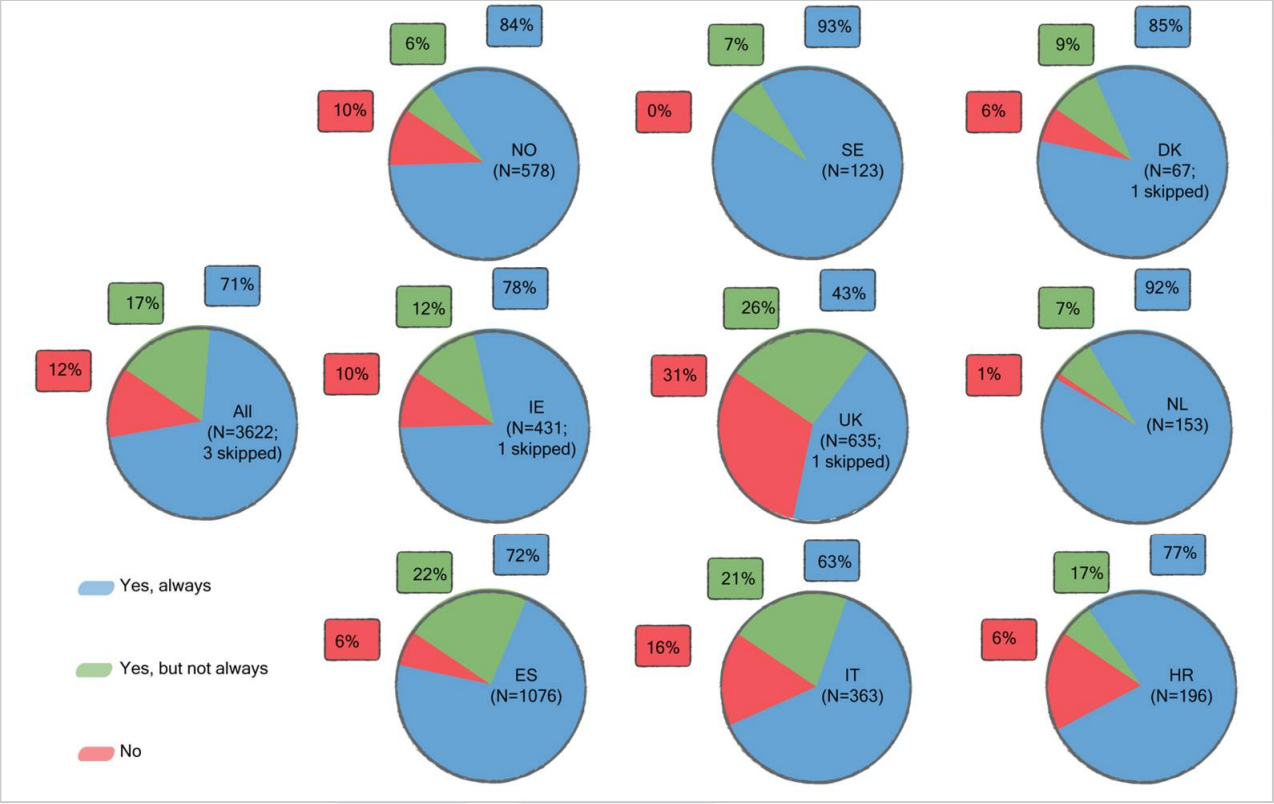


Figure 6.7.1. Results of Q30: Do you use an electronic system to prescribe or dispense medicines?

Presented per country. $p < 0.001$ (χ^2-test)

Table 6.7.1. Results of Q30: Do you use an electronic system to prescribe or dispense medicines? Presented per profession. p <0.001 (χ^2-test)

	GPs	Cardiologists	Pharmacists	Others	Total
Yes, always	1446 (82%)	94 (42%)	888 (68%)	145 (43%)	2573 (71%)
Yes, but not always	290 (16%)	70 (32%)	186 (14%)	73 (22%)	619 (17%)
No	30 (2%)	58 (26%)	223 (17%)	119 (35%)	430 (12%)
Total	1766 (100%)	222 (100%)	1297 (100%)	337 (100%)	3622 (100%)

6.7.2 Q31: How often do you use the following options to keep your medicines knowledge up to date?

In total, twelve options (thirteen in NO) were presented to the respondents on how they could keep themselves up to date with new medicines knowledge. The most favoured option was a medicines reference book, used on a daily basis (Figure 6.7.2.2). However, Italian HCPs indicated using it much less frequently (monthly or less). The SmPC (Figure 6.7.2.3), national clinical guidelines (Figure 6.7.2.4), medical journals (Figure 6.7.2.9), NCA website/newsletter (Figure 6.7.2.6) and international guidelines (Figure 6.7.2.5) were still, by a fair proportion, used on at least a weekly basis. However, approximately 40% of Dutch HCPs had never used the NCA website or (drug-specific) newsletter. In NO, the regional drug information centre (RELIS) was also used to a similar extent (Figure 6.7.2.13). There was little use of medicine advisory committees (Figure 6.7.2.8) or company representatives (although in IT, 50% of HCPs receive them on a weekly basis) (Figure 6.7.2.10), and the EMA website (Figure 6.7.2.7), mobile phone apps (Figure 6.7.2.11) and blogs (Figure 6.7.2.12) were rarely, if ever, referenced.

There were statistically significant differences among HCPs in how often they used the different options (Table 6.7.2). The use of a mobile app was the only option that did not significantly differ among HCPs. Pharmacists more often used a medicines reference book, SmPC and NCA website/newsletter, whereas GPs more often used national clinical guidelines and medicine advisory committees. International clinical guidelines and medical journals were more often used by cardiologists.

The UK did not include this question.

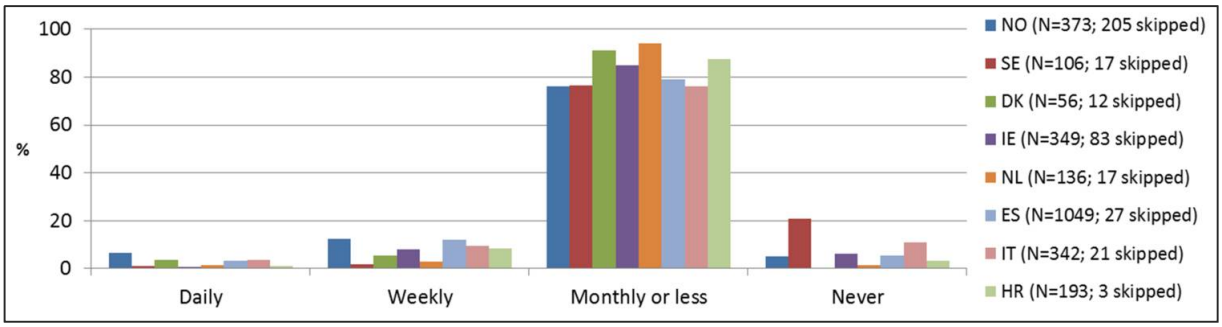


Figure 6.7.2.1. Training or courses, organised by e.g.: … p <0.001 (χ^2-test)

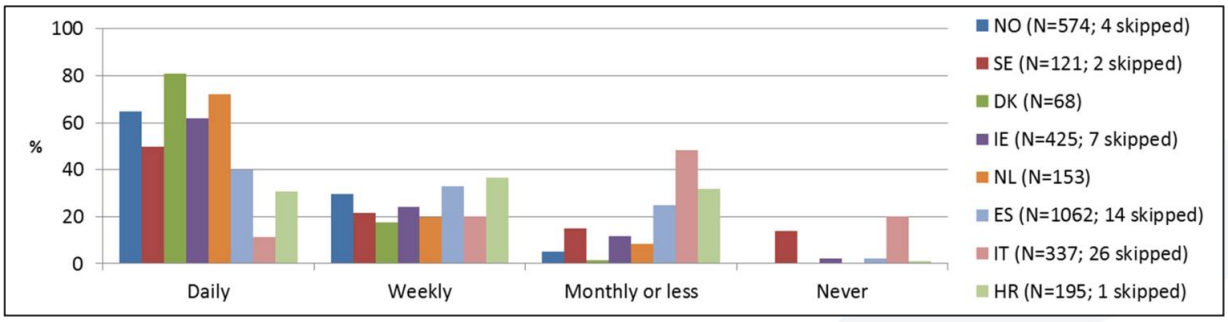


Figure 6.7.2.2. A medicines reference book. p <0.001 (χ^2-test)

Examples of reference books that were presented to the respondents are Farmakoterapijski priručnik (HR), Medicin.dk (DK), BNF, MIMS, Irish Medicines Formulary (IE), Guida all'uso dei farmaci, British Formulary (IT), Farmacotherapeutisch Kompas of Informatorium Medicamentorum (NL), Felleskatalogen, Legemiddelhåndboka (NO), Medimecum, Guía Terapéutica en Atención Primaria (Ed. semFYC) (ES), Fass (SE).

