GIMS model for the screening and rating of Medication Safety in a country

Master thesis Research Project

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The Netherlands

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Content

Abstract

Introduction
The inappropriate, prescription, dispensing and patient use of medicines are global problems with large influence on patient safety according to researches by the World Health Organization (WHO). This problem will grow in the future, because of increasing use of medication, especially in low- and middle-income countries.
While most research is focused on pharmacovigilance, data is lacking about all processes and structures influencing appropriate use, also called Medication Safety (MS).
A structured overview of all these processes and structures is needed. The aim of this research is to create a (internationally applicable) screening and rating model concerning MS in a country in collaboration with GIMS foundation.

Methods
During phase 1, a framework provided by the GIMS foundation was used as base to create the model. The framework consisted of alpha, beta, and gamma actors and delta factors. They were sorted on their direct and indirect influence on patient and consumer. Literature was searched via PubMed and the WHO with keywords 'Pharmacovigilance', 'Medication Safety (AND stakeholders OR healthcare practitioner)' to create the critical dynamics and their conditions. Conditions for a rating system were created to finalize model 0.1. During phase 2 panel members were identified by purposeful sampling. They were selected on their broad view on MS and gave feedback via mail and phone conversation about GIMS model 0.1. The feedback was processed into GIMS model 1.0.

Results
Information of nine WHO documents and four researches was used. To create the critical dynamics for the alpha actors, the Knowledge, Attitude and Tools formulation was used based on the found literature. For the rating a five point Likert scale was added. Seven panel members from the Netherlands were chosen. Feedback of the panel members was processed to create model 1.0. The final model consisted of 247 critical dynamics for 29 stakeholders.

Conclusion
A comprehensive qualitative model (internationally applicable) concerning the actual status and improvement possibilities about Medication Safety in a country is created. To establish whether this model can be used in the international setting, it needs to be tested in different countries. National adaptations are likely needed to increase fitness.

1. Introduction

1.1. From pharmacovigilance to patient safety

Approximately 50 years ago modern pharmacovigilance started in the shape of the first program of drug monitoring by the World Health Organization(WHO).[1] Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine related problem.[2] See table 1.1 for all definitions. In the nineties pharmacovigilance expanded from the Western world, to Asia and Africa, [1] which resulted in the opening of the first collaborating centre of the WHO in 2010 which provided a pharmacovigilance centre in Ghana, Africa.[3]
The expanding interest in pharmacovigilance and the improved access to medicines gave an increasingly positive effect on health the last decades. This improved access is leading to a reduction in mortality and burden of disease; consequently it is improving the quality of life. However, the inappropriate use of medicines, prescription, dispensing and patient use are global problems with large influences on patient safety.[4] Especially when local conditions, which include professionalism of health care practitioners and IT support, are less favorable.

Table 1.1 Definitions

Term	Definition
Medication Safety	Minimize health risks originated from the global use of medicine.[5]
Pharmacovigilance	The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine related problem.[2]
Medication error	A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labeling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use''. [6]
Adverse drug reaction	A harmful response in the patient caused by the drug itself given in the recommended manner (dose, frequency, route, administration technique).[7]
Adverse drug event	Medical occurrence temporally associated with the use of a medicinal product, but not necessarily causally related.[8]

1.2. Research about global inappropriate use of medication and follow-up

To investigate the issue of safe medication usage among patients, the WHO conducted the first global study in 2009 to investigate the impact of inappropriate use of prescription medicines in long-term therapies in developing and transitional countries.[9] The WHO defines rational medicine use as: "Medicine use is rational (appropriate, proper, correct) when patients receive the appropriate medicines, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost both to them and the community. Irrational (inappropriate, improper, incorrect) use of medicines is when one or more of these conditions is not met." Studies between 1990 and 2006 about medicine use in developing and transitional countries were examined. The outcomes of this study showed that inappropriate use of medicine is still a widespread problem in developing and transitional countries. Approximately 50% of all patients were failing to take their medicines correctly. There was not much improvement in prescribing and patient care from 1990 till 2006 and it was expected that the overall situation is worse than reported.[9]

However, other researches show that inappropriate use of medicine does not only have a large impact in developing countries, but also in high income countries. Medication errors are still the leading cause of harm to patients in hospitals. On every five doses given to patients in typical US hospitals, one medication error occurs.[10] Also medication incidents are the second highest reported type of incident in Australian hospitals with error rates of 18%. The United Kingdom and the United States have similar figures.[11]

In response to the research of the WHO a report was published in 2012. It is a technical report which was prepared to be applied to the Ministers Summit at the International Pharmaceutical Federation congress in Amsterdam in October 2012 about '' The Benefits of the Responsible Use of Medicines'.[12]
Responsible use of Medicines implies that the capabilities, existing resources and activities of stakeholders in the health system are aligned to ensure that patients will receive the right medicines at the right time, benefit from the medication and use them appropriately. Thus, stakeholders have a responsibility to ensure appropriate use of medicines.

The aim of the summit was to explore and identify solutions to improve outcomes for patients about the use of medicines and to support sustainable and cost-effective healthcare around the world. Finally, the summit resulted into four recommendations, which were generally supported:

- The first recommendation was **to coordinate and incentivize better alignment between health care practitioners (HCPs) to create continuity of healthcare and improvement of management of medicines**. This implies better collaboration between HCPs and to promote this collaboration.
- The second recommendation was **to ensure that policies to manage safe use of medicines are determined by patient needs**. An example is investigating strategies and interventions to improve adherence of medication. This can provide patient education or tools to support adherence.
- The third recommendation showed that **policy makers should commit to successful initiatives in pharmaceutical innovation and learning**. Policy makers should be more focused on patient centered care and effective allocate resources to improve safe use of medicines.
- The last recommendation was to **support evidence-driven policy making by investing more into health care data in order to plan and evaluate effective intervention policies**. Information technology should be improved, to store all data.

In 2016 the 'Global challenge of Medication Safety to improve patient safety and quality of care' was discussed during a side event of the World Health Assembly. The goal of this side event was to emphasize the global burden of the unsafe medication practices and highlight all the obstacles towards safe medication use and practices. It is the run-up to the launch of the WHO Global Patient Safety Challenge, which started after the research of the WHO about rational drug use. During this event, different stakeholders, from non-governmental organizations to policy makers, were brought together to review this global problem and discuss this with each other in order to raise awareness among all stakeholders.[13]

1.3. Hospital admissions related to medication in the Netherlands

In the Netherlands, the Hospital Admissions Related to Medication (HARM)-Wrestling report was published in 2009 by researchers of Utrecht University, pharmaceutical sciences in request of the Society of Medical Specialists and Dutch Association of Hospital Pharmacists. The HARM-Wrestling report made recommendations as follow up to the HARM study. These recommendations are mainly to improve Medication Safety for the long term and focuses on the current and future healthcare professionals in the Netherlands.[14]

The HARM study focuses on interventions on the short term to improve appropriate use of medicines. This research showed how many observed drug-related hospitalizations could have been potentially avoidable. It concluded that 2,4% of all hospital admissions and 5,6% of all emergency admissions were medicine related. Of these medicine related admissions 46% was potentially avoidable. The total costs of these admissions were 85 million euros each year.[15]

1.4. Lack of data about Medication Safety

The previous examples show the global scale of the issue of inappropriate use of medicines. However, these and most other researches mainly focus on the urge of improving pharmacovigilance and adverse drug events. Mostly they do not mention other aspects influencing safe medication usage. If the search term 'Medication Safety AND Patient Safety' is used in PubMed, 13064 documents are available. However, they mostly only mention healthcare practitioners and their role in the medication safety system in primary and secondary healthcare. Other stakeholders, such as insurance companies or patient and consumer organizations, are hardly mentioned in any scientific paper about Medication Safety or Patient Safety.

The WHO, through its pharmacovigilance network guided by the Uppsala Monitoring Centre, mainly focuses on collaborating with pharmacovigilance centers to register mostly only adverse drug reactions. This is very useful, especially for new products, but leave out a medication system approach. Other focus points such as essential medicines and patient safety do not discuss all processes and structures influencing appropriate use of medicine.
Also, in the report 'Reporting and learning systems of medication errors: the role of pharmacovigilance centers' the WHO shows an overview of all stakeholders influencing pharmacovigilance, but stakeholders influencing all structures and processes of appropriate use of medicines are again not provided.[16]

For the first time the role of technology and interprofessional collaboration was discussed on an international level during the Ministers Summit in 2012.[12] Furthermore, some scientific researches as Mansur *et al.*[10] mention the urge of creating a global medication safety framework and names technology and interprofessional collaboration, but also education as important aspects influencing appropriate use of medicines.[10] Even though, a clear overview of all aspects influencing safe use of medicines is still not mentioned in any research.
The technical report 'The pursuit of responsible use of medicines: sharing and learning from country experiences' notifies the importance of improving activities, capabilities and even the existing resources of all stakeholders in the health system. They should take their responsibility and recognize the challenge of finite resources to ensure appropriate use of medicines. However, the report does not mention what they imply with 'all stakeholders in the health system'.[4]
In 2006 the Expert Group on Safe Medication Practices of the Council of Europe presented the first international report on safe medication practices with focus on Europe to enhance safe medication use. They noted that the prevalence of medication errors is not very well managed in Europe. Safe medication practices on national and local level are poorly implemented and developed in most of the European countries.[17]
The first aim of the report was to foster safe medication practices at European level. Other aims were to create awareness in European countries to recognize this problem as an important system-based public health issue and to provide guidance to authorities, governments, agencies and other European companies to implement safe medication practices.[17]
They stated in the report that a system approach was needed and they encourage collaboration between stakeholders involved in the medication system to improve the patient safety and the quality of the use of medication. Still, they do not mention what they imply with 'all stakeholders within the medication system'.[17]

1.5. Creating a helicopter view

As seen in the examples, a lack of data exists about Medication Safety. The information which is available, can be found in different articles, but never in an overview. A helicopter view of all stakeholders involved in the system is still missing.
While many researchers and policy makers now call for a more comprehensive view on the actual situation of all structures and processes influencing appropriate use worldwide, there is no theoretical frame work yet on how to get an accurate and structured view.

