

WEB-RADR WP 3B STUDY RESULTS

User-based evaluation

Study 1. Qualitative evaluation of a mobile app to assess side effects

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1 Introduction

1.1 Purpose of the document

The purpose of this document is to present the results of the qualitative study of the Work Package 3B team.

1.2 Version history

Table 1. Version history

Version	Date	Comments/Changes from previous version	Authors
1	28-8-2015	First draft manuscript	WP3B team
2	15-9-2015	Second draft	WP3B team
3	16-10-2015	Results added	WP3B team
4	29-10-2015	Discussion added	WP3B team
5	13-11-2015	Methods + results of each country completed	WP3B team
6	30-11-2015	Revised version based on comments and suggestions after F2F meeting and TC	WP3B team
7	04-12-2015	Agreement on changes -> final version	WP3B team

1.3 Definitions and abbreviations

For definition and abbreviations in this document, please refer to the WEB-RADR Definitions and Abbreviations Document.

2 Introduction

2.1 Background

Reporting of adverse drug reactions (ADRs) by patients has been shown to be a valuable addition to the reports provided by healthcare professionals (HCPs) [1,2]. However, knowledge in the general population about reporting ADRs e.g. through the Yellow Card Scheme in the UK is limited [1]. It is widely accepted that new tools should be developed that facilitate reporting of ADRs by patients and HCPs. Intensive web-based monitoring of patient experiences with new drugs provides one such tool to increase the number of reported ADRs [3,4]. A mobile application or a so-called app provides another.

When ADR reports or findings from clinical trials result in the identification of a new and important drug safety signal that information does not always reach the HCP or affect his clinical behaviour [5,6]. In the EU, important new safety issues are primarily communicated by sending paper-based warning letters by the Marketing Authorisation Holder (MAH) to HCPs; i.e. Direct Healthcare Professional Communications (DHPCs). DHPCs are increasingly sent in collaboration with the European Medicines Agency (EMA) [7]. Although many National Competent Authorities (NCAs) publish these safety-warnings on their website, this is not sufficient to reach all stakeholders as a recent study showed that Dutch physicians rarely visit their NCA website [8]. In addition, the

European Federation of Pharmaceutical Industries and Associations (EFPIA) is keen to establish new mechanisms and policies for these communications with a view to reducing future costs. This is why additional channels need to be explored through which stakeholders can be informed about drug risks. Ideally, risk communication is two-way and it is for that reason attractive that a tool for reporting ADRs also provides useful information for the user of the tool, such as existing benefit/risk information [9,10]. Especially when that source is considered trustworthy, information may be more readily accepted [8,11].

Still, it is largely unknown how the target populations of patients and HCPs value a mobile app for both reporting ADRs and as a source of drug safety information. HCPs may not always have the same needs regarding safety information as lay people [12]. A more sophisticated language, or/and references could be given to scientific background information, when communicating to this collective [13]. Also, large differences can be expected in how much a mobile application will be used between patient groups; e.g. younger patients, highly-informed patients (e.g. those with an orphan disease, who belong to a powerful patient community) or elderly patients with often multi-morbid disease (e.g. those with heart failure, type II diabetes mellitus). Actually, it was suggested by the EURORDIS patient platform, that due to the relevance for rare disease patients, more information about off-label treatments could be provided. Format and wording may affect the response to risk information by HCPs [14]. User-friendliness, wording and format should be attuned to the target audience not only by considering health literacy but possibly also visually-disabled patient populations. Another challenge is how to get a mobile app adopted by the larger public.

In this project, a mobile app to report ADRs **and** to provide ADR information – i.e. *two-way risk communication* – has been developed. Four studies will be conducted to assess potential barriers and facilitators of a mobile app of two-way risk communication, the impact of wording and format on the usability of an app, and experiences of actual users of the developed app. This document provides the results of the first study.

2.2 Purpose

The primary objectives of this first, qualitative study were:

- to explore patients' and HCPs' needs and preferences for a mobile app on two-way risk communication (what are facilitators and barriers for using a mobile app on two-way risk communication);
- to explore patients' and HCPs' perspectives on such a mobile app prototype.

3 Methods

The study was conducted in Spain, France, the UK, the Netherlands, Portugal and Sweden. In each country, the needs and preferences of a mobile app for two-way risk communication were assessed. Different methods were used across the countries (see table 2).

3.1 Population

The study focused on HCPs and different patient populations across the participating countries (table 2). Below, an overview is given of the included type of patients and HCPs.

The following type of patients were included:

Patients with an orphan/rare disease: In general, patients with an orphan/rare disease are highly informed about their disease/treatment. Therefore, their preferences and needs for a mobile app were expected to differ from the general population. In addition to patients, *caregivers of such patients* were included.

Adolescents: Adolescents often use mobile apps and are expected to have different preferences and needs to the general population.

Patients with type 2 diabetes (T2DM): Patients with T2DM are often elderly patients with multi-morbid disease, which increases their risk of experiencing ADRs. In general, elderly patients have limited experience with mobile apps. Due to these factors, this patient population was of interest for exploring preferences and needs for a mobile app.

We selected HCPs serving these populations; i.e. professionals related to patients with a rare disease, paediatricians, hospital doctors and pharmacists for adolescents, and GPs, internists, pharmacists, and nurse practitioners for patients with T2DM. In addition, the opinion of pharmacovigilance specialists was explored since their opinion may differ from the opinion of healthcare professionals. Participants were recruited through different channels (table 2).

3.1.1 Inclusion criteria

Study participants had to be in the possession of a smartphone or tablet and they had to be able to use such technology. A specific inclusion criteria for patients was that they had ever experienced (or detected, in case of caregivers) an ADR from any drug they (or their children) had used. It was not necessary that they ever reported the ADR.

3.1.2 Exclusion criteria

Patients and HCPs were excluded when they:

- could not speak/read/write the local language;
- did not give informed consent or a parent did not give informed consent (in case of adolescents aged ≤ 16 years);
- did not have a smartphone or tablet or could not handle apps on these;
- were aged < 18 years (not applicable in the study with adolescents).

3.2 Study design

A qualitative study design was used. Focus group discussions were conducted in most of the countries. The other qualitative method used was face-to-face interviews.

3.2.1 Patient demographics/other baseline characteristics

Patient and HCP characteristics were recorded on the consent form. For patients, the characteristics that were asked for were their gender, age and education level. HCPs were asked about their gender, age and profession.

3.2.2 Variables of interest

The study explored 1) patients' and HCPs' needs and preferences for a mobile app on two-way risk communication, and 2) their perspectives on such a mobile app prototype. The qualitative study contained three steps (adapted from [15]):

Step 1. Introduction: e.g. an outline of the program of the study was given and participants completed the consent form.

Step 2. App for ADRs: Discussion about an app for ADRs and about two-way risk communication in general using a semi-structured interview guide. Questions in this interview guide focused on facilitators and barriers to increase the participants' intention to use a mobile app for ADR reporting. Themes that were discussed are:

- Reasons for reporting ADRs (e.g. when do people report?);
- Opinions about receiving risk information;
- Positive and negative aspects of an app to report ADRs;
- What aspects in such an app are needed to be useful;
- When participants would use such an app;

- What should be done by whom with the entered information.

Step 3. Opinion about prototype app: Participants used the prototype app on a tablet/phone provided by the researchers or they used their own tablet/phone. HCPs were asked to report a (fictitious) ADR whereas patients were asked to enter their own prescribed drugs and to report the ADR they currently experience or have experienced in the past. It was mentioned that these reports were used as test reports instead of real reports. The app was not available in all the languages of the included countries in the project. If a language was not available, the UK version could be used. This option was suitable for the study with HCPs. Another option was to use screenshots of the app in which the text was presented in the language of the country. In this case, the focus group leader presented the screenshots to the participants. This option was more suitable for the study with patients. After this testing, the app to be used for two-way risk communication was discussed using a semi-structured interview guide. Questions in this interview guide focused on the evaluation of the mobile app prototype. The following themes were discussed:

- Positive and negative aspects of the mobile app prototype;
- User-friendliness of the app;
- Usefulness of the app and options to improve usefulness;
- What participants expect after reporting an ADR.

The themes that were discussed in step 1 and 2 were somewhat different for the focus group discussions with pharmacovigilance specialists conducted in Portugal and Sweden.

3.2.3 Power assessment

Focus group discussions and face-to-face interviews were planned until theoretical saturation was reached at an overall level. This means that theoretical saturation was based on the whole project instead of individual country/population level.

3.3 Data analysis

3.3.1 Analysis sets

The focus group discussions and face-to-face interviews were video- or audio-recorded and transcribed verbatim by one of the researchers. In most countries, two researchers analysed (a sample of) the transcripts separately and subsequently compared and integrated their analysis to extract themes from the data or describe the results. In Spain and Portugal, one researcher performed this analysis and data extraction.

3.3.2 Analysis of the variable(s)

The data were analysed using thematic analysis [16]. In the end, the analysed data was arranged according to a theoretical model. For facilitators and barriers to increase the participants' intention to use a mobile app for two-way risk communication, the Unified Theory of Acceptance and Use of Technology (UTAUT) [17] (Figure 1) was used as a theoretical model using a deductive (top down) approach.

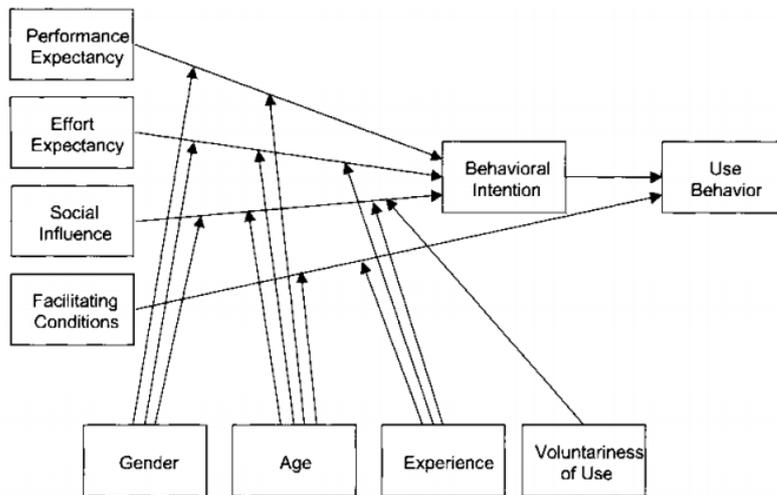


Figure 1. Unified Theory of Acceptance and Use of Technology (UTAUT) [17]

A description of four variables in the model is given below.

Performance expectancy: Degree to which an individual believes that using the system will help her or him to attain gains (perceived usefulness, extrinsic motivation, relative advantage, outcome expectations)

Effort expectancy: Degree of ease associated with the use of the system (perceived ease of use, complexity, ease of use)

Social influence: Degree to which an individual perceives that important others believe he or she should use the new system (subjective norm, social factors, image)

Facilitating conditions: Degree to which an individual believes that an organizational and technical infrastructure exists to support use of the system (perceived behavioral control, facilitating conditions, comparability).

The model describes the following variables as moderating variables: Gender, age, experience and voluntariness of use.

For each variable of the model, the data were analysed and arranged into subthemes. Differences among the researchers were discussed and resolved by the research team.

3.4 Ethical considerations

3.4.1 Regulatory and Ethical compliance

The workpackage lead is responsible to ensure regulatory and ethical compliance of this study, in accordance with regulations in place in the country(ies) where the study will be run. The general advisory board is responsible to ensure ethical adequacy of this protocol and related documents.

3.4.2 IRB/IEC

In each country, the study protocol was submitted to a local ethics committee who provided a waiver of full ethical approval.

Table 2. Methods per country

	Study design	HCPs	Patients	Recruitment of participants	Compensation	Ethical approval	Recording
Spain	Focus group discussions	HCPs in the focus groups will be included in the focus groups from the Hospital Sant Joan de Déu from Barcelona.	Patients with an orphan/rare disease and caregivers of such patients	EURORDIS will be recruiting all participants (patients, caregivers and HCPs) with the collaboration of Federación Española de Enfermedades Raras (FEDER) from Madrid and the Hospital Sant Joan de Déu from Barcelona.	Participants will be compensated for their time and travel, according to the established budget for the EURORDIS involvement in the IMI Web-RADR project.	Fundació Sant Joan de Déu	Audio
France	Focus groups discussions	HCPs in the focus groups will be included in the focus groups from EURORDIS database	Patients with an orphan/rare disease and caregivers of such patients	Patients and caregivers' identification was done in coordination with Alliance Maladies Rares, the French national alliance of Rare Diseases. French members of the Drug Information, Transparency and Access Task Force also contributed. The EURORDIS contact database contains 125 contacts within French patient organizations. HCPs, who correspond to the diseases of the patients, were invited as suggested by the patients themselves and using the Orphanet tools to search for experts/HCPs.	Participants will be compensated for their time and travel, according to the established budget for the EURORDIS involvement in the IMI Web-RADR project.	Inserm Institut national de la santé et de la recherche médicale	n/a
The UK	Face-to-face interview	Lead Pharmacist Medication Safety	n/a	Pharmacists were contacted In person or email. Information sheet/reply form were sent inviting participation in a focus group, Due to circumstances outside our control the focus group did not take place and a face-to-face interview was scheduled with the one pharmacist who could participate albeit within a very narrow timeframe.	n/a	UCL Research Ethics Committee	Audio
	Focus group discussions	Paediatricians Hospital doctors	Adolescents	Adolescents aged 11-18 years old were approached through Young People Advisory Groups (YPAGS) who share their views/comments on medical treatments and health research. Information leaflets/sheets and consent forms were sent to parents and adolescents inviting participation in a focus group. Paediatricians and pharmacists were contacted in person or by email. Information leaflets and consent form were sent inviting participation in a focus group.	Adolescents were compensated travel expenses and refreshments/lunch for participating in the focus group. A thank you letter was sent to each adolescent following the session. Paediatricians, hospital doctors and pharmacists were not offered any compensation.		

The Netherlands	Face-to-face interviews	General practitioners Internists Pharmacists Nurse practitioners	Patients with T2DM	Patients: Letters send to patients via pharmacists, direct contact to patients from previous studies, article in journal (GezondNu) advertisements on the internet: http:// groningen.dvn.nl/nieuws ; www.lareb.nl ; https://www.diabetesfonds.nl/help-mee/andere-manieren-van-helpen/meedoen-aan-onderzoek HCPs: Google search for e-mailaddresses of professionals in Groningen -> direct contact via e-mail.	HCPs received a voucher of €75,- for their participation. Patients received a voucher of €50,-.	University Medical Center Groningen	Video
Portugal	Focus group discussions	Pharmacovigilance specialists	n/a	Pharmacovigilance specialists' identification was done with the collaboration of a local association APREFAR (associação dos profissionais dos registos e regulamentação farmacêutica), it is a local association from professionals in regulatory affairs and pharmaceutical legislation. 15 PV specialists were invited via e-mail and 5 have attended to the focus group. The informed consent was signed by all of them.	n/a	n/a	Audio
Sweden	Focus group discussions	Pharmacovigilance specialists	n/a	The participants were recruited from a pool of active members in the Pharmacovigilance network of LIF (Läkemedelsindustriföreningen) which is the trade association for the research-based pharmaceutical industry in Sweden.	n/a	n/a	Audio

T2DM = Type 2 diabetes mellitus; HCP = healthcare professional

4 Results

In total, 9 focus groups and 13 interviews were conducted in which 28 HCPs and 50 patients participated (table 3). Of the participating HCPs, the age ranged from 29 year in the UK to 60 year Spain. Most of the HCPs were female (range from 50% in the Netherlands to 100% in Sweden). The age of the participating patients ranged from 11 in the UK to 67 in Spain. Most of the patients were female with percentages ranging from 57 in Spain to 77 in the UK.

Table 3. Descriptive statistics per country

	Spain (rare diseases)	The UK (adolescents)	The Netherlands (type 2 diabetes)	Portugal (PV specialists)	Sweden (PV specialists)
<i>HCPs</i>					
N groups / interviews	1/0	1/1	0/8	1/0	1/0
Total N	5	8	8	5	3
N per profession	Medical doctor: 4 Biologist: 1	<i>Focus group</i> Paed: 2 Snr Paed: 3 Hosp Snr Dr: 1 Hosp Junior Dr: 1 <i>Interview</i> Pharmacist: 1	GP: 3 Internist: 3 Pharmacist: 1 Nurse pract: 1	5	3
N females (%)	3(60)	6 (75)	4 (50)	4 (80)	3 (100)
Median age (range)	51 (42-60)	35 (29-55)	48.5 (33-58)	39 (31-55)	
<i>Patients/carers</i>					
N groups / interviews	1/0	4/0	0/4	N/a	N/a
Total N	7	39	4	N/a	N/a
N females (%)	4 (57)	30 (77)	3 (75)	N/a	
Median age (range)	50 (33-67)	15 (11-18) + 11 did not state age but are between 11-18 years (mean=14.4)	51 (43-64)	N/a	N/a
Education (%)				N/a	N/a
Lower education	-	4 (10)	-		
Middle education	4(57)	30 (77)	2 (50)		
Higher education	3(43)	-	2 (50)		
Other	-	3 (8) Left school 2 (5) not stated	-		

HCP = Healthcare professional; GP = General practitioner; Paed = Paediatrician; Snr Paed = Senior Paediatrician; Hosp Snr Dr = Hospital Senior Doctor; Hosp Jnr Dr = Hospital Junior Doctor; PV specialists = pharmacovigilance specialists; Nurse pract = Nurse practitioner

4.1 Results Spain

4.1.1 Patients

4.1.1.1 Step 1. Introduction

This patient focus group consisted of 3 men and 4 women, divided in 3 caregivers and 4 patients. Therefore, they were all closely related to rare diseases. They were also experienced in the side effect, concept and have ever experienced a side effect. None of them have ever notified any adverse reaction to medication through any channel available, besides going to the doctor and reporting the episode to them.

4.1.1.2 Step 2. Discussion

To the question “What would make you report a side effect via a mobile app?” the group agreed in that needing information about their physiological condition is the main motivation to use tools like the proposed app. For rare disease patients, possible networks focused in providing information are strongly relevant in their lives. And, having a tool like the Yellow Card app could help them to keep updated any moment and to be aware of the different diseases possible evolution, as they assessed during the focus group.

The participants also commented different situations which are problematic in their routine, and having an app with these characteristics could help them avoid those problems. The most repetitive arguments were:

- to ease the path for them to update doctors about their specific situation between follow up visits.
- to have a quick and accessible source of information about the possible impact of the side effect on their concrete physiological situation.

It was also mentioned that the app should be able to classify the patients according to their disease, or even make a distinction for Rare Disease Patients. Patients and caregivers highlighted that the app must have this option because some sorts of medications could have a different physiological impact according to a specific disease. And collected reports should be contrasted between people under the same diagnose. After these clarifications, the whole group agreed in the utility of making side effects reports through the app.

When referring to what could prevent the users to make a side effect report via a mobile app, participants were mainly concerned about the management of the personal information provided, either when signing in the app or when reporting an adverse reaction through this via. On the other hand, the group also wanted to know how the collected information from the reporting activity will be handled, and therefore questioned the quality of the information the app is able to provide as a feedback from their own report. In consequence, the quality of the information became a need for the participants to find the app reliable for the intended use.

Participants also assessed that they would never use this type of app if it wasn't for their personal situation. Rare disease patients are strongly involved in any type of source providing information about either their concrete disease or rare diseases in general. And they will never use this app to report a side effect if their physiological situation was standard, because reaching the doctor would be the first and only option.