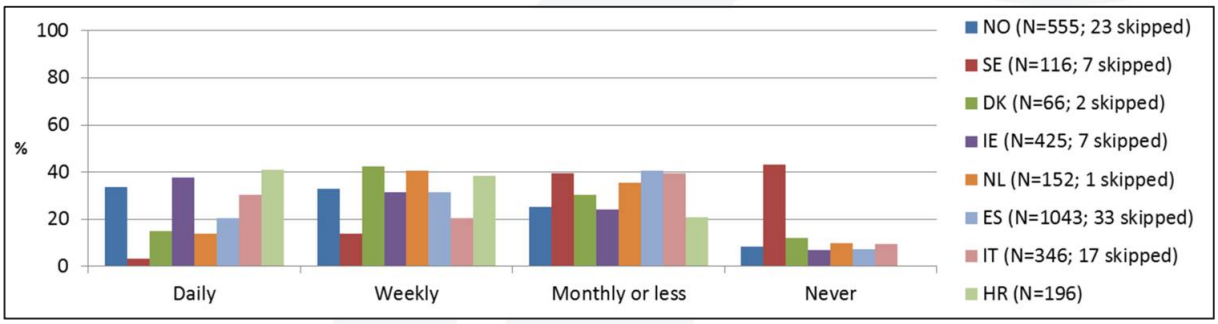


Figure 6.7.2.3. Summary of Product Characteristics/Patient information leaflets. p <0.001 (χ^2-test)

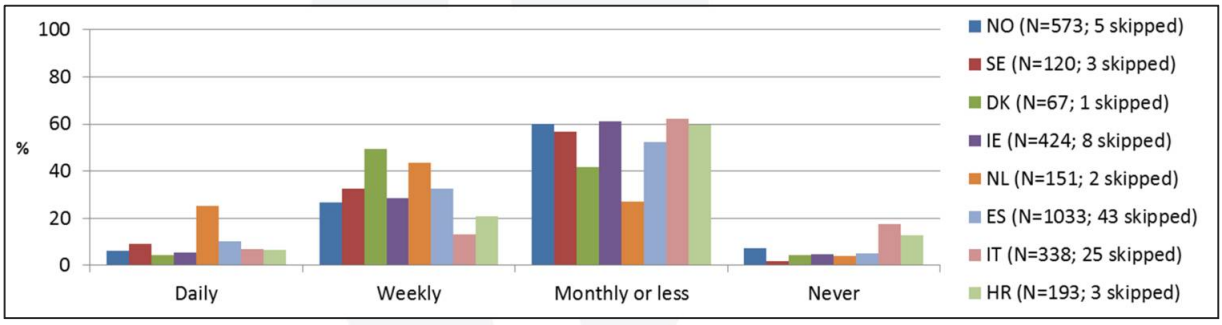


Figure 6.7.2.4. National clinical guidelines. p <0.001 (χ^2-test)

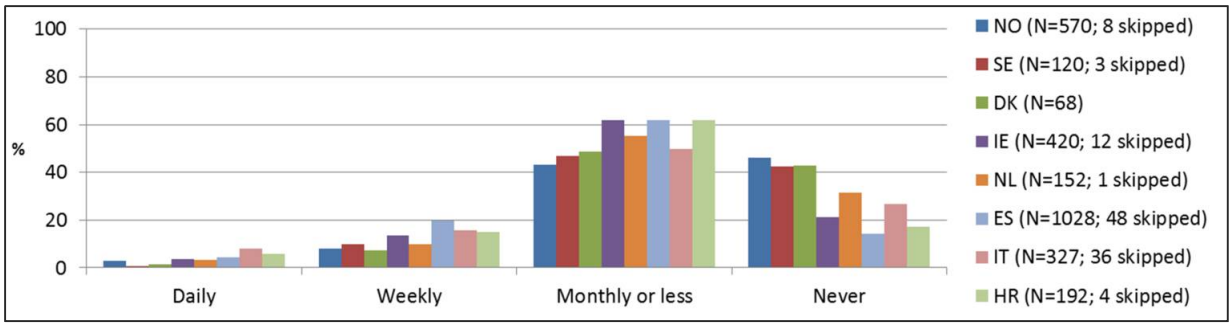


Figure 6.7.2.5. International clinical guidelines. p <0.001 (χ^2-test)

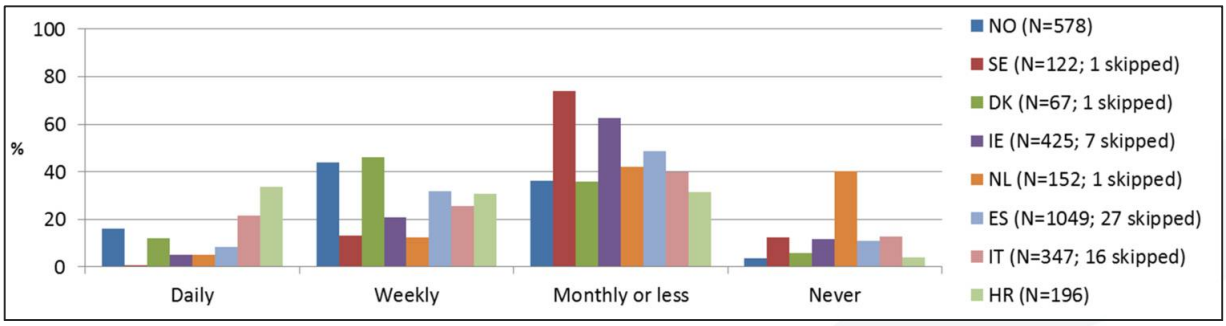


Figure 6.7.2.6. NCA website/newsletter. p <0.001 (χ^2-test)

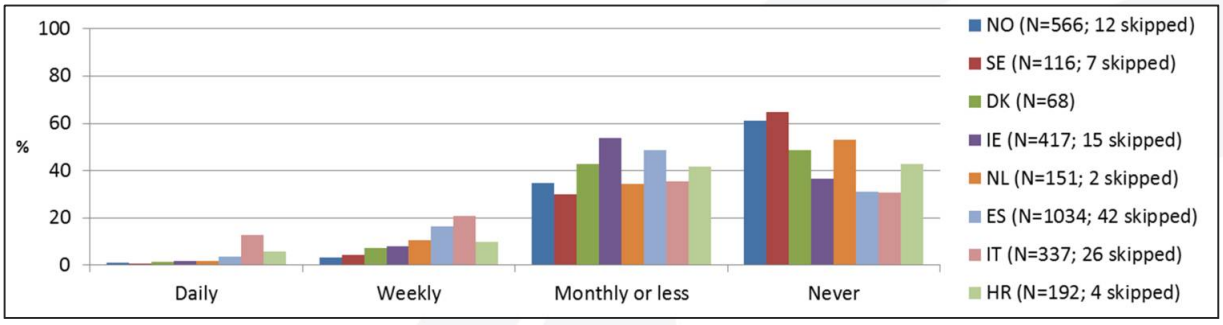


Figure 6.7.2.7. EMA website/newsletter. p <0.001 (χ^2-test)

