

WEB-RADR WP 3B STUDY PROTOCOL

User-based evaluation

Study 2. Quantitative evaluation of a mobile app on two-way risk communication

Type of document:

Protocol qualitative evaluation

Date:

February 22th, 2016

Authors:

WP3B team

(WEB-RAD-015-SPT Template - Version 1.0 – 30-Sep-2014)

TABLE OF CONTENTS

1	RATIONALE	3
1.1	BACKGROUND	3
2	INTRODUCTION	5
2.1	PURPOSE OF THE DOCUMENT	5
2.2	VERSION HISTORY	5
2.3	DEFINITIONS AND ABBREVIATIONS	5
3	RESPONSIBILITIES AND COORDINATION	5
4	OBJECTIVES	6
4.1	PRIMARY OBJECTIVES	6
5	GENERAL METHODS	6
5.1	STUDY DESIGN	6
5.1.1	Participants.....	6
5.1.2	Variables of interest	6
5.2	SURVEY.....	6
5.2.1	Survey distribution	6
5.3	TIMELINES	7
5.4	DATABASE MANAGEMENT AND QUALITY CONTROL.....	7
5.5	DATA ANALYSIS	8
5.5.1	Analysis sets	8
5.5.2	Sample size	9
5.6	ETHICAL CONSIDERATIONS	9
5.6.1	Regulatory and ethical compliance	9
5.6.2	Informed consent procedures	9
5.6.3	IRB/IEC.....	9
6	REFERENCES	10

1 Rationale

1.1 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 healthcare professionals. 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 healthcare professional 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 healthcare professionals; 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. For these reasons, additional channels need to be explored through which stakeholders can be informed about safety information. 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]. It may be that more sophisticated language should be used, and/or references could be given to scientific background information when communicating to this group [13]. Also, large differences can be expected as to how much a mobile application will be used between patient groups; e.g. younger patients, highly-informed patients (e.g. those with orphan diseases, 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 has been suggested by the EURORDIS patient platform that wider information about off-label treatments should be provided, due to its relevance to rare disease patients. 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 considering health literacy but possibly also visually-impaired patient populations. Another challenge is how to facilitate mobile app adoption by the wider public.

In this project, a mobile app to report ADRs **and** to provide medicinal product 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 (**Figure**).