During the discussion, participants highlighted the features they would like to have in the app in order to make it more useful for them. As mentioned above, rare disease patients and caregivers proposed to make a differentiation between types of patients. On the first place, the group decided that three categories should be offered to the user when signing in the app: HCPs, patients and rare disease patients. But as the discussion continued, their final proposal was to

offer the user, if patient, the chance to be classified into a diagnosed disease either rare or not. Making this feature opened for common chronic diseases. Participants came up with this conclusion because having a physiological condition makes the person to be under a treatment (drug treatment), and cataloguing the collected information under such parameters, might help to identify not only new side effects faster but also possible interactions between medicines.

Additionally, these patients and caregivers were looking forward to link the information they add to their app profile and their clinical file. Participants concluded that making such link, the efficiency of follow up visits to the doctor could be increased. Because, every time the doctor reaches the clinical file, it will always be updated from the patient perspective.

A brief discussion was maintained between participants about how relevant is for potential users the level of the language used because medical vocabulary can become significantly confusing. Besides such discussion, one of the participants expressed how important this tool could be for the pharmacists and how pharmacies should be involved in this process of side effects recognition and report. Because such offices, in Spain, are one of the most common and quicker places to go when having any question about drugs. The rest of the group strongly agreed with her.

Rare disease patients and caregivers would like to be updated on several fields according to their disease and/or medication (when possible): treatments being applied (either being experimental or not), news concerning their personal medication (either if it is a chronic treatment or a punctual solution), and receive feedback about the reports done by other people in the same situation they are (same diagnose, same drug treatment...).

Nonetheless, participants showed unconformity with how the feedback could be provided. During the discussion, it was frequently repeated how significant is for rare disease patients to collect and share information. For such reason, patients and caregivers thought about creating a data base to relate rare diseases and possible symptoms when being exposed to a medication. The whole group agreed in the great utility of the app, if the feedback provided could explain the following points according to the data collected through the reporting activity in the data base:

- whether or not the adverse reaction notified by the user is a normal physiological reaction to the medication, according to the patient's condition
- the severity of the reaction to the medication

All focus group participants described that when detecting a side effect, the most important thing for them is to have the necessary information to be able to evaluate the intensity and importance of the event. Therefore making these pieces of information cleared by the app and knowing the information received has been adequately contrasted and validated might help the user to evaluate the situation, and to have the appropriated reaction in order to avoid future consequences.

When confronting an uncommon reaction to a medication, rare disease patients and caregivers fell into an unknown field, where any help is welcome. In this way the recognition of any side effect will prompt them to use the app immediately, according to most participants' comments. However, some members of the focus group pointed out that an app in such a sensitive situation is too impersonal. Once the patient is over or partially over the episode caused by the side effect, they may reach the doctor in first place.

On the other hand, patients and caregivers highlighted that the provided information by the app could be strongly relevant for HCPs and scientific researchers. Helping them identifying new adverse reactions to medicines, predicting the possible reactions of rare disease patients when exposed to new medication and warning about possible unknown interactions between drugs.

4.1.1.3 Step 3. Power point presentation

During the screenshots presentation, participants revealed the following impressions:

1) It is needed to have an option to classify the patient either in a specific diagnosed disease or if not possible, the system should be able to recognize a rare disease patient from the personal data provided by the user.

2) It could be helpful to link the clinical file of the patient to the data in the patient app profile. Being the doctor or the responsible group of doctors, besides the patient, the only ones able to access to such data.

3) When reporting a side effect, the option of “death” in the consequences of the side effect must be removed and if necessary expressed in a different wording.

4) Users have to be able to personalize the type of information they want to be updated about: news from drugs of their interest, experimental treatments related to their disease, reports related to their personal medication...

5) Participants proposed the inclusion of experimental medication (biological drugs, biosimilar drugs...) and non-medicinal treatments (treatment which do not involve the use of drugs) in the app to either keep updated in these options or to be able to report a side effect on them.

After making a medication side effect report, participants would like to receive from the app any related reports to the one they just have done. But only if those reports were sent by individuals in similar conditions to them. Additionally, participants were interested in knowing the status of the notification to the competent European authorities of their report.

The group described the app in general as useful, interesting and potentially positive impact in the reporting adverse reactions to medications process, and in the efficiency of spreading information about medication safety in each level of the society (patients, caregivers, relatives and HCPs).

4.1.2 Professionals

This Healthcare Professionals (HCP) focus group consisted of 3 men and 3 women, divided in one pharmacist, one biologist and 4 specialists.

These HCP are members of the Hospital Sant Joan de Déu, in Barcelona. The main activity of this hospital is the treatment of rare or minority diseases, especially on pediatric patients. Participants selected for the focus group have a detailed knowledge of what an adverse drug reaction (ADR) is, are aware of the national and European pharmacovigilance system and in consequence are closely related to the official protocols established to report an ADR.

Every HCP included in this event have used, at least once, the actual reporting ADRs tools established by the AEMPS.

4.1.2.1 Performance Expectancy

Motivation to report

Healthcare Professionals (HCP) described the functions of this app as useful and efficient. In addition, they liked the direct and immediate access to quite relevant information when facing an adverse reaction to a Medicine.

Two fields were highlighted by this HCP as being the most relevant when using this developing tool: Patients under a Clinical Trial and patients under several medicines, easing in this way the quick detection of unexpected reactions to the drug under research, or possible interactions between the using drugs.

Prevention from reporting

Spanish HCP do not have any official prevention from reporting, as the law describes this activity as part of their duties. Nonetheless, participants had some opinions about the system proposed by the app to make an adverse drug reaction report.

HCP agreed that this tool may not be useful when reporting incidences develop by medicines rarely used. And therefore, this system is neither efficient for every type of patient. They may need to closely select patients and diseases to be included in this tool, in order to optimize the app functionality and provide the attention requested by the patient in the best way.

Participants also agreed in that, especially when suffering from a rare disease, the app might be a tool too cold to be used. Patients need to reach their personal doctor when going through a situation such as developing an adverse drug reaction (ADR).

HCP would like this system not to be one more source of information; they would like to have one official tool to make the reports needed and avoid receiving the same pieces of information through several sources. In this way, when referring to the patient, HCP couldn't see the point of this tool as a way to ease their lives. Patients need to fill the report through the app and then go to the doctor anyway to check how serious the ADR is and to find a solution for the problem.

Reports

Apart from the fact of who is reporting an ADR, all participants agreed that the essential data provided by the app feedback should be: when were similar cases reported, number of similar cases reported, and category of the ADR (to be able to make a balance of the emergency developed by the ADR).

When the patient reports

All participants were solid in that the reports made by rare disease patients should be validated by a HCP before sending it anywhere else.

In the same way, they thought it might be helpful to receive the information provided by the app when a patient, under their responsibility, reports an ADR.

If the patient reporting belongs to a Clinical Trial, HCPs were very interested in receiving a notification of such report in real time. In this way they could have enough time to register such report, notify it themselves and react to help the patient as soon as possible. If the patient reporting suffers from a rare disease, HCP agreed that they would also like to receive any report made by the patient as soon as possible in order not to miss any kind of data. Because most medications used by these patients are not common treatments, and therefore the notification of every step could help to avoid any kind of problematic situation.

In case of common patients, participants assessed that the main goal of this function in the app should be to make sure that the useful information provided by the app as a feedback, reaches the right person in order to provide an official tool for the HCP to help on time the patient who has just notified.

When the HCP reports

When a HCP reports, they expect to have a feedback from the app exclusively when the conclusions about the ADR or medical interactions reported are new or not previously described, relevant or urgent.

News

HCP were interested in receiving by this app just ultra-important information about the drugs of their interest. They would never be interested in this tool if the updates provided are duplicated by any other official media. Receiving this updates should be easy and quick to select in the app.

Additional functions

As previously mentioned, participants suggested that the notifications made by patients should be validated by a HCP before further movements. Therefore, reports should be storage in the users' app profile, creating a track of every report made. In this way, when attending to the HCP visit, they will be able to validate only the relevant reports and send them to the European Authorities. Another option suggested was to send the report to the HCP who belongs to the team in charge of a specific patient, validate the report if needed and send it or not to the EMA.

This data route proposed by the participants of this focus group could help to strengthen the on-line relation between patient and personal HCP.

It was also mentioned the increasing utility of the app if it could provide to the users valuable and common information to ease the drugs/treatment intake: posology, notifications as reminders of when to have the medication, how to take the medication (with food, before food, with water/milk/juice...).

4.1.2.2 Effort Expectancy

Usability

When discussing about how easy was to use the app, HCP highlighted how rare disease patients and/or caregivers trust ONLY in their personal doctor, and even some times patients are able to trust in a team of professionals looking for their specific situation. Therefore, participants didn't feel very confidence about the usability of this type of app due to the low confidence these patients have in a not related system to their health problem. Rare disease patients may consult their doctor or team of professionals in charge before using such an app with the goal functions.

Ease of use

According to the discussion during the focus group, HCP assessed that to ease the usability of the app, rare disease patients should be identified in their personal profile and linked to the profile of their personal doctor or HCP in charge of their follow up.

In this way, every ADR reported and/or consulted by the patient, or any possible interaction between the using medications could be notified to the HCP in real time and a solution to the problem can be provided as soon as possible.

App appearance

According to the participant's opinions, the appearance of the app is not friendly enough, asks for too much information either when signing in and when reporting in a form format, and uses a vocabulary not reachable for every kind of public. All these characteristics make the app not very attractive to the user.

HCP think that moving along the app should be based on intuition, therefore introducing images to click on, or using a different vocab than the official definitions established by the health authorities might help improving the app first impression and in consequence easing the use of it.

As a last instance, the option offered by the app of “death” as a consequence of the ADR reported caught all the attention of the HCPs participating in the focus group. They all agreed in that is a scary term for the user, and that the wording have to be carefully chosen before offering such kind of options.

4.1.2.3 Social Influence

Environment

HCP agreed that there are two concrete situations which prompt people reporting in a higher frequency, and where patients and caregivers do really provide a significant help in the pharmacovigilance field. These two situations are when the patients are in a clinical trial and when is a rare disease patient who needs to be closely controlled by a HCP.

Nonetheless, these types of patients already have tools available to provide connection to their doctor(s) or group of professionals when needed. And, according to the participants, this tool might offer a service to a need already covered by the Spanish system.

Data flow

HCP showed a complete confidence on the system regarding the safety of data both provided to the app and provided by the app. Such confidence was based on the official authorities regulating this project.

Although, during the discussion, participants were interested in the data flow when reporting and in making clear that HCPs need to also receive the relevant information about a report made by any of the patients under their supervision as soon as possible, in order to provide the best solution in the most efficient way.

Treatment adherence

HCP were concern about the availability of the information. Having access to every piece of information about a disease, and about the medicines part of the treatment suggested by the doctor could decrease the treatment adherence.

Rare diseases do not have many options for treatment in most cases. And professionals showed worry about possible patient reactions when reading such kind of information and not being able to give any alternatives.

4.1.2.4 Facilitating Conditions

HCP made the following suggestions to optimize the app options and provide a more efficient service to the users (patients, caregivers or HCP):

- Patients should be identified by categories. For instance: part of a Clinical Trial, Rare Disease Patients...
- People related to Rare Diseases should have a subcategory on their own, where patients, caregivers and HCP were included and with the chance to link their profiles between them
- A diary of the user: where to write everything related to the treatment followed (useful for patients on clinical trials), where to create personalized alerts (such as for the timing, posology, news about the medication of interest), receive pieces of advice on how to take the medication (before meals, after meals, best foods to improve the drug absorption, possible interactions with other medications...)

- Report other type of problems related to the drug such as organoleptic characteristics, or any other issue which could create an influence on the treatment adherence
- Based on that the technical files of the drugs are not useful when treating children/newborns, the app could provide a function to provide efficient information about how to use medication when dealing with this type of patients

4.2 Results France

France was not able to conduct any focus group discussion or face-to-face interview.

The protocol had been approved by an IRB, invitations to patients and professionals were sent, meetings had been planned but due to unexpected circumstances and cas-de-force-majeure the researcher was not in a capacity to run the focus groups.

4.3 Results the UK

4.3.1 Patients

Four adolescent focus groups were held in different locations across England.

A total of 39 children aged between 11 and 20 years old attended the groups. Consent to participate and be audio recorded was obtained from either the adolescent if they were 17 years and above or from their parent if 16 years old and below.

The audio-recorded focus group sessions were transcribed verbatim. Relevant topics of interest were derived from the transcriptions and coded. These coded data items were extracted and arranged into the following broad themes under the categories of the UTAUT model described earlier:

Performance Expectancy

- Motivators for using the app
- Barriers to using the app
- Who should see the submitted ADR reports

Effort Expectancy

- Wording and clarity
- Privacy, security and reliability

Social Influence

- Features
- Feedback/preferred information

Facilitating Conditions

- App presentation/appearance
- Data Tariff and storage

Each of these themes were examined and similar data items were further categorised into sub-themes.

4.3.1.1 Performance Expectancy

** Motivators for using the app*

Many adolescents said they would use a mobile app. Some, however, would use it not necessarily to report an adverse drug reaction but as a source of drug information. One child said she would use the app to see *“whether other people have experienced similar side effects with the same med.”*

Another child would use the app *“to see if it was a normal side effect.”* A few other children also commented to that effect, that they would use the app to check if the perceived side effect was common or *“definitely the side effect of the drug.”*

One boy said, *“I personally would use it before I take a medication as well to see what sort of side effects I may have in case it’s something severe I may not want to take the medication.”* This suggests the app could potentially influence compliance with taking medication and warrants further exploration.

The app was also seen as a form of reassurance with one boy commenting, *“It would help if you are sort of feeling side effects that are lower down the list, you would possibly be alerted to go to the GP*

and also if you are higher up then you would just accept that that's a common side effect." Another child added, *"so that you know what's not supposed to happen like your brain could be bleeding"*(girl).

One child perceived the app as a way to reduce the need for a verbal conversation with their health care professional, particularly if the condition was seen to be *"embarrassing."* Another girl agreed saying she would use the app if it were about an emotional problem and it was less embarrassing than talking to a healthcare professional. There may be ramifications for an unintended effect of the app contributing to young people avoiding direct engagement with their health professional, particularly if this is related to mental health conditions. This is another area that might need further exploration.

Many adolescents viewed the app as generally a good idea, that most people would find it easier than any other form *"now it's like modern day you wouldn't want leaflets about side effects"*(girl). Having the app to hand was seen as *"one of the most successful ways to write down the notes. Most people carry their mobile, (you) don't really need pen and paper, can do it straight away as soon as you get the side effects."*

Another reason given for using the app was if they couldn't access their regular healthcare professional or general practitioner, for example at the weekend. They viewed an app to be quicker in terms of communication and readily available *"like 24/7."* A number of young people said it was important the app was easy to use.

Being able to personalise the app was seen to incentivise use. That the app should be different from what was already available was also important. Others said that they would use the app if it was bright and colourful. *"If app was colourful and had pictures. If it was just pages and really bland like black and white writing and I didn't (sic) want to read it"* (Boy). Another girl commented, *"I use my apps because they are fun, they're creative and I like to use them. If I didn't like doing them and I didn't enjoy it I would just delete it."*

Many adolescents said that if the app was *"endorsed by a doctor then [it] would be used a lot."* *"If a doctor recommended having it whilst on a medicine then basically I would but if not I wouldn't really think of it myself."*

Others said they would be more likely to use it if *"it did something else"*, such as talk to friends as well as reporting side effects. This topic is further discussed in the features section.

Another incentive for using the app would be if the reported information benefited others, *"If I knew that the app that I was inputting all this information would benefit other people as well, then I would."*

Another girl would use the app if she received a response and others said people would be more likely to use the app if it was free.

** Barriers to using the app*

Several young people asked how difficult or how long it would take to complete an ADR report and this appears to be a determinant of whether the app would be used. The following comments illustrate this barrier, *"are all these pages ones you have to fill in when reporting a side effect? Because it might put some people off."*

"They want people to use this app but are asking too many questions which would make people give up."

"If I had to input all the information, if it took a lot of time I don't think I will" [use it].

"If it's hard to use we are less likely to use it."

Queries as to whether there was a time limit to complete an ADR report were raised by a number of young people. In some other apps if information is not entered quickly they could be timed out and have to start again. This was area of frustration for young people, particularly if lots of information was asked.

Additionally, the severity of the side effect would determine if the app would be useful, *“if your reaction was very severe or life threatening you wouldn’t waste time putting it into an app.”*

Barriers related to technology was another reason young people might not use the app, *“if your type of technology doesn’t have the software then we might not be able to use it.”* Themes related to data tariff and storage are discussed later.

** Who should see the submitted ADR reports*

Doctors and healthcare professionals were the preferred persons to view submitted ADR reports; one reason given was that information wouldn’t need to be repeatedly submitted. One child said, *“I’d just rather the information went to the people like the drug companies or you [researcher/HCP].”*

However, one girl expressed her preference to choose whether her GP could see her information and to be able to delete the report. Another girl said, *“should be able to turn off any time you want. So if you’ve like, I’m just feeling it I put it into my app but probably nothing serious so I don’t want my Dr to know and you should be able to turn off.”*

One boy said, *“would be good to see if a couple of other people have same thing as you –should have option to make your report public and you talk to them about what’s happening.”*

“I think that’s good you can feel a bit more comfortable that you’re not the only person going through those side effect and also maybe see extremes..oh ok my side effect isn’t as bad or is worse..maybe I should consult a Dr.” (girl)

Another girl suggested a *“sharing system then you could share it (the report) with people you want – parents would be an option.”*

Views were polarised about whether parents should be able to view the child’s ADR reports, generally older children preferred parents not to have access and younger children wanted parents to be informed.

4.3.1.2 Effort Expectancy

** Wording and Clarity*

Many of the young people in the focus groups wanted clarification on whether the symptoms they experience would be worth notifying or reporting. It appears that they were seeking reassurance their report would be valid. They expressed uncertainty about whether their experience of the side effect would be related to the medication if they felt unwell. They queried whether a common side effect of a drug should be reported and were worried at not being able to distinguish which would be causing the symptom if they were taking more than one medication. *“If you were taking 2 medicines at the same time how would you decide which side effect belonged to each drug?”* The key issue arising from this part of the discussion seems to be that young people feel they lack knowledge about medicines and what side effects or degree of severity was appropriate to report.

Some of the medical terminology was very difficult for the young people to understand, particularly those in the lower age range, e.g. 14 years and younger. One boy stated, *“it’s got advanced vocabulary”* while several girls commented that it was quite complicated and asked, *“what age*

group is this for?” and “the part that says would the reaction lead to any of the following confuses me!”

