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## Developing e-health applications to promote a patient-centered approach to medically unexplained symptoms

van Gils, Anne

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*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2019

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

van Gils, A. (2019). *Developing e-health applications to promote a patient-centered approach to medically unexplained symptoms*. [Thesis fully internal (DIV), University of Groningen]. Rijksuniversiteit Groningen.

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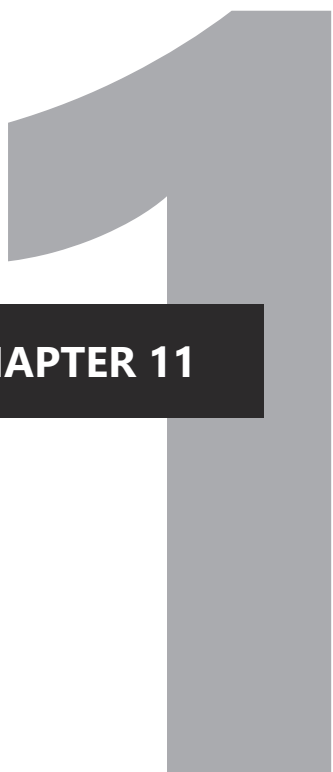
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# CHAPTER 11



## **General discussion.**

### Overcoming Treatment Obstacles with E-health Applications

Medically unexplained symptoms (MUS) constitute a major health issue because of their high prevalence, the suffering and disability they cause, the associated medical costs, and the lack of evidence-based treatment options. In the general introduction of this thesis (*Chapter 1*), three obstacles in the treatment of MUS were put forward, along with potential solutions (see table 1).

**Table 1.** Obstacles in the treatment of MUS with potential solutions, provided by e-health applications.

	I	II	III
<b>Obstacles</b>	Inadequate communication between patients and healthcare providers	Limited use of effective psychological treatments	Heterogeneity; inadequate match between problem and intervention
<b>Solutions</b>	Education & training for healthcare providers	Increasing reach and acceptability of psychological interventions	Personalizing explanation and treatment
<b>E-health applications</b>	Online course ('e-learning') for healthcare providers	Online self-help: 1) Self-help website 2) Guided self-help intervention	Online assessment: Reports and treatment algorithms, based on results of online questionnaires & diaries

In the projects, described in this thesis, advanced internet ('e-health') applications were developed to give shape to these solutions by approaching treatment obstacles from different angles (i.e. interventions aimed at patients and healthcare providers). In this final chapter, the solutions and their corresponding e-health applications will be reviewed in the context of the main findings of this thesis. Furthermore, methodological considerations, implications for clinical practice, and recommendations for future research will be discussed.

#### **Application I: Online Course to Educate and Train Healthcare Providers**

Discrepancies between patients' needs and healthcare providers' responses to patients with MUS are an important, but generally ignored, perpetuating factor for MUS (3). An innovative form of education that can be used to improve healthcare providers' knowledge, skills, and attitude, is online learning ('e-learning'). Reviews of the e-learning literature in various medical education contexts have shown that online learning is at least as effective as traditional

teaching methods, such as lectures or workshops (4-6). In addition, online learning is attractive for healthcare providers, because of its flexibility, convenience, and self-controlled learning pace (7). The first part of this thesis comprised a pilot study, describing the course content and user experiences of an online, interprofessional course we developed to promote a patient-centered approach to managing MUS (*Chapter 2*). A survey before the start of the course confirmed earlier findings that healthcare providers experience patients with MUS as difficult (8-10) and that many of them do not feel well equipped to manage these patients (11). This stresses the need for education and training on MUS. A survey at the end of the course revealed that pilot study participants – healthcare providers from various professions, with varying levels of experience – were extremely satisfied with the course. Previous studies on e-learning, both in the medical and nonmedical literature, have consistently demonstrated high satisfaction rates (4). In addition, self-reported learning gains regarding knowledge, skills, and attitude were generally rated very positive by our pilot study participants. Thus, from the perspective of healthcare providers, an online course is an effective and satisfying way to learn about MUS.

