STRIPA – THE POTENTIAL USEFULNESS OF A MEDICAL APP

Aarnoutse, Floor, Utrecht University, Princetonplein 5, Buys Ballotgebouw, 3584 CC Utrecht, the Netherlands, M.F.Aarnoutse@uu.nl

Renes, Cassandra, Utrecht University, Princetonplein 5, Buys Ballotgebouw, 3584 CC Utrecht, the Netherlands, C.A.M.Renes@uu.nl

Batenburg, Ronald, Utrecht University, Princetonplein 5, Buys Ballotgebouw, 3584 CC Utrecht, the Netherlands, R.S.Batenburg@uu.nl

Spruit, Marco, [1] Utrecht University, Princetonplein 5, Buys Ballotgebouw, 3584 CC Utrecht, the Netherlands; [2] Spru IT b.v., Meidoornlaan 22, Loosdrecht, the Netherlands, marco@spru.it

Abstract

Polypharmic patients are patients who chronically use five or more medicines. The number of polypharmacy patients continues to increase even though it is a risk factor for morbidity and mortality. A medication review is an important measure to mitigate medication risks. It is known to effectively reduce the number of drug related problems per (polypharmic) patient. STRIP is a Dutch method to perform a structured medication review. Based on this method, the STRIPA(ssistent) tool is developed. However, whether or not this app is considered useful by the healthcare professional is not known yet. In order to assess this, a systematic literature study is conducted. In addition, an effectiveness study design is described. The results show that there is indeed a need for medication reviews and Dutch healthcare professionals are likely to adopt new technologies, an effectiveness study based on a randomized controlled trial is necessary to assess the effectiveness of STRIPA.

Keywords: Polypharmic, STRIPA, Medication review, Dutch healthcare professionals.

1 Introduction

In the Netherlands around 10% of the pharmacy visitors are polypharmic patients, which mean they chronically use five or more medicines (KNMP, 2013). Research showed that the number of polypharmacy patients continues to increase and that it is a known risk factor for morbidity and mortality (Hajjar, Cafiero & Hanlon, 2007). In the Netherlands alone, polypharmacy costs society between 103 and 229 million euros (Zorginstituut Nederland, 2013). Polypharmacy can possibly lead to dangerous combinations of drugs, which can be harmful for the patients. Not only can certain drug-drug interactions be harmful, they can also neutralize the active substances in one another. The chronic use of multiple drugs increases patients' risks to experience adverse effects, under-prescription, overtreatment, and decreased drug adherence (Meulendijk et al., 2013). Besides that, using multiple drugs also leads to an increased chance of hospitalization (Meulendijk, 2012). Therefore it is of importance that general practitioners (GPs) scan for drug-drug interactions. This can be formally done via a periodic medication review, by which GPs together with pharmacists have to review their polypharmic patients' medicine use.

In the Netherlands there were two methods for medication reviews: the Prescribing Optimization Method (POM) and 'Gebruik-Indicatie-Veiligheid-Effectiviteit' (GIVE). There was a need for a unified method and that is why based on the POM method, STRIP (Systematic Tool to Reduce Inappropriate Prescribing) was developed (TPO, 2012). STRIP is a step-by-step method that aims at assisting GPs and pharmacists with determining the optimal medication for polypharmic patients (Meulendijks, 2013) and can be used in software for healthcare professionals. The rise of mobile technology brought exponential growth of software use by healthcare professionals (O'Hagan, 2012).

STRIPA, short for STRIP-Assistant, is a STRIP-based app for GPs and pharmacists to use when making a medication review for polypharmic patients. For these medication reviews STRIPA offers several functionalities:

- An overview of the suffered conditions, diseases and medication for each patient.
- Linking the prescribed medication to the associated diseases.
- Advice when to start new medication.
- Advice when to stop current medication.
- Linking side effects to the associated medication.
- Showing drug-drug interactions.
- Advice about medication dosage.

These functionalities will be further elaborated on in the STRIPA section.

In 2009 almost a third of all pharmacists did not do a single medication review (Inspectie voor de Gezondheidszorg, 2009). It is hypothesized that this is the case because it takes a lot of time for the pharmacists as well as for the GPs. STRIPA can help these healthcare professionals with making faster and more structured medication reviews. However, it is unknown if GPs and pharmacists see the potential benefits and are willing to adopt STRIPA as a support tool. Therefore the main research question for this paper is:

RQ 1: What is the potential usefulness of STRIPA for conducting medication reviews?

This research question will be answered based on several subquestions. First of all (i) *'why is medication reviewing important?'*. Answering this question will lead to a better understanding of the field. The second sub question (ii) is *'what can STRIPA offer?'*. Answering this questions will lead to a better understanding of the app. Sub question three (iii) is *'are there any apps similar to STRIPA?'*. This will deepen the understanding about STRIPA and help positioning it within the market. The fourth sub question (iv) is *'how can an effectiveness study for STRIPA be designed?*. By designing an effectiveness study, a foundation for future research is built.

The remainder of this paper is structured as follows; in the next section a systematic literature review will be conducted in order to give a state-of-the-art overview of the current situation regarding medication reviews, drug-drug interactions, polypharmic patients and the usage of e-health by healthcare professionals. This will give an answer to the first sub question. In the third section STRIPA will be introduced, in order to give an in-depth understanding of the app and therefore answer sub question number two. In the subsequent section STRIPA will be compared to existing apps, which answers sub question three. Thereafter an effectiveness study design will be presented. This will answer sub question five. The article concludes with a discussion, conclusion and future research.

2 Systematic Literature Review

A systematic literature study (SLR) is carried out in order to identify and select research relevant for STRIPA. This section will start with the explanation of the process of the SLR. After that the result of the SLR in the form of related literature is presented.

2.1 SLR procedure

The SLR used in this study is based on the study of Liberati et al. (2009) and is therefore divided in four successive phases; identification, screening, eligibility, included. Appendix A gives an overview of the phases along with the yielded results per phase.

Identification. Two databases, Google Scholar and PubMed, are searched for relevant articles. PubMed comprises a large number of citations for biomedical literature from MEDLINE, life science journals and online books and thus is purely focussed on medical literature. Google scholar indexes articles across an array of publishing formats and disciplines and includes most peer-reviewed online journals of Europe and America. In addition to that Scholar also includes many scholarly publishers, books and other non-peer reviewed journals. By not limiting the search to only the more on-subject database, PubMed, a far larger number of articles can be searched through for the SLR.

Two reviewers independently scanned the electronic records to identify potential articles. In Appendix B, the used search keys and their underlying relationship can be found. These search keys are selected based on their relevance to the subject. Supporting healthcare professionals with making *'medication review(s)'* is the main functionality of STRIPA. These reviews are focussed on patients who chronically take more than five medicines, called *'polypharmacy'*. STRIPA makes these medication reviews based on the STRIP method, whereby *'drug interaction'* (how do drugs interact with each other), *'medicine criteria'* (when to start and stop medication and dosage information), and *'medicine disease connection'* (which medicines should be used for what disease) are of importance.
For each search key subject, there are five layers of identified search keys. In the first layer the *'general'* search keys for that subject are identified. The second and third layer combine the subjects with the words *'app'* and *'e-health'* which is respectively short for application and electronic health. Since STRIPA is ought to be an app to help general practitioners and pharmacists conduct medication reviews, and therefore falls in the category of e-health, these search keys are included. The last two layers combine the subjects with the words *'general practitioner information system'* and *'clinical decision support software'*. STRIPA is a clinical decision support software which can be integrated with the general practitioner information system. By also including these four extra layers literature based on similar projects can be found.
For each search key the two databases were scanned. These search keys yielded a total of 3.005.135 results divided over PubMed (112.847) and Google Scholar (2.892.288).

