The value of tailored communication in promoting medication intake behavior

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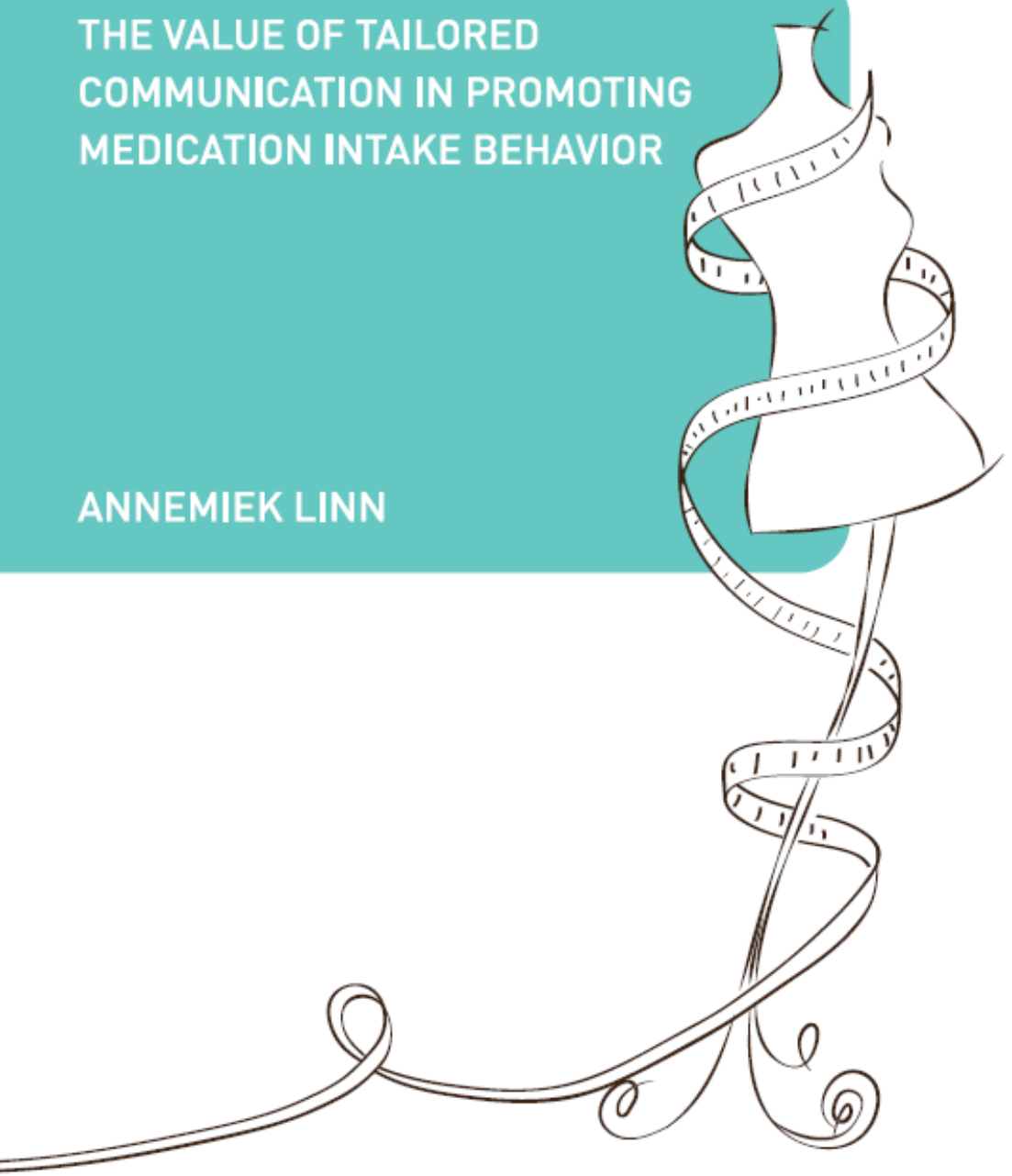
ANNEMIEK LINN



The value of tailored communication in promoting medication intake behavior

Annemiek Linn

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The value of tailored communication in promoting medication intake behavior

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Faculteit der Maatschappij en Gedragswetenschappen

Voor mijn drie musketiers,
Oma, Mama en Marjolijn

Contents

Chapter 1

Introduction

“Just as cats chase mice but don’t necessarily eat them, humans chase medicines but don’t necessarily take them” (Misselbrook, 2001, p. 173).

Introduction

"Just as cats chase mice but don't necessarily eat them, humans chase medicines but don't necessarily take them"(Misselbrook, 2001, p. 173).

Hippocrates described the concern with patients not taking their prescribed medication over 2000 years ago; however, this issue continues to generate intense debate today (Brown & Brussel, 2011). Many patients, especially those with chronic illnesses, experience difficulty with taking their medication as prescribed. Therefore, it is not surprising that the average successful medication intake rates for long-term treatment are low. One of the proposed strategies for improving medication intake behavior is tailoring. Sabaté (2003) proposed that interventions should be tailored to the needs of a patient to achieve maximum impact. To accomplish this tailoring, health care systems and providers need to develop means for accurately assessing the determinants of medication intake behavior. Although tailoring is regarded as the most promising strategy (Sabaté, 2003; Van Dulmen, 2011), little is known about appropriate methods, how messages should be tailored, and how content should be adapted to the individual receiver. In this chapter, medication intake behavior will be discussed first; the importance of tailored communication for encouraging successful medication intake behavior will be discussed second; and types of media that can be used for promoting successful medication intake behavior will be discussed last.

Medication intake behavior

Appropriate medication intake behavior can aid patients by reducing the risk of relapse (Ediger et al., 2007). For example, Kane, Huo, Aiekns and Hanauer (2003) found that patients with inflammatory bowel disease (IBD) who failed to adhere to a maintenance medication schedule had a 61% probability of relapse compared with patients who took their medication as prescribed. However, despite the strong association between successful medication intake behavior and health outcome, poor medication intake behavior remains a significant problem. Reports of the World Health Organization (WHO) and the National Institute for Health and Clinical Excellence (NICE) reveal that 30–50% of patients with chronic long-term illnesses do not take their medication as prescribed (Nunes et al., 2009; Sabaté, 2003). What are the reasons for this behavior?

Medication intake behavior is complex. Several terms are used to describe the concept of medication intake behavior. Compliance, adherence, concordance, persistence, and medication intake behavior have all been used to describe whether a patient is taking or not taking his or her medication as prescribed. However, the terms differ slightly in connotation and/or content. *Compliance* can be interpreted as a patient's competence for following the providers' recommendations. This competence suggests a potentially

distressed relationship with the provider. Taking medication as prescribed depends on the quality of the instructions given and the role of the patient in following the provider's orders (Horne, 2006; Vermeire, Hearnshaw, Van Royen, & Denekens, 2001; Vrijens et al., 2012). *Adherence* is defined as the extent to which patient behavior corresponds to the *agreed* recommendations of the provider. The definition of adherence implies that patients have the freedom to decide whether they agree with the treatment regimen (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008; Kane & Robinson, 2010; Vermeire et al., 2001; Vrijens et al., 2012). *Concordance* focuses on the cooperation between the patient and the provider and is predominantly used in the United Kingdom (Horne, 2006). In this definition, the terms communication, patient support for taking medication, shared decision-making, patient beliefs, and preferences have been emphasized and considered (Horne, 2006; Vrijens et al., 2012). *Persistence* is used to describe the length of time between the first and the last dose, which immediately precedes discontinuation of the medication (Urquhart & Vrijens, 2005; Vrijens et al., 2012). Last, the act of taking or not taking the medication as prescribed is a behavior (DiMatteo, Haskard-Zolnierek, & Martin, 2012). *Medication intake behavior* is defined as the extent to which patients succeed or fail to take medications as prescribed. Compared with the previously defined terms, this definition is based on a simple but wide-ranging approach in which both the provider and the patient play a role. For this reason, the term medication intake behavior will be used throughout this dissertation.

Similar to the Information-Motivation-Strategy model of Dimatteo and colleagues (2012), medication intake behavior can be considered a result of cognitive, affective, and behavioral factors. The cognitive component highlights the importance of patient knowledge and its achievement through effective provider-patient communication. The affective component includes a patient's (lack of) motivation or a negative or positive attitude towards medication. The behavioral component includes a patient's (lack of) workable strategy for following treatment recommendations (Dimatteo et al., 2012).

Barriers to successful medication intake behavior

To improve medication intake behavior, specific reasons for poor medication intake behavior need to be addressed. Patients may report unintentional (e.g., when a patient is not able to recall medication instructions due to memory problems) and intentional (e.g., when a patient decides not to take medication due to a fear of side effects) poor medication intake behavior (Sabaté, 2003). Barriers to successful medication intake behavior can be practical (cognitive and/or behavioral) and/or perceptual (affective) and are considered important determinants of taking the medication as prescribed. Existing evidence suggests that patients' perceptual barriers are more predictive of intentional poor medication intake behavior than of unintentional poor medication intake behavior, and practical barriers are more predictive of unintentional poor medication intake

behavior than of intentional poor medication intake behavior (Horne, Parham, Driscoll, & Robinson, 2009; Wroe, 2002; Wroe & Thomas, 2003).

Practical barriers

Practical barriers (i.e., memory barriers or daily routine barriers) refer to cognitive or behavioral difficulties relating to medication intake behavior. *Memory barriers* are associated with a patient's cognitive information-processing problems, such as difficulty comprehending treatment information and recalling medication instructions (Kane & Robinson, 2010). According to Ley's cognitive model, medication intake behavior is largely determined by a patient's capability to memorize and understand medical information (Ley, 1979). The importance of remembering and understanding medical information for promoting successful medication intake behavior is emphasized in various research (Flocke & Stange, 2004; Kessels, 2003; Ley, 1976; Ley, 1979). If patients are unable to memorize specific information, even the most effective treatment recommendations may be useless (Bartlett et al., 1984; Flocke & Stange, 2004; Ley, 1979). As a consequence of poor patient recall, patients are more likely to misinterpret instructions, which may lead to misuse or unintentional poor medication intake behavior (Cameron et al., 2010; Kane & Robinson, 2010). Although the relationship between recall of medical information and medication intake behavior is often described in research (Kessels, 2003; Ley, 1979), only a few studies exist that have explicitly examined this relationship.

Daily routine barriers refer to the perceived inconvenience of taking medication according to the treatment regimen, which may be attributed to the difficulty of integrating the medication regimen into daily life (Kane & Robinson, 2010). This component may be influenced by a patient's belief in taking the medication as prescribed under certain conditions, such as interruptions of their normal daily routine (Cameron et al., 2010; Kane & Robinson, 2010). Recent studies have indicated that interruptions in a patient's daily routine are an important predictor for poor medication intake behavior (Vervloet, 2013). In this case, it is important that patients believe that they are capable of overcoming these obstacles.

Perceptual barriers

Perceptual barriers are based on an internal negotiation between the perceived necessity of the treatment and any related concerns and are considered proximal determinants of medication intake behavior (Clifford, Barber, & Horne, 2008; Horne & Weinman, 1999; Horne, Weinman, & Hankins, 1999; Horne et al., 2009; Menckeberg et al., 2008; Schüz et al., 2011). The necessity-concerns framework (NCF) is a framework used to improve our understanding of the relationship between a patient's beliefs and a patient's medication intake behavior (Clifford et al., 2008). A meta-analysis spanning 17 long-term conditions involving over 10,000 patients showed showed that the framework had good exploratory value in both cross-sectional and prospective studies (Horne et al., under review).

Necessity barriers are associated with a patient's lack of belief in the need for medication. More specifically, beliefs represent the perceived role of medication in protecting against deterioration of the present and future health status of a patient (Horne et al., 1999). It can be thought of the answer to two questions: 'How much do I need this potential benefit?' and 'Can I manage without it?'. These beliefs influence a patient's motivation to begin and continue treatment. Patients with a stronger belief in the necessity of taking their medication as prescribed are less likely to believe that they can cope with their disease without medication (Clifford et al., 2008; Horne et al., 1999).

Concern barriers refer to the expected side effects or the fear of becoming too dependent on the medication (Kane & Robinson, 2010). Concerns are a measure of the perceived relevance of the costs and their emotional impact (e.g., how much they worry about potential side effects). It is especially important to consider patients' concerns because patients often report their concerns with medication as the primary reason for poor medication intake behavior (Horne & Weinman, 1999). Concerns are primarily explicit, can be considered a verbalization of an unpleasant emotional state (Zimmermann, Del Piccolo, & Finset, 2007) and are mainly intentional (Kane & Robinson, 2010). An emotional cue (i.e., verbal indication of an underlying unpleasant emotion) can be considered an indicator of concerns. A review of patients' emotional cues concluded that patients generally verbalize one to seven emotional cues during each medical consultation (Zimmermann et al., 2007). Adequate response to a patient's emotional cues is essential because it may reduce a patient's anxiety (Butow, Brown, Cogar, Tattersall, & Dunn, 2002). In addition, it may promote coping with illness (Zachariae et al., 2003), satisfaction with treatment (Uitterhoeve et al., 2008), disclosure of emotions, fewer concerns and worries (Roter & Larson, 2002), and increased recall of information (Jansen et al., 2010). Moreover, responding to a patient's emotional cues offers providers a better understanding of a patient's concerns, which facilitates more adequate responses to these cues and tailoring of information to a patient's emotional needs (Uitterhoeve et al., 2008).

The value of tailored communication

The word *tailoring* is used more frequently by researchers in the field of health communication. *Tailor* stems from the Latin word talea, which means 'to cut' (Kreuter & Skinne, 2000). Today, the word 'cut' indicates that a message fits an individual. Tailoring may be defined as "any combination of strategies intended to reach one specific person, based on characteristics that are unique to that person, related to the outcome of interest" (Kreuter, Farrell, Olevitch, & Brennan, 1999, p. 176). The definition should not be used interchangeably with the concept of personalization or targeting. Personalized messages are often generic messages that are used with a person's name to elicit attention, whereas targeted messages are messages for a specific subgroup that are usually based

on a set of demographic characteristics (Kreuter & Skinne, 2000; Maslowska, Putte, & Smit, 2011).

The elaboration likelihood model (ELM) explains the processes underlying the efficacy of tailored persuasive messages. Tailoring provides an opportunity to address the specific preferences and needs of patients; people tend to pay more attention to information that they perceive as personally relevant (Kreuter et al., 1999; Kreuter & Wray, 2003), which may stimulate elaboration via a central route (Petty & Cacioppo, 1986b). A central route leads to deeper processing and more persistent persuasion (Pettey, Priester, & Brinol, 2002). When information is tailored to the specific needs of patients, it will be more useful than nontailored information in helping patients implement their desired behavioral changes (Kreuter et al., 1999).

Tailored messages can be useful in the context of health care because poor recall of medical information is often reported as a major problem (Kessels, 2003). Patients are often confronted with a substantial amount of detailed and complex information about their treatment, which is often difficult to understand and recall (Kessels, 2003). Tailored messages will receive more attention; thus, they will be better processed and, consequently, better recalled.

In the past decade, numerous interventions designed to improve successful medication intake behavior have been developed and implemented. These interventions have been delivered through a variety of media. The most typical media used to deliver interventions comprise the Internet (i.e., eHealth), mobile phones (i.e., mHealth), and interpersonal communication. Although tailoring is often associated with the Internet, tailored messages can also be delivered via various alternative media. The manner in which the message can be tailored, however, differs by method.

eHealth

With the introduction of eHealth in the 1990s, opportunities for using communication technology to improve health and the health care system have grown (Oh, Rizo, Enkin, & Jadad, 2005). One of the advantages of eHealth is the ability to efficiently support patients over time. This support is especially relevant to patients living with chronic diseases, which require patients to engage in long-term self-management behavior. Moreover, eHealth has the advantages of being inexpensive, easy to access, and accessible to large populations (Petrie, Perry, Broadbent, & Weinman, 2012).

Computer technology, especially the Internet, can be used to tailor health messages to the personal situation of patients, and may result in a significant contribution to the development of tailored message strategies (Lustria, Cortese, Noar, & Glueckauf, 2009). Computer technology can be used to create tailored health messages that derive from an individual assessment (Kreuter & Skinne, 2000). For example, data from individuals regarding a number of determinants can be collected and can be conceptually or empirically based. Computer-driven algorithms can be used to process patients' data

and generate tailored feedback to meet their needs (Kreuter & Skinne, 2000). By selecting specific determinants related to the behavior, tailoring can be used to enhance cognitive acceptance, preconditions for message processing, and message impact (Hawkins, Kreuter, Resnicow, Fishbein, & Dijkstra, 2008). A review of computerized tailored health interventions concluded that the Internet provides the optimal technology for implementing interventions because it has the capability to assess potential barriers and provides the patient with immediate and tailored feedback (Lustria et al., 2009). Studies of various health behaviors have shown that computer-generated materials that are tailored to the unique needs and interests of patients are more effective than conventional health communication messages (Bull, Kreuter, & Scharff, 1999; Cortese & Lustria, 2012; Prochaska, DiClemente, Velicer, & Rossi, 1993; Smit, de Vries, & Hoving, 2012).

mHealth

In addition to eHealth, another technology that is receiving considerable attention is mHealth. mHealth focuses on the use of mobile communication for health information and services (Nacnovich, 2011). Mobile devices are one of the most significant recent developments in the field of information and communication technology (Chomutare, Fernandez-Luque, Årsand, & Hartvigsen, 2011). According to Nacnovich (2011), mobile devices offer four distinct applications for international development: monitoring of patient medication intake behavior, support, diagnostic treatment, and data collection. With the introduction of mHealth, it also became possible for patients to monitor their health, improve their treatment outside of the hospital, and access health care services anytime and anywhere (Preuveneers & Berbers, 2008). Furthermore, by being ‘always on’ and ‘always worn’, mobile phones can provide an intimate and detailed picture of a patient's daily routines and offer affordable, proximate, personalized, and continuous measurement in context (Ramanathan, Swendeman, Comulada, Estrin, & Rotheram-Borus, 2012).

Interventions that employ mobile devices are primarily based on the principles of behavioral learning theory. From this perspective, medication intake behavior depends on stimuli or cues that generate a response that will reinforce successful medication intake behavior (Leventhal & Cameron, 1987). Examples of behavioral interventions include reminders, such as reminders by email, telephone or computer (Peterson, Takiya, & Finley, 2003). Based on a recent review of mobile applications, the enhanced usability and pervasiveness of mobile devices has resulted in a renewed interest in the development of new applications (Chomutare et al., 2011). With the opportunity to use new communication technologies, we can better understand patients and translate this understanding into tailored health messages sent by mobile phones. Computer-mediated algorithms are often used to generate these reminders but can also be used to generate tailored text messages.

Interpersonal communication

The importance of interpersonal communication was acknowledged during the era of Hippocrates. According to the Greek physician and philosopher Hippocrates, "the patient, though conscious that this condition is perilous, may recover his health simply through his contentment with the goodness of the physician" (Blasi, Harkness, Ernst, Georgiou, & Kleijnen, 2001, p. 757). Bensing and Verhaak (2004) justifiably argue that the words of Hippocrates have lost remarkably little of their former appeal. Balint added "not only the medicine…or the pills…but the way the doctor gave them to the patient—in fact the whole atmosphere in which the drug was given" (Blasi et al., 2001, p. 757) and emphasized the importance of interpersonal communication for promoting medication intake behavior. For decades, it was generally thought that patient-provider communication was adequate and that there was no cause for concern. However, evidence suggests otherwise (Stewart, 1995). For example, it was determined that communication is often not tailored to a patient's needs (Ong, De Haes, Hoos, & Lammes, 1995). It was also determined that poor medication intake behavior is more common among patients whose provider is a poor communicator (Zolnierek & DiMatteo, 2009). These examples not only stress the importance of effective communication but also highlight the consequences of poor communication.

What is adequate patient-provider communication? When seeking a provider, patients have two basic needs: the need to know and understand (i.e., instrumental communication) and the need to feel acknowledged and understood (i.e., affective communication) (Bensing & Verhaak, 2004). Instrumental communication refers to the provision of information and advice; affective communication refers to the expression of empathy or concern (Bensing & Verhaak, 2004). Previous research on health communication has emphasized the importance of exchanging information (instrumental communication) *and* creating a good relationship (affective communication) (Ong et al., 1995) because many medical problems cannot be solved by only one type of communication. However, many providers do not use both types of communication behavior adequately (Barber, Parsons, Clifford, Darracott, & Horne, 2004; Bernstein et al., 2011; Ong et al., 1995).

First, patients often report unmet informational needs at the time of their diagnosis (Bernstein et al., 2011) or when beginning their medication (Barber et al., 2004). High levels of unmet informational needs are reported in studies of cancer patients (Sanson Fisher et al., 2000; Van Weert et al., 2009), patients with cardiovascular disease (van Geffen et al., 2011), patients with asthma (Koning, Maille, Stevens, & Dekker, 1995), and patients with IBD (Irvine, 2004). An explanation for this finding may be that patients do not clearly express their informational needs. Patients may assume that the provider has informed them of everything or worry that they will appear foolish or consume too much of the provider's time (Fallowfield & Jenkins, 1999). Patient education should be based on individual preferences, for instance, by directly asking patients about their needs.

However, a previous oncology study determined that providers generally do not adequately explore a patient's personal situation and information needs (Posma, Van Weert, Jansen, & Bensing, 2009). Consequently, providers cannot tailor information to their patients' needs and an information gap may result.

Second, although affective communication is important for predicting patient satisfaction and quality of health care (Bensing, 1991), providers often do not employ affective communication during consultations (Heaven & Maguire, 1996). It has been frequently reported that providers underestimate the affective needs of patients (Heaven & Maguire, 1996; Uitterhoeve et al., 2008). Moreover, providers often find it difficult to address patient concerns (Heaven & Maguire, 1996). As a result, patients may become worried and dissatisfied with their treatment (Suominen, Leino-Kilpi, & Laippala, 1995) and/or with the communication with their providers (Krishnasamy, 1996).

Although evidence suggests that tailoring is important, reviews of patient-provider communication conclude that communication by providers is often not tailored to a patient's needs (Hack, Degner, & Parker, 2005; Ong et al., 1995). Providers fulfilling a patient's needs may lead to symptom resolution, better functional and physiological status and pain control (Stewart, 1995), improved patient satisfaction (Kessels, 2003; Ley, 1979), higher recall levels of medical information (Kessels, 2003; Van der Meulen, Jansen, van Dulmen, Bensing, & Van Weert, 2008), and appropriate medication intake behavior (Barber et al., 2004; Bartlett et al., 1984). Although evidence suggests that tailoring is essential, how we should tailor messages and how message content should be adapted to patients was not determined until recently.

Multimedia interventions

As previously described, various media have advantages regarding the promotion of medication intake behavior. For example, computer technologies can be used to create tailored health messages derived from individual assessments. As a result, this can be used as a tool for providers to optimize the extent to which they tailor interpersonal communication to the needs and barriers of patients. In particular, eHealth and mHealth interventions should not be considered separate interventions, but should rather be considered tools that both patients and providers can use to tailor information to a patient's needs. In marketing and advertising literature, the term synergy is an important concept when considering the effectiveness of persuasive communication. Synergy occurs when the combination of multiple media exceeds the sum of their individual effects (Naik & Raman, 2003; Voorveld, Neijens, & Smit, 2011). However, this concept has rarely been applied to the development of interventions that are designed to improve medication intake behavior. In line with the synergy concept, Sabaté (2003) suggests that these strategies are expected to be most effective when used as components of multimedia programs and implemented in a tailored manner.

Patients with inflammatory bowel disease

Patients with inflammatory bowel disease (IBD) are identified as the target population for the empirical studies in this dissertation. IBD is a complex chronic inflammatory disorder. The two most common inflammatory bowel diseases are Ulcerative Colitis and Crohn's disease. Data concerning the prevalence of IBD estimate that the worldwide prevalence rate of IBD (i.e., the total number of cases of IBD worldwide) is approximately 396/100,000 persons (Lakatos, 2006). The way that IBD affects a patient's life is highly variable and may depend on the severity of the inflammation in the affected area. Symptoms include abdominal cramps, weight loss, acute urgency to have a bowel movement, pain and fatigue.

IBD patients represent a high-risk group for poor medication intake behavior (Robinson, 2008). Non-adherence rates of 20% to 40% for long-term therapies have been reported (Horne et al., 2009; Sewitch et al., 2003; Shale & Riley, 2003). Several determinants are associated with non-adherence: chronic illness, age (individuals are often diagnosed at a relatively young age), an unpredictable course for the disease, long inactive periods, inconvenient therapies, and side effects (Ediger et al., 2007; Kane, 2007; Van Dulmen et al., 2007; Vermeire et al., 2001). Appropriate medication intake can reduce the probability of relapse for IBD patients (Ediger et al., 2007). Previous research has suggested that patients who do not take their medication as prescribed have a 61% probability of relapse compared with an 11% probability of relapse for patients who adhere to a prescribed medication schedule (Kane et al., 2003).

The treatment of IBD has become complex since the introduction of immunosuppressive and biological therapy (Johnson et al., 2007). For example, biological therapy is prescribed earlier and more frequently as combination therapy than five years ago (Cosnes et al., 2005). Remission of disease is now the primary therapeutic aim, which can be achieved through intensive treatment strategies (Danese, Colombel, Reinisch, & Rutgeerts, 2011). In addition, using immunosuppressive or biological therapy to initially treat IBD is associated with an increased risk of potentially adverse reactions, such as cancer. The likelihood of developing cancer as a result of taking immunosuppressive or biological therapy to treat IBD is very low; however, as soon as these adverse reactions are discussed, this issue may become the focus of attention for patients at the cost of other vital information (Johnson et al., 2007; Wessel, De Kooy, & Merckelbach, 2000). When medication regimens evoke concerns or become more complex, patients are more likely to forget how and when they have to take their medication. Patients are less likely to perform the directives, even though these medications are often administered in the hospital or by other organizations (DiMatteo et al., 2012).

Role of nurses in educating IBD patients

In the Netherlands, nurses play an increasingly important role in educating IBD patients about immunosuppressive and biological therapy and have a key position in understanding and addressing patient barriers to medication intake behavior. When immunosuppressive or biological therapy is prescribed, nurses (primarily nurse practitioners) inform patients about their prescribed medication. Accumulating evidence indicates that the relationship between patient and provider can play a crucial role in influencing satisfaction (Bartlett et al., 1984), recall (Kessels, 2003), and successful medication intake behavior (Hulka, Cassel, Kupper, & Burdette, 1976; Ley, 1979; Ware, Snyder, Wright, & Davies, 1983).

According to guidelines from the National Institute for Clinical Excellence (NICE), nurses should offer all patients the opportunity to be involved in the decision-making process concerning their prescribed medication (Nunes et al., 2009). Based on the Information-Motivation-Strategy model of Dimatteo and colleagues (2012), clinical actions of nurses should address the following points: 1) ensuring that patients have accurate information, 2) assisting patients to overcome perceptual barriers, and 3) assisting patients to overcome practical barriers. For example, nurses are expected to inform patients about the name of the medication and its possible side effects and provide instructions on how to take the prescribed medication. In addition, nurses should be aware that patients will have concerns about their medication and have different perceptions about their personal needs for medication (DiMatteo et al., 2012; Nunes et al., 2009). Nurses are therefore recommended to use a patient-centered approach that enables patients to disclose their concerns (Nunes et al., 2009).

Aims and outline of this dissertation

Aims

This dissertation aims to develop a theoretical and evidence-based tailored multimedia intervention to improve medication intake behavior. In addressing this aim, this dissertation gains insight into patient barriers to successful medication intake behavior and investigates the various methods and types of media (i.e., eHealth, mHealth and interpersonal communication) that can promote successful medication intake behavior.

Outline

The main aim of **Chapter 2** is to investigate which tailored Internet interventions are effective in improving medication intake behavior. Insight into the current developmental stage of these interventions is obtained. Selected studies are assessed for their effectiveness regarding medication intake behavior and to what degree medication intake behavior is determined by the level of tailoring of the intervention. The relationship between the characteristics of the studies and the reported effectiveness of the interventions is also investigated. The main aim of **Chapter 3** is to examine the effectiveness of interventions that use electronic reminders for improving medication intake behavior. To achieve this objective, existing data about the effectiveness of electronic reminders for improving patients' medication intake behavior are synthesized and critically appraised. In addition, the characteristics of electronic reminders that are associated with their effectiveness are investigated. In **Chapter 4**, we investigate how and if tailored communication can be useful for improving medication intake behavior. To achieve this goal, a new communication typology for addressing barriers to successful medication intake behavior is developed, and the relationship between the use of the typology and the barriers to successful medication intake behavior is examined. In **Chapter 5**, the relationship between patient satisfaction regarding communication with nurses and their medication beliefs is investigated. More insight is gained into patients' beliefs about the immunosuppressive or biological therapy that is prescribed for IBD; the results for the same group of patients are compared over a period of 6 months. Next, the relationship between patient satisfaction regarding communication with nurses and their beliefs is examined. **Chapter 6** explores the relationship between recall of medical information and medication intake behavior. Prescribing consultations between nurses and IBD patients are analyzed in a naturalistic environment, and the recall scores of IBD-patients are related to self-reported medication intake behavior. In **Chapter 7**, a multimedia intervention aimed at addressing patients' individual barriers to successful medication intake behavior is described. The development of this intervention is based on

the results of the previously described chapters (see Figure 1) and guided by the Medical Research Council framework.

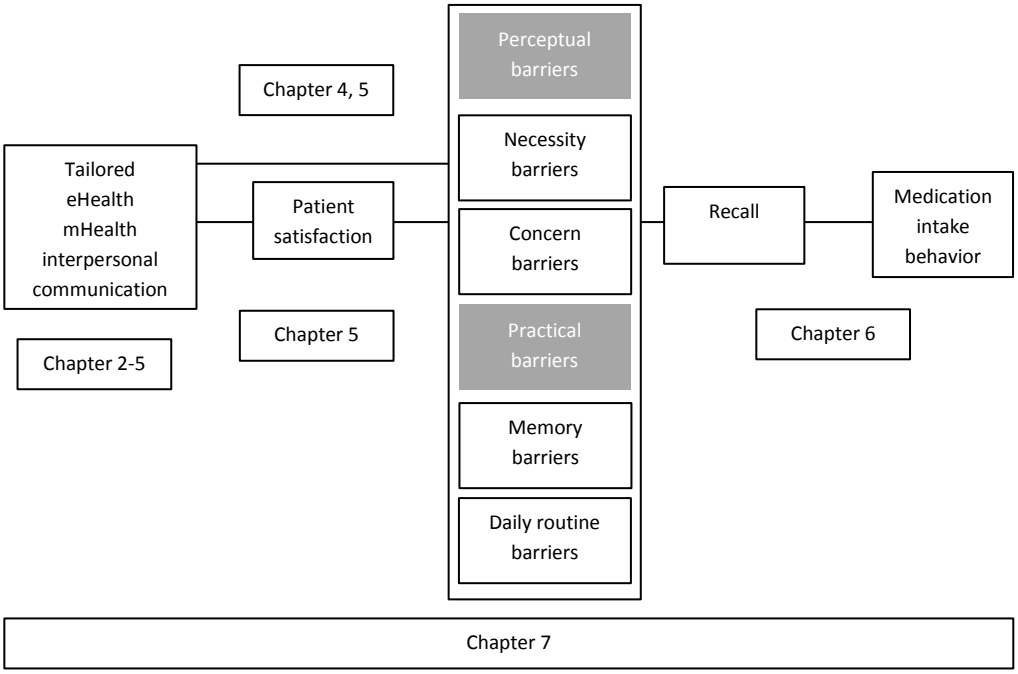

Figure 1. *Dissertation outline.*

In the final chapter, **Chapter 8**, the findings and the implications of the results of this dissertation are discussed. Moreover, directions for future research and practice are outlined.

The described studies in chapter 4-6 are based on the same dataset and used to structurally develop an intervention (described in chapter 7) to tailor the communication to IBD patients' barriers and needs. The intervention is currently being evaluated, but this evaluation is behind the scope of this dissertation. Figure 2 shows all the measures used in the described studies, a more detailed description of the measures is given in the chapters concerned. Moreover, Figure 2 displays the time when these measures were assessed.

Time of measurement	T0 Prior the consultation		T1 Directly after the consultation	T2 Telephone interview three weeks after the consultation	T3 Telephone interview six months after the consultation
Measurement	1. Informed consent 2. Demographics	1. Consultation characteristics 2. Content analysis	1. Recall 2. Satisfaction about nurses' communication	1. Perceptual barriers 2. Practical barriers 3. Self-reported medication intake behavior 4. Recall	1. Satisfaction about nurses' communication 2. Self-reported medication intake behavior

Figure 2. *Study overview.*

Chapter 2

Effects of eHealth interventions on medication intake behavior[1]: a systematic review of the literature

Patient: "Do you have any advice? How I can monitor my health?" Nurse: "If you like, there is an application for your smartphone […]. You can make notes, there is a map of nearby bathrooms and you can write down your symptoms" (male, 27 years old, Colitis).

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[1] For the purpose of this dissertation, the term adherence is changed into medication intake behavior

Abstract

Background: Poor medication intake behavior is considered to be an important health risk. Numerous interventions to improve medication intake behavior have been developed. The use of Internet-based interventions to improve medication intake behavior has increased rapidly. Internet interventions have the potential advantage of tailoring the interventions to the needs and situation of the patient.

Objective: The main aim of this systematic review was to investigate which tailored Internet interventions are effective in improving medication intake behavior.

Methods: We undertook comprehensive literature searches in PubMed, PsycINFO, EMBASE, CINAHL, and Communication Abstracts, following the guidelines of the Cochrane Collaboration. The methodological quality of the randomized controlled trials and clinical controlled trials and methods for measuring medication intake behavior were independently reviewed by two researchers.

Results: A total of 13 studies met the inclusion criteria. All included Internet interventions clearly used moderately or highly sophisticated computer-tailored methods. Data synthesis revealed that there is evidence for the effectiveness of Internet interventions in improving medication intake behavior: 5 studies (3 high-quality (HQ) studies and 2 low-quality studies (LQ)) showed a significant effect; 6 other studies (4 HQ studies and 2 LQ studies) reported a moderate effect; and 2 studies (1 HQ study and 1 LQ study) showed no effect. Most studies used self-reported measurements to assess medication intake behavior, which is generally perceived as a low-quality measurement. We did not find a clear relationship between the quality of the studies or the level of sophistication of message tailoring and the effectiveness of the intervention. This might be explained by the great difference in study designs and the way of measuring medication intake behavior, which makes results difficult to compare. There was also large variation in the measured interval between baseline and follow-up measurements.

Conclusion: This review shows promising results on the effectiveness of Internet interventions in improving medication intake behavior. Although there is evidence according to the data synthesis, the results must be interpreted with caution due to low-quality medication intake behavior measurements. Future studies using high-quality measurements to assess medication intake behavior are recommended to establish more robust evidence for the effectiveness of eHealth interventions on medication intake behavior.

Introduction

Recent reports of the World Health Organization and the National Institute for Health and Clinical Excellence reveal that 30%–50% of patients with chronic illnesses do not take their medication as prescribed (Sabaté, 2003). Other studies also show that rates of poor medication intake behavior are very high and depend on the type of disease. The highest successful medication intake behavior rates are found for patients with human immunodeficiency virus infection, while diabetes patients have the lowest rate (DiMatteo, 2004). As such, poor medication intake behavior can be considered an important health care problem. This is especially true for patients with a chronic illness because successful medication intake behavior is a crucial factor in the effectiveness of a therapy (DiMatteo, 2004). Consequently, many patient-centered interventions are developed to improve medication intake behavior, and the impact of the Internet in the development of these interventions is increasing. It is therefore important to understand how these interventions work and to know whether they are effective in improving medication intake behavior. To our knowledge, no recent review has studied the effectiveness of patient-centered Internet interventions on patients' medication intake behavior. Therefore, we conducted a systematic literature study in which we reviewed evidence from studies on Internet interventions that were developed to assist patients in their medication management. The purpose of our study was fourfold: first, to gain insight into the current stage of development of these interventions; second, to assess the included studies for their effectiveness on medication intake behavior; third, to investigate to what degree successful medication intake behavior is determined by the characteristics of the intervention; and fourth, to investigate whether there is a relationship between the characteristics of the study and the reported effectiveness of the interventions.

Different terms are used in the literature to describe the concept of successful medication intake behavior—for example, compliance, adherence, and persistence. They have all been used to indicate that the patient is using the medication following the prescribed regimen. These terms differ in exact meaning. In this paper, we use the term successful medication intake behavior. According to this definition, poor medication intake behavior is a wide concept that varies from missing an occasional dose to never taking the prescribed medications (Kane & Robinson, 2010). Patients have different reasons for being nonadherent. These different reasons have something in common: the patient does not execute the treatment plan and does not persist. Execution is a continuous process where the actual dosing history corresponds to the ideal doses (Urquhart & Vrijens, 2005; Wroe, 2002). To improve medication intake behavior and develop target interventions, it is important to address the specific reasons why a patient is not able or willing to execute the treatment plan. From this perspective, interventions should be personalized or tailored to address individual needs and beliefs. The definition

of tailoring describes the features that make tailored health messages different from other approaches: “It is assessment-based and as a result the message can be individual-focused” (Kreuter & Skinne, 2000). In other words, tailoring is based on gathering and assessing personal data related to health outcomes or several determinants in order to determine the most effective strategy to meet that person’s needs (Lustria et al., 2009). With these characteristics, a tailored message is able to provide personal feedback, commands greater attention, is processed more deeply, and is perceived as more likable by patients than a general message (Lustria et al., 2009; Noar, Benac, & Harris, 2007). Because of these possibilities, tailored health messages are also more likely than generic information to be read, remembered, and viewed as personally relevant (Kreuter & Skinne, 2000; Kreuter & Wray, 2003).

Computer technologies can be used to tailor health messages to the personal situation of the patient and might therefore contribute significantly to the development of tailored message strategies. The Internet is potentially a powerful medium for delivering those tailored messages. The management of a chronic disease should be personalized to an individual because the person is ultimately responsible for the success of the intervention (Wantland, Portillo, Holzemer, Slaughter, & McGhee, 2004). The technology provides an opportunity to tailor the information in several formats and modalities, which enhances the user’s experience of the material and will result in a better understanding (Lustria et al., 2009; Noar et al., 2007). Moreover, Internet interventions have the advantage that they can provide interactive and responsive programs (Wantland et al., 2004). These interventions can provide effective data and information provision and retrieval. The advantages of tailored message strategies can contribute to the incorporation of interactive and continued self-monitoring, feedback, and information exchange, which play an increasingly important role in changing patients’ behavior.

Methods

For this review, we used the guidelines of the Cochrane Collaboration to assess the studies on their internal validity and to summarize the existing evidence about Internet interventions to improve medication intake behavior in patients. The Cochrane Collaboration method is described in more detail in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins, Green, & Collaboration, 2008).

Inclusion Criteria

We included a study when the following inclusion criteria were met: (1) the study described a patient-centered Internet intervention, (2) the study described an intervention for patients who use prescribed medication for a chronic condition, (3) at least one of the outcome measures was medication intake behavior, (4) the study was quantitative, and (5) the study was published in either the English or Dutch language.

Search Methods

We conducted a systematic literature search to identify articles containing information about the effect of Internet interventions on medication intake behavior. Comprehensive literature searches were undertaken in the databases PubMed, PsycINFO, EMBASE, CINAHL, and Communication Abstracts. The search strategies used the following keywords: (medication therapy management OR medication adherence OR patient compliance OR self-care) AND (Internet) AND (intervention study OR randomized controlled trial OR clinical controlled trial). We then continued with the snowball method by looking for references in publications, especially those of the included studies and reviews on interventions to promote medication intake behavior. The search was conducted in June 2010. Since Internet interventions is a relatively new topic, no time limits were applied. Application of the search strategy to the specified databases resulted in a total of 620 hits (Table 1). In total, we selected 13 studies from these results.

Table 1.
Results of database searches.

Source	Hits per strategy	Unique studies	Relevant studies
PubMed	388	388	11
Communication Abstracts	0	0	0
PsycINFO	47	40	0
EMBASE	169	82	0
Snowball method	3	0	1
CINAHL	13	10	1
Total	620	520	13

Reference Manager version 11.0 (Thomson Reuters, New York, NY, USA) was used to manage the citations. Duplications were logged, leaving 520 unique results (see Figure 1). On the basis of title and abstract, two researchers (pairs of AL, MV, LvD, JvW) independently selected studies for inclusion. If the study seemed to meet the inclusion criteria or if there were doubts about the inclusion, the full text of the article was obtained. Based on the full articles two reviewers independently reviewed whether these studies fit all the inclusion criteria. Disagreements were solved by discussions between the two researchers. For a more detailed description of the excluded studies see Appendix 1.

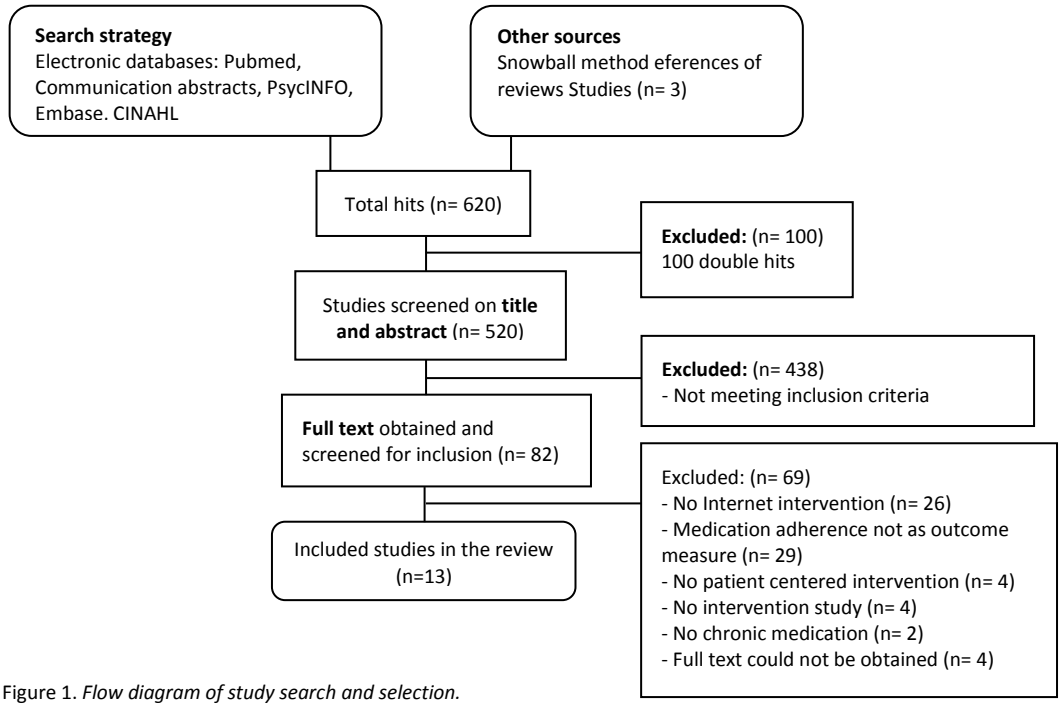

Figure 1. *Flow diagram of study search and selection.*

Assessment of Methodological Quality

The methodological quality of included randomized controlled trials (RCTs) and clinical controlled trials (CCTs) was independently reviewed by two researchers (AL and JvW) using the list from the Cochrane Collaboration Back Review Group (Van Tulder, Furlan, Bombardier, & Bouter, 2003). The list consists of 11 criteria for internal validity, namely:

- 3 criteria regarding selection bias: whether (a) randomization was adequate, (b) treatment allocation was concealed, and (c) groups were similar at baseline regarding the most important indicators,
- 4 criteria for performance bias: whether (d) patients were blinded to the intervention, (e) care provider was blinded to the intervention, (g) co-interventions were avoided, and (h) compliance with the intervention was acceptable,
- 2 criteria regarding attrition bias: whether (i) the dropout rate after baseline was acceptable, and (k) the analysis included an intention-to-treat analysis, and,
- 2 criteria for detection bias: whether (f) the outcome assessor was blinded to the intervention, and (j) outcome assessments in all groups were similar.

For each included study, all criteria were scored as “yes,” “no,” or “unclear.” All unclear scores were later rated as “no.” Studies were rated as high quality (HQ) when at least 6 of the 11 criteria for internal validity were met. Otherwise, studies were considered of low

quality (LQ). Disagreements were discussed until consensus was reached. If disagreement or indistinctness persisted a third reviewer (LvD) was consulted.

In addition, two researchers (AL and LvD) independently assessed the quality of the methods for measuring medication intake behavior to a medical regimen. A standard method to assess medication intake behavior does not exist and every method has its limits (Sluijs et al., 2006; Wetzels, Nelemans, Schouten, Van Wijk, & Prins, 2006). In clinical trials, medication intake behavior can be measured based on, for example, interviews, diary, questionnaire-based self-reporting, prescription refills, pill counts, or electronic monitoring (Farmer, 1999; Wetzels et al., 2006). We categorized the measurements in high- and low-quality medication intake behavior assessments based on previous findings concerning the objectivity of these measurements (Farmer, 1999; Wetzels et al., 2006). In this review electronic monitoring and physiological/biomedical measures are defined as high-quality medication intake behavior assessment. These measurements are considered the most objective standard (Farmer, 1999). Previous research has shown that data from pill counts and electronic monitoring are strongly correlated (Velligan et al., 2007). Yet, others consider pill counts not to be accurate (Pullar, Kumar, Tindall, & Feely, 1989; Rudd et al., 1989). In addition, meta-analyses have shown that self-reported medication intake behavior is also strongly correlated with electronic monitoring (Shi, Liu, Fonseca et al., 2010; Shi, Liu, Koleva et al., 2010). Like pill counts, the accuracy of self-reported measurements is debatable. Some argue that self-reports may be an accurate measurement for measuring medication intake behavior (DiMatteo, Giordani, Lepper, & Croghan, 2002; Grymonpre, Didur, Montgomery, & Sitar, 1998), while others state that the use of self-reported measurements is not an accurate method (Farmer, 1999; McMahon et al., 2011; Sajatovic, Velligan, Weiden, Valenstein, & Ogedegbe, 2010; Wetzels et al., 2006). Taking all arguments into account, we considered self-measurements, such as questionnaires, pill counts, prescription refills, interviews, and diaries, to be most subjective for measuring medication intake behavior (Sluijs et al., 2006). We therefore considered these measurements low-quality medication intake behavior assessment. However, if two or more different low-quality medication intake behavior measurements were used in the same study, such as a combination of questionnaires and prescription refills, the method was considered high-quality medication intake behavior assessment.

Data Extraction

One researcher (AL) documented the following characteristics of the included studies: (1) method (type of study), (2) participants (total number of participants, sex per group, mean age per group, type of disease), (3) intervention (name of experimental intervention, name of control condition, period, number of times/minutes per week), (4) outcome measures (type of outcome measures, time of measurement), (5) results (short description), and (6) author's conclusion.

Data Synthesis

Due to diversity in the features of the interventions and the methods used to measure medication intake behavior, it was not possible to pool the data. Therefore, we conducted a best evidence synthesis (see Textbox 1) based on (Van Tulder et al., 2003) and adapted by a Dutch study (Steultjens et al., 2009). The best-evidence synthesis was conducted by attributing various levels of evidence to the effectiveness of the interventions. The synthesis takes into account the design, methodological quality, and outcomes of the studies. Textbox 1 shows that at least 1 HQ RCT or 2 HQ CCTs were needed to establish robust evidence for the effectiveness of an intervention.