It would be desirable if an (international applicable) analytical tool, which can provide the needed data and insights, is realized. Ideally, the international applicability can facilitate both international academic discussions as well as giving benchmarking possibilities.

1.6. Creating a screening and rating model regarding Medication Safety

The Global Initiative for Medication Safety (GIMS) foundation, a pharmacovigilance (PV) organization based in the Netherlands, has a focus on the theme of Medication Safety. Its aim is to create awareness, analyses, insights and responsibility in the whole of the medical chain regarding Medication Safety on a global level. It drafted its own definition for Medication Safety (MS): 'Minimize health risks originated by the global use of medicines'.[5] To achieve better insights and data on the theme of Medication Safety, the GIMS foundation started a collaboration with University of Utrecht (UU) to attempt to create an international applicable screening and rating model (GIMS model) of all structures and processes concerning Medication Safety in a country during this research project. Besides creating insights and data, the GIMS model also helps to facilitate individual countries to identify strengths and weaknesses and with that good practices and room for improvements
Further aims are to evaluate and adapt the screening model using the Netherlands as a case study.

It must be possible for every country to apply the GIMS model and create an overview of the situation of their country regarding MS. The outcome of the model can result in publication, which can stimulate stakeholders to improve themselves.
If the model is applied on multiple countries, not only an overview can be created on national level, but also on international level. This can improve the situation of all stakeholders regarding MS worldwide.

2. Methods

2.1. Phases of the development of the GIMS model

The development of the model has been divided in five phases (see figure 2.1):

Phase 1: Creating a draft of GIMS model 0.1. During this phase literature will be read and questions will be constructed about stakeholders influencing MS. They will be sorted in the model and an introduction with additional information will be added.

Phase 2: Improving the quality of the model by a panel of different stakeholders. A panel will be gathered to give feedback about the first version of the model. The feedback will be processed in to a new version of the GIMS model 1.0.

Phase 3: The model will be applied on a country by someone with a broad view on MS. To examine if the model works appropriately, it will be first applied on the Dutch situation.

Phase 4: The answers of the model will be evaluated by a panel of different stakeholders within the evaluated country. Adaptations can be made, if the panel considers it as necessary.

Phase 5: Identifying strengths and weaknesses and with that good practices and room for improvements regarding MS in the evaluated country. This phase will provide the final outcome of the model.

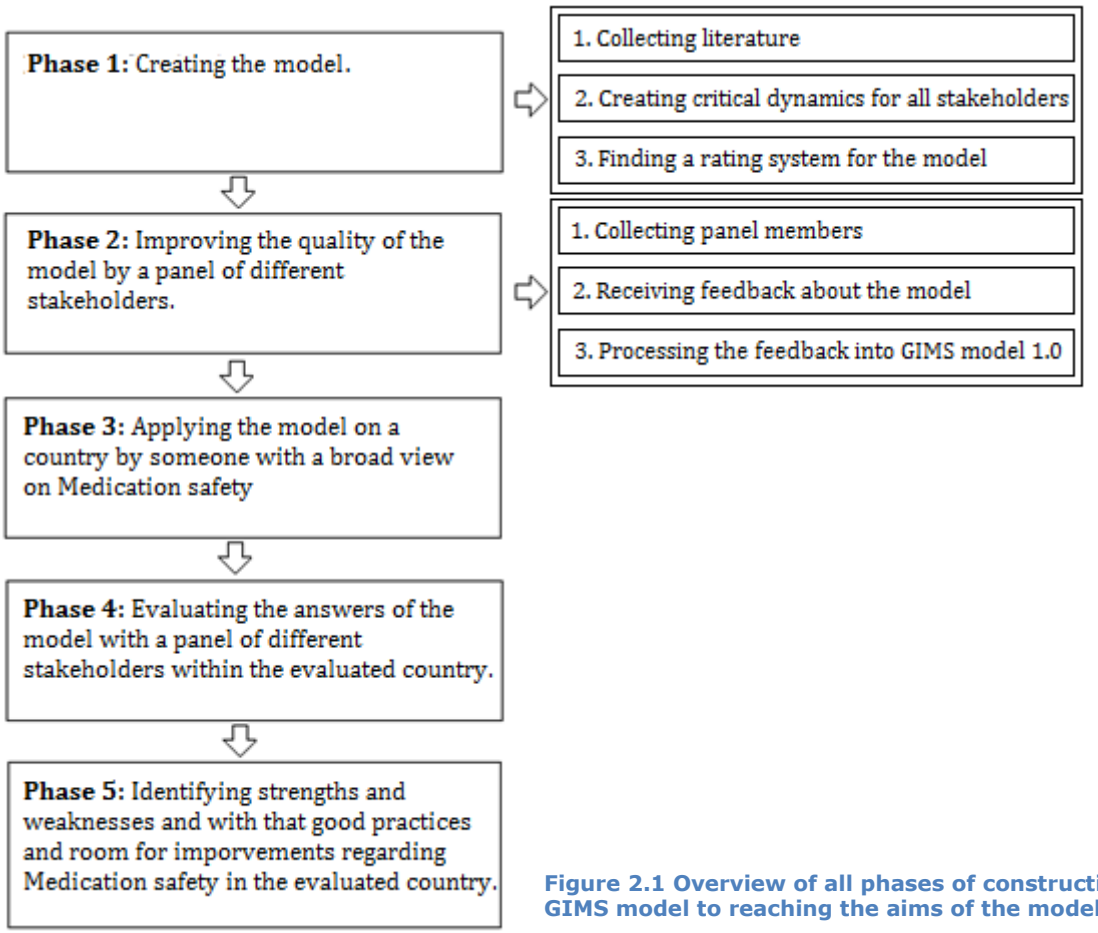

Figure 2.1 Overview of all phases of constructing the GIMS model to reaching the aims of the model

2.2. Phase 1: Creating the model

2.2.1. Framework GIMS model

The framework made by GIMS is used as base to create the model and find stakeholders (see figure 2.2).[5] This framework is created by the founders of GIMS with their own broad view on Medication Safety and reading (scientific) literature.
The foundation defines an actor as an entity which can have influence on a situation. Examples are a company, an organization or an individual. A factor is a circumstance which has influence, but is not a true entity with corresponding possibilities of making choices. Examples are culture, religion and politics.

The stakeholders are sorted based on their direct and indirect influence on patient and consumer regarding Medication Safety. They are called alpha, beta and gamma actors and delta factors (see figure 2.2). Alpha actors have the most direct influence on patient and consumer regarding Medication Safety, therefore they are nearest to the actor patient and consumer in the model. For example, a doctor has direct contact with the patient, just as a pharmacist, a retailer and a nurse. Therefore, they are Alpha actors. A professional organization of health care practitioners (HCPs) mostly has influence on patients and consumers via HCPs, in this case doctors and pharmacists. Therefore, they are Beta actors. Gamma actors have influence on Beta actors. For example, a national medicines regulatory body provides information and has direct influence on all beta actors. The Delta factors are not true entities and mostly have an indirect influence on patient and consumer and therefore they are placed in the outer ring.
This is based on the researchers' scientific view.

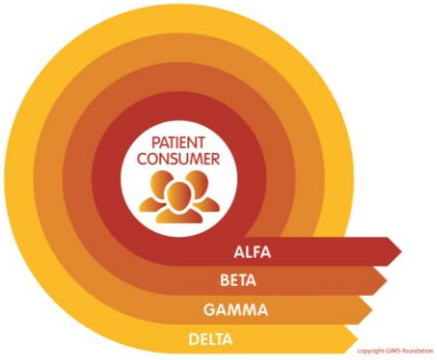

Figure 2.2 GIMS actors and factors concerning Medication Safety in a country.[6]

Alpha actors: patient and consumer, health care practitioner (doctor, pharmacist, nurse), hospital and retail.
Beta actors: professional organization of health care practitioners, national health care institute (like NICE for the UK), health care software provider, pharmaceutical retail formula, pharmaceutical wholesaler, pharmacovigilance organization.
Gamma actors: national medicines regulatory body, national inspectorate, ministry of health, academia, patient & consumer organization, national laboratory, pharmaceutical industry, insurance body and/or company, international bodies like WHO, EMA, EFPIA, PGEU, Cochrane.
Delta factors: national medicines and healthcare legislation, technology, culture, religion, economics, politics, stability and prosperity of a society and media.

2.2.2. Creating the critical dynamics for GIMS model 0.1

For each actor or factor, questions are formulated. The questions about the stakeholders, are called critical dynamics. Critical dynamics were not implemented in the GIMS framework and are created during this research. The GIMS foundation defines critical dynamics as part of an actors behavior or status which potentially have strong effects, and should give a complete overview of the situation and interaction with other actors or factors regarding Medication Safety. The critical dynamics are created by searching scientific literature and with discussing with the daily supervisor.

2.2.3. Collecting (scientific) literature

As mentioned in the introduction, scientific literature and documents of the WHO are available about actors and factors influencing Medication Safety. To create the critical dynamics, all the literature is further analyzed on potential components which can lead to a useful question.