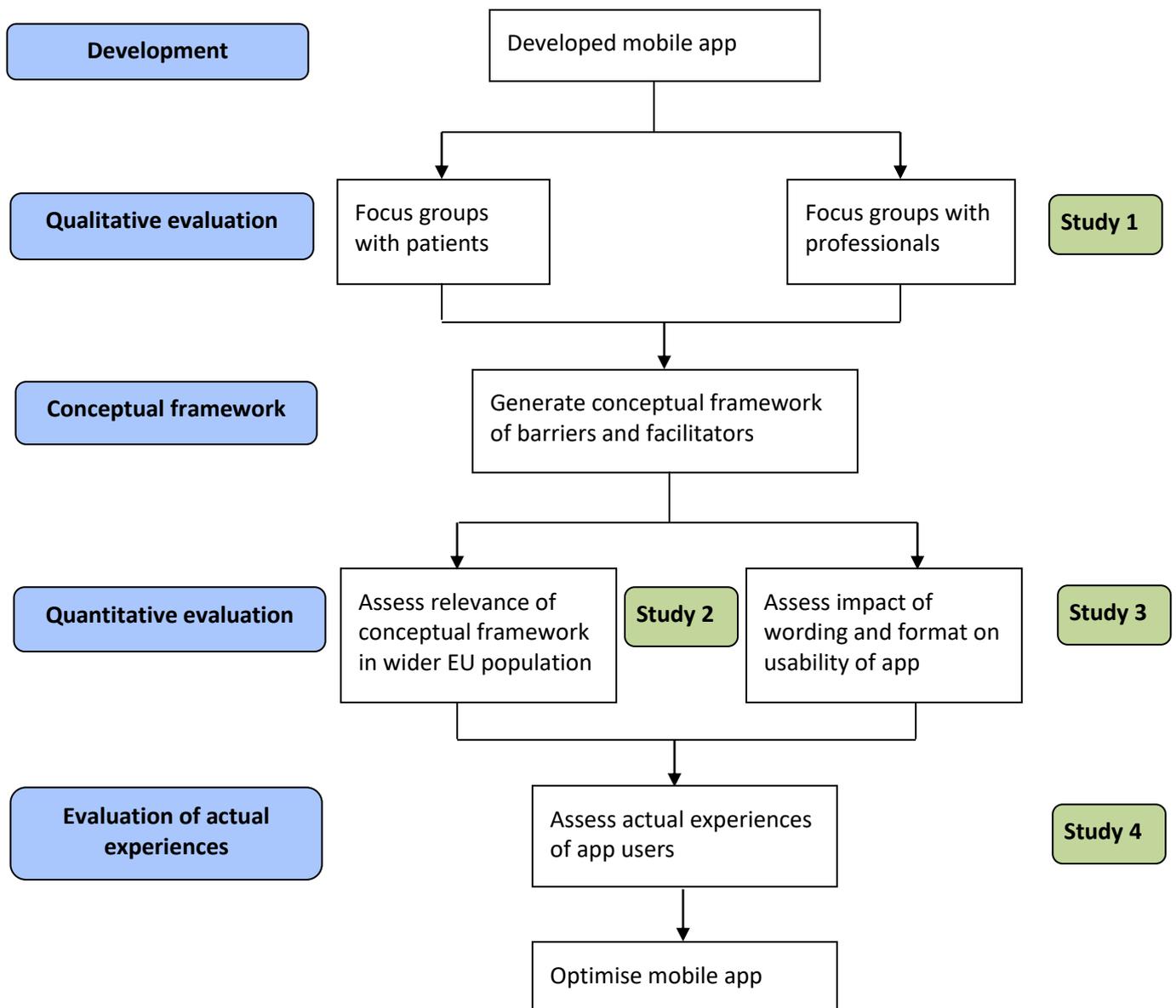


Figure. Flow-chart of studies in the project (study 3 and 4 will be conducted by the Dutch team only)

2 Introduction

2.1 Purpose of the document

This document includes the protocol for the following study planned within Work Package (WP)3B:
- Study 2: Quantitative evaluation of barriers and facilitators of a mobile app for two-way risk communication.

2.2 Version history

Table 1 Version history

Version	Date	Comments/Changes from previous version	Authors
01	27 February 2019		WP3B

2.3 Definitions and abbreviations

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

3 Responsibilities and coordination

This study is under the responsibility of:

Study supervisor:

Peter Mol (University Medical Center Groningen, Dutch Medicines Evaluation Board)

Study coordinators:

Alastair Sutcliffe (Institute of Child Health)

François Houyez (EURORDIS)

Raphael van Eemeren (AMGEN)

Other staff involved includes:

Sandra Fernandes (Sanofi)

Lisa Wong (Institute of Child Health)

Faiza Afsal (Institute of Child Health)

Carmen Lasheras Ruiz (EURORDIS)

Denis Costello (EURORDIS)

Karin Hace (AMGEN)

Sieta de Vries (University Medical Center Groningen)

4 Objectives

4.1 Primary objectives

The primary objective of this study is:

- to quantify to what extent the identified facilitators and barriers in study 1 are considered relevant for healthcare professionals (HCPs) and patients across a wider EU population.

5 General methods

5.1 Study design

Study 1 of WP3B revealed several potential facilitators and barriers to using a mobile app for two-way risk communication. In study 2, a survey will be constructed to quantify the relevance of these facilitators and barriers.

5.1.1 Participants

Patients, carers, and HCPs can participate in this study. Patients and carers can participate if they are familiar with mobile apps.

For HCPs it is assumed that they are familiar with mobile apps. The only inclusion criteria for HCPs is that they should be working with patients and distribute, prescribe, inform or advise patients about drugs.

5.1.2 Variables of interest

Quantitative information will be generated on the barriers and facilitators for using a mobile app on two-way risk communication.

5.2 Survey

The information will be collected via a web-based survey that will be developed using the Unipark software (<http://www.unipark.de>). The content of the survey will be based on the findings of the first study within WP3B. WP3B members developed a draft, English version of the survey in which the content will be finalized after feedback and input from WP3A and the various patient and HCP associations involved in the distribution of the survey. This version will be piloted in a small number (~10) of people who are not involved in the project (e.g. other colleagues, relatives of WP3B members). The survey can be adapted based on this pilot testing. WP3B members will decide whether adaptations are desirable.

This finalized English version will then be translated by an official translation agency located in the Netherlands. The survey will be translated into Spanish, French, German, Dutch, Croatian, Portuguese. Members of the WEB-RADR project who have one of these languages as native language will perform the back-translation. This back-translation will be used to assess whether the meaning of the questions in the different versions is equivalent.

The Dutch team will enter the survey in the Unipark software and will keep track of the survey. The paper-based version of the patient survey is presented in Appendix 1 and the HCP survey is presented in Appendix 2.

5.2.1 Survey distribution

The survey will be distributed to patients and HCPs in Europe via various European patient and HCP associations (e.g. European Society of Cardiology, European Academy of Neurology, European

Federation of Allergy and Airways Diseases Patients' Associations). These associations will send a direct e-mail to their members and/or they will advertise the study on their websites and/or newsletters.