Sensitivity Analysis

We conducted a sensitivity analysis to identify how sensitive the results of the best-evidence syntheses were to changes in the way the study quality was assessed. For the sensitivity analysis, the best-evidence synthesis was repeated in two different ways, using the following principles: (1) LQ studies were excluded, (2) studies were rated as HQ if they met at least 4 of the 11 criteria of internal validity instead of 6. We then compared the results of the sensitivity analysis with the results of the best-evidence synthesis and described the sensitivity of the results (Steultjens et al., 2009; Verkaik, Van Weert, & Francke, 2005).

Effectiveness

Study effectiveness was categorized as significant effect on medication intake behavior, moderate effect on medication intake behavior, and no effect on medication intake behavior. We defined a study effect as moderate if the authors reported a positive effect of the intervention on medication intake behavior but there were limitations, such as the following: improvement of medication intake behavior was found only in a subgroup of the intervention group; medication intake behavior was measured indirectly (e.g., the study drew conclusions about the use of beta-agonist indicating that medication intake behavior was improved); or the significance of the results in medication intake behavior was not tested, but the authors used convincing arguments to explain the effectiveness of the intervention (see results section for explanation per study).

Textbox 1. *Principles of Best Evidence Synthesis*

Evidence:
Provided by consistent, statistically significant findings in outcome measures in at least two high quality RCTs.
Moderate evidence:
Provided by consistent, statistically significant findings in outcome measures in at least one high quality RCT and at least one low quality RCT or high quality CCT
Limited evidence:
Provided by statistically significant findings in outcome measures in at least one high quality RCT
Or
Provided by consistent, statistically significant findings in outcome measures in at least two high quality CCTs (in the absence of high quality RCTs)
Indicative findings:
Provided by statistically significant findings in outcome measures in at least one high quality CCT or low quality RCT (in the absence of high quality RCTs)
No/Insufficient evidence:
If the number of studies that have significant findings is less than 50% of the total number of studies found within the same category of methodological quality and study design
Or
In case the results of eligible studies do not meet the criteria for one of the above stated levels of evidence
Or
In case of conflicting (statistically significantly positive and statistically significantly negative) results among RCTs and CCTs
Or
In case of no eligible studies

Intervention: Tailoring Level of Sophistication of the Website

Tailored Internet interventions differ in how they deliver their message (Lustria et al., 2009). The difference is based on the sophistication of the way the message is tailored. We categorized the interventions in being low, moderate, or high in sophistication. Some interventions involve a form of online assessments (low sophistication), and others use online assessments, tailored feedback, and content matching (moderate sophistication). The third group of interventions provides instant feedback and a complex tailored health program with several tools and activities that would enable patients to achieve their health goals (high sophistication; see Figure 2; Lustria et al., 2009).

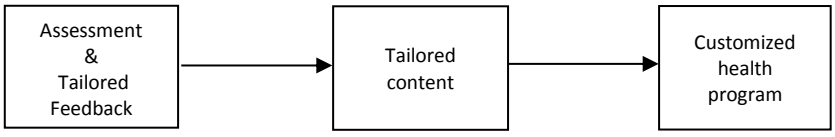

Figure 2. *Level of Sophistication* (Lustria et al., 2009).

Results

The main characteristics of the included studies (Artinian et al., 2003; Chan, Callahan, Sheets, Moreno, & Malone, 2003; Chan et al., 2007; Cherry, Moffatt, Rodriguez, & Dryden, 2002; DeVito Dabbs et al., 2009; Dew et al., 2004; DiIorio et al., 2009; Guendelman, Meade, Benson, Chen, & Samuels, 2002; Jan et al., 2007; Joseph et al., 2007; Ross, Moore, Earnest, Wittevrongel, & Lin, 2004; Van der Meer et al., 2009; Van der Meer et al., 2010) are presented in Table 2 and further described below (for a more detailed description of the included studies see Appendix 2).

Methodological quality: assessment of internal validity

For this review 10 RCTs were included, and 9 of them were assessed on their internal validity (Chan et al., 2003; Chan et al., 2007; DeVito Dabbs et al., 2009; Guendelman et al., 2002; Jan et al., 2007; Joseph et al., 2007; Ross et al., 2004; Van der Meer et al., 2009; Van der Meer et al., 2010; See Table 3). We included 1 RCT with no data on our primary outcome variable (i.e., medication intake behavior) for the control group (Artinian et al., 2003). This means that for this tenth study, we could not assess validity criteria. Moreover, we reviewed 2 prospective cohort designs and 1 survey. A total of 7 RCTs met 6 or more of the 11 validity criteria and therefore qualified as HQ studies.

Intervention: tailoring level of sophistication of the website

All Internet interventions reported computer-tailoring methods. Interventions were categorized as having low sophistication (online assessments), moderate sophistication (online assessments, tailored feedback, and content matching), and high sophistication (a more complex tailored health program; see Figure 2; Lustria et al., 2009).

Online assessment and feedback

Online assessment and feedback are used in interventions with single-incident computer-assisted risk or health assessments. For example, feedback is emailed to the patients or provided online (Lustria et al., 2009). In addition, these interventions are brief and usually done once at the beginning of the intervention. None of the reviewed studies used online assessment and feedback.

Tailored content

With tailored content a program provides (1) tailored text messages composed in a unique way according to how patients respond to certain questions, or (2) restricted access to content sections per patient (Lustria et al., 2009). Tailored content was used by 9 of the studies we reviewed; 1 study (Jan et al., 2007), Blue Angel for Asthma Kids, conducted an Internet-based interactive asthma educational and monitoring program in which patients were able to complete an electronic diary, record symptoms and need for rescue

medication, and upload their videos when they were using their inhaler. Based on these outcomes, the program comprised both an action plan with a warning system and a written treatment plan. A similar customized educational and monitoring website for patients with asthma was conducted in 2 studies (Chan et al., 2003; Chan et al., 2007), and 1 study (Joseph et al., 2007) tested the asthma management program Puff City. The program used tailoring to alter behavior through individualized health messages based on the patients' beliefs, attitudes, and personal barriers to change or maintain the behavior. Another form of a tailored website, System Providing Access to Records Online (SPPARO), was examined in 1 study (Ross et al., 2004). This website provided the medical record, an educational guide, and a message system for patients. Moreover, patients could contact the health provider by email. The telemedicine diabetes disease management program Health Buddy was tested in 2 studies (Cherry et al., 2002; Guendelman et al., 2002). However, the modality used in the diabetes program was different from the previously mentioned monitoring programs. Patients answered personalized questions that enabled them to monitor their disease symptoms, medication intake behavior, and disease knowledge by pressing buttons for response. The 2 studies using the Health Buddy differed in the intensity of the feedback. One study (Artinian et al., 2003) tested a medication compliance device. Data and answers to questions were recorded by the device and uploaded daily to a central server. Based on these answers health providers were able to monitor the patients, provide advice, and update the treatment regimens in the Med-eMonitor devices. One study (DeVito Dabbs et al., 2009) also tested a handheld device, Pocket Personal Assistant for Tracking Health (PATH), developed for patients after lung transplantation to record health data, review data trends, and report their condition changes to the transplant team. The device included decision-support programs to promote self-care behaviors.

Table 2.

Characteristics of included studies

Study; method	**Intervention**[a]	**Participants; sex; mean age**	**Medication intake behavior measurement; timing of measuring**	**Main conclusion**
(Artinian et al., 2003); RCT[b]	Web-based monitoring system; tailored content; nature of expert/therapist contact	N = 18 (17 males; mean age 68 years); intervention group n = 9, control group n = 9	Pill counts; baseline and 3 months	Medication intake behavior rate was 94% for the monitor group as measured by the monitor system
(Jan et al., 2007); RCT[b]	Blue Angel for Asthma Kids variability; tailored content; nature of expert/therapist contact	N = 164, intervention group n = 88 (35 males; mean age 10.9 years); control group n = 76 (28 males; mean age 9.9 years)	Self-reported at baseline and 12 weeks	The Blue Angel for Asthma Kids has the potential for improving asthma outcome compared with conventional treatment over a period of 12 weeks
(Chan et al., 2007); RCT	Customized educational and monitoring Web site; tailored content; nature of expert/therapist contact	N = 120; intervention group n = 60 (37 males; mean age 10.2 years); control group n = 60 (38 males; mean age 9.0 years)	Computerized prescription refill record at baseline, 26 weeks, and 52 weeks	No difference in medication intake behavior between groups
(Chan et al., 2003); RCT	Customized educational and monitoring Web site; tailored content; nature of expert/therapist contact	N = 10; intervention group n = 5 (1 male; mean age 6.6 years); control group n = 5 (4 males; mean age 8.7 years)	Self-reported asthma diary and computerized prescription refill record at 90 days and 180 days	After the intervention, the use of beta-agonist decreased, which is an indication of better medication intake behavior
(Joseph et al., 2007); RCT[b]	Web-based asthma management program; tailored content; user control	N = 314 (36.6% male; mean age 15.3 years); intervention group n = 162; control group n = 52	Self-reported at baseline and 12 months	Positive changes in controller medication intake behavior were seen
(Ross et al., 2004); RCT[b]	SPPARO (System Providing Access to Records Online); tailored content; nature of expert/therapist contact	N = 104; intervention group n = 54 (80% male; mean age 57 years); control group n = 50 (74% male; mean age 55 years)	Self-reported at baseline, 6 months, and 12 months	Providing patients access to an online medical record improved medication intake behavior
(Cherry et al., 2002); prospective design	Telemedicine diabetes disease management program; tailored content; nature of expert/therapist contact	Intervention group n = 169 (39 males; mean age 53 years); historical group (usual care)	Self-reported	Outcomes offer encouraging evidence that telemedicine technology coupled with daily remote monitoring may improve appropriate use medication
(Guendelman et al., 2002);RCT[b]	Health Buddy, an interactive device connected to a home telephone; tailored content; nature of expert/therapist contact	N = 134; intervention group (40 males; mean age 12.2 years); control group (37 males; mean age 12.0 years)	Self-reported at baselines, 6 weeks, and 12 weeks	Patients were more likely to take their asthma medication without additional reminders

(DeVito Dabbs et al., 2009); RCT[b]	Pocket Personal Assistant for Tracking Health (PATH); tailored content; nature of expert/therapist contact	N = 30; intervention group n = 15 (60% male; mean age 55 years); control group n = 15 (60% male; mean age 57 years)	Self-reported at baseline and 2 months	Patients who received the PATH were more likely to show high medication intake behavior to the medical regimen
(Van der Meer et al., 2009); RCT[b]	Internet-based self-management program; customized health program; user control	N = 200; intervention group n = 101 (29% male; mean age 36 years); control group n = 99 (29% male; mean age 37 years)	Self-reported at baseline, 3 months, and 6 months	After 3 months asthma control improved
(Van der Meer et al., 2010); RCT[b]	Internet-based self-management program; customized health program; user control	N = 200; intervention group n = 111 (28 males; mean age 36 years); control group n = 89 (28 males; mean age 36.6 years)	Self-reported at baseline, 3 months, and 1 year	Weekly self-monitoring leads to improved medication intake behavior in patients with partly and uncontrolled asthma at baseline and tailors asthma medication to individual patients' needs
(Dilorio et al., 2009); Survey	WebEase; customized health program; user control	N = 35 (40% male; mean age 37.5 years)	Self-reported at baseline and 6 weeks	Participants showed some improvement in medication intake behavior following the program
(Dew et al., 2004); prospective design	Website including skills workshops, discussion group, ask an expert, question and answer, health tips, recourses, and references; customized health program; nature of expert/therapist contact	N = 64; intervention group n = 24 (18 males; mean age 45.8 years); control group n = 40 (30 males; mean age 57.5 years)	Self-reported at baseline and 4 months	The intervention appeared to be weakly associated with improved medication intake behavior

[a] Sophistication of tailoring classification based on Figure 2.

[b] Randomized controlled trial.

Table 3.
Results of methodological quality

Study		Validity criteria[a] met	Study quality[b]	Quality measurement medication intake behavior
Randomized clinical trials				
	(Artinian et al., 2003)	Not applicable[e]	Low	Low
	(Jan et al., 2007)	a, b, c, d, i, j	High	Low
	(Chan et al., 2007)	a, b, f, i, j	Low	Low
	(Chan et al., 2003)	a, b, c, f, h[c], i, j	High	High
	(Joseph et al., 2007)	a, b, c, d, e, h, i, j	High	Low
	(Ross et al., 2004)	a, b, c, d, e, h[d], i, j, k	High	Low
	(Guendelman et al., 2002)	a, b, d, i, j	Low	Low
	(DeVito Dabbs et al., 2009)	a, b, c, e, i, j	High	Low
	(Van der Meer et al., 2009)	a, b, c, i, j, k	High	Low
	(Van der Meer et al., 2010)	a, c, h[f], i, j, k	High	Low
Prospective design/clinical trial or cohort design				
	(Cherry et al., 2002)		Low	Low
	(Dew et al., 2004)		Low	Low
Survey				
	(DiIorio et al., 2009)		Low	Low

[a] a: randomization adequate; b: treatment allocation concealed; c: groups similar at baseline regarding most important indicators; d: patients blinded to intervention; e: care provider blinded to intervention; f: outcome assessor blinded to intervention; g: co-interventions avoided; h: compliance with intervention acceptable; i: dropout rate after baseline acceptable; j: outcome assessed similarly in all groups; k: intention-to-treat analysis included.

[b] That is, 6 of 11 validity criteria were met.

[c] Compliance was acceptable in the first interval (<90 days).

[d] Compliance was acceptable in the first interval (6 months).

[e] No data on medication medication intake behavior for the control group and therefore judged as low quality.

[f] Compliance was acceptable in the first interval (3 months).

Customized health programs

Interventions that provide not only tailored content but also individualized instructions for meeting certain health goals, self-management goals, or goal-setting activities are so-called customized health programs (Lustria et al., 2009), used by 4 of the included studies. Of these, 2 studies (Van der Meer et al., 2009; Van der Meer et al., 2010) tested the effects of an Internet-based self-management program for asthma patients. This website allowed monitoring through the website, text messages, use of an Internet-based treatment plan, online education, and the possibility to communicate with the health provider. The intervention WebEase (DiIorio et al., 2009) consisted of three modules that were designed to assess an individual's status related to self-management practices and create a plan for change or to maintain the behavior. The modules in WebEase required the patient to answer questions related to these topics. Feedback was provided based on these responses. Patients entered data into MyLog, which is a screen for recording data about medication-taking behavior, stress, etc. In addition, the intervention included a knowledge component and a discussion board. This means that each patient was directed

to another path (DiIorio et al., 2009). Another study (Dew et al., 2004) tested a customized health program where patients chose which components of the website they wanted to use. The website included a home page, post-transplant skills workshops, discussion groups, "ask an expert," question-and-answer possibility, healthy-living tips, resources, and reference library. The way the patients used the website was based more on voluntary participation than in the study that used MyLog (DiIorio et al., 2009). Table 4 and Table 5 show for each study which method for delivering the tailored message was used (see column 2).

Table 4.
Effectiveness of short-term interventions (<6 months)

Study	Study quality	Sophistication of tailoring	Quality measurement medication intake behavior	Short-term effectiveness (<6 months)[a]
(DeVito Dabbs et al., 2009)	High	Moderate	Low	++
(Jan et al., 2007)	High	Moderate	Low	++
(Dew et al., 2004)	Low	High	Low	–
(DiIorio et al., 2009)	Low	High	Low	++
(Artinian et al., 2003)	Low	Moderate	Low	+
(Guendelman et al., 2002)	Low	Moderate	Low	++

[a] ++ = significant effect on medication intake behavior; + = moderate effect on medication intake behavior; – = no effect on medication intake behavior.

Role of health providers

Interventions also differ in the type and extent of health provider involvement. User control allows individuals to take a major role in managing their own care, whereas in expert control an expert or therapist takes a more directive role (Lustria et al., 2009). Only 4 of the interventions were based on user control and 9 interventions used contact with the health provider. A web-based asthma management program was developed in 1 study (Joseph et al., 2007). The program used tailoring to alter behavior through individualized health messages based on the user's beliefs, attitudes, and personal barriers to change. The health provider did not interfere. Three studies were also user based with treatment algorithms to give feedback (DiIorio et al., 2009; Van der Meer et al., 2009; Van der Meer et al., 2010). In contrast, in the Blue Angel for Asthma Kids, a customized educational and monitoring website site providing secure email contact between patients and their therapist, the therapist had a more directive role (Jan et al., 2007). Like the Blue Angel for Asthma Kids, SPPARO included a messaging system that made it possible to exchange secure messages with the health provider (Ross et al., 2004). The intervention manager who reviewed the data, sent emails about the peak flow, inhaler technique, and symptoms, and forwarded them the website. Patients (the virtual group as well as the

Table 5.
Effectiveness of long-term interventions (>6 months)

Study	Study quality	Sophistication of tailoring	Quality measurement medication intake behavior	Long-term effectiveness (>6 months)[a]
(Van der Meer et al., 2009)	High	High	Low	+
(Van der Meer et al., 2010)	High	High	Low	+
(Chan et al., 2003)	High	Moderate	High	+
(Joseph et al., 2007)	High	Moderate	Low	++
(Ross et al., 2004)	High	Moderate	Low	+
(Chan et al., 2007)	Low	Moderate	Low	–
(Cherry et al., 2002)	Low	Moderate	Low	+

[a] ++ = significant effect on medication intake behavior; + = moderate effect on medication intake behavior; – = no effect on medication intake behavior.

office-based group) had access to their case manager 24 hours a day, 7 days a week. One study (Dew et al., 2004) conducted a website including skills workshops, discussion group, ask an expert, question and answer, health tips, recourses, and references. In this case, the role of health providers was to provide the possibility for a patient to ask an expert. Several interventions used a special device to exchange information between patients and health care providers. The Med-eMonitor recorded data and answers to questions that could be uploaded by the health provider. Based on these outcomes, the health provider provided advice and updated the treatment regimens (Artinian et al., 2003). The PATH (DeVito Dabbs et al., 2009) recorded data and provided a tailored decision-support program and email contact with the health provider. The Health Buddy device in 2 studies (Cherry et al., 2002; Guendelman et al., 2002) is like the Med-eMonitor and PATH based on the feedback and participation of the health provider, but there is a difference in the intensity of participation of the health provider. In 1 study (Cherry et al., 2002) the health provider contacted the patient only when necessary, while in the other 2 studies (DeVito Dabbs et al., 2009; Guendelman et al., 2002) the patient received feedback instantly after sending a question. Our analysis to examine the extent to which medication intake behavior is determined by different tailoring levels revealed no clear relationship between the intervention's level of sophisticated tailoring and the extent to which the intervention was effective (Table 4).

Summary of effects on successful medication intake behavior

We found 5 studies with a significant effect on medication intake behavior (3 HQ studies and 2 LQ studies; DeVito Dabbs et al., 2009; DiIorio et al., 2009; Guendelman et al., 2002; Jan et al., 2007; Joseph et al., 2007). The first study (Jan et al., 2007) concluded that the intervention had a positive and significant effect on use of the inhaled corticosteroid and that this effect significantly differed from the baseline. In addition, the second study (Joseph et al., 2007) found positive changes in controller medication intake behavior. The third study (DiIorio et al., 2009) tested the WebEase intervention and found a significant

effect on successful medication intake behavior. The fourth study (Guendelman et al., 2002) found that patients were more likely to take their asthma medication when they used the Health Buddy. In the fifth study (DeVito Dabbs et al., 2009), patients who received the PATH intervention were more likely to adhere to their medical regimen. A moderate effect on successful medication intake behavior was reported in 6 studies (4 HQ studies and 2 LQ studies). The SPPARO proved to be feasible and improved general medication intake behavior. Improved medication intake behavior showed a similar trend but these results did not reach significance (Ross et al., 2004). The second study (Chan et al., 2003) concluded that, after the intervention, the use of beta-agonist decreased, which is an indication of improved medication intake behavior. The third study (Cherry et al., 2002) reported that medication intake behavior improved from 65% at pre-test to 94% at post-test, but the difference was not statistically tested. The medication intake behavior rate in the fourth study (Artinian et al., 2003) was 94% for the monitor group as measured by the monitor system. However, because there was no pre-test and the data of the control group were not available, it is unknown whether the results were significant as compared with the pre-test or the control group. The intervention of the last 2 studies (Van der Meer et al., 2009; Van der Meer et al., 2010) improved medication intake behavior in patients with partly and uncontrolled asthma at baseline. The authors concluded that the intervention was most effective in improving medication intake behavior for patients with partly or uncontrolled asthma at baseline. No significant results on patients' successful medication intake behavior were found in 2 studies (1 HQ and 1 LQ) (Chan et al., 2007; Dew et al., 2004).

Assessment of medication intake behavior measurements

Regarding the measurement of medication intake behavior, the 13 studies we reviewed showed a large variability of methods: 12 studies used a low-quality measurement to assess medication intake behavior and 1 used a combination of these methods (i.e., a high-quality measurement to assess medication intake behavior; Table 3).

Low quality of medication intake behavior measurement

In 10 studies, self-reported scales were used to obtain the medication intake behavior rate. Although 5 studies (Guendelman et al., 2002; Jan et al., 2007; Joseph et al., 2007; Van der Meer et al., 2009; Van der Meer et al., 2010) used self-reports to measure medication intake behavior, they did not describe what kind of instrument they used. One study (Dew et al., 2004) used self-reported data by asking questions regarding medication intake behavior during the initial interview. Reports of therapist and patients were compared. In addition, 1 study (Cherry et al., 2002) used a self-developed medication intake behavior survey on the Health Buddy appliance. The other 3 studies chose existing, valid, self-reported medication intake behavior scales. One study (Ross et al., 2004) used a

combination of the Morisky scale and the General Adherence Scale from the Medical Outcomes Study, and one study (DeVito Dabbs et al., 2009) used the Health Habits Assessment, a self-reported scale to measure medication intake behavior. One study (DiIorio et al., 2009) used the self-report USCF Adherence Questionnaire and the Antiretroviral General Adherence Scale. Finally, two studies used measurements such as counting pills (Artinian et al., 2003), and one study (Chan et al., 2007) used a computerized prescription refill record (after evaluation of the pilot study in which completing the diary turned out to be time consuming and inconvenient (see Chan et al., 2003).

High quality of medication intake behavior measurement

One study used a combination of methods. This study (Chan et al., 2003) used a diary in combination with a computerized prescription refill record. Table 3 shows the results of the assessment of the internal validity and the quality of medication intake behavior measurement.

Relation between quality of medication intake behavior measurement and effectiveness

Our investigation of the relationship between the quality of the medication intake behavior measurement and the effectiveness of the interventions revealed no clear relationship (there was only 1 study using a high-quality method to assess medication intake behavior), although self-reported medication intake behavior measurements seemed to result more often in significant effects than did pill counts and pharmacist medication intake behavior measurements (Table 4 and Table 5). Of the 10 studies using self-reports (low-quality medication intake behavior measurement), 5 reported a significant effect of the intervention on medication intake behavior (DeVito Dabbs et al., 2009; DiIorio et al., 2009; Guendelman et al., 2002; Jan et al., 2007; Joseph et al., 2007), 4 a moderate effect (Cherry et al., 2002; Ross et al., 2004; Van der Meer et al., 2009; Van der Meer et al., 2010), and 1 no effect (Dew et al., 2004). From the 2 studies in which pharmacist data or pill counting was used, 1 reported a moderate effect (Artinian et al., 2003) and 1 no effect (Chan et al., 2007). The 1 study that used a combination of methods to measure (Chan et al., 2003) found a moderate effect on medication intake behavior.

Relation between interval of medication intake behavior measurement and effectiveness

There was no clear relationship between the timing of the medication intake behavior measurements and the effectiveness of the intervention. The intervals between baseline and follow-up measurements differed between projects. Short-term medication intake behavior (i.e., within 6 months) was measured in 6 studies. The first study (DiIorio et al., 2009) showed that WebEase improved medication intake behavior 6 weeks after baseline. Patients who used PATH were more likely to show better medication intake behavior than the control group after an interval of 8 weeks after baseline (DeVito Dabbs et al., 2009).

The third study (Jan et al., 2007) found a significant effect on successful medication intake behavior after 12 weeks, and the fourth study (Guendelman et al., 2002) reported an improvement in medication intake behavior after 12 weeks. The fifth study (Artinian et al., 2003) found a successful medication intake behavior rate of 94% in the experimental group after 12 weeks. Because of the lack of medication intake behavior data for the control group and the lack of a pretest, the effects on medication intake behavior could not be established. The sixth study (Dew et al., 2004) examined the proportion of nonadherent patients in both an intervention and a control group after 16 weeks. That study's authors found uniformly small and nonsignificant differences between the control and intervention groups. However, they found an important difference within the intervention group. Subgroup differences appeared when the intensity of using parts of the intervention was related to the effectiveness. For example, patients who used the Managing Medical Regimen Workshop more often or intensely appeared to improve their medication intake behavior than those using the intervention less often or intensely (Dew et al., 2004).

Long-term medication intake behavior was measured in 7 studies—that is, medication intake behavior with an interval of 6 months or longer, mostly of 1 year or more. Two studies (Chan et al., 2003; Van der Meer et al., 2009) reported a moderate effect in their pilot on medication intake behavior after 6 months. In 2 studies (Joseph et al., 2007; Ross et al., 2004), they found a moderate (Ross et al., 2004) and significant (Joseph et al., 2007) improvement in medication intake behavior after 1 year. Two studies (Cherry et al., 2002; Van der Meer et al., 2010) found a moderate effect on medication intake behavior after 1 year. This means that all of the included studies using an interval of 6 months or longer showed an effect (significant or moderate) on long-term successful medication intake behavior. One study (Chan et al., 2007) did not find an effect on successful medication intake behavior after 1 year.

Table 4 and Table 5 give an overview of the methodological quality of the studies, the level of sophistication of each intervention, the quality of measurement of medication intake behavior, and an overview of the short-term and long-term effects.

Data synthesis

Using the principles of the best-evidence synthesis (see Textbox 1), taking into account the design, methodological quality, and outcomes of the studies, the following conclusions can be drawn. In total, 7 studies were considered HQ. We found 3 HQ studies (DeVito Dabbs et al., 2009; Jan et al., 2007; Joseph et al., 2007) and 2 LQ studies (Dilorio et al., 2009; Guendelman et al., 2002) that had a significant effect on improved medication intake behavior and that met 6 of 11 criteria. This means that there is evidence that tailored Internet interventions are successful in improving medication intake behavior.

Sensitivity analysis

The sensitivity analysis showed the same results as the best-evidence synthesis. The results remained the same when the analysis was repeated with the 6 LQ studies excluded (i.e., taking only the 7 HQ studies into account). Moreover, when studies were rated to be HQ if 4 instead of 6 criteria of interval validity were met, results stayed the same.

Discussion

Principal results

First, our objective was to gain insight into the current state of the use of Internet interventions to improve medication intake behavior. Results of this review indicate that this is still a new field. This is visible in the differences in interventions with respect to crucial aspects such as the level of sophisticated tailoring and the role of health care providers. Despite the differences, it is remarkable that none of the interventions used a low level of tailoring and the majority (nine of thirteen) provided the opportunity to contact a health provider.

Second, the studies were assessed on their effectiveness on medication intake behavior. There is evidence that Internet interventions can improve medication intake behavior. This evidence comes from three HQ studies and two LQ studies, finding significant results on medication intake behavior.

Third, we wanted to investigate to what degree medication intake behavior is determined by the characteristics of the intervention. All interventions discussed in this review used tailored methods and used a moderately or highly sophisticated tailored intervention. These types of health programs, especially customized health programs, are more complex, generally long-term, allowing the patients to access the programs several times (Lustria et al., 2009), and are considered appropriate for difficult-to-influence behaviors. We did not find a clear relationship between how sophisticated the tailoring of the intervention was and the extent to which the intervention appeared to be effective, possibly due to the various methods that were used.

Last, we wanted to investigate whether there is a relationship between the characteristics of a study and the reported effectiveness of the interventions. We found that there was variation not only in the level of tailoring, but also in the measurement of medication intake behavior, the timing of measuring medication intake behavior, and the intensity of the intervention. The included studies used self-reporting measurements (i.e., interviews, diary, self-reporting via questionnaires) or pill counts, or prescription refills, or a combination. No study used electronic monitoring, which is perceived as a high-quality method for assessing medication intake behavior (Farmer, 1999). Of the thirteen studies we reviewed, seven measured long-term medication intake behavior, using an interval of six months or longer. There is no clear evidence that the duration of the intervention is related to the effectiveness of the intervention. Nevertheless, of the seven studies

measuring long-term medication intake behavior, one HQ study showed positive effects and four HQ studies and one LQ study showed moderate effects on successful medication intake behavior. This indicates that long-term interventions are promising. However, more research in this field is needed.

There is evidence that Internet interventions can be effective in improving medication intake behavior. The evidence comes from thee HQ studies. However, the results should be interpreted with caution. Self-reported scales were used in 10 studies, which is considered a low-quality medication intake behavior measurement: five reported a significant effect of the intervention on successful medication intake behavior, four a moderate effect, and one no effect. Self-measurements can contribute to overestimating of the effects of interventions (Nieuwkerk & Oort, 2005). This could be explained by the possibility that patients may forget that they missed a dose. Biases that appear most prominent in estimating medication intake behavior by the patient from structured questionnaires are social desirability and social approval (Sluijs et al., 2006; Urquhart & Vrijens, 2005). In other words, studies relying on self-reporting may have a tendency to err on the optimistic side when it comes to medication intake behavior, certainly compared with more objective pill-counting studies. However, it must be noted that anonymous self-report questionnaires are found to be significantly correlated with electronic monitoring (Hugen et al., 2002) and virologic response (Nieuwkerk & Oort, 2005), considered more objective methods. Research also shows that using specific strategies, such as ensuring patients that their responses will be kept confidential (Nieuwkerk & Oort, 2005) or stratifying patients according to their socially desirable response (Nieuwkerk, De Boer-Van der Kolk, Prins, Locadia, & Sprangers, 2010), improves the prediction of medication intake behavior by self-reports. This indicates that self-reports are not useless, but future research should examine more strategies to reinforce accurate reporting by patients (Nieuwkerk & Oort, 2005). On the other hand, we included RCTs and, consequently, self-reported medication intake behavior can be expected to be overestimated in both treatment arms. Thus, the intervention effect (i.e., difference between intervention and control group) was not necessarily overestimated. Additionally, a distinction can be made between valid self-report measurements and measurements that are not. If self-reported measurements are used, for instance because this is a cost-effective method, using validated measurements is recommended.

Electronic monitoring or observation is considered to be more accurate. It electronically records the time and date of the actual dosing events. Because every single method has its limitations, the best approach is to use multiple assessment techniques concurrently, as a way to improve the accuracy of medication intake behavior assessment (Wetzels et al., 2006). One study in our review (Chan et al., 2003) used self-reported diary and prescription refills to measure medication intake behavior and made a distinction in interpreting the results. They used a self-reported diary to assess how the patients used

their inhaler, based on the idea that when patients are not using their inhaler according to the health providers' advice, they can be considered nonadherent. In addition, they used prescription refills to measure how many refills the patient was obtaining. In line with this method of measuring medication intake behavior, the optimal approach could be suggested to be a combination of self-reports and more objective measurements (Drotar, 2000). In addition, every single measurement needs a different interpretive approach because it has different relationships to clinical outcomes (Sluijs et al., 2006).

Of the studies we reviewed, six measured short-term medication intake behavior that varied from six weeks to four months: four of them were found highly effective and one moderately effective regarding medication intake behavior. The question is whether medication intake behavior improved in the long term, because the period was too short to measure persistence. According to an international expert forum on medication intake behavior (Sluijs et al., 2006), it is not easy to identify adherent and nonadherent patients beforehand. There is a large body of evidence dominated by reports identifying factors that are predictive or associated with nonadherence. Medication intake behavior could be seen as a dynamic behavior that is determined or influenced by unrelated factors that fluctuate and change over time (Reynolds, 2004). As an adherent patient can become nonadherent over time, the importance of time (i.e., persistence) has been emphasized (Urquhart & Vrijens, 2005). The quality of execution of the treatment plan can influence persistence. Factors such as perceptions of treatment outcomes, beneficial effects, and adverse effects can influence the quality of execution over time. Therefore, conducting interventions that address long-term medication intake behavior and overcome reasons why a patient is not able or not willing to adhere are recommended.

Methodological limitations

The search method was top-down in that we relied on existing databases and search terms. This approach has the possibility of missing important articles due to miscoding of search terms. A bottom-up strategy is more time consuming but has the advantage of being more comprehensive.

Clinical implications

Monitoring medication intake behavior to optimize effects and minimize nonadherence could be time consuming. Computers, however, are very good at collecting data concerning the monitoring of medication intake behavior. Internet interventions can be tailored, collect data, and monitor medication intake behavior. In addition, based on this systematic literature review, there is evidence that tailored Internet interventions can be an effective method to improve medication intake behavior. This means that Web-based interventions can be effective at increasing medication intake behavior among chronically ill patients. Health providers, who want to enhance patients' medication intake behavior,

are encouraged to use tailored websites or reminder systems. They could use these interventions in addition to their everyday work.

Implications for research

Because we did not find a clear relationship between the effectiveness and the degree of tailoring, we recommend that future studies should be conducted with variation in the level of sophistication of tailoring to further test which characteristics of the tailored messages have the most positive effects on successful medication intake behavior. Moreover, website compliance is often not completely reported. While the frequency in which the patient used the website is often reported, studies do not describe how exactly patients used the website. Therefore, it is difficult to compare the results of different interventions, because the way patients use the website can have implications for the effectiveness of the website.

Conclusion

With more than 40 million people using the Internet for a variety of purposes, health communication programs in the future are more likely to be delivered online (Kreuter & Wray, 2003). These types of interventions especially have the potential to address difficult-to-change behaviors such as successful medication intake behavior. This review shows promising results on the effectiveness of tailored Internet interventions to enhance successful medication intake behavior of chronically ill patients. There is evidence that these interventions can enhance successful medication intake behavior. But it remains a relatively new field, and studies using more objective measurements to assess medication intake behavior are recommended.

Chapter 3

The effectiveness of interventions using electronic reminders to improve medication intake behavior[2] to chronic medication: a systematic review of the literature.

Patient: "I cannot remember those things, and then, my mother asks what you told me, and I just don't remember…". Nurse: "Well, there is something like a SMS-alert that you can use so that you cannot forget" (male, 25 years old, Crohn's disease).

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[2] For the purpose of this dissertation, the term adherence is changed into medication intake behavior

Abstract

Background: Many patients experience difficulties in adhering to long-term treatment. Although patients' reasons for not being adherent are diverse, one of the most commonly reported barriers is forgetfulness. Reminding patients to take their medication may provide a solution. Electronic reminders (automatically sent reminders without personal contact between the healthcare provider and patient) are now increasingly being used in the effort to improve medication intake behavior.

Objective: To examine the effectiveness of interventions using electronic reminders in improving patients' medication intake behavior to chronic medication.

Methods: A comprehensive literature search was conducted in PubMed, Embase, PsycINFO, CINAHL and Cochrane Central Register of Controlled Trials. Electronic searches were supplemented by manual searching of reference lists and reviews. Two reviewers independently screened all citations. Full text was obtained from selected citations and screened for final inclusion. The methodological quality of studies was assessed.

Results: Thirteen studies met the inclusion criteria. Four studies evaluated short message service (SMS) reminders, seven audio-visual reminders from electronic reminder devices (ERD), and two pager messages. Best evidence synthesis revealed evidence for the effectiveness of electronic reminders, provided by eight (four high, four low quality) studies showing significant effects on patients' medication intake behavior, seven of which measured short-term effects (follow-up period <6 months). Improved medication intake behavior was found in all but one study using SMS reminders, four studies using ERD and one pager intervention. In addition, one high quality study using an ERD found subgroup effects.

Conclusion: This review provides evidence for the short-term effectiveness of electronic reminders, especially SMS reminders. However, long-term effects remain unclear.

Introduction

Medication intake behavior is the extent to which a person's behavior taking medication and/or executing lifestyle changes corresponds with agreed recommendations from a healthcare provider (Sabaté, 2003). Many patients, especially those with chronic illnesses, experience difficulties in adhering to prescribed treatment. Average medication intake behavior rates to long-term treatment are low (DiMatteo, 2004; Sabaté, 2003). Poor medication intake behavior compromises the effectiveness of medication treatment and results in suboptimal illness control. This can lead to increased use of healthcare services, reduction in patients' quality of life, and increased healthcare costs (Roebuck, Liberman, Gemmill-Toyama, & Brennan, 2011; Simpson et al., 2006; Sokol, McGuigan, Verbrugge, & Epstein, 2005). Numerous interventions aimed at improving medication intake behavior have been conducted, but these were mostly complex and not very effective (Haynes et al., 2008). Complex interventions are often time consuming, labour intensive and costly, thus not feasible in busy clinical practice. According to experts in the field of medication intake behavior, simple interventions, i.e. interventions that are workable in daily practice and that are easy for both professional and patient, appear to be most promising in furthering patients' medication intake behavior (Van Dulmen et al., 2008). An example of a simple intervention is reminding patients of their medication intake. Reminders can especially provide a solution for patients who are unintentionally non-adherent, i.e. patients who are willing to take their medication but forget it or are inaccurate with their timing (Wroe, 2002). Forgetfulness is commonly reported as a barrier to successful medication intake behavior in various patient populations (Bartlett, 2002; Bregnballe, Schiøtz, Boisen, Pressler, & Thastum, 2011; Lawson et al., 2011; Nair et al., 2011; Odegard & Gray, 2008; Olthoff, Hoevenaars, van den Borne, Webers, & Schouten, 2009; Roberts, 2000; Walker et al., 2006; Wu, Moser, Lennie, & Burkhart, 2008; Zelikovsky, Schast, Palmer, & Meyers, 2008). Albeit the range of patients reporting this barrier varies from 22% to 73% across the studies, in all studies forgetting to take a dose was the most frequently cited reason for non-adherence.

Two reviews on the effectiveness of 'reminder packaging', which refers to any medication package (e.g., a pill box, blister package, bottle) that physically incorporates a system for the day and/or time for medication to be taken, reported modest improvements in medication intake behavior to long-term medications (Mahtani, Heneghan, Glasziou, & Perera, 2011; Zedler, Kakad, Colilla, Murrelle, & Shah, 2011). However, patients are not actively reminded with this type of packaging. Studies evaluating the effect of personal and thus active reminders, such as telephone calls or emails from healthcare providers to patients, revealed positive effects on medication intake behavior rates (Contreras et al., 2005; Waalen, Bruning, Peters, & Blau, 2009). However, personal reminders can require an extensive time investment from healthcare

providers. Electronic reminders, on the contrary, are automatically sent to patients at the appropriate time without interference of a healthcare provider. Examples are reminder messages automatically sent to a patient's mobile phone with a short message service (SMS), an electronic reminder device (ERD) that provides patients with an audio and/or visual reminder at predetermined times, or text messages sent to patients' pager to alert them of their medication. This type of reminding does not require additional effort from professionals and may be easy to integrate in patients' daily life.

Interventions using reminders are primarily based on the principles of behavioral learning theory (Leventhal & Cameron, 1987). According to this theory, behavior depends on stimuli or cues, either internal (thoughts) or external (environmental cues), suggesting that non-adherent behavior can be modified after sufficient repetition of external stimuli or cues such as reminders.

With the increasing use of electronic reminders aimed at improving medication intake behavior, there is a need to gain insight into the effects of this type of reminding. Previous reviews evaluating strategies for improving medication intake behavior among electronic reminders often focused on specific patient populations. For example, Gray and colleagues (2009) found that a reminder device might be beneficial to patients with glaucoma. Wise and Operario (2008) showed that half of the studies included in their review reported significantly improved medication intake behavior in HIV patients as a result of ERD. Misono and colleagues (2010) reviewed studies using healthcare information technology interventions to improve medication intake behavior to cardiovascular and diabetes medication, and showed that of these interventions, reminder systems provided the best evidence for increasing medication intake behavior. To our knowledge, no review has been conducted that systematically studied the effects of specifically electronic reminding (e.g., via SMS, ERD, pager/beeper systems) on patients' medication intake behavior to a range of long-term medication. Therefore, in this systematic review, we aim to synthesize and critically appraise the existing evidence on the effectiveness of electronic reminders in improving patients' medication intake behavior to chronic medication. In addition, we aim to investigate the characteristics of electronic reminders that are associated with their effectiveness.

Methods

This review was conducted according to the guidelines of the Cochrane Collaboration described in the Cochrane handbook for systematic reviews of interventions, version 5.1.0 (updated March 2011; Higgins et al., 2008).

Inclusion criteria

A study was included in this review if it met the following inclusion criteria: (1) the intervention was aimed at patients who were prescribed chronic medication; (2) the intervention involved an electronic reminder aimed at improving medication intake behavior; (3) the reminder was directed to the patient; (4) one of the outcome measures was medication intake behavior; (5) the study design was either a randomized controlled trial (RCT) or a controlled clinical trial (CCT); (6) the study was published in English. Studies using historical controls were excluded, as possible bias may be introduced due to factors (other than the intervention) that may have changed over time. We defined an electronic reminder as an automatically sent reminder without personal contact between healthcare provider and patient. Consequently, telephone calls, emails or SMS personally sent by healthcare providers were excluded.

Search strategy

We conducted a comprehensive literature search in PubMed, Embase, PsycINFO, CINAHL and the Cochrane Central Register of Controlled Trials. We used the following MeSH terms and keywords for searching PubMed: (medication adherence OR patient compliance OR medication therapy management) AND (cellular phone OR reminder systems OR text message OR electronic reminder) AND (intervention study OR randomized controlled trial OR controlled clinical trial). Advanced search, allowing for explosion search, mapping to preferred terminology, searching keywords or in all text was used in the other databases whenever possible. No restriction on publication date was applied. The electronic databases were last searched on 7 March 2011. Electronic searches were supplemented by manual searching of reference lists of relevant reviews ('snowball method').

Review procedures

Reference Manager 11.0 was used to manage all citations. Independently, three reviewers (MV as first reviewer and either AJL or LvD as second reviewer) screened all citations (title and abstract) identified by the electronic and manual searches. Full text was obtained for the potentially eligible studies and for those for which we had insufficient information. The interrater agreement between MV and AJL and MV and LvD was 92% and 97%, respectively. Full text articles were reviewed independently by AJL and MV for final inclusion in the review according to the inclusion criteria mentioned earlier. Reasons for exclusion of studies at this stage are given in supplementary Appendix 3. Disagreements between reviewers were resolved by discussion.

Data extraction

MV extracted the following study characteristics (see table 1 and supplementary Appendix 4):

1. General information (first author, year of publication)
2. Study design
3. Study population (sample size, age, gender, medication/disease)
4. Intervention (description of experiment and control condition, type of reminder)
5. Medication intake behavior measure (type of measurement, follow-up period)
6. Main study results
7. Authors' conclusion.

Methodological quality

The methodological quality of the studies was assessed independently by AJL and MV according to the criteria list from the Cochrane Collaboration Back Review Group (Van Tulder et al., 2003). This list addresses 11 criteria for identifying potential sources of bias:

1. Selection bias (three criteria), referring to systematic differences between participants in the different groups: (a) proper generation of allocation sequence; (b) proper concealment of treatment allocation; and (c) comparability of groups at baseline.
2. Performance bias (four criteria), referring to systematic differences between the groups in the care provided to participants, apart from the intervention that is evaluated: (d) participants kept blind to treatment allocation; (e) care providers kept blind to treatment allocation; (g) co-interventions were avoided or were similar for all groups; (h) compliance was acceptable in all groups.
3. Attrition bias (two criteria), referring to systematic differences between the groups in participants who drop out and those who remain: (i) proper description of and acceptability of drop-out rate; (k) analysis according to intention-to-treat principle.
4. Detection bias (two criteria), referring to bias in how outcomes are ascertained, diagnosed or verified: (f) outcome assessor kept blind to participants' exposure to intervention; (j) timing of outcome assessment was similar in all groups. Each criterion was scored with a 'yes', 'unclear ' or 'no', where 'yes' indicates the criteria have been met and thus suggest a low risk of bias. The methodological quality of a study was considered high when six or more criteria were met. Disagreements between the reviewers were resolved by discussion.

Data syntheses and sensitivity analysis

It was not possible to perform a meta-analysis because of the heterogeneity of methods and interventions used. Therefore, a best evidence synthesis (BES) was conducted, based on the one proposed by van Tulder et al (2003) and adapted by Steultjens and colleagues (2009). This synthesis takes the design, methodological quality and outcomes of the studies into account and attributes various levels of evidence to the

effectiveness of interventions. Box 1 presents the principles of BES. Sensitivity analysis was performed to identify how sensitive the results of BES are to changes in the way this synthesis was performed. For the sensitivity analysis, BES was repeated in two ways: low quality studies were excluded; studies were classified as high quality if they met four instead of six internal validity criteria.

Textbox 1: Principles of Best Evidence Synthesis

Evidence: Provided by consistent significant findings in outcome measures in at least two high quality RCTs.
Moderate evidence: Provided by consistent significant findings in outcome measures in at least one high quality RCT and at least one low quality RCT or high quality CCT.
Limited evidence: Provided by significant findings in outcome measures in at least one high quality RCT **or** provided by consistent significant findings in outcome measures in at least two high quality CCTs (in the absence of high quality RCTs).
Indicative findings: Provided by significant findings in outcome measures in at least one high quality CCT or low quality RCT (in the absence of high quality RCTs).
No/Insufficient evidence: If the number of studies that show evidence is less than 50% of the total number of studies found within the same category of methodological quality and study design **or** if the results of eligible studies do not meet the criteria for one of the above stated levels of evidence **or** in case of conflicting (significantly positive and significantly negative) results among RCTs and CCTs **or** in case of no eligible studies.

Categorization of intervention study outcomes

We categorized the type of electronic reminder in three categories: SMS reminder; audio/visual reminder from ERD; and reminder via pager systems. The effect of the intervention was also categorized in three categories: overall effect; subgroup effect; and no effect on medication intake behavior. Any effect, either overall or in subgroups, needed to be statistically significant ($p < 0.05$). Furthermore, we investigated both short-term (follow-up period < 6 months) and long-term (follow-up period > 6 months) effects.

Results

A total of 813 hits, 527 of which were unique, resulted from the electronic database searches. Searching references from reviews provided six potentially relevant studies. After screening the title and abstract, 491 references were excluded because they did not meet the inclusion criteria. Of the remaining 42 references, full text was obtained and assessed for inclusion in the review. Details on excluded studies in this stage are given in supplementary Appendix 3. Finally, a total of 13 studies met all inclusion criteria (see Figure 1).