Scientific literature

1. Search has been done through PubMed with the words 'Medication Safety', 'Medication Safety AND Stakeholders', 'Health care practitioner AND Medication Safety', 'Pharmacovigilance', 'Pharmacovigilance AND Stakeholders', 'Pharmacovigilance AND healthcare practitioner' and 'Pharmacovigilance AND doctor OR pharmacist'. Only a few articles, which can be found in the Methods and bibliography of the GIMS model, have been used to collect stakeholders.

Documents of the WHO

1. Searching continued on the website of the WHO. The WHO is considered as a reliable source, because it is an agency of the United Nations and acts as a coordinating authority on international public health. Their literature and documents are based on scientific research and they are one of the largest organizations investigating health topics.[18]
2. On the website of the WHO the topic 'Pharmacovigilance', 'Medication Safety' and 'Patient Safety' were studied and the attached documents read.
3. Also the search continued via Google. The words 'stakeholders AND Medication Safety AND WHO' and 'stakeholders AND Medication Safety AND World Health Organization' were used to find literature. Some stakeholders from the image of GIMS were also used as searching words. Such as 'insurance companies AND World Health Organization'.

Other literature

1. Websites of stakeholders were studied to gain more information. These were mostly Dutch stakeholders. Examples are the national healthcare inspectorate and national medicines regulatory body.
2. Also international organizations involving MS were studied. Examples are: World Health Alliance for Patient Safety, International Society of Pharmacovigilance, East African Community and the website of the European Commission about Patient Safety.

2.3.1. Creating the critical dynamics

Conditions will be created and a systematic search will be done to find the most adaptable formulation to create the critical dynamics.

Conditions to formulate critical dynamics

1. Every critical dynamic is supported with a source, which can be found in the bibliography.
2. It is prioritized that the questions were as open as possible, to not create a limitary rating. The words 'To what extent' and 'How' are used to create these open questions. For example: To what extent do doctors feel their responsibility in MS and PV? This question can't be answered with yes or know, but needs a more detailed answer.
   If an open question could not be asked, a closed question was formulated. For example: Does a pharmacovigilance center exist in your country? This question can only be answered with 'yes' or 'no'.
3. The critical dynamics should be formulated in a manner that a high rating implies 'not an issue' and a low rating implies 'an issue'. If the complete model is rated, it must be immediately visible which stakeholders and critical dynamics need improvement, because everything on the left side is an (slightly) issue and everything on the right side is (slightly) not an issue.
4. Furthermore, the model is examined on suggestive questions. If a critical dynamic was considered suggestive, it was formulated differently.
5. During phase 2 the panel members will look at the critical dynamics and will give feedback about the formulation.

2.2.4. Finding a rating system for the GIMS model

A rating system needed to be added, to value every critical dynamic. Also the rating system was not implemented in the GIMS image and created during this research.

After discussing several rating systems, the Likert scale was finally chosen to implement as rating system in the model. It is a reliable rating method which is often used in scientific literature.[19, 20] It is a scale where respondents can express their strength of agreement with each of the statements; in this case the critical dynamics.[19, 20] Conditions to reach the requirements for the Likert scale have been set up.

2.3. Phase 2: improving the quality of the model by an expert panel

2.3.2. Function and selection of the panel members

To find out whether the GIMS model 0.1. (both structure, formulated questions, rating method, introductional texts) was practically feasible and/or needed further improvements a key-expert view in the form of a panel was needed.

Panel members were found based on purposeful sampling; the researcher, the daily supervisor and the referee decided which stakeholders were key experts on Medication Safety and interested to participate as a panel member. It was important that the panel member had a broad view on Medication Safety and that they originated from different sectors. This was taken in consideration when the stakeholders were collected.

2.3.3. Receiving feedback about GIMS model 0.1

The panel members should give written or spoken feedback. It was the responsibility of the researcher that all feedback was well recorded.
The model would be send to the members with a small amount of questions.

The priority questions which were asked:

1. Do you understand the structure and content of the introduction?
2. Do you understand the structure and content of this model?
3. Does this model give you a good overview of the (f)actors?
4. Are stakeholders missing?
5. Do you understand the questions? If not, do you have suggestions to formulate the questions differently?
6. Are the right questions asked for each stakeholder?

The panel members were invited to answer these questions and could also give other feedback about the model and the introduction of the model.

2.3.4. Processing the feedback into GIMS model 1.0

All feedback of the panel about GIMS model 0.1 was gathered. The researcher and the daily supervisor would discuss which feedback would be added to the model. This would finally result in creating the GIMS model 1.0.

3. Results

3.1. Phase 1: Creating the model

3.1.1. Collecting (scientific) literature

Literature identified about the stakeholders and used to create critical dynamics and as such model 0.1 are shown in table 3.1.

Table 3.1 Overview of all literature used to create the GIMS model

Source	References
WHO	World Health Organization, Geneva. Public-private roles in the pharmaceutical sector: Implications for equitable access and rational drug use. 1997. Available at: http://apps.who.int/medicinedocs/pdf/whozip27e/whozip27e.pdf
	World Health Organization, France. Reporting and learning systems for medication errors: the role of pharmacovigilance centers. 2014. Available at: http://apps.who.int/iris/bitstream/10665/137036/1/9789241507943_eng.pdf
	World Health Organization. Patient Safety Curriculum Guide.2011. Available at: http://apps.who.int/iris/bitstream/10665/44641/1/9789241501958_eng.pdf
	World Health organization. Patient Safety (2016). http://www.who.int/patientsafety/en/
	World Health Organization. Looking at the pharmacovigilance: ensuring the safe use of medicines. 2004. Available at: http://www.who-umc.org/graphics/24753.pdf
	World Health Organization. Assessing national medicines regulatory systems. 2016; Available at: http://www.who.int/medicines/areas/quality_safety/regulation_legislation/assesment/en/.
	World Health Organization. National drug regulatory systems. 1999. Available at: http://www.who.int/medicines/technical_briefing/tbs/National_drug_regulatory_legislation_Annex8TRS885_en.pdf
	World Health Organization. Chapter 6 Pharmaceutical regulations and legislation. 2012. Available at: http://apps.who.int/medicinedocs/documents/s19583en/s19583en.pdf
Scientific literature	Mansur J. Medication Safety Systems and the Important Role of Pharmacists. Drugs Aging. 2016; 33:213–21.
	Lapkin S, Levett-Jones T, Gilligan C. Using the Theory of Planned Behaviour to examine health professional students' behavioural intentions in relation to medication safety and collaborative practice. Nurse Educ Today 2015 Aug;35(8):935-940.
	Harmark L, Raine J, Leufkens H, Edwards IR, Moretti U, Sarinic VM, et al. Patient-Reported Safety Information: A Renaissance of Pharmacovigilance? Drug Saf 2016 Oct;39(10):883-890.
	Alhomoud F, Dhillon S, Aslanpour Z, Smith F. South Asian and Middle Eastern patients' perspectives on medicine-related problems in the United Kingdom. Int J Clin Pharm 2015 Aug;37(4):607-615.
Other literature	GIMS foundation. GIMS image. 2015. Available at: www.gimsfoundation.org
	Shutterstock. Poor prescription practices across Africa are putting patients at risk. 29/09,2016; Available at: http://theconversation.com/poor-prescription-practices-across-africa-are-putting-patients-at-risk-64250
	Médicins du Monde. The KAP Survey Model (Knowledge, Attitudes, and Practices). 2011. Available at: https://www.spring-nutrition.org/publications/tool-summaries/kap-survey-model-knowledge-attitudes-and-practices
	Inspectie voor de Gezondheidszorg. Inspectie voor de gezondheidszorg. 2016. Available at: http://www.igz.nl
	World Health Alliance for Patient Safety. 2016. Available at: http://www.who.int/patientsafety/worldalliance/en/
	International Society of Pharmacovigilance. 2016. Available at: http://isoponline.org/
	European Commission. Patient Safety. 2016. Available at: http://ec.europa.eu/health/patient_safety/policy/index_en.htm
	East African Community. Health. 2016. Available at: http://www.eac.int/sectors/health

3.1.2. Formulating the critical dynamics

Additional information

Formulating the critical dynamics proved to be quite difficult. It resulted for example in adding additional information in the form of an attachment to the model in which for each question further explanation is provided on how to interpretate the question.

KAT Formulation[21]

To formulate the critical dynamics, conditions and models have been searched. Finally, the knowledge, attitude and practice (KAP) formulation on www.spring-nutrition.org, created by medicines du monde in 2011 was considered as the most applicable formulation.[21] The knowledge, attitude and tools (KAT) model is derived from the KAP formulation. Instead of focusing on the quality of practices of the stakeholders, it focuses on the quality of the tools they are using. It seemed more valuable, because the practices were also partly discussed in the attitudes. Tools are important to examine how HCPs carry out their tasks. Because this also has consequences for the Medication Safety of the patient.

3.1.3. Finding a rating system

Conditions Likert scale

1. A five point Likert scale was chosen, which is more often the standard in other scientific literature.
2. Each critical dynamic can be rated on a 5 point Likert scale. If 1 is rated, the critical dynamic is not at all present or not an issue in your country. If 5 is rated, it is very much present or an important issue in your country. Each question must be rated based on the scientific view of the participant evaluating the model.
3. In order to create continuity, the model will be filled in by one person with a broad view of Medication Safety in the researched country. If opinions are needed of stakeholders, they will not rate the critical dynamic based on their opinions. Opinions of the stakeholders will be gathered and only the one authorized to fill in the model will rate the critical dynamics.