Screening. Of the roughly 3 million results, 4.759 records are screened. This is done by reading the titles and when deemed maybe relevant for this research, also the abstract. Per relevant keyword the first 100 results were searched trough for PubMed as well as Google Scholar. However, some keywords did not yield 100 results and other keywords were deemed not relevant enough. This was

the case when after 40-60 results none of the screened titles were slightly interesting for this research, at which case the search stopped. Therefore divided over the 34 search key and two databases, 4.759 records are screened. Based on this title and abstract screening, 105 articles were deemed interesting for this research. 38 of which originated from PubMed and 67 of Google Scholar. Consequently, 4.654 screened articles were deemed not interesting enough and are dismissed.

Eligibility. In order to access the eligibility of the remaining 105 articles, the full texts of these articles are sought. Of 34 articles no full text could be found and were thus excluded from further analysis. The full texts of the remaining 71 articles were further analysed on their added value to the literature review. The articles are divided into four different categories; (1) duplicates, (2) not applicable and (3) not relevant and (4) include in review. Duplicates are articles which came up in Google Scholar as well as PubMed and were in both cases included in the results. In total, there were eight duplicate articles. Seven articles were deemed not applicable. These articles were often solely based on countries apart from the Netherlands, and could not be generalized due to their research approach or because they were based on a device not used for STRIPA, for example PDAs. The last category in which articles are excluded are the articles which are deemed not relevant. An article is deemed not relevant when it is too specifically aimed at a disease, technique, target group etcetera. Also articles which were too general or did not fit in after all were deemed not relevant. In total 29 articles belong to this group.

Included. A total of 27 articles were left to include in the literature review. When analyzing these articles some general concepts can be distinguished compliant with the search keys. In appendix C, the references to the included literature as well as the concepts they entail, can be found. E-health is identified in most of the articles. A broad view of e-health is used, in which also apps, clinical decision support software and general practitioners information systems are reckoned in this term. The only search key missing in the concept table, is medication disease connection, because none of the selected articles are found based on this search key. In the next section, related literature, the result of the analysis of the included articles can be found.

2.2 Related literature

There are a lot of papers reporting about side-effects of different drugs. Scanlin (2013) stated: “The more powerful a drug is, the more likely it is to have harmful side effects. The Institute of Medicine (IOM) of the National Academies estimates (...) that there are between 44.000 and 98.000 hospital deaths annually attributed to medical errors, more than 7.000 of which are due to medication errors.” Based on this it can be stated that reviewing medication is important, the question remains whether or not it is also effective. Multiple studies have been conducted to measure the effectiveness of these medication reviews (Seidling et al., 2011; Krska et al., 2001; Vinks, Egberts, de Lange & de Koning, 2009; Bindoff, Tenni, Peterson, Kang & Jackson, 2007). In a randomized control trial in the United Kingdom 332 records of patients aged 75 years and above or those who uses multiple medicines were reviewed. The results showed that all patients had at least two drug related problems (Krska et al., 2001). A study about the effectiveness of medication reviews in the Netherlands between GPs and pharmacists, showed a positive influence in reducing potential drug related problems for elderly. The results showed a significant reduction in the mean number of drug related problems per patient. The mean number of drugs per patient did not significantly reduce after the medication review (Vinks, Egbert, de Lange & de Koning, 2009). Another effectiveness study about medication reviews in Australia showed that not only significantly less drug related problems per patients were found, but also that a decision support system (DSS) for medication review found significantly more potential drug related problems than healthcare professionals without a DSS (Bindoff, Tenni, Peterson, Kang & Jackson, 2007). A medication review is an important measure to mitigate medication risks, but not all patients can be reviewed. A research in Sweden looked at the potential drug-drug interactions and concluded that there was a strong correlation between drug related problems and the use of multiple

drugs. The pronounced increase in polypharmacy over time implies a growing reason for prescribers and pharmacists to be aware of drug-drug interactions (Åstrand, Åstrand, Antonov & Petersson, 2007).

A conclusion can be drawn that medication reviews can substantially improve patient safety and that information systems positively support the medication review process by reducing drug error rates (Kaushal, Shojania & Bates, 2003; Bates & Gawande, 2003; Miller, Gardner, Johnson & Hripcsak, 2005; Drenth-van Maanen, van Marum, Knol, van der Linden & Jansen, 2009; McInnes, Saltman & Kidd, 2006). The main driver behind implementing a computerized physician order entry for Dutch physicians is patient safety (Aarts & Koppel, 2009). Ko et al., (2007) stated "both prescribers and pharmacists indicated that the CPOE [Computerized Prescriber Order Entry] system had a neutral to positive impact on their jobs". Even though these information systems are useful, they are not always adopted by the users. A research about the implementation of DSS or CPOE systems in seven western countries showed that the United States and the Netherlands have the highest use rates. Healthcare professionals in the United States, the United Kingdom, Switzerland, and the Netherlands are most likely to have integrated decision support systems (Aarts & Koppel, 2009).
An American survey held under 1.745 pharmacists concluded that DSSs often fail to protect patients from harmful drug-drug interactions. The potential risk of drug-drug interaction depends on a number of drug and patient specific factors. DSSs should pay attention to these factors (Horn et al., 2013; Smithburger, Buckley, Bejian, Burenheide, Kane-Gill, 2011). In addition, "the effectiveness of computerized clinical decision support systems (CDSSs) depends on the quality of the knowledge they refer to" (Mille, Degoulet & Jaulent, 2007), it is important to include the knowledge of healthcare professionals in the system.

One major problem with the adoption of DSSs is that users ignore the alerts and advises the system produces. A lot of research has been done to study how many alerts and advises are ignored and more importantly why they are being ignored (Ko et al., 2007; Kmetik, Chung, Sims & Found, 2007; Ahearn & Kerr, 2003). Through a questionnaire the reasons for overriding drug alerts by GPs in the UK are examined. 236 GPs participated in this study. 22% of the GPs admitted they frequently to very frequently override drug alerts. The main reason for overriding drug alerts was that the drug alert was not relevant. 90% of the GPs stated that it should be harder to ignore drug alerts (Magnus, Rodgers & Avery, 2002). When tiering the alerts into categories based on severity, alerts were not as quickly ignored. In an American research, 71.350 alerts were investigated. A correlation was found between tiering the alerts and overriding the alerts. From the 31.876 tiered alerts, 100% of the most severe alerts were accepted against 34% of the total 39.474 non tiered alerts. Also moderate severe alerts had a higher acceptance rate with tiered alerts (29%) against non tiered alerts (10%) (Paterno et al., 2009). In Australia the opinion of 191 GPs and 138 Pharmacists about alerts were analysed. The vast majority of the respondents wanted to be able to differentiate the alerts by severity. The research states that it should also be harder for physicians to override alerts for severe interactions and that it should be mandatory to provide a reason when they do override an alert (Yu, Sweidan, Williamson & Fraser, 2011).
Another aspect that should be taken into consideration with these kinds of systems is that "Doctors may not be aware of all the drugs their older patients are taking. Frank and colleagues reported that in a study in Canada 37 per cent of patients were taking drugs without their doctors' knowledge, and 6 per cent of patients were not taking medications that were on their doctors' lists" (Duerden, Avery & Payne, 2013). STRIPA does not include these aspects in their assessment, while these aspects do influence the interaction with other drugs.