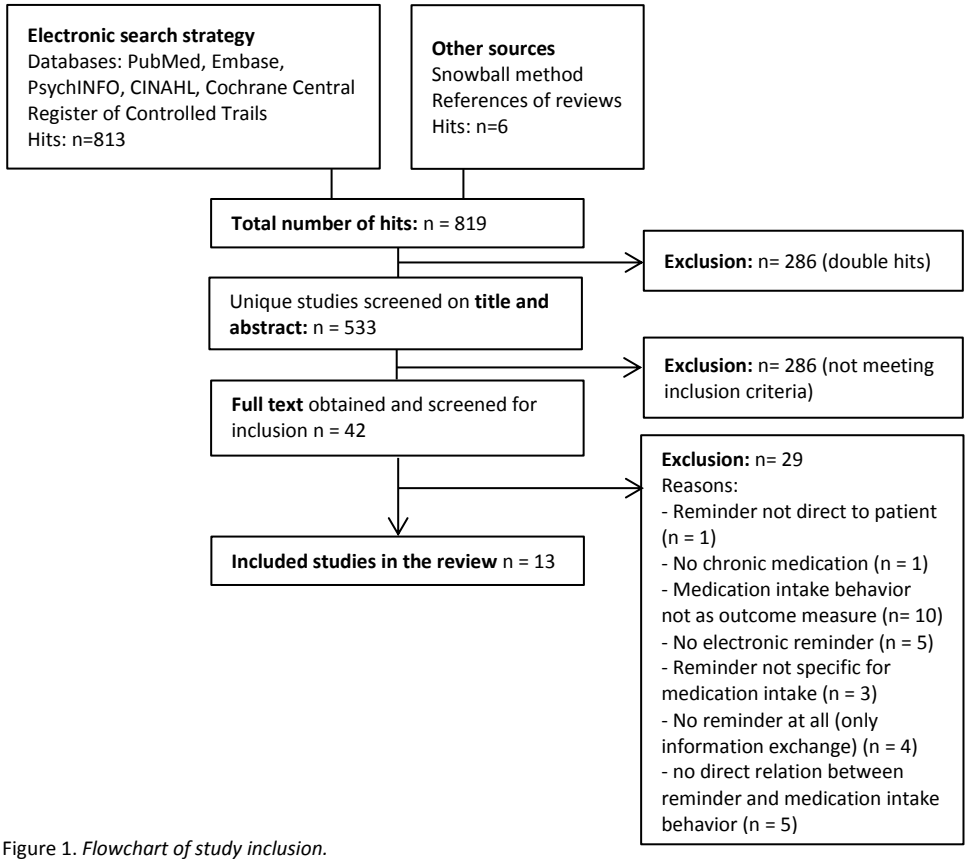

Figure 1. *Flowchart of study inclusion.*

Description of the studies

Table 1 shows the main characteristics of the 13 included studies (for a more detailed description, see supplementary Appendix 4). The study population varied: patients on antiretroviral therapy (five studies; Andrade et al., 2005; Hardy et al., 2011; Pop-Eleches et al., 2011; Safren, Hendriksen, Desousa, Boswell, & Mayer, 2003; Simoni et al., 2009) patients with hypertension (three studies; Christensen et al., 2010; Costa et al., 2005; Santschi, Wuerzner, Schneider, Bugnon, & Burnier, 2007) patients with asthma (two studies; Charles et al., 2007; Strandbygaard, Thomsen, & Backer, 2010), patients with glaucoma (two studies;Ho, Camejo, Kahook, & Noecker, 2008; Laster, Martin, & Fleming, 1996), and women using oral contraceptives (one study; Hou, Hurwitz, Kavanagh, Fortin, & Goldberg, 2010). All studies involved adult patients, except for one study that also included adolescents aged 13 years or older (Charles et al., 2007). The duration of medication use varied across the studies and also within the studies. Seven studies included patients initiating or changing treatment (Andrade et al., 2005; Charles et al., 2007; Christensen et al., 2010; Ho et al., 2008; Hou et al., 2010; Pop-Eleches et al., 2011;

Simoni et al., 2009), four studies included patients currently using medication (Costa et al., 2005; Hardy et al., 2011; Laster et al., 1996; Safren, Hendriksen, Desousa, Boswell, & Mayer, 2003), and two studies included both new and current users (Santschi, Wuerzner, Schneider, Bugnon, & Burnier, 2007; Strandbygaard et al., 2010). Four interventions tested the effect of SMS reminders on patients' medication intake behavior (Hardy et al., 2011; Hou et al., 2010; Pop-Eleches et al., 2011; Strandbygaard et al., 2010) seven studies evaluated an ERD with audiovisual medication reminders (Andrade et al., 2005; Charles et al., 2007; Christensen et al., 2010; Costa et al., 2005; Ho et al., 2008; Laster et al., 1996; Santschi et al., 2007) and two studies concentrated on the effect of a pager reminder (Safren et al., 2003; Simoni et al., 2009). Almost half of the studies used multiple measures to assess medication intake behavior. Electronic monitoring (electronically registering the date and time of every medication intake) was used in 11 studies. Six studies exclusively used electronic monitoring (Charles et al., 2007; Ho et al., 2008; Pop-Eleches et al., 2011; Safren et al., 2003; Santschi et al., 2007; Strandbygaard et al., 2010), four combined electronic monitoring with self-report (Andrade et al., 2005; Christensen et al., 2010; Hou et al., 2010; Simoni et al., 2009) and one combined electronic monitoring with both pill count and self-report (Hardy et al., 2011). One study exclusively used pill count (Costa et al., 2005), one study assessed bottle weight (medication in soluble form) with self-report (Laster et al., 1996). Only three studies followed patients for a period of 6 months or longer (Christensen et al., 2010; Pop-Eleches et al., 2011; Simoni et al., 2009).

Methodological quality

The methodological quality (risk of bias) of the thirteen included RCTs was assessed. Seven studies were classified as high quality studies, six studies were considered low quality (Table 2).

Effectiveness of interventions

Tables 3 and 4 summarize the effects on medication intake behavior, methodological quality of the studies, and characteristics of the intervention (studied medication, type of electronic reminder, and type of medication intake behavior measurement), by length of follow-up period. Eight (four high and four low quality) studies reported significant overall effects on patients' medication intake behavior as a result of an electronic reminder. Hardy and colleagues (2011) compared the medication intake behavior of HIV patients receiving SMS reminders with patients using a beeper as a reminder and found a significant difference in favor of SMS reminding. Strandbygaard and colleagues (2010) revealed that medication intake behavior rates of asthma patients who received daily SMS reminders were higher than those of patients who were not reminded. The third study also focused on asthma patients and found that an ERD with an audiovisual reminder significantly improved medication intake behavior (Charles et al., 2007).

Table 2.
Methodological quality of included RCTs

Study	Validity criteria met[a]	Methodological quality[b]
Hardy 2011	a, b, c, g, h, i, j	High
Pop-Eleches 2011	a, c, g, h, i, j, k	High
Hou 2010	a, b, c, f, g, h, i, j, k	High
Strandbygaard 2010	a, c, g, h, i, j	High
Simoni 2009	a, b, c, g, h, i, j, k	High
Charles 2007	a, b, c, g, h, i, j	High
Andrade 2005	c, g, h, i, j, k	High
Christensen 2010	c, g, h, j	Low
Ho 2008	g, h, j	Low
Santschi 2007	a, g, h, i	Low
Da Costa 2005	c, g, h, j	Low
Safren 2003	c, g, h, j, k	Low
Laster 1996	g, h, i, j	Low

[a] selection bias: criteria a, b, c; performance bias: criteria d, e, g and h; attrition bias: criteria i and k; detection bias: criteria f and j.
[b] high quality: 6 or more criteria met; low quality: 5 or less criteria met

Two other studies also used an ERD with audiovisual reminders, both in patients with glaucoma, and found higher medication intake behavior rates in patients receiving these reminders (Ho et al., 2008; Laster et al., 1996). Da Costa and colleagues (2005) reported significant differences in medication intake behavior between patients with hypertension who used a reminder alarm card that produced a beep at predetermined times, and patients who did not. Safren and colleagues (2003) revealed improvements in medication intake behavior in patients with HIV as a result of reminder messages sent to patients' pagers. The last study found that patients who were reminded once a week had higher medication intake behavior rates than patients reminded daily or patients not reminded at all (Pop-Eleches et al., 2011). One (high quality) study revealed significant effects in a subgroup of the intervention group; Andrade and colleagues (2005) found that an ERD with audiovisual reminders significantly improved medication intake behavior in memory-impaired patients (assessed with neuropsychological tests), but not in memory-intact patients. Finally, four (two high and two low quality) studies, two of which measured the impact of the reminder on multiple time points, showed no effects on medication intake behavior at any time point (Christensen et al., 2010; Hou et al., 2010; Santschi et al., 2007; Simoni et al., 2009).

Table 1.

Main characteristics of included studies (ranked according to type of reminder and year of publication)

Author, year of publication, study design	Study population	Type of reminder	Description of intervention	Type of medication intake behavior measure	Timing of medication intake behavior measurement	Main findings
Hardy 2011 RCT parallel	Adult patients with HIV (n=19)	SMS (versus beeper)	Daily personalized (by adding info on topic chosen by patient, e.g. news, weather, sports) text messages sent for each dose scheduled by caregiver. Response with text message required. If no response given, the phone would beep every 15 min.	Self-report, pill count, electronic monitoring, CAS	Baseline, week 3 and week 6.	Significant difference in medication intake behavior at week 3 and 6 were found in favor of the SMS, when measured with electronic monitoring and CAS. No differences were found with self-report nor pill count.
Pop-Eleches 2011 RCT parallel	Adult patients with HIV (n=428)	SMS	Four interventions: 1) daily short reminder; 2) daily long reminder; 3) weekly short reminder; 4) weekly long reminder. Short message: "This is your reminder", long message providing additional support: "This is your reminder. Be strong and courageous, we care about you". Message was sent at 12:00. No response required.	Electronic monitoring	Every 12-week period in 48 weeks.	Weekly reminders significantly increased percentage of participants achieving 90% medication intake behavior by 13–16%. No differences were found between long and short reminders. Daily reminders did not improve medication intake behavior.
Hou 2010 RCT parallel	Women on oral contraceptives (n=73)	SMS	Daily text message "Please remember to take your birth control pill" sent at a designated time chosen by patient. No response required.	Self-report and electronic monitoring	Every month for 3 months.	No difference in mean number of missed pills per cycle with either self-report or electronic monitoring between women who received SMS reminders and women who did not.

Author, year of publication, study design	Study population	Type of reminder	Description of intervention	Type of medication intake behavior measure	Timing of medication intake behavior measurement	Main findings
Strandbygaard 2010 RCT parallel	Adult patients with asthma (n=26)	SMS	Daily text message "Remember to take your asthma medication morning and evening. From the Respiratory Unit" sent at 10:00. No response required.	Electronic monitoring	Week 4 and week 12.	Patients who received a daily SMS reminder remembered to take, on average, significantly more doses (about 18%).
Christensen 2010 RCT cross-over	Adult patients with hypertension (n=398)	ERD with audiovisual reminder	Use of HHDC device operated with tablet blister packs which gives an audiovisual reminder when it is time to take the medication.	Self-report and electronic monitoring	At month 6 and month 12 (after cross-over).	Use of the HHDC device with reminders did not lead to significant improvement in medication intake behavior.
Ho 2008 RCT parallel	Adult patients with glaucoma (n=42)	ERD with audiovisual reminder	Use of TDA which has a LCD screen that displays a flashing eye drop symbol on the front and emits a beep when patients are supposed to give themselves a dose of medication.	Electronic monitoring	At 3-5 weeks.	Significant differences in mean adherence and rate of missed doses between patients using TDA with reminders and patients using TDA without reminders.

Author, year of publication, study design	Study population	Type of reminder	Description of intervention	Type of medication intake behavior measure	Timing of medication intake behavior measurement	Main findings
Charles 2007 RCT parallel	Adult and adolescent patients with asthma (n=90)	ERD with audiovisual reminder	Use of SmartInhaler which emitted a beep at predetermined times (selected by patient) once every 30 sec for 60 min and stopped if device was actuated or after 60 min. Device had a light which was green before actuation, changing to red once the dose was taken.	Electronic monitoring	Baseline and week 6, 12, 18 and 24.	Use of SmartInhaler with reminders significantly improved medication intake behavior from 74% to 93%. Around 1 in 4 patients using the device with reminders had <50% medication intake behavior, compared with 1 in 20 patients using it without reminders.
Santschi 2007 RCT cross-over	Adult patients with hypertension (n=24)	ERD with audiovisual reminder (versus MEMS caps)	Use of IDAS II that accommodates blister packs. Visual reminder (indicating time elapsed since last dose) and audible reminder, which sounds at chosen time for 1 min or until device is opened, and can be deactivated upon request.	Electronic monitoring	Baseline and month 2 and 4 (after cross-over).	Median taking adherence was high and did not differ between patients using IDAS II and patients using MEMS caps. Regularity of drug intake timing was significantly higher with IDAS II compared to MEMS.
Andrade 2005 RCT parallel	Adult patients with HIV (n=58)	ERD with audible reminder	Use of DMAS device programmed with reminder messages and dosing times for each medication in the HAART regimen.	Self-report and electronic monitoring	Week 4, 8, 12, 16, 20 and 24.	No differences in medication intake behavior between patients who used DMAS and patients who did not. Stratified to memory impairment: significantly higher medication intake behavior in memory-impaired patients using DMAS than memory-intact patients using DMAS.

Author, year of publication, study design	Study population	Type of reminder	Description of intervention	Type of medication intake behavior measure	Timing of medication intake behavior measurement	Main findings
Da Costa 2005 RCT parallel	Adult patients with hypertension (n=71)	ERD with audible reminder	Use of alarm card set up to beep every day at fixed time, preselected by pharmacist and/or patient. If alarm was ignored, it would beep every 20s for 3h, then stop and re-initiate 8h later, beeping every 20s for 1h.	Pill count	Baseline and month 1, 2 and 3.	Medication intake behavior of patients using the reminder alarm card was higher at all timepoints than that of patients not using this card, reaching statistical significance at the third month (mean medication intake behavior difference 10%).
Laster 1996 RCT cross-over	Adult patients with glaucoma (n=13)	ERD with audiovisual reminder	Use of TimeCap, a medication alarm device serving as cap on medication bottle. It has a digital display that shows time and day of week when the vial was last opened and an alarm that beeps when a dose is due. If the beep is ignored, the digital face flashes to provide a visual reminder that a dose has been missed.	Self-report and amount of solution used estimated by weighing of bottle	At day 30 and 60.	Patients using TimeCap with reminders administered significantly more eye drops (about one additional dose of pilocarpine per day) than patients who did not use TimeCap.

Author, year of publication, study design	Study population	Type of reminder	Description of intervention	Type of medication intake behavior measure	Timing of medication intake behavior measurement	Main findings
Simoni 2009 RCT parallel	Adult patients with HIV (n=224)	Two-way pager system	Three interventions: 1) peer support: 6 peer meetings and weekly phone calls from peers to participants. 2) use of two-way pager system: study coordinator customized message schedule to patients' daily regimen. In addition to dose reminders, 3 other messages were sent: a) educational; b) entertainment; c) medication intake behavior assessments. Minimum of 3 pager messages sent daily for 2 months. Pages gradually tapered in third month. Confirmation page was requested. 3) peer support and pager combined.	Self-report and electronic monitoring	At month 3, 6 and 9.	Pager support did not have a significant effect on medication intake behavior at 3, 6, or 9 months either measured with self-report or EM.
Safren 2003 RCT parallel	Adult patients with HIV (n=70)	One-way pager system	Study staff used website to input patients' schedule of daily pages which is linked to paging service delivering messages (e.g. ''Take 2 Combivir with water'' every day at 9:00, ''Take the 2 blue pills now'') to patients' pagers at designated times. Study staff could incorporate other reminders (e.g. timing of meals, appointments). No response required.	Electronic monitoring	Baseline and week 2 and 12.	Patients using the pager system revealed greater improvements in medication intake behavior at week 2 and 12 than patients who are only monitored. But at both assessment points, medication intake behavior was less than optimal (<70%).

CAS, composite medication intake behavior score; DMAS, disease management assistance system; ERD, electronic reminder device; HAART, highly active antiretroviral therapy; HHDC, helping hand data capture; IDAS II, intelligent drug administration system; RCT, randomized controlled trial; SMS, shortmessage service; TDA, travatan dosing aid.

Table 3.

Characteristics and effectiveness of interventions with a short-term follow-up period (<6 months)

Study	Medication for	Type of reminder	Study quality	Short-term effect[a] on medication intake behavior measured with:		
				EM[b]	self-report	pill count
Hou	contraception	SMS	high	–	–	
Hardy	HIV	SMS	high	++	–	–
Strandbygaard	asthma	SMS	high	++		
Charles	asthma	ERD	high	++		
Andrade	HIV	ERD	high	+	–	
Ho	glaucoma	ERD	low	++		
Santschi	hypertension	ERD	low	–		
Da Costa	hypertension	ERD	low			++
Laster	glaucoma	ERD	low		++	++[c]
Safren	HIV	pager	low	++		

[a] ++ = overall effect; + = subgroup effect; – = no effect.

[b] EM = electronic monitoring

[c] amount of eye drops left estimated by bottle weight

Table 4.

Characteristics and effectiveness of interventions with a long-term follow-up period (≥6 months)

Study	Medication for	Type of reminder	Study quality	Long-term effect[a] on medication intake behavior measured with:	
				EM[b]	self-report
Pop-Eleches	HIV	SMS	high	++	
Simoni	HIV	pager	high	–	–
Christensen	hypertension	ERD	low	–	–

[a] ++ = overall effect; + = subgroup effect; – = no effect.

[b] EM = electronic monitoring

Relation between type of reminder and effects

Four studies used SMS reminders, three of which showed significant positive effects on medication intake behavior. Those studies used either personalized text messages that requested a reply from patients when taking the medication (Hardy et al., 2011), or standardized text messages without requiring acknowledgment (Pop-Eleches et al., 2011; Strandbygaard et al., 2010). The study revealing no effect used standardized messages without requesting a reply (Hou et al., 2010). Four of the seven studies evaluating audio/visual reminders from ERD significantly improved patients' medication intake behavior. Three of them used an ERD that produced both an audible and visual reminder (Charles et al., 2007; Ho et al., 2008; Laster et al., 1996), the fourth used an ERD that only emitted an audible reminder (Costa et al., 2005). The one study that found a subgroup effect evaluated an ERD with an audible reminder (Andrade et al., 2005). Two studies showed no effects, both of them used an ERD that accommodated blister packs (Christensen et al., 2010; Laster et al., 1996). Two interventions used pagers, one of which revealed a significant effect (Safren et al., 2003). This study delivered standardized text messages to patients' pagers at predetermined times and requested no reply (Safren et al.,

2003). The pager intervention revealing no effects delivered a minimum of three pager messages daily and a confirmation return page was requested for every message (Simoni et al., 2009).

Relation between length of the follow-up period and effects

Ten studies had a follow-up period shorter than 6 months. Within this group, all but two studies revealed significant overall effects (Andrade et al., 2005; Charles et al., 2007; Costa et al., 2005; Hardy et al., 2011; Ho et al., 2008; Laster et al., 1996; Safren et al., 2003; Strandbygaard et al., 2010) or a subgroup effect (Andrade et al., 2005). The follow-up period varied from 3 weeks to 3 months. In contrast, only one of three studies following patients for over 6 months reported significant effects. That study followed patients for 48 weeks (Pop-Eleches et al., 2011). The two studies reporting no effects followed patients for 9 (Simoni et al., 2009) and 12 months (Christensen et al., 2010).

Relation between type of medication intake behavior measurement and effects

Eleven studies used electronic monitoring as a method to measure medication intake behavior. Six of them reported significant overall effects, (Charles et al., 2007; Hardy et al., 2011; Ho et al., 2008; Pop-Eleches et al., 2011; Safren et al., 2003; Strandbygaard et al., 2010) one found a subgroup effect (Andrade et al., 2005). In addition to electronic monitoring, five studies used self-report to measure medication intake behavior. Two of those studies showed inconclusive results between the two methods: significant effects were only found when medication intake behavior was measured with electronic monitoring, not with self-report (Andrade et al., 2005; Hardy et al., 2011). One study also used pill count as a third method for measuring medication intake behavior, but again effects were only found with electronic monitoring (Hardy et al., 2011). One study exclusively using pill count (Costa et al., 2005) as well as a study using 'pill count' (or weight of medication solution) combined with self-report (Laster et al., 1996) showed significant effects on medication intake behavior.

Other characteristics

The number of patients participating in the studies was often limited: six studies included fewer than 30 patients in each arm. Despite this limited sample size, four of them revealed significant effects (Hardy et al., 2011; Ho et al., 2008; Laster et al., 1996; Strandbygaard et al., 2010) and one a subgroup effect (Andrade et al., 2005) on medication intake behavior. In addition, four studies included between 30 and 50 patients in each arm, three of which showed significant effects (Charles et al., 2007; Costa et al., 2005; Safren et al., 2003). Of the three studies that included more than 50 patients in each arm, one study reported significant effects (Pop-Eleches et al., 2011).

BES and sensitivity analysis

Seven of the 13 included RCT were classified as high quality studies. Four of them reported significant overall effects, three of which were effects measured short term (<6 months follow-up). In addition, four low quality studies found significant effects, all short term. Only one high quality study found significant effects measured long term (6 months or longer follow-up). Using the principles of BES (see box 1), these results indicate that there is evidence of the short-term effectiveness of electronic reminders in improving patients' medication intake behavior to medication. Regarding the type of electronic reminder, there is evidence resulting from three high quality studies of the effectiveness of SMS reminders in improving medication intake behavior (Hardy et al., 2011; Strandbygaard et al., 2010). Moderate evidence was found for audiovisual reminders from ERD as a strategy to improve medication intake behavior, as one high quality and three low quality studies found significant effects (Charles et al., 2007; Costa et al., 2005; Ho et al., 2008; Laster et al., 1996). There is insufficient evidence for the effect of pager reminders in particular, as the low quality study reported significant effects (Safren et al., 2003). As sensitivity analysis, BES was first repeated using seven high quality RCT (thus disregarding six low quality RCT). Evidence for the short-term effectiveness as well as evidence for the effectiveness of SMS reminders in particular remained. However, limited evidence is now found for the effectiveness of ERD with audiovisual reminders. Second, BES was repeated using four instead of six (out of 11) validity criteria for classifying RCT as high quality studies. Again, evidence for the short-term effectiveness as well as evidence for SMS reminders remained. In addition, evidence was also provided for audiovisual reminders from ERD.

Discussion

This review provides evidence for the short-term effectiveness of electronic reminders in improving medication intake behavior in patients using chronic medication. Significant improvements in medication intake behavior were found in all but two studies following patients for a period of less than 6 months (four high and four low quality studies). Only one (with a high quality) of three studies with long-term follow-up reported significant effects on patients' medication intake behavior. The electronic reminders evaluated in those studies included SMS reminders, audio/visual reminders from ERD and reminders delivered to pagers. Stratified by the type of electronic reminder, our review shows that SMS reminders in particular but also ERD can be effective strategies for improving patients' medication intake behavior in the short run.

Most studies included in this review followed patients for a period of less than 6 months. It is, however, important to investigate whether the effects of electronic reminding remain for a longer time period. Patients who are adherent at first can become non-adherent over time (Vrijens, Vincze, Kristanto, Urquhart, & Burnier, 2008).

Furthermore, all 13 studies included in this review automatically sent electronic reminders regardless of whether or not patients took their medication. This may negatively influence the long-term effects of electronic reminders, as these automated reminders can become a routine resulting in habituation. This may be the reason that Pop Eleches and colleagues (2011) found that SMS reminders sent once a week significantly improved the medication intake behavior of HIV patients whereas daily reminders did not. Further research is needed to investigate the influence of the frequency with which reminders are sent in improving of medication intake behavior. Moreover, real time medication intake behavior monitoring is now upcoming (Haberer et al., 2010; Haberer et al., 2012), offering the possibility to intervene only when patients miss a dose, thus avoiding the reminders becoming routine. The effectiveness of this non-automated type of electronic reminding on medication intake behavior is currently being investigated (Vervloet et al., 2011).

With technology evolving rapidly, the use of older technologies such as pager systems is likely to decrease and new technologies may arise, such as applications for smart phones. Currently, SMS reminding is increasingly being implemented in interventions aimed at improving medication intake behavior as mobile penetration is high. The effectiveness is influenced by patients' willingness to receive SMS reminders. Two of the included studies reported patient experiences with SMS reminding (Hou et al., 2010; Strandbygaard et al., 2010). Both studies reported a positive evaluation of this type of electronic reminding, although in one of the studies the majority of patients indicated that the predetermined time at which the reminder was sent daily was unsuitable (Strandbygaard et al., 2010). In addition, three included studies evaluating ERD reported that these devices were well accepted by patients (Andrade et al., 2005; Laster et al., 1996; Santschi et al., 2007), which is in line with other research (Christensen et al., 2009; Sahm, MacCurtain, Hayden, Roche, & Richards, 2009).

Our review showed that SMS reminders are effective in increasing medication intake behavior. There are, however, differences in the SMS reminders sent. One study used personalized text messages that requested a reply (Hardy et al., 2011), the other two studies yielding significant effects sent standardized text messages without requiring acknowledgment (Pop-Eleches et al., 2011; Strandbygaard et al., 2010). Earlier research showed that a tailored message is usually more effective than a standard text (Kreuter & Wray, 2003). This cannot be confirmed by our findings. However, more studies are needed to investigate the influence of the content of reminder messages on adherence behavior. Reminders can especially be used to modify the behavior of unintentionally non-adherent patients, i.e., patients who are willing to take their medication but forget it or are inaccurate (Wroe, 2002). Nonetheless, none of the included studies focused specifically on this patient group, implying that the intervention was possibly not suited for some of the patients; those who deliberately miss or alter their doses and make a rational decision to do so by weighing pros and cons of the medication. Interventions using reminders may be

more effective when they are solely focused on patients who are unintentionally non-adherent. On the other hand, using text messages, for example, to stimulate patients who doubt the effectiveness of medication by stressing the importance of the intake in the message may provide a solution for intentionally non-adherent patients (Petrie et al., 2012).

Reminders can be beneficial for improving medication intake behavior in patients of all ages. Elderly patients may be at risk of forgetting to take their medication because of memory problems. Adolescents, on the other hand, may be at risk for forgetting their dose because of their busy (social) lives. Zelikovsky and colleagues (2008) reported that being out with friends and participating in activities were reasons for forgetting among adolescent renal transplant candidates. Furthermore, as adolescents extensively use mobile phones, SMS reminders might be particularly useful for reminding them. Miloh and colleagues (2009), for example, showed improved medication intake behavior rates as a result of text messaging in pediatric liver transplant recipients. None of the studies included in our review, though, specifically targeted the pediatric population. Future studies involving the pediatric population are recommended.

Electronic monitoring is currently seen as the most reliable and objective method in measuring medication intake behavior, while self-report is considered less reliable as this measure tends to overestimate medication intake behavior (Farmer, 1999; Osterberg & Blaschke, 2005). Most studies included in the review used electronic monitoring for medication intake behavior measurement, sometimes combined with self-report. In two studies, in which medication intake behavior was measured with both electronic monitoring and self-report, effects were only found when medication intake behavior was measured with electronic monitoring, while no effects were found for self-report. A possible explanation may be that with self-report patients report a high medication intake behavior rate from the beginning, leaving no or insufficient room for improvement. These findings emphasize the importance of incorporating objective methods for medication intake behavior measurement into studies whenever possible (Haynes et al., 2008).

Limitations of the included studies

The methodological quality of the studies varied. In studies identified as low quality, mostly the risk of selection and attrition bias is present. By using a BES, this methodological quality was taken into account in attributing levels of evidence to effects found in studies.

The electronic database searches provided five studies in which a more complex intervention was used, with an electronic reminder as one of the aspects of the intervention (Düsing, Handrock, Klebs, Tousset, & Vrijens, 2009; Fairley et al., 2003; Franklin, Waller, Pagliari, & Greene, 2006; Ostrop & Gill, 2000; Simoni et al., 2011). Those studies only reported the total effect of the complex intervention on patients' medication intake behavior, no direct relation between the reminder and medication intake behavior

was reported. Therefore, those studies could not contribute to this review, thus we decided to exclude those studies.

The primary aim of electronic reminders is to improve patients' medication intake behavior. Therefore, we focused not on clinical outcomes, but on medication intake behavior as (one of the) main outcome measures. In medication intake behavior research, a patient is often classified as adherent when an medication intake behavior rate of over 80% is reached (Karve et al., 2009). This cut-off point indicates the minimum level of medication intake behavior needed for therapeutic effect. In the HIV population, the cut-off point is 90%. Although often used, these cut-off points are arbitrary. Only two studies in our review used a cut- off point for medication intake behavior. Pop-Eleches and colleagues (2011) used a binary indicator of whether HIV patients achieved more than 90% medication intake behavior as a primary outcome. Charles and colleagues (2007) used cut-off points of over 50%, over 80% and over 90% medication intake behavior for asthma patients. Both studies, however, did not link their findings to clinical outcomes nor reported on the clinical significance of the effects found. Trials aiming to evaluate the effects on patients' medication intake behavior usually have insufficient power to detect significant differences in clinical outcome measures. Of the nine studies that showed an effect on medication intake behavior, three studies also reported clinical outcomes (Andrade et al., 2005; Costa et al., 2005; Strandbygaard et al., 2010), of which one found a significant improvement in the intervention group (Andrade et al., 2005). Although medication intake behavior appears to be an intermediate outcome, there is evidence of the association between increased medication intake behavior rates and positive health outcomes (Rozenfeld, Hunt, Plauschinat, & Wong, 2008; Simpson et al., 2006).

Limitations of the review

A methodological limitation of our review may be that we used a 'top-down' approach in our search strategy, which means that we relied on existing databases and their search terms for identifying relevant studies. This may lead to missing relevant studies due to miscoding of search terms. A 'bottom-up' strategy, relying on searching existing databases in the broadest way possible, is significantly more time and labor-intensive but has the advantage of being comprehensible. To reduce this potential problem, we used the snowball method to identify studies that we possibly missed with our top-down strategy in addition to the electronic database searches.

Clinical implications

After providing patients with the electronic reminders, no additional effort is needed from healthcare providers, making this an intervention easy to implement in daily practice. Furthermore, electronic reminders and especially SMS reminders appear to be easily integrated into patients' lives. As such, this seems to be a simple intervention for both patient and professional for enhancing medication intake behavior. However, the healthcare system needs to be ready to include the use of electronic reminders in usual care for patients using chronic medication.

Implications for further research

Future studies should aim specifically at patients who are unintentionally non-adherent in examining the effects of electronic reminders on medication intake behavior. In addition, further research is needed to identify for which patient groups electronic reminding is most beneficial, for example, studies involving the pediatric population and studies involving patients with other types of chronic illnesses. Moreover, the included studies mostly found short-term improvements. Future studies should investigate the long-term effects of electronic reminders and search for additional features of electronic reminding to improve medication intake behavior in the long-term. One example may be not to send patients reminders daily at predetermined times, but to intervene only when necessary, by sending patients reminders only when they forget to take their medication (Vervloet et al., 2011). Another example may be to tailor the content of the reminder message to the needs of the patients based on their illness and treatment beliefs (Petrie et al., 2012).

Conclusions

This review shows that electronic reminders lead to short-term improvements of patients' medication intake behavior to chronic medication, while the long-term effects remain unclear. The increasing opportunities of new technologies make it possible to tailor reminding both in timing (only when needed) and in content (tailored messages). In this way, long-term improvements in medication intake behavior may be achieved.

Chapter 4

Words that make pills easier to swallow: a communication typology to address practical and perceptual barriers to medication intake behavior

Patient: "I would prefer to take as little medication as possible because taking medication is just plain bad for your body, especially because we don't know what kind of medication will come next." Nurse: "Yes, that is certainly true, and that's a very natural feeling, eh.., that you want to take as little medication as possible" (male, 41 years old, Colitis).

Nurse: "Well, then, we will find something that suits you better […]. If you think that this will not work out, I will ask [doctor's name] what your options are."

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Abstract

Background: The barriers to patients' successful medication intake behavior could be reduced through tailored communication about these barriers. The aim of this study is therefore (1) to develop a new communication typology to address these barriers to successful medication intake behavior, and (2) to examine the relationship between the use of the typology and the barriers to successful medication intake behavior.

Methods: Based on a literature review, the practical and perceptual barriers to successful medication intake behavior typology (PPB-typology) was developed. The PPB-typology addresses four potential types of barriers that can be either practical (memory and daily routine barriers) or perceptual (concern and necessity barriers). The typology describes tailored communication strategies that are organized according to barriers and communication strategies that are organized according to provider and patient roles. Eighty consultations concerning first-time medication use between nurses and inflammatory bowel disease patients were videotaped. The verbal content of the consultations was analyzed using a coding system based on the PPB-typology. The Medication Understanding and Use Self-efficacy Scale and the Beliefs about Medicine Questionnaire Scale were used as indicators of patients' barriers and correlated with PPB-related scores.

Results: The results showed that nurses generally did not communicate with patients according to the typology. However, when they did, fewer barriers to successful medication intake behavior were identified. A significant association was found between nurses who encouraged question-asking behavior and memory barriers ($r = -0.228$, $p = 0.042$) and between nurses who summarized information ($r = -0.254$, $p = 0.023$) or used cartoons or pictures ($r = -0.249$, $p = 0.026$) and concern barriers. Moreover, a significant relationship between patients' emotional cues about side effects and perceived concern barriers ($r = 0.244$, $p = 0.029$) was found as well.

Conclusion: The PPB-typology provides communication recommendations that are designed to meet patients' needs and assist providers in the promotion of successful medication intake behavior, and it can be a useful tool for developing effective communication skills training programs.

Introduction

Medication is a keystone of modern treatment, especially for patients with chronic intestinal illness such as inflammatory bowel disease (IBD) (Kane & Robinson, 2010). Despite the proven effectiveness of medication, nonadherence has been reported in over 40% of patients taking maintenance therapies for IBD (Horne et al., 2009). Poor medication intake behavior can be either unintentional or intentional. For example, if a patient is not able to recall medical information due to memory problems, this could result in unintentional nonadherence (Horne et al., 2009; Kane & Robinson, 2010). If, on the other hand, a patient chooses not to take the medication because of a fear of side effects, this would be intentional nonadherence. Both unintentional and intentional nonadherence can be the result of practical or perceptual barriers. These types of barriers can contribute to the problem of unintentional and intentional nonadherence and must be addressed if adherence rates are to be improved (Sabaté, 2003). Practical barriers (e.g., memory barriers due to limitations in cognitive capacity and resources) influence the ability to implement the instructions to follow the treatment. Perceptual barriers (e.g., the lack of belief in the necessity of the medication) are based on an internal negotiation between the perceived necessity of the treatment and any concerns relating to it, and these factors influence a patient's motivation to start and continue the treatment (Kane & Robinson, 2010).

Communication is a powerful tool to promote successful medication intake behavior. Zolnierek and Dimmatteo (2009) show that the patients of providers who communicate well have a 19% higher medication adherence than patients whose providers do not communicate effectively (Zolnierek & DiMatteo, 2009). "Words that make pills easier to swallow," i.e., the ways in which effective communication leads to successful medication intake behavior, have been described in previous studies. These studies have mainly focused on the exchange of information during prescription medication consultations (Richard & Lussier, 2006). Although these studies have provided valuable information on medical communication, they have not related communication strategies to specific barriers to successful medication intake behavior. These barriers vary between patients and patient groups and require the development of effective communication strategies that are designed to meet the needs of patients (Van Dulmen et al., 2008). Because poor medication intake behavior is considered to be a widespread problem (Sabaté, 2003), it is remarkable that no study has adequately described which different communication strategies designed to meet the specific needs of the patient, can be used in addressing specific barriers to successful medication intake behavior.

The purpose of this study is therefore (1) to develop a new communication typology to address the barriers to successful medication intake behavior, and (2) to examine the relationship between the use of the typology and these barriers. To address

the second aim, we formulated two research questions: (1) to what extent do nurses communicate according to the practical and perceptual barriers to successful medication intake behavior (PPB-typology), and (2) to what extent is the use of these communication strategies related to barriers to successful medication intake behavior?

Developing the typology

To address the first aim we reviewed the literature concerning communication and medication intake behavior. Table 1 describes the possible practical and perceptual barriers to successful medication intake behavior that might be intentional or unintentional. Within the category of practical barriers we distinguished between "memory barriers" (mostly unintentional) and "daily routine barriers" (mostly intentional), and within the category of perceptual barriers we distinguished between "necessity barriers" (mostly unintentional) and "concern barriers" (mostly intentional). Table 2 gives an overview of the PPB-typology.

The typology describes restructured communication strategies that are organized according to the barriers on the one hand and the communication strategies, divided into provider versus patient and instrumental versus affective communication, on the other hand. These types of communication strategies are further elaborated in the following sections.

General communication strategies

Effective communication serves the patients' need to understand (instrumental or cognitive needs) and to be understood (affective or socio-emotional needs; Bensing & Verhaak, 2004). Regardless of the type of barriers a patient may have, providers should always use general instrumental and affective communication strategies (Roter & Larson, 2002). General instrumental communication strategies include using medication intake-promoting communication, such as stressing the importance of taking the medication, and avoiding medication intake-hindering communication, such as saying it is acceptable for the patient to decide to take the medication on any given day. Moreover, the literature suggests that provider-centered communication, such as interrupting the patient, may have a negative effect on health outcomes (Kaplan, Greenfield, & Ware Jr, 1989; Ong et al., 1995). Instead, providers should allow open discussions about potential difficulties and/or a poor medication intake history. Because prior poor medication intake behavior is an independent predictor of successful medication intake behavior (Geers, 2012), exploring whether a patient has a poor medication intake history is essential. Consequently, it is important that providers respond adequately to patients who indicate that they have a poor medication intake history, e.g., by exploring the reasons for the previous poor medication intake behavior. From the patients' perspective, it is important for them to verbalize any poor medication intake history they have.

Table 1.
Types of practical and perceptual barriers

Practical barriers	**Example**
Memory barriers	"Sometimes I forget to take my medication"
(e.g., limitations of capacity and recourses)	"It is not easy for me to understand how to take the medication"
Daily routine barriers	"If I have a party, I sometimes decide not to take my medication"
(e.g., inconvenience of the medical regime)	"It is not easy for me to implement the medication regimen in my daily life"
Perceptual barriers	**Example**
Necessity barriers	"Sometimes I quit taking medication to discover if I still need the medication"
(e.g., lack of belief in the necessity of the medication)	"I don't need this medication"
Concern barriers	"I am concerned about the side effects"
(e.g., concerns and beliefs)	"I am worried that I will become too dependent on these medication"

In addition, many studies in patient-provider communication stress the importance of using general affective communication by patients and providers in medical consultations (Bensing, 1991). Affective communication refers to encouraging the patient to talk by showing concerns, establishing agreement, engaging in social conversation, and making jokes (Roter & Larson, 2002). The ability to use affective communication is considered to be a necessary condition for adequate patient education, as well as an important predictor of the success of a consultation (Bensing, 1991). It enhances relationships, creates a safe atmosphere, generates trust, improves the comprehension and recall of information, and allows the decision-making process to occur (Ong et al., 1995; Roter & Larson, 2002) and, is therefore expected to improve medication intake behavior (Zolnierek & DiMatteo, 2009).

Communication addressing memory barriers

Memory barriers are distinguished as the first type of practical barriers (see Tables 1 and 2) and relate to the patients' lack of self-efficacy regarding their ability to remember to take the medication, due to difficulties reading instruction leaflets and/or labels, comprehending treatment information, and recalling medication instructions and various combinations of medication. The term "self-efficacy" refers to one's belief in one's ability to successfully execute a behavior required to produce a certain outcome (Bandura, 1977; Cameron et al., 2010). Memory barriers are practical and mostly unintentional, because they are often the result of cognitive processing problems. Recall of information (i.e., the ability to understand and reproduce medical information) is a prerequisite for successful medication intake behavior (Kessels, 2003). Unfortunately, between 40% and 80% of medical information is almost immediately forgotten, and almost half of medical information is incorrectly recalled (Kessels, 2003) after it has been prescribed, which is likely to contribute to patients' incorrect medication intake. Communication strategies

that aim to address memory barriers should focus on enhancing the comprehension and recall of medical information.

There are several instrumental communication strategies that can reduce memory barriers. Recall-promoting techniques include summarizing, categorizing, structuring, providing written information, using cartoons or pictures, emphasizing and repeating information, checking with patients for understanding, and avoiding recall-hindering techniques such as technical jargon (Houts, Doak, Doak, & Loscalzo, 2006; Silberman, Tentler, Ramgopal, & Epstein, 2008).

Furthermore, patient participation is considered to be an important factor, as it is expected to result in improved recall of information (Brown, Butow, Dunn, & Tattersall, 2001). Providers can increase patient participation by encouraging question-asking behavior during or after consultations or by involving the patient in the problem-solving and decision-making process. Problem-solving is defined here as the search for the correct solution to a problem. Decision-making is defined as a situation in which "a choice must be made between several alternatives, often involving trade-offs of harms and benefits (Deber, 1994)". Involving a patient in the problem-solving and decision-making process may lead to higher levels of recall (Kaplan et al., 1989). In addition, it is important that providers ask the patient questions about used information sources, such as websites, and that they recommend reliable sources to prevent patients' exposure to inaccurate information (Eysenbach & Diepgen, 1999).

Patients can also contribute to the patient-provider interaction in several ways. For example, they can improve the decision-making process and enhance information recall by obtaining information and educating themselves prior to the consultation, e.g., by seeking information from various sources, such as the Internet or written educational material from the hospital (Ilic, 2010; Silberman et al., 2008). In addition, patients can interrupt the provider to direct the flow of information and ask for clarification when information is unclear (Feldman-Stewart, Brundage, & Tishelman, 2005; Roter & Larson, 2002). Displaying proactive behavior, such as asking questions and verbalizing possible difficulties, has been shown to result in higher comprehension and improved recall of information (Brown et al., 2001).

Table 2. *PPB-Typology: Communication strategies addressing barriers to medication intake behavior*

	Provider		**Patient**	
	Instrumental communication	**Affective communication**	**Instrumental communication**	**Affective communication**
PRACTICAL BARRIERS				
Memory barriers (e.g., limitations of capacity and recourses)	**1. General instrumental communication** **2. Instrumental communication addressing barriers** - Recall-promoting techniques - Encouraging question-asking behavior - Involving the patient in the problem-solving and decision-making process - Asking the patient questions about used information sources	**1. General affective communication**	**1. General instrumental communication** **2. Instrumental communication addressing barriers** - The use of Internet and written education of the hospital - Patient participation, especially interrupting the provider when information is unclear or asking questions - The verbalization of difficulties reading instruction leaflet/labels, comprehending treatment information, recalling medication instructions, combinations of medication	**1. General affective communication**
Daily routine barriers (e.g., inconvenience of the medical regime)	**1. General instrumental communication** **2. Instrumental communication addressing barriers** - Asking questions whether patients' are able to implement the treatment regime in daily life - Giving information and advice how to implement the treatment regimen in daily life - Involving the patient in the problem-solving and decision-making process	**1. General affective communication**	**1. General instrumental communication** **2. Instrumental communication addressing barriers** - The verbalization of difficulties concerning treatment regimen, taking medication, costs medication - Asking questions how to implement the treatment regimen in daily life - Participating in the problem-solving and decision-making process	**1. General affective communication**
PERCEPTUAL BARRIERS				
Necessity barriers (e.g., lack of belief in the necessity of the medication)	**1. General instrumental communication** **2. Instrumental communication addressing barriers** - Giving information and advice about medical condition and the necessity of (changing the) therapeutic regimen - Involving the patient in the problem-solving and decision-making process - Emphasizing and repeating the most important reasons to change medication, checking with patients for understanding	**1. General affective communication**	**1. General instrumental communication** **2. Instrumental communication addressing barriers** - Asking questions about the reasons to change medication and possible alternatives - Participating in the problem -solving and decision-making process	**1. General affective communication** **2. Emotional cues**
Concerns barriers (e.g., concerns and beliefs about medication)	**1. General instrumental communication** **2. Instrumental communication addressing barriers** - Motivational interviewing techniques - Emphasizing and repeating important information once possible concerns and fears are reduced	**1. General affective communication** **2. Cue responding to emotional cues** - Actively address patients' emotional cues - Reactively address patients' emotional cues - Avoiding disaffirming reactions in response to patients' emotional cues	**1. General instrumental communication** **2. Instrumental communication addressing barriers** - Actively asking questions about the concerns	**1. General affective communication** **2. Verbalizing emotional cues**

Communication addressing daily routine barriers

Daily routine barriers are the second type of practical barriers. These barriers refer to patients' self-efficacy with regard to taking their medication. These types of barriers are mostly intentional, because patients often actively decide not to take the medication, due to, for example, the costs of the medication or the inconvenience of the treatment regimen (Kane & Robinson, 2010). Communication strategies should focus primarily on addressing the daily routine barriers using instrumental communication to explore and reduce possible problems in incorporating the medication regimen into daily practice.

By asking whether the patient perceives these barriers, the provider can assess which practical barriers the patient is experiencing. In addition, the provider can provide information and advice on how patients can implement the treatment in their daily life. Practical advice on how to manage treatment at home is one of the most prevalent needs of patients (Van Weert et al., 2009). Patients, especially those with chronic illnesses, often make decisions about their treatment that fit their own personal circumstances (Vermeire et al., 2001). It is therefore important to encourage the patient to be involved in the problem-solving and decision-making process. If possible, daily routine barriers should be discussed, and the treatment regimen should be understood and agreed upon, which may reduce patients' perceptions of these difficulties in their daily lives.

From a patient's perspective, it is essential to verbalize difficulties and actively ask for advice regarding how to manage expected difficulties, how to implement the treatment regimen in everyday life, and how to integrate medication protocols into his or her lifestyle (Feldman-Stewart et al., 2005; Wroe, 2002). It is also important for patients to actively participate in the problem-solving and decision-making process.

Communication addressing necessity barriers

Necessity barriers are the first type of perceptual barriers. These barriers refer to a lack of belief in the necessity of using medication and are mostly unintentional. Communication strategies that address these barriers should focus on adequate patient education about the treatment regimen and shared decision-making (Kane & Robinson, 2010).

Patients may have erroneous ideas about the need for medication, based on, for example, previous negative experiences or stories of other patients. Information and advice about the patient's medical condition and the rationale behind the therapeutic regimen may change these beliefs (Smets, Nieuwkerk, & Hoos, 2006). Moreover, patients' belief in the necessity of the medication will be higher if they feel involved in the problem-solving and decision-making process, and if they eventually make a mutual agreement regarding their treatment (Feldman-Stewart et al., 2005; Wroe, 2002). In addition, the use of specific recall-promoting techniques by the provider, such as repeating and emphasizing the most important reasons to prescribe the medication and checking whether the patient has understood the importance of taking the medication, is recommended (Silberman et al., 2008). From a patient's perspective, it is important to

actively ask questions during the consultation about the reasons for taking the medication, to inquire about possible alternatives, and to take an active role in the problem-solving and decision-making process (Wroe, 2002).

Communication strategies addressing concern barriers

The fourth type of barrier that patients may encounter, which is the second type of perceptual barriers, is related to a patient's fears or concerns, e.g., about the side effects of the medication or about becoming dependent on the medication. These barriers are mostly intentional (Kane & Robinson, 2010). General affective communicative strategies are especially important in addressing concern barriers, because they not only create a safe atmosphere between the provider and the patient but also encourage patients to disclose their emotions, concerns, and worries (Roter & Larson, 2002). In addition, motivational interviewing techniques can be used to create a nonjudgmental and supportive environment in which the patient can be an active partner and feels free to express both motivation and reluctance or concerns about the treatment (DiIorio et al., 2003). It is important that the provider listens and reflects on what the patient says and points out discrepancies between the patient's current and required behavior. These techniques can help the patient to resolve ambivalence about his or her own behavior and to identify factors that are barriers to following the treatment plan (DiIorio et al., 2003).