5.3 Timelines

The study will start after data collection for study 1 has been finished. The study will end by November 2016. More specific timelines are presented below.

When	What
February 2016	- Finalizing protocol quantitative study - First contact with patient and HCP associations - Finalize content survey (with input from WP3A and the various associations)
End of February/Beginning of March 2016	Pilot-testing of survey
March 2016	- Translation of survey by official translation agency in the languages: Spanish, French, German, Dutch, Croatian, Portuguese - Back-translations of the survey
April 2016	- Finalize surveys - Enter surveys in Unipark - Start recruitment procedures and data collection
May - August 2016	Data collection
August/September 2016	Data analyses
September/October 2016	Draft version report
November 2016	Final report

5.4 Database management and quality control

The following activities will be used to ensure sufficient quality of the data:

- The translation of the English version into other languages by an official translation agency and back-translation by the researchers will ensure that the questions in the different versions are equivalent in their meaning.
- Participants complete a web-based survey. Therefore, the data is directly entered in a database. This eradicates potential data-entering errors by the researchers.

The data collection will start in April 2016 and end in August 2016. The research team in the Netherlands is responsible for data storage. This team will store the raw data on the survey on a local, secured disk in Stata format. A copy of the raw data will be used for the data cleaning and data analyses. Due to this, the primary source of the data remains available. The first step in using this copy of the raw data is to delete email addresses entered by the responders. So, the working file will not contain any e-mail addresses.

Cleaning of the data includes deletion of responders who did not complete the survey and where necessary/desirable (re)naming of variables, labeling of variables, labeling of values, etc. The data cleaning process will be documented in a Stata syntax. The data cleaning will be conducted by one of the researchers in the Netherlands. This data cleaning process will be checked by a second researcher in the Netherlands. In case of any errors, the syntax of the data cleaning will be adapted

by the first researcher and checked by the second researcher. This procedure will be repeated until no errors are detected. WP3B members will receive a copy of the cleaned dataset if they ask for it.

All the data and the syntaxes will be stored by the researchers in the Netherlands for a minimum of 15 years after the end date of data collection and each WP3B member could request the cleaned dataset at any time during this period. After these 15 years, all data and syntaxes will be deleted permanently.

The results of this study will be documented in a WEB-RADR report format. Once the WEB-RADR final report is available, the results will also be published in a scientific paper. The researchers in the Netherlands will write the first draft of the scientific paper and will be responsible for the different steps in the submission and publication process. Other WP3B members will be involved in the reporting/writing process and can be considered as co-authors if they fulfill the requirements of a co-author as defined in the research code of the University Medical Center Groningen in the Netherlands (<https://www.umcg.nl/SiteCollectionDocuments/English/Researchcode/UMCG-Researchcode,%20basic%20principles%202013.pdf>). In the acknowledgement section of any publication, the following information will be reported: “The WEB-RADR project has received support from the Innovative Medicine Initiative Joint Undertaking www.imi.europa.eu under Grant Agreement n°115632- resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme FP7/2007-2013 and EFPIA companies’ in kind contribution, www.imi.europa.eu, United Kingdom”.

In the survey, responders can indicate if they would like to receive the study results. Researchers in the Netherlands will provide the study results in Dutch language to responders from the Netherlands. In addition an English translated version will be made available by the researchers in the Netherlands for responders from other countries than UK, France, Spain, Portugal and Germany. Responders from one of these five countries will receive the results from the local WP3B members (UK: Lisa Wong/Faiza Afsal, France: François Houyez, Spain: Carmen Lasheras Ruiz, Portugal: Sandra Fernandes, Germany and Austria: Karin Hace).

In case a prize draw is used to stimulate participation, the research team in the Netherlands will take care of the prize draw: i.e. selecting the winners, informing the winners and providing the coupon to the responders who won a prize.

5.5 Data analysis

5.5.1 Analysis sets

The data analyses will start after the data cleaning is deemed accurate.

Descriptive statistics will be used to describe demographic characteristics of the respondents. In addition, descriptive statistics will be used to quantify the extent to which the barriers and facilitators are considered relevant: The answers to all the different closed-ended questions will be presented. For the open-ended questions, a short summary will be presented if relevant. Open-ended answers that are provided in languages other than Dutch or English will be evaluated by other WP3B members, i.e. in the case of Spanish, French, Portuguese or German answers. Surveys that are completed in other languages will be analyzed only on the answers given to the closed-ended questions.

Additional analyses will be performed to determine differences in preferences and expectations of the app among stakeholder groups (type of patient, HCP and nationality).