2.3 Lessons learned

There are several lessons learned from the analysis depicted in the previous section. First of all, medical errors due to medication errors are not uncommon and polypharmacy is increasing in frequency. The dangers accompanying polypharmacy can be reduced due to medication reviews, since these reviews improve patients' safety substantially. This is proven to be true in multiple countries

including the Netherlands. DDSs supporting these medication reviews can significantly increase the chance of identifying potentially harmful drug-drug interactions. These DDSs have a chance to do well in the Netherlands, since a study about the implementation of DSS or CPOE systems in seven western countries showed that the United States and the Netherlands have the highest use rates. However traditional DSSs (not aimed at medication reviews) often fail to protect patients from harmful drug-drug interactions, therefore future (versions of) DSSs should take the number of drugs, their interactions and specific patient factors into account. In addition, the effectiveness of a DSS also depends on the quality of knowledge they refer to. However one major problem with the use of DDS's by healthcare professionals is that they often ignore the alerts and advises the system produces. This can be overcome by tearing the alerts into categories based on severity, this leads to less ignored alerts and advices. Besides that, health care professionals are not yet aware of all the drugs patients are taking. This is because some drug can be bought without a prescription and patients are not sharing this with their doctors or because patients are without informing their doctors stop taking their prescribed medicine.

3 STRIPA

STRIPA is an online software service to support GPs when prescribing medication and to support GPs and pharmacists when reviewing the medication of their polypharmic patients. STRIPA is based on the STRIP method for medication review. The STRIPA tool can be used as an integrated software program which interacts with the information system of the GPs and the pharmacies. The medication reviews performed by the GPs and pharmacists are used to improve the generated advises when performing another medication review. Next to this integrated software, an app version is also available.

3.1 STRIPA Drivers

Polypharmacy is associated with several medical problems, like under-prescription, overtreatment, increasing risk of adverse effects, and decreased drug adherence. These medical problems are also described as drug related problems. When performing medication reviews, drug related problems can be identified. Previous research shows that out of 1.489 medication reviews, an average 3.1 drug related problems were found per patient. In this research pharmacies did not include all problems they identified, therefore the actual amount of drug related problems per patient is even higher (Service Apotheek, 2012). KNMP (2013) investigated 507 medication reviews in the Netherlands and found an average of 3.6 drug related problems per patient. Identifying these problems and adjusting the medication leads to less medication usage and less hospital admissions. Booz (2012) stated that when 10-12% of the medicine usage can be stopped and 15-17% of the unplanned hospital admissions can be prevented when executing a medication review, the Netherlands can save up to €150-200 million. To support medication review a decision support system, STRIPA is designed. Meulendijk (2012) stated that after implementation of STRIPA in the Netherlands, mortality can be expected to decrease by 3 to 19 persons on a yearly basis, morbidity by 4 to 28 persons, and the financial cost by 10 to 45 million euros per year. To encourage GPs and pharmacists to perform medication reviews, in the Netherlands healthcare providers financially reward the GPs and pharmacists whenever they perform a medication review (Inspectie voor de Gezondheidszorg, 2009). They can send an invoice to the healthcare providers for each medication review they performed. Through a step-by-step method GPs are forced to critically review the medication use of their polypharmic patients. All the patient information is included in the STRIPA system.

3.2 STRIPA Functionalities

All screenshots mentioned in this section about STRIPA can be found in Appendix D, this includes an overall screenshot of STRIPA which is screenshot 1. In this case the dossier of Mrs. Kwarten is shown. Mrs. Kwarten is 93 years old and suffers from several conditions. These conditions are

visualized at the top of the screen. She suffers from flatulence, nausea and an impaired kidney function. Next to the conditions, the lab results for several functions, like heart rate and blood pressure, are stated. These results help the GP with diagnosing the patient. The GP has previously diagnosed several diseases with Mrs. Kwarten. These diseases are shown at the left side of the system. The GP can enter more diseases if deemed necessary. For some of these diseases the GP has prescribed medication. The medicines are listed at the right side.

Besides an overview of the conditions, diseases and medication, STRIPA has several other functionalities. First, the STRIPA makes it possible to link the prescribed medication to the diseases. In screenshot 2, all the medicines are linked to the diseases. This process highlights redundant medication. STRIPA holds data about the lab results and conditions of the patients, with this information STIRPA gives advice about when a patient should start with a new medicine. Because Mrs. Kwarten suffers from atrial fibrillation, a new medicine should be prescribed. STRIPA suggests several medications which addresses the condition and do not interfere with other prescribed medication. The GP can choose whether to add the new medicine to the prescription or to ignore the condition. When the GP adds the medication, the medicine is automatically linked to the disease in the disease overview, this is shown in screenshot 3. In addition, STRIPA advises when a patient can stop using a certain medicine. In screenshot 4 STRIPA advises to stop using *acetylsalicylic acid* because the patient has no history of coronary, cerebral or peripheral vascular symptoms. Again, the GP can choose to accept or deny the given advice. The subscribed medication has several side effects. The GP can connect these side effects to the associated medication. Screenshot 5 shows the GP drag the side effect nausea to the medicine euthyrox tablet. Furthermore, STRIPA shows drug-drug interaction warnings. When prescribing multiple medicines to a patient, the consequences of using these medicines together are not always clear. Whenever a drug has an unwanted effect, a warning is given, shown in screenshot 6. In the example of Mrs. Kwarten four drug-drug interactions are identified. STRIPA advices another medication which has the same effect but has different constituents. The GP can choose whether to ignore the interaction warning and prescribe the drug he wanted, or listen to the advice of the STRIPA. Based on values like weight and age, medications have a certain dosage. After checking for drug-drug interactions, STRIPA checks for under- and overdosage. In the case of Mrs. Kwarten only two tablets of *calci chew d3* are allowed while two and a half tablets are prescribed (Screenshot 7). After these steps, the medication is optimized. STRIPA shows an overview, visualized in screenshot 8. On the left side all the medications are connected to the diseases and any potential side effects are listed with their associated medication. On the bottom the bin is located, which shows all the deleted or changed medication during the process. In this overview the GP can check if everything is correct and if necessary reverse the made changes or make new changes.

3.3 STRIPA Status

The STRIPA system is currently being tested through a clinical experiment and a one-year longitudinal study. The results of these tests will become available in 2015. Next to the STRIPA system, an app is being developed. This app currently is in the development phase. O'Hagan (2012) stated "there is tremendous potential for customized care through mobile devices". Therefore transforming the STRIPA system into an app can be an added value. The app will work on both Android and iOS and is developed for tablets (10 inch or bigger). The app is not designed for smartphone use. Because the app contains a lot of information, fitting it on a screen of 10 inch or smaller would indicate leaving out important information. All the information addressed in STRIPA is of equal importance therefore no information can be left out.

3.4 Preliminary results

Looking at the lessons learned in section 2.3 and the information about STRIPA, some tentative conclusions can be formulated. Since there is an increasing amount of people with polypharmacy, and medication errors are not uncommon, there is a market for tools, software, procedures etc. which helps

prevent these medication errors. Especially medication reviews are proven to reduce the amount of drug related errors. Therefore it can be stated that there is a use for an app that focuses on medication reviews, like STRIPA. DDS and CPOE systems have the highest use rates in the Netherlands, this positively influences the chances STRIPA is adopted by Dutch healthcare professionals. It is suggested that DDSs should take the number of drugs, their interactions and specific patients factors into account in order to protect the patient better from harmful drug-drug interactions. STRIPA considers both the drug and patient specific factors, and therefore addresses this issue. In addition, the effectiveness of a DSS also depends on the quality of knowledge they refer to. The generated advises by STRIPA are based on the medication reviews performed by the healthcare professionals themselves, this insures the quality of the advices are continuously improved and of a high standard. A problem with DDS's is that advises and alerts are often ignored by the healthcare professionals. This can be overcome by tearing the alerts into categories based on severity, which is proven lead to less ignored advices and alerts. STRIPA does not differentiate its alerts and advices by severity, it should be a good alternation in future releases.