In general, responding adequately to patients' emotional cues is essential. Emotional cues are verbal indications of an underlying unpleasant emotion or an explicit and a clear verbalization of experiencing an unpleasant emotional state (Zimmermann et al., 2011). Providers can actively (i.e., on their own initiative) or reactively (i.e., in response to the patients' emotional cues) address patients' emotional cues. If a patient expresses emotional cues, it is important for the provider to exhibit facilitating behavior (i.e., addressing these emotional cues by exploring or acknowledging them (Heaven & Green, 2001) or offering minimal encouragement [e.g., "aahhh" and "mmm"]; Eide, Quera, Graugaard, & Finset, 2004). An adequate response to these cues may encourage patients to further disclose their perspectives on the treatment (Uitterhoeve et al., 2008). It is important that providers actively (without an emotional cue) demonstrate the aforementioned facilitating behavior.

As the ability of patients to recall information can be negatively influenced by stress (Kessels, 2003), it is not only important to address patients' psychosocial and emotional needs, beliefs, concerns, and emotional cues but it is also recommended to emphasize and repeat important information after concerns and emotional cues have been addressed (Silberman et al., 2008).

From a patient's perspective, it is important to clearly verbalize emotions such as fear. Patients are generally more likely to disclose their emotions indirectly as opposed to directly, which creates the risk that their emotional cues will not be detected by the

provider (Jansen et al., 2010). This failure of communication could have a negative effect on the patient's recall of information (Jansen et al., 2008; Jansen et al., 2010). In addition, it is important that patients actively ask questions about any concerns or emotional issues they may have about treatment.

Testing the typology

In this section we turn to the second aim of this study by describing the methods used to test the typology. We describe how we analyzed the consultations between nurses and patients using the PPB-typology and the measures that were used to examine the barriers to patients' successful medication intake behavior.

Design

In this study, the communication skills of the nurses were investigated during their educational consultations with IBD patients at the start of immunosuppressive or biological therapy. Eight specialized IBD nurses at five hospitals participated in this study. The PPB-typology was tested in consultations with IBD patients, because these patients represent a high-risk case with regard to not taking their medication as prescribed, particularly medications that are used for long-term therapies. This high-risk condition is due to the characteristics of the illness, which includes (long) inactive periods alternating with (chronic) active periods, and to medical therapy that is often inconvenient due to side effects (Ediger et al., 2007). Taking immunosuppressive or biological therapy is associated with an increased risk of rare but potentially serious adverse reactions such as cancer. Although the likelihood of developing cancer as a result of taking a medication for IBD is very low, as soon as these words are mentioned, patients are often struck with fear and do not hear much more of what is said afterwards (Johnson et al., 2007). Therefore, nurses have an increasingly important role in educating IBD patients about their treatment regimen.

The patient inclusion criteria for this study included: (1) a diagnosis of Crohn's disease or ulcerative colitis according to classical clinical, endoscopic, radiographic, and/or pathohistological criteria, as determined by an experienced gastroenterologist; (2) starting treatment with azathioprine, 6-mercaptopurine, infliximab, methotrexate, 6-thioguanine, or adalimumab for the first time; and (3) fluency in Dutch. Patients with prior acknowledged or diagnosed limited cognitive abilities were excluded. The Medical Ethical Committee of the VU Medical Center, Amsterdam, The Netherlands, granted permission for this study, which was supplemented with local feasibility statements (Trial No NTR2892). The data were collected from September 2009 until January 2012.

Procedure and participants

Patients were asked for written permission to videotape their consultation with an IBD nurse. First, anonymous questionnaires were collected prior to the consultation. In the questionnaire, patients were asked to specify their age, gender, education, diagnosis, and the length of time since diagnosis. Second, the consultations were recorded on video. Third, a follow-up questionnaire, containing questions concerning the barriers perceived by the patients, was administered during a telephone interview 3 weeks after the videotaped consultation.

When the patient entered the consultation room, the researcher switched on the video camera and left the room before the consultation started. Although the providers noted some stress at the beginning of the study, they did not report stress afterwards. Providers usually described each consultation as a typical consultation reflecting an average situation.

Of the 110 eligible patients, 19 (17.3%) refused to participate: 8 did not want their consultation to be videotaped, five felt too sick or too tired, and 6 felt overwhelmed or were too busy. Another 11 participants (10.0%) were excluded: seven patients decided not to start the prescribed medication after the consultation, three video recordings were missing due to technical problems, and one patient appeared to have cognitive problems. The consultations of all of the remaining patients (N = 80) were analyzed (see Figure 1). A non-response analysis revealed that nonparticipating patients were younger (mean [*M*] = 35.6, standard deviation [*SD*] = 11.4) than participating patients (*M* = 40.1, *SD* = 14.6; *P* . 0.05). There was no difference in gender between participants and nonparticipants.

Analyzing the consultations

All of the consultations were transcribed. The verbal content was analyzed using a protocol that was based on the PPB-typology. Categories of several validated coding instruments were used as a basis for the developed typology. Only those items in which previous research suggested that there is a relationship between communication and medication intake behavior were included. Because some of the communication strategies of the several validated instruments overlap, certain categories are based on more than one instrument. Only utterances that contained a topic that fitted in one of the categories of the protocol were scored. An utterance is a communicative unit that conveys one thought or is related to one specific interest. An utterance can vary in length from one word to a sentence. Each utterance was considered to be mutually exclusive (Schouten, Meeuwesen, & Harmsen, 2009). The complete protocol can be obtained from the first author. Tables 3 and 4 show the primary instruments and the literature on which the protocol was based.

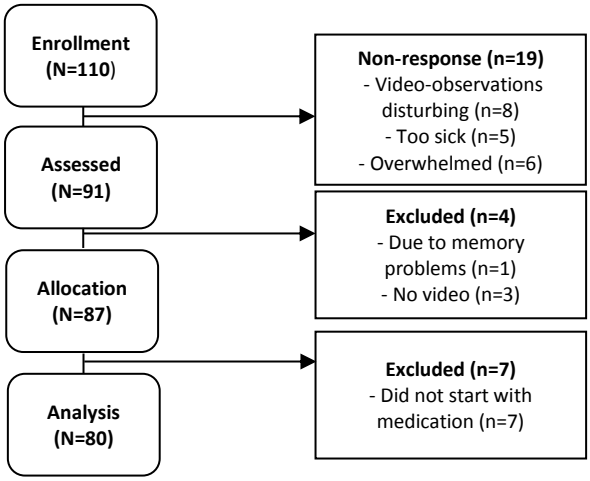

Figure 1. *Consort Flow Diagram patients' non-response (N = 80).*

The conversations between the nurse and the patient were coded by the first author and a trained research assistant. The first author, a university graduate in communication science and experienced in coding nurse-patient communication, trained the research assistant to code nurse-patient communication using the protocol. Guidelines were followed to minimize observer bias and reactivity. After 5 days of training, the "real" observations began. In addition, regular meetings of the team were held to discuss and resolve coding issues.

Reliability was tested using intraclass correlation coefficients (ICC) using a two-way mixed-effect model of consistency and single measure statistics. The ICC is often used to measure the reliability between two interval variables. To determine intercoder reliability, the observers both coded the same 13 (16%) video recordings. Intercoder reliability was measured for the communication categories that accounted for more than 1% of all utterances. Based on κ statistics criteria (Altman, 1991) values between 0.21 and 0.40 are considered fair, values between 0.41 and 0.60 are considered moderate, and values > 0.61 are considered good. The ICC ranged between 0.6 and 1, with a mean ICC of 0.9, which is considered good (Altman, 1991).

Instrumental communication

Nurses' instrumental communication consisted of eleven main categories, which included all categories with respect to information or advice about medical conditions, treatment, lifestyle, and information about the ward, administration, and services. General instrumental main categories were medication intake-promoting communication intake-hindering communication, avoiding provider-centered communication, actively exploring poor medication intake history and reaction after a poor medication intake history (Kaplan et al., 1989). Providers' instrumental communication addressing barriers were: using recall-promoting and recall-hindering techniques (Ediger et al., 2007; Houts et al., 2006; Silberman et al., 2008), promoting patient participation (Deber, 1994), asking the patient

questions about used information sources (Eysenbach & Diepgen, 1999), giving information and advice, and using motivational interviewing techniques (DiIorio et al., 2003). The general instrumental communication of the patients consisted of one main category: the verbalization of medication intake behavior. Patients' instrumental communication addressing barriers consisted of two main categories, which were the verbalization of difficulties and patient participation (Feldman-Stewart et al., 2005).

Affective communication

The nurses' general affective communication categories referred to those aspects that were needed to establish a trusting relationship between the provider and the patient, including showing concerns, establishing agreement, engaging in social conversation, and making jokes (Roter & Larson, 2002). The nurses' response to emotional cues (cue responding) consisted of two categories, which were actively and reactively addressing cues. Based on the Medical Interview Aural Rating Scale system (Heaven & Green, 2001), we distinguished exploring and acknowledging as modes of active response and exploring, acknowledging, neglecting, and providing minimal encouragement as modes of reactive responses (Uitterhoeve et al., 2008). Patients' general affective communication included one main category, which consisted of establishing agreement, engaging in social conversation, and making jokes. Patients' emotional cues consisted of one main category, which included emotional cues (Heaven & Green, 2001; Zimmermann et al., 2011) We made a distinction between emotional cues that pertained to previous or current medication and emotional cues that pertained to the new prescribed medication.

Measures of barriers

The questionnaire that was administered prior to the consultation included socio-demographic background characteristics and medical background characteristics. The questionnaire that was administered 3 weeks after the consultation included the Medication Understanding and Use Self-Efficacy Scale (MUSE) (Cameron et al., 2010) and the Beliefs about Medicine Questionnaire (BMQ) (Horne et al., 1999).

Table 3. *Communication strategies nurse (N = 8)*

Nurse	M[1]	SD	%[2]	Based on
General instrumental communication				
Medication intake- promoting communication	**.7**	**1.4**	**0.2**	Zolneriek and Dimatteo (2009)
Medication intake-hindering communication	**.1**	**.5**	**0.0**	Zolneriek and Dimatteo (2009)
Provider-centered communication	**.5**	**1.4**	**0.2**	Kaplan and colleagues (1989)
Interrupting patient	.1	.4	0.1	Kaplan and colleagues (1989)
Neglecting question patient	.0	.2	0.1	Kaplan and colleagues (1989)
Active: poor medication intake history	**.1**	**.5**	**0.2**	MIARS
Active: exploring poor medication intake history	.5	.4	0.2	MIARS
Active: acknowledging poor medication intake history	0	0.1	0	MIARS
Reactive: after poor medication intake history	**.2**	**.9**	**0.1**	MIARS
Reactive: exploring poor medication intake history	.1	.4	0.0	MIARS
Reactive: acknowledging poor medication intake history	.1	.4	0.0	MIARS
Reactive: minimal reaction	0	.2	0.0	MIARS
Reactive: neglecting	.1	.3	0.0	MIARS
General affective communication nurse				
Affective communication	**4.8**	**6.5**	**1.6**	RIAS
Showing concerns	.1	.5	0	RIAS
Establishing agreement	2.4	2.1	0.9	RIAS
Engaging in social conversation	1.4	2.4	0.5	RIAS
Making jokes	1.0	1.5	0	RIAS
Instrumental communication addressing barriers				
Recall-promoting techniques	**27.9**	**12.8**	**9.3**	RPT; MI
Summarizing	2.7	2.4	0.7	RPT
Categorizing	.6	1.0	0.2	RPT
Structuring	2.1	1.9	0.8	RPT
Providing written information	5.3	4.0	1.8	RPT
Using cartoons or pictures	3.1	4.8	1.0	RPT
Emphasizing en repeating information	12.3	7.1	4.2	RPT
Checking with patients for understanding	1.8	2.0	0.6	RPT
Recall-hindering techniques	**22.6**	**11.3**	**7.5**	RPT
Promoting patient participation	**4.7**	**3.9**	**1.5**	RIAS
Encouraging question-asking behavior during consultation	1.4	1.2	0.4	Deber (1994)
Encouraging question-asking behavior after consultation	1.2	2.5	0.4	Deber (1994)
Involving the patient in the problem-solving process	.2	.5	0.1	RIAS; Deber (1994)
Involving the patient in the decision-making process	.8	1.4	0.3	RIAS; Deber (1994)
Involving the patient in the problem-solving logistic process	.6	1.1	0.2	RIAS; Deber (1994)
Involving the patient in the decision-making logistic process	.5	1	0.2	RIAS; Deber (1994)
Asking the patient questions about used information sources	**.3**	**.7**	**0.1**	Deber (1994)
Giving information and advice	**180.0**	**64.5**	**60.8**	RIAS
Giving information (e.g. about therapeutic regimen)	137.9	59.9	46.3	RIAS
Giving advice (e.g. about treatment regimen)	2.9	4.2	0.9	RIAS; MI
Giving general information (related to (medical) paperwork)	25.8	17.3	8.8	RIAS
Giving general advice (related to (medical) paperwork)	.2	.9	0.1	RIAS
Asking questions	13.2	7.3	4.7	RIAS
Motivational interviewing techniques	**1.0**	**1.8**	**0.3**	MI
Listening and reflecting	0.9	1.6	0.3	MI
Pointing out discrepancies	.1	.4	0	MI
Nurses response to emotional cues (cue responding)				
Actively addressing emotional cues	**5.1**	**4.1**	**1.6**	MIARS; RIAS
Active: exploring emotional cues	.4	.9	0.1	MIARS; RIAS;
Active: acknowledging emotional cues	4.7	4.0	1.5	MIARS; RIAS; MI
Reactively addressing emotional cues	**9.6**	**9.1**	**3.2**	
Reactive: exploring emotional cues	.5	1	0.2	MIARS
Reactive: acknowledging emotional cues	3.3	3.9	1.1	MIARS
Reactive: minimal encouragement	2.4	3.6	0.8	MIARS; Jansen and colleagues (2010)
Reactive: neglecting	3.4	4.5	1.2	MIARS; Jansen and colleagues (2010)

The Roter Interaction Analysis System (RIAS; Roter & Larson, 2002), Medical Interview Aural Rating Scale (MIARS; Heaven & Green, 2001), Motivational Interviewing (MI; Dilorio et al., 2003), Recall Promoting Techniques (RPT; Silberman et al., 2008)

[1] Mean number of utterances per category per consultation

[2] Percentage based on the mean number of coded utterances that appeared in the consultations

Table 4.
Communication strategies patient (N = 80)

Patient	M[1]	SD	%[2]	Based on
General instrumental communication				
The verbalization of poor medication intake behavior	**.2**	**.7**	**0.1**	Zolneriek and Dimatteo (2009)
General affective communication				
Affective communication	**7.3**	**6.0**	**2.7**	RIAS
Establishing agreement	4.5	4.7	1.5	RIAS
Engaging in social conversation	2.5	1.4	0.7	RIAS
Making jokes	1.7	1.2	0.5	RIAS
Instrumental communication addressing barriers				
The verbalization of difficulties	.5	1.4	0.2	Feldman-Stewart and colleagues (2005)
Concerning reading instruction leaflet/labels	.0	.0	0	Feldman-Stewart and colleagues (2005)
Concerning comprehending treatment information,	.0	0.2	0	Feldman-Stewart and colleagues (2005)
Concerning recalling medication instructions	.0	0.2	0	Feldman-Stewart and colleagues (2005)
Concerning combinations of medication	.0	.16	0	Feldman-Stewart and colleagues (2005)
Costs medication	.1	.5	0	Feldman-Stewart and colleagues (2005)
Concerning treatment regimen	.3	1.6	0.1	Feldman-Stewart and colleagues (2005)
Patient participation	**19.9**	**11.2**	**6.6**	RIAS; Deber (1994)
Problem solving	.2	.6	0.1	RIAS; Deber (1994)
Decision making	.3	.7	0.1	RIAS; Deber (1994)
Problem solving logistic	.5	.9	0.2	RIAS; Deber (1994)
Decision making logistic	.4	.9	0.2	RIAS; Deber (1994)
Interrupting the provider	.4	.9	0.1	Kaplan and colleagues (1989)
Asking questions	17.2	10.0	5.5	RIAS
The use of Internet	.5	1.0	0.2	Eysenback and Diepgen (1999)
The use of written education hospital	.5	1.0	0.2	Eysenback and Diepgen (1999)
Patients' emotional cues				
Verbalizing emotional cues	**11.2**	**10.0**	**3.8**	Uitterhoeve and colleagues (2008)
Emotional cue well-being patient	3.6	4.8	1.2	Uitterhoeve and colleagues (2008)
Positive emotional cue previous medication	.7	1.3	0.2	Uitterhoeve and colleagues (2008)
Emotional cue towards side effects previous medication	1	1.6	0.3	Uitterhoeve and colleagues (2008)
Emotional cue towards administration previous medication	.4	.8	0.2	Uitterhoeve and colleagues (2008)
Emotional cue towards dependency previous medication	.0	.2	0	Uitterhoeve and colleagues (2008)
Emotional cue towards necessity previous medication	.2	.5	0.1	Uitterhoeve and colleagues (2008)
Emotional cue: reassurance previous medication	.1	.6	0.1	Uitterhoeve and colleagues (2008)
Emotional cue towards necessity previous medication despite education	.1	.3	0	Uitterhoeve and colleagues (2008)
Emotional cue towards side effects	.8	1.5	0.3	Uitterhoeve and colleagues (2008)
Emotional cue towards administration	.7	1.3	0.2	Uitterhoeve and colleagues (2008)
Emotional cue towards dependency	.1	.3	0	Uitterhoeve and colleagues (2008)
Emotional cue towards necessity	.2	.5	0.1	Uitterhoeve and colleagues (2008)
Emotional cue towards necessity despite education	.1	.5	0.1	Uitterhoeve and colleagues (2008)
Emotional cue: reassurance	.4	.6	0.1	Uitterhoeve and colleagues (2008)
Emotional cue other	3.1	4.1	1.0	Uitterhoeve and colleagues (2008)

The Roter Interaction Analysis System (RIAS; Roter & Larson, 2002), Medical Interview Aural Rating Scale (MIARS; Heaven & Green, 2001), Motivational Interviewing (MI ; Dilorio et al., 2003), Recall Promoting Techniques (RPT; Silberman et al., 2008)

[1] Mean number of utterances per category per consultation

[2] Percentage based on the mean number of coded utterances that appeared in the consultations

Medication Understanding and Use Self-Efficacy Scale

The MUSE measured patients' self-efficacy in understanding and using prescription medication (Cameron et al., 2010). The scale consisted of two subscales, each including four items: (1) "MUSE-understanding self-efficacy" (α = 0.80), measuring patients' self-efficacy related to their understanding of the medication (e.g., "It is easy for me to understand instructions in medication leaflets"), and (2) "MUSE-use self-efficacy" (α = 0.91), measuring patients' self-efficacy with regard to the action of taking their medication (e.g., "It is easy to set a schedule to take my medication") (Cameron et al., 2010). Memory barriers referred to patients' cognitive information-processing problems (Kane & Robinson, 2010). Therefore, the "understanding self-efficacy" subscale was considered an indicator

of perceived memory barriers. Daily routine barriers referred to the perceived inconvenience of taking the medication according to the treatment regimen (Kane & Robinson, 2010). The "use self-efficacy" subscale measured possible barriers to the action of taking medication and was therefore considered an indicator of daily routine barriers. Scores on each scale were summed to give a score ranging from 4 to 16. A higher score indicated a lower level of self-efficacy.

The Beliefs about Medicine Questionnaire

The adapted version of the BMQ, known as the Dutch BMQ-specific, was used (Heijmans, 2006). The BMQ measured patients' attitudes and beliefs regarding taking their medication and consisted of two separate subscales: (1) "BMQ-necessity," measuring beliefs about the necessity of taking medication (e.g., "My life would be impossible without medication"; five items; $\alpha = 0.76$), and (2) "BMQ-concerns," measuring patients' concerns about taking medication (e.g., "Having to take the medication worries me"; six items; $\alpha = 0.74$). Necessity barriers referred to patients' lack of belief in the necessity of the medication (Kane & Robinson, 2010). Therefore, the BMQ-subscale "necessity" was considered an indicator of necessity barriers. Concern barriers referred to concerns about the medication (Horne et al., 1999). The BMQ-subscale "concerns" was therefore considered an indicator of concern barriers. Scores on the necessity subscale were summed to give a score ranging from 5 to 25 and a scale midpoint of 15. Scores on the concerns subscale were summed to give a score ranging from 6 to 30 and a scale midpoint of 18. A higher score indicated a stronger belief in the necessity or more concerns, respectively.

Data analysis

The data were analyzed using SPSS 20.0 (SPSS, Inc, Chicago, IL). The frequencies of the utterances were calculated and on interval level. The scores on the BMQ and MUSE were correlated with the scores for the communication categories using Pearson's bivariate correlations, with a significance level of $p < 0.05$. Pearson's correlations were calculated for the categories that occurred, on average, one or more times during a consultation. In total, 28 communication strategies occurred, on average, one or more times during a consultation and were correlated with the four barriers.

Results

Participants' characteristics

Two-thirds (66.3%) of the sample was female. Fifty-nine patients (73.8%) were diagnosed with Crohn's disease and 20 with ulcerative colitis (25.0%). The mean age was 40.1 (*SD* = 14.6) years, and almost half of the patients were highly educated (see Table 5). All of the eight nurses were female, with a mean age of 43.0 (*SD* = 11.9) years. The nurses had worked for an average of 4.7 (*SD* = 2.9) years as IBD nurses.

Communication characteristics

To investigate the first research question, we analyzed to what extent nurses communicate according to the PPB-typology. The consultations lasted, on average, 1780 (*SD* = 564.4) seconds, which means that the average consultation lasted 29 minutes. The mean number of coded utterances of each consultation was 295.5 (*SD* = 87.6*).* Nurses mostly employed instrumental communication during the consultations. A total of 60.8% of the coded utterances (*M* = 180.0) referred to provider categories giving information and advice, whereas 9.3% (*M* = 27.9) were devoted to recall-promoting techniques, and 7.5% (*M* = 22.6) were devoted to recall-hindering techniques. General affective communication was rarely found: 1.6% (*M* = 4.8) of the coded communication was coded as affective communication, and 3.2% (*M* = 9.6) was coded as cue-responding communication. Of all the cue-responding communication, 5.2% (*M* = 0.5) was exploring, 34.7% was acknowledging (*M* = 3.3), and 25.3% was minimal encouragement (M = 2.4); in addition, 35.4% of the emotional cues of the patients were neglected (*M* = 3.4).

Regarding patients' communication, patient participation was evident in 6.6% (*M* = 19.9) of the coded communication during the consultations, and 3.8% (*M* = 11.2) referred to verbalized emotional cues. Only 0.2% (*M* = 0.5) of the utterances were coded as verbalizing difficulties, and 2.7% (*M* = 7.3) were coded as general affective communication. Tables 3 and 4 give the mean scores of providers' and patients' verbal utterances within each communication category, respectively.

Perceived barriers

To investigate the second research question we first measured patients' perceived barriers, and then we analyzed to what extent those barriers were associated with the communication strategies according to the PPB-typology.

Mean scores on the MUSE ($M_{\text{MUSE-understanding}}$ = 7.17; *SD* = 2.37; $M_{\text{MUSE use self-efficacy}}$ = 7.25; *SD* = 1.76) indicated that patients perceived relatively few memory and daily routine barriers. The results also showed that patients reasonably believed in the necessity of the medication ($M_{\text{BMQ-necessity}}$ = 18.51; *SD* = 3.28) but still had concerns and worries regarding the treatment regimen ($M_{\text{BMQ-concerns}}$ = 17.21; *SD* = 4.19).

Table 5.
Patient characteristics

Patient characteristics		***N* = 80**	**%**
Gender	Male	27	33.7%
Age	M (*SD*)	40.1 *(14.6)*	
	Range	18-80	
Type of Disease	Crohn's disease	59	73.8%
	Colitis Ulcerosa	20	25.0%
	Other	1	1.3%
Diagnosed in years	*M(SD)*	9.93	(10.01)
	Range	0-40	
Educational level	Low	21	26.6%
	Moderate	27	34.2%
	Higher education	31	39.2%
	Other	1	1.3%
Living arrangements	Alone	17	21.3%
	With partner	20	25.0%
	With partner and child(ren)	20	25.0%
	With child(ren)	9	11.3%
	Other	14	17.5%
Children	Yes	39	48.8%
Employed	Yes	56	70.0%
Ethnicity	Dutch	70	87.5%
Religious	Yes	20	25.0%

As expected, a significant negative relationship was found between nurses encouraging question-asking behavior and memory barriers, indicating that with more nurse encouragement for the patients to ask questions, fewer memory barriers were perceived by patients (r = −0.228, p = 0.042). However, other expected relationships between communication strategies and memory barriers were not found.

Unexpectedly, no relationship between perceived daily routine barriers and communication strategies was found.

An unexpected significant negative relationship was found between checking with patients for understanding and perceived necessity barriers, suggesting that the

more nurses asked whether the patients understood the medication instructions, the less patients believed that the medication was necessary (r = −0.276, p = 0.013). However, other expected relationships between communication strategies and necessity barriers were not found.

The use of two recall-promoting techniques, i.e., summarizing and using cartoons or pictures during the consultation, was significantly associated with fewer perceived concern barriers (r = −0.254, p = 0.023 and r = −0.249, p = 0.026, respectively). These findings indicate that the more nurses summarized information or used pictures to illustrate the information, the fewer concerns patients had about the medication. Moreover, we found a significant positive relationship between the emotional cues of patients about side effects concerning previous medication and perceived concern barriers, indicating that the more patients expressed worries about side effects based on previous medication use, the more concerns they had regarding the new prescribed medication (r = 0.244, p = 0.029). An unexpected significant negative relationship was found between involving the patient in the decision-making process and perceived concerns (r = −0.225, p = 0.045). In other words, patients who were more involved in the decision-making process about their treatment showed more concerns than patients who were less involved. Other expected relationships between communication strategies and concern barriers were not found.

Discussion

In the current study, we developed and tested a new communication typology to promote successful medication intake behavior. To address the first research question, we found that, in general, the nurses and the patients did not use many of the communication techniques that, according to the PPB-typology, were expected to be related to fewer barriers. A possible explanation may be that the nurses are not aware of the specific barriers that patients perceive, and they are therefore unable to structure their communication accordingly. They may possibly make no distinction between the various barriers. These distinctions are not as straightforward as originally believed (Gadkari & McHorney, 2012). Patients may experience memory and daily routine barriers and necessity and concern barriers simultaneously (Clifford et al., 2008). It may be rather difficult for nurses to identify which barriers a patient perceives, particularly if the nurses are not trained in the detection of such barriers.

The level of patient participation was found to be high in our sample. This was predominantly due to the high number of questions that patients asked and the high number of emotional cues they expressed. IBD patients verbalized several emotional cues, primarily about their health. We found a mean of 11.2 emotional cues per consultation, compared with a mean ranging from one to seven emotional cues per consultation, which

was reported in a literature review by Zimmermann and colleagues (2007). An explanation for this result may be that patients who are starting with immunosuppressive or biological therapy, are in an active phase of their disease. Although the introduction of these medications most likely provides patients with a more effective therapy, the medications are also known to show some rare but potentially serious adverse side effects (Johnson et al., 2007). This issue may have caused a relatively large number of emotional verbalizations. However, the nurses neglected one-third of the emotional cues (e.g., by switching the topic of conversation), which has been shown to be an inhibiting response. Moreover, exploring patients' emotional cues, which is recognized in the literature as a facilitative communicative behavior, was only incidentally found.

Furthermore, IBD patients have previously been described as a group of patients who prefer to be actively involved in the decision-making process concerning their treatment (Baars, Markus, Kuipers, & van der Woude, 2010). However, in the current study, patients, in general, did not actively participate in the decision-making process. This may be explained by the fact that every IBD treatment has its own possible benefits, risks, and side effects. It may therefore be difficult to implement shared decision-making in the treatment of IBD. This makes the active involvement of patients a challenge (Baars et al., 2010) and a training goal for further communication skills training. Previous research showed that communication skills training in general affective communication strategies, such as showing interest, listening carefully, taking the patient seriously, and asking questions in a safe atmosphere, resulted in a 19% decrease in nonadherence (Zolnierek & DiMatteo, 2009). A more recent study showed that communication training was successful in enhancing nurses' exploration of patients' medication beliefs and concerns (Latter et al., 2010). This effect may increase if nurses learn how they can identify both perceptual and practical barriers to successful medication intake behavior.

To address the second research question, the results showed that when communication strategies were used according to the developed typology, this was associated with fewer barriers. Our findings indicated that when the nurses encouraged patients to ask questions, fewer memory barriers were perceived. Previous research also found that active patient participation and more question-asking resulted in increased recall of information (Brown et al., 2001). If patients are encouraged to actively ask questions, they receive opportunities to direct the information flow, which will result in more tailored communication and thus in higher recall (Kessels, 2003). Our findings also showed that the use of the recall-promoting techniques was related to fewer concern barriers. When patients perceive concern barriers, they may have false beliefs about the probability of side effects, which can hinder the proper absorption of adequate information (Kessels, 2003). However, the use of recall-promoting techniques seems to be able to reduce this effect.

Shared decision-making initiated by the nurse was related with fewer concern barriers. This relationship was not expected prior to the study, but, intuitively, it does

make sense. When nurses involve patients in the shared decision-making process, the nurses shift away from attempting to encourage patients to take the prescribed medication toward asking questions about how they can contribute to the individual decisions that the patients make (Vermeire et al., 2001). Patients may have individual preferences for taking or not taking the medication as prescribed, and whether the patients have concerns may play a role in this process. For that reason, nurses should acknowledge that patients make decisions based on their individual concerns (Gadkari & McHorney, 2012). Involving patients in the decision-making process allows patients to discuss their concerns, which might ultimately result in consensus and agreement about the treatment, and, consequently, fewer concerns. Although we did not find literature on this relationship when developing the PPB-typology, it seems plausible that decision-making is associated with fewer concern barriers. We believe that these results can contribute to the further refinement of our typology, and these communication strategies will be added to the PPB-typology.

Unexpectedly, we found low mean scores for memory and daily routine barriers, which indicates that patients experience relatively few practical barriers. As a consequence, there was not much variability within these barriers. This may be one of the reasons why we did not find stronger relationships between the use of tailored communication strategies and reduced practical barriers. This could be explained by our sample. Almost 40% of the patients were highly educated, and the majority were relatively young (with a mean age of 40 years). Memory barriers, in particular, may be different in older patients and patients with a lower degree of education. For this reason, it is desirable to replicate this study among older patients and/or patients with a lower degree of education in other patient samples. Moreover, it is plausible that the patients who refused to participate in the study because they were too busy might experience more practical barriers than the patients who participated. This may have contributed to an underestimation of the results.

Limitations

Some limitations of this study should be considered. First, we focused on verbal communication, because this type of communication is still of great importance in medical consultations. However, we did not include nonverbal communication in the scoring system. As shown by the literature review of Hall and colleagues (1994) nonverbal indicators of provider interest are associated with patient satisfaction and indirectly associated with medication intake behavior. Future research on communication strategies to reduce barriers to successful medication intake behavior should include nonverbal measures as well.

A second limitation is that we measured perceived barriers only after the consultation. Therefore, we were not able to measure possible changes over time. This

might be an explanation for some findings that were not predicted by the developed typology. For example, checking whether the patient had understood the given information was associated more frequently with necessity barriers. It is possible that although the nurses used this communication technique to decrease those barriers, they might not have been able to remove them successfully. In other words, it is possible that the patients scored relatively high on these barriers after the consultation, but lower than they would have scored before the consultation. Therefore, future research should include pre-measurements of perceived barriers regarding medication, which may help to further refine the developed typology.

Conclusions

To conclude, although the PPB-typology provides promising communication recommendations, many of the communication strategies according to the typology were minimally used and should therefore be prioritized in future communication skills training. Interpersonal health communication could be improved by providing training programs to teach health care providers how to identify barriers to successful medication intake behavior, how to adequately respond to emotional cues, how to encourage patient participation, and how to actively involve patients in the decision-making process. The results of this study suggest promising ways to use the PPB-typology in interventions that address patients' barriers by using tailored communication to promote successful medication intake behavior.

Chapter 5

Understanding patients' medication beliefs: the importance of patient satisfaction

Nurse: "First, I will tell you how and why the medication works." Patient: "IF it works." Nurse: "Are you cynical about that?" Patient: "YES, I have used as much medication as there seems to exists on this planet and nothing has helped so far, so no, I am not convinced" (male, 25 years old, Crohn's disease).

Patient: "Well, yes.. cancer is a side effect that frightens me. […] Yes, the word cancer has been on my mind a lot lately" (female, 26 years old, Crohn's disease).

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Abstract

Background: To gain more insight into patients' beliefs that are held about maintenance medication prescribed for inflammatory bowel disease (IBD) at start of the treatment and after six months, and to explore the relation between patients' satisfaction with providers' communication concerning the newly prescribed medication and patients' beliefs.

Methods: This is a longitudinal study in which telephone interviews were conducted with 84 IBD patients. The questionnaire included the Beliefs about Medicines Questionnaire (BMQ-specific) and measurements of patients' satisfaction with their providers' communication. In addition, patients were asked to indicate to what extent the information was tailored to their needs.

Results: More than half of the patients perceived concerns about, or little personal need for the prescribed medication. Especially concerns were salient. Their beliefs remained stable after six months. A higher level of patient satisfaction with provider's communication and the perceived level of tailoredness was significantly related to more positive beliefs about the medication.

Conclusions: This study provides valuable insights into the beliefs held by IBD patients about their maintenance therapy. The results of this study highlight the significant role of patient satisfaction with provider communication and the perceived level of tailoredness in relation to medication beliefs.

Introduction

The importance of positive beliefs towards the desired behavior has been emphasized in a number of health psychology theories such as the theory of planned behavior (Ajzen, 1991; Fishbein & Yzer, 2006), the integrative model of behavior prediction (Fishbein & Yzer, 2006) and the behavioral model for medication adherence (Bruin, Hospers, Borne, Kok, & Prins, 2005). Empirical research also revealed that beliefs about medication are significantly related to medication intake behavior (Clifford et al., 2008; Ediger et al., 2007; Horne & Weinman, 1999; Horne, 2003; Horne et al., 2004; Horne et al., 2009).

Research involving beliefs about medication suggests the use of the necessity-concerns framework (NCF) in predicting medication intake behavior (Clifford et al., 2008; Horne et al., 1999; Horne & Weinman, 2002; Horne, Cooper, Gellaitry, Date, & Fisher, 2007). According to the NCF, patients' willingness to start and continue to take prescribed medication is influenced by the way in which they judge their personal need for the treatment relative to potential adverse consequences of taking it (Clifford et al., 2008). Necessity is a summative belief representing the individuals' evaluation of the importance of the perceived beliefs. It can be thought of the answer to two questions: 'How much do I need this potential benefit?' and 'Can I manage without it?'. Concerns are a measure of the perceived relevance of the costs and their emotional impact (e.g., how much they worry about potential side effects; Horne, 2003). A meta-analysis spanning 17 long-term conditions involving over 10,000 patients showed that poor medication intake behavior was related to necessity beliefs and concerns. This meta-analysis also showed that the framework had good exploratory value in both cross-sectional and prospective studies. However, relatively few studies have used prospective designs measuring beliefs when starting the treatment (Horne et al., under review).

Providers have a key position in understanding and addressing patients' specific concerns and beliefs about the necessity of medication intake (Latter, Maben, Myall, Young, & Baileff, 2007). The link between communication and medication intake behavior has been studied extensively (Hulka et al., 1976; Latter et al., 2010; Zolnierek & DiMatteo, 2009). There is accumulating evidence that providers' communication can play a crucial role in influencing satisfaction (Bartlett et al., 1984), and medication intake behavior (Bartlett et al., 1984; Hulka et al., 1976; Korsch, Gozzi, & Francis, 1968; Ley, 1988; Zolnierek & DiMatteo, 2009). For example, Bartlett and colleagues (1984) found a positive effect of providers' communication skills on medication intake behavior, and this effect was mediated by patient satisfaction. Although patient satisfaction with the providers' communication is positively related to medication intake behavior (Bartlett et al., 1984), the relation between satisfaction with providers' communication and medication beliefs is still unexplored. To our knowledge there is one study that concluded that providers' collaborative communication style (e.g., a non-authoritarian manner of problem-solving

and conflict resolution) was positively related to beliefs about medication (Bultman & Svarstad, 2000). However, the researchers did not measure patients' satisfaction with providers' communication, and they suggest further research to unravel the relationship between satisfaction with providers' communication and beliefs about medication (Bultman & Svarstad, 2000). The aim of this study is to gain more insight into beliefs patients have about their newly prescribed medication at start of the treatment and after six months and into the relation between satisfaction with providers' communication concerning the newly prescribed medication and medication beliefs.

Methods

Design

Between December 2008 and March 2012, inflammatory bowel disease (IBD) patients and eight nurses from six hospitals in the Netherlands were recruited. In the Netherlands, nurses have a key role in IBD management and educating IBD patients about newly prescribed medication such as immunosuppressive and biological therapy. Nurses are expected to inform the patients about the prescribed medication (e.g., about possible side effects, and to give instructions on how to take the medication). Therefore, this study focuses on nurse consultations around IBD immunosuppressive or biological therapy. Moreover, we focused on IBD patients because only a few studies have measured beliefs about medication among IBD patients (Hall, Rubin, Hungin, & Dougall, 2007; Horne et al., 2009). These studies did not, however, investigate changes in beliefs over time.

To be eligible for this study, patients had to meet the following inclusion criteria: (1) diagnosed with Crohn's disease or Ulcerative Colitis according to classical clinical, endoscopic, radiographic and/or path histological criteria as determined by an experienced gastroenterologist, (2) going to start with immunosuppressive or biological therapy (i.e., Azathioprine, 6-mercaptopurine, Infliximab, Methotrexaat, 6-thioguanine, and Adalimumab) for the first time and, (3) being able to read and write in Dutch. All patients (N = 84) gave written informed consent. The Medical Ethical Committee of the VU University Medical Centre Amsterdam granted permission for this study, which was supplemented with local feasibility statements (trial number NTR2892).

Measurements

The Beliefs about Medicines Questionnaire

The Beliefs about Medicines Questionnaire (BMQ-Specific) was used to assess patients' beliefs and attitudes towards immunosuppressive or biologic therapy prescribed for IBD (Heijmans, 2006; Horne et al., 1999). The BMQ-Specific was administered during telephone interviews when patients started taking their medication; three weeks after the consultation (T1) and 6 months after (T2; see Figure 1). The BMQ-Specific comprises two subscales, a 5-item Necessity scale measuring patients' beliefs about the *necessity* of

taking the medication (5-item scale, α = .75), and a 5-item Concerns scale measuring patients' *concerns* about the potential adverse consequences of taking the medication (5-item scale, α = .67). Examples of the Necessity scale included: 'My health at present depends on my medication' or 'My medication protects me from getting worse'. Examples of the Concerns scale included: 'I sometimes worry about becoming too dependent on my medication' or 'Having to take medication worries me'. Patients were able to indicate their level of agreement on a 5-point Likert scale ranging from 'strongly disagree' (1) to 'strongly agree' (5). Higher scores on the scales indicate stronger beliefs (i.e., high perceived necessity and more concerns, respectively). The patients' scores on each scale were summed, resulting in a scale ranging from 5 to 25 for necessity and concerns. Based on the mid-point (15) of the two BMQ-Specific subscales, we divided patients in four different groups: ambivalent (high necessity, high concerns), sceptical (low necessity, high concerns), indifferent (low necessity, low concerns), and accepting (high necessity, low concerns; Clifford et al., 2008; Horne et al., 1999; Horne et al., 2009; Menckeberg et al., 2008). A necessity-concerns differential (NCD) was calculated per patient by subtracting his/her concerns score from his/her necessity score, resulting in a range from -20 to 20. The NCD provides a numerical assessment of how the patient judges their perceived need for treatment, relative to their concerns. Positive scores indicate that necessity was valued higher then concerns and negative scores indicate that concerns were rated higher than perceived need (Clifford et al., 2008; Horne et al., 1999; Menckeberg et al., 2008).

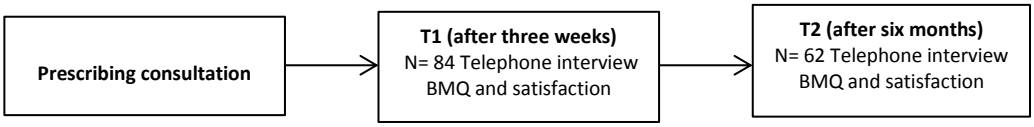

Figure 1. *Procedure.*

Patient satisfaction

To measure satisfaction, we used 29 statements belonging to three scales concerning satisfaction with the general information about one's disease and treatment (12 items, α = .85 Range 12-48), support regarding medication use (7 items, α = .67 Range 12-28), and the affective communication (9 items, α = .82 Range 9-36). Examples of statements concerning general information about disease and treatment were: 'The nurse educates me about my disease' and 'The nurse informs me about the potential side effects'. Examples of the medication use scale were: 'The nurse asks whether I experience adverse reactions' and 'The nurse discusses whether the treatment is effective'. Examples of the affective communication scale were: 'The nurse takes me seriously' and 'The nurse treats me with respect'. The possible answers ranged from '1 = poor' to '4 = very good' (Hendriks, Vervloet, & van Dijk, 2005). Thus, a higher score on this scale indicated that a patient was more satisfied. In addition, we asked patients to assess the consultation on a scale of 1 to 10, to indicate to what extent the consultation was tailored to their specific needs.

Demographic characteristics

Participants were asked to specify their age, gender, and education. Education was divided into low level of education, middle level of education and high level of education.

Statistical analyses

For the non-response analysis, Chi-square (χ^2) tests and independent sample *t*-tests were conducted to determine differences between participants and non-participants. Descriptive statistics were used to describe the sample. To address our aims, mean scores and standard deviation (*SD*) for BMQ-specific Necessity and Concerns scale and the NCD were calculated at T1 and T2 and compared at the two time points using paired samples *t*-tests. Moreover, differences within the attitudinal groups between patients who continued the treatment and patients who stopped taking the medication (drop-out) were calculated using paired sample *t*-tests. Repeated measures were used for within comparison to compare attitudinal beliefs and satisfaction ratings at T1 and T2. Multiple regression analysis was used to examine the relationship between satisfaction and beliefs. Since there was a moderate positive relationship between the different components of satisfaction with the perceived level of tailoredness (mean r = .496, range= .362-.651 p < .001) at T1 and a strong positive relationship between the different components of satisfaction with the perceived level of tailoredness (mean r = .661, range = .605-.728 p < .001) at T2, we conducted separate regressions. Multiple regressions were conducted with the NCD at T1 resp. T2 as dependent variable and the following two sets of variables as independent variables, entered as separate blocks: (i) background characteristics, (ii) satisfaction with the general information or satisfaction with support regarding medication use or satisfaction with affective communication or the perceived level of tailoredness. For the regression analyses, we dummy coded the three levels of education with high education as a reference group.

Results

Non response

Of the 114 eligible patients, 20 (17.5%) refused to participate in the study. Seven did not want their consultation to be videotaped, five felt too sick or too tired, and eight felt overwhelmed or were too busy. Afterwards, we excluded ten participants because they decided not to start with the medication, or because they stopped with their medication within three weeks. Three weeks and six months after the consultation, the patients were contacted for a telephone interview. A total of 84 patients filled out the questionnaire at the start of their treatment (T1). If patients indicated during the follow-up telephone interview in the next measurement (survey at T2) that they had stopped with their medication (n = 22), they were excluded. Reasons mentioned for drop-out were side

effects, ineffectiveness of the medication or pregnancy. This resulted in a total of 62 of 110 patients who completed both questionnaires (see Figure 2). Non-participating patients (n = 20) or patients who stopped taking their medication (n = 22) did not differ significantly in terms of age and gender from participating patients (n = 84).

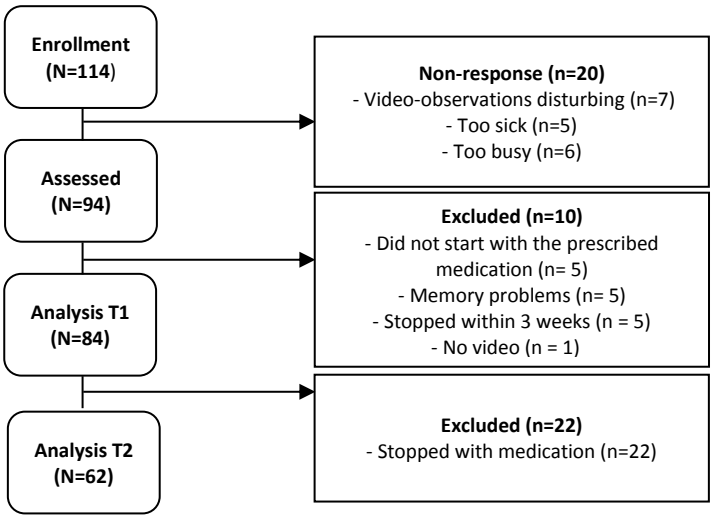

Figure 2. *Flow chart.*

Sample characteristics

The characteristics of the patients are presented in Table 1. More than two-thirds (63.1%) of the sample was female, 62 patients (73.8%) were diagnosed with Crohn's disease and 22 patients (21.8%) with Ulcerative Colitis. The mean age was 40.6 years (*SD* = 14.5*)* and one third of the patients were moderately educated (34.2%).

All nurses were female with a mean age of 40.6 years (*SD* = 14.3). On average, they had worked as IBD nurses for approximately 4.7 years (*SD* = 2.9).

Table 1.
Patient characteristics

Patient characteristics		*N* = 84	%
Gender	Female	53	63.1%
Age	M (*SD*)	40.6 *(14.3)*	
	Range	19-81	
Type of disease	Crohn's disease	62	73.8%
	Colitis Ulcerosa	22	25.0%
Diagnosed in years	M*(SD)*	10.1	*(9.8)*
Educational level	Low	21	25.0%
	Moderate	31	36.9%
	Higher education	32	38.1%
Living arrangements	Alone	19	22.6%
	With partner	20	23.8%
	With partner and child(ren)	21	25.0%
	With child(ren)	10	11.9%
	Other	14	16.7 %
Children	Yes	44	52.4%
Employed	Yes	61	72.6%
Ethnicity	Dutch	73	86.9%
Religious	Yes	20	23.8%

Beliefs about immunosuppressive or biological therapy

Patients were categorized into four attitudinal groups based on their specific beliefs about immunosuppressive or biological therapy. Figure 3 shows that, at the start of their treatment with immunosuppressive or biological therapy, more than half of the patients accepted their treatment (55%; high necessity, low concerns). A third of the patients was ambivalent (27%; high necessity, high concerns). The smallest groups of patients were indifferent (16%; low necessity, low concerns) or sceptical (2%; low necessity, high concerns). After six months, the results largely remained the same. More than half of the patients accepted their treatment (55%) and a third of the patients was ambivalent (28%). The smallest groups were again indifferent (15%) and skeptical (2%; see Figure 3). A

within-subjects (GLM repeated measures) test showed that the difference in attitudinal beliefs was not significant, $F(1,61) = 0.110$, $p = .472$, $\eta^2 = .002$.