3.1.4. Adding remarks and sources

'Remarks and sources' is added to the model. The applier of the model should always add a reference where the information is found, to enhance the objectivity. If opinions are asked, it should also be added to the model. The one rating the model should always be free to add remarks to each of the critical dynamics.

3.1.5. Summary GIMS model 0.1

The GIMS model 0.1 consists of alpha, beta, gamma actors and delta factors, also called stakeholders. Critical dynamics for every stakeholders are made. The summary of the result of the model is shown in table 3.2.

Table 3.2 Summary of GIMS model 0.1

Section	Content GIMS model 0.1
Introduction	*Introduction*
	- Aims of the GIMS foundation - Goals of research project - Goals GIMS model
	Explanation of the model
	Actors and factors - Collecting stakeholders - Sorting stakeholders into the GIMS model - Image GIMS model
	Critical dynamics - KAT model - Collecting literature to create the critical dynamics
	Remarks - Explanation how to use Remarks and Sources
	Rating of the model - Definition Likert scale - Explanation how to use the rating system of the model
Alpha actors	*Doctor; Pharmacist*
	Knowledge - Education MS and PV - Average actual knowledge about MS and PV
	Attitude - MS and PV considered as relevant themes - Responsibilities regarding MS and PV; interprofessional collaboration - Relationship governmental agencies
	Tools - Availability of electronic patients files - Availability of electronic guidelines and formularies
	Nurse
	Knowledge - Education MS and PV - Average actual knowledge MS and PV
	Attitude - MS and PV considered as relevant themes - Responsibilities regarding MS and PV; interprofessional collaboration
	Retailer
	Knowledge - Training to sell over-the-counter (OTC) medication
	Tools - (ICT) tool for diagnosis and product - Market authorizations rules for OTC products
Beta actors	*Healthcare practitioner-organizations*
	- MS and PV considered as relevant themes - Well respected - Quality of the guidelines concerning MS and PV
	Pharmacovigilance organizations
	- Well respected - Stimulate save medication practices; provide therapeutic guidelines and up-to-date information - Focus on adverse drug reactions (ADRs)
	National Healthcare Institutes
	- MS and PV an area of focus
	Pharmaceutical wholesale
	- Wholesale market exist of a few entities - To what extent is Good Distribution Practices (GDP) the standard - Battling against counterfeit products
	Database & Software provider
	- ICT products used in primary and secondary care
	Retail formulas
	- Pharmaceutical Patient Care used as an Unique Selling Point towards general public

Gamma actors	*Medicines Regulatory Authority*
	- Well respected and independent - Liaised with the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA)
	Inspectorate
	- MS and PV are an area of focus - Enforcement power
	Ministry of Health
	- MS and PV are an area of focus - Enforcement power - License to work as HCP - Working on 'Universal Health Coverage' plans
	Academia
	- MS and PV are an area of focus for scientific research
	Patient and Consumer organizations
	- MS and PV are an area of focus - Influential towards governmental agencies
	Healthcare Insurance companies
	- MS and PV taken up in their contracts with HCPs
	Pharma Industry
	- Deploy extra activities concerning MS and PV
	International entities
	- Influence on national policy and legislation development - Warm/functional relationship with governmental agencies
Delta factors	*Legislation concerning medicines and healthcare*
	- Sufficient to optimally protect against risks from using medication
	Technology
	- Country with high developed ICT-technology - Technology equally available throughout the country - ICT tools for prescribing and dispensing
	Culture
	- Sensitivity of privacy-aspects of big ICT databases - Existence of influence of alternative medication of choice of medication - Personal use of medicines. Perspective about use of medication. - Not a big difference in appreciation of different forms of medicines
	Religion
	- Religion as a factor taken into account concerning MS and PV
	Economics
	- Availability of both public- and private facilities; private pharmacies more valued - Patients bound to go to one specific pharmacy - Business model focused upon selling more products - The law and financial ties and prescription bonuses
	Politics
	- Sensitivity of political system towards national business interests - Political awareness regarding MS and PV
	Media
	- The law and advertisement for prescription medicines - Influence of OTC advertisements towards the public
	Stability and prosperity
	- Is the country political stable and generally prosperous

3.2. Phase 2: improving the quality of model 0.1 by a panel

3.2.1. Collecting panel members

Panel members who met the requirements were searched.

Due to a lack of time, there have been a number of considerations:

1. Every stakeholder of the panel needed to be contacted to discuss his or her comments on the GIMS model and introduction of the model. Getting in contact with the panel member, the examining of the model by the panel member and discussing his or her comments would require a large amount of time. Therefore, a small panel of 8 panel members is chosen.
2. The stakeholders need to be easy reachable and reach the required standards. Therefore, the key experts were Dutch and mostly a connection of the referee or daily supervisor.

The panel members which were selected for feedback about the model are shown in table 3.3. One panel member did not respond and is left out of the research. Therefore, there are 7 panel members.

Table 3.3 Panel members

Function	Why added to the panel?
Pharmacist working in health consultant	Specialization in pharmacy business and medication management. Change management in profitable and sustainable healthcare business.
Pharmacist in public pharmacy	View of a healthcare professional (HCP). Has direct contact with patient and consumer.
Master Pharmacy student at the University of Utrecht	Did research about policies on essential medicines. Provides a scientific view of the model.
Doctor working in health consultancy	Works with organizations and companies involving health and Healthcare practitioners. Topics include human resources, operations, governance, financing, coding and marketing.
Dr. pharmaceutical sciences at the University of Utrecht	Scientific view on the model.
Environmental engineer and economist	Worked for the GIMS foundation. Broad view on all different aspects influencing Medication Safety.
Pharmacist and HCP worked in developing countries	Worked in developing countries in different capacities on policy, strategy and implementation on issues surrounding access to care and treatment.

3.2.2. Receiving feedback about GIMS model 0.1

After the construction of GIMS model 0.1, feedback was gathered of all panel members. The feedback was five times given vocally and twice as well vocally as written. During the conversation it was the responsibility of the researcher to write everything down.
A summary of the most important feedback and which of them is added to the GIMS model is shown in table 3.4. All feedback of all stakeholders can be found in attachment 7.2.

Table 3.4 Summary of all feedback from the panel members

Section	Subsection	Feedback	Feedback applied to the model?
Introduction	*Goals*	The goal of the model is different. The aim of the model should be that a country can be facilitated to create an overview of the situation regarding MS to identify the strengths and weaknesses (and with that good practices and room for improvements). It is important to clearly state this in your introduction.	Yes
	Introduction	Explain clearly that someone with a broad view on MS will apply the model on a country. Also the applier of the model should add the search strategy to find answers on the critical dynamics.	Yes.
		Annotate which sources, also of the WHO, are used for the actors and factors. And notify where your key documents originate from. What is the search strategy?	Yes.
	Critical dynamics	Definition is wrong. Critical dynamics are dynamics between different parties in society who have influence op MS. Education is a hygiene factor, therefore it is not necessary to add to the model. The critical dynamics now more focus on the quality of execution of the work by stakeholders and the level of education. However, the questions must be about the dynamics between different parties (for example doctor, pharmacist and patient).	No. Definitions are made at the beginning of the research. If the definitions must be changed, the whole construction of the model need to be changed as well.
		All questions have to be in connection with the patient. For every critical dynamic need to be asked: 'How is this question in connection with the stakeholder and the safety of the patient?'	Yes.
		Start with explaining how the actors and factors are sorted in the GIMS model in connection with patient and consumer. Explain why alpha actors are the nearest to patient and consumer.	Yes.
		Clearly explain how the model has to be rated. If the stakeholder is asked about his opinion on a critical dynamic, will he or she also rate the question? Or will the applier of the model decide the rating of the critical dynamic? Ask continuously how reliable the answer is.	Yes. Added that someone with a broad view about MS will fill in the model.
		Some critical dynamics stakeholders will always answer with 'yes'. But the applier of the model needs a reliable answer. For example, if you ask the pharmaceutical wholesaler if they battle counterfeit products, the pharmaceutical wholesaler will always answer this question with 'yes'. Instead of asking the pharmaceutical wholesaler about his opinion, the national medicine regulatory authority can be asked. This gives a higher probability of a honest answer.	No. Someone with a broad view on MS will rate the critical dynamics.
		General comments	
		Can't you apply the KAT model to all actors and factors?	No. It was not possible to apply the KAT formulation to all actors and factors.
		This is an international model, so don't look at the questions with a Dutch view. For example: in many countries (also in Europe) many patients do not have a fixed pharmacy.	Yes.
		The applier of the model has to know a lot about all different actors/factors/groups regarding MS. Are the answers not too much based on your own experiences instead of an objective view? Not everybody knows what is happening behind the scenes of companies and people regarding MS.	Yes. Added that (scientific) literature has to be searched, before asking opinions of stakeholders. The applier the model can not add his/her own opinion.
		If you answer a critical dynamic with 'no', some critical dynamics of the same stakeholder are not necessary to be answered. It can be a possibility to refer to other questions. For example: if you answer this question with 'no', please continue with question X.	Yes. If critical dynamics do not need to be answered, the applier of the model can write under remarks: 'does not apply'.
		The national healthcare institute and healthcare software providers are not part of beta actors, but gamma actors. These stakeholders do not have a large direct influence on patient and consumer. A national healthcare institute is mainly responsible for the quality, safety and cost effectiveness.	No. The actors and factors were already fixed. They could not be adjusted.
		Some countries have strong regulatory bodies. It is recommended to add them not to gamma, but to beta actors. National inspectorate: has a direct impact on MS, so it would be better to place it at beta.	No. The actors and factors were already fixed. They could not be adjusted.