Many questions were asked about what certain terms meant like *“prolonged”, “concomitant”, “congenital anomaly”, “I know what head deformity is but I don’t know what NOS stands for”, “some people may not know what incapacity means”, “what if you don’t know it’s life threatening?”* Another child exclaimed, *“..some bits sound traumatic, like ‘life-threatening’ for a child. Filling that in oh my gosh I’d be thinking I’m going to die!”*

A few remarked that plainer language should be used, *“I just think it should be a bit more simple because different ranges of people are using this.”*

Lists of word choices were suggested as helpful since *“spelling words might be difficult”* and would help to standardise terminology *“a lot easier to have pre like inputted ones otherwise... the slang people use to describe things I think you’d find it quite difficult.”*

As with the paediatricians’ focus group, there was discussion about what the ‘strength’ field meant on the reporting page of the app. One young person commented, *“it’s a bit vague.”* There was also debate about the word ‘route’. *“Wait what is that, what is route?”* and *“what is a route?”* with a suggestion that the language *“could be simpler, like ‘how did you take the medicine?’”* Drop down boxes were suggested to facilitate easier entry of information, *“there should definitely be those [drop downs] for strength and for those [route] as well!”*

It appears some of the questions lack clarity, for example *“what do they mean ‘what else did you do?’ but you might not have done anything!”* Also some young people said they did not understand the question ‘Where was the medicine taken’ asking *“Does that mean where you bought it?”* There was also misinterpretation of the option to indicate if they were a health professional, *“I mean, your body doesn’t change whether you’re a physician or not.”*

One girl did not agree with the word ‘report’ and suggested it should be changed to ‘report symptoms’ because it had negative implications, *“it’s kinda like if someone made a nasty comment or something or someone was mean to me.”* Another girl commented, *“I’m not being picky here but I just noticed it says ‘has the medicine caused a similar reaction before’.. should be yes or no instead of ON or OFF.”*

The section where country input was requested also raised questions on why it was asked and also interpretation of its function with one child remarking, *“it’s a good idea as you may be on holiday or something.”* Other comments include, *“I don’t understand the address section. There should be a hospitals list too.”* Others in the group agreed with her comment. Someone also queried why they needed to give their initials, this question also cropped up in other groups. There was also some mild confusion with the word ‘Watchlist’ with one girl commenting, *“what are you watching?”* *“I don’t know if it’s linked to the news page. This is much more complicated.”*

** Privacy, security and reliability*

Several mentions of incorporating the NHS logo into the app came from the different groups. The general view was that if the NHS endorsed the app it was more trustworthy and secure. Some comments relating to this theme are:

“would look better if endorsed by NHS, recognisable as a health app,”

“should have NHS colours too, people will trust it more if they know it is from NHS,”

“it needs to have NHS on it otherwise people might think this is some dodgy guy.”

There were mixed views about receiving information from the app. On the one hand many young people liked the idea of having a forum to go to for information, on the other they were reticent as to whether the source was trustworthy.

“You might question the reliability of it, the sources of information, there should be a facility for telling them it isn’t recognised.”

“You can’t always trust these people on the forum.”

A number of young people wanted to be able to see other users’ reports but remain anonymous. One boy said that it should be anonymous, *“just in case people don’t want others to know they are taking certain medication.”*

To enhance security, all agreed that the app should have a login code or password or pin number so *“people messing around on your phone can’t log onto the account, so people can’t just get into it and send random side effects.”* A four-digit pin number was preferred for log on.

One boy questioned what information would actually be stored *“if it’s your medical information you need better security because people could just hack into it if the firewall’s not that good.”*

Four children agreed with the app storing their location with a condition, *“it’s ok if you can turn it off”*. One child was not sure if she would share her location.

Recorded messages were proposed as a means of delivering information on some common side effects of a selected medicine. However, one child stated she did not want this to be used to ask her more questions.

The issue with anonymity was raised several times leading to suggestions to be assigned a number instead of using their name. Some questioned the reason for using initials with concerns how people with the same initials would be identified, i.e. *“which ones is which.”*

Privacy was very important to the young people and a few said they wouldn’t give their postcode or use the app if *“I knew there was a risk of someone coming to my house.”* One child said she found it annoying to have to give her email address and another said she would not use her real name but *“put in a false name.”*

4.3.1.3 Social Influence

* Features

A number of ideas for preferred features on the app were suggested. Most young people liked the idea of a personal account or profile. One girl said there could an option to archive some of the information. *“You put in certain details you want to keep on the app for a long time but others you could delete.”*

A reminder to report a side effect or to take medication was also suggested a number of times. A prompt to report a side effect if the young person was on a certain medication was seen to make *“it easier for people to report.”*

Having a list of possible side effects relevant to the drug would also be useful, in addition to prompts to further questions to elicit any other symptoms they might not have thought to describe. In essence, many young people expressed high preference for a more interactive and responsive app.

The news section of the app generated less enthusiasm with comments such as *“seems like you’re giving us a lot of information,” “that’s very detailed”* and *“I wouldn’t care. The parents would be more interested in that.”* Comments were also made that there were too many medical terms.

Alerts were viewed by some young people to be useful if they were related to the medicines they were taking.

Chat forums

The idea of a chat forum to discuss their experiences of medicines and their side effects was put forward by a number of young people. Boys in particular favoured the idea of a chat forum.

However, having a forum does not necessarily mean young people would participate on it. One girl said it would be useful to see what people are saying about their experience of a particular medicine (a source of user information) without engaging with other users.

A forum was seen as a place to obtain advice, although some young people wanted this to be anonymous *“because it’s quite personal.”* One girl gave an example, *“if your weight affected the medicine you were taking that could be really awkward to put on app because it’s really personal.”*

One boy also suggested that it would be useful to have *“statistics of occurrence of people who have had it in the past to see how common it is or how likely it is you might have that side effect.”*

Buzzwords

One boy suggested an option to be able to change the settings on the app to specific age ranges *“so could more friendlier for kids in the sense you could have buzz words.”* He also said that for adults it could be more independent, this is have more free text options. A boy in another group also brought up the same term saying that there should *“buzzwords for different symptoms to describe how you’re feeling.”*

“Any side effects information on what could happen, how.. serious the thing is or information on what you’re feeling.”

Lists of different brand names were deemed to be useful.

Comparison of drugs

One boy asked, *“will it [app] be able to look at your drug history so that you could see whether or not drugs are affecting other drugs you’re taking so far...to show to a health care professional or pharmacist.”* This may indicate that some basic information of drug-drug interactions would be useful and ties in with the discussion earlier about what side effects should be reported.

Diary/calendar/reminders

Many young people from the different focus groups suggested a diary or calendar feature would give added value to the app. One boy says, *“like a diary of some sort and then you could be given information whether that would interfere with another or have effects that are unknown.”* One child also commented that it *“would be good if you could make a Dr’s appointment”* on the app.

An option to type in location to find their local or nearest GP or notification to pick up a prescription were incentives which would encourage use, although they also wanted *“to be able to search the medical condition and be private”* (be anonymous). Another child would like something to remind her to take medication and said she would use this type of app more with this feature, e.g. special ringtone or a visual like a text message.

Rating/sliding scale

There was a fair bit of discussion about a rating or sliding scale from 1-10 or a list of drop downs for medicines causing discomfort *“how badly you can put it”* and *“cause someone’s 5 could be someone else’s 10.”* A pain threshold was given as an example.

A timeframe to show when a report should be sent according to how serious the side effect was perceived was seen as very useful.

Categories/dropdowns/click options

To make the app a bit more attractive and encourage uptake, a dropdown list for reactions and symptoms to explain *“how you are feeling if don’t know what you’re feeling, if you don’t know how to describe it,”* generated wide agreement. One girl said there *“should be a setting where you can type in any drugs you’re taking e.g. if take inhaler for asthma, symptoms drop-down will only be applicable to asthma.”*

Another said that people find it easier when the words are there.

Click on and drop down options were put forward in all of the groups. These features enable faster completion of the report:

“got to be quick”,

“tick boxes rather than typing,”

“tick boxes for medications you’re on,”

“could have click on instructions and really really simple explanations...like little speech things next to each little link.”

“...and if you click on the drug then there’s a list of side effects and you click which ones you have.”

“...and another box just in case one side effect that you’re having isn’t listed.”

“I think to make it easier to the one or you don’t want to describe them you should have categories like rashes and stuff, so it ‘s not just a massive list.”

Alternatively the question *“did you mean?”* could be asked in case of misspelling *“because they (drugs) have really complicated names.”*

However, some young people said the information should be balanced, as too much information would cause anxiety. The recurring sub-theme of a drop-down choice list suggests that many young people may not have the vocabulary to describe their experienced symptoms.

Functionality over aesthetics was seen as more important to one child, *“not about making it attractive.. if you’ve got a condition then you’re going to have side effects, it’s about making it practical and useful basically.”*

A tick box to indicate pregnancy was also considered useful in the profile information.

Getting Drs to promote app

A few young people suggested advertising the app at GP surgeries and encouraging doctors to ‘like’ it. There was general enthusiasm for an option to “like” the app as with Facebook as that would encourage uptake. One boy said, *“get your doctor to set it up for you...so he supervises you...show you the ropes.”* Another child said a trial launch could be carried out with patients on certain medications by their GP or health care professional who would give them an access code to the app.

A number of times the question of why initials were required came up. The young people viewed this as repetitive and said it should come up automatically if it was already entered once in the profile.

Pictures/ presentation

A concern frequently raised by young people across all the focus groups was getting the spelling of the medicine right. The following are a selection of comments pertaining to this theme, *“would you have pictures of actual medicines, because of someone mistyped or something...it would be easier for them to tell if was wrong.”*

“would you search for brand or actual drug name?”

“you could have a...most common side effect for most common illnesses...so you don’t have to search it everytime.. if you’re always taking one medicine. You can favourite it.”

“would like pictures of drug when you click on name of drug.”

Three girls suggested bullet points as a way to make the information clearer. Three girls in one group said it would be useful to have a general overview of a drug and what it is used for.

One child asked why there was a separate link to information away from the app and thinks *“people wouldn’t be bothered to click on a link.”* Another girl said the comment about the link was quite vital as no one would click on it if it were not *‘straight on the app’*; two other girls agreed saying, *“that’s too much effort”* and *“yeah, people won’t do it.”*

An option for entering weight in both kilograms and stones was suggested as it was unclear which one the app was asking for. Also a request for an input box of how many times a day and dose the medicine is taken.

In response to a child’s comment that *“the app doesn’t feel that intuitive,”* a demonstration or *“a walk-through on using the app”* as with some games was suggested by others in the group as a solution.

4.3.1.4 Feedback/preferred information

A number of children stated they would like feedback about the reports, even if it were just an acknowledgment the report was received, *“short and sweet”*, or *“we don’t think it is harmful.”*

How soon a reply could be expected was raised and a quick reply was preferred with information on how to deal with the side effect and how long the side effect would last. A quick response after sending an ADR report was seen as a beneficial app feature.

Some concern was raised that a reply might come too late if the ADR was serious. They suggested that a serious ADR could be flagged up on the GP’s database to contact the patient.

One child said that regular updates or alerts would be *“really useful because you’d wanna know what’s going on with that medication.”* Others however, said that once they felt better they *“might not be bothered by that point and don’t need it anymore.”*

One girl suggested being able to view other users’ reports to compare dosages. There was disagreement about this and some young people said that it was more important the app sends information to the person who submitted the report rather than allowing the reports to be used in that way. However, another child said she would still like to know if others had the same side effect.

Most young people preferred feedback from a doctor, nurse or health care professional. One boy said receiving a feedback message on the app would be easier than email. Another child suggested a pre-set response could be sent when an ADR report is received but others countered this saying it would be less personal.

4.3.1.5 Facilitating Conditions

** App presentation/Appearance*

There were mostly positive views about the general appearance of the app. The young people liked the design saying it was nice, clean, simple, professional, and did not look too complicated. They also liked the colour of the app and one child said it was *“very chifty”*, meaning child-friendly.

However, others thought the app looked *“very boring. It’s all letters and numbers.”* They suggested an option to change the font size to accommodate the visually impaired as some found it *“hard to see the writing on the boxes.”* One child said *“it’s good if you are an adult, if not then it is hard. My mum would love this app.”* Another agreed saying it *“looks like a parent’s kind of page.”*

More pictures were preferred throughout the app. With reference to the appearance of the watchlist page one child said, *“it’s good. At least it’s got a picture on it. It’s not even a good picture, but at least it’s a picture.”*

** Data tariff and storage*

Questions were raised about whether Wi-Fi was required to use the app and several children said it was not always easy to access Wi-Fi. One suggestion was to be able to add the report without Wi-Fi then transmit when access was available. They were also worried about forgetting what happened if they were not able to report the side effect at the time of occurrence or fairly soon.

There was also discussion on how much space or memory the app would use. Perception of the app taking up space on their device or not being used often was a disincentive, *“I’m not sure it would get used that much so I’m not sure I’d want it on my device cause it would just be waste of space.”* One child suggested an option of just downloading information about the medicines being taken to reduce the size of the app.

There was agreement that information overload should be kept to a minimum and only necessary information sent out.

After reviewing the screenshots of the prototype app, one child commented that it did not look as helpful as it could be *“you give information but you don’t get much out of it.”*

Miscellaneous

There were a few questions and comments that do not quite fit into the above themes but may be of interest. The young people briefly discussed what age groups would have a mobile phone. Some said they received their first phone aged 9 – 11 years old, others at age 12 and above. Therefore many young people will be familiar with mobile technology at a very young age and wouldn’t find it difficult to use an app. However, young people thought that adults might not find it so easy, *“someone in the older generation might find it hard, not me.”*

A few children said they were only allowed access to their mobile phone during break or lunchtime so reporting a side effect during school hours would be difficult. They asked if a doctor’s note was required to access the app to report a side effect during school hours. Further discussion generated advice to see the school nurse if side effects were affecting them during school hours.

Summary

Many young people across the four focus groups engaged very well with the sessions and liked the idea of the app. The collective key issues raised are about the app being relevant to their age group and fit for purpose, particularly in terms of visual presentation and language, being authentic (i.e. different from what is already available), and assurance of privacy and security. Themes and suggestions overlap in some areas. All the groups said they would be interested in getting feedback about the end product and some would like to be involved in the design of the app.

4.3.2 Professionals – focus group

Seven HCPs attended the focus group, which was held at University College Hospital, London. Three attendees are senior paediatricians; two are junior paediatricians, one a senior hospital doctor and one a junior doctor. Initially more participants had attended, however, due to a clinical emergency some were called away.

Following the focus group the audio was transcribed verbatim and coded. A total of 78 items were identified from the transcript. Each item was sorted into topics and a common theme was applied to groups of similar topics.

The following themes were identified under the categories of the UTAUT model:

Performance Expectancy

-Action post-reporting

-App presentation/additions

Effort Expectancy

-Accessibility

-User experience

Social influence

-Degree of severity of ADR/Perceived patient understanding of ADR

Facilitating Conditions

-Data tariff/space on device

-Information overload (subthemes - filtering/validation/relevance/reliability)

4.3.2.1 Performance Expectancy

** Action post-reporting*

On asking what HCPs expected to happen after they send an ADR report the immediate response was to ask who would pick up the information. They were then asked who they thought should pick up that information. A key comment was that it should be someone who could act to reduce the side effect like the MHRA or a regulatory body should pick it up. Another HCP reiterated, *“it’s something you need to act upon so you can have a set of clinical outcomes”*.

Feedback to the patient about the ADR report was seen as important, in addition to receiving feedback as HCP’s. They would also like to know if their particular side effect had been reported by another HCP. Participants said they would also want to know about the side effects their patients were reporting on the drugs they had prescribed, *“if patients were reporting ADRs of drugs I’d started it would be useful to know. Definitely”*.

One concern was that patients might report the ADR through the app and take no further action, *“don’t want them to just report it and then carrying on with their life...don’t want it to be a replacement for seeing their HCP”*.

There was general agreement a useful feature would be linking the ADR report to the patient’s electronic records which could then be accessed by the patient’s HCP.

Receiving feedback about the outcome of the ADR report was also expressed as an incentive to use the app. This point generated discussion among the group that they would want something in return for using the app to report an ADR – for both patients and doctors, *“yes completely, because*

if you're sending your news, if you're spending your time, you're spending your data then you want something back!"

** App presentation/additions*

Participants liked the overall presentation of the prototype app describing it as "clean", "nice and clean", although the discussion raised questions about the clarity and complexity of language in some areas.

One participant asked, *"what is the difference between strength and dosage, I'm not sure whether that is obviously clear"*. Group discussion eventually resolved this question, *"yeah, yeah is it 240mls in 5mls of paracetamol or 120 cause there's two different suspensions?"* However, others pointed out that a layman or a young person might not know and *"often in children, cause it's in suspension the parents will say 5ml but then have to find out the strength of the medication"*. A drop down menu of different strengths of medication was suggested and this generated a positive response, *"would make a big difference, would clarify yeah, that would make sense."*

The meaning of one phrase in the app caused some confusion in the group. *"What is equivalent to suspect stroke or concomitant?; "I don't know what that means"; "I suppose it might mean is that the drug you wanted to report?"; "that's unintelligible to a room of exceptionally intelligent health professionals!"*.

A different interface for patients and HCPs was suggested as the current prototype was seen to be *"a bit complicated for a patient"*. This was generally agreed by most of the group, *"fundamentally...view is this app has to be a different one for patients and HCPs, also they are for different aims and purposes"; "use of app is very very different, patient is specific only for drug they are on, HCP wants to know about larger range of drugs"*.

Making the process of filling in information easier by having more drop-down menus and less free text was proposed as a feature to encourage app use.

Another clarification to the language was suggested for the outcome section, *"add life or limb threatening rather than just life threatening"*.

4.3.2.2 Effort Expectancy

** Accessibility*

Under the accessibility theme HCPs raised questions about the ease of mobile app use. This came up 3 times during the short session.

Participants said it was a good way to report side effects and that it would be *"easier to find the drugs"* they would be looking for.

One participant questioned how easy it would be to enter the information. Another commented, *"not everyone will have a mobile phone"*.

** User Experience*

Participants tended to deviate into discussion about use of the app from the patients' perspective despite reminders that it was their perspective as HCPs we were interested in. Suggestions were put forward as to how to improve the patients' experience as a user such as entering their medical condition, drugs they are and creating a profile that they would only be required to set up once.

These suggestions were made before participants were shown the screenshots of the prototype app.

Participants commented that people would not want to spend a lot of time going through a lengthy process, *“for the patient, really must be simple and short as possible otherwise they will not do it”; “the more info you want, the longer it will take to complete”*.

In relation to adolescents, professionals said that the length of time needed to fill in a report would determine whether the process would be completed, *“adolescents may just use [their] full attention span to get through the first couple pages and then they’ll be like ‘What is this man?’”*

HCPs also suggested that a link to a patient forum would be useful, *“maybe have a link to a patient forum so they can talk about whoever’s taking that medicine, how it’s tolerated, personal experiences. It incentivises them”*. Again the discussion came back to the patient’s perspective.

4.3.2.3 Social Influence

* Degree of ADR severity/patient understanding of ADR

The severity of an ADR is a factor that HCPs suggested might determine whether or not they would use the app to report. A few participants were unsure they would use the app to report the lesser side effects of medicines, *“depending on the severity of the reaction or the side effect so if it’s just a little bit of nausea and they are not violently sick so maybe that would put you off”; “if there’s a less severe side effect you’re less likely to”*. Participants were unsure if lesser side effects required reporting.

The discussion on the severity of the ADR that required reporting lead to a debate on patients’ understanding of what an ADR is. Participants questioned patients’ ability to report appropriately, *“many patients say they’re allergic to medicines they’re on. When you ask them on the ward, it’s diarrhoea or you know, something else, then you have to reassure them it’s not a side effect.”* This issue then lead to a discussion on validity, detailed later.

4.3.2.4 Facilitating Conditions

* Data tariff/How much space will it take on the device?

How much data in terms of tariff and memory the app would need was a topic of interest that generated a lot of discussion.

Participants asked if the app was *“cumbersome”* – this word came up twice.

“Will it clog up your phone”, “take up loads of memory”, “how cumbersome or big is the app”; “What is the size of sending an average response (report). Is it in terms of just a few kilobytes?” They also pointed out that not every mobile phone has data as part of their package.

One participant said that they assume the app will be free as *“it would be expected that if the app is not free nobody will want to use it”*.

From these comments, the amount of space the app takes up on an individual’s device, and the tariff or cost to use the app seems to be a factor that will influence uptake of the app to report ADRs.