Results also showed that there was no significant difference within the attitudinal groups between patients who continued the treatment and patients' who stopped taking the medication (drop-out; see Table 2; n=22).

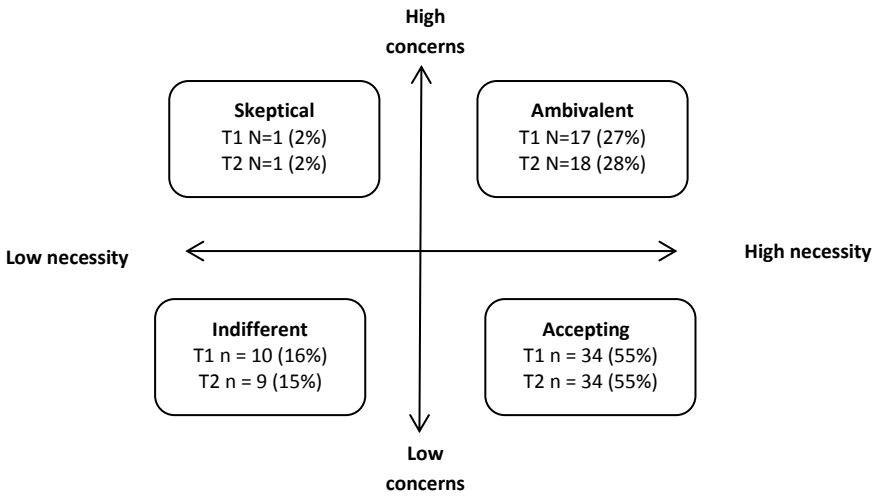

Figure 3. *Attitudinal analyses of beliefs about immunosuppressive or biological therapy over time.*

To explore the changes in the NCD over time, only patients who completed both questionnaires at T1 and T2 ($N = 62$) were included. On average, there was no difference between experienced concerns at the start ($M = 13.56$, $SD = 3.75$) and after six months ($M = 13.58$, $SD = 3.43$), t (57) =-.04, $p = .966$. There was also no difference between patients' personal need for medication at start of their treatment ($M = 18.41$, $SD = 3.21$) and after six months ($M = 18.27$, $SD = 3.49$), t (57) = 0.28, $p = .781$. According to the NCD, patients thought that the benefits of taking the medication outweighed the costs at T1 ($M = 4.84$, $SD = 4.11$) and T2 ($M = 4.68$, $SD = 4.67$), t (57) = 0.24, $p = .807$. These differences were not significant.

Table 2.
Differences in attitudinal groups for drop-out and participating patients

	Attitudinal groups			
Did the patient stop with the treatment?	**Sceptical**	**Ambivalent**	**Indifferent**	**Accepting**
Yes	1 (4.5%)	8 (36.4%)	2 (9.1%)	11 (50.0%)
No	1 (1.6%)	17 (27.4%)	10 (16.1%)	34 (54.8%)

Patients' satisfaction

To analyse satisfaction over time, only patients who completed both questionnaires at T1 and T2 (n = 62) were included. At the beginning of the treatment, patients were satisfied with nurses' general information about their disease and treatment (*M* = 3.63, *SD* = 0.42, range 1-5) and about nurses' affective communication (*M* = 3.74 *SD*= 0.37 range 1-5) and with nurses' support with their medication use (*M*= 3.47 *SD*= 0.42 range 1-5). (*M* = 7.8, SD = 1.0, range = 5 – 10 at T1) and after six months (*M* = 7.7, *SD*= 1.0, range = 5 - 9 at T2). An Anova with repeated measures showed that patients significantly rated the components of the satisfaction scale differently, Wilks' Lamba = .638, $F(2,68) = 19.278$, $p < .001$, $\eta^2 = .632$.

After six months, patients were generally most satisfied about nurses' general information about their disease and treatment (*M*= 3.70 *SD*= 0.43 range 1-5) and affective communication (*M*= 3.71 *SD*= 0.42 range 1-5) and support with their medication use (*M*= 3.44 *SD*= 0.56 range 1-5). The difference between patients' satisfaction at start of the treatment and after six months was not significant. An Anova with repeated measures showed that patients significantly rated the components of the satisfaction scale differently, Wilks' Lamba = .040, $F(1,61) = 621.006$, $p < .001$, $\eta^2 = .960$.

Table 3.
Medication beliefs

Scale	Range of score	Mean Score	*SD*	Minimum score	Maximum score	*N*
Necessity (t1)	5 to 25	18.47	3.26	10	25	84
Necessity (t2)	5 to 25	18.24	3.64	5	25	62
Concerns (t1)	5 to 25	13.75	3.64	6	25	84
Concerns (t2)	5 to 25	13.66	3.43	7	20	62
Differential (t1)	- 20 to 20	4.70	4.20	-4	19	84
Differential (t2)	- 20 to 20	4.58	4.80	-11	15	62

Satisfaction and medication beliefs

To investigate the relationship between satisfaction and patients' beliefs (NCD) towards their medication at T1, all patients who completed the questionnaire at T1 (*N* = 84) were included. Patients' satisfaction with the general information about their disease and treatment had a significant, positive relation with beliefs towards medication (β = .31, *p* = .012). This indicates that the more satisfied patients were with their nurses' information about their disease and treatment, the more positive beliefs they held towards their medication. Patients' satisfaction regarding the perceived level of tailoredness was significantly related to a more positive belief towards medication (β =.25, *p* = .024). This indicates that patients who were more satisfied about the level of tailoring in the consultation had more positive beliefs towards their medication. To measure the relation between satisfaction and patients' beliefs after six months, we repeated the analyses with the 62 patients who completed the questionnaire at T2. Results showed that patients'

satisfaction with the general information about their disease and treatment at T2 was significantly related to more positive beliefs towards medication after six months (β = .35 p = .015). However, the relation between the perceived level of tailoredness and positive beliefs towards medication disappeared.

Discussion

This study provides insights into IBD patients' beliefs about immunosuppressive or biological therapy and explored the relation between patient satisfaction with provider's communication and beliefs about medication. Our results can be summarized into three key findings. First, almost half of the patients perceived problems with taking the medication. Second, beliefs remained stable after six months. Third, patients' satisfaction with nurses' communication is significantly related to their beliefs about the medication.

At the start of their treatment, most patients accepted the medication, but almost half of the patients reported problems with believing that the medication was necessary and/or had concerns about the medication. Similar results in IBD patients taking maintenance medication have been reported (Ediger et al., 2007; Horne et al., 2009). Horne and colleagues (2009) compared the reported medication intake behavior across the four attitudinal groups. Results indicated that the 'accepting' group had the highest levels of successful medication intake behavior, which was significantly higher than all the other groups. Patients in all other attitudinal groups were significantly more likely to be nonadherent. To improve medication intake behavior through targeted interventions, it is important to identify patients who have negative beliefs about their medication. It may however be rather difficult for nurses to identify these beliefs, particularly if the nurses are not trained in the detection of such beliefs. A recent study developed an online preparatory assessment (OPA) which gains more insight into patients' beliefs and assists nurses in determining the most effective strategy to meet patients' specific beliefs. Based on the results of the OPA, nurses are informed about the perceived beliefs and specific communication strategies that should be used in order to address these negative beliefs (Linn, Weert, Smit, Perry, & Van Dijk, 2013).

According to the common-sense model of health and illness (Leventhal, Brissette, & Leventhal, 2003) and the NCF (Clifford et al., 2008), patients starting their treatment receive information about the medication and develop new beliefs based on new information and experiences. For example, a decrease in symptoms of one's illness can lead to less adaptive responses, such as lower perceived necessity (Leventhal et al., 2003). According to these models it seems plausible that medication beliefs may change over time. Our results show no statistical differences in the BMQ-Specific after six months. This is in contrast with other studies in which changes over time were measured. One study found more positive beliefs about antidepressants after six months (Aikens & Klinkman,

2012). Another study found more negative beliefs about medications for cardiovascular disease after twelve months (Allen LaPointe et al., 2010). However, these results were found in in other diseases. IBD patients starting with immunosuppressive or biological therapy can expect to experience improvement in their health after two to four months, depending on the type of medication (Mertens, Hertel, Reuther, & Ricker, 1981) which may explain why we did not observe any changes in beliefs. Another explanation may be that, according to the Elaboration Likelihood Model (ELM), patients engage in central-route processing if involvement is high, which means that one is willing to elaborate on the message. Attitudes formed via the central route are more stable (Petty & Cacioppo, 1986a). As IBD patients especially prefer to be actively involved in the decision-making process concerning their treatment (Baars et al., 2010), it seems plausible that IBD patients are more likely to engage in the central route, which makes beliefs more difficult to change. Moreover, the beliefs in the previous mentioned studies and in our study population were not targeted. This might be due to the failure of health care providers to apply appropriate techniques to change those beliefs. Communication skills training for health care providers should prioritize exploring, identifying and addressing patients' beliefs.

Our results indicate that patients' satisfaction with nurses' communication is significantly related to medication beliefs. In addition, our results indicate that patients' satisfaction regarding the extent to which the consultation was tailored to their needs was significantly associated with medication beliefs. Especially high quality information may prevent inaccurate information and thus negative beliefs. Previous studies in this field have consistently demonstrated a positive relationship between satisfaction and successful medication intake behavior (Bartlett et al., 1984; Hulka et al., 1976; Korsch et al., 1968; Ley, 1988; Zolnierek & DiMatteo, 2009). It is often assumed that this is also the case for patients' beliefs about medication.

Patients often report unmet information needs when starting with their medication (Irvine, 2004). Educating patients should be based on individual preferences, by directly asking patients about their needs. Previous studies showed that tailored information, which relates to the specific information needs of the patient, improves patient satisfaction (Kessels, 2003; Ley, 1979), recall of medical information (Kessels, 2003; Van der Meulen et al., 2008) and therefore may result in more successful medication intake behavior (Linn et al., 2012; Ownby, Hertzog, & Czaja, 2012). To improve medication intake behavior, our results indicate that it is important that providers use a tailored patient-centred approach; especially since it enables patients to discuss their beliefs, explaining benefits and risks of the medication (Nunes et al., 2009). As a consequence, patients may have more positive beliefs towards their medication. When patients were asked how satisfied they were with their nurses' information provided the past six months, the relation with medication beliefs remained. With these results in mind we can assume that communication may especially be important in the initiation of the treatment for

example, when the patient takes the first dose of a prescribed medication. Indeed, a review of reviews concluded that educational interventions such as interpersonal education appear to have a favourable impact on medication intake behavior. However, most of the effects decrease over time (Van Dulmen et al., 2007).

There was a moderate to strong positive relation between satisfaction and the perceived level of tailoredness. This may indicate that patients who are more satisfied about the information given during the consultation may perceive fulfilled information needs. This is in line with the work of Linder-Pelz (1982) who considers satisfaction as a multidimensional concept in which patient satisfaction is a positive attitude or a positive evaluation of health care services. In this view, patients' evaluate distinctive aspects of their care, for example the quality of the information and the degree to which the providers' information meets the patients' needs (Sixma, Kerssens, Campen, & Peters, 2002).

Limitations

Our study is limited because we measured the BMQ-Specific at a six months interval in IBD patients receiving immunosuppressive biological therapy. Since patients may form or change their beliefs based on an increase or decrease in symptoms of the illness, IBD patients starting with their medication have not sufficiently noticed the effectiveness of the medication after six months. Measuring the BMQ-Specific after six months may be too short for patients to notice significant changes in their health. This, in turn, may result in underestimating the results. Further research should include an interval of one year or even longer to measure changes in beliefs.

Conclusions

This study underlines that effective communication matching patients' needs and preferences leads to more positive beliefs about medication. Thus, the provision of tailored information makes patients more positive towards their prescribed medication. Thus adequate, high quality information which is tailored to the patients' needs is important when addressing beliefs about medication. Successful interventions should therefore focus on tailored adequate information to modify these beliefs.

Practical implications

With almost fifty percent of the patients experiencing problems with either their personal need for medication and/or concerns about their intake, this suggests the need for supporting patients with their beliefs and concerns. Responding adequately to patients' concerns is essential, because it reduces anxiety (Butow et al., 2002) and may promote satisfaction (Uitterhoeve et al., 2008), increases disclosure of emotions, concerns and worries (Roter & Larson, 2002), and gives providers a better understanding of patients' concerns which makes it easier to respond more adequately to these cues (Uitterhoeve et al., 2008). A previous study showed that adequate communication strategies, tailored to the patients' concerns are related to less concerns (as indicated by the BMQ-Specific; Linn et al., 2012). Especially since medication beliefs are associated with medication intake behavior, adequate, high quality information which is tailored to the patients' needs seems to be important in addressing patients beliefs and may also result in higher satisfaction with health care.

Chapter 6

May you never forget what is worth remembering: the relation between recall of medical information and medication intake behavior in patients with inflammatory bowel disease

Nurse: "All in all, I will tell you quite a lot of information, and therefore, I will repeat the most important information so that you do not have to remember everything at once".

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Abstract

Background: Nurses play an important role in educating patients with inflammatory bowel disease (IBD) about immunosuppressive or biological therapy during prescribing consultations. The education for immunosuppressive or biological therapy often contains complex information. Poor medication intake behavior can be a result of poor information recall, which is often caused by complex information.

Objectives: The aim of this study is to measure information recall by IBD patients, and to investigate the relationship between recall and medication intake behavior.

Methods: Data collection took place from September 2009 until March 2012. Eight nurses at six Dutch hospitals and 68 IBD patients participated in this study. Prescribing consultations were videotaped and patients completed surveys immediately after the consultation and after three weeks. Information recall was based on the actual communication in video recordings of the consultations. Medication intake behavior was measured by self-report.

Results: Issues most frequently discussed were side effects and how patients had to administer their medication. IBD patients could reproduce half of the information given. Recall of medical information was a significant predictor for self-reported medication intake behavior (β = .37, p = .007), indicating that higher recall of medical information relates to improved self-reported medication intake behavior.

Conclusions: This study revealed a significant relation between IBD patients' recall and self-reported medication intake behavior. When educating IBD patients about their newly prescribed medication, providers should consider recall-promoting techniques to increase medication intake behavior.

Introduction

It is increasingly recognized that medication intake behavior is complex. Taking medication is a process in which three phases can be distinguished: the initiation (the patient takes the first dose), the implementation or execution (the patient's behavior corresponds with the prescribed regimen) and the discontinuation (the end of the regimen is marked) (Urquhart & Vrijens, 2005). Although appropriate medication intake behavior can reduce the chance of relapse in inflammatory bowel disease (IBD) patients, the patients often do not take their medication as prescribed (phase 2). For example, Kane and colleagues (2003) found that patients who failed to adhere to their maintenance medication had a 61% chance of relapse, compared with just 11% among those patients who did take their medication as prescribed. A review involving patients with IBD showed nonadherence rates varying from 7% to 72% for long-term therapies, with most studies reporting 30% to 45% nonadherence (Jackson, Clatworthy, Robinson, & Horne, 2009). Although some associations have been found, demographic variables (e.g., age and gender) as well as disease and treatment factors (e.g., administration and complexity) are considered to be poor indicators of medication intake behavior (Vermeire et al., 2001).

The treatment of IBD has become more complex since the introduction of immunosuppressive or biological therapy (Johnson et al., 2007). When their treatments become more complex, patients are more prone to forget how and when they must take their medication (DiMatteo et al., 2012). A study measuring patients' knowledge about their immunosuppressive or biological therapy found that of the 354 participating patients, only 60% understood the role of immunosuppressive or biological therapy (Hilsden, Verhoef, Best, & Pocobelli, 2003). Efforts to improve patients' knowledge include the use of information leaflets (Hawkey & Hawkey, 1989) or physician education (Waters, Jensen, & Fedorak, 2005).

To optimize the initiation process and the implementation or execution process for newly prescribed medication, nurses play an increasingly important role in educating IBD patients about their immunosuppressive or biological therapy during consultations at which medication is prescribed. These prescribing consultations contain complex and important information about, for example, medication instructions, which are often difficult to remember (Ley, 1979; Wessel et al., 2000). While information about prescribed medication is important in promoting medication intake behavior, it can be considered to be useless when the recall of medical information, i.e., the ability to understand and reproduce the medical information, is poor (Kessels, 2003; Ley, 1988). In other words, patients who do not know how to take the medication as prescribed because they are not able to understand or reproduce the information are not likely to behave appropriately (Kessels, 2003). Thus, the recall of medical information is expected to influence the quality of the initiation and implementation processes for taking medication. This is in line with

Ley's cognitive model, assuming that medication intake behavior can be determined by the recall of medical information (Ley, 1988). Although the relationship between the actual recall of medical information and medication intake behavior has previously been suggested in the literature (Ley, 1988), neither recall has been accurately measured (Bartlett et al., 1984; Pickney & Arnason, 2005) nor measured in IBD. When the relationship between medication intake behavior and recall was studied, either recall was measured using only three items (Bartlett et al., 1984) or it was assessed many months after the information was provided, both of which make the results less accurate (Pickney & Arnason, 2005). To improve medication intake behavior and develop target interventions, it is important to understand the relationship between the recall of medical information and medication intake behavior. The aim of this study is therefore to investigate the relationship between the recall of medical information and medication intake behavior in IBD patients by comprehensively measuring the recall of medical information.

Methods

Design and Population

This study was part of a larger study aiming to develop an intervention to tailor the communication to IBD patients' needs and barriers to medication intake behavior. The recommendations for this intervention are based on an investigation of care-as-usual, including patients' recall of medical information and medication intake behavior .

Data were collected from September 2009 until March 2012. Eight IBD nurses at six hospitals participated. Patient inclusion criteria were being diagnosed with Crohn's disease or Ulcerative Colitis according to classical clinical, endoscopic, radiographic and/or pathological histological criteria as determined by an experienced gastroenterologist, starting with Azathioprine, 6-mercaptopurine, Infliximab, Methotrexaat, 6-thioguanine, or Adalimumab, and fluency in Dutch. The Medical Ethical Committee of the VU Medical Center granted permission for this study, which was supplemented with local feasibility statements of all participating hospitals (trial number NTR2892).

Procedure

Eligible patients were sent a letter with information about the study. Prior to the consultation, a written informed consent was obtained from both the patient and the nurse. Furthermore, patients completed a written questionnaire containing background information and disease characteristics. A researcher started a video camera (n = 59) or tape recorder (n = 9) and left the room before the consultation started. Immediately after the consultation, the patients were asked to complete another written questionnaire. Three weeks after the consultation, the patients were contacted for a telephone interview.

Measurements

Background characteristics

The background measures included age, gender, level of education, type of disease, years since diagnosis, and administration of the medication (e.g., pills, infusion, or injection).

Content analysis

The information discussed in the videotapes was analyzed using an extensive observation checklist based on comparable studies in oncology (Jansen et al., 2008; Van Weert, Jansen, Spreeuwenberg, van Dulmen, & Bensing, 2010). The categories in the checklist covered ten primary domains: 'general information about the disease', 'information about the medication', 'side effects', 'information about corticosteroids', 'administration', 'information leaflet', 'recommendations', 'additional necessary medication/checks', 'impact of the medication on patients' daily life' and 'need for blood monitoring'. Each primary domain consisted of several subcategories. The subcategories for the primary domain 'information about the medication' were, for example, 'name of medication', 'duration of the treatment', 'purpose of the treatment', and 'effect of the treatment on patients' health'. Additional subcategories could be added to each primary domain on the checklist.

Recall of medication information

The recall of medical information was measured using an adapted version of The Netherlands Patient Information Recall Questionnaire (NPIRQ), which was originally used in oncology settings and checked against the actual consultation using the observation checklist (Jansen et al., 2008). For the purpose of this study, the NPIRQ was adapted for the IBD setting. To ensure content relevance, the questionnaire was designed to include questions that were representative of the main topics discussed in the consultations and, at the same time, relevant to patients starting immunosuppressive or biological therapy. We generated questions using pilot observations from videotaped consultations (N = 15). Examples of topics on the questionnaire are as follows: purpose of the medication, name of medication, duration of treatment, frequency of administration, and when to expect an effect from the medication. The content validity of the questionnaire was tested by nine nurses (not involved in the current study). These nurses were asked to indicate topics that, according to them, are discussed in a consultation. Based on their input, the items of the questionnaire were revised or deleted. This review process resulted in thirteen questions, which were assessed directly after the consultation *(immediate recall*). Each question started with a multiple-choice indication of whether the topic was discussed. The answer options were 1) "No, not discussed", 2) "Yes, it was discussed but I don't remember what was said", and 3) "Yes, namely…". With the latter selection, the patient was invited to

write down what he or she recalled about the topic (for example, “Can you describe the purpose of the treatment?”).

Three weeks after the consultation, *delayed recall* was measured by telephone using thirteen questions. The consultations were analyzed in a naturalistic environment, which meant that the nurses provided some standard introductory information but that the content and the amount of information varied per patient. For this reason, a different version of the delayed questionnaire was developed for each patient based on his or her videotaped consultation. The basis of the questionnaire was the immediate recall questionnaire. Almost all the questionnaires contained questions about ‘the name of the medication’ , ‘what kinds of side effects may occur’, ‘the frequency of administration’ and ‘when to contact the nurse’. Topics from that questionnaire that were not or limited discussed were replaced with questions about the most important other topics discussed in that specific consultation. This resulted in more personal relevant questions (e.g., “What information is given by the nurse about the possibility of getting pregnant when using your medication?” or “What information is given by the nurse about vaccinations when travelling while you are using your medication?”).

Two coders first assessed whether the topic was discussed during the visit based on the videotapes. Second, each item recalled was compared with the specific items mentioned by the nurse (Jansen et al., 2008; Jansen et al., 2008). The percentage of accurate recall was calculated by dividing the sum of the accurately recalled items by the total number of items discussed (Jansen et al., 2008). Finally, a total recall score was established, which is the mean recall percentage per patient for immediate and delayed recall.

Interobserver reliability

To determine the interobserver reliability of the immediate and delayed recall measurements, two observers randomly coded nine identical transcriptions of the consultations (13%) (Zandbelt, Smets, Oort, & De Haes, 2005). The first author, experienced in coding nurse-patient communication, trained the research assistant in using the observational protocol and coding scheme for the recall questions. After six days of training, the real observations began. Regular meetings were held to discuss and resolve coding issues. Reliability was assessed using Cohen's Kappa, which corrects for agreements due to chance. The mean inter-observer reliability was .91. For immediate recall, the mean interobserver reliability was .85 (Range = .72-1) and for delayed recall, the mean inter-observer reliability was .97 (Range = .89-1), illustrating a good interobserver reliability (Altman, 1991).

Medication intake behavior

We measured self-reported medication intake behavior with a single item (i.e., "Please indicate on a scale from 1 to 10 the extent to which you are taking the medication as prescribed", with 1 representing very poor and 10 representing very good). A previous study showed that this self-report measure is significantly related to the scores obtained using a more objective method to measure medication intake behavior: the Medication Event Monitoring System (Hugen et al., 2002).

Statistical Analysis

A non-response analysis was conducted using *t*-tests and Chi-square tests to examine the differences between the responders and the non-responders in terms of age and gender. Descriptive statistics were used to describe the sample, the consultation characteristics and the recall scores. The administration of the medication was dummy coded for a regression analysis for 'injection' and 'infusion therapy,' with 'pills' as the reference category. An ANOVA analysis was carried out to compare recall scores between patients taking pills, injections or receiving infusion. A multiple regression analysis was used to examine the predictors of medication intake behavior. The predictors for self-reported medication intake behavior in the regression were pre-selected for each of the patients' demographic variables using a backward selection procedure. In the pre-selection, a significance level of p =.15 was chosen (Zandbelt, Smets, Oort, Godfried, & De Haes, 2006). Three background characteristics (age, education and type of administration, i.e., injection or infusion therapy) as well as the delayed recall of medical information were retained. Subsequently, pre-selected variables were included in the final model by entering the following two sets of variables as separate blocks: (i) background characteristics as control variables and (ii) delayed recall of medical information.

Results

Patient characteristics

Of the 100 eligible patients, 22 refused to participate. Nine did not want their consultation to be videotaped, five felt too sick or too tired, and eight felt overwhelmed or were too busy. Another ten patients were excluded because they decided not to start with the prescribed medication.

The non-participating patients did not significantly differ in age or gender from the included patients. The consultations for all remaining patients (N = 68) were analyzed. Almost two thirds (n = 42) of the sample were female, and 54 patients (79.4%) were diagnosed with Crohn's disease. The mean age was 40.5 years (*SD* = 14.9), and over half of the patients had received a higher education. A total of 20.6% of the patients received

their medication through infusion, 42.6% had to take pills, and 36.8% had to inject themselves (see Table 1).

Table 1.
Demographic Characteristics.

Patient characteristics		*N* = 68	%
Gender			
	Male	26	37.7%
Age			
	M (*SD*)	40.5 *(14.9)*	
Type of Disease			
	Crohn's disease	54	79.4%
	Colitis Ulcerosa	13	19.1%
	Unknown	1	1.5%
Diagnosed in years			
	M*(SD)*	9.6	*(10.3)*
Medication administration			
	Infusion	14	20.6%
	Pills	29	42.6%
	Injection	25	36.8%
Educational level			
	Low	18	20.6%
	Moderate	24	42.6%
	High	26	36.8%
Living arrangements			
	Alone	16	23.5%
	With partner	16	23.5%
	With partner and child(ren)	16	23.5%
	With child(ren)	8	11.8%
	Other	12	17.6%
Employed			
	Yes	51	75.0%
Ethnicity			
	Dutch	63	91.2%

Content analysis

The consultations lasted an average of 29.5 minutes (*SD* = 8.5). In all of the consultations, the nurses discussed the side effects (100%). In almost all consultations, the nurses discussed the name of the medication (98.5%) and its administration (97.1%). The medication intake behavior was discussed in 44.1% of the consultations. In almost half of the consultations, the duration of treatment was not discussed (48.5%; see Table 2).

Table 2.
Recall scores (N = 68)

Category	No of items discussed *(M)*	(*SD*)	Not discussed[1]	% of consultation in which the topic was not discussed	Recall score[2] (%)	*SD*
Immediate recall					**52.6**	**15.0**
Purpose of the medication	5.2	1.9	7	10.3	32.7	37.2
Name of medication	0.9	0.3	1	1.5	83.6	37.3
Duration of treatment	0.5	0.5	35	51.5	59.8	43.3
Frequency administration	3.8	3.1	2	2.9	85.9	24.1
Influence of the medication on the immune system	0.8	0.3	8	11.8	69.2	41.1
When to expect an effect from the medication	0.8	0.4	13	19.1	66.8	41.4
The need for blood monitoring	3.3	2.3	13	19.1	63.6	36.6
Side effects	9.0	3.1	0	0	26.7	18.1
When to contact the nurse	3.7	2.2	4	5.9	39.2	30.4
The possibility of experiencing side effects	0.5	0.5	36	52.9	78.8	42.0
The impact of the medication on the patients' daily life	3.6	2.7	14	20.6	5.5	17.9
medication intake behavior advice	0.8	1.1	38	55.9	15.0	32.5
Delayed recall					**53.8**	**15.7**

[1]Number of consultations in which the item was not discussed
[2]% of correctly recalled information compared with total amount of given information by the nurse, measured only for the consultations in which the category was discussed

Recall of information

Patients recalled 52.6% (*SD* = 15.0) of the information presented by the nurse immediately after the consultation and 53.8% (*SD* = 15.7) after three weeks. There were no significant differences between the immediate and the delayed recall. The type of information that was most accurately recalled immediately was the administration of the medication; on average, 85.9% of this information was reproduced. Furthermore, 83.6% of the information about the name of the medication was accurately recalled. The information that was reproduced the most poorly was the impact of the medication on the patient's daily life (5.5%), the advice about the medication intake behavior (15.0%) and the potential side effects (26.7%; see Table 2). An ANOVA analysis showed no significant difference between patients receiving injection, infusion or pills on delayed recall. On average, patients using injection recalled (*M* = 48.2, *SD* = 12.8) less than patients who received their medication through infusion (*M* = 59.7, *SD* = 15.4) or oral medication (*M* = 51.9, *SD* = 16.3), however this difference was not significant ($t(66) = 2.27$; p = .083).

Predictors of self-reported medication intake behavior

The patients rated their medication intake behavior on average as 9.1 (*SD* = 1.2), indicating that most of the patients rated themselves as being quite highly adherent. Thirty-seven patients (54.4%) rated themselves as completely adherent. Nevertheless, the scores were normally distributed with skewedness and kurtosis below 1.5 (Field, 2009).

The delayed recall of medical information was significantly related to the self-reported medication intake behavior (β = .37, *p* = .007). This relationship indicates that the patients with lower recall scores three weeks after the consultation rated themselves as less adherent than the patients with higher recall scores. Moreover, the patients who had to inject the medication rated themselves as less adherent compared to those who had to take pills (*β* = -.25, *p* = .052; see Table 3).

After entering the first set of background variables, we found a significant negative relationship between age and self-reported medication intake behavior (*β* = -.29, *p* = .020). The relationship between age and medication intake behavior disappeared when controlling for the recall of medical information, implying that there may exist a mediated relationship between age and self-reported medication intake behavior through recall. This mediated effect was tested using Hayes' PROCESS macro (Hayes, 2012). The analysis indeed showed an indirect effect from age on self-reported medication intake behavior through recall. Age was related to recall (B -.44 *p*=.000), and recall was related to self-reported medication intake behavior (B =.02 *p*= .03). The indirect effect of age on self-reported medication intake behavior was significant, 95% CI [-.024, -.001], point estimate =-.009. This result indicates that the older patients are, the less they recall, and the more likely they are to rate themselves as non-adherent.

Table 3.

Relationship between recall of information and medication intake behavior (N = 68)

	Medication intake behavior				**Medication intake behavior**			
	Model 1				**Model 2**			
	B	*SE*	β	*p*	*B*	*SE*	β	*p*
Constant	10.26	.63			8.6	.83		
Age	**-.02**	**.01**	**-.29**	**.020**	-.01	.01	-.15	.243
Education	-.01	.07	-.01	.929	-.06	.07	-.09	.432
Injection[1]	-.46	.32	-.19	.155	**-.61**	**.31**	**-.25**	**.052**
Infusion therapy[2]	-.09	.38	-.03	.802	-.02	.36	-.01	.952
Delayed recall					**.03**	**.01**	**.37**	**.007**
Participants	68				68			
R^2	.09				.19			
Adjusted R^2	.04				.13			
p	.153				**.017**			

[1] bold type indicates which relations were significant

[2] 0,1; 1 = injection; pills = reference category

[3] 0,1; 1 = infusion therapy; pills = reference category

Discussion

This study combines video observations of nurse-patient prescribing consultations about immunosuppressive or biological therapy with post-visit questionnaires to comprehensively measure the recall of medical information. This study investigates the relationship between recall and self-reported medication intake behavior.

Our data support previous research concerning provider-patient communication when prescribing medication (Bezreh, Laws, Taubin, Rifkin, & Wilson, 2012; Latter, Maben, Myall, & Young, 2007; Tarn et al., 2006). The most frequently discussed topics included side effects and the name of the medication. The topics that were often not mentioned were the duration of intake, the advice about medication intake behavior, and the possibility of experiencing side effects. As in a previous study indicating that only 60% of the patients understood the role of immunosuppressive or biological therapy (Hilsden et al., 2003), it appears to be important to train providers to discuss the relevant information necessary to improve their patients' knowledge, which may result in successful medication intake behavior (Waters et al., 2005).

To the best of our knowledge, this is the first study that measured the recall of medical information in IBD patients extensively. Our results demonstrate that the patients reproduced approximately half of the information provided during consultations. Whether these results are consistent with other studies is difficult to determine. Studies measuring patients' recall of medical information often find inconsistent results, varying in their periods for measuring recall, (unclear) measurements, the type of consultation, and the type of patient (Jansen et al., 2008). Previous studies in populations with diseases other than IBD reported recall rates ranging from 23% for older cancer patients receiving chemotherapy (Jansen et al., 2008) and 50% for patients receiving health behavior advice (Flocke & Stange, 2004) to 86% for patients receiving information about their newly prescribed medication (Tarn & Flocke, 2011). These findings indicate that our results are within the range of previously reported recall rates.

The information that was recalled most poorly was the impact of the medication on the patients' daily lives. This result is particularly interesting because previous studies have shown that one of the most prevalent information needs of patients receiving new medication is information about its possible impact on their daily life (Berry, Gillie, & Banbury, 1995; Nair et al., 2002; Van Weert et al., 2009). Such personally relevant information is expected to be better recalled (Petty & Cacioppo, 1986b). An explanation may be that the patients may not have recognized that the nurses discussed the impact of the medication on their daily life. To improve the recall of medical information, providers should try to explicitly categorize information (e.g., "I am going to tell you how the medication can affect your daily life and how to minimize these effects") since previous research has shown that this is related to an increase in recall (Ley, 1979). Moreover,

information should be categorized into meaningful chunks so that the number of informational items can be reduced (Lang, 2006; Miller, 1956).

The results of this study indicate that the level of recall is a significant predictor for medication intake behavior, thereby supporting Ley's cognitive model (Ley, 1988). Our results emphasize the importance of patients' recall in promoting medication intake behavior. Previous research also suggested a relationship between recall and patient's medication intake behavior (Bartlett et al., 1984; Pickney & Arnason, 2005). However, the method used to measure recall was limited. We found a relationship between delayed recall and medication intake behavior, but not between immediate recall and medication intake behavior. The explanation might be straightforward. If a patient is not able to correctly remember the information over time, he or she will most likely also not be able to take the medication as prescribed over time. An additional explanation can be found in the recall measurement. The questions asked after three weeks were particularly developed for each patient based on their videotaped consultation. Thus, those questions could be more related to personally relevant information than the standard recall questions directly after the consultation. This personal information may include barriers for medication intake behavior. For example, a woman who asks questions about the possibility of becoming pregnant while taking medication is possibly expressing a medication intake barrier. The information given about this barrier is, due to the personal relevance of the topic, expected to lead to deeper processing(Petty & Cacioppo, 1986b) and, consequently, the higher recall of medical information and better medication intake behavior. This might also explain why there were, on average, no significant differences between immediate and delayed recall, while previous research (e.g., McGuire, 1996) found that patients remembered more information immediately after the information provision than after one week and one month.

In contrast to the studies that found that younger patients were more likely to be nonadherent (Shale & Riley, 2003), our findings show that age was negatively related with self-reported medication intake behavior. This result indicates that older patients are more likely to rate themselves as nonadherent. Indeed, older adults are found to be more prone to misunderstanding medical information due to declines in basic cognitive abilities (Brown & Park, 2003; Jansen et al., 2008). The majority of the patients were relatively young, which may indicate that the mediated effect of age on self-reported medication intake behavior through recall may be even stronger when studying age differences in a more heterogeneous group with more variance in age.

Our results also show that the necessity of injecting the medications was negatively related to the self-reported medication intake behavior. An explanation for the relation between the necessity of injecting and medication intake behavior may be that injections may cause some degree of discomfort or negative beliefs such as concerns about injection-side pain which may result in higher nonadherence (Mohr, Boudewyn, Likosky, Levine, & Goodkin, 2001). This difference may explain why patients who had to

inject their medication rated themselves as being less adherent compared to those who had to take pills (Mohr et al., 2001).

Limitations

Our study is limited because the questions varied between the immediate and the delayed recall questionnaires. Therefore, we were not able to compare scores between immediate and delayed recall. Further research should include standardized educational consultations and questionnaires to compare recall scores.

A self-reported measurement was used to assess medication intake behavior. The many methods used to measure medication intake behavior include physiological/biomedical measures, refill records, pill counts, or electronic monitoring (DiMatteo et al., 2012; Sluijs et al., 2006). Some scholars state that self-reported medication intake behavior can be an accurate measurement (DiMatteo et al., 2002) and is likely to correlate with more 'objective' measurements (Hugen et al., 2002; Shi, Liu, Fonseca et al., 2010; Shi, Liu, Koleva et al., 2010). In addition, medication intake behavior in this study was measured using one item. Rossiter (2002) proposes that if the concept can be conceptualized as concrete and singular, it does not require multiple items to represent it in the measure. Thus, we can assume that the method used to measure the patients' medication intake behavior may be accurate; however, other measurements such as refill data or electronic monitoring may enhance the validity of our findings. Future research should include refill data obtained one year after start to gain more insight into IBD patients' medication intake behavior and to compare the patients' self-reported medication intake scores with more 'objective' methods.

Practical implications

This study indicates that medication intake behavior can be improved if IBD patients are better able to recall the information that they receive. Previous research has shown that patients who received adequate and high-quality information about their prescribed medications were more adherent (Hulka et al., 1976), which might be partly explained by the higher recall of medical information. This finding implies that communication skills training and guidelines might be useful. The Practical and Perceptual Barriers to medication intake behavior typology describes how practical barriers (memory and daily routine barriers) and perceptual barriers (concerns and perceived necessity barriers) can be addressed with tailored communication to promote the recall of medical information and improve medication intake behavior (Linn et al., 2012).

Conclusion

The results of this study reveal that almost half of the medication information presented by nurses cannot be reproduced by patients and that the patients' recall of medical information is related to medication intake behavior. It is therefore important to consider recall-promoting techniques, such as summarizing, categorizing, or supplementing consultations with written information (Bernstein et al., 2011; Silberman et al., 2008), as a way to improve medication intake behavior.

Chapter 7

1+1=3? The systematic development of a theoretical and evidence-based tailored multimedia intervention to improve medication intake behavior.

Nurse: "Shall we work through the list [the Question Prompt List] now?" Patient: "Yes, I think that will be the best […] It should be easier to work through this while we talk because the things I have the most questions about are on this list" (male, 66 years old, Colitis).

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Abstract

Objectives: To describe the development of a theoretical and evidence-based tailored multimedia intervention to improve medication intake behavior in patients with inflammatory bowel disease (IBD). The intervention integrates interpersonal and technology-mediated strategies with the expectation that this will work synergistically.

Methods: The development followed the Medical Research Council's framework. Three literature reviews and three pre-tests among 84 IBD patients and eight nurses were conducted to guide the development of the intervention. A feasibility study was carried out among four nurses and 29 patients.

Results: The components include: 1) an online preparatory assessment (OPA); 2) tailored interpersonal communication; 3) tailored text messaging. To support the development, the feasibility was tested. Results indicated that the OPA was comprehensive and could be a helpful tool for both patients and nurses to prepare for the consultation. The training was evaluated as being instructive and applicable with a mean mark of 8.5. Of the developed messages, 65.6% received positive evaluations and were used in the intervention.

Conclusion: By applying the framework, we were able to describe the logic behind the development of a tailored multimedia intervention to improve medication intake behavior. This study could serve as a guide for the development of other health interventions.

Introduction

The odds of a good health outcome for patients who are taking their medication as prescribed are, on average, 2.9 times higher than the odds of a good outcome for non-adherent patients (DiMatteo, 2004). Despite this strong association, poor medication intake behavior remains a significant problem. Although interventions to improve medication intake behavior are common, effective interventions are scarce. Reasons for the ineffectiveness of interventions include 1) lack of theoretical foundation; 2) failure to identify the types of non-adherent behavior; and 3) inability to support patients to overcome barriers to successful medication intake behavior over time (Van Dulmen et al., 2007).

First, according to previous literature involving medication intake behavior interventions, and especially technology-mediated interventions, are often developed in an ad-hoc manner without reference to a theoretical foundation (Chavannes, Sont, Van der Boog, & Assendelft, 2012; Elliott, Barber, & Horne, 2005; Haynes et al., 2008). Research conducted across diseases has demonstrated that a robust theoretical foundation contributes to the effectiveness of interventions (Gallant & Maticka-Tyndale, 2004). Given the number of ineffective interventions developed to promote medication intake behavior (Van Dulmen et al., 2007), the theoretical foundations and feasibility of these interventions should be established before other costly trials are initiated (Robinson et al., 2005).

Second, to improve medication intake behavior, it is important to address specific reasons for poor medication intake behavior. Patients may report both unintentional (the patient does not take the medication unconsciously) and intentional (the patient actively decides not to take the medication) reasons for poor medication intake behavior (Clifford et al., 2008; Gadkari & McHorney, 2012; Unni & Farris, 2011). In addition, both intentional and unintentional poor medication intake behavior can be the result of practical and/or perceptual barriers (Linn et al., 2012). Practical barriers could be memory barriers (difficulties remembering to take the medication) or daily routine barriers (difficulties integrating the medication regime in daily life). Perceptual barriers could be necessity barriers (a lack of belief in the necessity of taking the medication) or concern barriers (fears or concerns about the medication; Kane & Robinson, 2010; Linn et al., 2012).

Third, persuasive communication can be important to support patients in overcoming their barriers to successful medication intake behavior (Van Dulmen et al., 2007). In the marketing and advertising literature, synergy is an important concept when considering the effectiveness of persuasive communication. Synergy refers to the effect that occurs when the combination of multimedia exceeds the sum of their individual effects (Naik & Raman, 2003). When exposed to multimedia, two psychological processes - forward encoding and multiple source perception - are stimulated (Voorveld et al., 2011).

Forward encoding occurs when a message in the first medium 'primes' the interest for, and attention to, a message in the second medium. For example, when a patient reads instructions about medication use, this may prime their interest in the information provided during a consultation and stimulate deeper processing (Dijkstra, 2002). This suggests that patients may more deeply process the message offered during a consultation if they have been provided with some form of preparatory communication beforehand. Multiple source perception refers to the notion that a message conveyed via different media may make the message appear more convincing and credible (Voorveld et al., 2011). This suggests that the persuasive power of the message could be enhanced if a multimedia approach is used, i.e. the message is delivered across different media. In the past decade, numerous interventions designed to improve medication intake behavior have been developed and implemented. These interventions have been delivered across a variety of media, including the Internet (Linn, Vervloet, van Dijk, Smit, & Van Weert, 2011), interpersonal communication (Van Dulmen et al., 2008) and, mobile telephones (Vervloet et al., 2012). In line with the synergy concept, Sabaté (2003) suggests that these strategies are most effective when used as components of multimedia programs and implemented in a tailored matter.

This paper describes the development of a theoretical and evidence-based tailored multimedia intervention aimed at addressing patients' barriers to successful medication intake behavior. By using different media to provide tailored information, it is proposed that the psychological processes of forward encoding and multi-source perception may be stimulated, thereby increasing patients' medication intake behavior.

Methods

We used the Medical Research Council's (MRC) framework to guide the development of this intervention. This framework was chosen because it acknowledges the importance of a theoretical understanding of the likely process of behavior change by drawing on existing evidence and theory, supplemented if necessary by new primary research (Campbell et al., 2007). The MRC framework distinguishes the following four phases: 1) development, 2) feasibility/piloting, 3) evaluation, and 4) implementation (see Figure 1) (Craig et al., 2008). In this paper, we will focus on the development, feasibility/piloting and evaluation of the intervention. First, the methods of these separate phases will be described (see paragraph 2.1 to 2.3), next the results (see paragraph 3.1 to 3.3).

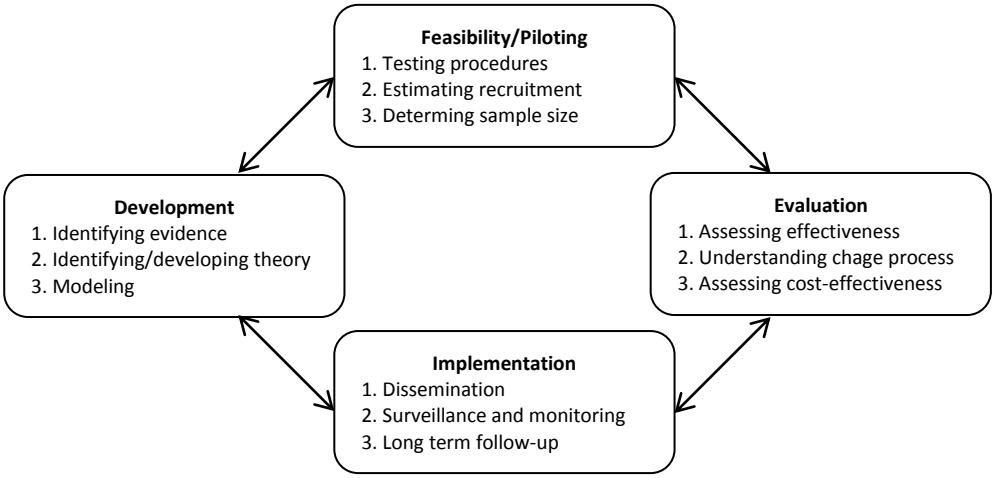

Figure 1. *Medical Research Council's evaluation Framework (MRC).*

Development

Identifying evidence

Because a theoretical understanding of the likely process of change was needed, we identified existing evidence and theory by conducting three reviews. To identify the available evidence concerning the effectiveness of interventions designed to improve medication intake behavior, two systematic literature reviews were conducted that investigated the effectiveness of tailored Internet-based interventions (Linn et al., 2011) and electronic reminders by mobile phones or electronic reminder devices (Vervloet et al., 2012) in improving medication intake behavior. We undertook comprehensive literature searches in PubMed, PsycINFO, EMBASE, CINAHL, and Communication Abstracts, following the guidelines of the Cochrane Collaboration. The search strategy included all possible search terms for Internet interventions or electronic reminders and medication intake behavior. In addition, a third literature review was conducted to gain more insight into what is known about communication in relation to medication intake behavior (Linn et al., 2012).

Identifying and developing theory

Because we believed that the existing evidence was not sufficient, we supplemented the existing evidence and theory with three pre-tests (Craig et al., 2008).

The Medical Ethical Committee of the VU Medical Center granted permission for these pre-tests and retrieved local feasibility statements (trial number NTR2892). The data were collected from September 2009 until March 2012. Patients with inflammatory bowel disease (IBD) were identified as a target population for the pre-tests as high rates of poor medication intake behavior among this patient group have been reported (Ediger et al.,

2007). In the pre-tests eight nurses of six different Dutch hospitals participated. Eligible patients were sent a letter with information about the study before the consultation. Written informed consent was obtained from both patients and nurses.

The intervention aims to support patients in overcoming their barriers to successful medication intake behavior. Since poor medication intake behavior can be the result of practical (memory and daily routine) or perceptual (concerns and lack of necessity) barriers, indicators of these barriers were needed. Concepts that are related to these practical and perceptual barriers are self-efficacy and beliefs. The importance of self-efficacy and positive beliefs towards the desired behavior in achieving health behavior change has been emphasized in a number of health psychology theories such as the Theory Planned of Behavior (TBP; Ajzen, 1991) and The Behavioral Model for Medication Adherence (Bruin et al., 2005). In the pre-tests two scales measuring patients' self-efficacy and beliefs were used as indicators for patients' barriers to successful medication intake behavior.

First, the Medication Understanding and Use Self-Efficacy (MUSE) was used. This scale consists of two four-item subscales assessing patients' self-efficacy of *understanding* (referring to memory barriers; $\alpha = 0.80$) and *using* prescribed medication (referring to daily routine barriers; $\alpha = 0.90$; Cameron et al., 2010). Responses to each statement were scored on a four-point Likert scale (1 = 'strongly agree' to 4 = 'strongly disagree'). Mean scores were calculated and a score of higher than two was considered as an indicator for practical barriers.