4 Related apps

There are two other apps for general practitioners and pharmacies to support the medication review process similar to STRIPA: Epocrates and MicroMedex Drug Information (O'Hagan, 2009), both apps focus on healthcare professionals. There are multiple other applications available but these applications only focus on one aspect of medication reviews.

Epocrates has a free version, which provides information on drugs, interactions and a pill ID function. According to the Epocrates website "nearly 1 in 2 U.S. physicians rely on Epocrates routinely to help inform their decisions in the moments of care, making it the #1 medical app available to U.S. physicians" (Epocrates, 2014). Epocrates also has a premium version with features like suggesting alternative drugs, insight in lab results and disease information. Epocrates is available for Android and iOS. For Android alone, Epocrates has been downloaded over a million times with an average rating of 4.3 out of 5 (n = 19.356) (Google Play, 2014a). For iOS the average rating is 3 out of 5 stars (n = 46.934) (iTunes, 2014a).

MicroMedex Drug Information is a subscription based app and costs $2.99 a year. It provides an extensive index of medications, which includes information about dosage, drug-drug interactions and a tool for pill identification (Micromedex, 2014). MicroMedex Drug Information has been downloaded over 5000 times for Android, with an average rating of 4.2 (n = 56) (Google Play, 2014b). For iOS the average rating is around 2 stars (n = 176) (iTunes, 2014b).

In Appendix E, the apps are compared according to functionality and rating. This table shows the uniqueness of STRIPA. STRIPA is the only app with information about the condition of the patient, start and stop criteria of the all medication and a functionality which links the medication to the diseases. Only pill identification, information about other healthcare professionals and general drug information is not included in STRIPA. However, these functionalities are not of importance when conducting a medication review.

5 Effectiveness study design

An effectiveness study should be carried out in order to test whether or not STRIPA is deemed effective for GPs and pharmacists. This effectiveness study should focus on the perceived effectiveness of STRIPA. In order to test this, the development of STRIPA should be finished first.

There are several study designs possible for researching effectiveness (Baxter & Jack, 2008). Based on research of Stolberg, Norman and Trop (2004) and the University of Ottawa (uOttawa, n.d.) the randomized controlled trial (RCT) is chosen to test the effectiveness of STRIPA. In RCT a predefined group of subjects is randomly allocated to two or more groups. One group is assigned as a control group, while the other groups are assigned to an intervention. After the experiment, outcomes of both groups are measured and compared to each other. An advantage of RCT above other study designs, is

that it is considered to be the most reliable form of scientific evidence (Akobeng, 2005), since it reduces bias (uOttawa, n.d.). This is the case because the subjects are randomly allocated to one of the two groups, which ensures homogeneity between the groups. Therefore, when comparing the groups to each other after the experiment, the difference between those groups must be caused by the experiment. There are also some disadvantages to RCTs. For example, the external validity can be not sufficient enough. This is for instance the case when only comparing groups in a specific country, then it may not be generalizable to another country with different norms, believes et cetera. In the STRIPA experiment however, this is not a threat. Since STRIPA is intended to use within specific boundaries (in the Netherlands, by GPs and pharmacists) these boundaries can serve as an input for the experiment. Another disadvantage of RCTs is the narrowness of the studied question. RCTs usually only inspect one variable or very few variables, rarely looking at the full picture (Singh, Kumar & Sarkar, 2011).

When conducting an experiment about STRIPA the subjects are GPs and pharmacists. It is estimated that in the Netherlands there are 9.115 GPs and 2.644 pharmacists (Nederlandse patiënten consumenten federatie, 2014). In order to have a representative sample for an effectiveness study, 396 GPs and 336 pharmacists should participate in the experiment. This is calculated based on the standard sample size formulae, with a confidence interval of 5 and a confidence level of 95%. The participating GPs and pharmacists should both be randomly divided in two equal sized groups. Both groups should be presented with the two cases discussed in the end-user survey section, since those cases are representative for the problems that can arise when conducting a medication review for polypharmic patients. The control group should perform the STRIP method with pen and paper and the intervention group by means of STRIPA. When comparing the results of the two groups there are several measurements that should be taken into account. The time to complete the two cases is of importance, since it is claimed that STRIPA reduces the time to complete a medication review. In addition, also the medication and dosage changes should be measured. In this way it can be measured if one of the groups makes significantly more errors than the other. An error is deemed as such, whenever a healthcare professional does not change a medication or medication dosage when it forms a threat to the patient or when a healthcare professional changes the medication or medication dosage into a (still) harmful combination. In addition, also not optimal changes in medication should be deemed as errors. Whether one of the groups makes significantly more errors than the others can be calculated with any statistical significance test.

The costs for such an experiment can be high, when paying all subjects their normal hourly wage in addition to the costs of the researchers themselves and the distribution of STRIPA to the intervention group. In order to suppress the costs, the healthcare professionals should be asked to participate voluntarily. Since only 4.05% of the GPs and 12.7% of the pharmacists in the Netherlands are needed to conduct this experiment, it should be possible to at least move a part of the healthcare professionals to participate voluntarily. This voluntary group will do so based on intrinsic drivers, like ‘the feeling to give something back’ and ‘the feeling of accomplishment’ (Noels, 2001), or the possibility to get to try STRIPA free-of-charge. When the intended amount of subjects is not reached, the healthcare professionals should be promised a financial compensation, in order to move them to participate.

6 Discussion

In this research, there are some threats to the validity of the results. First of all, the SLR could be extended by including more specific search keys. However, the most crucial parts are already included in this version. Besides a more thorough SLR, from the 39 analyzed respondents, there were only four pharmacists. To give more accurate conclusions about the adoption of STRIPA, the overall sample size needs to be bigger and especially more pharmacists should be included. STRIPA is an extensive tool to support medication reviews. It gives alerts whenever a drug related problem is present. In STRIPA healthcare professionals can easily ignore these alerts. Previous research has shown that

tiering these alerts into categories according to severity help healthcare professionals to make the right decisions. Alerts from the most severe category are rarely ignored. STRIPA should add these tiered alerts. Furthermore, STRIPA does not include information about the reliability of a patient. How frequent a patient takes their medication has great consequences on the overall treatment. Taking the patient reliability into account could be an added value for STRIPA since alternative treatments may be more effective.
In the experiment and end-user survey mentioned in this research two cases were used to test the potential usefulness of STRIPA. To measure the effectiveness, a RCT should be performed. The RCT clearly shows the effectiveness of STRIPA but it remains an experiment in a controlled environment. All the participants use the same cases to perform a medication review and the differences between the control group and the intervention group are measured. The narrowness of the studied question within a RCT does not examine the 'complete picture'. Therefore this type of experiment does not include how healthcare professionals use STRIPA in their daily life for real patients. This includes that in practice GPs and pharmacists will regularly work together whenever they perform a medication review. In the experiments mentioned before the differences between usage of GPs and pharmacists is measured but how these groups collaborate is not known.

7 Conclusions

Based on the research described in this paper, the main research question of this paper '*what is the potential usefulness of STRIPA for conducting medication reviews?'* can be answered.

There are between 44.000 and 98.000 hospital deaths annually attributed to medical errors, of which more than 7.000 are due to medication errors. These medication errors cost a lot of money and certain errors can be avoided. A medication review is one way of reducing the amount of medication errors. Multiple studies have proven the effectiveness of medication reviews. To support GPs and pharmacists when performing medication reviews for polypharmic patients STRIPA offers a step by step-by-step method. STRIPA has several functionalities, including an overview of the patient with the condition and medication; linking the medication to the associated diseases; advice when to start and stop with a certain medication; linking side effects to the associated medications; drug-drug interactions; and advice about medication dosage. There are some similar apps to STRIPA, but none of these apps has all the functionalities combined in one app like STRIPA does. Furthermore, research showed that after implementation of STRIPA in the Netherlands, mortality can be expected to decrease by 3 to 19 people on a yearly basis, morbidity by 4 to 28 people, and the financial costs by 10 to 45 million euros a year. An effectiveness study should be carried out in order to test whether or not STRIPA is deemed effective for GPs and pharmacists.