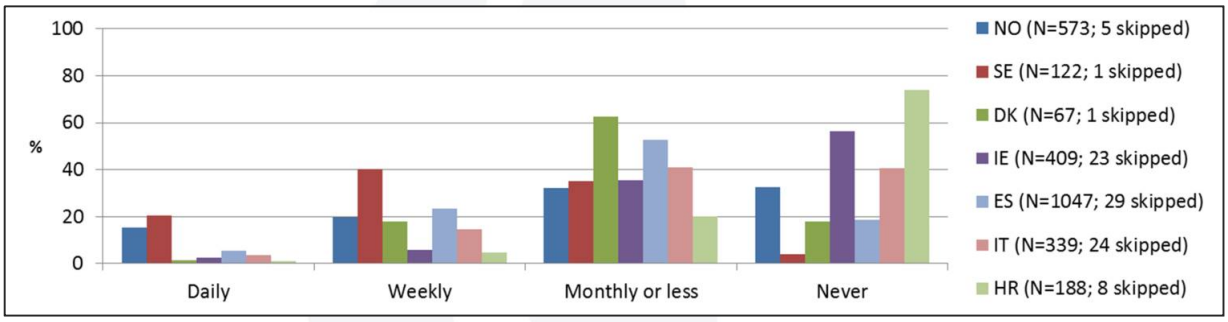


Figure 6.7.2.8. Medicines advisory committees (not included by the NL). p <0.001 (χ^2-test)

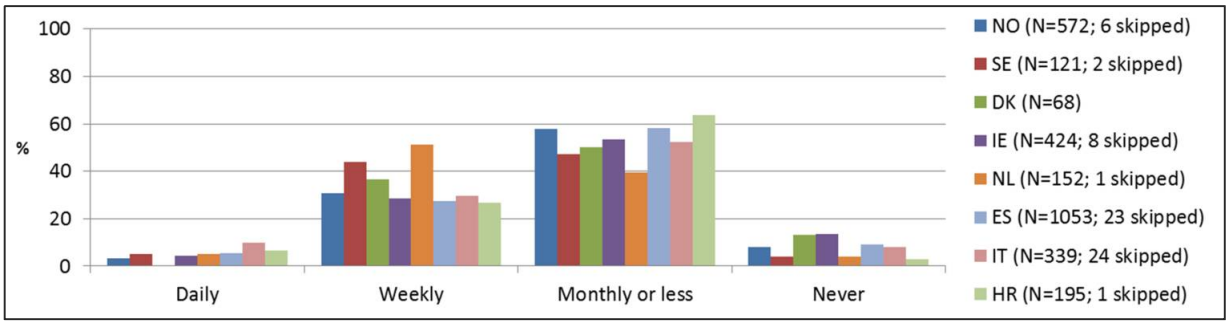


Figure 6.7.2.9. Medical journals. p <0.001 (χ^2-test)

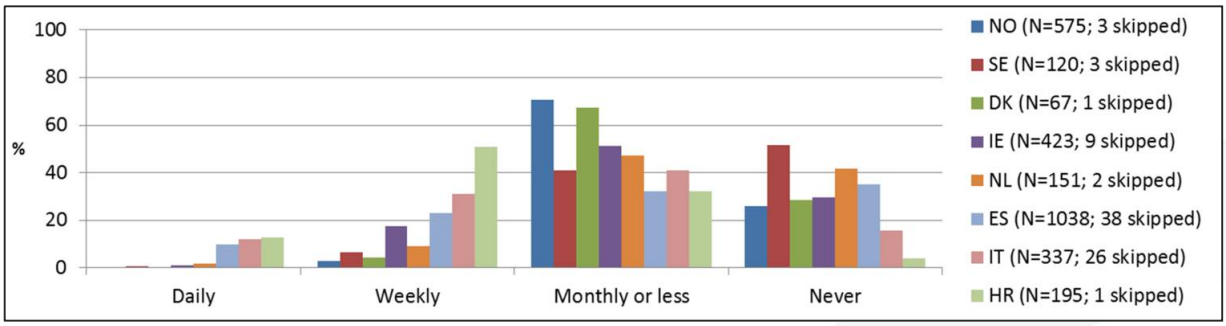


Figure 6.7.2.10. Company representatives. p <0.001 (χ^2-test)

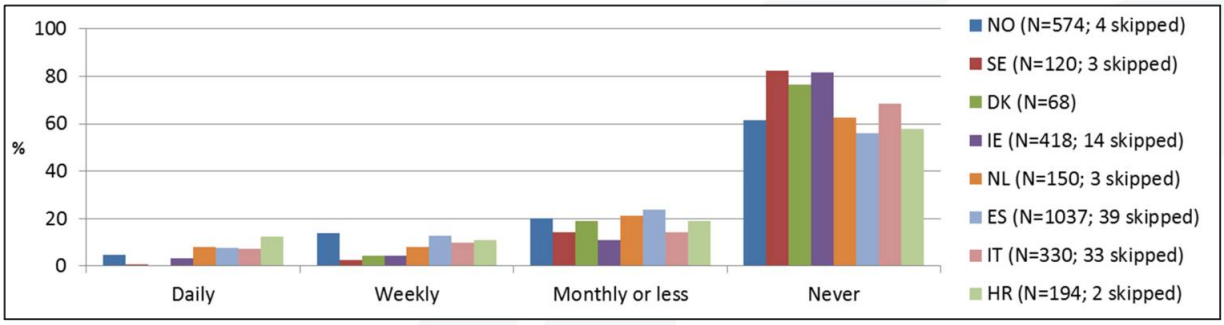


Figure 6.7.2.11. A mobile phone app. p <0.001 (χ^2-test)

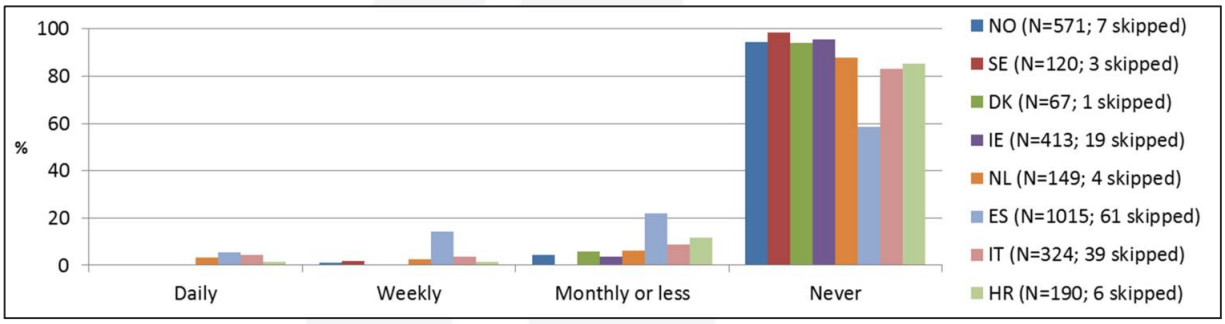


Figure 6.7.2.12. Blogs. p <0.001 (χ^2-test)

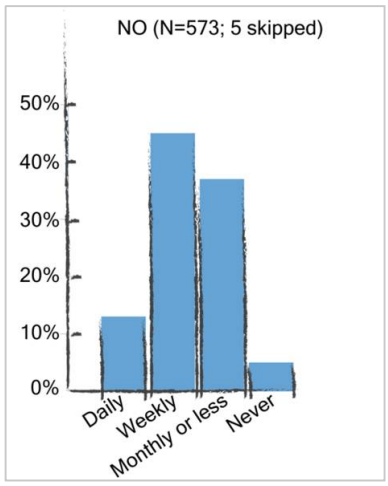


Figure 6.7.2.13. RELIS (De regionale legemiddelinformasjonssentre; Regional drug information centres).

