

Aspects influencing patients' preferences for the management of drug–drug interactions: A focus group study



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ABSTRACT

Objective: The management of drug–drug interactions (DDIs) involves a complex risk–benefit assessment, in which patients' preferences should be taken into account. The aim of this study was to examine the aspects influencing patients' preferences with regard to DDI management options.

Methods: A qualitative study consisting of five focus groups with patients chronically using cardiovascular drugs was conducted. Key questions concerned preferences regarding DDI management options for a provided fictitious DDI. Thematic analysis of the verbatim transcripts was performed.

Results: Despite their limited knowledge with respect to DDIs, patients easily chose a management option for the presented DDI. When additional information was provided, preferences showed to be fluid. Ten interdependent aspects influencing preferences were derived from patients' argumentations: risk perception, fear, acceptance of uncertainty, openness to change, willingness to take risk, trust in health care professional, financial & practical burdens, health condition, experience, and knowledge & assumptions.

Conclusion: Patients' preferences regarding DDI management options were often determined by provided information. Preferences were dependent on an interplay of diverse aspects.

Practice implications: Tailored provision of information and individualized counseling is needed for active patient involvement in DDI decision making.

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1. Introduction

Clinical decision making on drug–drug interactions (DDIs) is complex. Health care professionals use DDI management guidelines which recommend one or more management options for every DDI. These options can include, for example, additional monitoring, switch to an alternative drug or dose adjustment. In daily practice, the choice between DDI management options is usually made by health care professionals with limited patient involvement.

DDI management recommendations are generally developed in the tradition of evidence based medicine, with a focus on risk–benefit assessments [1]. Although it has been acknowledged that

in essence evidence based medicine should also include the patient's perspective, in DDIs this is not often the case, yet [2–4]. Frameworks like Grading of Recommendations Assessment, Development and Evaluation (GRADE) can guide the development and presentation of clinical guidelines [5,6], including DDI management recommendations [7,8]. The assessment in the GRADE framework includes not only a weighing of clinical risks and benefits, but also the acceptability and feasibility of the intervention for the patient. These last two criteria may influence the strength of a recommendation, which in the GRADE framework is classified as weak (conditional) or strong.

In case of weak recommendations, the importance of shared decision making (SDM) is emphasized, as patient preferences may become a decisive factor [9]. Weak recommendations are not unusual in case of DDIs. Whereas this suggests that patients should be involved in decision making, patients seem to be rarely involved in DDI management in daily practice, neither by the physician nor by the pharmacist [10]. A potential explanation could be the complexity of DDI management, with at least two involved

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therapies and several management options with all their advantages and disadvantages. A second explanation could be found in the clinical decision support systems, which support health care professionals in the detection and clinical management of DDIs, but in which the patient perspective is barely represented [11,12].

For incorporating the patient's perspective in decision making on the individual level, awareness of potential preferences is needed [13,14]. Having insight in the reasoning and values behind the preferences could be helpful for health care professionals to understand and interpret them. Knowledge in this field is conspicuously absent. Therefore, the aim of this study is to examine the aspects influencing patients' preferences regarding DDI management options.

2. Methods

2.1. Study type

A qualitative study design was chosen for this explorative study. We used focus groups to stimulate patients to share their thoughts on the management of drug–drug interactions, as they might not be used to talking about that topic.

2.2. Patient selection and recruitment

Focus groups were conducted in five community pharmacies on different locations in the Netherlands.

Patients were eligible when they were 18–85 years old, Dutch speaking, and healthy enough to participate in a focus group meeting in the pharmacy (according to the clinical judgement of the pharmacist). Moreover, patients had to be experienced drug users, who had used cardiovascular drugs for over one year. In this patient group the occurrence of DDIs is frequent [15]. In each pharmacy patients with a specific profile of cardiovascular medication were selected to increase group homogeneity in order to enhance interaction among participants. Selections were made based on the pharmacy electronic patient records, including drug dispensing history and coded chronic conditions. The five selected groups were: 1) patients with heart failure, using a loop diuretic; 2) patients with diabetes, using a renin-angiotensin system inhibitor; 3) patients using a platelet aggregation inhibitor, without heart failure or diabetes; 4) patients using lipid lowering drugs, without heart failure, diabetes, or use of antithrombotic drugs; 5) patients with hypertension using antihypertensive drugs, without heart failure, diabetes, or use of antithrombotic drugs.