		Rating	
		Leave 'neutral (3)' out of the model. The applier of the model wants to know directly if a critical dynamic needs improvements or if it is not an issue in your country.	Yes.
		Some critical dynamics are more important than other critical dynamics. Do those questions have to be rated with more preference?	No. During the evaluation of the rating of the critical dynamics, more preference can be given to the answers.
		Actor social networks	
		Family also has a direct influence on patient and consumer. It should not be implemented with culture or religion. I would make this a separate actor.	No, but added family to the actor patient and consumer.
		Actor hospital	
		Add something about the electronic data exchange. At the moment it is not optimal between hospital and public pharmacy. This is mostly about patient files and process data.	Yes.
		How much discharge and admission medication?	No. No value for MS.
		How much trust does the patient have in the Medication Safety in the hospital?	Yes, but asked general for the actor doctor and pharmacist.
		Actor patient/consumer	
		Add the actor patient. I think it is quite extensive and most important stakeholders are reviewed, but I miss actually the patients behaviour. It is mentioned via the cultural and religious aspects and also via the patient organizations, but the individual patients role and his/her social network has an enormous influence in my opinion and is undervalued. How do patients look for information about medicines: internet, social media, neighbours, family and friends. These are the most direct actors in the patients network. Not (anymore) the HCP.	Yes.
		Are the choices about the medication therapy made by the patients conscious or unconscious choices?	Yes.
		Examine your critical dynamics by a panel of patients and patient organizations.	No.
		In the case of an ADE: does the patient stop using the medication? If the patient suffers from side effects, does he contact (or share with) the HCP or discusses which steps have to be taken?	Yes.
		Which aspects are most influential for the patient? Make them choose between the stakeholders, do not forget health care insurance.	Yes.
		How would the stakeholders help patients and consumers to optimize the use of medication? This can be an open question, or give the patient several choices.	No. This will be the outcome and is also the aim of the model.
		Formulating critical dynamics	
		Some critical dynamics are suggestive and need to be formulated in another way.	Yes.
		It is interesting to see how stakeholders describe themselves on their websites and to the public about how they 'really' work. Examine well how the stakeholders describe themselves on their websites how they function and what their view is of the patient.	Yes.
		Create more open questions to gain information as effective as possible.	No. We decided to use the Likert scale for each critical dynamic. Each critical dynamic will have a value. Open questions are difficult to value.
GIMS Model	Alpha actors	General comments	
		What does KAT mean? Explain this in the introduction of the model.	Yes.
		Nurses: No 'Tools' for the actor Nurse? What about dispensing tools? For example (electronic) registration of administration of medication? Try to apply the KAT formulation to this actor.	Yes.
		Pharmacists: Perceive pharmacists their relationship with doctors as effective?	Yes.
		Doctors and pharmacists: the tools which pharmacists use are different from doctors (also different storage systems). How is the communication when the tools differ from each other? How are the triangular relationships between doctor, pharmacist and	Yes.

		patient?	
		Nurse: How well is the collaboration with the doctor?	Yes.
		Retailer: Read documents about public private strategy and from the pharmaceutical industry. Also create critical dynamics about the conditions in a country of selling medication. For example, OTC medication can only be sold in pharmacies in Belgium .	Yes.
	Beta actors	General comments	
		HCP organizations: To what extent do pharmacists and doctors collaborate with each other?	Yes. Asked if they collaborate with each other.
		Pharmacovigilance organizations: Should you not add something about reporting side-effects? To what extent is it obligatory and stimulated to report side effects? Is there an open culture to report medication errors? Is all information reported back to the HCPs?	Yes.
		National healthcare institutes: I understand you have to make choices regarding the questions. However, at the moment they seem sometimes randomly chosen. How do you determine if the most important aspects are included? It should be based on literature and the panel, but that is also just a group of people with an opinion.	Yes.
	Gamma actors	General comments	
		Medicines Regulatory Authority: What is the link with MS/PV?	Yes. Added market authorization and risk assessment of medicines.
		Ministry of Health: I think you will find that they will answer all these questions with yes or rating 5.	No.
		Pharma industry: What is the commercial influence of the stakeholder in the country? If large pharmaceutical companies have more influences then small pharmaceutical companies, this can result in a monopoly of pharmaceutical companies in the country. These aspects can have influence on MS and corruption.	No.
	Delta factors	General comments	
		Culture: Are these the most important culture questions? Health literacy of the patient is also important to add.	Yes. Added at the actor patient.
		Politics: To what extent does politics have influence on the collaboration between HCPs?	No.
		Economics: Also the availability and reliability of medicines is important. How much medication is illegal?	Yes. Added to the actor wholesale and pharmaceutical companies.
		What is the amount of trained staff selling medication?	Yes.
		Legislation concerning medicines and healthcare: WHO guidelines should also be mentioned and to what extent countries abide the guidelines.	No.

3.2.3. Processing the feedback into GIMS model 1.0

GIMS model 1.0 is the model after implementing the feedback of the panel members and the daily supervisor. It is the final version for this research. The model can be found in attachment 7.1. The amount of critical dynamics and stakeholders (actors and factors) compared to GIMS model 0.1 can be found in table 3.5.

Table 3.5 Number of critical dynamics used in GIMS models 0.1 and 1.0

		Number of critical dynamics model 0.1	Number of critical dynamics model 1.0
Alpha actors	**Patient and consumer**	-	12
	Doctor	13	33
	Pharmacist	13	31
	Nurse	7	16
	Hospital board	-	8
	Retailer	4	7
Beta Actors	**Healthcare practitioner organizations**	8	17
	National healthcare institute	2	2
	Pharmaceutical wholesale	3	3
	Pharmacovigilance organization	6	18
	Pharmaceutical retail formula	2	5
	Healthcare software provider	3	3
Gamma actors	**National medicines regulatory body**	4	8
	National inspectorate	2	7
	Ministry of health	5	7
	Academia	2	7
	Patient & consumer organization	3	5
	Pharmaceutical industry	1	6
	Health insurance company/ public health insurance	1	4
	National laboratory	-	5
	International bodies	2	16
Delta factors	**National medicines and healthcare legislation**	1	7
	Technology	4	1
	Culture	4	4
	Religion	1	2
	Economics	8	4
	Politics	2	2
	Stability and prosperity of a society	2	1
	Media	2	3
Total		**105 critical dynamics for 26 stakeholders**	**247 critical dynamics for 29 stakeholders**

4. Discussion

The aim of this present study was to create a (internationally applicable) screening and rating model concerning Medication Safety in a country. Further aims were to evaluate and adapt the screening model using the Netherlands as a case study. The research contained finding and constructing actors and critical dynamics and a rating system to create the GIMS model.

4.1. Content of the GIMS model 1.0

A model is created based on the found literature and the framework of GIMS foundation, which consisted of actors and factors. After receiving feedback from the panel new actors are added, such as patient and consumer, hospital board member and laboratory. The actors and factors were sorted based on their direct influence on patient and consumer. To create an overview of the actual situation regarding the actors or factors, questions, also called critical dynamics, were created for each stakeholder. By reading (scientific) literature and receiving feedback from the panel, the model was examined on completeness regarding all critical dynamics. If a critical dynamic needed more background information, additional information is added as attachment. The questions were as open and objective as possible. The final version of GIMS Model 1.0 consisted of 247 critical dynamics for 29 stakeholders. This is a large increase in comparison to the GIMS model 0.1. Most critical dynamics were added to the alpha actors, because of their direct influence and contact with patient and consumer. Also more critical dynamics are created for HCP organizations, because of their direct influence on HCPs. Furthermore, a good report of the WHO 'Reporting and learning systems of medication errors: the role of pharmacovigilance centers' was found, which provided many critical dynamics for the actor pharmacovigilance center.
Finally, the Likert scale is added for the rating of each critical dynamic. Model 1.0 consists of a 4 point Likert scale, to stimulate the applier of the model to not choose for a neutral choice. 'Remarks and sources' is added to enhance the objectivity. To the model an introduction was added, which explains the development of the model, but also the aim and suggestions for search methods to answer the critical dynamics.

4.2. Literature

Despite a long search for (scientific) literature a good overview of all actors and factors influencing MS, could not be found. Also a model does not exist with the same content or aim as this research. However, literature with common grounds with this research did exist. Most useful information is found on the website of the WHO and PubMed. Surprisingly, not much research was available about the actor patient and consumer. Also, it was difficult to find information about the Delta factors.