This option was only available in NO.

Table 6.7.2. Results of Q31: How often do you use the following options to keep your medicines knowledge up to date?

Presented per profession. Some respondents skipped options for this question.

		GPs	Cardiologists	Pharmacists	Others	Total	p-value (χ^2-test)
Training or courses, organised by…	Daily	40 (3%)	3 (2%)	31 (4%)	6 (3%)	80 (3%)	<0.001
	Weekly	156 (11%)	11 (6%)	75 (10%)	16 (8%)	258 (10%)	
	Monthly or less	1162 (81%)	137 (75%)	647 (83%)	153 (75%)	2099 (81%)	
	Never	76 (5%)	31 (17%)	30 (4%)	30 (15%)	167 (6%)	
A medicines reference book	Daily	719 (47%)	44 (22%)	555 (57%)	63 (28%)	1381 (47%)	<0.001
	Weekly	421 (27%)	66 (33%)	253 (26%)	91 (40%)	831 (28%)	
	Monthly or less	340 (22%)	63 (31%)	132 (14%)	63 (28%)	598 (20%)	
	Never	61 (4%)	30 (15%)	26 (3%)	8 (4%)	125 (4%)	
Summary of Product Characteristics/ Patient information leaflet	Daily	286 (19%)	26 (13%)	435 (45%)	35 (16%)	782 (27%)	<0.001
	Weekly	450 (30%)	34 (17%)	354 (37%)	58 (26%)	896 (31%)	
	Monthly or less	605 (40%)	103 (51%)	156 (16%)	100 (45%)	964 (33%)	
	Never	173 (11%)	40 (20%)	15 (2%)	29 (13%)	257 (9%)	
National clinical guidelines	Daily	166 (11%)	18 (9%)	51 (5%)	17 (8%)	252 (9%)	<0.001
	Weekly	479 (32%)	52 (26%)	238 (25%)	63 (29%)	832 (29%)	
	Monthly or less	799 (53%)	111 (55%)	571 (59%)	125 (57%)	1606 (55%)	
	Never	75 (5%)	21 (10%)	100 (10%)	13 (6%)	209 (7%)	

		GPs	Cardiologists	Pharmacists	Others	Total	p-value (χ^2-test)
International clinical guidelines	Daily	53 (4%)	31 (15%)	26 (3%)	9 (4%)	119 (4%)	<0.001
	Weekly	228 (15%)	82 (40%)	74 (8%)	34 (16%)	418 (15%)	
	Monthly or less	895 (59%)	88 (43%)	479 (51%)	132 (61%)	1594 (55%)	
	Never	336 (22%)	4 (2%)	363 (39%)	43 (20%)	746 (26%)	
NCA website/newsletter	Daily	120 (8%)	11 (5%)	210 (22%)	20 (9%)	361 (12%)	<0.001
	Weekly	426 (28%)	37 (18%)	380 (39%)	48 (21%)	891 (30%)	
	Monthly or less	799 (52%)	107 (52%)	340 (35%)	118 (52%)	1364 (46%)	
	Never	183 (12%)	49 (24%)	46 (5%)	42 (18%)	320 (11%)	
EMA website/newsletter	Daily	43 (3%)	7 (3%)	55 (6%)	3 (1%)	108 (4%)	0.001
	Weekly	189 (13%)	20 (10%)	101 (11%)	28 (13%)	338 (12%)	
	Monthly or less	675 (45%)	79 (39%)	403 (42%)	83 (37%)	1240 (43%)	
	Never	598 (40%)	96 (48%)	393 (41%)	108 (49%)	1195 (41%)	
Medicines advisory committees	Daily	143 (10%)	4 (2%)	35 (4%)	12 (5%)	194 (7%)	<0.001
	Weekly	312 (22%)	22 (12%)	123 (14%)	44 (19%)	501 (18%)	
	Monthly or less	631 (44%)	78 (42%)	319 (36%)	117 (52%)	1145 (42%)	
	Never	359 (25%)	81 (44%)	412 (46%)	53 (23%)	905 (33%)	

		GPs	Cardiologists	Pharmacists	Others	Total	p-value (χ^2-test)
Medical journals	Daily	74 (5%)	30 (15%)	41 (4%)	12 (5%)	157 (5%)	<0.001
	Weekly	485 (32%)	88 (43%)	247 (26%)	73 (32%)	893 (31%)	
	Monthly or less	862 (56%)	76 (37%)	559 (58%)	123 (54%)	1620 (55%)	
	Never	112 (7%)	9 (4%)	114 (12%)	19 (8%)	254 (9%)	
Company representatives	Daily	145 (10%)	9 (4%)	22 (2%)	4 (2%)	180 (6%)	<0.001
	Weekly	354 (23%)	53 (26%)	120 (12%)	33 (15%)	560 (19%)	
	Monthly or less	533 (35%)	102 (51%)	575 (60%)	112 (50%)	1322 (45%)	
	Never	483 (32%)	37 (18%)	248 (26%)	76 (34%)	844 (29%)	
A mobile phone app	Daily	107 (7%)	15 (8%)	48 (5%)	12 (5%)	182 (6%)	0.004
	Weekly	157 (10%)	27 (14%)	83 (9%)	33 (15%)	300 (10%)	
	Monthly or less	312 (21%)	37 (19%)	162 (17%)	42 (19%)	553 (19%)	
	Never	933 (62%)	121 (61%)	665 (69%)	137 (61%)	1856 (64%)	
Blogs	Daily	59 (4%)	8 (4%)	11 (1%)	4 (2%)	82 (3%)	<0.001
	Weekly	142 (10%)	6 (3%)	18 (2%)	7 (3%)	173 (6%)	
	Monthly or less	231 (16%)	15 (8%)	56 (6%)	23 (10%)	325 (11%)	
	Never	1053 (71%)	170 (85%)	860 (91%)	186 (85%)	2269 (80%)	

7. Discussion

In this section we elaborate on potential explanations for the more salient findings from our study. In addition, some implications of the results for clinical practice are suggested and recommendations for improvement of risk communication are provided.

7.1 Three safety communication tools

Overall, HCPs were familiar with the three safety communication tools (i.e. DHPCs, NCA communications and educational materials) and considered them useful. HCPs were least familiar with educational materials, probably because they are not required for all medicinal products, meaning that HCPs may not have frequently encountered them. Therefore, less familiarity with this type of communication is to be expected. However, several HCPs claimed to have heard about the diclofenac safety issue via educational materials, despite these materials not being disseminated for this drug. This finding indicates that HCPs may have confused educational materials with other safety communication materials or may have had a broader interpretation of this term outside of the regulatory definition.

Cross-national differences were observed with regard to preferences for receiving safety information in general, for example, receiving DHPCs as hardcopies versus electronic versions. The preference for electronic versions was highest in ES and the UK. For ES, this may be related to the fact that in most cases DHPCs are no longer sent as hardcopy versions. Hardcopy versions seemed to be more appreciated in NL, SE and IE, although, interestingly, NL and SE have the highest level (92% and 93%) of electronic prescribing/dispensing systems. It might be that HCPs in these countries are suitably familiar with hardcopy versions of safety information and do not wish to change this practice. A tentative reason for this, offered in the open-ended answers, was that HCPs already receive a large volume of electronic information. The open-ended question answers also revealed several other reasons for their preference: ease of filing and the possibility to discuss/show the warning with/to colleagues/patients. However, these reasons appeared to apply as much to electronic documents as to the paper-based versions. Earlier research in the NL had shown that HCPs were quite receptive to receiving emails (10, 11). This inconsistency may have been influenced by the smaller sample of HCPs included in the current study, different terminology used (i.e. ‘electronically’ versus ‘email’) or the difference in specialist profession included in the survey (i.e. cardiologists versus internists).