In addition to improving patient-doctor communication (*obstacle I*), the online course also aims to promote the use of psychological interventions (*obstacle II*), and enable healthcare providers to match interventions to the specific problems of individual patients (*obstacle III*). Table 2 shows the learning goals of the course, addressing these three obstacles. By educating and training healthcare providers in all of these areas, application I reinforces the strengths of applications II and III, which will be discussed below.

### ***Application II: Online Self-help to Increase the Reach and Acceptability of Psychological Interventions***

Because highly trained mental healthcare professionals are not required, online self-help interventions have the potential to increase the use of evidence-based psychological interventions for MUS. The second part of this thesis started with a systematic review and meta-analysis, studying the effectiveness of self-help interventions for MUS (*Chapter 3*). This study showed that self-help significantly reduces symptom severity and improves QoL compared to usual care or a waiting list. Overall effect sizes were not inferior to those of conventional psychological treatments for MUS (12, 13). Self-help interventions might thus provide a solution to the limited availability of psychological interventions for MUS, while also being more acceptable to patients than a referral to mental healthcare.

**Table 2.** Learning goals from the online course, associated with the three treatment obstacles.

Obstacles	Learning Goals
<i>After following this module, the participant will:</i>	
I Inadequate communication between patients and healthcare providers	<ul style="list-style-type: none"> <li>• Be more aware of their attitude towards patients with MUS</li> <li>• Have gained insight into 10 common misconceptions about MUS</li> <li>• Be able to make informed decisions on diagnostic testing, avoiding unnecessary procedures</li> <li>• Be able to recognize signs that a patient feels unheard</li> <li>• Know how to use physical examination to effectively reassure a patient</li> <li>• Be able to explain the working diagnosis 'MUS' to a patient</li> <li>• Be able to recognize and prevent a common negative interaction pattern</li> </ul>
II Limited use of effective psychological treatments	<ul style="list-style-type: none"> <li>• Know methods to motivate patients for behaviour change</li> <li>• Know when and how to refer a patient with MUS to mental healthcare</li> </ul>
III Heterogeneity; inadequate match between problem and intervention	<ul style="list-style-type: none"> <li>• Have gained basic knowledge on the etiology of MUS</li> <li>• Be able to recognize and explore the five symptom dimensions (physical, cognitive, emotional, behavioral, and social)</li> </ul>

Subsequently, the development and content of two online self-help interventions were described. The first intervention was a self-help website for patients with minor head injuries, the occurrence of which is a common precipitating factor for MUS (*Chapter 4*). The second intervention was 'Grip self-help': a web-based, personalized, guided self-help intervention for MUS in primary care (*Chapter 5*). Both of these interventions include a combination of education and practical exercises to reduce the impact of unhelpful cognitions, emotions, behaviors, and social factors associated with physical symptoms. Although the effectiveness and successful implementation of these interventions will have to be demonstrated by future studies, both feature three important qualities that can increase the reach and acceptability of psychological interventions. First, the use of the internet as a medium makes both interventions accessible to a large group of patients. The website [www.headinjurysymptoms.org](http://www.headinjurysymptoms.org) can be used by all patients with command of the English language, suffering from symptoms after a minor head injury. Grip self-help can be used by Dutch patients with mild to moderate MUS, after referral by their primary care provider. Second, both are associated with (relatively) low costs, because involvement of highly trained mental healthcare providers, such as clinical psychologists, psychotherapists, or psychiatrists, is not needed. The website does not require any form of guidance. Grip self-help includes low-

frequency guidance by a general practice mental health worker (GP-MHW) (*Chapter 6*). Finally, when embedded into somatic healthcare settings, the interventions are probably more likely to be used and accepted by patients. General practitioners, clinicians in the emergency department, and neurologists can refer patients with a minor head injury to [www.headinjurysymptoms.org](http://www.headinjurysymptoms.org) and can use the information from the website to inform and reassure patients. General practitioners (GPs) and GP-MHWs can use Grip self-help to diagnose and treat patients with MUS in the primary healthcare setting. Integrating key elements of psychological interventions in somatic healthcare settings bypasses the stigma that many patients feel when visiting a psychologist or psychiatrist.