* Information overload/validity/relevance/reliability

The focus group raised a question about large numbers of ADR reports being made and expressed a

concern regarding filtering out those that are “not real”. *“I think the amount of noise would be tremendous and there will be huge IT costs in the development of algorithms to try to find the meaning of signals in all that noise”.*

HCPs asked whether unvalidated information might be made available to every user. They also queried the *“validity of ADRs reported directly from a patient to a database without it being filtered through a conversation with a healthcare professional..it may have nothing to do with the drug”* and commented, *“if, as the aim is to capture new or unknown side effects, some reactions will be idiosyncratic or very rare”.*

The theme of what is relevant to HCPs in terms of news generated a question on what constituted ‘news’ or *“how do you define news?”*. The group said they would not want every single notification, as that would be irrelevant. It was suggested that in the news section the known side effects of each drug should be listed. Then if an ADR occurred that was not listed, it would be reported, thereby *“acting as a filter to reduce irrelevant information”.*

A sub-theme around information overload is reiterated through the strands of validity and relevance. Again the idea that the app would have thousands and thousands of people producing reports of side effects seems to be a concern for HCPs, *“I do not see how you are going to police or organise them in a positive way to allow people to see this huge amount of information”,* and *“How immediately relevant or helpful that information, whatever that might be, could be to a single individual”.*

There was consensus that reliability was important, *“What’s reliable, what’s not?”*

Any information reported *“needs to be reviewed and put back out there for people to see”.*

As to the length of time that information should be made available, participants said no time restrictions were necessary, as consent would have been given to put that information out in the public domain by the user’s act of submitting the report.

** Miscellaneous*

A few miscellaneous items were raised during the focus group and for interest they are included here briefly. *“What’s being missed at the moment with the current system that this will improve on?”; “The evidence base behind those lists of side effects that currently exist – how strong is that?”*

One participant also suggested *“make the agenda of the project around educating HCPs around the new system that’s specifically designed to find that [ADR]. You can easily report idiosyncratic things you don’t think of as an ADR”.*

Summary

From this small sample of prescribers the main suggestions put forward were:

- 1) Data lite
- 2) Different versions for lay people and professionals
- 3) Feedback for any report sent.

4.3.3 Professionals – face-to-face interview

4.3.3.1 Performance Expectancy

** Possible facilitators of app use*

Generally, a mobile app to report ADRs was considered to be a good concept as people use their mobile phones everyday.

Has to be easy to use, so shouldn't necessarily require IT skills. Needs to have a simple approach. Does it connect with local systems, that is, primary care systems or trusts. There should be two-way communication.

Feedback is important, for example, does this drug cause this side effect, how many other people are reporting this.

Drop down boxes and lists are helpful providing they are intuitive and not too long. *"A list with more than 6-7 items won't work, if they're very lengthy people tend to just pick the first thing."*

Free text considered to be good for telling the story but on a hand held device this might not be easy to do.

Screenshots of the prototype app seen are *"clear, simple, appealing, intuitive."*

** Potential barriers to app use*

Login should be made as easy as possible, *"if you're made to log in every time it's going to create a barrier so.. the path of least resistance, ideally I wouldn't want to log in at all, so once the profile is created that's it."*

Amount of information required about the patient was seen as a barrier. From the Lead Pharmacist's for Medication Safety (LPMS's) experience of the Yellow Card, *"they want a lot of information. With a mobile you would probably need to find more information about the patient so if you're already at a hospital computer it would be just as easy to report through the online or web version, so why would you need to use mobile app anyway?"*

Usefulness/function. Would be unlikely to download the app to own personal device. LPMS considered her phone as personal, it's not a work phone, *"so I choose what I do or don't have on there and I don't particularly like having work things on there unless they are useful to me personally, would a mobile app for reporting ADR's be one of those? I don't know."* The LPSM would download app to a work iPad but not to a personal phone.

What ADRs to report. The LPMS said that some guidance around what should be reported would be useful. As the focus of the MHRA is very much on novel agents and newer agents in the first few years of marketing or black triangle drugs, some support on what is an adverse reaction and is expected to be reported.

4.3.3.2 Effort Expectancy

News page of app was too wordy, a lot of text. Prefers a simple clear message, *"It was difficult to find what it's trying to tell me, what I'd really like is a drug name, what the issue is, because clearly there's some kind of fault here, and who might this apply to..acute trusts, community or everyone..then I can decide whether or not it's of interest or relevance to me."*

App should be able to cope with both brand and generic names of drugs.

4.3.3.3 Facilitating Conditions

Benefit over local system. The first port of call for ADR reporting would be the LPMS's local reporting system due to the advantage of assurance that the patient would be managed appropriately. Also for local learning as national reporting learning system have mechanisms to share information with MHRA anyway.

Local reporting system was thought to be more beneficial than reporting directly to MHRA and Yellow Card as *"it's a bit of a black hole - a few years ago I tried to find out how many of my organisational reports had gone in through the yellow card reporting system to the MHRA. It took about two weeks... and the information I got back were numerical data, which is meaningless for me in my capacity as medication safety officer. That doesn't provide opportunity to learn or understand what's going on locally, so in that context if I were to report or encourage reporting it would be through local systems so that we could have the richness of the data."*

Two-way communication. In terms of two-way communication, the LPMS was in favour of HCP's receiving feedback about the reported ADR through the app. However the LPMS said that the patient should not receive information back via the app about the ADR a HCP makes. This was due to concern about information governance and the HCP's duty of care to keep the confidentiality of the patient's information. However, the view was that the patient also had a choice whether they wanted feedback.

Needs to cope with blank fields. The information the app asks may not be available at the time of making the report for example, *"you may not know the weight depending from where you're reporting from and whether you are the person experiencing the side effect or... may not have the age to hand so it needs to cope with blank fields and I don't know if it does or not."*

Clarity of Wording/Phrasing. The terminology of the app was considered to be very healthcare focussed. Needs to be in plainer English, *"Life threatening is simple to understand but it's a perception of whether you think it's life threatening or is it clinically life threatening for example. Similarly prolonged hospitalisation, if a patient was reporting themselves would they necessarily know that ADR calls for prolonged hospitalisation or not so I think it's a page that's written by healthcare professionals or people who want the data...rather than people who report the data."*

Abbreviations and jargon *"Obviously, nobody's going to know what ONS is."* Additionally, the interpretation of some terms differ from patient and HCP perspective, for example, *"patients say I'm feeling sick they don't say, some might say I'm nauseous it's using plain English really, cause I think if a patient is typing it might say feeling sick, threw up, vomiting, those kinds of words I suppose to nausea."*

HCP would tend to re-interpret what the patient tells them, *"so it's probably an element of distillation that goes on from what the patient reports and what you decide it is, which is not necessarily the wrong thing but again it comes back to what the data collection purpose is."*

Another example was if the patient said they felt 'a bit woozy,' the HCP would probably bring in their own objective assessment of what that meant, for example, hypotension, light-headedness or drowsiness, which might have different outcomes or interpretations.

On some of the option boxes the LPMS said that **On** and **Off** were the wrong words, that a tick box or yes/no was more appropriate. For example, *"...if it causes prolonged hospitalisation it should be yes or no, on and off are just the wrong words."*

Additionally, at the point of reporting, the HCP may not know whether the ADR will cause or prolong hospitalisation, *"so how would that be reported?"*. There was also the question of what

constitutes a medically important condition, who was it important to, and by whose definition.

In the profile page, although the list would be reflective of healthcare practice and terminology, there is no allowance for other categories of reporters, for example, allied health professionals. The term 'physician assistants' was considered a very American term as is 'physician.' The LPMS also queried whether a biomedical engineer would do an ADR report.

Additional clarity around some questions are needed, such as 'What else did you do?' *"What else did you do in respect to what? So this needs a bit of a qualifier."*

4.3.3.4 Social Influence

App may be a barrier to communication between patient and HCP. Important that the app is marketed appropriately and the patient informs the HCP first so that symptoms will be managed. Concern about preconception that if ADR is reported through the app by patient, then *"somebody somewhere will know what adverse events they're experiencing"* leading to patient not seeking health advice.

LPMS said that appropriate information and guidance as to what reporting means is important as the general public has the view that if their GP knows about an ADR, the hospital will also know which isn't necessarily the case.

4.4 Results the Netherlands

4.4.1 Patients

Interviews were conducted with four patients who had at least a diagnosis of T2DM (Table 3).

4.4.1.1 Familiarity with Lareb

During the introduction of the interviews, it became clear that several people are not familiar with Lareb. More specifically, only 50% of the participants were familiar with Lareb. This number is biased since these people were also recruited through the website of Lareb. One of these familiar patients mentioned that “a lot of people are not aware of the existence of Lareb” (patient 2).

4.4.1.2 Type of ADRs

Patients mentioned that they generally will report the following ADRs:

- those that are permanently;
- those that are not mentioned on the patient information leaflet;
- every ADR.

Reasons for not reporting an ADR were:

- uncertainty about which ADRs the authorities are interested in (“is this severe enough to report?”, “or they should say that you can report every ADR so that you don’t have to think about whether this is something that they intend to collect”, patient 4);
- uncertainty about details of the ADR (“only the HCP can measure the height [of e.g. glucose-levels]”, patient 4).

4.4.1.3 How to inform patients about the existence of the app

HCPs may inform patients about the existence of the app (patient 1,2,4). This is a reliable source for patients (patient 4). Another potential source is the diabetes association. Information can be provided through newsletters that are already used by the HCPs. Another idea that was mentioned was to inform people through a TV commercial.

4.4.1.4 Performance expectancy

* *Intrinsic motivation*

Patients report an ADR for intrinsic reasons (patient 1, 3). A financial compensation is expected to introduce bias by patients reporting every symptom that they experience (patient 3).

* *Interaction patient – NCA*

Feedback regarding the app by patients

It was indicated that it should be possible for patients to give feedback on the app (patient 4). This could be done by for instance indicating that a link could be used for providing feedback.

Feedback regarding ADRs by NCA

Patients indicated that they would like to receive feedback regarding the reported ADR. This may also help to honor patients and give them the feeling that they are taken seriously (patient 2, 3). There were two types of feedback mentioned, that is 1) general information about for instance the number of reported ADRs, the type of ADRs, which drugs causes most of the ADRs etc (patient 4), and 2) feedback after sending a report (patient 1, 2, 3, 4). The first type of feedback can be provided for instance every 6 months (patient 4). For the second type of feedback, patients like to receive a confirmation that their report has been successfully submitted (patient 1, 4) and/or

automatic news messages about the drug for which they did the report (patient 2) (see also “news items” below). Both could be done by providing a checkbox at the end of the report in which the patient can indicate him- or herself whether he/she wants to receive this information.

Follow-up

One patient indicated that it would be good whether a follow-up survey would be send to a patient who send a report. This information would provide information about the duration of the ADR and the actions that were taken to resolve/alleviate the ADR (patient 4).

** Patient-HCP communication/interaction*

The app may empower patients in the communication with their HCP as indicated by patient 3: “people who do not have the medical knowledge can have a look at their phone and they can see that it happens more often [a specific symptom], so I can discuss it with my doctor”. It might also give a patient trust in their idea of a symptom being an ADR also if a HCP is not aware of this association. The patient can then refer to the information in the app (patient 2).

Some patients do not want to visit the doctor for every symptom they experience. The app may help such patients to check whether symptoms can be related to drug use: “I have a new tablet and I have pain somewhere in my body and I do not know exactly what it is, and I do not want to go immediately to my doctor and that you have this and see what has been reported” (patient 2).

Patients did not feel that their ADR report should go to their HCP (patient 1, 2, 4). In their opinion the ADR is often already discussed with the HCP before the ADR will be reported (patient 1, 4). One patient noted, however, that it would be useful if HCPs receive a notification in case of new safety signals. The HCP should then search in his/her database for patients who might be of concern (patient 2).

The app itself might also be useful for HCPs. It was indicated that a HCP can have a quick look in the app to look whether the ADR mentioned by the patient has been reported more often in the app (patient 2). It may increase the speed to link an ADR to a drug (patient 2).

** Reports*

A patient indicated to expect that only a description of the ADR should be given (no detailed survey was expected) (patient 1).

The report should be send to an independent organization such as (the explained) Lareb. Lareb can then provide an overview of all the reported ADRs to the pharmaceutical industry (patient 4).

Patients like the option to store their previous reports (patient 1, 2). Especially to see everything that they reported so that they can check whether they have reported everything they wanted (e.g. did I report all the symptoms) (patient 1). However, others feel that only a short report is sufficient (patient 2). Patients should be able to decide themselves how long they want to store these since some patients want to be able to store them the rest of their live (patient 1, 2) while others do not want to store them endless (patient 3). It would be nice to have a function in the stored reports to sort the reports by drug name or ADR for instance. In addition, a search function would be nice (patient 2). Patients liked the idea to continue a report on at later moment (patient 4).

** News items*

Patients like to receive news items.

Type of news

The news could be about new developments of a drug, new ADR knowledge of a drug (patient 1), drugs that are taken off the market (patient 2), and an overview of comparable drugs with the lowest number of ADRs (patient 4). There was contradiction about news of newly marketed drugs where patient 2 would be interested in this information and patient 4 does not want this

information. Patient 4 indicated that there is always a standard treatment so it would not be of interest to know newly marketed drugs.

The information may be presented for all drugs (patient 1) or only the drugs that someone uses or that are related to someone's disease(s) (patient 2). In addition, the information could be presented both in newsletter format or a box that can be checked to view news items. A newsletter could for instance be sent 4 times a year (patient 1) and could be presented in the app itself. People should be aware that no medical terminology is used in the news items (patient 4). New items could be indicated by an icon on the logo of the app or for instance a short sound (patient 2). However, the sound may be annoying when you have a lot of apps (patient 2).

Source

The following instances were mentioned as good sources for the news items: diabetes association, independent institute or a university (patient 3). In addition, it was agreed that the CBG-MEB would be a good source (patient 3). There was some contradiction in the pharmaceutical industry as a source of the information where patient 3 prefers an independent source and patient 2 thinks that information about drug developments by the pharmaceutical industry might be interesting.

Prototype app

Three comments were given on the news items in the prototype version of the app:

- One patient indicated that the news item about acute pancreatitis with DPP4-inhibitors is misleading since the patient was searching for news about metformin and metformin is not a DPP4-inhibitor (patient 2). If you are searching for information about metformin, only this information should be presented.
- It is an additional step that the same information is presented after a click on the news item. This step should be deleted so that all information is presented directly after a click on the news item (patient 1, 2).
- One patient was surprised that each news item is presented individually instead of an overview of all the news for a drug (patient 1).

**Profile*

Some patients expected that they also had to enter their prescribed medication in the profile of the app user (patient 2, 4). This information can be used to already present the news about these drugs (patient 2). Also, this information can then be used in the ADR report which reduces the time a patient needs to complete reports (patient 4). This drug information may be useful to check whether co-medication might be influencing the ADR instead of a single drug entered by the patient (patient 4).

** Graph*

Patients liked the graph in the prototype app about the number of reported ADRs (patient 1-4). Most of the patients noted, however, that it would be more useful when the specific ADR was presented instead of the currently used high level categories (patient 1, 2, 3). One patient indicated that presenting the information the other way around (a list of drugs for an entered ADR) might cause an increase in reports that are no true ADRs (patient 2).

** Additional functionalities*

Other functionalities that patients expected in the app or that were mentioned as useful were:

- patient experiences with a drug (patient 1, 2) and the option to add own experiences (patient 1). The system should, however, not be too informal (patient 2). A professional may have a look at the messages provided by the patients in the app (patient 2).
- suggestion on possible actions to reduce/alleviate ADRs. This could be done by referring to an association such as the diabetes association (patient 2). This information would be useful since "it will scare less if you know which side-effects exist and that there are solutions for it" (patient 3).
- product information (patient 1-4): "[information for all drugs about] their function, ADRs, how

- often ADRs occur (preferably in percentages according to patient 3), the best way to take the drug” (patient 1). This can also be provided by using a link to the patient information leaflet (patient 2).
- background information about the development of drugs (e.g. are they tested on animals (patient 1)).
 - present alternative drugs for the one a patient experiences an ADR. According to this, the patient could ask the doctor about other options (patient 2): “In the past, you did what the doctor told you to do but people are now of course searching [for treatment options] and they want to talk with the doctor” (patient 3).
 - The option to add a photo could be helpful (patient 2).
 - A reminder function for when patients have to check their eyes and feet (patient 3). On the other hand, a reminder functionality for taking prescribed medication was not seen as relevant (patient 2).
 - information about what to do in case of hypoglycemia (patient 4).
 - functionality to track your glucose levels (patient 3).
 - advise about diet and lifestyle to keep your blood sugar low (patient 3).

4.4.1.5 Effort expectancy

* Login

Patients see some advantages of a login screen on the app: other people cannot enter the app/to protect the data (patient 1, 2). On the other hand, patients were not worried about other people seeing their data as indicated by patient 4: “it is not something that they can plunder your bank account” and patient 3 “there are no big medical secrets in it”. It would be preferred if there is the option to save the login details (patient 3, 4). One patient noted that asking for an e-mail address and password on the login screen may be confusing for those who use the app for the first time. It should be clearly stated that they have to create an account. Otherwise they may try to use the password that they have to access their e-mail (patient 4).

Two patients indicated that the details that are entered to create an account should also be used in your profile and as the personal details in the ADR report (see also report section above) (patient 2, 4). Patients do not want to enter these details over and over again. One patient mentioned that it would also be handy to link it to *DigiD* (patient 2).

* Accessibility

An app is easily accessible: “You are immediately there where you have to be, you don’t have to search on google, you don’t have to use paper and pen, you don’t have to call” (patient 4). In addition, a mobile phone is always there where the person is.

* Ease of use

Some keywords for a successful app are:

Comfortable: “You should make it as comfortable as possible” (patient 4).

Use as less steps as possible: More steps/proceedings makes it more difficult and people are also sometimes a little bit lazy (patient 3).

Easy: It should be very easy to use (patient 2, 4) and easily accessible (patient 2).

User-friendly (patient 2, 3).

Simple and clear: “it is better to keep it very simple and clear and that what is in it works (e.g. page not found is fatal)” (patient 4). The basis should work properly and it is ok that other options are added later on (patient 2).

Short sentences and simple words (patient 4).

Logicity: Illogicality in an app reduces the chance of reporting an ADR again (patient 2).

It should also have been designed for a mobile device (patient 2) and the app may work differently on a tablet or a mobile phone or a computer. So it should be tested on each device (patient 4).

Completing an ADR report should take approximately 2-3 minutes (patient 4). If it takes much longer it is expected that people report less quickly a report again. Also patient 2 mentioned that you should not have to answer to many questions in a report.

** Language*

Two patients mentioned that it would be useful to provide the app also in other languages than the Dutch language (patient 3, 4). Patient 4 indicated that people from several cultures live in the Netherlands and that some might be able to better read and write the English language. Patient 3 indicated that a translation of entered medication in Italian would be useful since this patient often goes to Italy and it would be more easy to present Italian HCPs an overview of the medication list in the app than to mention the whole list.

A patient had some problems with the prototype app since there were some English words in it (patient 1). Therefore, a closer look at the translation is needed.

** Current app*

Several comments and suggestions to the prototype version of the app were given. Below an overview of these comments and suggestions is presented.

Batchnumber

Patients were not familiar with the term batchnumber (patient 1, 4).

Yes/no button

The button that is used to indicate whether the reporter wants to answer yes or no () was not completely clear (patient 1). In addition, patient 4 indicated that it would be wise to report yes and no besides the button since 9 of the 10 people do not know this button.