8 Future research

Because the effectiveness study and the performed experiment mentioned in this research both include two predefined cases, an observational study would be a good addition. In the observation study the healthcare professionals use the system when conducting medication reviews on real patients. The RCT and observational study together give a complete picture how effective STRIPA is. This observation study includes studying the collaboration of GPs and pharmacists. To test if the functionalities of tiered alerts and taking the patient reliability into account is an added value for STRIPA, additional research should be performed. No research is available whether these two extra functionalities increase the value of STRIPA. This future research should examine how GPs and pharmacists handle the alerts when they are tiered into different categories according to severity. Moreover, not all patients take their medication according the prescription. This affects the overall treatment and should be included in the medication review. Missing in this research is the preference of healthcare professions for a mobile app. At the moment STRIPA is only available for a PC. In the future STRIPA will be available for tablets, both Android and iOS. However it can be the case that

healthcare professionals do not see the need to use STRIPA on tablets, this need exists should be researched. In this research, as well as previous research about STRIPA, only GPs and pharmacists are included. STRIPA could be beneficial for a broader audience. STRIPA is mainly focused on elderly patients, therefore STRIPA could be useful for other healthcare professionals like homecare nurses and even for informal care providers and patients themselves. Certain STRIPA functionalities, like the drug-drug interaction feature, can support these other user types. For example, functionalities like start and stop criteria for medication are not applicable for all types of users. A study should be conducted in order to understand the needs of the different user types. This need can be translated into different user profiles with different STRIPA functionalities. A reason for healthcare professionals to use STRIPA may also rely on a CE certification, which can cost a lot of money and time. Before determining the most appropriate level of CE certification, research should be conducted to examine the extent to which the attitude towards STRIPA changes positively with a CE certification level. This should also include a cost benefit analysis. STRIPA is tentatively scheduled for public release on the Dutch market in 2015.

9 References

Baxter, P., and Jack, S. (2008). Qualitative case study methodology: Study design and implementation for novice researchers. The qualitative report, 13(4), 544-559.

Booz & Company. (2012). The potential for pharmaceutical quality services. [Online]. Available from: http://www.knmp.nl/downloads/nieuws/nieuws-2012/booz-co-the-potential-for-pharmaceutical-quality-services.pdf/view [Accessed 17 June 2014].

Epocrates. (2014). Epocrates overview. [Online]. Available from: http://www.epocrates.com/products [Accessed 17 June 2014].

Google Play. (2014a). Epocrates. [Online]. Available from: https://play.google.com/store/apps/details?id=com.epocrates&hl=en [Accessed 18 June 2014].

Google Play. (2014b). Micromedex Drug Interactions. [Online]. Available from: https://play.google.com/store/apps/details?id=com.thomson.druginteractions&hl=en [Accessed 18 June 2014]

Inspectie voor de Gezondheidszorg. (2009). Het resultaat telt. [Online]. Available from: http://www.farmaactueel.nl/beleidsstukken/IGZ2009.pdf [Accessed 4 June 2014].

iTunes. (2014a). Epocrates. [Online] Available from: https://itunes.apple.com/en/app/epocrates/id281935788?mt=8 [Accessed 18 June 2014].

iTunes. (2014b). Micromedex Drug Interactions. [Online]. Available from: https://itunes.apple.com/us/app/micromedex-drug-interactions/id391763035?mt=8 [Accessed 18 June 2014]

KNMP. (2013) Medicatiebeoordeling. [Online]. Available from http://www.knmp.nl/downloads/organisatie-regelgeving/organisatie-regelgeving-normen-en-richtlijnen/richtlijnmedicatiebeoordeling.pdf [Accessed 10 June 2014].

Krska, J., Cromarty, J.A., Arris, F., Jamieson, D., Hansford, D., Duffus, P.R., ... and Seymour, D.G. (2001). Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. Age and Ageing, 30(3), 205-211.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P., ... and Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Annals of internal medicine, 151(4), W-65.

Meulendijk, M. (2014). [STRIPA]. Unpublished raw data.

Nederlandse patiënten consumenten federatie. (2014). Zorgkaart Nederland. [Online]. Available from: http://www.zorgkaartnederland.nl/apotheker [Accessed 24 June 2014].

Nederlandse Service Apotheek Beheer B.V. (2012) Analyse Medicatiebeoordeling t.b.v. de KNMP Richtlijn Medicatiebeoordeling. [Online]. Available from: www.serviceapotheek.nl [Accessed 5 June 2014].

Noels, K.A. (2001). New orientations in language learning motivation: Towards a model of intrinsic, extrinsic, and integrative orientations and motivation. Motivation and second language acquisition, 23, 43-68.

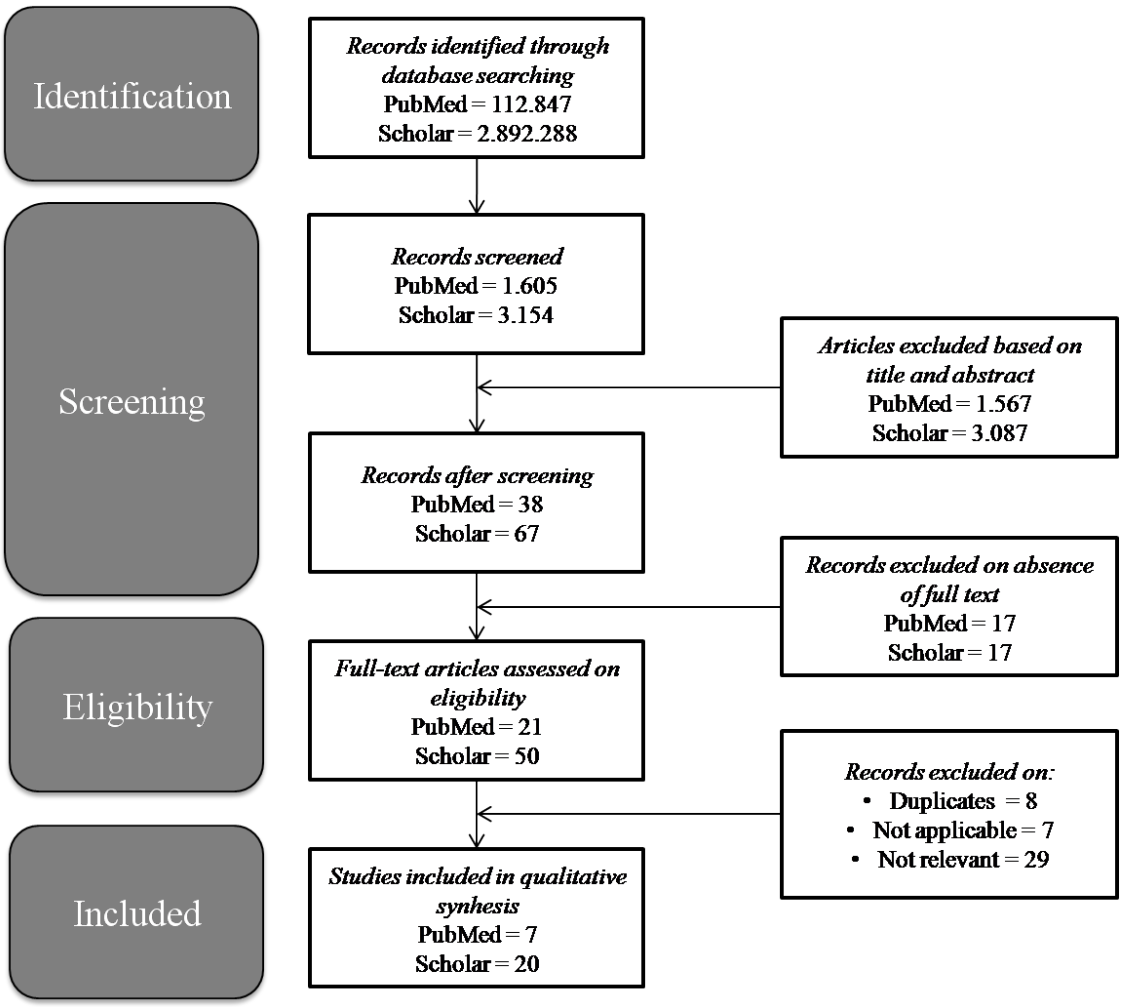
Stolberg, H.O., Norman, G., and Trop, I. (2004). Fundamentals of Clinical Research for Radiologists. AJR, 183, 1539-1544.