Per pharmacy, 60 randomly selected patients meeting the inclusion criteria were invited by letter. After one week patients were contacted by phone until at least eight patients had agreed to participate (additional patients who signed up afterwards were accepted until a maximum of ten per focus group). These patients received a confirmation letter, a short questionnaire on demographics, and an informed consent form. Patients received a reminder phone call one day before the meeting. After participating, patients received a 20 euro gift voucher.

2.3. Topic guide development

A topic guide was developed based on the research question. The first focus group meeting was used as pilot, leading to the final topic guide (Fig. 1). In the topic guide, several questions related to a fictitious DDI example with realistic DDI management options which covered all common aspects of DDI management in one example [16,17]. The options included risks, benefits and practical implications [5,6]. A DDI example was used to concretize the topic: because the occurrence of drug–drug interactions is generally

acute, there was no possibility to have a discussion based on the patients' current DDI experience and patients are often not aware of the occurrence of a DDI.

2.4. Conduction of focus groups

The focus groups (one in the morning, four after working hours) were conducted in the community pharmacies and lasted two hours. The focus groups were run by three researchers/pharmacists: a moderator who had a training on focus group moderation (MH), an observer (making field notes), and a technical leader (at least one of the latter two was experienced in focus groups, being AF or MB). The participants did not know the moderator; she was introduced as a researcher in drug–drug interactions, interested in patients' opinions on DDI management in the context of patient centered care. The questions were asked following the topic guide. The case description (Fig. 1) was provided in writing to the participants, with oral explanation. The additional information was provided orally, supported by flip chart notes.

2.5. Data analysis

After every focus group the attending researchers discussed the results. Focus groups were audiotaped and transcribed ad verbatim. The analysis was performed in NVivo qualitative data analysis software (QSR International Pty Ltd. Version 11, 2015). Inductive thematic analysis with open codes was applied [18,19]. Thus a rich thematic description of the data was reached. This approach is suitable for situations where the participants' views of the topic are unknown. The method consists of six phases: familiarizing with the data; generating initial codes; searching for themes; reviewing themes; defining and naming themes; producing the report [18].

One focus group was independently coded by MH and AF, and consensus on the coding scheme was reached. The other focus groups were coded by MH, and in case of doubt discussed with AF. Codes were thematically clustered into aspects influencing preferences. Applicability of these aspects to the coded fragments was continuously verified. Determined aspects and interpretation of findings were repeatedly discussed in the research team and verified with the data until consensus was reached. Reporting was conducted taking into account the Consolidated criteria for reporting qualitative research (COREQ) [20].

3. Results

3.1. Participants and focus groups

Five focus groups with 5, 8, 10, 7 and 8 participants were conducted. Because after the first pilot focus group no substantial changes in the topic guide were needed, this focus group was included in the analysis. Data saturation was likely to be reached as no new aspects were derived from the last focus group. Sixteen participants were male and 22 female, their age ranged from 49 to 84. The educational level was diverse: 25 participants were low educated, 8 medium, and 5 high. Thirty seven of 38 participants were native Dutch. For patient and pharmacy characteristics, see Appendix A in supplementary material. All participants expressed their opinion on the key questions from the topic guide.

3.2. Patients' preferences and decision making

The participants had little knowledge about the subject of DDIs. When confronted with the example, patients intuitively decided on their preference for a management option. They expressed hardly any need for additional information preceding their