The overall response when asked how often **action is taken by HCPs** to these safety communications seems unrealistically high and is different from the previously reported mixed (or delayed) responses to regulatory warnings in the NL (12) and the USA (13). These two systematic reviews indicated that uptake of and action on safety messages was often more modest. Finally, in a review of 58 DHPCs issued between 2000 and 2008 for 46 drugs in the NL, in only 20 (35%) cases was long-term use changed (14). These differences in action taken may be due to differences among European countries. The country-specific results in the current study show, for instance, that Dutch HCPs take action least often compared to HCPs in other countries. Another reason may be due to the broad nature of the questions used in the current study. As indicated through open-ended questions, some HCPs do not take action where they do not use/prescribe the concerned medicine, and their response may depend on the situation (e.g. ADR characteristics, patient characteristics, patient preferences). Therefore, it may have been difficult for HCPs to indicate how often they take action in general. This may be the case for pharmacists, in particular, since their action is not related to prescribing but to providing information to HCPs and patients. Also, HCPs may have provided socially desirable responses or the respondents themselves may be a more engaged group compared to previous studies, and thus not representative of the general HCP population.

Considerable variability was observed in the frequency with which HCPs preferred to receive safety-related information. While 45% indicated that they would prefer an immediate update, approximately one quarter preferred a weekly update and the same proportion preferred a monthly update of all safety issues. Consequently, while the majority of responding HCPs indicated that repetition of a safety message would be useful after a period of time, a recommendation on the frequency or timing of this reminder is hampered by a lack of consensus on the frequency with which HCPs prefer to receive safety-related information. This is further complicated by the fact that a number of HCPs stated that the usefulness of repetition was conditional on the fact that there is evidence that HCPs had not sufficiently changed their prescribing practice, or that the earlier communication had not reached all target groups. Uptake of safety information may be improved with repetition, especially if the message is slightly adapted (15).

It was widely suggested that point-of-care alerts that are generated when a specific product is prescribed or dispensed might be an attractive option to communicate safety information to HCPs. In addition, they were one of the most preferred alternative safety information channels. Point-of-care alerts act as a timely and relevant reminder of important safety information (i.e. at the moment HCPs need it) and facilitate the provision of sustained information over time. In Norway, the NCA is a provider of the content for the national electronic prescribing system, something highly appreciated according to the survey findings. However, attention should be given to avoiding ‘alert-fatigue’, which may occur if warnings are received too often. Examples to prevent this include careful selection of the issue to be communicated, ensuring that it is not used too often and possibly only for a limited period of time (16). These issues should be considered and solved nationally and may depend on the specific safety issue.

Another suggestion made by respondents was that NCAs should maintain easily accessible repositories of safety communications on their web-portals/websites. A number of HCPs indicated that the availability of an easily accessible central repository of DHPCs, NCA communications and educational materials on the NCA website would be a valuable tool to facilitate subsequent retrieval of the materials after initial dissemination. It would also act as an indicator that these safety communications were non-promotional and had been approved by the NCA. This appears to be particularly relevant to educational materials as a number of respondents stated that these materials are difficult to distinguish from promotional materials produced by pharmaceutical companies. NCAs were considered a trusted source of safety information and it is therefore logical that the NCA provides and maintains an easily accessible repository. The majority of European NCAs already publish DHPCs on their websites (WP6 – Audit of National methods for communication survey report). Although many HCPs had a mostly neutral view on websites as a potential information channel, a website seems to be a reasonable source as a repository. Raising awareness of such a repository should be encouraged, in addition to increasing awareness of NCA websites in some countries. For instance, a large proportion of Dutch HCPs, especially GPs, do not visit the NCA's website (10).

All safety communications should be clearly identified as **non-promotional safety information**. In some countries this is indicated on the envelope in which a DHPC is sent, so that it is distinguished from promotional materials. This is supported by HCPs indicating that they primarily read safety information that is relevant to them, or only read DHPCs where it is clearly indicated that they contain non-commercial safety information. A consistently used symbol or text could help to avoid confusion for HCPs on what is an official – agreed/approved by the NCA – safety communication.

With regards to the content of safety communications, HCPs indicated that **summarised safety information and actionable recommendations**, with a distinguished layout, would be an important tool to help the busy reader to grasp the core message quickly.

HCPs considered that the information provided in educational materials should focus on the safety risk, how to prevent it, and how the medicine should be taken properly. Information on both benefits and risks could also be included, according to some respondents, for example, drug fact boxes that summarise the main drug benefits and risks in short bullet points (17). However, this may require further research, as not all HCPs were equally in favour of including such information.

7.2 General preferences

A clear message was that **trusted senders**, such as NCAs or professional bodies, are the preferred sources of safety information. The pharmaceutical industry, in particular, was not a preferred sender. In the field of (risk) communication, it is well-established that trust in the sender is associated with a greater uptake of the message conveyed (10, 18, 19). The NCA as a trusted sender of safety information was consistently reported throughout the survey. This finding is important since, currently, DHPCs sent by the pharmaceutical industry are the only way of sending pro-active information on safety issues in most countries.

The most **preferred** safety information **channels** were **emails**, **point-of-care alerts** (i.e. alerts through prescription systems) and, irrespective of electronic or paper-based format, **reference books** and **national clinical guidelines**. Consistent with the preference for DHPCs and educational materials, a large proportion of Dutch, Swedish and Irish HCPs retain a preference for paper-based materials.

If using email as a communication channel, up-to-date email address lists need to be maintained. This may be more challenging than acquiring regular resident addresses. In some countries (DK) HCPs are required to maintain a specific email address dedicated to messages from regulatory authorities, which could include drug (safety) messages. Professional societies or certification boards could be instrumental in maintaining up-to-date address lists. In fact, it is already current practice to email DHPCs in ES, where they are sent through relevant professional societies.

7.3 Specific safety issue updates

In general, Ivabradine was the least known of the four safety issues presented in this survey; however, only 9% of the cardiologists (the principle prescribers) were unaware of the issue. In comparison to the other three examples used, ivabradine is a newer active substance and authorised in relatively narrow subpopulations of patients with angina, and recently in patients with heart failure. This may explain the lower awareness of ivabradine compared to the other examples used. The issue was best known in IE, UK, ES and IT, although it is not clear if differences in (relative) market penetration of the product could explain some of the observations. In general, it is not unexpected that knowledge of safety issues seem to be related to the **extent of use** of a product. The extent of use is also an important factor in determining the communication strategy, where for more frequently used drugs, alternative communication channels to DHPCs may be relevant.

Cardiologists were clearly better informed of the safety communication for ivabradine than other HCPs. Cardiologists are the principal prescribers of this product and were thus specifically targeted in this safety communication. In line with their professional expertise they were also informed through other channels, e.g. medical journals and professional societies, on the safety issue.

Familiarity may thus be greater for drugs belonging to the professional's usual **pharmacotherapeutic toolkit**. Generalists (GPs and pharmacists) were less aware of safety issues with more specialised drugs, valproate and ivabradine, than CHCs or diclofenac. Finally, cardiologists were not very familiar with new updates on diclofenac-related cardiovascular safety issues. This may indicate that cardiologists are less focused on safety issues related to cardiovascular symptoms than safety issues for cardiovascular drugs.

Across all countries, the safety issues were best known through the **'official' channels**: DHPC, NCA websites or NCA direct communications/newsletters. However, Dutch HCPs mentioned professional bodies and medical journals as their principal information channels on the diclofenac and oral contraceptives safety issues. This finding suggests the importance for NCAs to intensify collaboration with professional bodies to disseminate safety information. Moreover, they should consider publishing safety information updates in medical journals, especially where this concerns such extensively used medicines such as diclofenac and oral contraceptives, which may attract a lot of media attention and could be a cause for concern amongst the general public. National sensitivities may exist, where certain topics – e.g. appropriate use of third-generation CHCs – may have previously received a lot of local attention. This could explain why a large proportion (40%) of Swedish HCPs were unaware of the recent update on the venous thromboembolism (VTE) risk of CHCs, as they may have considered this 'old news'.