WHO
Finding useful information on the website of the WHO was difficult. Not many information was applicable for this research under the topic Patient Safety. Under the topic 'Essential medicines and health products' two interesting reports were found called 'The Pursuit of Responsible Use of Medicines: Sharing and Learning from Country Experiences' and 'Reporting and learning systems of medication errors: the role of pharmacovigilance centers'. [4, 16]
An old report from 1997 was found via Google: 'Public-private roles in the pharmaceutical sector: Implications for equitable access and rational drug use'.[22]

The documents of the WHO contained information about the stakeholders, mostly influencing pharmacovigilance. The report of 1997 also provided other stakeholders which also influence Medication Safety. The document targets mostly policy makers and managers in a country on regional and international levels. However, it provides practical guidelines how public and private roles have effect on drug accessibility and rational drug use. It provides many stakeholders influencing rational drug use in the public and private sector in the pharmaceutical

market, which are not mentioned in any other document or report, such as government, healthcare insurance and pharmaceutical wholesale companies.[4, 16, 22]

PubMed
Via PubMed was searched for scientific literature. While searching on the key terms 'Pharmacovigilance', 'Medication Safety' and 'Medication Safety and stakeholders OR healthcare practitioner' 4 useful articles were found. However, the articles more focused on healthcare practitioners and not on other stakeholders.
In Mansur *et al.* and Lapkin *et al.* Medication Safety was discussed. However, both only focused on HCPs and not the other processes and structures involving MS.[10, 11] Lapkin *et al*. mostly discussed about the behavior of health professionals (and students) in relation to medication safety and collaborative practice. Critical dynamics about collaborative practice between HCPs are formulated by reading this research.[11] Mansur *et al.* published a research about the role of the pharmacist in the Medication Safety System. Mansur, contrary to most researches, focuses on the system contributors regarding medication-related adverse events. He notes that errors can occur during the storage, prescribing, transcription, preparation and dispensing, or the administration and monitoring of medication. He also writes that constructing a global Medication Safety framework is important. Furthermore, the importance of technology and education is notified. This study focused on HCPs, and especially (clinical) pharmacists. Many critical dynamics about the role of HCPs and especially pharmacists are formulated by using Mansur *et al.*.[10]

4.3. Positive aspects and room for improvement of the research

Positive aspects
Most pharmaceutical researches are quantitative. This research project is one of the less qualitative studies. The outcome does not provide data, but a tool to create data for all countries. The aim of this research project is a new and innovative concept, which is still not created in any other research project.
Also this research had a good structure from having the GIMS framework till creating the GIMS model 1.0. Because of a lack of literature about this topic, a large amount of time was used to decide how the model would be created within the timeframe. Finally, several phases could not be executed, but these phases are elaborated as seen in image 2.1.
Furthermore, definitions are created for new terms introduced in this research. The terms Medication Safety, KAT formulation, critical dynamics, actors and factors are defined and their function in the model.
To create a structure for all critical dynamics for the alpha actors, the KAT formulation is created. The structure gives a better overview of all questions asked about a stakeholder.
Finally, key experts were used. Because scientific literature was lacking about this topic, the model is not improved by literature. These key experts provided important feedback to improve the model. Every key expert was personally contacted via phone or face-to-face to improve the discussion about the feedback of the content of the introduction and the model itself.

Room for improvements
The execution of this research project was not an easy process. First of all, a lack of data existed about this topic. A large amount of time was spend in searching similar researches about this topic. Unfortunately, no research has been found which discusses specific about the aim of this research. The search term 'Medication Safety AND Patient Safety' in PubMed shows 13064 scientific articles. However, most of these articles focus on the role of healthcare practitioners within the medication safety system in primary and secondary healthcare. As seen in this research, the reality is different. Not only healthcare practitioners, but also other stakeholders are involved with Medication Safety and Patient Safety. Finally, only four scientific articles were used. These articles were not limited to the role of healthcare practitioners within the medication safety system, but also discussed the role of culture, education, and even discussed an overview of all systems concerning Medication Safety in a global framework. Scientific

literature about the role of other stakeholders (for example insurance companies and patient and consumer organizations) does hardly exist. Therefore, in the GIMS model is mostly referred to documents of the WHO as source to validate the stakeholders and critical dynamics.
As stated before, the report 'Reporting and learning systems of medication errors: the role of pharmacovigilance centers' has most common ground with this research. However, the report mostly focuses on pharmacovigilance and less on Medication Safety as stated by GIMS foundation.[16] Due to this lack of data, most of the content of this research and the GIMS model is self-designed, including definitions of actors, factors and critical dynamics and formulating them. Some critical dynamics even have the source 'AUTHOR' as reference which refers to the researcher of this research project, because of the lack of data. The lack of data about Medication Safety shows the importance that more research needs to be done about this topic.
Also the KAT formulation could not be applied to all actors and factors. The KAT formulation is preferred to be applied to people. To apply the formulation to other entities is more difficult and sometimes even impossible. Finally, there is decided to only use it for the alpha actors. To create the critical dynamics for the other (f)actors, conditions are self-invented and applied.
Furthermore, conditions how to add sources to 'Remarks and sources' is not added. This can be confusing for the applier of the model. In the introduction must be noted that the source must always be written in Vancouver Style.
To conclude, due to a lack of time just a small amount of Dutch panel members were contacted. It took often a large amount of time to reach the panel members. If they were reached, they needed to give feedback about introduction and the GIMS model itself; this also took time. The panel also only consisted of Dutch panel members. In future the panel needs to be international, larger and more time needs to be implemented in the research period to contact the panel members and receive their feedback.

4.4. Further research

Phase 1 and 2 are executed during this research (see figure 2.1). The model needs to be applied on the Dutch situation to validate if the model works properly. The answers of the model need to be discussed with a panel of different Dutch stakeholders. Finally, the outcome of the model must give an overview of the strengths and weaknesses and with that good practices and room for improvements of the evaluated country. This outcome could demonstrate that the model works properly for the Dutch situation and also determine if this model can be tested in other countries.
If the model will be tested in other countries, the international applicability of the model will be determined. Through other international academia the GIMS model 1.0 needs to be applied on other countries. It should be assessed if the introduction is clear, if critical dynamics are well designed and to what extent national adaptations need to be made for the right outcome to reach the aim in other countries.

5. Conclusion

A first version of an innovative comprehensive qualitative model (internationally applicable) concerning the actual status, and improvement possibilities, on the theme of Medication Safety in a country has been created. This is the first model ever created which gives an overview about the actual status of Medication Safety in a country. Until now, not much information was available about this innovative concept. To establish whether this model is of real practice value in the international setting, it needs to be tested in different countries. Also it must be determined if the model will facilitate individual countries to identify strengths and weaknesses and with that formulate good practices and room for improvements.
It is likely that national adaptations are needed to increase fitness for use in the different countries. Hopefully, by applying the model on different countries by collaborating with international academia, more information can be provided about the international applicability in the future.

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7. Attachments

7.2. Feedback panel members

Section	Subsection	Feedback	Applied to the model?
Introduction	*Goals*	The goal of the model is different. The aim of the model should be that a country can be facilitated to create an overview of the situation regarding MS to identify the strengths and weaknesses (and with that good practices and room for improvements). It is important to clearly state this in your introduction.	Yes
	Introduction	Give an abbreviation of Medication Safety (MS)	Yes
		Long sentences used in the introduction.	Yes, changed the introduction.
		'Minimize health risks originated by the global use of medicine' is the goal and not the definition of MS.	No. This definition of MS according to the GIMS foundation
		Introduction needs to be more 'to the point'. Maybe you can use enumerations?	Made it more to the point. No use of enumerations.
		Explain what MS and PV are. Important to know, when someone needs to answer the questions.	Yes.
		Explain clearly that someone with a broad view on MS will apply the model on a country. Also the applier of the model should add the search strategy to find answers on the critical dynamics.	Yes.
		Explain clearly under explanation: remarks are free comments. If a source supports the rating, this should also be shown (give an example).	Yes.
		Make a chart flow how the process from constructing the model till adapting the model and evaluating the answers takes place.	No. The chart flow must be part of the research project and not the model itself.
		An overview of the abbreviations.	Yes.
		Keep everything as visual as possible. More examples and pictures.	Yes.
		Give the abbreviation of pharmacovigilance (PV).	Yes.
		Annotate which sources have been used for the actors and factors. Note which sources of the WHO. Write down where your key documents originate from. What is the search strategy?	Yes.

	Critical dynamics	Definition is wrong. Critical dynamics are dynamics between different parties in society who have influence on MS. Education is a hygiene factor, therefore it is not necessary to add to the model. The critical dynamics now more focus on the quality of execution of the work by stakeholders and the level of education. However, the questions must be about the dynamics between different parties (for example doctor, pharmacist and patient).	No. Definitions are made at the beginning of the research. If the definitions must be changed, the whole construction of the model need to be changed as well.
		All questions have to be in connection with the patient. For every critical dynamic needs to be asked: 'How is this question in connection with the stakeholder and the safety of the patient?'	Yes.
		Give the sources where you found the KAT formulation.	Yes.
		'This model can measure the extent of a known situation. It provides information of a situations reality and in this case the reality of the situation of the stakeholders.' Formulate this question differently.	Yes.
		Start with explaining how the actors and factors are sorted in the GIMS model in connection with patient and consumer. Explain why alpha actors are the nearest to patient and consumer.	Yes.
		Example: Doctors: A3: is professional co-operation with pharmacists welcomed? Source(s): Koninklijke Nederlandse Maatschappij ter bevordering van de Pharmacie. Handvest van de apotheker. 14 mei 2013. Comment: but then is it welcomed by doctors, or by pharmacists?	Yes. Example is changed from doctor to pharmacist.
		Clearly explain how the model has to be rated. If the stakeholder is asked about his opinion on a critical dynamic, will he or she also rate the question? Or will the applier of the model decide the rating of the critical dynamic? Ask continuously how reliable the answer is.	Yes, added that someone with a broad view about MS will apply the model.
		Some critical dynamics stakeholders will always answer with 'yes'. But the applier of the model needs a reliable answer. For example, if you ask the pharmaceutical wholesaler if they battle counterfeit products, the pharmaceutical wholesaler will always answer this question with 'yes'. Instead of asking the pharmaceutical wholesaler about his opinion, the national medicine regulatory authority can be asked. This gives a higher probability of a honest answer.	No.
		General comments	
		Don't make the model to long. Keep it as short as possible. Five pages is the maximum.	No.