Currently, psychological interventions are reserved for patients with severe (i.e. multiple and chronic) MUS due to scarcity of healthcare resources. Both online self-help interventions, described in this thesis, might be particularly helpful for patients with mild MUS. This is important, because there are indications that the effectiveness of psychological interventions is greater in patients with a shorter duration of symptoms (14).

### ***Application III: Online Assessment to Promote Personalized Explanation and Treatment***

The effectiveness of psychological treatments might be improved by personalizing their contents. This is especially relevant in patients with MUS, since symptom characteristics and etiological factors vary greatly within this patient group. Personalization can occur on different levels: the level of symptoms and the level of etiological factors. Regarding the level of symptoms, many applications of psychotherapy have been described for a broad array of MUS. However, psychological interventions have also frequently been designed for specific symptoms (such as low back pain) and clusters of symptoms (such as irritable bowel syndrome, fibromyalgia, or chronic fatigue syndrome) (15). At the level of etiological factors, treatment can be personalized by focusing on a specific precipitating factor, such as a recent head injury. Adjusting the intervention to a specific trigger increases the likelihood that patients can identify with the provided information. For example, many patients with MUS suffer from health anxiety (i.e. the fear of having a serious illness). Patients who have suffered a head injury worry particularly about having permanent brain damage. By addressing these specific unhelpful cognitions, patients can be reassured more effectively. Treatments can also be personalized by focusing on specific perpetuating factors. For example, not all patients with MUS suffer from health anxiety. Thus, this is not a relevant treatment target for all patients. Previous studies have used profiles based on perpetuating factors to tailor treatment with positive effects on treatment motivation, adherence, satisfaction, and effectiveness (16-18).

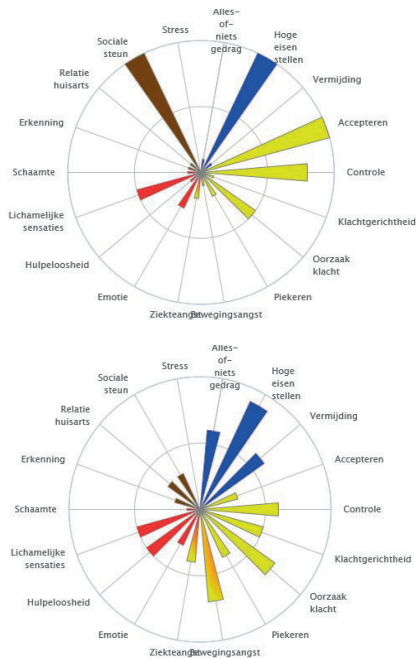
*Application Step I: Online Questionnaires and Diaries.* A first step in personalizing treatment is properly assessing symptom characteristics and etiological factors. Online self-report questionnaires are a thorough and efficient way to gather information on symptoms and

known risk factors for MUS. Two prospective general population cohort studies from this thesis show that childhood parental divorce, parental death (*Chapter 7*), and sexual abuse (*Chapter 8*) are risk factors for developing MUS. These studies also showed that these factors were neither required nor sufficient for the development of MUS, emphasizing the heterogeneity in this patient group. Gathering information on such predisposing factors can form a valuable contribution to a personalized explanatory model. Yet, because prior life events are impossible to influence with treatment (apart from adapting the perception and meaning of the events), we decided to exclusively assess perpetuating factors to personalize treatment in the Grip self-help intervention. In addition, establishing the presence of risk factors does not necessarily prove a causal link between the risk factor and the symptoms that have developed in a specific individual. We therefore suggest using electronic diaries to obtain further insight into individual factors contributing to symptom fluctuations. Time-series analysis using diary data of individual patients can establish the nature of the relationships between symptoms and perpetuating factors at the level of the individual. The two diary studies we performed illustrate the large inter-individual differences with regard to the influences of daily stress (*Chapter 9*), worry, and anxiety (*Chapter 10*) on MUS. In some individuals, increases in stress, worrying, and/or anxiety preceded an increase in MUS. In others, we found a reversed association: an increase in MUS preceded increases in stress, worrying, and/or anxiety. In addition, some individuals did not show any association between MUS and stress, worrying, or anxiety. Time series analyses can thus contribute to personalization of psychological interventions for MUS, by suggesting relevant treatment targets for specific individuals.