Finally, HCPs in Southern European countries, the UK and IE were more aware of the valproate safety issue. Reasons for a higher awareness in these countries is unclear. Anti-epileptics are likely initiated in all countries by neurologists, where GPs may renew these prescriptions. Consequently, DHPCs were addressed in most countries to neurologists and GPs (and/or pharmacists). One explanation may be that HCPs in Southern European countries generally follow official channels, such as DHPCs and NCA communications, better. However, it is not clear from the literature that prescribing behaviour is more affected by regulatory safety warnings in Southern Europe, the UK or IE compared to other regions (12). Another explanation may be that these HCPs gave more socially desirable answers and, despite the anonymous nature of the survey, wanted to appear fully informed.

In conclusion, targeted distribution of safety information aligns with the preference of HCPs for reading safety communications related to their clinical practice. In particular, for the more specialised drugs, the official regulatory safety communication channels seem the most important source of information. However, if a drug safety issue is widely discussed, or the product is extensively used, such as diclofenac and combined hormonal contraceptives, other channels (medical journals and professional bodies) are also likely sources of information. Consequently, it may be valuable to write editorials or comments for these journals and professional bodies in such cases. This should be adapted according to national preferences and to national organisation of the healthcare system.

7.4 Current practice

Currently, medicine reference books are the most cited source of drug information for HCPs, therefore NCAs may want to ensure good relations with the editors of such books. Moreover, as national and medical journals were also mentioned as important sources of drug information, NCAs might aim for a close, or closer, collaboration with their respective editors. It may be most efficacious to focus at a national level. Consistent with a survey performed in NL five years ago (10), modern communication tools, such as mobile phone apps or blogs, are largely unused or unappreciated as a source of drug information.

In conclusion, seeking collaboration with the most used national drug information sources seems to be a good communication strategy, given its independence on the familiarity of HCPs with national regulatory agencies.

7.5 Strengths and limitations

To date, this is the largest multi-national study on safety communication tools in Europe. In this study 3,625 HCPs from nine European countries gave their opinions on common safety communication tools. The study allows a comparison of views on communication strategies between HCPs from different countries, although generalised conclusions may be difficult to propose given the low response rates in some countries. Moreover, it provides an exploration of views between different groups of HCPs: GPs, pharmacists, cardiologists and a group of 'other' practising HCPs. Not all groups of HCPs were equally represented, nor was each surveyed country. The smallest group, the cardiologists, still included 222 respondents, thus allowing robust between-group comparisons. Pharmacists were not included in the Spanish and Swedish surveys, however, in five of the seven countries that did target pharmacists, they were the largest group of responders.

The study was developed using a single protocol with careful translation (eight languages) and back-translation of survey questions, which facilitated comparable responses. Small differences in translation and interpretation of *useful/very useful* (or *positive/very positive*) among countries may have had an effect on responses. There were also some small differences among the countries in the questions included in the survey due to, for instance, the consideration that the survey would become too lengthy. However, most of the respondents (65%) who started the survey, also completed it. Some countries did not include certain questions, however, a general picture of the view of HCPs on safety communication tools per country could be investigated.

This study, although not conducted in all EU countries, had a favourable distribution of three northern, three western and three southern countries. Extrapolation to other countries should be made with care, but a broad picture of safety communication from NCAs can be obtained. National differences exist, mostly with respect to preferences for electronic and paper-based formats of communication, frequency of reminders, and possibly in the – self-reported – level of action taken.

Recruiting HCPs for the survey proved difficult, meaning that different methods per country had to be used. Comprehensive email lists were not available nor obtainable through third-party suppliers, such as IMS Health, therefore various and sometimes multiple distribution methods were used per country. Distribution through professional organisations required additional efforts, with varying results. An especially successful recruitment strategy was explaining the scope of the project at a conference. Ultimately, the final sample size was large enough to assess even small differences between countries and subgroups. The difference in response between countries can in part be explained by the difference in the number of HCPs in each country. Still, the results in countries with a low absolute number of responders should be interpreted with care (see Table 6.1.1).

Unfortunately, it was impossible to determine a response rate, as HCPs were not individually approached. Moreover, a direct comparison between responders and non-responders – for those HCPs that were individually approached – was not possible since no information about the non-responders is available. For planning purposes, the authors used a sample size calculator, which indicated that approximately 100 respondents per profession per country would provide adequate statistical power in order to draw meaningful conclusions for each group. However, from Table 6.1.1 it becomes clear that some countries and professions are better represented than others. This should be taken in account when interpreting the results.

Ultimately, the study may represent the views of a more involved group of HCPs. Indeed, the large number of open-ended answers that were received for many of the questions suggests an engaged responder group.

The high percentage of reported action taken in response to safety communications and familiarity with the four cases presented may be explained by two factors. Firstly, HCPs receive many DHPCs, and may indeed have taken action in response to them at some point in time, though not necessarily always immediately or when indicated. A large proportion of respondents provided open-ended answers that indicated HCPs were quite familiar with NCAs' safety communication tools, which provided insight into why HCPs had certain preferences. Of course, they may also have a genuine interest in safety communications on medicinal products.

Secondly, respondents may have given socially desirable answers. In an earlier Dutch survey, it was found that 30% of the time respondents took action in response to DHPCs compared to 60% reported in this survey (10). The self-reported action taken in other European countries was even higher. It is unclear why HCPs would give more socially desirable answers here, compared to a previous survey, especially considering similar HCP groups were approached and surveys were strictly anonymous. Still, three years after the Pharmacovigilance Risk Assessment Committee (PRAC) was initiated, attentiveness and responses to drug safety issues may have truly increased, enhancing awareness and interest from HCPs. Socially desirable answers may also explain, for instance, the finding that pharmacists were more aware of educational materials than other HCPs, while they are often not the main target of these materials. However, such a finding may have been influenced by confusion about, or a broader interpretation of, educational materials.

In conclusion, a certain level of socially desirable responses cannot be excluded. This observation underscores the importance of evaluating risk communication or risk minimisation measures at various levels. This study, a survey intended to evaluate knowledge of, preference for, and intended behaviour following, safety communications provides a first step in improving how safety communications are best disseminated. Drug utilisation studies or clinical outcome studies in HCP databases, using, for example, interrupted time series designs, may be used to evaluate effectiveness with more robust outcomes (2, 6, 20).

Finally, linking heterogeneity in the HCP responses in this survey to preferences for communication methods of national regulatory agencies, as identified in the WP6 topic 1 (Audit of national reporting systems) report, remains elusive. Many agencies employ overlapping communication strategies and therefore identifying the most effective strategy is difficult. Nevertheless, NCAs that have a direct link to electronic prescribing systems, such as NOMA, the NO agency, may have an important advantage with respect to generating ‘point-of-care’ alerts. Moreover, close collaboration with national guideline developers, professional societies and journal editors could be of real value. Further work is needed to evaluate the most valuable national communication strategies (topic 1) with regard to specific outcomes, e.g. action taken and knowledge of specific safety issues.

8. Recommendations

In this section a number of recommendations are given. Some can be more easily implemented, others reinforce already existing practices, and some require legal or technical issues to be resolved.

In general:

- Trust in the sender is key. HCPs clearly indicated that NCAs and/or professional bodies were the preferred senders of safety information. In addition, trust in the sender was one of the most important factors in determining whether or not HCPs read and take action in response to safety communications. Consequently, NCAs should explore the option of sending DHPCs directly to HCPs. A greater role for national professional societies and national medical journals in disseminating safety information should also be actively pursued.
- Differentiation of safety communications from promotional materials produced by the pharmaceutical industry is recommended, particularly as a number of respondents indicated an element of distrust in relation to pharmaceutical companies.
- Of the three types of safety communication tools, HCPs were least aware of educational materials and responses suggest that there is confusion regarding what educational materials are, along with their objectives. Therefore, it is recommended that awareness/knowledge about this type of safety communication tool should be enhanced. Moreover, the sender of these materials should be reconsidered and HCPs should be made aware of the availability of materials for specific medicines (e.g. by a link in the prescribing system).
- Preferences for electronic versus hardcopy safety communications varied considerably across participating countries. Consequently, the format of distribution should be considered based on the national preferences. In general, emails were a preferred communication channel and can be used, provided up-to-date email addresses are maintained. Professional societies or certification boards could be instrumental in maintaining up-to-date addresses.
- Medicine reference books, national clinical guidelines, and point-of-care alerts were identified as valuable sources to aid HCPs in keeping up to date on medicines safety issues. The use of point-of-care alerts could be explored further by NCAs, as these alerts would be useful in providing timely reminders to HCPs about important safety information and educational materials at the point of prescription/dispensing. In the exploration phase, contact with NCAs who already use such alerts would be helpful.