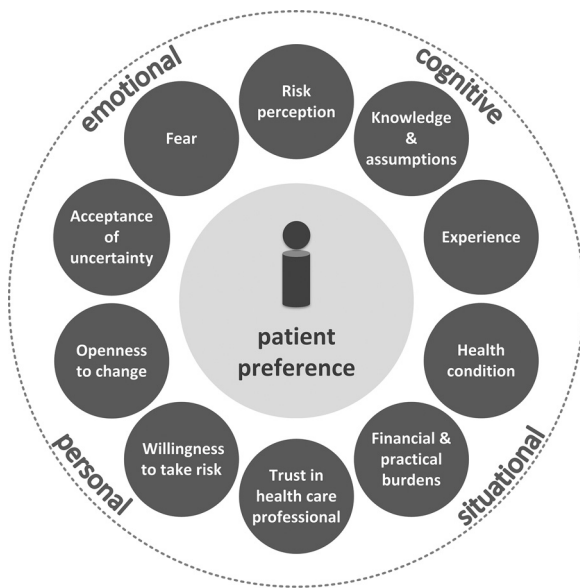
Introduction & transition (engagement questions)		
<ul style="list-style-type: none"> - Why do you join this meeting? - Have you ever experienced a situation in which two medications did not go well together (or other problems with medications), and how was it managed? 		
Case description		
<p>Imagine: you suffer from pneumonia. Your doctor suggests starting an antibiotic for 10 days. The combination of the antibiotic and your cardiovascular drug can cause muscle pain. In rare cases even serious muscle problems can occur (with hospitalization and risk of permanent kidney damage).</p> <p>What to do? (management options)</p> <ul style="list-style-type: none"> A. No action. Use the antibiotic and your cardiovascular drug concurrently B. Switch to another cardiovascular drug C. Switch to a second choice antibiotic D. Use the antibiotic and your cardiovascular drug concurrently + two blood tests to detect emerging muscle problems 		
Key (exploration) questions		
<ul style="list-style-type: none"> - In this example: which management option do you prefer and why? - Would you like to have more information about the management options? Which one(s)? - Considering the information on risks and benefits: <ul style="list-style-type: none"> o Which risks do you consider to be frequent? o Which risks do you consider to be serious? - Which should, in your opinion, be the role of the health care professional and you in the management of drug-drug interactions? 		
Additional information (provided stepwise and written down on flipchart)		
Characteristics of management options	Option	
Risk of serious muscle problems with permanent muscle damage	3 out of 10.000	A
	1 out of 10.000	B, C, D
Chance of recovery from pneumonia without hospitalization	95 out of 100	A, B, D
	90 out of 100	C
Switch to another cardiovascular drug	Yes	B
	No	A, C, D
Blood sampling	Yes	D
	No	A, B, C
Moderate muscle pain	10 out of 100	A, D
	5 out of 100	B, C
Nonrefundable costs (to be paid by patient)	0 euro	A, B, C
	25 euro once	D

Fig. 1. Focus group topic guide and case description.

decision. Preferences, however, were fluid. After additional information was actively provided (Fig. 1), many patients switched (repeatedly) to another option. In most cases, provision of the actual risk estimates increased patients' willingness to take the risk; however, all kinds of switches were observed. Moreover, a few patients mentioned that their current preference could be different from the one in reality, because of the hypothetical nature of the example.

3.3. Aspects behind patients' preferences

Out of patients' rationales for their preferences, ten aspects were derived. The aspects were in the cognitive, emotional, personal and situational domain (Fig. 2). The ten aspects were gradual concepts: they could be either low or high, positive or negative. The expressed preference was dependent on a complex interplay between the aspects. The aspects could apply to all



Aspects are described in detail in paragraph 3.3

Fig. 2. Aspects of patients' preferences regarding drug-drug interaction management options.

characteristics of the management options (e.g. fear could – to a different extent – apply to pneumonia, to muscle damage, or to replacement of current medication). Moreover, there was high mutual interdependency between the aspects, e.g. a bad experience could lead to fear, which could lead to unwillingness to take risk, etcetera. The interdependency is reflected in the citations below.

3.3.1. Risk perception

The analysis showed that the risk perception was a major aspect in the patients' preference construction. The perception whether presented risks were high differed between participants; both seriousness and incidence and in some cases duration influenced the perception of the risk magnitude. The patients expressed three types of considerations which contributed to the perceived seriousness of a risk: whether you could die from it, whether it could cause permanent (organ) damage, and whether the potential effect was short lasting or long lasting:

If you have muscle pain for only one week, and when it's the only option, you take the risk. But when muscle pain becomes chronic, it is a whole different story. [participant 5, group 1]

I assume you don't die from muscle problems, but you can die from pneumonia. [participant 2, group 1]

Patients generally perceived the risk of 1 or 3 out of 10,000 as very small; the difference between them mattered to some, but not to all patients. A likelihood that pneumonia is cured of more than 90% was generally perceived as high. Whether the difference between 90% and 95% mattered was variably perceived, but often the difference was irrelevant to the participants.