Other analyses are possible and will be discussed within the WP3B team.

All analyses will be conducted and documented in a second syntax by one of the researchers in the Netherlands. A second researcher will check the results and the syntax. In case of any errors, the

syntax of the data analyses will be adapted by the first researcher and checked by the second researcher. This procedure will be repeated until no errors are detected.

5.5.2 Sample size

We aim to include as many respondents from as many disciplines or with as many different diseases as possible to generate a wide range of views on barriers and facilitators in using an app on two-way risk communication.

5.6 Ethical considerations

5.6.1 Regulatory and ethical compliance

The WP lead is responsible to ensure regulatory and ethical compliance of this study, in accordance with regulations in place in the countries where the study will be run. The GAB is responsible to ensure ethical adequacy of this protocol and related documents.

5.6.2 Informed consent procedures

Participating patients and healthcare professionals are informed about the study via for instance a newsletter or e-mail. Participants can decide whether or not they wish to participate by entering the survey. In addition, they can stop answering the survey when they wish to. Completing the survey is considered to be providing consent to participate in the study. No formal consent form will be signed by participants.

5.6.3 IRB/IEC

In Spain, France, the UK and the Netherlands, the study protocol will be submitted to a local ethics committee to ask for a waiver of full ethical approval. Project members have to forward the approval of the local ethics committee for conducting the study to the WP leader(s). The WP leader(s) will store this information.

6 References

Ref No	Citation
1	Avery AJ, Anderson C, Bond CM, Fortnum H, Gifford A, Hannaford PC, et al. Evaluation of patient reporting of adverse drug reactions to the UK 'Yellow Card Scheme': literature review, descriptive and qualitative analyses, and questionnaire surveys. <i>Health Technol Assess</i> 2011;15(20):1-234, iii-iv.
2	van Hunsel F, Harmark L, Pal S, Olsson S, van Grootheest K. Experiences with adverse drug reaction reporting by patients: an 11-country survey. <i>Drug Saf</i> 2012;35(1):45-60
3	Harmark L, van Puijenbroek E, Straus S, van Grootheest K. Intensive monitoring of pregabalin: results from an observational, Web-based, prospective cohort study in the Netherlands using patients as a source of information. <i>Drug Saf</i> 2011;34(3):221-231
4	Harmark L, Puijenbroek E, Grootheest K. Longitudinal monitoring of the safety of drugs by using a web-based system: the case of pregabalin. <i>Pharmacoepidemiol Drug Saf</i> 2011;20(6):591-597
5	Goldman SA. Communication of medical product risk: how effective is effective enough? <i>Drug Saf</i> 2004;27(8):519-534
6	Piening S, Reber KC, Wieringa JE, Straus SM, de Graeff PA, Haaijer-Ruskamp FM, et al. Impact of safety-related regulatory action on drug use in ambulatory care in the Netherlands. <i>Clin Pharmacol Ther</i> 2012;91(5):838-845
7	Mol PG, Straus SM, Piening S, de Vries JT, de Graeff PA, Haaijer-Ruskamp FM. A decade of safety-related regulatory action in the Netherlands: a retrospective analysis of direct healthcare professional communications from 1999 to 2009. <i>Drug Saf</i> 2010;33(6):463-474
8	Piening S, Haaijer-Ruskamp FM, de Graeff PA, Straus SM, Mol PG. Healthcare professionals' self-reported experiences and preferences related to direct healthcare professional communications: a survey conducted in the Netherlands. <i>Drug Saf</i> 2012;35(11):1061-1072
9	Slovic P, Peters E, Grana J, Berger S, Dieck GS. Risk Perception of Prescription Drugs: Results of a National Survey. <i>Drug Information Journal</i> 2007;41(1):81-100
10	Edwards B, Chakraborty S. Risk Communication and the Pharmaceutical Industry: what is the reality? <i>Drug Saf</i> 2012;35(11):1027-1040
11	Lofstedt RE. The impact of the cox-2 inhibitor issue on perceptions of the pharmaceutical industry: content analysis and communication implications. <i>J Health Commun</i> 2007;12(5):471-491
12	Fischhoff B, Brewer NT, Downs JS. Communicating risks and benefits. An evidence-based user's guide [online]. http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM268069.pdf . Accessed January 6, 2015
13	Lundgren, R.E. & McMakin, A.H. Risk Communication. A handbook for communicating environmental, safety, and health risks. Third edition. ed.

	Columbus, Ohio, USA.: Battelle Press; 2004
14	Weatherby LB, Nordstrom BL, Fife D, Walker AM. The impact of wording in "Dear doctor" letters and in black box labels. Clin Pharmacol Ther 2002;72(6):735-742