- Repetition may be used to improve the update of safety issues. This can be done by providing different types of safety communication tools or using several channels for releasing the information. However, a balance should be made between repetition of safety information and inducing 'alert fatigue'. Immediate dissemination of DHPCs, followed by a monthly update on new safety issues, may be a reasonable approach. The concrete format and distribution may depend on the issue and on national preferences.
- A central repository of safety communications and educational materials, easily retrievable from an NCA's web-portal/website, or that of another recognised drug information centre, was consistently suggested by HCPs. This should facilitate accessing additional copies of, for example, educational materials, and would also reiterate the fact that these materials have been approved by the NCA.
- There may be valid reasons for HCPs not to take action in response to a safety issue (e.g. weighing the benefits and risks for an individual patient, patient preferences or unavailability of alternative therapies). It is recommended that this be taken into account when evaluating the effectiveness of safety communications.
- Safety communications should have a clear and focused message with a recognisable design and clear overview of actions to take. Use of an active voice, attractive layout and, where needed, pictures or graphs, could increase the uptake of the safety message. HCPs flagged that a summary box or key messages section outlining the most salient points was desirable.

9. Conclusions

The information provided in this report is part of the proposals for improvement of risk communication developed by the SCOPE WP6 members. This study highlights the familiarity of European HCPs with the main safety communication tools utilised by NCAs and industry. HCPs usually read the information, especially when it relates to their own daily practice. In addition, they find the information useful to very useful and have frequently taken the recommended action. Moreover, in four presented cases these safety communication tools were the main sources of drug safety information for HCPs. Overall, DHPCs are best known, followed by national regulatory agency communications and educational materials, although this varies among countries.

Trust in the sender, applicability for daily practice and the severity of a safety issue are the main reasons for reading and subsequently taking action in response to safety communications. As potential senders of safety information, NCAs particularly, as well as professional bodies, are indicated to be most trustworthy, while industry and public press ranked last. Electronic formats for safety communication are well accepted, although in three countries large groups of HCPs still prefer to receive paper-based materials. New and additional communication channels may be used. Most preferred are: email, point-of-care alerts in electronic prescribing systems, and national clinical guidelines or medical reference books. There was little enthusiasm for modern media (e.g. mobile apps). The results indicated targeted dissemination and tailoring of information would be of value. Some differences existed between countries, mostly on the desire for hard-copy material, frequency of reminders, extent of the information provided and how much self-reported action HCPs take.

9. References

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Annex 1. Survey

Screen 1
Welcome

Safety communications and their effectiveness

Survey of the views of healthcare professionals

If the survey is distributed via websites, add the following information from the invitation e-mail:
The aim of communicating safety information to healthcare professionals is to contribute to protecting public health by:
• promoting the rational, safe and effective use of medicines;
• preventing harm from adverse reactions.
This survey seeks to examine your experience with regulatory safety communications, your views on their effectiveness and what information channels you prefer. The survey is part of an EU-wide pharmacovigilance project called SCOPE (Strengthening Collaboration for Operating Pharmacovigilance in Europe) which aims to help medicines regulatory agencies (including <*insert NCA name*>) to fulfil the requirements of pharmacovigilance legislation introduced in 2012.
The following introduction will be used also when an invitation e-mail is sent:
In this survey we will ask you about three specific types of safety information that are used by national regulatory agencies:

- DHPCs (Direct Healthcare Professional Communications);
- national regulatory agency communications;
- educational materials

In addition, will we ask for your general preferences on safety communication about medicines and your response to such communication.
The next part is optional again:
By participating in the survey, you can win a € … coupon for …, if you fill in your e-mail address on the final page and tick the box to win the coupon.
Your answers will be used to optimise safety communication by these medicines regulatory agencies.
This survey is anonymous and will take approximately 15 minutes to complete.
When you start the survey, you cannot save your answers in between. It is not possible to come back later to where you have stopped.
If you require any further information regarding this research project or your participation in the survey, you may contact <*insert contact person/organization*>. If the results of the survey are published, your name will not be used. If you would like to receive a copy of the publication you can indicate this at the end of the survey by leaving your e-mail address.

We greatly appreciate your time and opinions.

<NCA logo + name> and/or <scientific body>

Screen 2

Direct Healthcare Professional Communications
(DHPCs, also known as 'dear doctor letters')
DHPCs are distributed by the pharmaceutical company once the content is agreed with the *<NCA name>*. These letters are sent to individual healthcare professionals. The letter indicates that it is sent in agreement with the *<NCA name>*.

Two examples of recent DHPCs:
<image>
Click here to view a larger version

1. **Are you familiar with this type of safety information?**
   - ○ Yes
   - ○ No, I have heard of DHPCs, but I have never seen one
   - ○ No, I have never heard of DHPCs
2. **Do you read the DHPCs you receive?** *Multiple responses possible*
   - ○ Yes, if they contain safety information that is important to me
   - ○ Yes, only when the envelope indicates it contains important, non-commercial information *Possible to customise to national practice*
   - ○ Yes, I read all letters from the pharmaceutical industry
   - ○ No, I do not read any letter from the pharmaceutical industry
   - ○ Not applicable

   If you have any comments, please let us know
   Optional
   [……..]

Screen 3

Usefulness of DHPCs

3. **How useful do you find a DHPC in general?**
   Not useful at all | Not useful | Neutral | Useful | Very useful
   Please specify why you think DHPCs are useful or not
   Optional
   [……..]

4. **How often do you take the action that is recommended in this type of communications?**
   Please click and move the slider to represent your position between the two options
   never……..always
   Please specify why you may or may not always take the recommended action
   Optional
   [……..]

5. **Would it be sufficient for you to only receive an electronic DHPC instead of a hardcopy version?**

   - ○ Yes
   - ○ No
   - ○ Other, please specify…

   If you have any comments, please let us know
   Optional
   [……..]

Screen 4
Optional

National regulatory agency communications
National regulatory agencies such as <*NCA name*> assess and monitor the efficacy, risks and quality of medicinal products. <*link to NCA website*>
National regulatory agency communications include <*insert country specific information*>
Two examples of national regulatory agency communication:
<*image*>
Click here to view a larger version.

6. **Are you familiar with this type of safety information?**
    - Yes, I have received this type of safety information and I am (somewhat) familiar with its content
    - Yes, I have received this type of safety information, but I have never read it
    - No

    If you have any comments, please let us know
    Optional
    [……..]

Screen 5
Optional

Usefulness of national regulatory agency communications

7. **How useful do you find national regulatory agency communications in general?**
   Not useful at all | Not useful | Neutral | Useful | Very useful
   Please specify why you think national regulatory agency communications are useful or not
   Optional
   [……..]

8. **How often do you take the action that is recommended in this type of communication?**
   Please click and move the slider to represent your position between the two options
   never……always
   Please specify why you may or may not always take the recommended action
   Optional
   [……..]

9. **Would it for you be sufficient to only receive an electronic version of national regulatory agency communication instead of a hardcopy version?** *Delete question if only an electronic version is available.*

   - Yes
   - No
   - Other, please specify…

   If you have any comments, please let us know
   Optional
   [……..]