Second, the Beliefs about Medicine Questionnaire (BMQ) was used (Heijmans, 2006; Horne et al., 1999). This scale consists of five items assessing patients' beliefs about the *necessity* of prescribed medication (referring to necessity barriers; $\alpha = .75$) and five items assessing *concerns* about medication (referring to concern barriers; $\alpha = .67$) (Heijmans, 2006; Horne et al., 1999). Responses to each statement were scored on a five-point Likert scale (1 = 'strongly disagree' to 5 = 'strongly agree'). Mean scores of the BMQ scales were calculated and the midpoint score of three or higher was considered as an indicator for patients' perceptual barriers (see Table 2). For the analysis in the pre-tests we used a significance level of $p = 0.05$.

With the results of the third literature review, the Practical and Perceptual Barriers to medication intake behavior-typology (PPB-typology) for effective communication was developed. Next, a pre-test was conducted to examine whether nurses communicated according to the typology. For this purpose, 80 educational consultations between nurses and IBD patients were videotaped and coded by independent observers using a codebook that was based on the PPB-typology. Subsequently, the relationship between the use of communication strategies according to the typology and barriers to successful medication intake behavior was examined (Linn et al., 2012). The verbal content of the consultations was analyzed using a coding system based on the PPB-typology. The MUSE (Cameron et al., 2010) and the BMQ (Horne et al.,

1999) were used as indicators of patients' barriers. The scores on the BMQ and MUSE were correlated with the scores for the communication categories using Pearson's bivariate correlations. To determine intercoder reliability, two observers both coded the same thirteen (16%) video recordings (Zandbelt et al., 2005). The intraclass correlation coefficients (ICC) ranged between 0.60 and 1.0, with a mean ICC of 0.90, which is considered good (Altman, 1991).

Previous studies indicated that patients' perceptual barriers are considered proximal determinants of medication intake behavior (Clifford et al., 2008; Horne & Weinman, 1999; Horne et al., 1999; Horne et al., 2009; Menckeberg et al., 2008; Schüz et al., 2011) and that patients' satisfaction about their providers' communication might be positively related to improved medication intake behavior (Bartlett et al., 1984). The aim of the second pre-test was therefore to explore the relation between patients' satisfaction and perceptual barriers (Linn, Van Weert, Van Dijk, Horne, & Smit, under review). Telephone interviews were conducted at the start of the treatment in which patients' perceptual barriers (Horne et al., 1999) and patients' satisfaction (Hendriks et al., 2005) were assessed (N=84). The BMQ was used as indicator for patients' perceptual barriers. Patients' satisfaction was measured with three subscales, i.e. satisfaction with general information about the disease and treatment (12 items; α = .85), with support regarding medication use (7 items; α = .67) and with affective communication (9 items; α = .82). In addition, patients were asked to indicate on a scale of 1 to 10 to what extent the consultation was tailored to their specific needs. Multiple regressions were used to measure the relation between satisfaction and perceptual barriers. Demographic variables were included as control variables.

Poor medication intake behavior can be a result of poor information recall, which is often assumed when complex information is given (Flocke & Stange, 2004; Kessels, 2003; Ley, 1976; Ley, 1979). It therefore seems important to explore this relation when developing an intervention aimed at improving medication intake behavior (Linn, Van Dijk, Smit, Jansen, & Van Weert, 2013). In total, 68 educational consultations concerning first-time medication use between nurses and patients were videotaped. Recall of information was measured using an adapted version of The Netherlands Patient Information Recall Questionnaire (NPIRQ; Jansen et al., 2008) and checked against the actual communication. Intercoder reliability was assessed and two observers randomly coded nine identical transcriptions (13%; Zandbelt et al., 2005). The mean intercoder reliability using Cohen's Kappa was .91 indicating a good intercoder reliability (Altman, 1991). Self-reported medication intake behavior was measured by asking patients to describe how precisely they took their medications as prescribed on a scale ranging from 1 to 10 (Hugen et al., 2002). Multiple regression was used to examine the relation between recall and medication intake behavior. Demographic variables were included as control variables.

Modeling

The different media studied in the literature reviews and pre-tests were 1) the Internet 2) interpersonal communication and 3) mobile phone. Based on the results, the different components of the intervention to be developed were determined: 1) an online component, i.e. Online Preparatory Assessment (OPA); 2) an interpersonal component, i.e. tailored interpersonal communication, learned during a communication skills training and 3) a text message component, i.e. tailored text messaging by mobile phone (see 3.1.3 for a more detailed explanation). The results of the reviews and pre-tests were also used to define each component of the intervention and to describe how each component of the intervention might alter behavior change (Craig et al., 2008).

Assessing feasibility and piloting methods

To test the feasibility of the online component, nurses (n=4) and patients (n=2) evaluated whether the various components of the OPA corresponded with the items discussed during educational consultations and barriers to successful medication intake behavior.

To test the feasibility of the interpersonal component, nurses (n=4) completed an evaluation questionnaire after the communication skills training. In addition, nurses were asked whether they perceived difficulties when integrating the intervention into their consultations.

The appropriateness and acceptability of the text message component was pilot-tested in IBD patients (N=29) and nurses (N=4). IBD patients were identified by an advertisement placed in the November 2011 online newsletter of the Dutch Crohn and Ulcerative Colitis association (CCUVN). Participants were asked to rate each of the 64 text messages on a four-point Likert scale (1 = 'extremely unhelpful' and 4 'very helpful'). Only the text messages that received an average rating of 'helpful' or 'very helpful' were selected for use. Nurses were asked during the training to reflect on the developed text messages and to think of alternatives.

Evaluating a complex intervention

After we established the theoretical basis, identified the main components of the intervention and pre-tested all the gathered evidence so far, a theoretically defensible and reproducible intervention was described. To objectify intervention effects several goals were formulated (see Table 1). The intervention will be implemented in a controlled setting. By exposing patients to either nurses who received the multimedia intervention (experimental condition), or to usual care (e.g., receiving standard information; control condition), the effectiveness of the intervention will be investigated. The primary outcome of interest is medication intake behavior, measured with pharmacy refill rates and self-reported measurements (Hugen et al., 2002).

Table 1.

Intervention Goals

Goals	Type of intervention	Component of the intervention
1. Improving communication skills (e.g. tailored information to the patients' needs and barriers, use affective communication, recall promoting behavior, promote patient participation)	Interpersonal and technology mediated	Communication skills training, OPA [a]
2. Encouraging the use of QPA	Interpersonal	Communication skills training
3. Identifying perceived barriers	Interpersonal and technology mediated	Communication skills training, OPA
4. Reducing patients' perceived barriers to successful medication intake behavior	Interpersonal and technology mediated	Communication skills training, OPA, text messages
5. Changing patients' medication beliefs	Interpersonal and technology mediated	Communication skills training, OPA, text messages
6. Improving patients' self-efficacy	Interpersonal and technology mediated	Communication skills training, OPA, text messages
7. Increasing recall of information	Interpersonal and technology mediated	Communication skills training, OPA
8. Improving satisfaction	Interpersonal and technology mediated	Communication skills training, OPA
9. Continuous support	Technology mediated	Text messages

[a] Online preparatory assessment

Results

Developing the intervention

Identifying evidence

The first systematic literature review (Linn et al., 2011) concluded that the Internet provides an optimal technology for implementing tailored interventions designed to improve medication intake behavior, because it has the capability to assess possible barriers.

The second systematic literature review (Vervloet et al., 2012) concluded that electronic reminders showed positive effects on medication intake behavior on the short-term. Intervention studies have mainly used text messages as reminders, focusing largely on patients who were unable to remember to take their medication as prescribed, i.e. patients that perceive memory barriers. However, new technologies make it possible to tailor text messaging content to address patients' individual barriers to successful medication intake behavior.

The third literature review lead to the development of the PPB-typology. The PPB-typology describes how to address patients' barriers to successful medication intake behavior with tailored communication. A detailed description of the PPB-typology is published elsewhere (Linn et al., 2012).

Identifying and developing appropriate theory

Results of the first pre-test demonstrated that nurses tended not to communicate according to the PPB-typology. Results also indicated that if communication strategies aligned to the PPB-typology were used, this was associated with less perceived barriers (Linn et al., 2012).

In the second pre-test (Linn et al., under review) we found that almost half of the patients perceived problems with believing that the medication was necessary and/or had concerns about the medication. Patients' satisfaction regarding nurses' communication and level of tailoredness was significantly related to a more positive attitude towards medication (β = .31, *p* = .012 resp. β =.25, *p* = .024).

In the third pre-test (Linn et al., 2013) a positive relation between patients' recall of information and medication intake behavior (β = .37, *p* = .007) was confirmed, indicating that higher recall of information relates to improved self-reported successful medication intake behavior.

Modeling

In this phase the components of the intervention are defined and described (Craig et al., 2008). Based on the first review, we concluded that the Internet may be a useful tool to alter patients' behavior. The first component of the intervention is therefore an OPA. This component may offer an opportunity for patients to prepare themselves for the consultation and nurses with tools to tailor information to patients' barriers to successful medication intake behavior. Information that is optimally tailored to the patients' barriers to successful medication intake behavior is expected to be more deeply processed, which might result in higher recall of information and, consequently, improved medication intake behavior (Linn et al., 2013).

The OPA consists of an online Question Prompt List (QPL) and two measurements: the MUSE (Cameron et al., 2010) and the BMQ (Horne et al., 1999) and is used to provide nurses with feedback on existing barriers and advices how to handle these barriers during the consultation. Patients received an email with a link to the OPA, varying between one week to two days before consultation. A QPL is a structured list with questions designed to aid patients' question asking behavior (Brown et al., 2001). By sending the QPL before the consultation, patients are leaving the time to read through the list and identify the questions they want to ask. The use of a QPL has been associated with a number of positive outcomes in previous research, such as, improved patient participation during consultation (Butow, Dunn, Tattersall, & Jones, 1994), improved patient empowerment (Dimoska, Tattersall, Butow, Shepherd, & Kinnersley, 2008), higher fulfillment of information needs (Van Weert et al., 2010), a shorter duration of consultation (Brown et al., 2001), reduced anxiety (Brown et al., 2001) and improved recall if information (Van der Meulen et al., 2008). The content of the QPL is based on a previous developed QPL in oncology (Van Weert et al., 2010) and items of the BMQ and MUSE. The QPL consists of 24

questions in total, divided in four main categories, corresponding with the four different types of barriers patients may encounter (i.e., memory barriers, daily routine barriers, necessity barriers and concern barriers). Statements include for instance 'I want more information about possible interferences in my daily life' (daily routine barriers) or 'I want to discuss my concerns about the side effects' (concern barriers). Patients are asked to identify the items they wanted to discuss by rating them on a four-point Likert scale (1 = 'not at all important' to 4 = 'very important'). There is also an opportunity for patients to add any additional questions. As soon as the patient completes the QPL, the nurse receives an email with the QPL. Patients can also print their own QPL and take it to the consultation.

To gain more insight into patients' barriers, patients fulfill the MUSE (Cameron et al., 2010) and the BMQ (Horne et al., 1999) directly after the QPL. If scores at that time (on baseline) indicate that a patient perceives barriers according to their scores on MUSE and/or BMQ, nurses are informed before the consultation by email with: 1) which barriers the patient perceives and 2) communication strategies that should be used in order to reduce or remove these barriers. The feedback about which communication strategies should be used, was based on the developed typology (see Linn et al., 2012 for a detailed description of the communication strategies). The execution of these communication strategies are trained during the communication skills training.

The second component of the intervention is interpersonal communication. Reviews have consistently concluded that communication is a powerful tool in promoting medication intake behavior (Zolnierek & DiMatteo, 2009) and that communication skills training often results in better communication behaviors among providers (Fellowes, Wilkinson, & Moore, 2001; Moore, Wilkinson, & Rivera Mercado, 2004). For this reason, a communication skills training with follow-up session was developed and executed. Nurses who participated in the pre-tests (N=8), were randomly assigned to the training (N=4). Prior to the training skills day, nurses received a complete reader by post containing a summary of the results of the pre-tests and practical exercises. The communication skills training was run by an experienced and qualified trainer. The first part of the training consisted of a presentation of the results of the three pre-tests. The second part of the training included a combination of learning methods such as role-play and reflection tasks. Afterwards the trainer discussed what the nurses learned. Twelve weeks after the communication skills training day, a half-day follow-up meeting was organized by the same trainer to provide the nurses with an opportunity to refresh and enhance the communication skills introduced during the training day. During follow-up nurses were also asked what the main changes where after the first day of training. Moreover, they discussed the successes and the barriers and received instructions about how to interpret the results of the OPA. As previous research indicates that the quality of healthcare interactions can be enhanced by the use of video-tapes and self-reflection (Marita, Leena,

& Tarja, 1999), the nurses were instructed to watch two video-taped consultations of their selves, recorded during the pre-tests, and to complete a self-reflection task. During the follow-up meeting, the self-reflection task was discussed.

The third component of the intervention is a tailored text message support system. Tailored text messages appear to offer promising possibilities for providing tailored feedback (Petrie et al., 2012). One of the advantages of text messaging is the ability to efficiently provide patients feedback over time. This may be especially relevant to patients living with chronic diseases that require the patient to engage in self-management behaviors over the longterm. Moreover, text messaging has the advantage of being inexpensive, easy to access and accessible to large populations (Petrie et al., 2012). For this reason, the third component of the intervention is a tailored text message support system. The development of these messages was based on the study of Petrie and colleagues (2012) and rewritten for patients with IBD receiving immunosuppressive or biological therapy. Patients receive one text message per week for six months, starting three weeks after the consultation. The type of text messages sent is determined by whether patients perceived barriers according to the scores on the MUSE and BMQ before and/or after the consultation. If a patient does not score high on one or more of the four targeted barriers, neither before nor after the consultation, the patient does not receive any text messages. If a patients scores high on one of the targeted barriers, before and/or after the consultation, he or she receives text messages from that specific barrier category. These text messages are chosen at random from that category that is designed to support patients with their barriers to successful medication intake behavior (see Table 2 for examples). If a patient scores high on multiple barriers, he or she receives text message chosen at random from the pool of messages for these barriers.

Assessing feasibility and piloting

To test the feasibility of the OPA, both nurses and patients reviewed the 24 items of the QPL. Results indicated that both nurses and patient thought that the items on the QPL corresponded with the items discussed during consultation and with patients' barriers, and that this was a helpful tool to prepare both nurses and patients before the consultation.

To test the feasibility of the communication skills training, participants completed a questionnaire. Results of the evaluation questionnaire indicated that all nurses evaluated the training as being instructive, practical, interesting and applicable. The training was evaluated with a mean mark of 8.5 (*SD* = 0.6), with 1 being not at all useful and 10 being extremely useful. The role-play with an actor was identified as the most meaningful component of the training.

Table 2.
Target barriers and text messages examples

Barrier	Measured with	Example of text messages
Memory barriers	MUSE patients' self-efficacy of understanding	"Put a note on the fridge or on the mirror above the sink. Replace the note occasionally or use a different color note, so it will stand out" "Think about your medication at regular intervals, for example, while brushing your teeth"
Daily routine barriers	MUSE patients' self-efficacy of using	"Keep some medication in your bag, purse or glove compartment in your car" "If you want to take an overseas trip, check with your IBD nurse if you need a doctor's statement to travel with your medication"
Necessity barriers	BMQ-Necessity	"Your medication helps to keep the inflammation in remission" "Your medication can help to enhance your quality of life"
Concern barriers	BMQ-Concerns	"Scientific research has shown that taking your medication is safe, even over a long period of time" "If you have questions about side effects, contact your IBD nurse"

In the beginning of the follow-up, nurses were asked what the successes were after the training. The nurses reported that they learned how to set transparent and structured agendas at the beginning of the consultation and were more likely to explore perceived barriers and to tailor their consultations to the patients' information needs and barriers. This resulted in more understanding and contact with the patient. The nurses also reported that they were more aware of the patient as an autonomous individual and felt the training gave them a better understanding of the patient. The nurses reported a number of difficulties that were addressed in the follow-up. These difficulties included integrating the communication skills into their consultations, working with patients who were not able to explicitly express their needs, managing consultations when the patient's agenda did not correspond with the agenda of the nurse and coping with workload. Some nurses indicated that in the beginning, when experimenting with the learned communication skills, they found it 'not natural' compared with their previous behavior.

Last, the feasibility of the text messages was tested. The four nurses reflected on the developed text messages during the follow-up training and believed that the tone of voice of some of the text messages was too positive. For example, they believed that text messages should not give false promises about the working of the medication. Instead, they suggested that the text messages should be more supportive, giving the patient advice what to do when they have, for instance, doubts about the effect of the medication. After adapting the text messages, 29 patients, i.e., eighteen with Crohn's disease and

eleven with Ulcerative Colitis (mean age of 26.6, *SD* = 8.1 with 85.0% being female), evaluated the text messages. In total 64 text messages were reviewed; 40 text messages (62.50%) received an average rating of 'helpful' or 'very helpful' (score $\geq$ 2.5) and were selected for use. In total 50 % of the messages targeting necessity, concerns and daily routine barriers were included and 62.50% of the messages targeting memory barriers. Patients had the possibility to add any comments about the text messages. Patients who were positive found the text messages useful, motivating or supportive. Some patients added that: 'The text message can help me with taking my medication, especially if the message are sent occasionally' or 'I like the text messages, especially how they are written: no difficult language, just simple and to-the-point'. Patients who were negative about the text messages reported: 'Some text messages are too positive, and therefore evoke resistance' or 'I do not believe in the text messages targeting my concerns, my fears are deeper than that'. Minor revisions in the selected text messages were made based on the recommendations of the reviews. Because we wanted 12 messages per barrier, we added new messages that were based on the evaluated messages that received high ratings, resulting in 48 text messages in total.

Evaluation

Outcomes will be measured after three weeks, six and twelve months. The results are expected to be available in December 2013 (see Table 3).

Discussion

This paper reports on the development of an innovative multimedia intervention to improve medication intake behavior. The strength of this intervention is that by following the guidelines of the MRC framework, we developed a good theoretical and evidence-based understanding of the likelihood that the intervention will be effective (Craig et al., 2008; Medical Research Council, 2000).

Each component of the intervention has its own specific value to improve medication intake behavior. This paper explained how technology-mediated and interpersonal communication can reinforce each other. The intervention integrated different media with their own specific value in tailoring the message with the expectation that this will work synergistically and thus will have added value as compared to stand-alone interventions. The OPA has the possibility to gain more insight into patients' barriers which assists in determining the most effective strategy to meet patients' specific barriers. This individual assessment gives providers more insight into patients' barriers and helps to provide tailored feedback during their consultations on both patients' barriers and patients' informational needs and concerns. We used new technologies to maintain support and send tailored text messages to assist patients with their medication intake in

daily routine. Recent research indicates that tailored messaging may be more effective than standard messaging at changing patient behaviors (Petrie et al., 2012).

Table 3.
Developing and evaluating the intervention according to the MRC framework

MRC: Feasibility and piloting/Development (September 2009 – October 2011)	
Systematic literature review: the effects of Internet interventions on medication intake behavior	
Systematic literature review: the effects of electronic reminders on medication intake behavior	
Development of the PPAB-typology	
Pre-tests	
Experimental group	Control group
3 hospitals, 4 nurses	4 hospitals, 5 nurses
Pre-test 43 IBD patients	Pre-test 43 IBD patients
MRC: Development	
Development intervention	
Pre-test text messages	
MRC: Implementation (November 2011 – January 2012)	
Experimental group	Control group
Intervention for nurses	Education as usual
Week 1: Communication skills training	
Week 2-11: Practice, reflection tasks	
Week 12: follow-up	
Intervention for patients	
OPA	
Text messages	
MRC: Evaluation (February 2012 – expected December 2013)	
Post-test	Post-test
3 hospitals, 4 nurses	4 hospitals, 5 nurses
43 IBD patients	43 IBD patients
Measurements:	*Measurements:*
Communication skills nurse	Communication skills nurse
Communication skills patient	Communication skills patient
Barriers medication intake behavior (Heijmans, 2006)	Barriers medication intake behavior
Recall	Recall
Satisfaction	Satisfaction
Anxiety	Anxiety
Background characteristics	Background characteristics

In adopting the multimedia approach this intervention capitalizes on the concept of synergy and the psychological processes of forward encoding and multiple source perception to enhance the persuasive power of the message. Empirical data is however needed to establish the effectiveness of a multimedia approach and future research should investigate the effects of this intervention.

A potential limitation of this intervention is the proposed design of this study. We chose to assign nurses and patients to the intervention group which is provided with the OPA, tailored interpersonal feedback and text messages. The control group continued receiving usual information. This was a practical consideration, because of the number of participating nurses (n=8). It would be interesting to assign nurses in the RCT to each of the separate components of the intervention. Although we assume that the integration of

these different modes of delivery may increase their effectiveness, it would also be interesting to test their effect in isolation to get insight in potential underlying mechanisms.

In this paper, the implementation phase of the MRC framework is not described. When implementing the intervention it is important to select people who are involved at the micro, meso, or macro level during the preparation, execution and/or continuation phase of the implementation, and who have insight into the factors that either impede of facilitate the implementation (Brug, van Assema, & Lechner, 2007). For example, nurses attended the training as a leisure activity. Although enthusiasm for the intervention can be an important facilitating factor for implementation (Meiland, Droes, de Lange, & Vernooij-Dassen, 2005), the imbedding of a communication skills training and activities to assure long-term continuation of the intervention requires commitment at organizational level.

Moreover, it is recommended to conduct a process evaluation during the implementation phase. Research conducted across diseases has demonstrated that a robust theoretical foundation contributes to the effectiveness of interventions (Gallant & Maticka-Tyndale, 2004) and helps to support the process evaluation of interventions. A process evaluation will gain valuable insights into the implementation process; whether the intervention was implemented according to plan and which adjustments are needed. This is critical when avoiding a Type III error and thus drawing incorrect conclusions about the effectiveness of a given intervention (Brug et al., 2007). For example, since our understanding of the facilitators and barriers to routinely use the OPA is still very limited, particularly in the IBD setting, without an appropriate process-evaluation this may result in incorrect conclusions about the ineffectiveness of the intervention (Brug et al., 2007). It can be recommended to use an implementation framework to conduct a process evaluation during the implementation phase. For instance, the Consolidated Framework for Implementation Research (CFIR) can be a useful framework to guide the exploration of the factors that positively or negatively influence the implementation (Damschroder et al., 2009).

Conclusion

By applying the MRC framework, we were able to describe the logic behind the systematic development and content of a feasible tailored multimedia intervention. In developing this intervention several study fields such as health communication, marketing and advertising were combined, which has led to an new view on how to address medication intake behavior.

Practical implications

While the pre-test is based on a sample of IBD patients, our intervention may be useful for all patients coping with chronic illness because the developed intervention is quite general and the content of the instruments could easily be applied to other diseases. This study could therefore serve as a guide for the development of other health interventions.

Chapter 8

Summary and general discussion

Nurse: "How often are you taking your medication?" Patient: "Not at all anymore, I stopped taking them, I don't like them and I would not recommend them to anyone" (male, 45 years old, Crohn).

Summary

This dissertation aimed to develop a theoretical and evidence-based tailored multimedia intervention to improve medication intake behavior. In addressing this aim, this dissertation gained insight into patient barriers to successful medication intake behavior and investigated the various methods and types of media: the Internet (i.e., eHealth), mobile phones (i.e., mHealth) and interpersonal communication, that can promote successful medication intake behavior.

Chapter 1 provided an overview of the theoretical background. First, the importance of successful medication intake behavior was described. Second, an overview of the concepts used to describe whether patients take their medication (or not) and possible determinants of this behavior were presented. Last, different media and the way in which messages can be tailored to the specific barriers of patients were discussed.

The effectiveness of eHealth interventions on medication intake behavior was evaluated in **Chapter 2**. We conducted comprehensive literature searches in PubMed, PsycINFO, EMBASE, CINAHL, and Communication Abstracts following the guidelines of the Cochrane Collaboration. The methodological quality of the randomly controlled trials, clinically controlled trials, and methods for measuring medication intake behavior were independently reviewed by two researchers. The thirteen selected studies focused on a variety of chronic conditions and mainly employed self-reported measurements of medication intake behavior, such as questionnaires, interviews, and diaries. The review provided insight into the current developmental stage of these interventions, assessed the effectiveness of the studies on medication intake behavior, and investigated the degree of medication intake behavior as determined by the characteristics of the intervention and the characteristics of the study. The results indicated that eHealth may be effective in promoting medication intake behavior. The evidence is derived from five studies (three high-quality studies and two low-quality studies), which revealed a significant effect on medication intake behavior. Six other studies (four high-quality studies and two low-quality studies) reported a moderate effect on medication intake behavior, and two studies (one high-quality study and one low-quality study) exhibited no effect on medication intake behavior. The results indicated that, despite the advancements in this field, the development of high-quality studies on the effectiveness of Internet interventions has improved over time. The studies included in this review used moderately or highly sophisticated tailored interventions. We did not establish a clear relationship between the sophistication of the tailoring of the intervention and the extent to which the intervention was effective. This review yielded promising results for the effectiveness of Internet interventions in improving a patient's medication intake

behavior. However, more research is needed to investigate the level of tailoring and the effect of Internet interventions.

In **Chapter 3**, we aimed to synthesize and critically appraise existing evidence on the effectiveness of electronic reminders for improving a patient's medication intake behavior. Many patients experience difficulty with adhering to long-term treatment. Although a patient's reasons for not adhering to treatment are diverse, one of the most commonly reported barriers is forgetfulness. Reminding patients to take their medication may therefore be the solution. Electronic reminders (i.e., reminders sent automatically without personal contact between the provider and patient) are increasingly used to improve medication intake behavior. A comprehensive literature search was conducted in PubMed, Embase, PsycINFO, CINAHL and the Cochrane Central Register of Controlled Trials. The methodological quality of the studies was assessed using the Cochrane Collaboration guidelines. The studies focused on a variety of chronic conditions. We aimed to investigate whether the characteristics of electronic reminders were associated with their effectiveness. In total, thirteen studies were included: four studies evaluated SMS reminders, seven studies evaluated audiovisual reminders from electronic reminder devices and two studies evaluated reminder messages delivered to pagers. The best evidence synthesis revealed evidence of the effectiveness of electronic reminders. This evidence was provided by eight (i.e., four high-quality and four low-quality) studies that demonstrated significant effects on successful patient medication intake behavior. Of these eight studies, seven studies measured short-term effects (i.e., follow-up period < 6 months). Electronic reminders have the ability to improve short-term medication intake behavior, especially for patients who unintentionally do not take their medication as prescribed. We also concluded that, when stratified by type of electronic reminder, short-message services are promising media strategies for improving medication intake behavior. However, the long-term effects remain unclear. Technological advancements, such as the tailoring of timing (only when needed) and content (tailored messages), may lead to long-term improvements in medication intake behavior.

The aim of **Chapter 4** was to develop a new communication typology that addresses barriers to successful medication intake behavior and to examine the relationship between the use of the typology in relation to these barriers. We reviewed research concerning communication and medication intake behavior, which resulted in the practical and perceptual barriers to successful medication intake behavior-typology (PPB-typology) for effective tailored interpersonal communication. The PPB-typology addresses four potential barriers to successful medication intake behavior: 1) memory barriers; 2) daily routine barriers; 3) necessity barriers; and 4) concern barriers. We analyzed the verbal content of prescribing consultations using a protocol based on the developed typology. Eighty consultations concerning first-time medication use between nurses and

inflammatory bowel disease (IBD) patients were videotaped. The verbal content of the consultations was analyzed using a coding system based on the PPB-typology. The Medication Understanding and Use Self-Efficacy Scale (MUSE) and the Beliefs about Medicines Questionnaire (BMQ) were used as indicators of patient barriers and were correlated with PPB-related scores. The scores on these scales were correlated with the scores for the communication categories. The results of this study indicated that most of the communication strategies based on the PPB-typology were hardly used. However, we found that if nurses encouraged patients to ask questions, fewer memory barriers were perceived by patients. Moreover, summarizing information and the use of cartoons or pictures during the consultation were significantly associated with fewer perceived concern barriers. The results of this study suggest that the PPB-typology is a promising tool for the development of interventions aimed at addressing patient barriers to successful medication intake behavior.

In the Netherlands, nurses play an important role in educating IBD patients about immunosuppressive or biological therapy in prescribing consultations. **Chapter 5** provided more insight into the relationship between patients' satisfaction regarding their communication with nurses and their perceptual barriers about the immunosuppressive or biological therapy prescribed for IBD. Telephone interviews were conducted with 84 IBD patients at the beginning of treatment and after six months of treatment. Patients completed validated questionnaires that assessed their satisfaction regarding their communication with nurses during prescribing consultations and their perceptual barriers to immunosuppressive or biological therapy. To measure patient satisfaction, we used 29 statements associated with three scales concerning satisfaction with nurse's general information about their disease and treatment, satisfaction with nurse's support regarding medication use, and satisfaction with nurse's affective communication. Moreover, patients were asked to what extent they thought that their communication with nurses was tailored to their needs. The BMQ was used to measure patients' barriers to their specific prescribed medication. The results indicated that more than half of the patients had concerns or little personal need for medication, or both. However, concerns were most salient among patients. Patients' perceptual barriers remained consistent after six months. Patient satisfaction about the extent to which the communication during the consultation was tailored to their needs was significantly related to fewer barriers. In addition, patient satisfaction about the information given during the consultation was significantly related to fewer barriers to successful medication intake behavior. The results of this study highlight the significant role of patient satisfaction with provider communication and the value of tailoring in relation to perceived barriers. Interventions to improve medication intake behavior should therefore consider the communication skills of the provider.

When immunosuppressive or biological therapy is prescribed, nurses educate patients about the prescribed medication. Nurses are expected to inform the patients about the name of the medication, possible side effects, provide instructions on how to take the prescribed medication, and provide emotional support. These prescribing consultations often contain complex information. Poor medication intake behavior can be a result of poor information recall. In **Chapter 6**, we investigated the relationship between recall of disseminated information and medication intake behavior for IBD patients by comprehensively measuring recall of information. Eight nurses from six Dutch hospitals and 69 IBD patients participated in this study. Video-observations of nurse-patient prescribing consultations, supplemented with post-visit questionnaires to measure recall of medical information, were used directly after the consultation and again after a period of three weeks. Recall of information was compared with the actual communication in the video recordings of the consultations and assessed using an adapted version of The Netherlands Patient Information Recall Questionnaire (NPIRQ). This questionnaire was administered directly after the consultation and again after a period of three weeks. The information discussed in the videotapes was analyzed using an extensive observation checklist. First, coders assessed whether the topic was discussed in the visit. Second, each topic recalled was compared with the specific items mentioned by the nurse. Self-reported medication intake behavior was measured by asking patients to describe exactly how they took their medications. The results revealed that approximately half of the information was recalled by patients immediately after the consultation or after a period of three weeks. Information about the type of administration and the name of the medication were most accurately recalled. The information that was recalled most poorly was the impact of medication on the patient's daily life and advice about medication intake behavior. Patient recall of medical information was significantly correlated with self-reported medication intake behavior. The importance of information recall needs to be considered when developing educational interventions aimed at improving medication intake behavior.

The systematic development of a theoretical evidence-based tailored multimedia intervention

In **Chapter 2** and **3** we concluded that both eHealth and mHealth have the potential to reduce poor medication intake behavior. **Chapters 4, 5** and **6** showed that providers' communication is important in addressing patients barriers to successful medication intake behavior. Using these results, we developed a multimedia intervention to improve medication intake behavior. In **Chapter 7** we described the development of a theoretical evidence-based tailored multimedia intervention aimed at reducing or removing barriers to successful medication intake behavior. The intervention includes three different components: 1) an online preparatory assessment (OPA) including a Question Prompt List (QPL); 2) tailored interpersonal feedback and; 3) tailored text messaging. To support the

implementation of the intervention, a one-day communication skills training and follow-up session was conducted for the nurses. In addition, the feasibility of the intervention was tested among nurses and patients. We assumed that interpersonal and technology-mediated components are most effective when used as components of a multimedia program and implemented in a tailored matter. The integration of these different media may increase their effectiveness compared to their use in isolation. We anticipated that this intervention will result in measurable effects in barriers to successful medication intake behavior, improved communication skills (e.g., communication that is tailored to the patients' needs and barriers, the use of affective communication, recall promoting behavior, increased patient participation in the consultation) and positive changes in practical and perceptual barriers.

The value of tailored communication

In **Chapter 8**, we reviewed the findings of this dissertation and noted some ways in which the results may contribute to our understanding of how tailored communication may be effective in improving medication intake behavior. Directions for future research and practice were also outlined. Many interventions to improve medication intake behavior have been developed. However, effective interventions for improving medication intake behavior are scarce. One of the reasons for this may be that barriers responsible for poor medication intake behavior vary among patients and patient groups and across different situations. Interventions should therefore be tailored to patients' barriers to successful medication intake behavior. The use of eHealth and mHealth in the development of these interventions is increasing and seems promising. Tailored messages can also be useful in the context of interpersonal communication because, as shown in this dissertation, patients' satisfaction regarding the extent to which a consultation was tailored to their needs was significantly related to fewer perceptual barriers to immunosuppressive or biological therapy. In addition, tailored interpersonal communication can be effective in assisting patients in overcoming barriers to successful medication intake behavior. Moreover, recall of information is a predictor of self-reported medication intake behavior. Tailored messages receive more attention and thus are more thoroughly processed by patients and therefore it is expected that they will be better recalled. Based on these findings, we developed a theoretical and evidence-based tailored multimedia intervention to improve medication intake behavior. We assumed that interpersonal and technology-mediated components are most effective when used as components of multimedia programs and implemented in a tailored manner. Because each medium has its own value with respect to how it can tailor a message, the integration of different media may increase their effectiveness compared to their use in isolation.

General discussion

Now that we have provided an overview of the main results of the studies comprising this dissertation, we would like to discuss the main findings in an integrative way. This general discussion will be framed as an overview of the theoretical considerations. We will also take the opportunity to discuss some limitations or the study designs and measurements. The discussion will be concluded with implications for practice and recommendations for future research in this field.

Many chronically ill patients experience difficulties in taking their medication as prescribed. It is increasingly recognized that medication intake behavior is complex and that there is not one intervention that is effective for all patients (Steiner, 2012). Poor medication intake behavior can be unintentional (e.g., when a patient is not able to recall medical information due to memory problems) and intentional (when a patient decides not to take the medication because of fear of side effects). To improve medication intake behavior, it appears to be important to address the specific reasons why a patient is unable or unwilling to follow the treatment plan. From this perspective, interventions should be tailored to address the individual barriers to successful medication intake behavior.

This dissertation aimed to develop a theoretical and evidence-based tailored multimedia intervention to improve medication intake behavior. We investigated how various methods and types of media: the Internet (i.e., eHealth), mobile phones (i.e., mHealth) and interpersonal communication, can promote successful medication intake behavior. Two systematic literature reviews were conducted and examined the effectiveness of tailored Internet-based interventions and electronic reminders in improving medication intake behavior. A third literature review was carried out to gain more insight into what is known about tailored communication strategies in relation to medication intake behavior. Because we believed that the existing evidence was not sufficient to develop a theoretical and evidence-based tailored multimedia intervention for patients with inflammatory bowel disease (IBD), we supplemented the existing evidence and theory with three empirical studies.

Barriers to successful medication intake behavior

Before developing this intervention, we sought to gain additional insight into IBD patients' practical and perceptual barriers to successful medication intake behavior. According to the necessity–concerns framework (NCF), patients' perceptual barriers can be categorized as a combination of beliefs about the necessity of taking the medication and their concerns (Clifford et al., 2008). Using the NCF, we found that concerns were most salient in IBD patients, rather than a lack of belief in the necessity of taking medication. The results showed that more than half of the patients perceived high levels of concerns, low levels of personal need, or both, concerning their medication.

The importance of addressing perceptual barriers to the desired behavior—in this case, medication intake—has been emphasized in a number of theories such as the theory of planned behavior (Ajzen, 1991; Fishbein & Yzer, 2006), the integrative model of behavior prediction (Fishbein & Yzer, 2006) and NCF (Clifford et al., 2008). Previous empirical studies have also underlined the importance of taking perceptual barriers in IBD patients into account (Ediger et al., 2007; Horne et al., 2009). In these studies, perceived perceptual barriers were correlated with self-reported poor medication intake behavior. One study (Horne et al., 2009) found that patients who had concerns or doubts about the necessity of the medication were more likely to report poor medication intake behavior than patients who accepted the treatment.

Previous research in this area has been mostly cross-sectional. As far as we are aware, this is the first study to contribute new insight into the perceptual barriers perceived by IBD patients at the start of treatment and after six months of treatment using immunosuppressive or biological therapy. Our findings indicated that patients' perceptual barriers remained stable over time. This is in contrast with the results of other studies, in which patients' perceptual barriers were observed to change over time. In one such study, patients taking antidepressants perceived fewer perceptual barriers about their medication after six months (Aikens & Klinkman, 2012). In another study, patients perceived more perceptual barriers about medications for cardiovascular disease after twelve months (Allen LaPointe et al., 2010). Because different groups of patients may experience different perceptual barriers to different medications or to the same medication at different times (Clifford et al., 2008), it is difficult to compare the results. In addition, the beliefs in the previous mentioned studies and in our study population were not targeted. This might be due to the failure of health care providers to apply appropriate techniques to change those beliefs. The results reported in **Chapter 4** confirm that little communication was used that was considered appropriate for changing or decreasing barriers (see also below).

The results described in **Chapter 4** also suggest that patients perceived relatively few practical barriers (barriers in understanding and using prescriptions in their daily routines). In addition, there was not much variability in the perception of these barriers. A review involving factors associated with poor medication intake behavior in IBD, reported that practical barriers are a strong predictor of poor medication intake behavior. The barrier 'costs of medication' was an especially salient barrier, according to this review (Ediger et al., 2007). In the Netherlands, however, health insurance covers almost all medication costs. In addition, most of the patients in our study were highly educated and relatively young. This may partly explain why patients in our study perceived relatively few practical barriers. As an indicator of perceived practical barriers, we used a scale that measured patients' self-efficacy in understanding (i.e., memory barriers) and using (i.e., daily routine barriers) prescribed medication. In **Chapter 6**, patients' recall of information

was measured using video observations of nurse-patient prescribing consultations, supplemented with questionnaires. We found that IBD patients were able to reproduce approximately half of the information given during consultation. Important information that is needed to take the medication as prescribed, such as the impact of the medication on patients' daily lives and advice intended to promote successful medication intake behavior, were most poorly recalled. This information can be considered useless when poorly recalled by patients. To the best of our knowledge, this is the first study that has extensively measured recall of information in IBD patients who are educated about their newly prescribed immunosuppressive or biological therapy. Although patients' self-efficacy concerning understanding and taking the medication was relatively high, almost half of the information was not recalled. The differences in patients' reported and observed barriers may be related to the method used to measure these barriers. Self-efficacy is measured by self-reporting, while recall of information is measured more objectively. The relation between self-efficacy and recall of medical information should therefore be further investigated.

The value of tailoring in different media

We investigated how different media can be effective in improving successful medication intake behavior. The results indicated that the different media strategies examined can be useful in reducing barriers to successful medication intake behavior and improving medication intake behavior.

In the last few years, eHealth interventions have become more professionalized (Atkinson & Gold, 2002; Snoei, Van Bodegraven, Oldenburg, Stijnen, & Kaptein, 2009). Studies of various health behaviors have shown that computer-generated materials tailored to the unique needs and interests of individuals are more effective in, for instance, addiction relapse prevention and smoking cessation (Bull et al., 1999; Cortese & Lustria, 2012; Prochaska et al., 1993; Smit et al., 2012). Previous research involving eHealth interventions has been extended by showing that eHealth can also be effective in improving medication intake behavior. The Internet offers the possibility of assessing personal data related to health outcomes or determinants. In this way, the message can be tailored to the personal situation of the patient, and the most effective strategy for meeting patients' needs can be determined (Kreuter & Skinne, 2000). The review involving eHealth interventions showed that the majority of the interventions provided the opportunity to contact the health provider, signifying the additional value of the provider when using Internet interventions. All interventions in the review tailored the health messages to some extent to the personal situations of the patients. In examining the level of tailoredness and the effectiveness of the intervention, no clear relationship was found. However, because all interventions tailored the message to some extent, the messages were, to that extent, personally relevant. According to the elaboration likelihood model (ELM), information that is personally relevant is more likely to be deeply processed, which

may lead to better recall of information (Petty, Cacioppo, & Goldman, 1981; Petty & Cacioppo, 1986b). Higher levels of recall is important because forgetfulness is commonly reported as a barrier to successful medication intake behavior in various populations. In studies in which reminder packaging (pill boxes, blister packages, or bottles) has been used, modest improvements in medication intake behavior have been reported. Personal active reminders, which require an extensive time investment, have been shown to have positive effects on medication intake behavior (Mahtani et al., 2011; Zedler et al., 2011). This dissertation extended previous research by showing that electronic reminders can also be effective in reducing unintentional poor medication intake behavior.

While past research involving mHealth has mainly focused on reminding patients to take their medication, new technologies make it possible to tailor text messaging content to address both patients' practical and perceptual barriers to successful medication intake behavior. In a recent study, asthma patients who received tailored text messages based on content reported greater personal need for their medication, more perceived control and displayed more successful medication intake behavior than patients who did not receive those messages (Petrie et al., 2012). We conclude that with the increasing opportunities offered by new technologies, it is also advisable to tailor messages based on timing (i.e., only when needed), in addition to tailoring messages in content. A recent study used real-time medication monitoring (RTMM) combined with SMS reminders. These messages were sent only if patients forgot to take their medication. This study showed that sending messages only when needed improved medication intake behavior and especially the precision with which patients followed their prescribed regimen (Vervloet et al., 2011; Vervloet et al., 2012). This method may be more effective compared to sending messages at fixed time intervals. Text messages at fixed time intervals may cause annoyance and may eventually lead to loss of effectiveness when the automated reminders become a routine. Thus, mHealth strategies that combine tailored content and reminders only when needed may increase the effectiveness of tailored messages even more (Pop-Eleches et al., 2011).

Although tailoring is often associated with new technologies, tailored messages can also be delivered via interpersonal communication. Interpersonal communication provides excellent opportunities to tailor information to the characteristics and needs of a specific patient, assuming that the provider pays attention to the individual needs, preferences and wishes of that patient. While the evidence suggests that tailoring to patients' instrumental and affective needs seems to be more and more important (DiMatteo, 2004; Haynes et al., 2008; Nunes et al., 2009; Van Dulmen, 2011), reviews involving patient-provider communication have concluded that providers' communication is often not tailored to patients' needs (Hack et al., 2005; Ong et al., 1995). We found that nurses often failed to mention important elements of medication use, such as duration of intake, medication intake-related behavior, and the possibility of side effects. This may

result in unmet information needs of the patient. A previous study in oncology found that providers do not explore patients' information needs sufficiently (Posma et al., 2009). As a consequence, providers cannot tailor information to patients' needs, and an information gap may exist.

The results of our study demonstrate the important role that the level of tailoredness in interpersonal communication plays in reducing barriers to successful medication intake behavior. Greater patient satisfaction with the extent to which the consultation was tailored to the patient's personal situation and preferences was significantly related to fewer perceptual barriers to immunosuppressive or biological therapy. We also found that greater satisfaction regarding nurses' instrumental communication was significantly related to fewer perceptual barriers to immunosuppressive or biological therapy. A previous study showed that the quality of providers' interpersonal communication skills resulted in improved medication intake behavior (Bartlett et al., 1984). However, to the best of our knowledge, the relationship between the level of tailoredness of the providers' information provision and the extent to which the patient perceives perceptual barriers has not been studied before. Because perceptual barriers are found to negatively influence medication intake behavior (Horne et al., 2009; Wroe, 2002; Wroe & Thomas, 2003), this finding provides opportunities for practical recommendations on how to improve medication intake behavior. To prevent or reduce perceptual barriers, it appears that nurses should tailor information to patients' personal situations, preferences, and information needs.

How providers should tailor their communication is often not described (Barber et al., 2004; Bernstein et al., 2011; Ong et al., 1995). A meta-analysis by Zolnierek and DiMatteo (2009) showed that patients of providers who communicate well have higher successful medication intake rates than patients whose providers do not communicate effectively. However, the studies reviewed in that meta-analysis mainly focused on the exchange of information during prescribing consultations and did not precisely identify which elements contributed to this effect and how. In our study, we have extended the existing literature by identifying the practical and perceptual barriers to successful medication intake behavior typology (PPB-typology). This typology provides tailored communication recommendations that are designed to meet patients' needs and assist providers in tailoring their communication to patients' barriers. The results of our study indicated that nurses generally do not address barriers to successful medication intake behavior in their communication with patients. This may be because nurses find it difficult to identify which barriers patients perceive and therefore are not able to tailor their communication (DiMatteo, 2004). The results also revealed that if nurses used tailored communication strategies that addressed patients' barriers to successful medication intake behavior, patients reported fewer perceived practical and perceptual barriers.

In conclusion, because IBD patients may have different reasons for their poor medication intake behavior, it is important that messages are tailored to patients'

individual barriers. New media strategies offer opportunities to tailor messages, and the effectiveness of these strategies is promising. In addition to eHealth and mHealth, tailored interpersonal communication can be a powerful tool in promoting medication intake behavior. For instance, effective communication that is tailored to patients' needs and preferences was found to be related to fewer perceptual barriers to medication intake behavior. Moreover, the importance of addressing barriers to successful medication intake behavior is emphasized. The proposed PPB-typology, which contains tailored interpersonal communication recommendations to reduce or remove barriers to medication intake behavior, has led to a unique view of *how* to reduce barriers to successful medication intake behavior in patients with chronic diseases.

The value of a theoretical and evidence-based tailored multimedia intervention

Finally, a theoretical and evidence-based tailored multimedia intervention was developed. This intervention enables providers to tailor their communication to patients' barriers to successful medication intake behavior. According to a review, interventions are often developed in an ad hoc manner without reference to a theoretical foundation (Elliott et al., 2005; Haynes et al., 2008). eHealth and mHealth interventions in particular are often lacking in theoretical foundations (Chavannes et al., 2012). Research conducted across diseases has, however, demonstrated that a theoretical foundation contributes to the effectiveness of interventions (Gallant & Maticka-Tyndale, 2004) and helps to support the process evaluation of interventions. **Chapter 7** described the development of a theoretically defensible evidence-based multimedia intervention aimed at addressing patients' barriers to successful medication intake behavior. The development followed the guidelines of the Medical Research Council (MRC) framework. Using the MRC framework, **Chapter 7** described the logic behind the systematic development and content of a new and innovative tailored multimedia intervention. This description could serve as a guide for other health care professionals when developing health interventions.