*Application Step II: Reports.* After assessment of symptom characteristics and etiological factors, the results of online questionnaires and diaries can be used to provide patients with insights into the nature, origin, and course of their symptoms. In Grip self-help, a report graphically displays which perpetuating factors are relevant to the individual (see figure 1). This so called 'Grip profile' is generated automatically, by comparing the patient's questionnaire results to norm scores from a group of primary care patients (*Chapter 5*). In addition, diary data can be used to depict the course of the symptoms over time, sometimes revealing interesting patterns.



**Figure 1.** Two examples of the Grip profile, showing which perpetuating factors are relevant in the individual.



Note. The larger the bar, the more problematic a factor is. Colors refer to different types of perpetuating factors. Blue: behavioral (all-or-nothing behavior, avoidance); yellow: cognitive (worrying, focusing on symptoms); red: emotional (helplessness, shame); brown: social (lack of acknowledgement, lack of social support).

*Application Step III: Treatment Algorithms.* The final step in personalizing treatment, is to use the information that was collected on symptom characteristics and etiological factors to personalize the intervention. In Grip self-help, patient-tailored selection of self-help exercises was enabled by algorithms, matching exercises to specific perpetuating factors (*Chapter 5*). An additional way of personalizing treatment in this stage, is to take patients' wishes into account. In Grip self-help, primary care professionals can adjust the type of exercises and their order, based on the patient's preferences. Accounting for patient preferences is likely to decrease drop-out and non-adherence.

### Methodological Considerations

In general, research on MUS is complicated by the great variety of terms and definitions used. Even though concepts such as MUS, various functional syndromes (i.e. irritable bowel syndrome, fibromyalgia, and chronic fatigue syndrome), and psychiatric classifications (somatoform disorders) show substantial overlap, they are certainly not identical. Choices regarding the inclusion criteria of participants affect study results. For example: in our

systematic review on self-help interventions, we incorporated medical as well as psychiatric diagnostic concepts in our search strategy (*Chapter 3*). In contrast, two important systematic reviews on traditional psychotherapy for MUS excluded functional somatic syndromes (12, 19). Because differences in the nature, duration and severity of symptoms may influence treatment outcomes, the results of these studies are difficult to compare. To a certain degree, these choices regarding study populations reflect the “lumping” versus “splitting” discussion in the field of MUS (20, 21). If we take the lumpers’ perspective and assume that all MUS share the same underlying construct, it makes sense to merge all of the available evidence. By reflecting the diversity in the group of patients with MUS, findings have a high ecological validity. Taking the splitters’ perspective however, one might argue that the heterogeneity that arises as a result of this approach is a major disadvantage.