List with drug names after entering some letters

Patients like it when a list with drug names appears after entering some letters, they think it is handy (patient 2, 4). For one patient it was confusing since the drug names in the list were not the one that this patient wanted to enter (patient 2). Therefore, the patient should enter the name of the drug instead of checking one from the list.

Illogicalities

Illogical things should be deleted from the app since people will not take you seriously (patient 2). Patients prefer a kind of decision tree where the entered information will influence which follow-up questions and options for specific questions will be presented (patient 2, 4). For example with lipid-lowering drugs the route of administration will be standardized to oral. A specific illogicality mentioned by patients was that in the report, it is asked for the end date of the drug. However, patients indicated that you should not have to complete this question when the drug was not stopped (patient 2, 4).

Wheel with answer options

Patients like the wheel with the answer options (patient 1, 4). However, it should be possible to immediately check the answer options instead of having to check "Gereed" (patient 2). In addition, it would be useful to also provide to option to enter your answer (patient 1, 2). This will be much faster in case of for instance your age (patient 1).

Problems/difficulties

- The terminology used for how the drug is taken is not clear for patients and there are too many

- options (patient 1, 2, 4). Patient 2 suggested also to change “route” into “toedieningsvorm”.
- Actions taken: “I take the drug at another point of time” (patient 4). This option was not presented and there was also no possibility to enter another answer. Another patient indicated that there was a switch to the former drug and that this answer was not one of the options (patient 1). Patient 4 also mentioned that it would be interesting to ask what has been done in case of the drug was stopped (e.g. other drug).
 - Patients didn’t see the bar in which they can enter their ADR. One patient mentioned that it seems like only serious ADRs are interesting to report since ADRs such as headache or heart palpitations are not in the list (referring to the list about seriousness) (patient 4). Another patient indicated that the app stated that at least one reaction should be added to the report whereas the patient thought that this was already done (seriousness was checked) (patient 2). Patient 4 suggested to present first the screen with entering your ADR followed by the consequences (e.g. hospitalization).
 - Not clear what was meant with “Land waar de reactie is begonnen” (patient 1; suggestion to use “bijwerking” instead of “reactie”).
 - It should be more clearly differentiated which reports are submitted and where a new report can be done (patient 4).
 - Dosage: 50mg but it is not asked how often per day (patient 4).
 - It would be useful to also add how often the ADR is experienced (e.g. 4 times a week) (patient 4).
 - The question “Did the drug cause a similar reaction before” was confusing for patient 1 since the patient had not taken the drug before. The patient therefore suggested to add the option “Unknown”.
 - A patient was confused with the question “Plaats waar het medicijn is verkregen” since it was prescribed in the hospital but obtained in the pharmacy (patient 1).
 - Start- and end date of the drug and ADR: patient 1 indicated that the specific dates were not known anymore.
 - In the field below the question of current and previous illnesses people had to delete the text “please describe...” before they could enter their answer. This was annoying (patient 2, 4).
 - Patient 2 indicated that it might be informative to also ask for country of origin since the prevalence of diabetes is higher in some populations than in others.

Tips/suggestions/tips

- A start page for new users with a short instruction about how to use the app (patient 1).
- It would be useful to add stars behind the obligatory questions (patient 4)/that it becomes clear which fields are obligatory (patient 2).
- It might be useful to add an information button behind some questions (e.g. batchnumber) with more information about what is asked for (patient 4).

Overall opinion

Some overall opinions:

- “ I like it” (patient 4).
- “You have to spend some time by assessing how things work, where to find stuff, what they mean with everything” (patient 1)
- “It is useable and there are some illogicalities but I assume that that will be solved” (patient 2).

It was indicated that a lot of questions are presented on the screen with the drug (patient 1). Also, a lot of information is asked for in the question about previous illnesses (patient 1, 2, 4). Patients are willing to enter this information (patient 1, 4) since they feel that it is important to do (patient 3). However, they only want to enter this information once: the app should be able to store this information and that you can add something in a later report (patient 4).

4.4.1.6 Social influence

* Contact other HCPs

One patient mentioned that the app could also provide advice to go to a psychologist in case of for instance problems with accepting (the consequences of) an ADR (patient 3). The patient gave the example of erectile dysfunction as ADR. Another idea was to refer to a patient organization in case of specific ADRs (patient 2). The patient organization can then be contacted for advice and about how to deal with the ADR. Such an organization can also be helpful in the app development itself (patient 2).

Patients have to order their drugs very often. It was suggested to include a link in the app to a person's pharmacy with the option to easily order their prescribed medication (patient 2).

* Prestige

In general, patients are not familiar with Lareb. Patient 4 indicated that it is important that a reliable instance is connected with the app and that people see this connection. This will provide trust in the app. It was also mentioned that people prefer to see an overview of reported ADRs from an official instance instead of reading symptoms on a forum accessed through google (patient 2).

* Independency

An independent source should assess the ADR reports (patient 1). Other information exchange (e.g. news items) should also not contain any commercial interest (patient 2).

4.4.1.7 Facilitating conditions

* Layout

The layout of the app was clear (patient 1). There were, however, several suggestions and tips:

- A general tip was to never use very bright colors. Bright colors are very annoying for a lot of people (e.g. people with epilepsy) (patient 4). Another patient indicated that it would be nice if the app user can change the colors him- or herself (patient 2). The same applies for the lettertype. These options will reveal that the app is not too formal.
- The menu is not on a separate screen now. It would be preferred to have a kind of home-screen were the different options are presented with nice buttons (patient 2). The button for an ADR report was not clear for this patient. The patient thought that this option would reveal all the ADRs reported in the world.
- An arrow to go to the previous page would be useful on each page in the app (patient 4).
- The logo of the app should be more recognizable and appealing (patient 4). It should be clear from the logo what you can do with the app. A suggestion for a logo was to present a phone with some drugs and a question mark (patient 4).

* Security/confidentiality of the data

A safe app is important and "the safer it is, the more people will use it" (patient 3). Patient 1 also indicated that personal information should not be available for everyone. However, patients are aware that the safety on such systems cannot fully be guaranteed (patient 3, 4). If the app is useful for the patient him- or herself than they would still use it (patient 3). Also, you can enter the information yourself. So, "if there is information that you do not want to provide, you do not have to" (patient 1).

* Cost

One patient noted that it would be a barrier for a lot of people to use an app if it is not freely accessible (patient 3).

4.4.1.8 Gender, age other characteristics

Different user characteristics may influence whether or not an app will be used. One of the factors might be the age of the patient. Age may influence whether or not a patient has access to the app. Patient 4 indicated for instance that her 93-year old father would not use the app. However, everyone with a mobile phone can be reached. Age may also influence the experiences and preferences within the app. Younger patients are more experienced with apps (patient 4). Therefore, the app may be more logic than for older patients. In addition, elderly are more often visually impaired than younger people. Therefore, it might be preferable to use a larger letter size for the elderly (patient 2). It would be an option that patients can select the letter size themselves (see also “layout” within the “facilitating conditions” theme). Two patients mentioned that they are curious, interested, and searching for information on the internet about medical things (patient 1, 3). These characteristics may influence whether people will use the app to search for information. Also, some patients are more anxious about entering personal data in an app. Such patients will probably be less inclined to use the app (patient 2).

4.4.1.9 Experience

Two patients indicated that they do not have a lot of experience with computers, telephones, apps (patient 1, 3). This reveals that they have to get used to for instance an app. Patient 1 indicated that she often asks other people to help her with such things.

4.4.1.1 Behavioral intention and Use behavior

Patients are generally quite positive about downloading and using such an app despite the various suggestions and things that should be improved in the prototype app. They like the idea (patient 2) and they think that there is a need for it (patient 3).

4.4.2 Professionals

Interviews were conducted with eight HCPs (Table 3).

4.4.2.1 Type of ADRs

The type of ADR influences whether or not HCPs are willing to report the ADR. This is independent of the medium of sending a report. HCPs indicate that they will report the following types of ADRs:

- New ADRs/ADRs that are unknown
- Serious ADRs
- ADRs of a new drug.

In addition, they will report an ADR when a patient explicitly wants them to report (HCP 1, 6). It also needs to be sure (HCP 7) or likely (HCP 8) that a specific drug is causing the ADR.

4.4.2.2 How to inform professionals about the existence of the app

Potential app users should be informed about the existence of the app. There are many apps available which introduces confusion as described by HCP 5: “the problem with apps is that there are so many that you don’t oversee it”.

Several channels can be used to inform HCPs about the app, that is via e-mail, articles, advertisements, letters, via the media, during professionals meetings and via word of mouth. These channels could be used by Lareb or professional associations. Examples of articles in national journals are Medisch contact, Huisarts en Wetenschap, Nederlands Tijdschrift voor Geneeskunde (HCP 2-8). It is important that a picture of the app is shown (HCP 7).

4.4.2.3 Performance expectancy

** Extrinsic/intrinsic motivation*

Professionals may report an ADR for intrinsic reasons as mentioned by HCP 5: “We are professionals so we have a certain faith so to speak” and HCP 7: “I do this [report an ADR] because I want to improve the care for all people so to speak” . It should also be communicated that ADR reporting is important, that it applies to good care and that it is a task of HCPs (HCP 7). Currently, it is always in addition to the structural tasks and reporting an ADR does not directly reveal any gains (HCP 8). An extrinsic motivation may positively influence the number of reports as indicated by HCP 2: “You can also use a kind of incentive. To encourage people”. However, incentives such as money are seen as stimulating the wrong motives to report (HCP 8).

** Reports*

Storage

Several reasons in favor of storing the reports were given:

- You can see that the report has been send
- You can see how often you report an ADR for a specific drug
- To see whether ADRs for a specific drug are more common than for another drug in the same therapeutic group. This may influence the preferences for a specific drug.

Storage of the reported ADRs may stimulate to report in the future as indicated by HCP 4: “In the last months, I always did 20 reports, this time it was 2, what is the cause of that? So that is also to stimulate to report”.

A HCP indicated that storage of the reports was not useful since he writes the reports already down somewhere else (HCP 4) such as in the medical dossier (HCP 7).

The report should contain all the information provided in the ADR report (HCP 2).

HCPs like to have the option to see their previous reports. It would be possible to present the reports of the last week, last month and longer (HCP 3) or per year (HCP 4). One HCP mentioned that it would be sufficient to store the reports only for half a year (HCP 6). Others would prefer to have the possibility to delete old reports themselves (HCP 2, 5). However, it should then be clear that the report will not be deleted from the database of the agency (HCP 6). There might also be regulations around the storage of the reports. Maybe the data should be stored for 15 years (HCP 8) as is a commonly used period for data storage. The drug name, date of the report and maybe the ADR at a higher level, but not the code [GB-MHRA-WEB-RADR1000...] should be indicated in the heading of the previous reports. Adding a patient number would also be useful and it would be useful to sort the reports on each of these (e.g. date, drug name, ADR) (HCP 6).

Feedback

Providing feedback about a report may also stimulate the reporting of ADRs. One HCP mentioned that feedback was only necessary in case of particularities but that she wanted to be sure that the patient is contacted by the NCA (HCP 2). Others always want feedback. Direct information should be provided in which it is mentioned that the report has been received successfully (HCP 1). In addition, this direct information should give an overview of the frequency of previous reports about

the reported ADR-drug association (HCP 2, 4, 6, 8). Whether or not an ADR is dose-related is also of interest since this may influence the prescribing behavior (e.g. the only option is to stop the drug since the same ADRs will occur with half of the dose (HCP 4)). All this direct information may help the HCP during his/her consult with a patient. In the long-term, it might be interesting to provide information about any consequences of the drug (e.g. the drug has been taken off the market (HCP 6)) or consequences of the report (HCP 8). Such information can be sent at the end of a year through an automatic message for instance (HCP 8).

One HCP was against any type of feedback: "I do not want to hear about it anymore" (HCP 7). Therefore, it might be wise to use checkboxes in the end of the report in which people can indicate whether or not and possibly which type of feedback they want to receive (see also section facilitating conditions – ideas/suggestions/tips).

** News items*

There was some diversity among the HCPs in their opinion about news items in the app. Some HCPs felt that news items could be useful (e.g. HCP 8: "I think that this can be a fast way to extra inform end-users, prescribers about new information that is known about it") whereas others felt that the goal of the app should simply be to report ADRs (e.g. HCP 2: "I would not directly link it to the app to my feeling, you have other sources for that").

Source

Reasons for not being in favor of news items were for instance the source and the independence of the provided information (HCP2). The news items should not come from the pharmaceutical industry (HCP 4, 7) but from Lareb, the FDA, or the EMA (HCP 4, 6). Another idea was to present news items about drugs in the media since this often influences patients' opinions/preferences (HCP 3). This information would be particularly helpful when an independent organization or person would provide feedback on the issues in the media (HCP 7).

Frequency

The frequency of providing news items may also influence the HCPs' opinion of the app. A HCP indicated that it would be preferred to indicate whether or not someone wants regular updates. The HCP indicated that it might scare when there are for instance 30 new news items (HCP 5).

Type of news

A HCP noted that the app could also be used by the agencies to communicate to prescribers (HCP 2, 8). The information in such communication could be about drugs in general that are often prescribed (HCP 1) but may also need to be more specific by focusing on regularly prescribed drugs at the HCP level (e.g. selecting on therapeutic group) (HCP 2).

Several HCPs indicated that the provided information should be about serious issues, such as drugs that are taken off the market and the reason for that, or newly identified life-threatening ADRs of a drug (HCP 3, 5, 6). Also, other types of information were considered as useful:

- Changes in guidelines (HCP 3)
- Changes in reimbursement of drugs (HCP 6)
- Changes in the frequency of an ADR with a drug (e.g. from rarely to often) (HCP 3)
- New interactions (HCP 8)
- It should not only advice to measure antibodies in the blood for instance, but also what you should do with it, what the consequences are (HCP 8)
- DHPCs (HCP 8).

A HCP mentioned that information about new drugs on the market would be useful (HCP 6) or about new applications of a drug (HCP 4). However, a HCP mentioned that such information is not directly necessary since the information is currently obtained in pharmacotherapeutic meetings

(*Farmacotherapeutisch Overleg*) (HCP7). Another HCP felt that such information should not be included at all and that the information should only be about reported ADRs (HCP 1). Not all the background information needs to be presented (HCP 1), but a link to the background information may be useful to increase the trust in the provided information.

A concern about providing information might be responsibility as indicated by HCP 5: “This saves you a lot of responsibility. Because if you do not report an important message [news item], why was this important message not in it. I have this thing, I look at it, an life-threatening ADR and you were too late, I have still prescribed that drug, although I use the app. That can be dangerous”.

* *Additional functionalities*

The HCPs reported several other functionalities that might be interesting in an app. Some HCPs felt, however, that the current app should be used only for reporting ADRs and that other apps should be developed for other functionalities (HCP 5). An option would be to provide links to other apps, websites etc to provide such additional functionalities (HCP 5).

An overview of other reported functionalities is provided below:

- No complete guidelines but an overview of preferred medication, summary of the guideline (e.g. start with drug A add drug B) (HCP 3)
- Present the conditions of starting a drug (e.g. when will it be reimbursed) (HCP 3)
- Dose-dependency of ADRs (HCP 1)
- Future reports (*terugrapportages*) about e.g. whether or not it was reversible after the patient stopped taking the drug (HCP 1)
- Details of previous reports (e.g. comedication)
- Overview of alternatives when a patient does not want to use a drug anymore (HCP 4)
- Providing an advise to resolve/reduce the ADR if this information is known (e.g. prescribe an additional drug to solve the ADR, take the drug with a glass of milk, divide the dose over the day)(HCP 8). The app may also present such information for the most frequent ADRs (HCP 8). Regulations should, however, be consulted in case such information is provided to patients (e.g. is it allowed to advise patients other drugs).
- Interactions between drugs (like in the British Medical Formulary) (HCP 5, 7). The app may also serve as a kind of warning system with a note after a report that the symptom may be due to an interaction between some of the drugs that the patient uses (HCP 7). According to this HCP it would therefore be more useful to enter prescribed drugs instead of medical history.
- A report by a patient can be send to his/her HCP. Although the HCP does not want to be bothered with all symptoms, it might be helpful to better structure the symptoms of a patient. Another option is that the patient shows his/her reports to the HCP during a clinical visit (HCP 8).
- Prediction model: after entering some information, how likely is it that this is an ADR? (HCP 2).

Several HCPs reported functionalities related to the Dutch pharmacotherapeutic compass (*farmacotherapeutisch kompas*):

- List of most important ADRs of the drugs (HCP 3, 7), literature search based on entering ADR and drug (HCP 5), entering an ADR and searching for related drugs (HCP 4, 7).
- A targeted search for a specific ADR (HCP 6).
- Interaction with other drugs (HCP 6). However, another HCP indicated that this would too much overlap with the *farmacotherapeutisch kompas* (HCP 8).
- Can it be prescribed to pregnant patients (HCP 6) or are there contraindications (HCP 7).

Graphs

In the current version of the app, graphs are presented with the number of reports provided per MedDRA System Organ Class.

In general, HCPs were enthusiastic about such graphs. However, the presented categories are too broad. HCPs would prefer to see more specific information for instance after checking one of the System Organ Classes (HCP 2, 4- 8). Such a graph is seen as useful to prepare for instance *farmacotherapeutisch overleg* or to answer questions from other HCPs (HCP 1). The more specific information may also include pictures of how the ADR looks like (HCP 8).

The numbers in the graph presented by gender and age categories were seen a less useful since it indicates who reports the ADR via an app instead of how often ADRs occur in specific populations. Moreover, the numbers are not corrected for the frequency of use within the population, indicating that a higher number of reports in for instance an age category may be due to a more frequent prescription in this group (HCP 8).

4.4.2.4 Effort expectancy

* Login

An app on two-way risk communication would be useful since it has been assumed that it is more easy to login in an app (HCP 3). It should be possible to login into your domain from different devices using your own login data (HCP 4). Some HCPs indicated that it would be preferred not to enter the details each time you want to enter the app (HCP 6-8). The most ideal situation would be that users can indicate themselves whether or not they want to save the login details.

* Accessibility

An app is easily accessible. It takes less effort to search for than for a (digital) reporting form (HCP 2, 6).

* Ease of use

Time constraints is a major issue for HCPs to report an ADR (HCP 3-8). Therefore, words that are mentioned for a successful app are:

- Simple: It should be as simple as possible (HCP 1, 2, 3, 7, 8). the app should focus. Unnecessary information or functionalities should be deleted (HCP 4). Some people will discontinue when it is too laborious (HCP 2). If it is simple, you do not have an excuse anymore (HCP 5). People are lazy, keep it simple (HCP 5).
- Short: The more information you want to collect, the higher the threshold to report (HCP 5, 7, 8).
- Easy to complete: A HCP noted that a previous report was not completed due to complex questions such as what was the exact date, how many days were between it, etc. The HCP did not know this information anymore (HCP 6). It should also be easy to identify the drug in a drug list (HCP 8).
- Quick: It should be possible to quickly check options (HCP 4), to do it fast (HCP 3, 7). The app should also work fast (HCP 6, 8).
- As less typing as possible: A reduction of the number of type moments using checkboxes or menu's or using sections to select for instance previous diseases would increase the ease of use (HCP 2, 4). It should be click, click, click (HCP 3, 4).
- Contact patient for details: It was suggested that the HCP only provides basic information and that the agency can contact the patient (of course after permission of the patient) for the details (e.g. drug/disease history) (HCP 3). Also another HCP mentioned that it would be handy when patients can report themselves (HCP 4).