		Can't you apply the KAT model to all actors and factors?	No. It was not possible to apply the KAT formulation to all actors and factors.
		Sometimes the actors look like each other. Does a big difference exists between legislation and politics of the delta factors? Can't you combine them?	No. Politics is about the political awareness on MS and PV. Legislation examines to what extent MS and PV is implemented in the national legislation.
		Create more critical dynamics about the differences between primary and secondary care.	Yes.
		I do understand the critical dynamics, but I do not see how this could provide an outcome towards taking corrective measures or making improvements.	Yes. Explained how the questions will result in an outcome regarding MS in a country.
		This is an international model, so don't look at the questions with a Dutch view. For example: in many countries (also in Europe) many patients do not have a fixed pharmacy.	Yes.
		The applier of the model has to know a lot about all different actors/factors/groups regarding MS. Will the answers not be based too much on your own experiences instead of an objective view? Not everybody knows what is happening behind the scenes of companies and people of stakeholders.	Yes. Added that (scientific) literature has to be searched, before asking opinions of stakeholders. The one filling in the model can not add his/her own opinion.
		It would be a possibility to change the lay-out. First, general critical dynamics about doctors and other actors can be asked, then the interactions between stakeholders. For example: Do doctors and pharmacists perceive each other as equal? Opinion doctor: …. And opinion pharmacist:… This will make the list with critical dynamics shorter and clear. And more honest answers of the stakeholders.	No.
		If you answer a critical dynamic with 'no', some critical dynamics of the same stakeholder are not necessary to be answered. It can be a possibility to refer to other questions. For example: if you answer this question with 'no', please continue with question X.	Yes. If the critical dynamics do not need to be answered, the applier of the model can write under remarks: 'does not apply'.
		When the model will be applied on the Dutch situation, open boxes can be added for: - Formulating different critical dynamics - To add or remove critical dynamics	No.
		The national healthcare institute and healthcare software providers are not part of beta actors, but gamma actors. These stakeholders do not have a large direct influence on patient and consumer. A national	No.

		healthcare institute is mainly responsible for the quality, safety and cost effectiveness.	
		Some countries have influential regulatory bodies. It is preferred to add them not to the gamma, but to the beta actors. National inspectorate has a direct impact on MS. It is preferred to add it to the beta actors.	No.
		Rating	
		Leave 'neutral (3)' out of the model. The applier of the model wants to know directly if a critical dynamic needs improvements or if it is not an issue in your country.	Yes.
		Yes/no questions can be added.	Yes.
		Explain for each Likert point the value. Likert point 1 is 'very less', point 2 is 'slightly less' and 3 is 'neutral' etcetera.	Yes.
		Some critical dynamics are more important than other critical dynamics. Do those questions have to be rated with more preference?	No. During the evaluation of the rating of the critical dynamics, more preference can be given to the answers.
		If all critical dynamics are answered, how are you going to interpretate the answers?	Yes. Added to the introduction.
		The introduction should give more explanation about rating.	Yes.
		The "not at all – very much" rating does not work for all questions.	Yes.
		Remarks are very important. If a critical dynamic is rated, an explanation or source should be added. Otherwise, the critical dynamic has no value. Especially if you want to compare countries with each other.	Yes.
		Actor social networks	
		Family also has a direct influence on patient and consumer. It should not be implemented with culture or religion. I would make this a separate actor.	No, but added family to the actor patient and consumer.
		Add an actor partner/family. Children also have influence, especially when their parents are old and can not take care of themselves.	No, but added it to the actor patient and consumer.
		You can also change it into actor social networks. Firstly, personal networks exist, for example neighbors and relatives. They can have influence on the use of medication. Secondly, social media exists, which has a large influence on the behavior of a patient. An example of a critical dynamic of the actor social networks: If you read something about your medication on social media, do you continue with the use of medication? If your neighbor recommends a drug, do you consider	No, but added it to the actor patient and consumer.

		buying it?	
		Actor hospital	
		What are the influences of the hospital on Medication Safety?	Yes.
		Add something about the electronic data exchange. At the moment it is not optimal between hospital and public pharmacy. This is mostly about patient files and process data.	Yes.
		How much discharge and admission medication?	No. No value for MS.
		How much trust does the patient have in the Medication Safety in the hospital?	Yes, but a general question it added to actors doctor and pharmacist.
		Actor patient and consumer	
		Add the actor patient. I think it is quite extensive and most important stakeholders are reviewed, but I miss actually the patients behaviour. It is mentioned via the cultural and religious aspects and also via the patient organizations, but the individual patients role and his/her social network has an enormous influence in my opinion and is undervalued. How do patients look for information about medicines: internet, social media, neighbours, family and friends. These are the most direct actors in the patients network. Not (anymore) the HCP.	Yes.
		It is important to know what the interests are of patients and consumers.	Yes.
		Critical dynamics for the actor doctor: How well does the patient follow your instructions? Critical dynamic for pharmacist: How well are the instructions followed which are given to the patient by the staff of the public pharmacy?	Yes.
		Are the choices about the medication therapy made by the patient conscious or unconscious choices?	Yes.
		Examine the perception and behavior of patients regarding MS in the literature.	Yes.
		Examine your critical dynamics by a panel of patients and patient organizations.	No.
		In the case of an ADE: does the patient stop using the medication? If the patient suffers from side effects, does he contact (or share with) the HCP or discusses which steps have to be taken?	Yes.
		What aspect is most influential for the patient? Make them choose between stakeholders, do not forget health care insurance.	Yes.
		How would the actors help the patients and consumers to optimize the	No. This will be the outcome and is the aim of the

		use of medication? This can be an open question, or give the patient several choices.	model.
		How do patients experience to be admissioned in the hospital and receive new medication? Also ask this critical dynamic for discharge medication. What is the quality of the conversations between HCP in the hospital and patient?	Yes. Quality of conversations between HCP and patient is added. There is no value to add admission medication in the hospital.
		Formulating critical dynamics	
		Some critical dynamics are suggestive and need to be formulated differently.	Yes.
		It is interesting to see how stakeholders describe themselves on their websites and to the public about how they 'really' work. Examine well how the stakeholders describe themselves on their websites how they function and what their view is of the patient.	Yes.
		Sometimes the structure of the sentences and the language is of inadequate quality.	Yes.
		Keep the critical dynamics as simple as possible. Some critical dynamics are too difficult to answer. You can refer to another document or a box with explanation in which is explained why you have asked this critical dynamic.	Yes. Additional information about the content of the critical dynamics is added.
		Create more open questions to gain more information as effective as possible.	No. We decided to use the Likert scale for each critical dynamic. Each critical dynamic will have a value. Open questions are difficult to value.
GIMS Model	*Alpha actors*	General comments	
		What does KAT mean? Explain this in the introduction of the model.	Yes.
		Nurses: No 'Tools' for the actor Nurse? What about dispensing tools. For example (electronic) registration of administration? Try to apply the KAT model for this actor.	Yes.
		Pharmacists: Do pharmacists perceive their relationship with doctors as effective?	Yes.
		Doctors and pharmacists: the tools which pharmacists use are different from doctors (also different storage systems). How is the communication when the tools differ from each other. How are the triangular relationships between doctor, pharmacist and patient?	Yes.
		Doctor: Handwriting.	Yes.

		Nurse: How well is the collaboration with the doctor?	Yes.
		Retailer: Read documents about public private strategy and from the pharmaceutical industry. Also create critical dynamics about the conditions in a country of selling medication. For example, OTC medication can only be sold in pharmacies in Belgium .	Yes.
		Actors	
		Actor 1: are medical students trained in Medication Safety(MS)/pharmacovigilance (PV)?	Yes.
		Actor 2: to what extent is MS / PV part of Permanent Education	Yes.
		Actor 2: What does '*' mean? Better explanation at the end of your model.	Yes. An attachment with additional information is added to the model.
		Actor 3: what is the average actual knowledge about PV/MS? Comment: Difficult question. It is recommended to ask if doctors receive enough trainings about MS and PV to apply in the work field. Also it is a subjective question and difficult to rate.	Yes. Changed the question.
		Actor 4: to what extent is PV/MS considered to be a relevant theme within the medical world? Comment: What is the "medical world"?	No. No explanation about the medical world is provided. It is a general term and not necessary to add an explanation.
		Actor 5: are doctors lawfully liable for (the quality of) their prescriptions? Comment: Is liable an attitude?	No.
		Actor 8: experience/perceive doctors the pharmacists as equal? Comment: why equal, why not as an expert in medicines? Also doctors and pharmacists are not equal, because they both have a different role regarding MS. A better question would be: To what extent perceives the doctor the pharmacist as expert in medication.	Yes. Changed the question into: To what extent accept doctors pharmacists as co-manager in medication therapy?
		Actor 9: is there a warm/functional relationship with governmental agencies? Comment: I suspect there is a hypothesis behind this question? Wouldn't everyone say 'yes' to this questions? This is better: How is the relationship with governmental relationship? Also 'warm' needs to be changed in 'cooperates'.	No. Removed the question. Asked about collaboration with stakeholders of the actor HCP organizations.
		Actor 10: is there a system of electronic patient-files? Comment: patient-files has to be patient-records.	Yes.
		Actor 12: are there electronic formularies available? Comment: What is the difference with T2: are there electronic	Yes. Critical dynamics about therapeutic guidelines are removed.