TPO. (2012). Nieuwe multidisciplinaire richtlijn polyfarmacie ouderen. Tijdschrift voor praktijkondersteuning. [Online]. Available from http://www.tijdschriftpraktijkondersteuning.nl/archief/volledig/id689-nieuwe-multidisciplinaire-richtlijn-polyfarmacie-ouderen.html [Accessed 10 June 2014].

uOttawa. (n.d.). Study Designs. [Online]. Available from http://www.med.uottawa.ca/sim/data/Study_Designs_e.htm [Accessed 23 June 2014].

Zorginstituut Nederland. (2013). Fact sheet polyfarmacie. [Online]. Available from: https://www.zorginstituutnederland.nl/binaries/content/documents/zinl-www/kwaliteit/meerjarenagenda/agenda-2013/agenda-2013/agenda-2013/zinl%3Aparagraph%5B7%5D/zinl%3Adocuments%5B4%5D/1306-fact-sheet-polyfarmacie/Fact+sheet+polyfarmacie.pdf [Accessed 11 June 2014]

Appendix A – Systematic Literature Review process



Appendix B – Search keys

	Drug interaction	**Polypharmacy**	**Medicine criteria**	**Medicine decease connection**	**Medication review**
General	Drug interaction Drug interactions Drug drug interaction Drug drug interactions Drug interaction study	Polypharmacy Polypharmacy elderly Polypharmacy APK Medicine multiplicity Polypharmaxy optimization method POM	Medicine criteria	Medicine disease connection	Medication review
App	Drug interaction app	Polypharmacy app	Medicine criteria app	Medicine disease connection app	Medication review app
E-health	Drug interaction e-health	polypharmacy e-health	Medicine criteria e-health	Medicine disease connection e-health.	Medication review e-health
General practitioners information systems	General Practitioners information system drug interaction	General practitioners information system polypharmacy	General practitioners information system medicine criteria	General practitioners information system medicine disease connection	general practitioners information system medication review
Clinical decision support software	Clinical decision support software Drug interaction	Clinical decision support software Polypharmacy	Clinical decision support software medicine criteria	Clinical decision support software medicine decease connection	Clinical decision support software medication review

Appendix C – Concept table

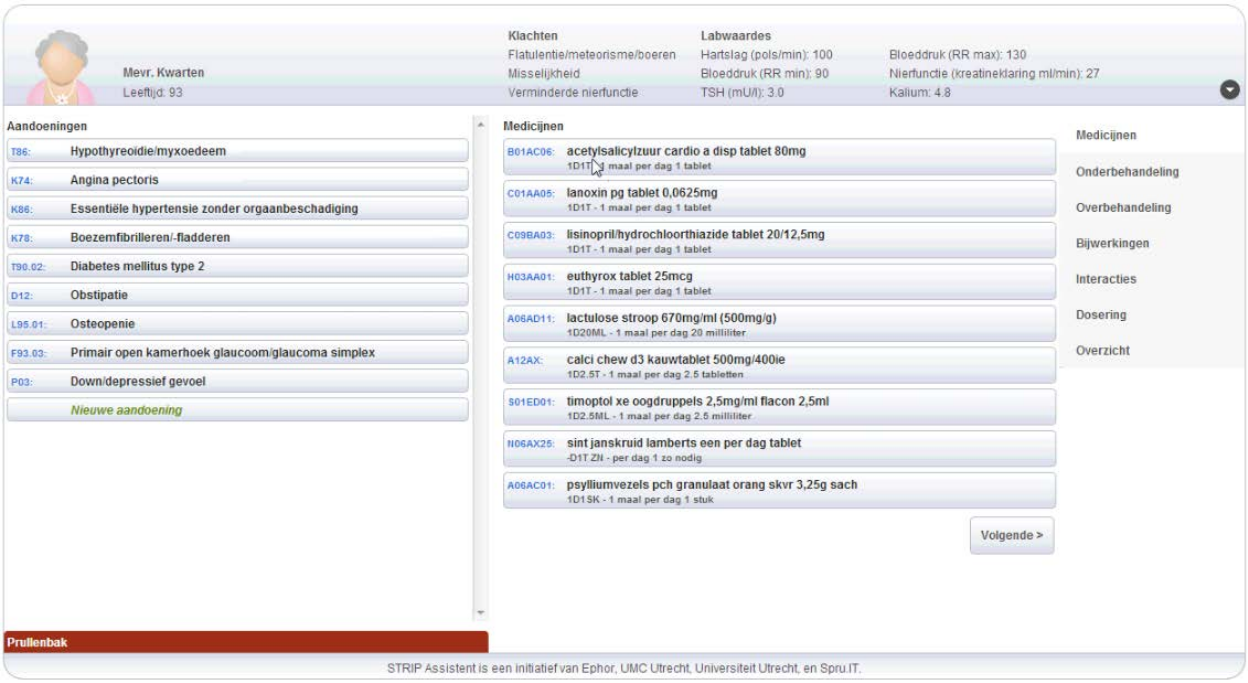
Reference	Drug-drug interaction	E-health	Health care specialists	Polypharmacy	Medication review
Magnus, D., Rodgers, S. and Avery, A. J. (2002). GPs' views on computerized drug interaction alerts: questionnaire survey. Journal of clinical pharmacy and therapeutics, 27 (5), 377-382.	✔	✔	✔		
Kmetik, K.S., Chung, J., Sims, S. and Found, N.R. (2007). Reasons provided by prescribers when overriding drug-drug interaction alerts. Am J Manag Care, 13, 573-580.	✔	✔	✔		
Paterno, M.D., Maviglia, S.M., Gorman, P.N., Seger, D.L., Yoshida, E., Seger, A.C., ... and Gandhi, T. K. (2009). Tiering drug–drug interaction alerts by severity increases compliance rates. Journal of the American Medical Informatics Association, 16(1), 40-46.	✔	✔			
O'Hagan, E. (2012). Getting started with medical apps: Apps you should know about. Journal of Hospital Librarianship, 12(2), 162-170.		✔			
Yu, K. H., Sweidan, M., Williamson, M. and Fraser, A. (2011). Drug interaction alerts in software-what do general practitioners and pharmacists want?. The Medical journal of Australia, 195(11-12), 676-680.	✔		✔		
Åstrand, E., Åstrand, B., Antonov, K. and Petersson, G. (2007). Potential drug interactions during a three-decade study period: a cross-sectional study of a prescription register. European journal of clinical pharmacology, 63(9), 851-859.	✔			✔	
McInnes, D.K., Saltman, D.C. and Kidd, M.R. (2006). General practitioners' use of computers for prescribing and electronic health records: results from a national survey. Medical Journal of Australia, 185(2), 88.		✔	✔		
Bates, D.W. and Gawande, A.A. (2003). Improving safety with information technology. New England journal of medicine, 348(25), 2526-2534.		✔			