Screen 6
Optional

Educational materials
Educational materials include prescriber checklists and booklets for healthcare professionals with information about certain risks. Educational materials may also include cards and/or brochures to give to patients to help explain an adverse drug reaction of a specific medicine. These are distributed by the relevant pharmaceutical companies once the content is agreed with *<NCA name>.*

Two examples of this type of communication:
<image>
Click here to view a larger version

10. Are you familiar with this type of safety information?

- ○ Yes, I have received this type of safety information and I am (somewhat) familiar with its content
- ○ Yes, I have received this type of safety information, but I have never read it
- ○ No

If you have any comments, please let us know
Optional
[……..]

Screen 7
Optional

Usefulness of educational materials

11. **How useful do you find educational materials in general?**
    Not useful at all | Not useful | Neutral | Useful | Very useful
    Please specify why you think educational materials are useful or not
    Optional
    [……..]

12. **If educational material for the patient is available, either for explanation during a consult or to be read at home, how do you value the following delivery methods?**
    - Hardcopy versions - Very negative | Negative | Neutral | Positive | Very positive
    - Online or web-based tools - Very negative | Negative | Neutral | Positive | Very positive

13. **Please tick all the following contents that you think should be included in educational materials for patients:**
    - Warnings about serious adverse drug reactions and how the risk may be minimized
    - Information on how to correctly use/take the product
    - A summary of both the benefits and risks of using the product
    - Other, please specify…
    - None of the above

14. **Have you ever used educational materials as part of a discussion about a medicine with a patient?** *Multiple responses possible*
    - Yes
    - No, I do not routinely prescribe medicines for which educational materials are available
    - No, I do not know if educational materials are available for the medicines I prescribe
    - No, I do not find these materials helpful for patients
    - No, I think the Patient Information Leaflet provides already sufficient information
    - No, because …

    If you have any comments, please let us know
    Optional
    [……..]

Screen 8 General preferences and behaviour towards medicines safety information
As a healthcare professional you may receive medicines safety information (e.g. DHPCs, national regulatory agency communications or educational materials) through different channels and from different sources. It is known that various factors may influence whether healthcare professionals take subsequent action in their daily practice. In this section, we would like to ask you about your preferences for channels and sources [who is sending the information] and the factors that may affect your response to the safety communications you receive.

<image>	*<image>*	*<image>*
DHPC	**National regulatory agency communication**	**Educational material**

15. **How do you value the following sources as a sender of safety messages?**
    Very negative | Negative | Neutral | Positive | Very positive
    - *<NCA name>*
    - European Medicines Agency (EMA)
    - Professional body (e.g. *<national example>*)
    - Pharmaceutical companies
    - Colleague
    - Public press (e.g. through local newspaper article or news program on television)
    - Independent researchers (e.g. through publications in a medical journal)
    - Other, please specify…
16. **In general, do you prefer to receive safety information in hardcopy (paper) or electronically?**
    - Hardcopy
    - Electronically
    - No preference
17. **Below you can find some channels, which can be both in a hardcopy and electronic format. Independent of the format, how do you value each channel to keep up to date on the safety of medicines?**
    Very negative | Negative | Neutral | Positive | Very positive
    - Personalised letter
    - Medical journal
    - Summary of Product Characteristics / Patient information leaflet
    - Medicines reference book (e.g. <national example>)
    - Newspaper
    - National clinical guidelines (e.g. <national example>)
18. **How do you value the following alternative channels to keep up to date on the safety of medicines?**
    Very negative | Negative | Neutral | Positive | Very positive
    - E-mail
    - Social media (e.g. Twitter)

- Mobile phone text (e.g. SMS)
- Point-of-care alerts (e.g. pop-up notification at the time of prescribing or dispensing)
- Website
- Television or radio
- Mobile app
- In person (e.g. face-to-face meeting, course, medical congress or seminar)
- Phone call
- Other, please specify…

19. In general, how often do you prefer to receive safety-related information?

- An **immediate** update of individual safety issues
- A **weekly** update of all safety issues
- A **monthly** update of all safety issues
- A **quarterly** update of all safety issues

20. Do you think it is useful when a safety message is repeated after a certain period of time?

- Yes
- No
- Other, please specify…

21. In general, how much do you agree with the following statements? I only read the safety information if, ...
Strongly disagree | Disagree | Neutral | Agree | Strongly agree

- I like the channel through which the information is sent (e.g. e-mail, hardcopy letter)
- I trust the sender of the safety message
- I like the lay-out of the document
- the document is not too lengthy
- I have enough time to read the information
- the safety information is relevant for my daily practice
- I do not receive a new safety message too often
- Other factors? Please specify…

22. In general, how much do you agree with the following statements about safety information? I only take action in response to a safety warning if, …
Strongly disagree | Disagree | Neutral | Agree | Strongly agree

- the adverse drug reaction is severe or causes irreversible harm
- I trust the sender of the safety message
- I receive sufficient background information on the basis for the safety message
- I agree with the recommendation in the safety information
- my colleagues or multidisciplinary team agree with the safety message
- the message is incorporated in clinical or professional society guidelines

- a patient requests an action in response to safety information she/he has found
- recommendations are clear
- a recommendation can easily be implemented in routine daily practice
- the safety information is relevant for my daily practice
- Other factors? Please specify…

23. Are you aware of updates to the safety profiles of the following medicines? If yes, how did you hear about them?

Please tick all that apply

No | Yes, via DHPC | Yes, via website or newsletter | Yes, via educational materials | Yes, via professional body | Yes, via a colleague | Yes, via medical journal | Yes, via lay media (newspaper/television) | Other, please specify below

- Combined Hormonal Contraceptives – update on the risk of venous thromboembolism
- Diclofenac – new cardiovascular precautions
- Valproate – further restrictions for use in women and girls
- Ivabradine – the need to take additional measures to minimize the risk of cardiovascular events and severe bradycardia

If you heard about one of the updates to the safety profiles of the medicines above via a channel that was not mentioned, please specify below

[……..]

If you have any comments, please let us know

Optional

[……..]

Screen 9 General questions

24. What is your gender?

- Male
- Female

25. What is your age?

- <35
- 35 – 45
- 46 – 55
- >55

26. What is your profession?

- General practitioner
- Cardiologist
- Pharmacist
- Other, please specify…

27. What is your primary employment setting? ***Tailor per country, employment settings differ***

- Community based - public practice
- Community based - private practice
- Hospital based - public practice
- Hospital/clinic based - private practice
- Other, please specify…

28. Where is your practice located?

- Rural area
- Urban area
- Other… (if applicable)

29. How long do you have a healthcare professional accreditation?

- <5 years
- 5 – 20 years
- >20 years

30. Do you use an electronic system to prescribe or dispense medicines?

- Yes, always
- Yes, but not always
- No

31. How often do you use the following options to keep your medicines knowledge up to date?
Daily | Weekly | Monthly or less | Never *tailor with examples per country*

- Training or courses, organised by e.g.: … <text field>
- A medicines reference book (e.g. “Farmacotherapeutisch Kompas” and “Informatorium Medicamentorum” in NL)

- Summary of Product Characteristics / Patient information leaflet
- National clinical guidelines (e.g. “NHG standaarden” in NL)
- International clinical guidelines (e.g. from the “European Society of Cardiology”)
- <NCA name> website/newsletter
- EMA website/newsletter
- If applicable: medicines advisory committees (e.g. …)
- Medical journals
- Company representatives
- A mobile phone app
- Blogs
- Other, please specify…

Screen 10 End of the survey

Thank you for your participation.

32. **We would be grateful for any additional comments you may have on how safety communications could be improved**
    [……..]
33. **If the results of the survey are published, would you like to receive a copy of the publication?**
    If yes, please also fill in your e-mail address below
    - Yes
    - No
34. **Do you want to participate to win a … coupon for …?**
    If yes, please also fill in your e-mail address below
    - Yes
    - No
35. **Please leave your e-mail address if you answered yes to one of the questions above. The e-mail address will be saved separately from your answers.**
    [……..]