		therapeutic guidelines available? Do electronic patient files exist or are they recorded in a different way (on paper). That has to be the first question, afterwards you can ask about the electronic patient records.	
		Actor 13: to what extent is an e-prescribing tool in use which (can) take into individual account; dosage, interactions, contra-indications, allergies? Comment: Change this question into two questions. First question: to what extent is an e-prescribing tool in use? Second question: to what extent are dosage, interactions, contra-indications, allergies taking into individual account? Maybe each aspect can be rated individually.	Yes.
		Actor 16: what is the average actual knowledge about PV/MS? Comment: Broad question. Probably you will only hear personal experiences.	No.
		Actor 17: is PV/MS considered to be a relevant theme within the pharmaceutical ~~world~~ field?	Yes.
		Actor 21: experience/perceive pharmacists themselves as equal to doctors? Comment: Why equal? Concerning MS /PV, medicines in general?	Yes. Changed the critical dynamic into: Is professional cooperation with doctors welcomed?
		Actor 22: is there a warm/functional relationship with governmental agencies? Comment: As above, do you not think everyone will say yes to the questions A1-A6?	No. Asked about collaboration with stakeholders with actor HCP organizations.
		Actor 23: what is the quality of the system of electronic patient-files? Comment: First question has to be: Is there a system?	Yes. First asked if the system is electronic.
		Actor 26: are I~~C~~T tools in use to act pro-actively? Comment: I do not know how many countries will understand this question.	Yes.
		Actor 34: is additional training required for retailers to sell OTC medicines? Comment: Additional to what?	Yes. Changed the sentence.
		Actor 35: is there a (I~~C~~T) tool which guides the retailer to a diagnosis and product?	Yes.
		Actor 36: Are there strict market authorisation rules for OTC products? Comment: In my opinion this is part of the factor legislation. And add policies.	Yes. Removed it from the actor Retailer and added this critical dynamic to the actor National Medicines Regulatory Body.

		Actor 37: Are they enforced vigoursly? Comment: How?	Yes. Removed the critical dynamic.
	Beta actors	General comments	
		Numbering is not correct.	Yes.
		HCP organizations: To what extent do pharmacists and doctors collaborate with each other?	Yes. Asked if they collaborate with each other.
		Pharmacovigilance organizations: Should you not add something about reporting side-effects? To what extent is it obligatory and stimulated? Is there an open culture to report medication errors? Is all information reported back to the HCPs?	Yes.
		Pharmaceutical wholesale: What is the commercial influence of the pharmaceutical wholesale in the country?	No. Commercial influence of medication is asked at the actor 'Media'.
		National healthcare institutes: I understand you have to make choices regarding the questions. However, at the moment they seem sometimes randomly chosen. How do you determine if the most important aspects are included? It should be based on literature and the panel, but that is also just a group of people with an opinion.	Yes.
		Actors	
		Actor 3: Are they well respected? Comment: Difficult question. Formulate it differently.	Yes. Critical dynamic removed.
		Actor 4: What is the quality of the guidelines concerning PV/MS? Comment: Can not be rated with not at all to very much. Difficult question. Would separate the question into two questions. First question: Do they have guidelines? Second questions: To what extent do they follow the guidelines?	Yes.
		Actor 5: Does an organisation of pharmaceutical professionals exist? Comment: This is a yes –no question, not applicable on the rating you provided.	Yes.
		Actor 6: If so, is PV/MS an issue? Comment: Subjective question.	Yes. Changed the question into: Are MS and PV one of its focus points?
		Actor 8: What is the quality of the guidelines concerning PV/MS? Comment: Difficult to rate with 'not at all' to 'very much'. You can better rate with 'low' and 'high'.	No.
		Actor 9: Does a national PV/MS organisation exist? Comment: Is a yes-no question. What would be an example?	Yes. Changed the critical dynamic into a yes-no question. Example is not added.

		Actor 12: Do they provide essential and up-to-date medicine information and therapeutic guidelines? Comment: Or be part of the platforms which develop and implement these guidelines and information.	No, but changed the question into: Does it have the authority to take further steps in the evaluation of ADRs and ADEs?
		Actor 14: Five stars are added to this critical dynamic, but no explanation.	Yes. Additional information added to the attachment of the model.
		Actor 17: Is the total wholesale market just existing of a few entities? Comment: Ambiguous question. I do not understand the question.	No. Additional information also not added to the attachment of the model.
		Actor 18: Is Good Distribution Practice the standard? Comment: Formulate the critical dynamic differently. Is GDP legally defined? If yes, to what extent is it obliged to abide these laws? Unclear. There could be GDP, but are they enforced?	No.
		Actor 19: Are counterfeit products battled against? Comment: Read Falsified Medicines Directive for more information. Depending on whom you ask, everyone will say yes (even in South Sudan). Add substandard products. Ask this question to national regulatory authorities. And examine well how to evaluate the answer of this critical dynamic.	Yes.
		Actor 20: Are there suppliers for medical-/pharmaceutical ICT products/services, which are also focussed at Medication Safety, in your country? Comment: If so, to which extent are these ICT products and services actually used?	Yes. Removed the critical dynamic.
		Actor 24: If so, is the availability and quality of Pharmaceutical Patient Care used as an Unique Selling Point towards the general public, by these formulas? Comment: Why is it interesting whether it is used as an USP? I would be more interested in their role of developing / maintaining and executing the guidelines, quality concerning MS/PV.	Yes. Removed the critical dynamic.
	Gamma actors	General comments	
		Medicines Regulatory Authority: What is the link with MS/PV?	Yes. Added market authorization and risk assessment of medicines.
		Ministry of Health: I think everybody will answer all these questions with yes/5.	No.

		Pharma industry: What is the commercial influence of the stakeholder in the country? If large pharmaceutical companies have more influences then small pharmaceutical companies, this can result in a monopoly of pharmaceutical companies in the country. These aspects can have influence on MS and corruption.	No.
		Actors	
		Actor 1: Does such a Medicines Regulatory Authority exist in your country? Comment: Do they have an updated national medicines list? And what are the key organization in developing countries?	No. To specific.
		Actor 3: Is it functionally liaisoned with entities like EMA and FDA? Comment: Only EMA and FDA? Explain why you are asking this question.	No.
		Actor 4: Is it independent? Comment: Independent from what?	Yes. Added to the additional information in the attachment of the model.
		Actor 6: Are they working on 'Universal Health Coverage' plans? Comment: What is the link with MS and PV?	Yes. Removed the critical dynamic.
		Actor 7: Do they have enforcement power? Comment: Sentence is unclear. Change the sentence.	Yes. Changed the critical dynamic into: Does it have the right and authority to intervene?
		Actor 8 and 9: Does one need a license to work as medical/pharmaceutical professional? Comment: This is a 'yes/no' question. Can not be ranked with Likert 1-5.	Yes. Added to the model: Does it have a license register system in which all licenses are stored of all HCPs of the country?
		Actor 12: Is PV/MS a focus area for scientific research? Comment: Would also be interesting whether they teach their students about the curricula of medical or pharmaceutical professions? Research about practice and policy?	No.
		Actor 16: Is it an influential organisation towards governmental agencies? Comment: Or directly towards the pharmaceutical industry?	No. But added: Do they collaborate with the government?
		Actor 19: How much influence do international entities (like WHO, FIP) have on your countries national policy and legislation development? Comment: Is this influence good or bad? If the WHO has much influence, this can also show that a country does not have a structured healthcare. This is mostly the case in developing countries. Does the WHO have influence in the decision making on law and regulations of the Dutch healthcare system?	Yes.

	Delta factors	General comments	
		Culture: Are these the most important culture questions? Health literacy of the patient is also important to add.	Yes. Added at the actor patient.
		Politics: To what extent does politics have an influence on the collaboration between HCPs?	No.
		Religion: Which medicines can the patient take for his/her religion?	No.
		Economics: Also the availability and reliability of medicines is important. How much medication is illegal?	Yes. Added to the actor wholesale and pharmaceutical companies.
		What is the amount of trained staff selling medication?	Yes.
		Legislation concerning medicines and healthcare: WHO guidelines should also be mentioned and to what extent countries abide these guidelines.	No.
		Actors	
		Factor 1: Is the actual legislation concerning medicines and healthcare considered to be sufficient in order to optimally protect against risks from using medicines? Comment: This is a difficult question to answer.	Yes. Changed the critical dynamic.
		Factor 2: Would you consider your country to be highly developed in ICT-support technology?	Yes.
		Factor 3: Technology is equally available throughout the country? Comment: Sentence is not clear. Formulate the question differently and use examples.	Yes. Removed the critical dynamic.
		Factor 5: ICT-tools for dispensing are widely used? Comment: Is the question not also asked in the alpha actors?	Yes. Already asked at alpha actors.
		Factor 6: Sensitivity about the privacy-aspects of big ICT databases in healthcare is very low? Comment Is this question about culture or ICT?	Yes. Removed the critical dynamic.
		Factor 8: Does the dominant culture in your society experiences the personal use of medicines as something LESS positive/favourable? In other words is the use of medications in a negative perspective in your country? Comment: It is better to separate these two questions into two critical dynamics.	Yes. Changed the critical dynamic.
		Factor 12: Are patients bound to/used to go to one specific pharmacy all of the time? Comment: First ask if there is a choice. In the Netherlands we have a	No.

		choice to go to one specific pharmacies, and the patient are loyal. This is not the case in other EU countries, for example Belgium, Spain, Portugal or UK.	
		Factor 15: Use private pharmacies Pharmaceutical Patient Care as an 'USP' in their competition? Unique selling point? Comment: Do you mean: do private pharmacies use Pharmaceutical Patient Care as an USP for competition in the (local) pharmacy market?	Yes. Removed the critical dynamic.
		Factor 22: Are advertisements for OTC medicines, which are directly focussed at the consumers, influential towards the public? Comment: Difficult question to answer.	No.