Miller, R.A., Gardner, R.M., Johnson, K.B. and Hripcsak, G. (2005). Clinical Decision Support and Electronic Prescribing Systems A Time for Responsible Thought and Action. Journal of the American Medical Informatics Association,12(4), 403-409.		✔			
Aarts, J. and Koppel, R. (2009). Implementation of computerized physician order entry in seven countries. Health Affairs, 28(2), 404-414.		✔			
Ko, Y., Abarca, J., Malone, D.C., Dare, D.C., Geraets, D., Houranieh, A., ... and Wilhardt, M. (2007). Practitioners' views on computerized drug–drug interaction alerts in the VA system. Journal of the American Medical Informatics Association, 14(1), 56-64.	✔	✔	✔		
Krska, J., Cromarty, J.A., Arris, F., Jamieson, D., Hansford, D., Duffus, P.R., ... and Seymour, D.G. (2001). Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. Age and Ageing, 30(3), 205-211.			✔	✔	✔
Vinks, T.H., Egberts, T.C., de Lange, T.M. and de Koning, F.H. (2009). Pharmacist-based medication review reduces potential drug-related problems in the elderly. Drugs & aging, 26(2), 123-133.			✔	✔	✔
Hajjar, E.R., Cafiero, A.C. and Hanlon, J.T. (2007). Polypharmacy in elderly patients. The American journal of geriatric pharmacotherapy, 5(4), 345-351.				✔	
Scanlin, A. (2013). Reducing the Risks of Medication Errors. BioSupply Trends Quaterly, 26-29.	✔				
Meulendijk, M. (2012). Development of a decision-support system in the primary care sector. In CAiSE (Doctoral Consortium).		✔	✔	✔	✔
Meulendijk, M., Spruit, M., Drenth-van Maanen, C., Numans, M., Brinkkemper, S. and Jansen, P. (2013). General practitioners' attitudes towards decision-supported prescribing: An analysis of the Dutch primary care sector. Health informatics journal, 19(4), 247-263.		✔	✔	✔	✔

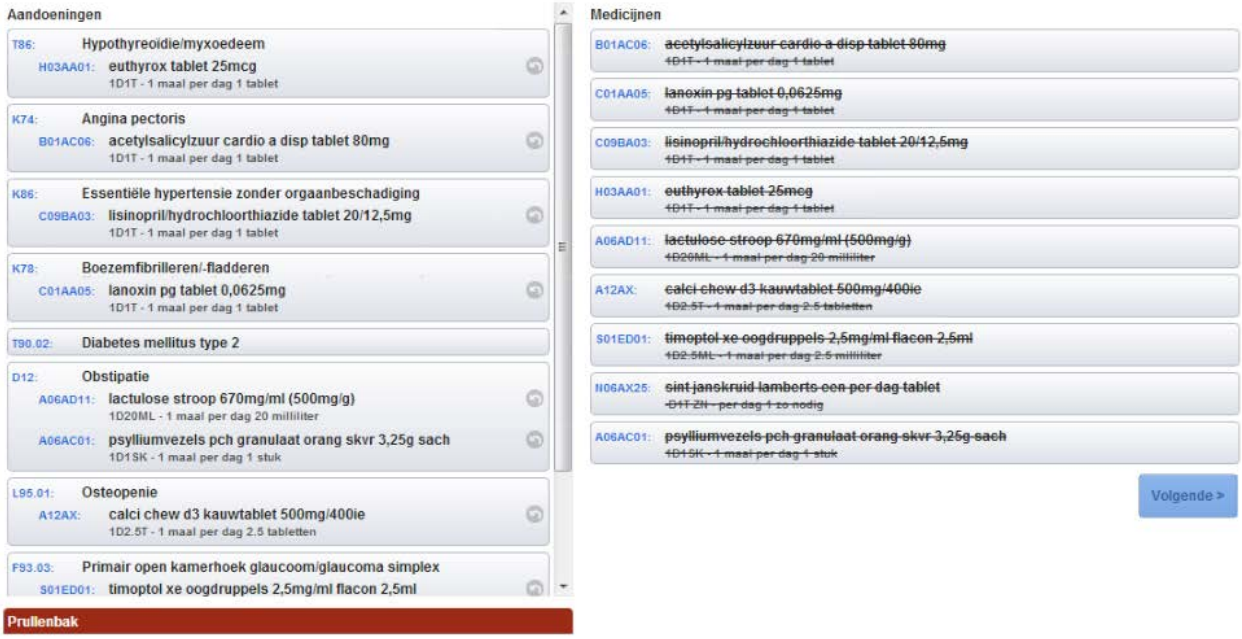
Horn, J.R., Gumpper, K.F., Hardy, J.C., McDonnell, P.J., Phansalkar, S. and Reilly, C. (2013). Clinical decision support for drug-drug interactions: Improvement needed. American journal of health-system pharmacy: AJHP: official journal of the American Society of Health-System Pharmacists, 70(10), 905-909.	✔	✔	✔		
Mille, F., Degoulet, P. and Jaulent, M.C. (2007). Modeling and acquisition of drug-drug interaction knowledge. In Medinfo 2007: Proceedings of the 12th World Congress on Health (Medical) Informatics; Building Sustainable Health Systems (p. 900). IOS Press.		✔			
Ahearn, M.D. and Kerr, S.J. (2003). General practitioners' perceptions of the pharmaceutical decision-support tools in their prescribing software. The Medical Journal of Australia, 179(1), 34-37.	✔		✔		
Smithburger, P.L., Buckley, M.S., Bejian, S., Burenheide, K. and Kane-Gill, S.L. (2011). A critical evaluation of clinical decision support for the detection of drug-drug interactions. Expert opinion on drug safety, 10(6), 871-882.	✔	✔			
Seidling, H.M., Phansalkar, S., Seger, D.L., Paterno, M.D., Shaykevich, S., Haefeli, W.E. and Bates, D.W. (2011). Factors influencing alert acceptance: a novel approach for predicting the success of clinical decision support. Journal of the American Medical Informatics Association, 18(4), 479-484.		✔			
Drenth-van Maanen, A.C., van Marum, R.J., Knol, W., van der Linden, C.M. and Jansen, P.A. (2009). Prescribing optimization method for improving prescribing in elderly patients receiving polypharmacy. Drugs & aging, 26(8), 687-701.		✔	✔	✔	
Duerden, M., Avery, T. and Payne, R. (2013). Polypharmacy and medicines optimisation.	✔		✔	✔	✔
Albrecht, U.V. (2012). Transparency of health-apps for trust and decision making. Journal of medical Internet research, 15(12), e277-e277.		✔			
Kaushal, R., Shojania, K.G. and Bates, D.W. (2003). Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review. Archives of internal		✔			

medicine, 163(12), 1409-1416.					
Bindoff, I.K., Tenni, P.C., Peterson, G.M., Kang, B.H. and Jackson, S.L. (2007). Development of an intelligent decision support system for medication review. Journal of clinical pharmacy and therapeutics, 32(1), 81-88.		✔	✔		✔
Meulendijks, E. A. (2013). Requirements Engineering for Medical Consumer Applications.	✔	✔	✔	✔	✔