The value of tailoring in each medium has been discussed previously in this chapter, and it can be concluded that each medium has its own value in improving medication intake behavior. Computer technologies can be used to create tailored health messages derived from an individual assessment (**Chapter 2**), such as the Question Prompt List (QPL) described in **Chapter 7**. A QPL is a structured list with questions asked before the consultation, giving patients the time to read through the list and identify the questions they want to ask. Because patients are provided with some preparatory tools beforehand, they can prepare themselves for the consultation and gain more insight into what they want to discuss. Nurses who are given the results of this assessment are provided with information on potential barriers to medication intake behavior. Based on the results of this individual assessment, nurses can more easily provide tailored feedback during the consultation (**Chapter 7**). The ability to tailor interpersonal communication

(**Chapter 4**) may result in higher levels of satisfaction (**Chapter 5**), more personally relevant information, and higher recall of information (Kessels, 2003; Van der Meulen et al., 2008). The results of our study showed that recall of information was related to more successful self-reported medication intake behavior (**Chapter 6**). This finding supports Ley's cognitive model, based on his argument that patients' successful medication intake behavior is largely determined by patients' recall of medical information (Ley, 1979). Moreover, new technologies can be used to send tailored text messages to support patients in their medication intake behavior (**Chapter 3 and 7**). Recent research has indicated that tailored text messaging may be more effective than standard messaging in changing patient behaviors (Bull et al., 1999; Cortese & Lustria, 2012; Prochaska et al., 1993; Smit et al., 2012). One of the advantages of text messaging is the ability of the medium to efficiently support patients over time. This may be especially relevant to patients living with chronic diseases that require the patient to engage in self-management behaviors on the long term. Communicating tailored messages via eHealth, mHealth, and interpersonal communication might result in the messages being perceived as more convincing and trustworthy (Voorveld et al., 2011). The persuasive power of the intervention developed in this dissertation is expected to be stronger because a multimedia approach is used (i.e., the message is delivered across different media) and the message is tailored to patients' barriers. In developing this intervention, several study fields, such as health communication, health psychology, marketing and advertising, were combined. We expect that by combining interpersonal and technology-mediated strategies, this approach will work synergistically to enhance medication intake behavior in comparison to either one strategy applied in isolation. This will be tested in future research.

Strengths and limitations

Strengths of the study

The results of the studies described in this dissertation provide useful insights into *how* barriers to successful medication intake behavior can be addressed by using tailored technology-mediated and interpersonal communication, and our studies provide insight into *which* communication elements are related to fewer practical or perceptual barriers to successful medication intake behaviour, and *how* this can be applied in practice.

To the best of our knowledge, this is the first study that has analyzed IBD patients' barriers to successful medication intake behavior at the start receiving immunosuppressive or biological therapy and again after six months. Because the study was conducted in a naturalistic environment and combines video observations of nurse-patient prescribing consultations with pre- and post-visit questionnaires, it permitted a precise and accurate analysis of patients' and nurses' behavior.

The proposed PPB-typology provides concrete recommendations for *how* to reduce barriers to successful medication intake behavior with interpersonal communication in patients with chronic diseases. Moreover, the PPB-typology can be a useful tool in developing communication skills training that is targeted to patients' barriers to successful medication intake behavior.

Persuasive communication can be important in supporting patients in addressing their barriers to successful medication intake behavior. In the past decade, numerous interventions using different media have been designed and implemented to improve successful medication intake behavior. The MRC framework offers the opportunity to describe the development of an intervention structurally and ensures that every step needed to develop an intervention is completed. The description of the intervention described in this dissertation provides useful insights into how barriers to successful medication intake behavior can be addressed using different media, each of which has its own value in improving successful medication intake behavior. By combining techniques from several fields, medication intake behavior is placed in an interdisciplinary perspective at the interface of marketing and medicine.

Limitations

First, we focused on verbal communication because this type of communication is still of great importance in medical consultations. However, we did not include non-verbal communication in the scoring system. Essential elements of patient-provider communication include both verbal and nonverbal communication (Roter, Frankel, Hall, & Sluyter, 2006). As a review by Hall, Roter, Ehrlich, and Miller (2006) showed, nonverbal communication is associated with patient satisfaction. The results of this dissertation showed that patients' satisfaction with nurses' communication was significantly related to fewer perceptual barriers to successful medication intake behavior. Because we did not take nonverbal communication into account, it is unknown whether nurses' nonverbal communication would have influenced these results.

Second, the many methods used to measure medication intake behavior include physiological/biomedical measures, refill records, pill counts, electronic monitoring devices, and self-reported measurements (DiMatteo et al., 2012; Sluijs et al., 2006). The accuracy of each of these methods has been debated. In this dissertation, self-reporting was used to measure medication intake behavior. Self-measurements can contribute to overestimation of the effects of interventions (Nieuwkerk & Oort, 2005). This could be explained by the possibility that patients may forget that they missed a dose. The biases that appear to be most prominent in patients' estimating medication intake behavior using structured questionnaires are social desirability and social approval biases. In other words, studies relying on self-reporting may have a tendency to err on the optimistic side (Urquhart & Vrijens, 2005; Wetzels et al., 2006) with regards to medication intake

behavior, especially compared with more objective pill-counting studies. Although self-reported measurements may be affected by recall and self-presentation bias (Urquhart, 1994), a meta-analysis showed that self-reported medication intake behavior is likely to correlate with more accurate measurements such as pill counts (Shi, Liu, Fonseca et al., 2010). We used an one-item measurement to assess short-term self-reported medication intake behavior. A previous study, however, showed that this self-reporting measure was significantly related to a more objective method to measure medication intake behavior: the medication event monitoring system (Hugen et al., 2002). However, the use of objective measurements would support the validity of our findings. Our future research will include refill data obtained one year after start of the treatment to gain more insight into IBD patients' medication intake behavior and to compare patients' self-reported medication intake scores with their perceptual barriers.

Third, we had a relatively small, convenient, sample. Most of the patients who participated in the study were highly educated and relatively young. Non-response analyses showed no differences between participating and non-participating patients in terms of gender and age. Both Crohn's disease and ulcerative colitis typically manifest during late adolescence or early adulthood, with a peak onset between 15 and 30 years of age (Russel & Stockbrügger, 1996). Because memory problems in particular may be different in older and poorly educated patients, it is desirable to replicate this study among older and/or less educated patients in other patient samples. Moreover, it is plausible that patients who refused to participate in the study because they felt too sick, tired, overwhelmed, busy, or because they had cognitive deficits, are individuals who are likely to be more in need of effective communication strategies to improve medication intake behavior than the patients who agreed to participate in this study. It is therefore plausible that these results are not generalizable to all those in need. This may have contributed to an underestimation of the barriers.

Last, a potential limitation of the intervention developed in this dissertation, is the proposed design of this study. We chose to assign nurses and patients to the intervention group provided with the OPA, tailored interpersonal feedback and text messages. The control group continued receiving the usual information. This was a practical consideration, because of the number of participating nurses (n=8). It would be interesting to assign nurses in the RCT to each of the separate components of the intervention. Although we assume that the integration of these different modes of delivery may increase their effectiveness, it would also be interesting to test their effect in isolation.

Implications for clinical practice

This dissertation outlined some problems and challenges in educating IBD patients about their newly prescribed medications.

Exploring the opportunities of using eHealth in hospitals

With the introduction of applications for smart phones and tablets, it has become possible for patients to monitor their health, improve their treatment outside the hospital, and access health care services anytime and anywhere (Preuveneers & Berbers, 2008). eHealth is expected to contribute significantly to further development of health systems. Moreover, it offers the opportunity for providers to stay in contact with their patients without much extra effort. Hospitals should therefore investigate the opportunities of using eHealth in their usual care.

Enhancing active patient participation during consultation

Many patients report unmet needs. In the literature, it is often assumed that patients do not clearly express their information needs because patients assume that the provider has told them everything or because patients worry that they will appear foolish or take up too much time of the provider (Fallowfield & Jenkins, 1999). Moreover, patients tend to utter their questions and opinions more spontaneously and need their providers to encourage them to express concerns (Butow et al., 2002; Zandbelt, Smets, Oort, Godfried, & de Haes, 2007). Patients can use the developed QPL or any other form of preparatory communication beforehand to prepare themselves for the consultation. The developed QPL is a structured list of questions that serves to prompt the patient to ask specific questions but also raise concerns during a healthcare consultation. Previous research has demonstrated that exposure to a pre-visit website with a QPL empowered patients by making them more assertive (Dimoska et al., 2008). Moreover, a QPL stimulates patient participation during the consultation, such as increasing question-asking behavior (Brown et al., 2001). Obtaining information prior to the consultation can benefit the decision-making process (Ilic, 2010). Furthermore, it is important for patients to express whether they do or do not believe that the medication is necessary or whether they have concerns about the medication.

Communication skills training

Reviews have consistently concluded that communication is a powerful tool in promoting medication intake behavior (Zolnierek & DiMatteo, 2009) and that communication skills training often results in better communication behaviors among providers (Fellowes et al., 2001; Moore et al., 2004). This dissertation notes some implications for developing

communication skills training and communicating effectively with patients when educating them about medication.

Effectively communicate critical elements

Many health communication theories consider knowledge a factor that can explain a large proportion of the variance of a behavior, such as medication intake behavior (Maibach & Cotton, 1995). In the Netherlands, IBD nurses play an important role in educating IBD patients about immunosuppressive and biological therapy during prescribing medication consultations. The importance of prescribing consultations was emphasized in a study by Tarn and colleagues (2006). They found that poor education about prescribed medication may contribute to an increase in misunderstandings about the prescribed medication (Tarn et al., 2006). Unfortunately, consistent with previous literature on provider-patient communication (Latter, Maben, Myall, Young, & Baileff, 2007; Tarn et al., 2006) this dissertation showed that IBD nurses often do not communicate critical elements of medication use. It is therefore important to mention important elements of medication use, such as duration of intake, medication intake-related behavior, and the possibility of side effects. Moreover, since recall of medical information was related to self-reported medication intake behavior, providers should consider recall-promoting techniques such as summarizing, categorizing, structuring, emphasizing, repeating medical information, providing patients with written (online) information, and using cartoons or pictures when explaining medical information. It is therefore advisable to communicate important need-to-know information to patients about their treatments, explore what patients want to know, tailor information to the individual needs of patients, and use recall-promoting techniques. These techniques should be prioritized in communication skills training.

Use of affective communication and adequate response to emotional cues

Literature on health communication emphasizes the importance of both instrumental *and* affective communication in promoting successful medication intake behavior (Ong et al., 1995; Zolnierek & DiMatteo, 2009). The ability to use affective communication is considered a necessary condition for adequate patient education as well as an important predictor of the success of a consultation (Bensing, 1991). Providers, however, often do not use affective communication during consultations (Heaven & Maguire, 1996). Consistent with previous research (Latter et al., 2010), the results of this study showed that IBD nurses mostly use instrumental communication; use of affective communication was hardly noted. Next to the lack of use of general affective communication, we found that nurses neglected one third of patients' emotional cues (e.g., by changing the subject), which has been recognized as an inhibiting response. Moreover, exploring patients' emotional cues, recognized in the literature as facilitative communicative behavior, was only incidentally found. Neglecting patients' emotional cues may lead to poorer patient recall (Jansen et al., 2009). An adequate response to patients' emotional cues may

encourage patients to more fully disclose their concerns (Butow et al., 2002; Mauksch, Dugdale, Dodson, & Epstein, 2008; Uitterhoeve et al., 2008), which may result in fewer concerns if adequately addressed. Thus, employing affective communication and responding adequately to patients' emotional cues are essential when communicating with patients who perceive perceptual barriers. For example, providers can create a nonjudgmental and safe environment, provide social support, show empathy, engage in social conversations, and make jokes.

Identify, explore, and address barriers to successful medication intake behavior

More than half of the patients starting to take a new medication perceive perceptual barriers. Moreover, half of the information given is poorly recalled. This suggests a need to address patients' barriers, especially because these barriers are associated with poor medication intake behavior. The results showed that nurses generally do not address barriers to successful medication intake behavior in their communication with patients. To identify patients' barriers, it is important that nurses ask patients whether they perceive barriers and that nurses respond adequately. Communication skills training for nurses should prioritize exploring, identifying. and addressing barriers. The PPB-typology can serve as a guide how to reduce these barriers.

Recommendations for future research

Measuring medication intake behavior

It is increasingly recognized that medication intake behavior is complex. Steiner (2012), for example, argues that medication intake behavior is a result of different determinants that interact with each other. Almost 200 different determinants have been studied, but none of them has been consistently related to poor medication intake behavior or has been found to be fully predictive (Donovan, 1995). This may be the reason why no gold standard for measuring medication intake behavior has been developed. For example, because different groups of patients may experience different barriers to different medications or to the same medication at different times, it does not seem logical to use one single scale for different groups of patients and different types of medication. A study in breast cancer patients using endocrine therapy found that a lack of personal need for the medication, measured using the Beliefs about Medicines Questionnaire (BMQ), was the best predictor for poor medication intake behavior (Grunfeld, Hunter, Sikka, & Mittal, 2005). However, a more recent qualitative study in breast cancer patients using endocrine therapy concluded that patients' beliefs, measured on the same scale (BMQ), appeared to be just as important as patients' own experiences and perceptions (Wouters et al., submitted). When measuring medication intake behavior, scholars are consistently using measurements that focus on only one or two determinants of a behavior. The advantage

of a more inductive approach, such as that used in a study by Wouters and colleagues (submitted), is that it may unravel more about people's experiences or reasons for poor medication intake. It is therefore recommended to use more qualitative approaches, such as interviews or focus groups, to gain more insight into the specific reasons for poor medication intake behavior that are relevant to a specific group. A scale to measure medication intake behavior should include several components and measure several determinants. Based on the interviews, one should choose the components of the scale that are most appropriate for that specific patient group, type of medication, and type of disease. This may result in more suitable and more predictive measures.

Multimedia tailoring

The combination of different tailored media is a relative new field in health communication. Future research should investigate the effectiveness of combining these strategies. Future research should also focus on the underlying processes of the effect of tailoring and the effects on various outcome measures, such as message processing (e.g., the role of involvement) and message factors (e.g., message content and style). In our review of the eHealth literature, we did not find evidence of a clear relationship between the level of sophistication of an intervention and the extent to which the intervention appeared to be effective. Future studies should be conducted with varying levels of tailoring to further test which characteristics of the tailored messages have the most positive effects on adherence. Moreover, it would be interesting to conduct tests to determine the optimal combination of different media and to determine for whom this combination may be most effective.

Refining the PPB-Typology

In this study, we made some first steps towards developing the PPB-typology, which should be refined and further developed in the future. Future research should include pre-measurements before consultations to measure perceived barriers regarding medication. Because we did not assess patients' barriers to successful medication intake behavior before the consultation, we were not able to measure possible changes in perceived barriers. This might also be an explanation for some findings that were not predicted by the typology developed. For example, checking whether the patient understood the information provided was associated with an increase in necessity barriers. It might be that nurses used these communication techniques to decrease those barriers but were not able to remove them. In other words, it is possible that patients still scored relatively high on these barriers after consultation, although less than before consultation. We believe that these results can contribute to the further refinement of our PPB-typology, and these communication strategies will be added to the PPB-typology. Moreover, further research should investigate whether nurses apply the communication strategies and whether this is related to fewer barriers.

New media strategies

The number of consumer health applications available for smartphone users is growing at an accelerated rate. For example, as of mid-April 2012, there were more than 13,600 consumer health apps available for the Apple iPhone (mobihealth news, 2012). However, until now, little research has investigated the effectiveness of these apps. Moreover, the applications are often developed in an unstructured manner, without any theoretical basis. With the introduction of applications for smart phones or tablets, it has become possible for patients to monitor their health, improve their treatment outside the hospital, and access health care services anytime and anywhere (Preuveneers & Berbers, 2008). It is important to know when patients have difficulties taking their medication as prescribed. With this information, providers can intervene at appropriate times. A recent study showed that interruptions in patients' daily routines, during weekends and holidays, may result in reduced intake of their medications and is an important risk factor for poor medication intake behavior (Vervloet, 2013). "Always on" and "always worn" mobile phones can provide an intimate and detailed picture of an individual's daily routines and offer affordable, proximate, personalized, and continuous measurement in context (Ramanathan et al., 2012). If it appears that a patient has an interruption in his or her daily routine, it will be possible, using these types of media strategies, to intervene at specific appropriate moments, which may result in better medication intake behavior. It would therefore be interesting to develop and systematically evaluate an evidence-based application for monitoring patients' health.

Concluding remarks

One of the proposed solutions for improving medication intake behavior is tailoring and it is important to address the specific reasons that a patient may be unable or unwilling to take medication as prescribed. Until now, not much was known about which medium should be used, how the message should be tailored and how the content should be adapted to the receiver. This dissertation showed that each medium (the Internet (i.e., eHealth), mobile phones (i.e., mHealth) and interpersonal communication) has its own value in tailoring the message. The results also indicated that many IBD patients starting receiving immunosuppressive or biological therapy perceive barriers to taking the medication as prescribed. To improve medication intake behavior, the message should not only be adapted to patients' perceptual and practical barriers but also to patients' information needs. This will increase patients' satisfaction and reduce perceptual barriers. Because recall of information is related to medication intake behavior, providers should provide information that is easy to understand and remember. Based on a theoretical foundation and empirical evidence, a tailored multimedia intervention was developed in this dissertation and implemented in a clinical setting. In the intervention developed, new

technologies are used to supplement prescribing consultations, with the expectation that this combination will work synergistically in increasing medication intake behavior.

Appendix 1

	Database	Authors	Title	Reason for exclusion
1.	PubMed	Bender BG, Apter A, Bogen DK, Dickinson P, Fisher L, Wamboldt FS, Westfall JM.	Test of an interactive voice response intervention to improve adherence to controller medications in adults with asthma.	No Internet intervention
2.	PubMed	Watson AJ, Kvedar JC, Rahman B, Pelletier AC, Salber G, Grant RW.	Diabetes connected health: a pilot study of a patient- and provider-shared glucose monitoring web application.	Medication adherence not as outcome measure
3.	PubMed	Mulvaney SA, Rothman RL, Wallston KA, Lybarger C, Dietrich MS.	An Internet-based program to improve self-management in adolescents with type 1 diabetes.	Medication adherence not as outcome measure
4.	PubMed	Svetkey LP, Pollak KI, Yancy WS Jr, Dolor RJ, Batch BC, Samsa G, Matchar DB, Lin PH.	Hypertension improvement project: randomized trial of quality improvement for physicians and lifestyle modification for patients.	Medication adherence not as outcome measure
5.	PubMed	McTigue KM, Conroy MB, Hess R, Bryce CL, Fiorillo AB, Fischer GS, Milas NC, Simkin-Silverman LR.	Using the Internet to translate an evidence-based lifestyle intervention into practice.	Medication adherence not as outcome measure
6.	PubMed	Decker V, Spoelstra S, Miezo E, Bremer R, You M, Given C, Given B.	A pilot study of an automated voice response system and nursing intervention to monitor adherence to oral chemotherapy agents.	No Internet intervention
7.	PubMed	Tamblyn R, Reidel K, Huang A, Taylor L, Winslade N, Bartlett G, Grad , Jacques A, Dawes M, Larochelle P, Pinsonneault A.	Increasing the detection and response to adherence problems with cardiovascular medication in primary care through computerized drug management systems: a randomized controlled trial.	Intervention not patient-centered
8.	PubMed	Yoo HJ, Park MS, Kim TN, Yang SJ, Cho GJ, Hwang TG, Baik SH, Choi DS, Park GH, Choi KM.	A Ubiquitous Chronic Disease Care system using cellular phones and the Internet.	Medication adherence not as outcome measure
9.	PubMed	McCarrier KP, Ralston JD, Hirsch IB, Lewis G, Martin DP, Zimmerman FJ, Goldberg HI.	Web-based collaborative care for type 1 diabetes: a pilot randomized trial.	Medication adherence not as outcome measure

10.	PubMed	Cho JH, Lee HC, Lim DJ, Kwon HS, Yoon KH.	Mobile communication using a mobile phone with a glucometer for glucose control in Type 2 patients with diabetes: as effective as an Internet-based glucose monitoring system.	Full text could not be obtained
11.	PubMed	Lorig KR, Ritter PL, Dost A, Plant K, Laurent DD, McNeil I.	The Expert Patients Programme online, a 1-year study of an Internet-based self-management programme for people with long-term conditions.	Medication adherence not as outcome measure
12.	PubMed	Ralston JD, Hirsch IB, Hoath J, Mullen M, Cheadle A, Goldberg HI.	Web-based collaborative care for type 2 diabetes: a pilot randomized trial.	Medication adherence not as outcome measure
13.	PubMed	Cocosila M, Archer N, Haynes RB, Yuan Y.	Can wireless text messaging improve adherence to preventive activities? Results of a randomized controlled trial.	No chronic medication
14.	PubMed	Lawrence DB, Allison W, Chen JC, Demand M.	Improving medication adherence with a targeted, technology-driven disease management intervention.	No Internet intervention
15.	PubMed	Faridi Z, Liberti L, Shuval K, Northrup V, Ali A, Katz DL.	Evaluating the impact of mobile telephone technology on type 2 diabetic patients' self-management: the NICHE pilot study.	Medication adherence not as outcome measure
16.	PubMed	Basheti IA, Armour CL, Bosnic-Anticevich SZ, Reddel HK.	Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique.	Medication adherence not as outcome measure
17.	PubMed	Schulz PJ, Rubinell S, Hartung U.	An Internet-based approach to enhance self-management of chronic low back pain in the Italian-speaking population of Switzerland: results from a pilot study.	Medication adherence not as outcome measure
18.	PubMed	Kim SI, Kim HS.	Effectiveness of mobile and Internet intervention in patients with obese type 2 diabetes.	Medication adherence not as outcome measure
19.	PubMed	O'Shea SI, Arcasoy MO, Samsa G, Cummings SE, Thames EH, Surwit RS, Ortel TL.	Direct-to-patient expert system and home INR monitoring improves control of oral anticoagulation.	No Internet intervention
20.	PubMed	Hee-Sung K.	Impact of Web-based nurse's education on glycosylated haemoglobin in type 2 Diabetic patients.	Medication adherence not as outcome measure

21.	PubMed	Kim HS, Jeong HS.	A nurse short message service by cellular phone in type-2 diabetic patients for six months.	Medication adherence not as outcome measure
22.	PubMed	Wangberg SC.	An Internet-based diabetes self-care intervention tailored to self-efficacy.	Medication adherence not as outcome measure
23.	PubMed	Wu AW, Snyder CF, Huang IC, Skolasky R, McGruder HF, Celano SA, Selnes OA, Andrade AS.	A randomized trial of the impact of a programmable medication reminder device on quality of life in patients with AIDS.	No Internet intervention
24.	PubMed	Cho JH, Chang SA, Kwon HS, Choi YH, Ko SH, Moon SD, Yoo SJ, Song KH, Son HS, Kim HS, Lee WC, Cha BY, Son HY, Yoon KH.	Long-term effect of the Internet-based glucose monitoring system on HbA1c reduction and glucose stability: a 30-month follow-up study for diabetes management with a ubiquitous medical care system.	Medication adherence not as outcome measure
25.	PubMed	Gerber BS.	The chronic disease self-management program: extending reach through the Internet.	Full text could not be obtained
26.	PubMed	Roumie CL, Elasy TA, Greevy R, Griffin MR, Liu X, Stone WJ, Wallston KA, Dittus RS, Alvarez V, Cobb J, Speroff T.	Improving blood pressure control through provider education, provider alerts, and patient education: a cluster randomized trial.	No patient centered intervention
27.	PubMed	Chatkin JM, Blanco DC, Scaglia N, Wagner MB, Fritscher CC.	Impact of a low-cost and simple intervention in enhancing treatment adherence in a Brazilian asthma sample.	No Internet intervention
28.	PubMed	Puccio JA, Belzer M, Olson J, Martinez M, Salata C, Tucker D, Tanaka D.	The use of cell phone reminder calls for assisting HIV-infected adolescents and young adults to adhere to highly active antiretroviral therapy: a pilot study.	No Internet intervention
29.	PubMed	Hornick TR, Higgins PA, Stollings C, Wetzel L, Barzilai K, Wolpaw D.	Initial evaluation of a computer-based medication management tool in a geriatric clinic.	Medication adherence not as outcome measure
30.	PubMed	Feldstein A, Elmer PJ, Smith DH, Herson M, Orwoll E, Chen C, Aickin M, Swain MC.	Electronic medical record reminder improves osteoporosis management after a fracture: a randomized, controlled trial.	Medication adherence not as outcome measure
31.	PubMed	Fonseca JA, Costa-Pereira A, Delgado L, Fernandes L, Castel-Branco MG.	Asthma patients are willing to use mobile and web technologies to support self-management.	Medication adherence not as outcome measure

32.	PubMed	Bray P, Roupe M, Young S, Harrell J, Cummings DM, Whetstone LM.	Feasibility and effectiveness of system redesign for diabetes care management in rural areas: the eastern North Carolina experience.	No patient centered intervention
33.	PubMed	Pines A.	Compliance with hormone therapy after Women's Health Initiative: who is to blame?	No intervention study
34.	PubMed	Ryan D, Cobern W, Wheeler J, Price D, Tarassenko L.	Mobile phone technology in the management of asthma.	No Internet intervention
35.	PubMed	Bush N, Donaldson G, Moinpour C, Haberman M, Milliken D, Markle V, Lauson J.	Development, feasibility and compliance of a web-based system for very frequent QOL and symptom home self-assessment after hematopoietic stem cell transplantation.	Medication adherence not as outcome measure
36.	PubMed	Hagström B, Mattsson B, Rost IM, Gunnarsson RK.	What happened to the prescriptions? A single, short, standardized telephone call may increase compliance.	No Internet intervention
37.	PubMed	Kwon HS, Cho JH, Kim HS, Song BR, Ko SH, Lee JM, Kim SR, Chang SA, Kim HS, Cha BY, Lee KW, Son HY, Lee JH, Lee WC, Yoon KH.	Establishment of blood glucose monitoring system using the Internet.	No intervention study
38.	PubMed	Fairley CK, Levy R, Rayner CR, Allardice K, Costello K, Thomas C, McArthur C, Kong D, Mijch A, Melbourne Adherence Group; Melbourne Adherence Group.	Randomized trial of an adherence programme for clients with HIV.	No Internet intervention
39.	PubMed	Larsen DL, Cannon W, Towner S.	Longitudinal assessment of a diabetes care management system in an integrated health network.	Medication adherence not as outcome measure
40.	PubMed	Cramer J, Rosenheck R, Kirk G, Krol W, Krystal J; VA Naltrexone Study Group 425.	Medication compliance feedback and monitoring in a clinical trial: predictors and outcomes	No patient centered intervention
41.	PubMed	Safren SA, Hendriksen ES, Desousa N, Boswell SL, Mayer KH.	Use of an on-line pager system to increase adherence to antiretroviral medications.	No Internet intervention
42.	PubMed	Akron General Medical Center, Akron, Ohio 44333, USA.	The use of non-face-to-face communication to enhance preventive strategies.	No intervention study
43.	PubMed	McAlindon T, Formica M, Kabbara K, LaValley M, Lehmer M.	Conducting clinical trials over the Internet: feasibility study.	No chronic medication

44.	PubMed	Hart T, Hawkey K, Whyte J.	Use of a portable voice organizer to remember therapy goals in traumatic brain injury rehabilitation: a within-subjects trial.	Medication adherence not as outcome measure
45.	PubMed	Stuart GW, Laraia MT, Ornstein SM, Nietert PJ.	An interactive voice response system to enhance antidepressant medication compliance.	No Internet intervention
46.	PubMed	Burkhart PV, Dunbar-Jacob JM, Fireman P, Rohay J.	Children's adherence to recommended asthma self-management.	No Internet intervention
47.	PubMed	Finkelstein J, O'Connor G, Friedmann RH.	Development and implementation of the home asthma telemonitoring (HAT) system to facilitate asthma self-care.	Medication adherence not as outcome measure
48.	PubMed	Andrade A.	HIV adherence strategies take a high-tech route.	Full text could not be obtained
49.	PubMed	Frances CD, Alperin P, Adler JS, Grady D.	Does a fixed physician reminder system improve the care of patients with coronary artery disease? A randomized controlled trial.	No Internet intervention
50.	PubMed	Bennett SJ, Hays LM, Embree JL, Arnould M.	Heart Messages: a tailored message intervention for improving heart failure outcomes.	No intervention study
51.	PubMed	Johnson BF, Hamilton G, Fink J, Lucey G, Bennet N, Lew R.	A design for testing interventions to improve adherence within a hypertension clinical trial.	No Internet intervention
52.	PubMed	Curtin K, Hayes BD, Holland CL, Katz LA.	Computer-generated intervention for asthma population care management.	Medication adherence not as outcome measure
53.	PubMed	Cramer JA, Rosenheck R.	Enhancing medication compliance for people with serious mental illness.	No Internet intervention
54.	PubMed	Legorreta AP, Hasan MM, Peters AL, Pelletier KR, Leung KM.	An intervention for enhancing compliance with screening recommendations for diabetic retinopathy. A bicoastal experience.	Medication adherence not as outcome measure
55.	PubMed	Milch RA, Ziv L, Evans V, Hillebrand M.	The effect of an alphanumeric paging system on patient compliance with medicinal regimens.	No Internet intervention
56.	PubMed	Casebeer L, Roesener GH.	Patient informatics: using a computerized system to monitor patient compliance in the treatment of hypertension.	Full text could not be obtained
57.	PubMed	Schectman G, Hiatt J, Hartz A.	Telephone contacts do not improve adherence to niacin or bile acid sequestrant therapy.	No Internet intervention

58.	PubMed	Skaer TL, Sclar DA, Markowski DJ, Won JK.	Effect of value-added utilities on prescription refill compliance and health care expenditures for hypertension.	No Internet intervention
59.	PubMed	Turner BJ, Day SC, Borenstein B.	A controlled trial to improve delivery of preventive care: physician or patient reminders?	No Internet intervention
60.	PubMed	Simkins CV, Wenzloff NJ.	Evaluation of a computerized reminder system in the enhancement of patient medication refill compliance.	No Internet intervention
61.	PubMed	Ascione FJ, Brown GH, Kirking DM.	Evaluation of a medication refill reminder system for a community pharmacy.	No Internet intervention
62.	PubMed	Heard C, Blackburn JL, Thompson MS, Wallace SM.	Evaluation of a computer-assisted medication refill reminder system for improving patient compliance.	No Internet intervention
63.	EMBASE	Viera AJ, Jamieson B	How effective are hypertension self-care interventions	No Internet intervention
64.	EMBASE	Shanovich KK, Sorkness CA, wise M, Pulvermacher AD, Bhattacharya A, Gustafson DH.	Internet telehealth for pediatric nurse case management improves asthma control.	No patient centered intervention
65	EMBASE	Benhamou PY, Melki V, Boizel R, Perreal F, Quesada JL, Bessieres-Lacombe S *et al*.	One-year efficacy and safety of Web-based follow-up using cellular phone in type 1 diabetic patients under insulin pump therapy: the PumpNet study	No Internet intervention
66.	EMBASE	Bond GE, Burr R, Wolf FM, Price M, McCurry SM, Teri L.	The effects of a web-based intervention on the physical outcomes associated with diabetes among adults age 60 and older: A randomized trial.	Medication adherence not as outcome measure
67.	EMBASE	McMahon GT, Gomes HE, Hohne SH, Hu TMJ, Levine BA, Conlin PR.	Web-based care management in patients with poorly controlled diabetes.	Medication adherence not as outcome measure
68.	CINAHL	Phillips A.	Web based care management improved glucose control in patients with poorly controlled diabetes.	Medication adherence not as outcome measure
69.	CINAHL	Pontin D.	An interactive monitoring device reduced asthma symptoms and functional limitations in inner city children with asthma	Medication adherence not as outcome measure

Appendix 2

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Artinian RCT	Patients with symptomatic left ventricular dysfunction	A web-based monitoring system	- Tailored content - Nature of expert/therapist contact	N=18 Mean age: 68 17 males Intervention group n=9 Control group n=9	- Pill counts -Baseline and 3 months	Medication compliance rate was 94% for the monitor group as measured by the monitor system
Jan RCT	Paediatric asthma patients	Blue Angel for Asthma Kids variability	- Tailored content	N = 164	- Self-reported use and test score for dry powder inhaler (DPI) or metered dose inhaler (MDI) with the spacer technique	The Blue Angel for Asthma Kids, has the potential for improving asthma outcome compared with conventional treatment over a period of 12 weeks
			- Nature of expert/therapist contact	Intervention group n= 88 Mean age 10.9 35 males Control group n=76 Mean age 9.9 28 males	- Baseline and 12 weeks	

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Chan RCT	Paediatric asthma patients	A customized educational and monitoring Web site	- Tailored content - Nature of expert/therapist contact	N=120 Intervention group n=60 Mean age 10.2 37 males Control group n= 60 Mean age 9.0 38 males	Computerized prescription refill record - Baseline, 26 and 52 weeks	No difference in adherence between both groups
Chan RCT	Paediatric asthma patients	A customized educational and monitoring Web site	- Tailored content - Nature of expert/therapist contact	N=10 Mean age: 7 5 males Intervention group n=5 Mean age 6.6 1 male Control group N=5 Mean age 8.7 4 males	- Self reported asthma diary and computerized prescription refill record - 90 days and 180 days	After the intervention, the use of β-agonist decreased, which is an indication of better adherence

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Joseph RCT	Patients with asthma	Web-based asthma management program	- Tailored content - User control	N=314 Mean age 15.3 36.6% male Intervention group: n= 162 Control group n= 152	- Self-reported - Baseline and 12 months	Positive changes in controller medication adherence
Ross RCT	Patients with Heart Failure	The SPPARO (System Providing Access to Records Online)	- Tailored content - Nature of expert/therapist contact	N= 104 Intervention group n= 54 Mean age 57 80% male Control group n=50 Mean age 55 74% male	- Self-reported - Baseline, 6 months, 12 months	Providing patients access to an online medical record improved adherence
Cherry Prospective design	Patients with diabetes	Telemedicine diabetes disease management program.	- Tailored content - Nature of expert/therapist contact	Intervention group n=169 Mean age 53 39 males Historical group (usual care)	- Self-reported - Baseline, 12 months	Outcomes offer encouraging evidence that telemedicine technology coupled with daily remote monitoring may improve appropriate utilization of healthcare services

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Guendelman RCT	Persistent asthma.	Health Buddy, an interactive device connected to a home telephone	- Tailored content - Nature of expert/therapist contact	N=134 Intervention group mean age 12.0 40 male Control group Mean age 12.2 37 male	- Self-reported - Baseline, 6 and 12 weeks	Patients were more likely to take their asthma medication without additional reminders
DeVito Dabbs RCT	Patients who received a lung transplantation	Pocket Personal Assistant for Tracking Health	- Tailored content - Nature of expert/therapist contact	N = 30 Intervention group n=15 Mean age 55 60% male Control group n=15 Mean age 57 60% male	- Self reported - Baseline, 2 months	Patients who received the PATH were more likely to show high adherence to the medical regimen
Van der Meer RCT	Patients with asthma	Internet-based self-management programme	- Customized Health program - User control	N = 200 Intervention Group n= 101 Mean age 36 29% male Control Group n=99 Mean age 37 29% male	Adherence: self-reported. Baseline, 3 months and 6 months	In the first 3 months, many patients had uncontrolled asthma and were advised to increase their inhaled corticosteroid doses. The improvement in asthma control after 3 months allowed a decrease in medication over the next 9 months without loss of asthma control. This suggests tailoring medication to patients' needs rather than increasing medication for the whole study sample

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Van der Meer RCT	Patients with mild to moderate persistent asthma	Internet-based self-management programme	- Customized Health program - User control	N= 200 Intervention n=111 Mean age 36 28 males Group 1 (well controlled) n=37 Group 2 (partly controlled) n=38 Group 3 (uncontrolled) n=36 Control group n = 89 Mean age 36.6 28 male Group 1 (well controlled) n=38 Group 2 (partly controlled) n=33 Group 3 (uncontrolled) n=28	- Self-reported - Baseline and after 3 months and 1 year	Weekly self-monitoring and subsequent treatment adjustment leads to improved asthma control in patients with partly and uncontrolled asthma at baseline and tailors asthma medication to individual patients' needs

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Dilorio Survey	Patients with Epilepsy	WebEase	- Customized Health Program - User control	N = 35 Mean age 37.5 40% male	- Self-reported - Baseline and 6 weeks	Participants showed some improvement in adherence following the program
Dew Prospective design	Heart recipients and their family caregivers	Website including skills workshops, discussion group, ask an expert, question and answer, health tips, recourses and references	- Customized Health Program - Nature of expert/therapist contact.	N=64 Intervention group n= 24 Mean age 45.8 18 males Control group n= 40 Mean age = 57.5 30 males	- Self-reported - Baseline, 4 months	The intervention appeared to be most weakly associated with medical compliance change

Appendix 3: List of excluded studies with reason for exclusion

Database	Year	Authors	Title	Reason for exclusion
PubMed	2011	Harris LT, Lehavot K, Huh D, Yard S, Andrasik MP, Dunbar PJ, Simoni JM.	Two-Way Text Messaging for Health Behavior Change Among Human Immunodeficiency Virus–Positive Individuals	Medication adherence not as outcome measure
PubMed	2010	Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, Jack W, Habyarimana J, Sadatsafavi M, Najafzadeh M, *et al*.	Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomized trial	Reminder not specifically for medication intake
PubMed	2010	Simoni JM, Chen WT, Huh D, Fredriksen-Goldsen KI, Pearson C, Zhao H, Shiu CS, Wang X, Zhang F.	A Preliminary Randomized Controlled Trial of a Nurse-Delivered Medication Adherence Intervention Among HIV-Positive Outpatients Initiating Antiretroviral Therapy in Beijing, China	Only total effect of intervention on adherence reported (reminder was one aspect)
PubMed	2010	Bender BG, Apter A, Bogen DK, Dickinson P, Fisher L, Wamboldt FS, Westfall JM.	Test of an Interactive Voice Response Intervention to Improve Adherence to Controller Medications in Adults with Asthma	Reminder not specifically for medication intake
PubMed	2010	Marciel KK, Saiman L, Quittell LM, Dawkins K, Quittner AL.	Cell phone intervention to improve adherence: cystic fibrosis care team, patient, and parent perspectives	Medication adherence not as outcome measure
PubMed	2009	Decker V, Spoelstra S, Miezo E, Bremer R, You M, Given C, Given B.	A pilot study of an automated voice response system and nursing intervention to monitor adherence to oral chemotherapy agents	No reminder (only information exchange)
PubMed	2009	Düsing R, Handrock R, Klebs S, Tousset E, Vrijens B.	Impact of supportive measures on drug adherence in patients with essential hypertension treated with valsartan: the randomized, open-label, parallel group study	Only total effect of intervention on adherence reported (reminder was one aspect)
PubMed	2008	Lawrence DB, Allison W, Chen JC, Demand M.	Improving Medication Adherence with a Targeted, Technology-Driven Disease Management Intervention	Reminder is not directed to patient (not patient-centered)

PubMed	2008	Tsur L, Kozer E, Berkovitch M.	The Effect of Drug Consultation Center Guidance on Contraceptive Use Among Women Using Isotretinoin: A Randomized, Controlled Study	No reminder (only information exchange)
PubMed	2008	Mollon B, Holbrook AM, Keshavjee K, Troyan S, Gaebel K, Thabane L, Perera G.	Automated Telephone Reminder Messages Can Assist Electronic Diabetes Care	Medication adherence not as outcome measure
PubMed	2006	Fonseca JA, Costa-Pereira A, Delgado L, Fernandes L, Castel-Branco MG.	Asthma patients are willing to use mobile and web technologies to support self-management.	Medication adherence not as outcome measure
PubMed	2005	Ryan D, Cobern W, Wheeler J, Price D, Tarassenko L.	Mobile phone technology in the management of asthma	Medication adherence not as outcome measure
PubMed	2003	Fairley CK, Levy R, Rayner CR, Allardice K, Costello K, Thomas C, McArthur C, Kong D, Mijch A, Melbourne Adherence Group.	Randomized trial of an adherence program for clients with HIV	Only total effect of intervention on adherence reported (reminder was one aspect)
PubMed	2003	Larsen DL, Cannon W, Towner S.	Longitudinal Assessment of a Diabetes Care Management System in an Integrated Health Network	Medication adherence not as outcome measure
PubMed	2003	Stuart GW, Laraia MT, Ornstein SM, Nietert PJ.	An interactive voice response system to enhance antidepressant medication compliance.	No reminder (only information exchange)
PubMed	1999	Cramer JA, Rosenheck R.	Enhancing Medication Compliance for People with Serious Mental Illness	No electronic reminder
PubMed	1993	Raynor DK, Booth TG, Blenkinsopp A.	Effects of computer generated reminder charts on patients' compliance with drug regimens	No electronic reminder
Ref from review	2006	Mannheimer SB, Morse E, Matts JP, Andrews L, Child C, Schmetter B, Friedland GH; Terry Beirn Community Programs for Clinical Research on AIDS	Sustained Benefit From a Long-Term Antiretroviral Adherence Intervention Results of a Large Randomized Clinical Trial	Medication adherence not as outcome measure

Ref from review	2003	Dunbar PJ, Madigan D, Grohskopf LA, Revere D, Woodward J, Minstrell J, Frick PA, Simoni JM, Hooton TM.	A two-way messaging system to enhance antiretroviral adherence	Medication adherence not as outcome measure
Ref from review	1991	Leirer VO, Morrow DG, Tanke ED, Pariante GM.	Elders' nonadherence: its assessment and medication reminding by voice mail.	No chronic medication
Embase	2006	Franklin VL, Waller A, Pagliari C, Greene SA.	A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes	Only total effect of intervention on adherence reported (reminder was one aspect)
Embase	2005	Ostojic V, Cvoriscec B, Ostojic SB, Reznikoff D, Stipic-Markovic A, Tudjman Z.	Improving Asthma Control Through Telemedicine: A Study of Short-Message Service	Medication adherence not as outcome measure
PsycINFO	2009	Basheti IA, Armour CL, Bosnic-Anticevich SZ, Reddel HK.	Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique	Medication adherence not as outcome measure
PsycINFO	2009	Enriquez M, Cheng AL, McKinsey DS, Stanford J.	Development and Efficacy of an Intervention to Enhance Readiness for Adherence among Adults Who Had Previously Failed HIV Treatment	No electronic reminder
PsycINFO	2000	Ostrop NJ, Gill MJ.	Antiretroviral Medication Adherence and Persistence with Respect to Adherence Tool Usage	Only total effect of intervention on adherence reported (reminder was one aspect)
PsycINFO	2006	Robertson L, Smith M, Castle D, Tannenbaum D.	Using the Internet to enhance the treatment of depression	Reminder not specifically for medication intake
PsycINFO	2009	Scherr D, Kastner P, Kollmann A, Hallas A, Auer J, Krappinger H, Schuchlenz H, Stark G, Grander W, Jakl G, Schreier G, Fruhwald FM; MOBITEL Investigators.	Effect of Home-Based Telemonitoring Using Mobile Phone Technology on the Outcome of Heart Failure Patients After an Episode of Acute Decompensation: Randomized Controlled Trial	No reminder (only information exchange)

Cochrane Register Controlled Trials	1999	Fulmer TT, Feldman PH, Kim TS, Carty B, Beers M, Molina M, Putnam M.	An intervention study to enhance medication compliance in community-dwelling elderly individuals.	No electronic reminder
Cochrane Register Controlled Trials	1998	Keder LM, Rulin MC, Gruss J.	Compliance with depot medroxyprogesterone acetate: A randomized, controlled trial of intensive reminders	No electronic reminder

Appendix 4: Detailed characteristics of included studies (ordered on type of reminder and year of publication)