Another stumbling block in scientific studies on MUS, is the assessment method. Establishing MUS requires adequate clinical evaluation in order to exclude the presence of underlying medical conditions. However, it is difficult to determine precisely what counts as ‘adequate’. Most studies, including the randomized controlled trial we have designed, studying the effectiveness of Grip self-help (*Chapter 6*), therefore rely on the judgement of individual clinicians. In addition, large cohort studies, including the TRAILS study (*Chapters 7 and 8*) and ‘HowNutsAreTheDutch’ (*Chapter 10*), do not allow for extensive medical evaluation of all study participants. Self-report questionnaires provide a commonly used alternative to assess the number and severity of MUS. Even though underlying organic pathology cannot be ruled out, the sum score of self-report questionnaires such as the Patient Health Questionnaire-15 (PHQ-15) highly correlates with distress, functional limitations, the presence of somatoform disorders, and the use of healthcare resources (22, 23). In addition, self-report questionnaires can be used to screen for psychiatric conditions, that are often accompanied by physical symptoms (depression, generalized anxiety, panic disorder, post-traumatic stress disorder) (*Chapter 6*).

When applying the principles of personalized medicine to psychological interventions for patients with MUS, reliable and valid assessment of symptom characteristics and etiological factors is an important prerequisite. For Grip self-help, we developed an assessment system to measure the relevance of perpetuating factors in individual patients (*Chapter 5*). A battery of self-report questionnaires was used (24). However, not all types of perpetuating factors were adequately represented. Perpetuating factors deemed important by clinicians (24) for which no validated questionnaires were found to assess them included excessive (online) information seeking, difficulty asking for help, and setting high standards. In addition, some of the questionnaires used were validated in specific patient populations, limiting their generalizability. Since time-series analysis of diary data is a relatively new method in the fields of medicine and psychology, literature on the reliability and validity of diary measures of

somatic symptoms and psychosocial factors, such as emotions, cognitions, and behaviors, is scarce.

### **Implications for Clinical Practice and Future Research**

The findings in this thesis stress the importance of developing a *personalized* explanation for MUS. Many healthcare providers, especially those in general practice, are familiar with the biopsychosocial model. Yet, the notion that MUS are simply the result of stress or anxiety is surprisingly persistent. The two diary studies we performed (*Chapters 9 and 10*) show that stress and anxiety indeed lead to an increase in MUS in some individuals. Yet, in others, stress and anxiety arise as a consequence of an increase in physical symptoms. Furthermore, some individuals did not show a relationship between stress or anxiety and MUS at all. These findings emphasize that generic and one-dimensional explanations of MUS (such as “*Your headache is caused by stress*”) are obsolete. Moreover, such ‘psychogenic’ explanations are perceived as threatening by patients and will often be disputed (26). Two of the e-health applications, described in this thesis, were designed to help clinicians to construct a more complex and personalized explanation. First, the online course teaches healthcare providers how to recognize and explore all relevant symptom dimensions (physical, cognitive, emotional, behavioral, and social) and how to adequately explain MUS to patients (*Chapter 2*). Second, the online assessments gather information on various types of etiological factors and establish their relationships with symptoms in the individual. This information can be used to facilitate the development of a personalized explanation. According to Burton et al, an explanation should 1) be plausible, 2) avoid blaming the patient, 3) promote therapeutic partnership or action, 4) apply a descriptive label, 5) address causation, and 6) be created through dialogue between doctor and patient (26). An example of the combination of these elements with information from online questionnaires and diaries can be found in box 1.

After developing a self-help website for patients with symptoms after a minor head injury (*Chapter 4*), an online self-help intervention for patient with MUS in primary care (*Chapter 5*) and an online course for healthcare professionals (*Chapter 2*), studying the effectiveness of these interventions is an obvious next step. A randomized clinical trial, examining the effects of the Grip self-help intervention on health-related quality of life and symptom burden, is currently being carried out (*Chapter 6*). Acceptability and cost-effectiveness will also be reviewed. In addition to healthcare provider satisfaction and self-reported learning gains, which were assessed in the pilot study of our online course (*Chapter 2*), a future study could establish improvements in knowledge, skills, and attitude as rated by patients or observers.

**Box 1.** Continuation of two cases (see *Chapter 1*), describing the course of treatment with the help of e-health applications.