I think 3 out of 10,000 is not a substantial risk. It leaves a lot of healthy people. It wouldn't keep me awake at night. [participant 2, group 5]

I prefer the option with another [second choice] antibiotic; 5% difference [in curation rate] is negligible. [participant 4, group 1]

To reduce the abstractness of risks, some participants compared them with rare events from other life areas (for example lotteries and earthquakes). The analysis showed that patients often used a binary approach in the interpretation of risks: they either focused

on the ever-present possibility of being affected, or they focused on the extreme unlikelihood of being affected.

It is said an earthquake happens only once in 10,000 years – it could happen tomorrow [but that would be very coincidental]. [participant 7, group 3]

It could be my neighbor and me [who are affected by a risk of 3 out of 10,000]. [participant 2, group 1]

3.3.2. Fear

The analysis showed that fear concerned reoccurrence of events patients had already experienced as well as the occurrence of new health problems (the participants especially expressed fear with regard to the permanent renal damage and potentially fatal pneumonia from the presented example). Fear increased by information about potential risks.

I'm scared. Eleven years ago, I got a mechanical heart valve, and I still live in fear. [participant 6, group 2]

It would scare me off that it can cause permanent kidney failure. [participant 3, group 5]

3.3.3. Acceptance of uncertainty

In the analysis it was seen that patients considered uncertainty about outcomes generally as unpleasant. Management options were assessed for the degree of certainty and whether the participants felt in control. Having certainty, or being in control, was an important consideration for preferring blood testing. Patients perceived mild adverse effects as more acceptable when the origin was known, thus providing certainty that they were not threatening. Opposite the wish for control and reassurance patients expressed that they realized that absolute certainty does not exist in life.

I prefer to be monitored. Then I am sure that things are going well. I think . . . I hope . . . [participant 1, group 4]

You never know which choice is best; when you are ill, you are at the mercy of the gods [participant 7, group 2]

There's no guarantee that you won't be affected. [participant 5, group 5]

3.3.4. Openness to change

One of the management options included change of current medication. Many participants expressed strong attachment to their current medication, because they wanted to maintain the current stable situation. A minority of patients were open to change, but only when it was advised by their trusted physician. The data suggested that openness for change was either related to the perception that the cardiovascular drug was not that essential, or by the perception that the importance of optimal treatment of the pneumonia could outweigh the initial resistance to the switch of the cardiovascular medicine.

I would be reluctant to switch the cardiovascular medicines. . . . it's a balanced combination – you should just keep your hands off. [participant 2, group 1]

The heart is doing well by now. So, let them adapt the antibiotic. You are already used to the cardiovascular medicine and when you change it, other complications may occur. [participant 4, group 2]

When it is the cardiologist's advice, I wouldn't mind to switch to another cardiovascular drug, [participant 6, group 2].

3.3.5. Willingness to take risk

The analysis showed that patients either accepted risks as an inseparable part of life, or wanted to eliminate any potential risk because of the importance of health.

Just try the combination – I'll be the guinea pig. [participant 3, group 1]

If you can potentially prevent something you should do so. Otherwise you play with people's health [participant 1, group 1]

3.3.6. Trust in health care professional

Patients would take certain management options only under consideration when they were advised by their prescriber. Furthermore, the analysis showed that the mere fact that a health care professional mentioned a certain risk (e.g. the DDI), was for some patients reason not to take a risk, even when patients perceived this risk as negligible. Especially the oldest participants expressed high trust in their physician and emphasized the importance of a trustful relationship.