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Hardy 2011 RCT parallel	Patients with HIV Intervention: n=10, mean age 42, 50% male. Control: n=9, mean age 44, 50% male.	Intervention: daily personalized text messages sent for each scheduled ART dose. Patients had to respond with a text message when taking ART. Control: use of beeper, which would beep for 30 sec at time ART dose should be taken and would not repeat if the reminder was not acknowledged. *Type: SMS versus beeper*	Self-report (SR), pill count (PC), electronic monitoring (MEMS) and composite adherence score (CAS). Baseline, week 3, week 6.	Baseline: no significant differences in PC and SR between two groups. Week 3: significant difference in MEMS adherence between intervention and control group: 85.3% vs. 57.2% (p=0.0129), and with CAS: 81.5% vs. 56.7% (p=0.0176). Week 6: significant difference in MEMS adherence: 89.7% vs. 56.3% (p=0.002) and with CAS: 83.4% vs. 53.6% (p=0.0094).	First RCT of a personalized cellular phone reminder system to show significantly better short term improvements in adherence to ART in comparison to a beeper reminder system.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Pop-Eleches 2011 RCT parallel	Patients with HIV Group 1: n=70, mean age 35.6, 67% female. Group 2: n=72, mean age 35.7, 69% female. Group 3: n=73, mean age 37.7, 59% female. Group 4: n=74, mean age 36.8, 69% female. Control: n=139, mean age 35.7, 66% female.	Intervention: 1) daily, short reminder; or 2) daily, long reminder; or 3) weekly, short reminder; or 4) weekly, long reminder; or Short messages were simple ("This is your reminder"), long messages provided additional support ("This is your reminder. Be strong and courageous, we care about you"). Control: no reminder *Type: SMS*	Electronic monitoring (MEMS). Every 12-week period in 48 weeks.	Over 48 weeks, participants with adherence >= 90% in 2 groups receiving weekly reminders was 53% vs. 40% in control group (P=0.03). Participants with adherence >= 90% receiving daily reminders was 41% vs. 40% in control group (P=0.92). Participants with adherence >= 90% was 47% in 2 groups receiving long reminders, 40% in the control group (P=0.24). Participants with adherence >= 90% in two groups receiving short reminders was 47% vs. 40% in control group (P=0.24).	Weekly SMS reminders increased percentage of participants achieving 90% adherence to ART by 13–16% compared with no reminder. A longer reminders was not more effective than either a short reminder or no reminder. Daily reminders did not improve adherence.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Hou 2010 RCT parallel	Women on oral contraceptives Intervention: n=36, mean age 22. Control: n=37, mean age 22.	Intervention: daily text message "Please remember to take your birth control pill" sent at a designated time chosen by the participant. Control: no reminder *Type: SMS*	Electronic monitoring (SIMPill) and self-report (diary). Every month for 3 months.	SIMPill: rate of missed pills per cycle for intervention and control group did not differ: 4.9±3.0 vs. 4.6±3.5 (P=.60). Number of missed pills increased with each cycle for entire cohort (P=.02) but did not increase according to arm (P=.58). Diary: mean of 1.4±1.9 missed pills per cycle in intervention group, and 1.1±1.2 in control group.	Although women receiving reminders felt that the text messages were useful and relied on them, there were no significant differences in mean number of missed pills per cycle between women who received daily text message reminders and women who did not.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Strandbygaard 2010 RCT parallel	Patients with asthma Intervention: n=12, mean age 34.4, 50% male. Control: n=14, mean age 30.7, 57% male.	Intervention: daily SMS reminder ("Remember to take your asthma medication morning and evening. From the Respiratory Unit"). Control: no reminder. All patients received education concerning necessity of ICS treatment, and were provided with knowledge of the disease mechanisms and correct inhaler technique. *Type: SMS*	Electronic monitoring (medicine dose-count on inhaler device). Week 4 and week 12.	Mean adherence rate in SMS group increased from 77.9% (week 4) to 81.5% (week 12); mean change: 3.6% (p=0.52). Mean adherence in control group decreased from 84.2% to 70.1%; mean change: -14.2% (p=0.01). Absolute difference in mean adherence rate between two groups after 12 weeks was 17.8% (p=0.019).	This study showed that asthmatic patients who receive a daily SMS reminder remember to take, on average, about 18% more doses of their anti-asthmatic medication compared with patients who do not receive a SMS reminder.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Christensen 2010 RCT cross-over	Patients with hypertension Intervention: n=219, age <45y 5.5%, 46-65y 60.3%, >65y 34.2%, 45.2% male. Control: n=179, age <45y 10.1%, 46-65y 62.5%, >65y 27.3%, 50.2% male.	Intervention: use of electronic monitoring device (Helping Hand Data Capture (HHDC)) which is operated with tablet blister cards. The device gives an audiovisual reminder when it is time to take medication. Control: standard therapy. After 6 months patients were crossed over. *Type: ERD with audiovisual reminder*	Self-report and electronic monitoring (HHDC). At 6 months and 12 months.	First 6 months: patients using HHDC reported 90.6% compliance vs. 85.1% in control group (NS). After crossover, patients using HHDC reported 86.3% compliance vs. 88.4% in control group (NS). Taking, dosing and timing compliance (electronic monitoring data) was 45-52% in group 1, and 32-38% in group 2. Group differences are close to significance. After 6 months, 50% of patients was persistent, 30% took their tablets on a daily basis.	Use of the HHDC device improved self-reported compliance in patients starting on treatment with telmisartan by 5.5% compared to usual care. BP values were unaffected. The HHDC device is most suitable for newly diagnosed patients.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Ho 2008	Patients with glaucoma Total group: n=42, mean age 69.1, 23 female Intervention: n=20 Control: n=22	Intervention: use of Travatan Dosing Aid (TDA) with audiovisual reminder. TDA has a LCD screen that displays a flashing eye drop symbol on the front as a visible reminder when patients are supposed to give themselves a dose of medication and it emits an audible beep as an audible reminder. Prescribed dosing time were programmed into the TDA. Control: use of TDA without audiovisual reminder. *Type: ERD with audiovisual reminder*	Electronic monitoring (TDA). At 3-5 weeks. Observation duration intervention group: 9-84 days (M=37.6), control group: 6-63 days (M=35.4).	Adherence rates were 87.9% and 79.7% (p=0.02), rates of missed dosing were 7.6% and 14.4% (p=0.03), rates of dosing at incorrect times were 7.1% and 9.8% (p=0.19), respectively for alarm on versus alarm off groups. Mean range of time between dose administration and scheduled dose time was 207 ± 108 minutes for the alarm on group and 424 ± 405 minutes for the alarm off group (p=0.08).	In the reminder group there were trends toward fewer days of dosing at incorrect times and smaller average range of time between scheduled dose time and drop administration. Difference in adherence rate and rate of missed doses was significant, suggesting that the presence of audible and visible alarms improved adherence and decreased likelihood of missing a dose.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Charles 2007 RCT parallel	Patients with asthma <u>Intervention</u>: n=44, mean age 39, 28 male. <u>Control</u>: n=46, mean age 35, 22 male.	<u>Intervention</u>: use of SmartInhaler with audiovisual reminder function (AVRF). The alarm was a single beep, which sounded at predetermined times (twice a day) once every 30 sec for 60 min after predetermined time and stopped if the device was actuated or after 60 min if not taken. The AVRF had a light, which was green before device was actuated, changing to red once the dose was taken. <u>Control</u>: use of SmartInhaler without AVRF. *Type: ERD with audiovisual reminder*	Self-report and electronic monitoring (SmartInhaler). Baseline and at 6, 12, 18 and 24 weeks.	Mean and median % medication taken in last 12 weeks: AVRF: 88% and 93%, control: 66% and 74%. Absolute difference in median: 18% (P< .0001). Taking >50% of their medication: AVRF: 95.5%, control: 71.7%. Taking >80% of their medication: AVRF: 88.6%, control: 39.1%. Taking >90% of their medication: AVRF: 63.6%, control: 19.6%. At all-time points, adherence was higher in AVRF group (difference in median adherence 7-21%; P< .0001). Last 4 weeks, underestimated mean missed doses: AVRF: 3, control: 12.2 doses. Median difference: 8 (P=.001).	AVRF improved adherence from a median of 74% to 93%, with a 2- to 3-fold greater number of subjects achieving 80% and 90% adherence with AVRF, respectively. Around 1 in 4 subjects had <50% adherence in the control group, compared with around 1 in 20 with AVRF.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Santschi 2007 RCT cross-over	Patients with hypertension Total group: n=25, mean age 58.0, 12 male.	Intervention: use of Intelligent Drug Administration System (IDAS II), an electronic device that accommodates blister packs. Electric foil is fixed upon the tablet slots, which activates recording of date and hour at which the drug was removed from the blister. Visual reminder (indicating time elapsed since last dose) and audible reminder, which sounds at chosen and fixed time for 1 min or until the device is opened, and can be deactivated upon request.Control: use of MEMS 6 SmartCap with LCD display on top indicating number of daily openings and number of hours elapsed since last opening.After 2 months patients were crossed over. *Type: ERD with audiovisual reminder*	Electronic monitoring (MEMS or IDAS II). Baseline and at the end of each two-month period (3 measurements).	Over the 4-month study, adherence was very high whatever the device, with a median taking adherence of 99.2% (range 62.7–100%). During the first 2-month period, median taking adherence was 100% (range 40.3–100%), with only two patients having a taking adherence <80%. During the last 2-month period, median taking adherence was 98.4% (range 84.1–100%). Median distribution index was lower with IDAS II, indicating that patients showed a stricter adherence to taking their drug at the same time, day after day with the IDAS II than with the MEMS device.	Both devices were considered to be reliable reminders supporting drug intake even though many patients had already established a daily routine for their drug intake. Overall adherence was very high and comparable with both devices. Our study shows that IDAS II is well accepted by patients and could represent a valuable device for the clinical management of patients with chronic diseases.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Andrade 2005 RCT parallel	Patients with HIV Intervention: n=29, mean age 38, 16 male. Control: n=29, mean age 38, 18 male.	Intervention: use of Disease Management Assistance System (DMAS) device, programmed with reminder messages and dosing times for each medication in the HAART regimen. Control: no use of DMAS All patients participated in an individualized, 30 min adherence counseling session each month and received adherence feedback from a clinical pharmacist. *Type: audiovisual reminder*	Self-report and electronic monitoring (eDEM caps). At 4, 8, 12, 16, 20, 24 weeks.	Overall mean adherence from EM data was not significantly different between DMAS (80%) and control (65%). Effect size: 0.51 (95% CI for Cohen's d, 0.26–0.76). Among memory-impaired subjects (DMAS n=14, control n=17), overall mean adherence was higher for DMAS (77%) than control (57%) (P=.001). Among memory-intact subjects, adherence did not differ significantly between DMAS (83%) and control (77%).	An electronic verbal prompting device can improve adherence to HAART by HIV-infected subjects who have memory impairment. The effect of the DMAS device at 24 weeks was only evident in the memory-impaired group, resulting in a 20% increase in adherence rate, compared with 6% for the memory-intact patients.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Da Costa 2005 RCT parallel	Patients with hypertension <u>Intervention</u>: n=35, mean age 57, 45.7% male. <u>Control</u>: n=36, mean age 59, 47.2% male.	<u>Intervention</u>: use of reminder alarm card set up to beep every day at the same time, preselected by pharmacist and/ or patient in accordance with prescription's specifications. The reminder card was similar in size to a credit card with a single button. If the patient failed to acknowledge the alarm, it would beep every 20s for 3h, then it would stop and re-initiate 8h later, beeping every 20s for 1h. <u>Control</u>: no alarm card. *Type: ERD with audible reminder*	Self-report and pill count. Baseline and at 1, 2 and 3 months.	Intervention group: compliance of about 97% throughout the study. Control group: compliance dropped from 94.9% after 1 month to 87.3% after 3 months. Compliance in the intervention group was higher at all time; reaching statistical significance at the third month (p=0.01). For the first and third month, 36 and 29 patients had compliance rates >80% and were rated as compliant. In both first and third month, 3 patients classified as compliant reported that they had stopped taking their medication. For the last month, 7 patients classified as non-compliant reported that they were still taking their medication.	This study indicates that reminder 'alarm' cards may have a positive effect on compliance with antihypertensive medication in patients taking ACE inhibitors once daily over three months. Mean compliance differences between groups were 10% in the last period of follow-up.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Laster 1996 RCT cross-over	Patients with glaucoma Total group: n=13, age not reported, 11 female.	Intervention: use of TimeCap, a medication alarm device serving as cap on conventional medication bottle. It has a digital display that shows time and day of week when the vial was last opened and an alarm that beeps when a dose is due. If the beep is ignored, the digital face flashes to provide a visual reminder that a dose has been missed. Control: no use of TimeCap After 30 days, patients were crossed over. *Type: audiovisual reminder*	Self-report and amount of solution used estimated by weighing of bottle. At 30 and 60 days.	Mean difference (±SD) between amount of medication used with TimeCap and amount used without TimeCap was +2.867g ± 2.138g ($p<0.0001$). Patients reported using their medication an average of 95.8% of the time with TimeCap and an average of 83.1% of the time without TimeCap.	Results indicate that patients used on average 2.867g more pilocarpine over the 30-day period with TimeCap. This results translates into 57 drops and into 29 medication doses or 1 additional dose of pilocarpine per day. The results indicate that a medication alarm device may effectively improve compliance in glaucoma patients.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Simoni 2009 RCT parallel	Patients with HIV Group 1: n=57; Group 2: n=56; Group 3: n=54; Control: n=57. Total group: n=224, mean age 40, 76% male.	Intervention: 1) peer support: 6 twice monthly 1-hour peer meetings held at the clinic with peers and participants, and weekly phone calls from peers to participants. 2) use of a 2-way pager system. The message schedule is customized to participants' daily regimen. In addition to dose reminders, including medication names and number of pills to be taken, 3 other types of messages were sent: 1) educational; 2) entertainment; 3) adherence assessments. Minimum of 3 pager messages sent daily for 2 months. Pages gradually tapered in third month. Confirmation page was requested. 3) combination of peer support and pager.	Self-report and electronic monitoring (MEMS). At 3 (directly post-intervention), 6 and 9 months.	Self-report 100% adherence last 7 days at 2 weeks, 3, 6, 9 months: Group 1: 63.2%, 56.1%, 42.1%, 43.9% Group 2: 80.4%, 57.1%, 42.9%, 58.9% Group 3: 70.4%, 70.4%, 55.6%, 50.0% Control: 64.9%, 47.4%, 63.2%, 43.9%. EM adherence last 7 days at 2 weeks, 3, 6, 9 months: Group 1: 61.7%, 47.0%, 37.2%, 32.3% Group 2: 63.0%, 41.8%, 36.9%, 36.5% Group 3: 63.2%, 50.1%, 35.4%, 32.1% Control: 63.0%, 38.7%, 41.0%, 29.1%. Peer support: a 2-fold increase in the odds of self-report 100% adherence for those receiving vs. not receiving peer support at post-intervention (OR=2.10, 95% CI 1.10-4.01, P=0.02). Peer support vs. no peer support was associated with 9% higher adherence	Findings indicated a 2-fold greater odds of self-reported 100% adherence at immediate post-intervention among individuals receiving peer support vs not receiving peer support. EDM data partially supported this finding. However, neither effect was maintained at follow-up.Receiving informational, emotional, affirmational support from peers might promote adherence, but that effect did not persist when the support was discontinued. The pager intervention did not seem to be successful in promoting adherence at any time point.

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
		Control: no peer support or pager. All patients participated in the HAART protocol (clinic-based program designed to provide education regarding HAART and adherence and to identify and correct adherence barriers before HAART initiation). *Type: pager*		at post-intervention with EM data (estimate=8.88, 95% CI 22.09-19.85, P=0.11). This did not persist at 6 and 9-month follow-up for self-report (P>0.77) nor EM adherence (P>0.74). Pager support did not predict improved odds of 100% adherence at 3 or 9 months (P> 0.74), but was associated with a decrease in 100% adherence at 6 months (OR=0.50, 95% CI 0.24-1.03, P=0.06). EM adherence also indicated no effect for pager support at 3, 6, or 9 months (P> 0.54)	

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Safren 2003 RCT parallel	Patients with HIV Total: n=70, 56 male, age not reported.	Intervention: website used to input patients' schedule of daily pages. A paging service delivered text messages (e.g. ''Take 2 Combivir with water'' every day at 9 AM, or ''Take the 2 blue pills now'') to patients' pagers at designated times. The system allowed staff members to incorporate other reminders (e.g. timing of meals or appointment reminders). Control: no reminders *Type: pager*	Electronic monitoring (MEMS). At baseline, 2 and 12 weeks.	For week 2 ($F(1,58)=8.24$, $p<0.01$) and week 12 ($F(1,43)=5.79$, $p<0.03$), there were significant interactions revealing greater improvement in the pager arm. On average, the intervention group started with 55% adherence, went up to 70% at 2 weeks and 64% at 12 weeks. The control group started with 57% adherence, and remained at 56% (week 2) and 52% (week 12).	A reminder device (pager) revealed improvements relative to monitoring alone at 2 and 12 weeks. However, at both assessment points, in both groups, adherence was less than optimal, revealing the need for more intensive intervention efforts among patients with pre-existing adherence problems.

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Nederlandse Samenvatting

Samenvatting

Het is algemeen bekend dat chronische patiënten moeite hebben met het goed innemen van hun geneesmiddelen. Eerder onderzoek wijst uit dat een derde tot de helft van de chronisch zieke patiënten therapieontrouw is. Dit kan leiden tot overbodige ziekenhuisopnames, onnodige extra onderzoeken, progressie van de ziekte, mislukking van de behandeling en extra kosten. Het bevorderen van therapietrouw is daarom een belangrijk aspect van de behandeling. Hierbij is het belangrijk te erkennen dat geen enkele therapieontrouwe patiënt hetzelfde is. Er is bijvoorbeeld onderscheid tussen onbewuste en bewuste therapieontrouw. Een patiënt die vergeet de geneesmiddelen in te nemen is een onbewust therapieontrouwe patiënt. Als een patiënt er zelf voor kiest om de geneesmiddelen niet te nemen, bijvoorbeeld vanwege zorgen over de bijwerkingen, wordt deze beschouwd als een bewust therapieontrouwe patiënt. Het onbewust of bewust niet innemen van geneesmiddelen is meestal het gevolg van praktische en/of perceptuele belemmeringen die de patiënt ervaart. Praktische belemmeringen zijn bijvoorbeeld vergeetachtigheid, het niet begrijpen van instructies of moeite hebben om het geneesmiddelengebruik te integreren in het dagelijks leven. Perceptuele belemmeringen zijn bijvoorbeeld het niet geloven in de noodzaak van het geneesmiddel of zorgen hebben over de bijwerkingen. Uit eerder onderzoek blijkt dat deze belemmeringen belangrijke determinanten voor therapieontrouw zijn.

Tot op heden zijn er weinig effectieve therapietrouw bevorderende interventies ontwikkeld. Redenen die in de literatuur hiervoor worden genoemd zijn: het ontbreken van een theoretische onderbouwing waardoor er geen aandacht wordt besteed aan onderliggende mechanismen, onvermogen van zorgverleners om een therapieontrouwe patiënt te herkennen en om patiënten blijvend te ondersteunen bij het geneesmiddelengebruik. De meeste interventies die zijn ontwikkeld richten zich op de communicatie tussen de zorgverlener en patiënt, websites en/of reminder services. Op basis van eerder onderzoek werd geconcludeerd dat, om optimaal effect te bereiken, deze interventies moeten worden afgestemd op de individuele patiënt. Hoewel maatwerk dus wordt beschouwd als een veelbelovende strategie in het bevorderen van therapietrouw, is er nog weinig bekend over de manier *waarop* de boodschap het beste gecommuniceerd kan worden en *hoe* de inhoud vervolgens kan worden aangepast aan de individuele ontvanger.

Dit proefschrift richt zich op het verbeteren van de therapietrouw van patiënten met de ziekte van Crohn of Colitis Ulcerosa (inflammatory bowel disease ofwel IBD). Geschat wordt dat 20% tot 40% van de IBD patiënten therapieontrouw is aan hun onderhoudsmedicatie. Remissie van de ziekte is in de behandeling van IBD het primaire

therapeutische doel. Dit kan worden bereikt door het inzetten van intensieve behandelingsstrategieën als immunosuppressiva of TNF-blokkers. Deze geneesmiddelen remmen de werking van het afweersysteem en worden vaak voorgeschreven. Patiënten die starten met deze geneesmiddelen krijgen een dertig minuten durend voorlichtingsgesprek met een verpleegkundige. Het doel van deze gesprekken is dat de verpleegkundige de patiënt informeert over alle belangrijke aspecten van de behandeling waardoor patiënten voldoende geïnformeerd zijn om de geneesmiddelen volgens voorschrift in te nemen.

Het **eerste hoofdstuk** van dit proefschrift leidt het onderwerp therapietrouw kort in en schetst een beeld van de mogelijke belemmeringen die patiënten kunnen ervaren bij het correct innemen van de geneesmiddelen. Vervolgens wordt ingegaan op de rol van op maat gemaakte communicatie in het bevorderen van therapietrouw. De afgelopen jaren zijn er verschillende interventies ontwikkeld om therapietrouw te bevorderen. Deze interventies worden via verschillende media gecommuniceerd: het internet (eHealth), mobiele telefonie (mHealth) en interpersoonlijke communicatie. Elk medium heeft zijn eigen waarde in het op maat maken van de communicatie naar de patiënt. Het doel van het proefschrift is om een op maat gemaakte, theoretisch onderbouwde, multimediale interventie te ontwikkelen die gebaseerd is op verschillende empirische studies. Eerst is door middel van drie literatuurreviews gekeken naar de effecten van internet (eHealth), mobiele telefonie (mHealth) en interpersoonlijke communicatie op therapietrouw. Deze reviews zijn als artikelen opgenomen in de hoofdstukken 2 tot en met 4. Vervolgens is een empirische studie gedaan. De resultaten van deze studie zijn beschreven in drie artikelen die zijn opgenomen in hoofdstukken 4 tot en met 6. Hoofdstuk 4 bevat dus zowel een literatuurreview als een deel van de empirische studie. Op basis van de resultaten is een interventie ontwikkeld en getest op uitvoerbaarheid die wordt beschreven in hoofdstuk 7.

Hoofdstuk 2 geeft een systematisch overzicht van de literatuur met betrekking tot de invloed van eHealth interventies op therapietrouw. Het doel van deze literatuurstudie is om meer inzicht te krijgen in a) de technologische kenmerken van de websites, zoals de mate van geavanceerbaarheid met betrekking tot de wijze waarop de website op maat gemaakt is; b) de effectiviteit van de interventies met betrekking tot therapietrouw; c) de relatie tussen de methodologische kwaliteit van de studies en de effectiviteit van interventies; en d) de samenhang tussen de kenmerken van de interventie en de effectiviteit. De databases PubMed, PsychINFO, EMBASE, CINAHL en Communication Abstracts zijn systematisch geraadpleegd. Dertien studies voldeden aan de inclusiecriteria en zijn systematisch geanalyseerd. Op basis van de resultaten wordt geconcludeerd dat eHealth interventies effectief lijken te zijn in het bevorderen van therapietrouw bij chronische patiënten. Dit blijkt uit vijf studies (waarvan drie studies van hoge

methodologische kwaliteit). Daarnaast rapporteren zes andere studies (waarvan vier studies van hoge methodologische kwaliteit) een matig effect op therapietrouw. Twee studies (waarvan een studie van hoge methodologische kwaliteit) toonden geen effect op therapietrouw aan. Ondanks het in de kinderschoenen staan van de ontwikkeling van eHealth interventies ten tijde van de literatuurstudie, was ruim de helft van de studies van hoge kwaliteit. De interventies waren allemaal middelmatig tot geavanceerd wanneer wordt gekeken naar de manier waarop de interventie op maat was gemaakt. Er zijn geen aanwijzingen gevonden dat geavanceerdere interventies effectiever zijn dan minder geavanceerde interventies. Aangezien er veel variatie was in het type interventie en de methodologie van de studies is meer onderzoek nodig naar de relatie tussen kenmerken van de interventie en de effectiviteit om hier met grotere zekerheid uitspraken over te kunnen doen.

Een veel genoemde belemmering voor patiënten om de geneesmiddelen goed in te nemen is vergeetachtigheid. Elektronische reminders bieden een mogelijkheid om patiënten hierbij te ondersteunen en worden steeds meer gebruikt. **Hoofdstuk 3** geeft een systematisch literatuuroverzicht van studies die de effectiviteit van elektronische reminders op therapietrouw bestudeerden. Daarnaast vond ook een kritische evaluatie van de methodologische kwaliteit van de gevonden studies plaats. Bovendien werd gekeken naar de relatie tussen het type elektronische reminder en de effectiviteit. De databases PubMed, PsychINFO, EMBASE, CINAHL en Cochrane Central Register of Controlled Trails zijn geraadpleegd. Van de dertien gevonden studies die de effecten van elektronische reminders onderzochten, maakten vier studies gebruik van Short Message System (SMS), zeven studies gebruikten audiovisuele reminders en twee studies maakten gebruik van een pager om patiënten te herinneren aan het innemen van hun geneesmiddelen. Uit de analyse blijkt dat elektronische reminders effectief zijn in het bevorderen van therapietrouw op korte termijn. Dit blijkt uit acht studies (waarvan vier studies van hoge methodologische kwaliteit). Van deze acht studies hebben zeven studies kortetermijneffecten gemeten en gevonden, waarbij de follow-up maximaal zes maanden was. Van alle type reminders blijkt de SMS het meest effectief. De literatuurstudie laat ook zien dat de langetermijneffecten van elektronische reminders nog onduidelijk zijn. Door technologische ontwikkelingen ontstaan nieuwe mogelijkheden in de ontwikkeling van elektronische reminders. Door deze nieuwe ontwikkelingen hoeven SMS berichten alleen te worden verstuurd wanneer dit nodig is. Zo kunnen patiënten bijvoorbeeld alleen een SMS ontvangen wanneer zij hun geneesmiddelen niet innemen of krijgen patiënten een SMS aangepast aan de belemmeringen die de patiënt ervaart. Dit is een verbetering ten opzichte van een situatie waarin iedere patiënt een SMS herinnering krijgt.

Interpersoonlijke communicatie is essentieel bij het bevorderen van therapietrouw. Hoewel eerdere studies waardevolle inzichten geven in de effectiviteit van de communicatie tussen zorgverleners en patiënten ten aanzien van therapietrouw, blijft onduidelijk welke specifieke communicatiestrategieën effectief zijn. Het doel van de studie in **hoofdstuk 4** is a) het in kaart brengen van mogelijk effectieve interpersoonlijke communicatiestrategieën; en b) het relateren van het gebruik van deze communicatiestrategieën aan de belemmeringen die IBD patiënten ervaren ten aanzien van het geneesmiddelengebruik (immunosuppressiva of TNF-blokkers). Op basis van een literatuuronderzoek is allereerst een typologie ontwikkeld die zorgverleners handvatten biedt voor het identificeren van belemmeringen en het adequaat reageren op deze belemmeringen. De typologie onderscheidt vier typen belemmeringen: 1) moeite hebben met het begrijpen en onthouden van het geneesmiddelengebruik; 2) problemen hebben met het integreren van het geneesmiddelengebruik in het dagelijks leven; 3) het hebben van zorgen over het geneesmiddelengebruik; en 4) niet overtuigd zijn van het nut van het geneesmiddelengebruik. De eerste twee typen zijn praktische belemmeringen en de laatste twee typen zijn perceptuele belemmeringen. In de typologie worden communicatiestrategieën beschreven die zorgverleners en patiënten kunnen hanteren wanneer er sprake is van een of meerdere type(n) belemmeringen. De typologie is vervolgens getest onder 80 IBD patiënten die voor het eerst informatie kregen van hun verpleegkundige over het gebruik van immunosuppressiva of TNF-blokkers. De praktische en perceptuele barrières zijn gemeten aan de hand van gevalideerde vragenlijsten: de *Medication Understanding and Use of Self-Efficacy Scale* (MUSE) en de *Beliefs about Medicine Questionnaire*. Alle gesprekken zijn op video opgenomen, getranscribeerd en gecodeerd. De inhoud is gecodeerd aan de hand van een observatieprotocol dat is gebaseerd op de ontwikkelde typologie. De resultaten laten zien dat verpleegkundigen voornamelijk instrumentele communicatie (zoals het geven van informatie of advies) gebruiken tijdens het voorlichtingsgesprek. Zij passen veel minder affectieve communicatie (zoals het tonen van begrip of empathie) toe. In het algemeen hanteren verpleegkundigen maar weinig van de in de typologie voorgestelde communicatiestrategieën. De resultaten laten echter wel zien dat als verpleegkundigen deze communicatiestrategieën gebruiken, de patiënten minder belemmeringen ervaren. Verwacht wordt dat therapietrouw kan worden verbeterd als de communicatie is gericht op de specifieke belemmeringen ten aanzien van het geneesmiddelengebruik. Communicatie op maat kan worden gestimuleerd door het volgen van communicatietrainingen waarin de nadruk ligt op het aanleren van de strategieën uit de typologie.

Tijdens voorlichtingsgesprekken hebben zorgverleners een belangrijke rol in het identificeren, begrijpen en bespreken van perceptuele belemmeringen die patiënten

mogelijk ervaren, zoals zorgen over de gevolgen van het gebruik van het geneesmiddel en/of het niet geloven in het nut van het geneesmiddel. Accurate informatie en effectieve communicatie is van essentieel belang om eventuele belemmeringen weg te nemen. Het doel van **hoofdstuk 5** is om a) inzicht te krijgen in de perceptuele belemmeringen die IBD patiënten ervaren bij de start en na zes maanden van het gebruik van immunosuppressiva of TNF blokkers en b) te onderzoeken of tevredenheid over voorlichting van de verpleegkundige samenhangt met deze belemmeringen. In totaal hebben 84 IBD-patiënten die startten met immunosuppressiva meegedaan aan dit onderzoek. De belemmeringen zijn gemeten aan de hand van een gevalideerde vragenlijst. De vragen meten de volgende twee belemmeringen: de noodzakelijkheid van het gebruik van het geneesmiddelengebruik en de zorgen over het gebruik van het geneesmiddel. Om de mate van tevredenheid over de verpleegkundige voorlichting te meten, is aan patiënten gevraagd hoe tevreden zij waren over a) de informatievoorziening over de ziekte en de behandeling in het algemeen; b) de ondersteuning bij het geneesmiddelengebruik; en c) de affectieve communicatie. Ook is aan patiënten gevraagd hoe tevreden zij waren over de mate waarin de voorlichting van de verpleegkundige op de patiënt persoonlijk was afgestemd. De resultaten tonen aan dat de helft van de patiënten zorgen heeft over het gebruik van het geneesmiddel, of niet gelooft dat het geneesmiddel zal bijdragen aan een betere gezondheid. Na zes maanden zijn deze twijfels nog steeds aanwezig. Deze belemmeringen blijven dus stabiel gedurende de behandeling als er geen interventies worden ingezet die zich richten op deze belemmeringen. Uit de resultaten blijkt ook dat patiënten die tevredener zijn over de algemene informatievoorziening en de mate waarin de voorlichting op hen is afgestemd ook positiever zijn over het gebruik van het geneesmiddel.

Informatie over geneesmiddelen is vaak complex en moeilijk te begrijpen. Zo bevat een voorlichtingsgesprek in veel gevallen medisch jargon. Het begrijpen, onthouden en kunnen reproduceren van medische informatie (‘recall’) wordt beschouwd als een belangrijke voorspeller van therapietrouw. Het doel van **hoofdstuk 6** is daarom inzicht te krijgen in de hoeveelheid en het type informatie dat IBD patiënten kunnen reproduceren na afloop van het verpleegkundig voorlichtingsgesprek. Daarnaast is de relatie tussen recall en therapietrouw onderzocht. In totaal zijn 68 op video opgenomen patiëntgesprekken geanalyseerd door middel van een inhoudsanalyse. De patiënten beantwoordden direct na het consult dertien vragen over onderwerpen die tijdens het gesprek besproken waren. Na drie weken werden de patiënten gebeld en werden de recall vragen opnieuw gesteld. Een aantal vragen over bijvoorbeeld de naam van het geneesmiddel, de wijze van toediening en bijwerkingen, kwamen standaard in de recall vragenlijst na drie weken terug. Omdat niet alle onderwerpen uit de eerste recall vragenlijst bij elk gesprek besproken werden, werden aanvullende vragen gebaseerd op de

informatie uit de video-observaties. Bijvoorbeeld informatie over de mogelijkheid tot zwanger worden tijdens het gebruik van het geneesmiddel, of waar de patiënt op moet letten als hij/zij gaat reizen. De juistheid van de antwoorden is vervolgens beoordeeld aan de hand van hetgeen daadwerkelijk besproken was tijdens het consult en omgerekend tot een recall percentage. Na drie weken werd de therapietrouw gemeten door aan de patiënten te vragen om op een schaal van 1 tot 10 aan te geven in hoeverre zij de geneesmiddelen innemen zoals voorgeschreven. Uit de resultaten blijkt dat ongeveer de helft van de informatie over deze geneesmiddelen direct na het consult met de verpleegkundige kon worden naverteld (52.6%). Na drie weken was het percentage informatie dat gereproduceerd kon worden hetzelfde gebleven (53.8%). De onderwerpen die het beste gereproduceerd werden, waren de wijze van toediening en de naam van het geneesmiddel. Adviezen over het integreren van de behandeling in het dagelijks leven en het volhouden van de behandeling werden het meest vergeten. Het belang van het reproduceren van informatie voor therapietrouw wordt in dit proefschrift bevestigd: patiënten die informatie over de geneesmiddelen beter begrijpen en onthouden, vinden zichzelf therapietrouwer.

Op basis van bovenstaande resultaten is in **hoofdstuk 7** een op maat gemaakte interventie ontwikkeld. Het doel van deze interventie is het optimaliseren van het communicatieproces tussen de IBD-verpleegkundige en de patiënt, wat kan resulteren in het beter onthouden en begrijpen van informatie, het ervaren van minder belemmeringen en het verbeteren van therapietrouw. De interventie gebruikt drie verschillende vormen van gemedieerde communicatie: het internet, mobiele telefonie en interpersoonlijke communicatie. Door het combineren van deze verschillende communicatiemiddelen, wordt optimaal gebruik gemaakt van de unieke mogelijkheden van elk medium om de informatie aan te passen aan de individuele patiënt. De interventie bevat een *Online Preparatory Assessment* (OPA). Deze bestaat in de eerste plaats uit een online lijst met onderwerpen (*Question Prompt List ofwel QPL*) waarop patiënten voorafgaand aan het consult kunnen aangeven wat zij belangrijk vinden om tijdens het consult te bespreken met de verpleegkundige. Daarnaast bevat de OPA twee korte, gevalideerde vragenlijsten (MUSE en BMQ; zie hoofdstuk 4) die inzicht geven in de mate waarin patiënten praktische en perceptuele belemmeringen ervaren. Zoals beschreven in hoofdstuk 4 kunnen hiermee vier typen belemmeringen worden geïdentificeerd met bijbehorende communicatiestrategieën. De uitkomsten van de OPA en de vragenlijsten worden voorafgaand aan het consult naar de verpleegkundige gestuurd, samen met een advies welke communicatiestrategieën de verpleegkundige kan gebruiken om belemmeringen weg te nemen. Daarnaast bevat de interventie een communicatietraining voor IBD-verpleegkundigen waarin zij worden getraind in de specifieke communicatiestrategieën. De in hoofdstuk 4 ontwikkelde typologie fungeerde als basis voor deze

communicatietraining. De training is positief geëvalueerd door de deelnemende verpleegkundigen. Tot slot is een SMS-support system ontwikkeld, waarbij patiënten gedurende een half jaar één keer per week een op maat gemaakte SMS ontvangen met daarin een tekst die is aangepast op de specifieke belemmeringen die zij ervaren. Op basis van de OPA die patiënten voorafgaande aan het gesprek invullen en de score op de MUSE en BMQ na drie weken, wordt beoordeeld of patiënten belemmeringen ervaren. Als hieruit blijkt dat patiënten één of meerdere belemmeringen ervaren, krijgen ze één keer per week een SMS bericht die hoort bij één van de type belemmeringen. De SMS berichten zijn door de leden van de patiëntenvereniging voorafgaande aan de interventie getest en positief geëvalueerd. Door op maat gemaakte boodschappen via verschillende media te communiceren, wordt verwacht dat de boodschap als overtuigender en betrouwbaarder wordt gezien en dat een synergetisch effect zal optreden. Over de effectiviteit van de ontwikkelde interventie zal in de toekomst worden gepubliceerd.

Tenslotte wordt in **hoofdstuk 8** gereflecteerd op de bevindingen van dit proefschrift en worden aanbevelingen voor zowel wetenschap als praktijk gedaan.

Belangrijkste aanbevelingen en conclusies

Wetenschappelijke aanbevelingen

Meten van therapietrouw

In toenemende mate wordt erkend dat therapieontrouw een complex fenomeen is. Bijna 200 verschillende determinanten voor therapietrouw zijn tot op heden onderzocht, maar de resultaten zijn voor geen enkele determinant consistent. Omdat patiënten diverse belemmeringen kunnen ervaren, lijkt het niet logisch om één meetinstrument te gebruiken dat slechts gericht is op één belemmering. Het is daarom belangrijk om meer kwalitatieve benaderingen, zoals interviews of focusgroepen toe te passen om meer inzicht te krijgen in de specifieke redenen voor het niet nemen van de geneesmiddelen voor die desbetreffende patiëntengroep. Een meetinstrument zou meerdere componenten moeten bevatten die verschillende belemmeringen meet. Gebaseerd op interviews, zouden onderzoekers de componenten kunnen kiezen die het meest geschikt zijn voor die specifieke patiëntengroep, dat type geneesmiddel en type ziekte.

Maatwerk

Het combineren van verschillende media om communicatie op maat te leveren is relatief nieuw in de gezondheidscommunicatie. Uit toekomstig onderzoek moet blijken of dit inderdaad effectiever is dan het gebruik van een afzonderlijk medium. Als dat zo is, wordt aanbevolen om nader onderzoek te doen naar de onderliggende processen die leiden tot het effect van op maat gemaakte communicatie. Op deze manier wordt meer inzicht

verkregen in de (meer of minder) werkzame elementen van de interventie. Uit onze literatuurstudie bleek geen duidelijke relatie tussen de mate van geavanceerdheid van de eHealth interventies en het effect op therapietrouw. Om meer inzicht te krijgen in de relatie tussen communicatie op maat en therapietrouw is het wenselijk om in experimenteel onderzoek te variëren in de mate van geavanceerdheid van bijvoorbeeld een op maat gemaakte website. Bovendien kan het interessant zijn te bepalen wat de optimale combinatie van verschillende media is voor individuele patiënten.

Verfijning van de typologie

In dit proefschrift zijn een aantal eerste stappen gezet in de richting van de ontwikkeling van een typologie om door middel van communicatie op maat, belemmeringen weg te nemen. Het verdient aanbeveling deze typologie in de toekomst verder te ontwikkelen. Toekomstig onderzoek zou voormetingen moeten meenemen om het verschil in belemmeringen voor en na een gesprek te meten. In het huidige onderzoek kon bijvoorbeeld niet worden vastgesteld of er een verschil was in het aantal belemmeringen dat patiënten ervaren voor en na een voorlichtingsgesprek met de verpleegkundige. Dit kan een verklaring zijn voor het feit dat een aantal resultaten waren gevonden die niet waren voorspeld. Een voormeting kan nader inzicht geven in de relatie tussen het gebruik van communicatiestrategieën en de mate waarin belemmeringen worden ervaren door de patiënt.

Praktische aanbevelingen

Verken de mogelijkheden van eHealth in ziekenhuizen

eHealth zal naar verwachting een belangrijke bijdrage gaan leveren aan de verdere ontwikkeling van de gezondheidszorg. eHealth draait primair om het verbeteren van de kwaliteit van de zorg en gezondheid met behulp van technische hulpmiddelen. Een belangrijk aspect hierbij is dat eHealth nieuwe kwaliteiten toevoegt aan de huidige zorg. Deze nieuwe manier van communiceren kan een bijdrage leveren aan het op maat maken van de communicatie. Bovendien kan eHealth een bijdrage leveren aan arbeidsbesparing en meer doelmatigheid in de zorg. Tenslotte ondersteunt eHealth zorgverleners bij het in contact blijven met hun patiënten. Nader onderzoek naar de mogelijkheden van het gebruik van eHealth in de zorg kan waardevolle inzichten geven in de voor- en nadelen van eHealth.

Het aantal gezondheidsapplicaties (apps) dat beschikbaar is voor smartphonegebruikers groeit in een snel tempo. Met de introductie van deze apps is het mogelijk geworden voor patiënten om hun gezondheid te controleren en te monitoren, hun behandeling buiten het ziekenhuis te verbeteren en altijd en overal toegang tot gezondheidsinformatie te hebben. Tot nu toe is er weinig onderzoek gedaan naar de effectiviteit van deze apps. Bovendien zijn deze apps vaak zonder theoretische basis

ontwikkeld. Een recente studie toont aan dat onderbrekingen in de dagelijkse routine, bijvoorbeeld in het weekend en/of op feestdagen, kan leiden tot verminderde inname van geneesmiddelen. Hiermee is het doorbreken van de dagelijkse routine een belangrijke risicofactor voor therapieontrouw. Apps maken het gemakkelijker de patiënt in het dagelijks leven te ondersteunen bij het geneesmiddelgebruik. Doordat smartphones altijd worden meegedragen kan het verzamelen van deze informatie een goed beeld geven van het dagelijks leven van de patiënt. Een app kan bijvoorbeeld vragen stellen aan de patiënt zodat meer inzicht wordt verkregen in het geneesmiddelgebruik, intoleranties of de dagelijkse routine. Met deze informatie kunnen SMS interventies nog beter op maat worden ingezet.

Bevorderen van patiëntparticipatie

Veel patiënten hebben onvervulde informatiebehoeften. In de literatuur wordt vaak betoogd dat patiënten hun informatiebehoeften niet duidelijk uiten, bijvoorbeeld omdat patiënten ervan uitgaan dat de zorgverlener hen alle noodzakelijke informatie vertelt of dat ze te veel tijd van de zorgverlener in beslag nemen. Het gebruik van een *QPL* of een andere vorm van voorbereiding voorafgaand aan het gesprek met de zorgverlener kan een middel zijn om de participatie van de patiënt tijdens het consult te verhogen. Eerder onderzoek heeft aangetoond dat het gebruik van een QPL de patiënt assertiever maakt en het stellen van vragen stimuleert.

Training in communicatieve vaardigheden

Verschillende literatuurstudies hebben aangetoond dat interpersoonlijke communicatie een krachtig instrument is bij het bevorderen van therapietrouw en dat een communicatietraining resulteert in kwalitatief betere communicatie. In dit proefschrift worden een aantal aanbevelingen voor het ontwikkelen van een communicatietraining beschreven.

Communiceer belangrijke need-to-know informatie

Veel theorieën beschouwen kennis als een belangrijke factor, welke een groot deel van de variatie in gedrag kan verklaren. In lijn met eerdere studies laat dit proefschrift laten zien dat IBD-verpleegkundigen belangrijke *need-to-know* informatie niet communiceren. Het is daarom belangrijk dat verpleegkundigen alle informatie, die nodig is om de geneesmiddelen goed in te nemen, overbrengen aan de patiënt. Omdat het begrijpen en herinneren van medische informatie gerelateerd is aan therapietrouw, is het aan te bevelen dat zorgverleners recall-bevorderende strategieën gebruiken, zoals samenvatten, categoriseren en/of structureren. Het gebruik van deze strategieën kan worden aangeleerd tijdens een communicatietraining.

Gebruik affectieve communicatie en reageer adequaat op emotionele signalen
Eerder onderzoek op het gebied van gezondheidscommunicatie benadrukt het belang van zowel affectieve als instrumentele communicatie wanneer zorgverleners in gesprek gaan met patiënten. Het gebruik van affectieve communicatie wordt beschouwd als een noodzakelijke voorwaarde voor adequate voorlichting. Veel zorgverleners passen affectieve communicatie echter maar weinig toe tijdens een consult. In lijn met eerder onderzoek toont dit proefschrift aan dat IBD-verpleegkundigen vooral instrumentele communicatie gebruiken. Daarnaast geven verpleegkundigen niet altijd aandacht aan de emotionele signalen die patiënten geven. Doordat deze emotionele signalen vaak een belemmering vormen voor het innemen van geneesmiddelen, is het belangrijk dat de zorgverlener adequaat op deze signalen reageert. Een zorgverlener kan bijvoorbeeld de geuite zorg erkennen, of laten blijken dat er naar de patiënt wordt geluisterd. Een adequate reactie op deze emotionele signalen kan de patiënt tevens stimuleren om meer zorgen te uiten.

Identificeer en bespreek de belemmeringen voor goed geneesmiddelengebruik
Meer dan de helft van de patiënten die een behandeling met immunosuppressiva of TNF-blokkers begint, ervaart perceptuele belemmeringen. De resultaten tonen aan dat verpleegkundigen over het algemeen de belemmeringen niet identificeren en/of bespreken terwijl deze wel samenhangen met therapietrouw. Communicatiestrategieën die gericht zijn op identificeren en verkennen van deze belemmeringen en het adequaat reageren op deze belemmeringen, kunnen worden aangeleerd tijdens een communicatietraining.

Belangrijkste conclusies

Het is belangrijk om aandacht te schenken aan de belemmeringen die patiënten ervaren bij het nemen van geneesmiddelen. Tot nu toe zijn studies er nog niet in geslaagd om aan te geven *welk* medium hiertoe kan worden gebruikt en *hoe* de inhoud kan worden aangepast aan de ontvanger. Op basis van de zes artikelen in dit proefschrift vullen de volgende drie conclusies de bestaande literatuur aan.

Ten eerste geeft dit proefschrift inzicht in de vraag *welk* medium (eHealth, mHealth en interpersoonlijke communicatie) kan worden ingezet in het bevorderen van therapietrouw door middel van een op maat gemaakte boodschap. Het proefschrift laat zien dat elk medium een eigen waarde heeft in het afstemmen van de boodschap op de behoefte en belemmeringen van de patiënt. Het internet kan bijvoorbeeld worden gebruikt ter voorbereiding op een gesprek tussen zorgverlener en patiënt en is daarmee van waarde bij het verkrijgen van inzicht in de belemmeringen die patiënten ervaren door middel van

een vragenlijst (hoofdstuk 2). Mobiele telefonie biedt de mogelijkheid om patiënten te ondersteunen bij het geneesmiddelengebruik in het dagelijks leven. Door nieuwe technologieën is het bijvoorbeeld mogelijk om patiënten alleen een SMS te sturen wanneer zij de geneesmiddelen daadwerkelijk vergeten zijn, en/of een SMS te sturen die ingaat op de specifieke belemmeringen van een patiënt (hoofdstuk 3). Door het verbeteren van de communicatie tussen de IBD verpleegkundige en de patiënt zal dit naar verwachting resulteren in minder belemmeringen, betere recall (hoofdstuk 4 en 5) en verbeterde therapietrouw (hoofdstuk 6).

Ten tweede toont dit proefschrift aan dat de helft van de IBD patiënten die starten met immunosuppressiva of TNF-blokkers, perceptuele belemmeringen ervaren zoals het niet geloven in de noodzaak van het geneesmiddel of het hebben van zorgen over de bijwerkingen. Deze belemmeringen blijven stabiel gedurende de behandeling wanneer geen interventies worden ontwikkeld en/of worden ingezet die gericht zijn op het wegnemen van deze belemmeringen (hoofdstuk 5). Daarnaast reproduceren patiënten maar de helft van de informatie (hoofdstuk 6) die noodzakelijk is om de geneesmiddelen in te nemen als voorgeschreven (praktische belemmering).

Ten slotte geeft dit proefschrift inzicht in de vraag *hoe* de boodschap door een verpleegkundige in een consult op maat kan worden gemaakt. Dit proefschrift beschrijft een nieuwe innovatieve interventie om therapietrouw te verbeteren. Op basis van theoretische onderbouwing en verschillende empirische studies, is een op maat gemaakte multimediale interventie ontwikkeld. Met een online lijst met onderwerpen waar de patiënt kan aangeven wat hij/zij wilt bespreken kan de verpleegkundige de informatie aanpassen aan de behoeftes van de patiënt. Door de patiënt vooraf ook vragenlijsten in te laten vullen die inzicht geven in de belemmeringen worden verpleegkundigen gesteund bij het identificeren van deze belemmeringen (hoofdstuk 7). Hierdoor kunnen zij beter op deze belemmeringen inspelen. De ontwikkelde typologie biedt tevens handvatten voor communicatiestrategieën die zij kunnen gebruiken om deze belemmeringen adequaat te bespreken (hoofdstuk 4). Een automatisch op maat gemaakt SMS-support systeem kan vervolgens verpleegkundigen ondersteunen om patiënten op langere termijn in het dagelijks leven te begeleiden bij goed geneesmiddelengebruik. In de ontwikkelde interventie worden nieuwe technologieën gebruikt in aanvulling op de aangeleerde interpersoonlijke communicatiestrategieën die kunnen worden ingezet tijdens het voorlichtingsgesprek met de verwachting dat deze combinatie synergetisch zal werken (hoofdstuk 7).

Dankwoord

Dankwoord

Een concept wat centraal stond in het ontwikkelen van de op maat gemaakte multimediale interventie, is synergie. Volgens het een online woordenboek is een synergie-effect het gevolg van een samenwerking waarbij het effect van het totaal groter is dan wat de afzonderlijke partijen bereikt zouden hebben. Tijdens mijn promotie ben ik zoveel mensen dankbaar en ik mag wel zeggen dat door de support van, en samenwerking met mijn begeleiders en collega's, vrienden en familie mijn proefschrift velen malen beter is geworden dan wanneer ik het alleen gedaan zou hebben.

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Curriculum Vitae

Annemiek Linn was born on the 18th of January 1984 in Heemstede, the Netherlands. After finishing secondary education (atheneum) at College Hageveld in Heemstede in 2003, she studied Communication Science at the University of Amsterdam and specialized in Persuasive Communication. Her master thesis about recall and treatment adherence in patients with inflammatory bowel disease received a 'Best Paper Award'.

In 2009, she started working at the University of Amsterdam as a lecturer in Persuasive Communication. In addition to her teaching duties, she started with the research described in this dissertation, under the supervision of prof. dr. Edith Smit, dr. Julia van Weert and dr. ir. Liset van Dijk. She applied for several grants for the PhD project, resulting in two grants and additional financial support of the Amsterdam School of Communication Research / ASCoR. In 2011, she formally became a part-time PhD student.

After finishing her dissertation she will remain working at the Department of Communication Science of the University of Amsterdam as an assistant professor Health Communication. In her future research she wants to combine insights from health communication, marketing and computer-mediated research to gain more insight and understanding into the effectiveness of tailored new media strategies and interpersonal communication, and their effect on health behavior.

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Little is known about appropriate methods to address medication intake behavior in individual patients and how content should be tailored to the needs of these patients. This dissertation aims to develop a theoretical and evidence-based tailored multimedia intervention to improve medication intake behavior. The studies discussed in this dissertation provide insight into specific barriers for not taking medication as prescribed and investigate how different types of media (i.e., eHealth, mHealth and interpersonal communication) can address these barriers and promote successful medication intake behavior in patients with inflammatory bowel disease.