Ideally, most of the data would immediately be uploaded (HCP 4).

A suggestion was that the report should be easy and fast, with only a few questions to answer. In special cases (e.g. serious ADRs, unusual ADRs, or products under surveillance), the agency can contact the reporter for more information or to complete additional answers (HCP 5, 8). It is also

possible to add a checkbox at the end of the report where reporters can indicate whether or not they can be approached for additional questions (HCP 8).

In the current app, HCPs were dissatisfied with the question to enter the whole disease and medication history of the patient since this is a lot of work (e.g. HCP 2, 3, 4, 8). An option to increase its feasibility is to use sections that reporters can check general areas [e.g. CV disease] with the option to drill down to more specific diseases (HCP 2). Other options are presented in the theme “facilitating conditions” which is presented below.

Overreporting

Overreporting was mentioned as a possible concern of a very easy to use app (HCP 1, 5). If the app would be very easy to use, people might think more easily that the agency should know the information (HCP 1). However, overreporting might not be a big problem in the current app since there is still a lot of information asked for (HCP 1). Another HCP mentioned that overreporting would not be of concern due to underreporting (HCP 4). In addition it was said: “If everybody says that he or she get hiccups, just an example, than you cannot say this is not relevant but if everybody says it, it still means something. Although you cannot explain it so you should something with it. And if everybody says that he or she gets itches, yeah then there are still a lot of people for whom this is bothersome in one way or another. So, as a manufacturer you should do something with it” (HCP 4).

** Type of user*

The content of the app should depend on its user (HCP 8). HCPs suggest to use different terminology in an app for patients and HCPs (HCP 5). Words like oral and dental are not clear for patients whereas they are common language for HCPs (HCP 3, 4). In addition, questions should also be reformulated in a HCP- or patient-specific app. A question such as “when did you start the drug” is applicable for patients but should be changed into “when did the patient start” in the app for HCPs (6). The current app was seen as professional-oriented due to some difficult words used in the app (HCP 2). Sending a report may be less bothersome for patients than for HCPs, so patients could be asked more questions than HCPs (HCP 7). Also, the questions could be formulated differently. HCPs could for instance be asked for relevant medical history, whereas patients could be asked for the entire medical history (HCP7). However, in both cases it is important to only ask the questions that are really important (HCP 7).

Some HCPs seem to be worried about the quality of patient reports. It was for instance suggested to ask additional questions in a patient report such as whether it has been discussed with the HCP, whether other causes have been examined, etc (HCP 3). The HCP could also be send an automatic invitation to report an ADR when his/her patient has reported an ADR (HCP 5). This could be a sort of check on the probability of a symptom being an ADR. Such a check is desirable since the reported symptoms by patients should not just be linked to the drug (HCP 8).

Besides differences between patients and HCPs, it is also possible to expect differences among professions of the HCPs. A HCP noted for instance that the reason of prescribing a drug is not always clear for a pharmacist (HCP 1). A possible solution to solve this issue would be to make it clear that questions can be skipped (see section ‘Skip questions’ below). Also, the news items in the app may be relevant for some HCPs whereas it might be less relevant for others (HCP 7).

** Language*

It was suggested that the app would be available in both Dutch and English language since an increasing number of people (also doctors and nurses) do not properly speak, read and/or write the Dutch language (HCP 5).

Several words were not yet translated in the current version of the app. It was mentioned that these English words would be difficult to interpret for the patients (HCP 2).

** Current app*

Several aspects of the current app have been discussed during the interviews. Below, an overview of the main themes is given. An important thing is that the goal of the app and what to achieve with it should be clear.

Batchnumber

Several HCPs mentioned that entering the batchnumber of a drug is not very feasible since it is not easily known by patients and HCPs (HCP 2, 4-6). It would take a lot of effort to find out this number (HCP 1).

News items

For the news items, it was expected that the additional information would be available in the app after a click on the news item (HCP 3, 6). At the moment, the same information appears after the click and another click should be done to go to the information. This increases the number of clicks that need to be done to see the information. In addition, it was difficult to return to the app after the news item was opened (HCP 2). The information is presented on the internet and it takes several steps to return to the app.

A suggestion was given to present news items also for selected diseases and that checking sections would be useful (HCP 3). For instance the section diabetes with subsections of metformin, SU-derivates, GLP 1, DPP4 etc in which information about new drugs can be presented or information about new associations between drugs and ADRs.

A HCP mentioned that only information about the selected drug should be given and no information about drugs for the same disease (HCP 7). An example is information about DPP4-inhibitors when searching for information about metformin.

Yes/no button

The button that is used to indicate whether the reporter wants to answer yes or no () was not clear for several HCPs (HCP 1-5).

Continue a report at a later moment

HCPs mentioned that it would be easy to continue a report at a later moment (HCP 2, 5, 8). Sometimes there is not sufficient time to complete the report and it would be annoying when all the entered information is lost. In the current app, the data are already stored so people can continue their report at a later moment. It is suggested to add information about this in the app or to explicitly add a kind of save button so that reporters are aware of this option.

In addition, it was mentioned that it would be useful to add information to a previously submitted report (HCP 4, 6-8). This additional information could be about things that were forgotten in the previous report but could also be about new knowledge such as additional symptoms or later use of the same drug. It should, however, be clear that the entered information is useful and that it is not just to add to a dossier (HCP 8).

Red button with white stripe

It was not clear for some HCPs what was meant with the red button with the white stripe behind an entered symptom (HCP 2, 5). It was suggested to use a bin.

Skip questions

Although most of the questions are not mandatory in the current app, this was not immediately clear for the HCPs (HCP 1, 6). At least, it was not clear which questions were mandatory and which

were not. It was suggested to mark questions that are mandatory, present the mandatory questions in another color (HCP 7), or add an information button with a short instruction about the question (HCP 4) and information about whether or not it is mandatory (HCP 1). This may also solve the issue raised by a HCP that the question about the end date of the ADR indicates that you should only report when the ADR has been stopped (HCP 7).

HCPs were confused about a mandatory field on the page of the seriousness of the ADR. They thought it was mandatory to check one of the serious events (e.g. hospitalization, life-threatening, death) since they did not see the button to add a symptom (HCP 3, 5, 7).

List with drug names after entering some letters

Several options of drugs appear after entering some letters in for instance the drug name field. This functionality was seen as useful by the HCPs (HCP 1, 3, 5).

Problems/difficulties

The first page in the app is an instruction page. A HCP was confused by this information. The HCP was not sure what was meant with news items, create your list with products, etc (HCP 5). It was indicated that the app should be clear by itself without an information screen at the start.

One HCP mentioned that you should not be able to delete drugs from the list since general information should not be deleted (HCP 4). Maybe it should be more clearly described that it will only be deleted from your own created list.

Another HCP indicated that it is difficult to report a specific date for when the symptoms started (HCP 6). This is difficult for HCPs and patients. It is more easy to indicate that it was for instance about 3 months ago.

People like the menu's in which they can select the answer. However, a HCP indicated that free text options should be available for instance for the question about actions taken (HCP 6).

One HCP asked what the difference between a report and the watchlist was (HCP 3). Also for other HCPs it was not (immediately, entirely) clear what a watchlist was (HCP 7, 8). This issue might be solved by rephrasing the title Watchlist into a Dutch title.

After entering a drug name, the drug was presented three times in the list at the search function. The HCP expected that this had to do with different types of the drug (e.g. tablet, crème). However, it turned out that the drugs were the same (HCP 8).

There were also some words in the Dutch text that were not clear or confusing:

- Effect van de reactie (HCP 4, 5)
- Ondernomen actie met betrekking tot het medicijn (HCP 5)
- Plaats waar het medicijn is verkregen (HCP 6)
- Route (HCP 3).

Ideas/suggestions/tips

- The drug mentioned in the report can be directly added to the watchlist (HCP 4).
- If a report is started after a click of the link within the information of a drug, the drug name should already be entered in the report (HCP 8).
- The app should recognize both generic and brand names (HCP 2).
- You should be able to report the whole profile of ADRs, not only one symptom (HCP 2).
- After entering a drug, it would be useful that the known ADRs for that drug are visible and that you can select one of them (or enter another one) (HCP 2).
- For sex it would be better to present M and F and that you just can select one of the two instead of using the menu (HCP 4, 6, 7).
- Not everyone likes the wheel for the age and weight question. Some HCPs preferred to type the

answers, to have both options (the wheel and typing option), or to use categories that can be checked (HCP 3, 6-8).

- A calendar can be used for the question when you started the drug (HCP 4).
- The entered date of the start of the drug could be presented at the calendar of entering the start date of the reaction. This might increase the feasibility if you do for instance know that the reaction started after 3 days (HCP 4).
- It might be nice to see your progress in reporting an ADR. How many pages are left for instance (HCP 4).
- It would be nice if you can also swipe to the next page instead of only using the next button (HCP 4).
- Some questions may not be relevant for some drugs (e.g. allergic reactions, dose-dependency). If this is not important information for a drug, you can just leave it out (HCP 4).
- Make as much use of the touchscreen as possible, so as little typing as possible (HCP 4).
- The screen on which to enter the drug name scares. A lot of questions are asked. It might be an idea to first ask for the drug and then ask for the other questions on a different page. This additional page could then also present the drug-specific information such as 500, 850, 1000 mg for metformin so that you can select (HCP 4, 7). The same applies for the intake of the drug, metformin is oral, etc (HCP 4, 7).
- You cannot easily find the option that applies to you in the wheel with the options for the question where the drug has been obtained. It would be more easy to immediately present all the options and that you can check the one that applies (HCP 4).
- For weight you could set the wheel on the average weight in the population. Then you have to scroll less (HCP 4).
- It is inconvenient if you have the click on Done after you have selected the option that applies to you in the wheel. After the selection it should be done already (HCP 1).
- It was not clear why patient initials had to be entered (HCP 7).
- Several questions were seen as unimportant in an ADR report (e.g. where the drug has been obtained, reason of prescription) (HCP 7).
- With each question you should ask yourself whether the information is essential for the purpose. It should not be added for other purposes such as do HCPs prescribe correctly (HCP 7).
- It would be more logical to first report the ADR and then which actions were taken (HCP 7).
- A question asking for the time between the start of the drug and the start of the experienced ADR would be better than two separate questions asking for start date of the drug and start date of the ADR (HCP 7).
- Whether or not the ADR caused work absenteeism might be added to the seriousness (HCP 7).

Overall opinion

Some overall opinions:

- Clear, nice (HCP 1)
- Intuitive program (HCP 2)
- Not sufficiently user-friendly yet (HCP 3)
- First screen scares, some other small things should be adapted, but you start a report and you go through it and that is what you want (HCP 5).
- "I would not use this one" (HCP 7). The HCP did not like the layout of the app (boring and did not like the grayish letters). There is too much information in it.

4.4.2.5 *Social influence*

** Prestige*

The use of the app is expected to increase when it is clear that an organization with a great prestige is involved. In the Netherlands, this can be Lareb or Lareb in collaboration with for instance the

University Medical Center Groningen to increase the prestige (HCP 3,5).

** Type of ADR*

One HCP noted that agreement among HCPs at national level may stimulate the reporting of also other, less important ADRs (HCP 6). The reporting of such ADRs may be useful to see whether the documented numbers are correct (HCP 7). The goal of collecting ADR reports should be clear (HCP 8). For instance, is it about detecting rare ADRs or also quantifying the number of already known ADRs.

** Permission*

A HCP mentioned that permission of the patient is necessary to report the ADR through the app (HCP 1).

** Comparison*

It was indicated that comparing the number of reports in a year with colleagues (a kind of benchmarking) might stimulate to report in the future (HCP 7). It is important that the right terminology is used in such a report (HCP 8).

4.4.2.6 *Facilitating conditions*

** Layout*

The layout of the app may influence whether persons will use the app and will keep using the app. The following words were mentioned about the feeling that the layout of the app should create:

- Solid
- Classical
- Scientific
- Useful
- Professional
- Not old-fashioned
- Not overdone.

In addition, there should be a large button that users can press to report an ADR. (HCP 5).

Logo of the app

One HCP indicated that the logo of the app would be irrelevant (HCP 4). However, another HCP indicated that it should be clear that it has something to do with a drug, pill, tablet. In addition, it was suggested to link the logo to the agency that receives the reports (HCP 3).

** Security/confidentiality of the data*

The security of the app has been mentioned as a factor that influences the use of an app together with personal identifying information (HCP 2, 3, 6). However, most of the HCPs did not worry a lot about the security since they expect (or want to be sure) that no patient-identifiable details need to be entered and that the data will be handled confidentially (HCP 1, 2, 5, 6): "I should of course say that it should be a safe network etcetera, basically, you do not use the name of a patient, you use sex, date of birth, so I do not see any, no" (HCP 1). Storage of the report is ok when there is no patient-identifiable information in it or when you have permission of the patient (HCP 8).

** Operating system*

The developed app should be available for all operating systems on mobile phones/tablets (e.g. Android, iOS) (HCP 4).

* *Ideas/suggestions/tips*

Several ideas, suggestions or tips were provided by the HCPs to increase the facilitating conditions.

The first is to incorporate the option to make photos or to enter information using a dictaphone (HCP 3, 6, 7). Photos can be made of a computer screen showing the disease history or a list of the prescribed drugs of a patient. It will save a lot of work and it is easy to use, but the photo should be anonymous (HCP 8). The use of photos can also be useful for the agency who collects the reports since it may clarify the symptoms (e.g. HCP 8). However, it is questionable what will be done with the information (e.g. how is information extracted) (HCP 8).

Another idea was to connect the computer or another system (such as the electronic patient dossier or the GP information system (*huisartsen informatie systeem*) to the app (HCP 3, 4, 8). With such a connection, disease histories or medication lists may be uploaded into the app.

Ideas related to the reporting of ADRs are:

- After entering a drug, the ADRs that are known for that drug can be presented in the field to report the ADR using a drop-list. With such a functionality, it might be easy to just check the ADR and send the report (HCP 8). This functionality may also be useful to make a selection of ADRs for which additional information would be relevant (HCP 2).
- After entering a drug, reasons for using the drug can be pre-loaded. There should, however, always be the option to enter something else (HCP 6).
- In the end of the report it can be added whether or not the reporter wants additional information, 1) a first automatic report and 2) a more specific report in the future. HCPs might want to have such specific information for serious ADRs or special ADRs (HCP 5).
- Option to e-mail the feedback about the report and/or the submitted report to oneself (HCP 5).

Other ideas that were mentioned are:

- An overview of the frequency of ADRs associated with a drug (rarely, 1 in 10, less than 1%, etc) (HCP 2).
- The actual medication list of the patient in the app (HCP 4).
- Link in other medical apps (e.g. *farmacotherapeutisch Kompas*) to the new app to be able to directly report an ADR (HCP 5).
- Information about drugs (e.g. other statins) (HCP 6).

4.4.2.7 *Gender, age other characteristics*

Different user characteristics may influence whether or not an app will be used. The HCPs mentioned that younger professionals generally more often use smartphones and apps and that they are less fast in learning such new systems than younger HCPs (HCP 2, 3). In the future, however, the number of users will increase (HCP 2).

The HCPs also mentioned that a certain patient group will be reached with an app. The following characteristics were mentioned: Age, education level, intelligence, socio-economic status, ambition, dutifully, and assertiveness (HCP 1, 2, 3, 5). Patients with a lower socio-economic status for instance, will not be reached since they do not have a smartphone or they do not have the knowledge to use such technology. In addition, some patients may not dare to report an ADR, some may be unsure about whether they are able to report, some will not be able to report and some possibly do not feel like doing it (HCP 5).

4.4.2.8 *Experience*

Experience with mobile phones in general and apps more specifically may influence whether an app will be used to report an ADR. In addition, past experience will influence how easy to use the app is for the user. A HCP might not have much experience with mobile phones (HCP 2) or apps (HCP 1, 5).

In addition, some HCPs barely use health-related apps (HCPs 2), whereas others already use several of such apps (HCP 4).

4.4.2.9 Behavioral intention

Curiosity is one of the main reasons for HCPs to download the developed app (HCP 3, 4, 6). In its current stage, some HCPs felt the user-friendliness should be increased and/or additional things as discussed previously should be incorporated (HCP 2-4).

4.4.2.10 Use behavior

An app may be especially useful when a HCP is not sitting behind his or her desk (HCP 7). In the end, when the app is used, there should also be attention to stimulate reuse of the app. This could be done by sending app updates once in a while (HCP 2).

4.5 Results Portugal

4.5.1 Pharmacovigilance specialists

Rational for the app/ general concept

4.5.1.1 Patients

In terms of general concept of the app the opinions were different in the group for patient target.

- a) Available safety information to the patients would not be helpful and safe as a lot of patients have not knowledge to understand what it means and we can run risks in terms of treatment compliance. Patients shouldn't be access to this kind of information. How this kind of information may cause doubts to the patients. The information must reach the people who really need it. The information has to be balanced for the different target if patients or healthcare professionals.
- b) It is a benefit to have all safety information available to the patients as a transparency practice. Patients should know if they should have any action. On the other hand, patients who are using devices to upload the app have enough knowledge to understand also what would be available on the app. Nowadays, this information is already available on the local Health Authorities website. Besides safety information also quality information (alerts) should also be available on the app for this target. Language used on the information for patients should be different, easier than for Healthcare professionals.
- c) Patients should be very well trained in the app in order to understand its potential and how to use the available information. For its efficacy the app disclosure should be done through healthcare professionals (physicians) but in the real life it will be more difficult due their unavailability. Awareness campaigns are mandatory for its success in quantitative and qualitative aspects for this target.
- d) With no or mild impact on reporting rate by patients unless by young patients if there is an intensive awareness campaign through patient associations.
- e) The app should allow healthcare professional's validation.
- f) Patient must be able to delete the application if desired.

4.5.1.2 Healthcare Professionals

- a) Healthcare professionals must receive all safety alerts with no medical expertise discrimination as all clinical information is very important. Healthcare professionals must choose whether to receive or not.
As very important aspect this functionality allows receiving information more quickly and easily.
- b) All safety information disseminated should be evaluated in terms of its global impact. It is an imperative that the information is evaluated and balanced before its dissemination.
- c) It will be an added value for pharmacists if quality alerts are also available in the same way. Quality and safety alerts should appear as an option to select or for instance with different colors. Quality alerts are also important for prescribers.
- d) Training sessions should be conducted by local Health Authorities as well as very good disclosure and awareness campaigns and through professional associations. The best app disclosure will be by sharing experiences. Periodic updates will be also important in order to create usage habits.
- e) Slight impact on reporting rate unless the app allows to report in a time less than 5 minutes. In fact under reporting is still a reality in Portugal and lack of time is always mentioned as main cause for it.
The app will not change the type of reaction to report, serious and unknown (not unexpected) by the physician.

- f) Confidentiality, customization will be concerns over the reporting through this app. It is crucial that the information regarding personal data protection is very clear and concise.
- g) In order to be appealing the app should be quick, with no many fields to fill, few screens and user friendly.
- h) Healthcare professional must be able to delete the app as desired.