It is explicitly told that the situation entails a risk. That triggers me and gets stuck in my mind. [participant 3, group 5]

I won't mind [changing my lipid lowering drugs] when it is my cardiologist's advice. I trust him, and that's important for me [participant 6 group 2]

3.3.7. Financial & practical burdens

Most patients expressed the opinion that health was too important to save costs on monitoring like blood testing. The participants did, however, assume that some people would decline blood testing when they had to pay the costs themselves. Patients perceived venipuncture itself generally not as a burden: most participants were used to it. The analysis showed that practical and financial burdens were a minor aspect in patients' reasoning.

Buckets of blood have already been sampled. [participant 5, group 1]

I won't mind to pay 25 euros, I prefer to eliminate all risks [participant 3 group 5]

3.3.8. Health condition

Current health condition influenced patients' preferences. In general, the analysis showed that suboptimal health led to increased risk averseness, in order to prevent further deterioration. Participants took into account the seriousness of the indication of the cardiovascular medicine (e.g. primary or secondary prevention). With regard to the option to replace the cardiovascular medicine, patients using it as secondary prevention seemed to be more reluctant.

When your physical situation is less than optimal, you want to prevent any further deterioration. [participant 3 group 4].

I always have muscle pain, so it doesn't matter [whether the risk of muscle pain is 5% or 10%]. [participant 2, group 3]

3.3.9. Experience

In the analysis, former experiences – either related to health care or not – were shown to be a major part of the argumentation for current preferences. Patients considered both positive and negative experiences as a forecast of future outcomes. Not only own experiences were taken into account, but also experiences of relatives and acquaintances.

In the past, I used some other medicines and I had a venipuncture. That will have had a reason. So I prefer the option with blood testing. [participant 7, group 2]

Once, I have experienced serious side effects. I just don't want that ever again. [participant 6, group 5]

My father-in-law suffered from pneumonia. He was in his bed, wheezing all the time, while using antibiotics. It took an entire week or even longer before the wheezing reduced. [participant 3, group 3]

3.3.10. Knowledge and assumptions

Participants' knowledge about health and medicines influenced their preferences. The knowledge which patients introduced in the discussion included both correct information and incorrect assumptions. Some patients stuck to incorrect assumptions even when information falsifying their assumptions was presented.

[after presentation of the different curation rates] *There isn't any difference between this and that antibiotic, is there? I think an antibiotic is just antibiotic.* [participant 1, group 3]

When you are diagnosed with pneumonia, I think that your doctor wants to see you within a few days. When you tell him that you have serious muscle pain, he has all information he needs. [participant 8, group 2]

For most drugs, the chance of adverse events is higher than 3 out of 10,000. [participant 2, group 4]

4. Discussion and conclusion

4.1. Discussion

DDI management is a specialist field which is unfamiliar to most patients. Patients in our study could easily express their intuitive preferences for DDI management options; however, these preferences were fluid. Preferences were influenced by ten interdependent aspects from the cognitive, emotional, situational and personal domain. In thinking on risk, the main considerations expressed were the seriousness, incidence and duration of the risk and whether to avoid any risk or to accept risks because of its inevitability.

It is well known that the understanding of risk measures is complicated and subject to many biases. Framing of outcomes affects choices. However, effects seem to vary across situations and to depend on the exact presentation of information [21]. In our study, serious risks described in terms of loss were often perceived as relevant for the assessment (even if the risk was small, e.g. muscle damage in 1 or 3 out of 10,000). Curation rates of 90% and 95% were quite often perceived as comparable and therefore less relevant for the overall assessment. More in general, outcomes that give negative feelings – like health problems – lead to high risk estimates [22]. In addition, having to choose in health issues can cause stress, and hasty, irrational choices can be a way to cope with the decisional conflict [22].

We showed that patients' preferences for DDI management were dependent on a broad range of aspects, related to thinking (cognitive), feeling (emotional), character (personal) and current situation (situational). In general terms, the aspects we found were consistent with the aspects and domains which have been shown to be relevant in other investigations. This includes the combination of both cognitive and emotional aspects [22–24], and the wide range of aspects involved in risk perception [25]. Although several frameworks and models in the field of health decision making, preference construction and risk taking have been published, none of these models focuses on the combination which was the scope of our investigation. Available models on preference construction with regard to risk often originate from fields like behavioral economics rather than from health care [26]. Models related to patient decision making generally cover the complete decision making process, while we focused on one of the steps: the 'preference construction' [22–24]. Frameworks for the development of clinical recommendation like GRADE focus on factors in the risk-benefit assessment rather than the underlying rationale [5,6]. Models for health behavior have a focus on motivation and capability to undertake action [25,27,28]. In models related to SDM, process and knowledge are generally central factors, rather than

aspects behind patients' preferences [29–32]. For more details, see Appendix B in supplementary material.