**Case 1: a 41-year-old woman with irritable bowel syndrome**

After hearing her story and performing physical examination, the GP concludes that the symptoms are most likely an exacerbation of the patient's irritable bowel syndrome. He explains to the patient she is vulnerable to developing gastrointestinal symptoms due to her familial predisposition and that recent life stressors might have triggered an increase in symptoms by disrupting the signals between the brain and the gut. In order to enhance her coping strategies and facilitate recovery, the GP proposes to use 'Grip self-help'. Filling out the online questionnaires reveals the following maintaining factors: feelings of shame, experiencing a lack of control, all-or-nothing behavior, a lack of social support, and not asking for help. In addition, the diary report shows a significant increase in symptoms after prolonged physical activity. With the help of the GP-MHW, the patient subsequently works on these factors with Grip self-help. Exercises include learning to balance rest and activity and learning to ask for help. Over the course of five months, she pays monthly visits to the GP-MHW to discuss her treatment goals and progress.

**Case 2: a 22-year-old man with persistent symptoms after a concussion**

After reviewing the severity of his injury based on the Glasgow coma scale, the duration of loss of consciousness, and the duration of post-traumatic amnesia, the neurologist explains that the patient has suffered a mild traumatic brain injury. Even though most patients recover within a few weeks, a complicated course, as experienced by the patient, is far from unusual. He reassures the patient this does not indicate brain damage and does not mean that he will not recover. The neurologist explains that, even though understandable in the acute phase, inactivity and avoidance can ultimately worsen the symptoms. He suggests gradually increasing both mental (reading, watching TV, having conversations) and physical activities (walking, running, playing baseball). The patient is referred to [www.headinjuriesymptoms.org](http://www.headinjuriesymptoms.org) for further information, tips, and tools.

At least as important as studying the effectiveness of interventions, is the implementation of interventions that have been proven to be effective. Many online interventions that were developed in the context of scientific studies remain unused after termination of the study. An important cause is the lack of funding for the maintenance of such online applications. However, a recent Delphi study shows that implementation barriers in the field of MUS exist on many levels; the level of the patient, intervention, healthcare provider, organization, and external context (27). In order for interventions to really impact healthcare practice, implementation barriers and facilitators should be carefully addressed. Throughout the development and pilot phases of Grip self-help, various barriers on different levels became apparent and were taken into account. For example, GPs and GP-MHWs indicated they

experience a lot of time pressure in daily practice. Therefore, Grip self-help was developed to actually save time. Instead of exploring all symptom dimensions during a consultation, self-report questionnaires and automatically generated reports were developed to assess relevant perpetuating factors. In addition, Grip self-help provides patients with practical exercises, which were designed to be carried out with minimal guidance. Secondly, GPs and GP-MHWs stated that they felt insufficiently capable to treat patients with MUS, which could hamper successful implementation of Grip self-help. This was one of the reasons for developing an online course for healthcare providers. In conclusion, we hope to have developed not only a user-friendly, useful and effective, but also a sustainable set of e-health applications.

### **Concluding Remarks**

Most patients with physical symptoms seek help from doctors. Most doctors consider diagnosing and treating *disease* as their fundamental tasks. A problem arises when diagnostic testing does not reveal a biomedical cause for the symptoms. Doctors find it hard to explain MUS, leaving patients with many unanswered questions (*"What is going on with me? What is causing my symptoms? Will my symptoms go away? What can I do about the symptoms?"*). In contrast to the field of medicine, thoroughly exploring the patient's experience, perspective, and life story, and analyzing the interaction between the patient and healthcare provider are key areas of concern in the field of psychotherapy. Given the fact that such psychosocial factors can play an important role in the perpetuation of physical symptoms, this approach is of major value in the context of MUS. It is this conclusion, combined with an endless fascination for the puzzling phenomenon of MUS that has led me, as a medical doctor, to engage in psychotherapy training. I strongly believe that integrating knowledge from the field of psychotherapy into the field of medicine will advance care for patients with MUS. This thesis shows that e-health applications have the potential to promote a patient-centered approach by facilitating this integration.

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