4.5.1.3 Review of the app

Functionalities improvement

- Portuguese (from Portugal) language available on the app is an imperative.
- It is not clear which fields are mandatory on the app. They should be defined with an * or a different color for instance. During the first approach it was considered as no user-friendly
- It is confused to have patient in the middle of the healthcare professionals list. There should be a profile division like HCP button and Patient button and then on the field of HCP should appear a drop-down list. It doesn't make sense to have other on this field.
- Clear instructions for its fill are missed. The app must have clear instructions for the user in order to fill all fields. "Medically important event" must be clarified as for patients and for some HCPs PV seriousness criteria are not the same. Sometimes what it is severe is considered serious.
- It was also considered to be slow which will be an important issue to solve. It was identified need to make faster tool.
- Age button must have units (i.e years, months, days) as we also receive cases regarding babies and they are not just from breast feeding. This button may have years as units in default.
- Date of birth is important information to identify duplicate cases so; it should be added but as not mandatory field because sometimes we cannot get it. Date of birth and patient initials are important fields to search duplicates cases.
- Age group field is missed and sometimes when we don't know the date of birth and age we know the age group.
- Patient initials field is not the most relevant information to be mandatory.
- It is not clear if the age means age at the reporting time or age when the ADR occurred.
- The app must require just essential information in order to reduce the number of the fields, screens and time. It is a complex tool with a lot of information request. Each screen must have basic information and additionally a button like "more" in order to complete the information when it is available. This functionality would create a more appealing image on the first contact.
- Route information is too much complex, with a lot of options and some of them will not be understood by patients in general.
- Rotation screen is not active on the app, sometimes it is useful mainly we are using a smartphone.
- Too much information (MedDRA terms) on the ADR field, which will not be easy for patients. On the other hand, it is not easy to understand that we need click in "done" to select the correct option. It would be easier select directly on the term.
- "Yes" and "No" button is not clear. We don't know which is "yes" or "no".
- The risk information for all products must be available not just for the products that the ADR is being reported. For instance in case of HCP desired to know about other drugs that are prescribing. We cannot deny information as it is better to have access to validated and reliable information. For HCP this information must be more detailed than for patients. For patients it is not important to give ADR incidence.
- After reporting it would be nice to provide an acknowledgement email to the reporters in order to give them feedback like a summary explanation regarding their report. For patients these messages could include information like visit your doctor regarding this adverse event, for instance.
- The app should allow to do follow ups. Consent field should be added in order patient allow to contact the HCPs giving their contacts.

- New information should be available immediately and not in a periodic basis.
- There should be an open field for HCPs write what it is real relevant in order to increase the quality of the reported case.
- Login is easy but patient registration should allow an automatic fill of the patient fields.

4.5.1.4 General overview of the focus group

The app may have a high potential among young healthcare professionals and patients.
Important tool in terms of Public Health.
It has a nice layout in terms of font and color.
It is easy to access.
No any comment to the logo.

4.6 Results Sweden

4.6.1 Pharmacovigilance specialists

4.6.1.1 Motivation for patients/HCP

2 types of patients

- Those who look for info by reporting the AE (often also via asking question)
Possible motivator is to have the Safety alerts as a part of the news feed that provide some info to the patients. These patients are likely to be motivated if they can find on the app if a specific AE has been reported before: Though some of the data on the News feed could seem sometimes a bit too complicated for patients so the question is whether it would be advantageous to have a separate app for HCPs and Patients.
- Those who want to report an AE because they want to warn others.
This is the “more active” group that could probably use the app easier just to report an AE. But for these patients it is also important to understand what happens with the info that they have submitted. So any clarification of the “AE processing” process might be helpful so that they for example clearly understand what the tables really mean that display per product how many AEs of a certain type have been reported. Though this latter, clarify what has been reported already before might also be helpful for the patients who look for some more info on the products.

HCPs

- In Sweden, it is mandatory for HCPs to report adverse reactions so the app as such might not change the driving factor HCPs would report.
- But if HCP would indeed be using mobile devices in a frequent way during their day to day work it might ease the uptake of the app significantly.
The problem is just that we don't have a very good idea how much HCP are using mobile devices during their work.
- The news feed seems on the other hand indeed like a feature that definitely could motivate HCPs to use the app because they can get an “smart way”, i.e. not via traditional mailings, safety updates on products that they are interested in.
The app has also features that makes it very easy for a user to save some of the Safety updates content easily in a note or send it as a message/email so that data seems very well accessible.

4.6.1.2 Detailed feature review of the app

Following did look like errors/bugs

- users have to enter very frequent their email address and password each time
- if you entered weight, and then you don't want to have the details left there on the weight then you're not able to clear the field
- sometimes the keyboard is hiding certain field

Here is a list with proposals to improve the app

- To submit follow up info to a report that was previously submitted
It was not clear from the test version how that would work.
- “Medically important event”, for a patient everything is important, so everything would be serious, maybe there is a need to clarify further what all these different seriousness criteria really mean
- if I reported something, it would be good to send a receipt to my email for example. As a reporter it could be interesting to transfer the info of my report from the app to an email.
- Comment regarding the overview of AEs that were submitted previously to the agency
Here you have information of adverse reaction reported to the health authority previously but it does not say anything about that these are or are not confirmed reactions. (it might be that these are all AEs submitted to the agency but that for a lot of them there was no proof of causality) So

the patients could say “oh my god” all these reports are not in fass.se and they seem to have been reported from another system

- The news feed’s most missing part is the product information that doesn’t seem to be here. Having some normal product information (SmPC or PIL) was felt as a big miss and it could be a big advantage to have indeed that info available in the app because that could be another motivator for HCP/patients to use the app

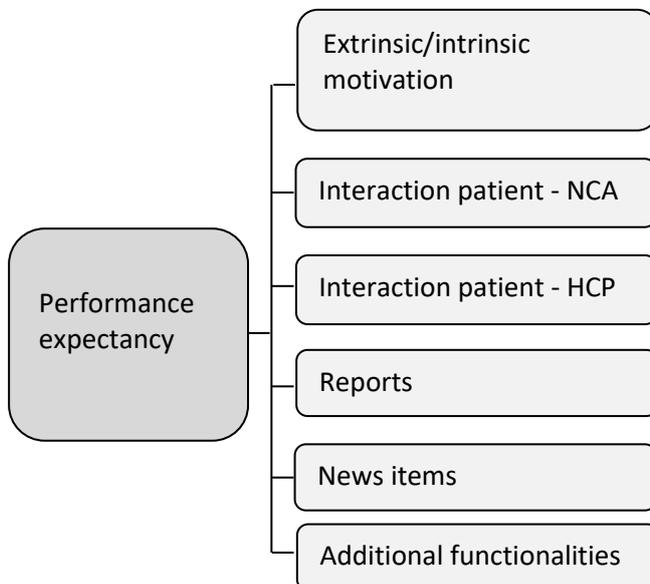
Overall impression of the focus group members

Overall it’s easy to use and it has a lot of potential

4.7 Overall conceptual framework of barriers and facilitators

An overall conceptual framework of barriers and facilitators for using a mobile app on two-way risk communication has been developed based on the presented results. The extracted themes were arranged according to the themes in the UTAUT model. Below, the extracted themes are presented and a summary of each extracted theme is given.

4.7.1 Performance expectancy



Extrinsic/intrinsic motivation

There was some discrepancy in motivation to report ADRs. Most patients and HCPs indicated to report an ADR based on intrinsic reasons and that extrinsic reasons should not be the motivation to report an ADR (e.g. *"We are professionals so we have a certain faith so to speak"*, the Netherlands, HCP 5; *"If I knew that the app that I was inputting all this information would benefit other people as well, then I would"*, the UK, focus group with patients). However, there were also some HCPs who suggested that extrinsic reasons may stimulate the reporting: *"You can also use a kind of incentive. To encourage people"* (the Netherlands, HCP 2). It was stated that ADR reporting is always in addition to structural tasks and that it does not directly reveal any gains (the Netherlands, HCP 8). Reporting ADRs through the local system was considered more beneficial by a HCP (face-to-face interview UK) as the app, *"doesn't provide opportunity to learn or understand what's going on locally so in that context if I were to report or encourage reporting it would be through local systems so that we could have the richness of the data"*.

Interaction patient – NCA

It was indicated that it should be possible to provide feedback on the app. Also, feedback from the NCA to the patient was mentioned as possible stimulus to use the app. This can be 1) feedback in general about for instance the number of reported ADRs over a period of time and which drugs causes most of these ADRs, and 2) feedback after sending a report (see section 'reports' below).

Interaction patient – HCP

The app may empower patients in the communication with their HCP: *"People who do not have the medical knowledge can have a look at their phone and they can see that it happens more often [a specific symptom], so I can discuss it with my doctor"* (the Netherlands, patient 3). It might also give

a patient trust in their idea of a symptom being an ADR, also if a HCP is not aware of this association.

Some patients indicated that they do not want to visit the doctor for every symptom they experience. The app may help such patients to check whether symptoms can be related to drug use: *“I have a new tablet and I have pain somewhere in my body and I do not know exactly what it is, and I do not want to go immediately to my doctor and that you have this and see what has been reported”* (the Netherlands, patient 2) and *“It would help if you are sort of feeling side effects that are lower down the list, you would possibly be alerted to go to the GP and also if you are higher up then you would just accept that that’s a common side effect”* (the UK, focus group with patients). However, this may be related to a concern of HCPs that patients might report the ADR through the app and take no further action: *“Don’t want them to just report it and then carrying on with their life...don’t want it to be a replacement for seeing their HCP”* (the UK, focus group with HCPs). This concern seems to be justified in some cases since it was mentioned by adolescents that the app may reduce the need for a verbal conversation with a HCP, particularly in case of embarrassing conditions (e.g. emotional problems) (the UK, focus group with patients).

Some patients did not feel that their ADR report should go to their HCP. In their opinion the ADR is often already discussed with the HCP before the ADR will be reported. However, some HCPs were worried about the quality of patient reports: *“I think the amount of noise would be tremendous and there will be huge IT costs in the development of algorithms to try to find the meaning of signals in all that noise”* (the UK, focus group with HCPs). Therefore, they suggested to perform some quality checks such as inviting the HCP to also report the ADR for a particular patient or to ask additional questions in the patient report (e.g. whether it has been discussed with the HCP, whether other causes have been examined). HCPs caring for rare disease patients stated that reports of their patients should be validated by a HCP before sending it anywhere else (Spain, focus group with patients). It was mentioned several times that a link of the reports to a patient’s clinical file would be useful. HCPs would immediately be up-to-date when opening a clinical file of a patient. Also, they may be willing to know what has been reported by their patients: *“If patients were reporting ADRs of drugs I’d started it would be useful to know. Definitely”* (the UK, focus group with HCPs) (also Spain, focus group HCPs).

Reports

It was indicated that it should be easy to report an ADR with as little questions to answer as possible: *“The more info you want, the longer it will take to complete”* (the UK, focus group with HCPs). Reporting an ADR may be less bothersome for patients than for HCPs, so patients could be asked more questions than HCPs (the Netherlands, HCP 7).

After a report, most of the people want some kind of feedback. This can be a confirmation that the report has been successfully send and/or an overview of how often this report has been made previously and/or automatic news messages about the drug for which they did the report and/or information on the long-term about any consequences for the drug or of the report. Others expected some kind of action from HCPs and concerns were raised that feedback might come too late if the ADR was serious (the UK, focus group with patients). They suggested that a serious ADR could be flagged up on the GP’s database to contact the patient.

Feedback was seen as distracting to some people. It is therefore useful to provide checkboxes in which people can indicate whether or not they want to receive such information.

Most of the people preferred to keep having access to their reported ADRs and to store unfinished reports so that they can continue these at a later moment.

News items

There was some diversity in opinions about news items in the app. Some people felt that news items could be useful (e.g. *“I think that this can be a fast way to extra inform end-users, prescribers about new information that is known about it”*, the Netherlands, HCP 8) whereas others felt that

the goal of the app should simply be to report ADRs (e.g. *"I would not directly link it to the app to my feeling, you have other sources for that"*, the Netherlands, HCP 2; They would never be interested in this tool if the updates provided are duplicated by any other official media, Spain, focus group HCPs; Available safety information to the patients would not be helpful and safe as a lot of patients have not the knowledge to understand what it means and we can run risks in terms of treatment compliance, Portugal, focus group PV experts).

People who were interested in news items reported various types of news items that were of interest. Some examples are:

- ADRs not on the list of known ADRs of a drug;
- Changes in the frequency of an ADR with a drug (e.g. from rarely to often);
- New interactions;
- DHPCs;
- Drugs that are taken off the market;
- Newly marketed drugs or new applications of a drug;
- Changes in guidelines.

However, not all people were interested in each type of information. In addition, some people wanted to see information for each type of drug whereas others were only interested in those that they take/prescribe. Therefore, it is suggested that app users are able to personalize the type of information they want to be updated about.

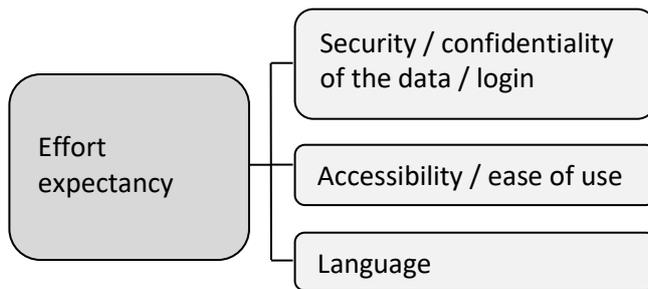
An important aspect for news items is the source of the information (see section Prestige / reliable, independent source below).

Additional functionalities

Several other functionalities were reported as being useful in such an app. Some examples are:

- Product information of drugs (e.g. *"[information for all drugs about] their function, ADRs, how often ADRs occur, the best way to take the drug"* (the Netherlands, patient 1). This may, however, also negatively influence adherence: *"I personally would use it before I take a medication as well to see what sort of side effects I may have in case it's something severe I may not want to take the medication"* (the UK, focus group with patients)(Spain, focus groups with HCPs);
- Experiences with a drug and option to add experiences: *"whether other people have experienced similar side effects with the same med"* (the UK, focus group with patients). For instance using a (link to) a forum;
- Present alternative drugs to the one an ADR is experienced;
- Present also quality alerts (added value for pharmacists and prescribers);
- Summary of guidelines;
- Information about how to resolve/alleviate the ADR;
- Interactions between drugs;
- A kind of a prediction model presenting the likelihood of a symptom being an ADR after entering some information. This would be useful for HCPs but also for patients: *"If you were taking 2 medicines at the same time how would you decide which side effect belonged to each drug?"* (the UK, focus group with patients);
- A function to remind for instance to report an ADR, an appointment with a HCP, or to take drugs (the UK, focus group with patients). Although it was also mentioned that a reminder functionality for taking prescribed drugs was not relevant (the Netherlands, patient 2);
- The option to store a list of (previous) prescribed drugs *"so that you could see whether or not drugs are affecting other drugs you're taking so far...to show to a health care professional or pharmacist"* (the UK, focus group with patients). This can provide an actual drug list for HCPs, which is useful for both HCPs and patients (the Netherlands, HCP 4). The drug list can be added to the ADR report which is useful to check whether co-medication might be influencing the ADR instead of a single drug entered by the patient (the Netherlands, patient 4).

4.7.2 Effort expectancy



Security / confidentiality of the data / login

A safe app was mentioned as important and *“the safer it is, the more people will use it”* (the Netherlands, patient 3). However, most of the people did not seem to worry a lot about the security since they expect (or want to be sure) that no patient-identifiable details need to be entered and that the data will be handled confidentially: *“I should of course say that it should be a safe network etcetera, basically, you do not use the name of a patient, you use sex, date of birth, so I do not see any, no”* (the Netherlands, HCP 1). Storage of the report was seen as ok when there is no patient-identifiable information in it or when there is permission of the patient (the Netherlands, HCP 8).

People with or involved in the care of patients with a rare disease and adolescents seemed to be more concerned about the security of the app and the personal information in it. It was for instance mentioned that they would not use their real name but *“put in a false name”* (the UK, focus group with patients). Using login details to enter the app was seen by them as an advantage to protect the data: *“people messing around on your phone can’t log onto the account, so people can’t just get into it and send random side effects”* (the UK, focus group with patients). Some of the other people found it annoying to always enter the login details and they were not so worried about data in the app: *“There are no big medical secrets in it”* (the Netherlands, patient 3). It is suggested that the user can indicate him-/herself whether or not to save the login details.

Accessibility/ease of use

An app was seen as easily accessible: *“You are immediately there where you have to be, you don’t have to search on Google, you don’t have to use paper and pen, you don’t have to call”* (the Netherlands, patient 4). However, there should be attention to inform potential app users about the existence of the app since there are (too) many apps available: *“The problem with apps is that there are so many that you don’t oversee it”* (the Netherlands, HCP 5).

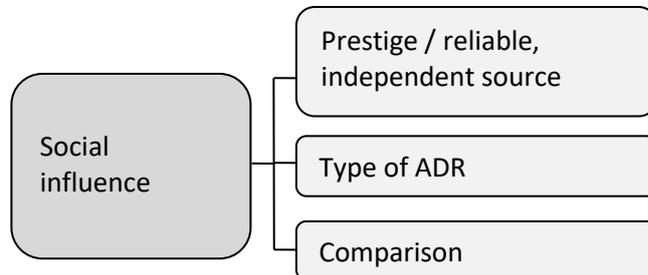
Some keywords for a successful app that were given are: Easy, simple, short, clear, logical. Such an app may increase the reporting of ADRs since time constraints was often mentioned by HCPs as a factor for not reporting an ADR (the Netherlands, HCP 3-8). Time was also mentioned by patients, specifically related to reporting an ADR: *“If I had to input all the information, if it took a lot of time I don’t think I will [use it]”* (the UK, focus group with patients). In general, apps that do not work like the mentioned keywords will not be used (again).

Examples of functionalities that were mentioned as increasing the ease of use and which were appreciated were presenting a list with for instance drug names after entering some letters and providing a list with answer options from which the person can select his/her answer (click on and/or drop down options). For this latter option, people often preferred to also have the option to enter their answer or at least to be able to provide another answer than the once provided. Illogicalities such as presenting pregnancy questions to a person who entered being a male, were seen as very annoying and such illogicalities introduced the feeling of not being taken seriously. Over-reporting was mentioned as a possible concern of a very easy to use app.

Language

The language in the app has been mentioned as an important factor of using the app. It was mentioned more often that the language in the app should be different for patients and HCPs. For HCPs and patients the terminology that should be used is respectively medical terminology and laymen terminology. Some HCPs as well as patients indicated that it would be useful when the app could be used in other languages.

4.7.3 Social influence



Prestige / reliable, independent source

It was mentioned that a clear link of the app to an organization with a great prestige increases the use of the app: *“people will trust it more if they know it is from [e.g.] NHS”* (the UK, focus group with patients). In addition, a reliable source should be linked to the app and this link should be clear to its users. A reliable source was first of all mentioned as important to inform people about the existence of the app. Moreover, it was mentioned by patients that if the app was *“endorsed by a doctor then [it] would be used a lot”* (the UK, focus group with patients) indicating that HCPs may increase app use among their patients. In addition, it was seen as important that ADR reports are sent to and that information in the app is provided by a reliable source. This will provide trust in the app. The ADR reports should be assessed by an independent source and any other information exchange should not contain any commercial interest. The source should be familiar to the users. A topic that specifically came up during the focus group discussion with adolescents was whether parents should be able to view their child’s ADR reports. In general, older children preferred parents not to have access and younger children wanted parents to be informed.