In situations with weak evidence (which is often the case in DDI management), guidelines advice SDM [9]. We observed that patients often did not ask for information, but that their preferences changed when information was actively provided. To enable and foster SDM, provision of information to patients is essential. This is challenging, as a neutral presentation of information about risks and benefits without any framing is hardly possible [33]. Moreover, research showed that people generally do not realize to what extent their decisions are based on (in)correct assumptions [34]. Incorrect assumptions were common in patients' argumentations in our study.

SDM includes much more than provision of information. Health care professionals should be aware of patients' preferences, goals and values. Our study showed that the range of aspects influencing preferences is broad. It will depend both on the patient and the present choice which aspects are decisive. SDM can be expected to be most appropriate for DDIs with several equivalent management options [4,14]. For other drug therapy related problems, similar considerations can be applied.

Our study has strengths and limitations. A strength is that we presented an integrated situation involving both the DDI itself and its management options. Therefore, advantages and disadvantages of the overall situation were assessed, consistent with the multifactorial complexity of the management of drug therapy related problems in daily practice.

A limitation is that the focus groups were about a hypothetical example. When patients are confronted with a DDI in real-life, their preference could be different. In addition, we used only one example of a DDI. Moreover, only patients chronically using cardiovascular medicines who were able to come to the pharmacy participated in the focus groups and therefore our results concern this patient group. The majority of participants were low educated, but this is consistent with the educational level of older cardiovascular patients in general. In other patient groups (e.g., homebound frail elderly, users of other types of drugs) or in real-life situations, patients can have other preferences than expressed during the focus groups. We expect that the general aspects which we identified will also be relevant to other patients groups and in other situations; however, it is possible that additional underlying aspects will exist. Finally, our study was an explorative investigation. For validation of the resulting aspects, additional research in other patient groups and real life situations is needed.

4.2. Conclusion

Patients' preferences regarding DDI management options were determined by provided information and therefore fluid. The preferences were dependent on the interplay of ten aspects, from the cognitive, emotional, personal and situational domain. The interdependency between the aspects was high, and many of them were related to risk assessment. Tailored provision of information and individualized counseling is needed for active patient involvement in DDI decision making.

4.3. Practice implications

In our study, patients did not ask for additional information themselves. However, their preferences changed when more information was actively provided. Therefore, health care professionals should invest in informing patients about drug therapy related problems in a way and extent appropriate for the individual patient. Health care professionals should realize that they may unintentionally influence patients' preferences when providing

information about risks and benefits. Moreover, they should be aware that in addition to cognitive aspects, both emotional and personal aspects are important. Therefore, health care professionals need excellent communication skills to assess patients' preferences and values and to integrate them in the decision making process. Trustful relationships between physician, pharmacist and patient are essential. Moreover, tools like clinical decision support systems should pay attention to the patient perspective in order to support health care professionals [13].

Contributors

All authors contributed to the study design, the study protocol, the analysis and the manuscript. All authors approved the final manuscript.

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Ethics

The Institutional Review Board of the Division of Pharmacoeconomics and Clinical Pharmacology of the Utrecht University approved the investigation and the work was conducted in compliance with its requirements. All participating patients signed informed consent and all data were anonymized during transcription. Formal testing of the study protocol by a Medical Ethics Committee was not necessary, as the study did not fall within the scope of the Dutch Act on Medical Research Involving Human Subjects.

I confirm all patient/personal identifiers have been removed or disguised so the patient/person(s) described are not identifiable and cannot be identified through the details of the story.

Competing interests

The authors have no conflicts of interest that are directly relevant to the content of this study.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.pec.2017.11.010>.

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