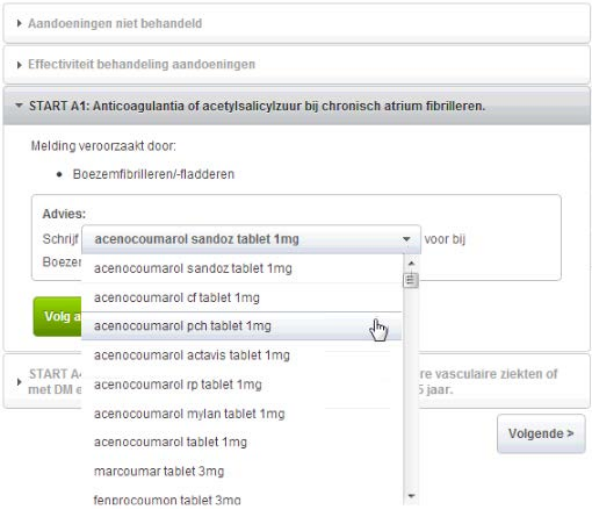
Appendix D – Screenshots STRIPA



Screenshot 1: STRIPA

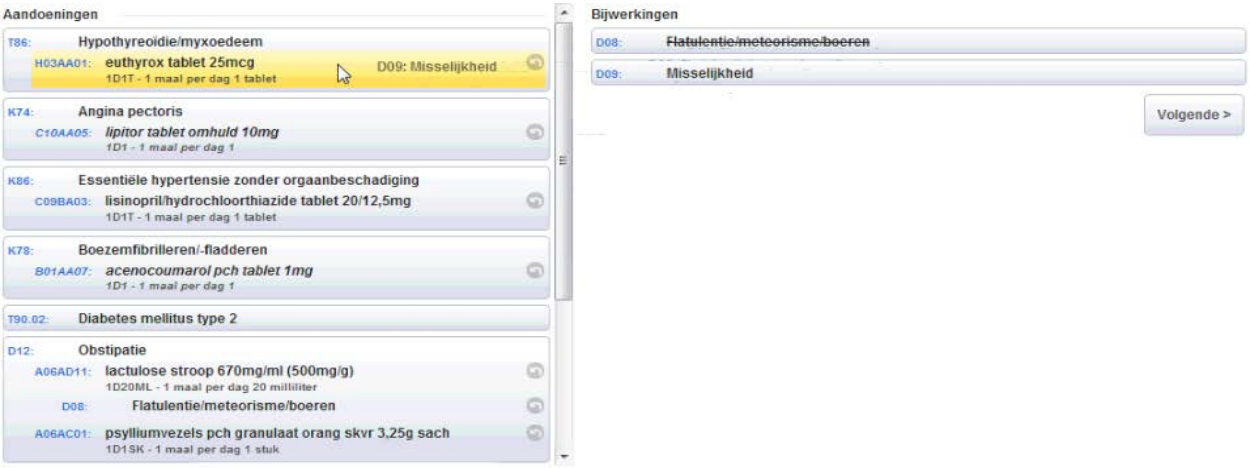


Screenshot 2: Drug-medication combination

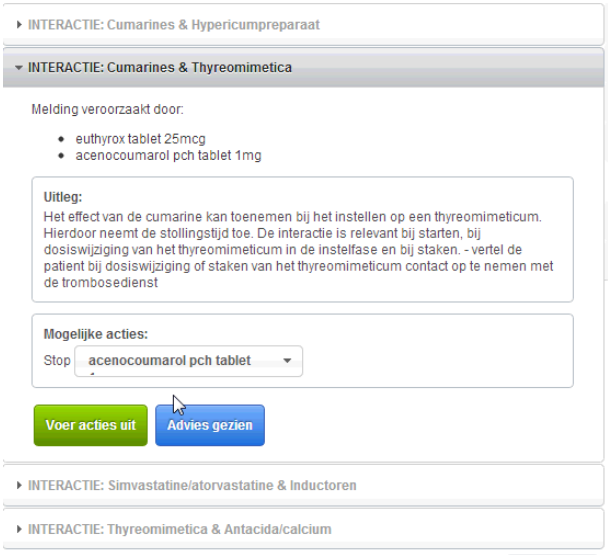


Screenshot 3: Start criteria medication

Screenshot 4: Stop criteria medication

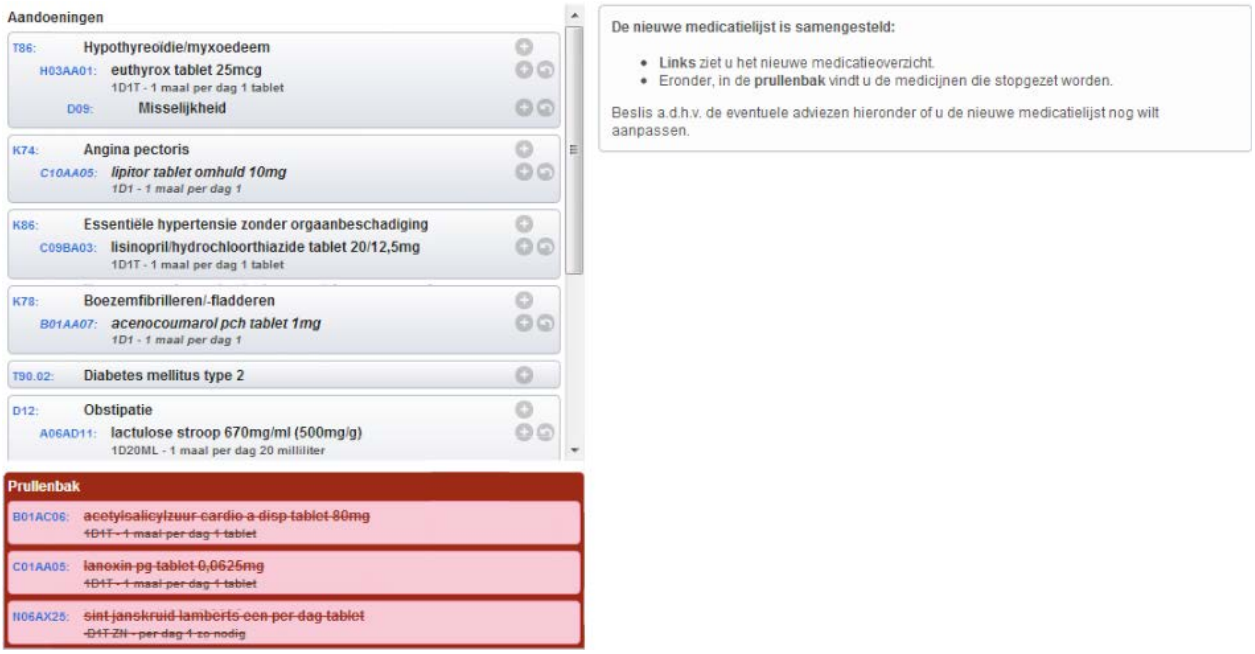


Screenshot 5: Connection effect to medication



Screenshot 6: Drug-drug interaction alert

Screenshot 7: Dosage medication alert



Screenshot 8: Overview

Appendix E – App comparison

Features	STRIPA	Epocrates	MicroMedex Drug information
Overview conditions patient	✔		
Overview diseases patient	✔	✔ *	
Overview lab results patient	✔	✔ *	✔
Overview medication patient	✔	✔	
Linking medication to the diseases	✔		
Advice start new medicine	✔		
Advice stop current medicine	✔		
Drug-drug interactions	✔	✔ *	✔
Advice about medication dosage	✔		✔
Pill identification based on its imprint and physical characteristics		✔	✔
Information about other health care professionals		✔	
General drug information		✔	✔
Costs	Unknown	Free version or a premium version for $159.99 a year	$2.99 a year
Rating	Unknown	Android: 4.3 (n = 19.356)	Android: 4.2 (n = 56)
		Apple: 3 (n = 46.934)	Apple: 2 (n = 176)

* This is a premium only feature