Type of ADR

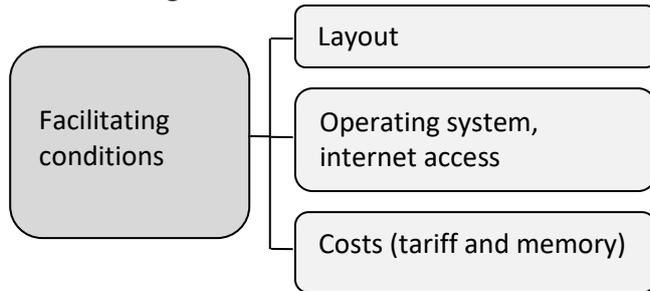
Currently, HCPs mentioned that they would report new ADRs/ADRs that are unknown, serious ADRs and ADRs of a new drug. The goal of collecting ADRs should be clear. For instance is it about detecting rare ADRs or also to quantify the number of already known ADRs. Participants were unsure if less severe ADRs required reporting: *“Depending on the severity of the reaction or the side effect so if it’s just a little bit of nausea and they are not violently sick so maybe that would put you off”, “if there’s a less severe side effect you’re less likely to”*(the UK, focus group with HCPs).

Also patients seemed to be unsure about which ADRs to report: *“Is this severe enough to report?”, “or they should say that you can report every ADR so that you don’t have to think about whether this is something that they intend to collect”* (the Netherlands, patient 4).

Comparison

It was mentioned by a HCP that comparing the number of reported ADRs with colleagues (a kind of benchmarking) might stimulate to report in the future. Also, a HCP’s comparison with his/her own previous reports may stimulate the reporting: *“In the last months, I always did 20 reports, this time it was 2, what is the cause of that? So that is also to stimulate to report”* (the Netherlands, HCP 4).

4.7.4 Facilitating conditions



Layout

The layout of an app was seen as important and as an influencing factor for whether people will use the app and will keep on using the app. In general, it was suggested to never use very bright colours. Such colours are annoying for a lot of people (e.g. people with epilepsy). It was indicated that it would be attractive that people can change the colours as well as the lettertype and font size themselves. Such a personalized app would incentivise its use. The font size is particularly important for people with impaired vision.

The logo of the app should be recognizable and appealing. It should be clear from the logo what you can do with it and it may be linked to the agency that receives the reports.

Operating system, internet access

It was mentioned that the app should be available for all operating systems on mobile phones and tablets and that they should have been tested on each system before an app will be launched. Adolescents were the only group who mentioned that it should be possible to make an ADR report without internet access. The report can be send later when there is internet access. Internet access may be related to the following topic, that is, costs in the sense that adolescents may only use WiFi on their mobile phone.

Costs (tariff and memory)

It was indicated that the app should be free of charge to stimulate its use. A topic that was mentioned only by adolescents or HCPs treating adolescents was the amount of space the app takes up on an individual's device: "Will it clog up your phone", "take up loads of memory", "how cumbersome or big is the app", "what is the size of sending an average response (report). Is it in terms of just a few kilobytes?" (the UK, focus group with HCPs).

4.7.5 Moderating variables

Several user characteristics are described in the UTAUT model as moderating factors, that is age, gender, experience and voluntariness of use. Age and experience were also mentioned in our study. Compared to younger people, it was mentioned that older people are less often in the possession of a mobile phone or tablet, are more often visually impaired and are generally less experienced with apps. These factors influence whether such patients will be reached through an app and influences their preferences within the app (e.g. font size). In addition, it was indicated that a user's experience also influences how easy it is to use the app.

In our study, also other characteristics were mentioned as influencing factors in whether or not an app can/will be used. Characteristics such as education level, cognitive skills, socio-economic status, ambition, dutifully, assertiveness, curiosity, being interested and anxiousness were mentioned as influencing factors on being in the possession of a mobile phone or tablet, having the knowledge to use an app, looking for information on the app, and (dare to, being able to, willing to) reporting ADRs through an app.

4.7.6 Behavioral intention

In general, people were quite positive about such an app. They liked the idea and indicated that there seems to be a need for it.

4.8 Practical recommendations to improve the WEB-RADR app

General

- * The more personalizable an app is, the better. Users should have the option to indicate their preferences in the app (e.g. whether or not they want to receive feedback after a report, store login details and how they app should look like).
- * Answering the question about whole disease and medication history is too much work. Patients seem to be willing to enter it once. So the entered information should appear again in a later report. For HCPs there should be other options to provide this information (e.g. that the patient is contacted for the information or by a dictophone, photo function or to connect/link to the clinical file).
- * Different language should be used in an app for patients and HCPs. There should be differences in terminology (whether medical terminology is used) and questions should be rephrased (when did you start the drug vs when did the patient start the drug). Moreover, answer options may differ between both versions (the option of “death” in the consequences of the ADR must be removed or if necessary expressed in a different wording in the patient version). Furthermore “Medically important event”, for a patient everything is important, so everything would be serious, maybe there is a need to clarify further what all these different seriousness criteria really mean.
- * The logo of the app should be more recognizable and appealing. It should be clear from the logo what you can do with the app.
- * Some users prefer a kind of home-screen where the different options are presented with nice buttons. The buttons ‘Report’ and ‘Watchlist’ were not clear to everyone.
- * An arrow to go to the previous page would be useful on each page in the app.
- * The developed app should be available for all operating systems on mobile phones/tablets.
- * It was seen as useful if someone can change the language of the app.
- * The app was considered as slow, it should be a faster tool.

Information screen

The information screen was not entirely clear and a bit confusing. It was indicated that the app should be clear by itself without an information screen at the start.

Profile

Patient is in the middle of the healthcare professionals list which is confusing. There should be a profile division like HCP button and Patient button and then on the field of HCP should appear a drop-down list. Also some of the professionals on the list might not be appropriate, for example a HCP asked whether a biomedical engineer would submit an ADR report (UK face-to-face interview).

News items

- * If someone is searching for news about a specific drug, news about other related drugs should not be presented. Such news items can be presented when people have to select for instance a disease or a drug class but not when they enter a specific drug.
- * After a click on the news item, the news should be immediately presented. It should not be necessary to click on ‘keep reading’ (this is an additional step). In addition, it was difficult to return to the app after the news item was opened. The information was presented on the internet and it took several steps to return to the app.

Report

General

- * A report should take as less time as possible. The app must require just essential information in order to reduce the number of fields, screens and time. Currently, it is complex with a lot of

information request.

- * Illogicalities should be deleted from the app (e.g. not asking for end date of the drug when the drug was not stopped). It would be preferred that the entered information will influence which follow-up questions and answer options are presented. For example with lipid-lowering drugs the route of administration will be standardized to oral.
- * It should be clear which questions are not obligatory (e.g. by using stars behind obligatory questions).
- * Several questions were seen as unimportant in an ADR report (e.g. where the drug has been obtained, reason of prescription; initials). Providing some background information per question why it is asked for instance may reduce resistance to complete the question.
- * It would be more logical to first report the ADR and then which actions were taken.
- * The age button must have units (i.e. years, months, days). And it should be clarified whether it is age at the reporting time or age when the ADR occurred.
- * Date of birth is important information to identify duplicates (suggestion to add but not as mandatory).
- * The severity of the ADR may reveal addition, important information to ask for in a report.

Terminology

- * People were not familiar with the term batchnumber. It would be useful to provide information boxes explaining terms like this.
- * Terminology for how the drug is taken is not clear to patients and there are too many options.

Symbols

- * The symbol  is not clear to everyone and confusing for others since it indicates on/off. Suggestion to use or add the text "yes/no".
- * The red button with the white stripe behind an entered symptom was not clear. Suggestion to use a bin.

(wheel with) Answer options

- * People should also be able to enter a drug name instead of being forced to select a drug from the list.
- * After a click on the answer option in the wheel it should be immediately checked instead of having to click on 'done' (this is an additional step). It would be useful to provide also the option that users can enter the answer themselves (instead of being forced to use the wheel).
- * The answer options for the question on actions taken are not complete. Some users wanted to enter that they take the drug at another point of time or that they had a switch to the former drug. Suggestion to add Other, namely.
- * The question "Did the drug cause a similar reaction before" was confusing since the person had not taken the drug before. It was suggested to add the option "Unknown".

Layout

- * Several users didn't see the bar which they had to click to enter their ADR. Layout of the bar can be adapted.
- * It should be more clearly differentiated which reports are submitted and where a new report can be done.

Feasibility

- * In the field below the question of current and previous illnesses people had to delete the text "please describe..." before they could enter their answer. This should be immediately deleted when someone wants to enter information.
- * It is difficult for people to report a specific date (e.g. for when the symptoms started). It is more easy to indicate that it was for instance about 3 months ago. Suggestion to add the option to provide this information instead of being forced to check a date. Or a calendar can be used. The entered date of the start of the drug could be presented at the calendar of entering the start date

of the reaction.

- * Do also use drop down menu's for strength.
- * If weight was entered and it should be removed, it was not possible to clear the field.
- * Sometimes the keyboard is hiding certain field.
- * If a report is started after a click of the link within the information of a drug, the drug name should already be entered in the report.
- * After entering a drug, it would be useful that the known ADRs for that drug are visible and that you can select one of them or enter another one.
- * For sex it would be better to present M and F and that you just can select one of the two instead of using the menu.
- * It would be nice to see the progress in reporting an ADR.
- * It would be nice if you can also swipe to the next page instead of only using the next button.
- * For weight you could set the wheel on the average weight in the population. Then you have to scroll less.

Storage of reports

- * It should be possible to store previous ADR reports in the app.
- * The drug name, date of the report and maybe the ADR at a higher level, but not the code [GB-MHRA-WEB-RADR1000...] should be indicated in the heading of the previous reports. Patient number would also be useful and it would be useful to sort the reports on each of these (e.g. date, drug name, ADR).
- * It would be useful if a report could be continued at a later moment. In addition, it would be useful to add information to a previously submitted ADR report.

Other

- * Dosage: 50mg for instance but it is not asked how often per day.
- * The app should recognize both generic and brand names.
- * You should be able to report the whole profile of ADRs, not only one symptom.

Graph

- * The graph would be more useful when the specific ADRs are also presented (not only the SOC levels), for instance after a click of a SOC.
- * It is not clear whether the overview of ADRs are confirmed reactions or just all the previously submitted ADRs.

Search function

After entering a drug name, the drug was presented three times in the list at the search function. This was confusing.

Specific suggestions to UK app

- * There was discussion about what the 'strength' field meant on the reporting page of the app.
- * There was also debate about the word 'route'.
- * Confusion about the question 'Where was the medicine taken'.
- * Report might be changed to report ADRs.
- * The meaning of one phrase in the app caused some confusion in the group. "What is equivalent to suspect stroke or concomitant?".
- * Add life or limb threatening rather than just life threatening.

Specific suggestions to Dutch app

- * Change "route" into "toedieningsvorm".
- * Not clear what was meant with "Land waar de reactie is begonnen" (suggestion to use "bijwerking" instead of "reactie").
- * It was indicated that the question "Plaats waar het medicijn is verkregen" was confusing since the

drug was prescribed in the hospital but obtained in the pharmacy.

* Unclear or confusing sentences: Effect van de reactie; ondernomen actie met betrekking tot het medicijn; plaats waar het medicijn is verkregen.

5 Discussion

This study revealed 1) general knowledge about barriers and facilitators to use a mobile app on two-way risk communication and 2) feedback on the prototype app. The study had a qualitative design in which the opinion and ideas of a small number of patients and HCPs was addressed. The results of the study are input for a quantitative study among a larger number of patients and HCPs to quantitatively assess barriers and facilitators to use a mobile app on two-way risk communication. The feedback on the prototype app is input for other work packages within the WEB-RADR project to improve the app.

5.1.1 Barriers and facilitators according to the UTAUT model

In our study, the UTAUT model was used as a theoretical base. The UTAUT model describes four variables that influence the behavioural intention to perform a certain behaviour or here to use a mobile app for two-way risk communication. The four variables are performance expectancy, effort expectancy, social influence and facilitating conditions. According to these four variables, an overview of detected barriers and facilitators in the current study for using an app on two-way risk communication is presented in table 4.

Most of the detected barriers and facilitators will be further addressed in follow-up studies, in particular during the upcoming, quantitative study (table 4). Barriers and facilitators related to the accessibility/ease of use and layout of the app will be assessed in a follow-up study using a discrete choice experiment. No further assessment will be performed on the themes language and operating system, internet access since it is expected that everyone will agree that an app should be available for and tested on all operating systems and that a different language should to be used in an app for patients and HCPs.

From the current study it became clear that there were some discrepancies in importance attached to the various barriers and facilitators. The upcoming, quantitative study will be used to assess at least the following discrepancies:

- Link the ADR report to clinical file or present it to HCP. There was some discrepancy in whether or not an ADR report of a patient should be presented to his/her HCPs.
- The type of news people would like to receive. Some people indicated that the app should just focus on ADR reporting whereas other people wanted as much news in the app as possible. In case they want to receive news: which type of news do they want? A lot of ideas were given (e.g. drugs that are taken off the market, new applications of a drug) but there was discrepancy in the type of news people were interested in.
- Most of the people stated that they want a kind of feedback after submitting a report. There was, however, discrepancy on the type of feedback (e.g. immediately that the report has been successfully send, an overview of previous related reports, a follow-up survey about changes in the ADR over time). For more information about the feedback one can provide to reporters, it is also proposed to explore the results of the survey conducted by the SCOPE Joint Action on patient reporting, where 15 member states reported sending some kind of feedback to patients who report suspected ADRs.

From the current study it also became clear that there may be differences 1) between patients and HCPs, 2) between patients and HCPs for the different disease types in this study, and 3) among countries in perceived barriers and facilitators and other relevant aspects regarding a mobile app for two-way risk communication. Therefore, the quantitative study will be used to test at least the following aspects:

- Worry about the security of the app (using login codes for entering the data). Adolescents and patients with or HCPs treating patients with a rare disease and adolescents seemed to be more worried about the security of the app than other patients and HCPs. It will be assessed whether these populations are indeed more worried about the security of an app.
- The costs in terms of space on someone's device has only been mentioned by adolescents or HCPs treating adolescents. It might be that this is particularly an issue for younger persons or for people in the UK.
- There was confusion about which type of ADRs people are expected to report. In Sweden and Spain, it is mandatory for HCPs to report ADRs and it has been defined which ADRs they are expected to report. This may influence which type of ADRs people are willing or intend to report. It will be assessed whether there are differences among countries in the type of ADRs HCPs are willing to report.

Table 4. Overview of detected barriers and facilitators per variable of the UTAUT model

Variable	Barriers	Facilitators	Assessed in future study?
<i>Performance expectancy</i>			
Extrinsic/intrinsic motivation	Extrinsic reasons (e.g. financial rewards) should not be the motivation to report	Extrinsic reasons may stimulate the reporting	Study 2: Quantitative assessment (only in HCP survey)
Interaction patient – NCA		* It should be possible to provide feedback * Feedback from NCA to patient may stimulate	Study 2: Quantitative assessment (only in patient survey)
Interaction patient – HCP	* Patients may report an ADR through the app and take no further action * Some patients did not feel that their ADR report should go to their HCP * Concerns about quality of ADR report if patient sends directly	* App may empower patients in communication with HCP * App can help patients check if a symptom might be an ADR * App may help those who do not want to visit the doctor for every symptom	Study 2: Quantitative assessment
Reports	* Feedback may be distracting	* As few questions as possible * Provide feedback after a report * Store reports on app * Continue unfinished reports at a later moment	Study 2: Quantitative assessment
News items	* Goal of the app should simply be to report ADRs * Not all people were interested in any type of news	* News could be useful * Different types of news items were suggested * Source of the information	Study 2: Quantitative assessment Study 3: Discrete choice experiment
Additional functionalities	* Other functionalities may have negative effects (e.g. reducing adherence)	* Several other functionalities were seen as useful	Study 2: Quantitative assessment
<i>Effort expectancy</i>			
Security/confidentiality of the data/login	* Concerns about security of the app * Concerns about personal information in it	* A safe app * No need to enter patient-identifiable details * Confidential handling of the data	Study 2: Quantitative assessment

	* Annoying to always enter login details	* Login detail protect the data	
Accessibility/ease of use	* (too) many apps available (how to inform people about the app) * Time constraints * Illogicalities in doing a report	* App is easily accessible * Easy, simple, short, clear, logical app * Functionalities such as presenting a list after entering some letters	Study 3: Discrete choice experiment
Language		* Different language for patients and HCPs * Option to use the app in other languages	No further assessment
<i>Social influence</i>			
Prestige/reliable, independent source	* Older children did not want their parents to have access to their reports	* Linkage of the app to an organization with a great prestige * Link the app to reliable source * Report send to independent source * News items should come from independent source * Source should be familiar to app user	Study 2: Quantitative assessment
Type of ADR		* Clear goal of collecting ADRs	Study 2: Quantitative assessment (which type of ADRs people are willing to report)
Comparison		* Compare number of reports (e.g. with colleague, with someone's past number of reports)	Study 2: Quantitative assessment (only for HCPs)
<i>Facilitating conditions</i>			
Layout	* Very bright colours	* Option to let the user change the layout to own preferences * Recognizable and appealing logo	Study 3: Discrete choice experiment
Operating system, internet access		* Available for and tested on all operating systems * No need to have internet access to report an ADR	No further assessment
Costs (tariff and memory)	* If a large amount of space is taken on one's device	* App should be free of charge	Study 2: Quantitative assessment

5.1.2 Features and functionalities

During the current study it turned out that several features may influence the use of an app. A list of such features is presented as practical recommendations to improve the WEB-RADR app on two-way risk communication in section 4.8.

Additional functionalities may also influence the use of a mobile app. Various suggestions have been made but they may not be (immediately) implementable in an app on two-way risk communication. Some examples of additional functionalities are:

- * Product information of drugs;
- * Experiences with a drug and option to add experiences;
- * Present alternative drugs to the one an ADR is experienced;
- * Summary of guidelines;
- * Information about how to resolve/alleviate the ADR;
- * Interactions between drugs;
- * A kind of a prediction model presenting the likelihood of a symptom being an ADR after entering some information;
- * A function to remind for instance to report an ADR, an appointment a HCP, or to take drugs;
- * The option to store a list of (previous) prescribed drugs.

5.1.3 Breadth of focus, segmentation of target groups

In the current study, barriers and facilitators were assessed among different target populations. Among them were patients with a rare disease, patients with type 2 diabetes, adolescents, GPs, pharmacists, internists, nurse practitioners, hospital doctors and pharmacovigilance specialists. From the study, it became clear that these different populations were generally positive about an app for two-way risk communication. The participants indicated that several factors could influence whether or not someone will (be able to) use such an app. First of all, people who are not in the possession of a smartphone or tablet will not be able to use the app. This applies particularly to children and the elderly. Examples of other patient characteristics that were mentioned as influencing the use of an app are education level and experience. A previous study conducted in the US demonstrated that these factors indeed influence the use of health apps [18]. More specifically, it was shown that younger people, those with higher incomes, and higher educated people are more likely to use health apps [18]. In the upcoming, quantitative study in various European countries, it will be assessed whether these patient characteristics also influence the intention to use a mobile app for two-way risk communication.

5.1.4 Strengths and limitations

A strong aspect of the current study is that different European countries and different patient and HCP groups were involved in the study. However, no focus group discussions were conducted in France as was the initial plan. A limitation of the study is that each patient or HCP group was assessed in different countries. Therefore, it is unclear whether differences that seem to exist among for instance patient groups are really due to the type of patient or to differences among countries. Also, there were differences in the method used to assess the barriers and facilitators with most of the countries using focus group discussions but also some countries using face-to-face interviews. This may have resulted in some differences between the countries. These limitations will be eliminated in the follow-up, quantitative study in which the same survey will be used in the participating countries to assess the opinions and preferences of the same patient and HCP groups. Another limitation of the current study is related to the UTAUT model which was developed to assess user acceptance for new technology in the workplace that may not necessarily apply to technology in healthcare. However, the model provided us a structured approach to identify important themes on perceived barriers and facilitators of a mobile app for two way risk communication.

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