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

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CHAPTER 1



General introduction.

Medically Unexplained Symptoms: a Common Phenomenon

Experiencing physical symptoms is a normal part of life. In population surveys, around 95% of adults report at least one physical symptom in the preceding weeks (1, 2). This concerns symptoms such as pain, fatigue, gastrointestinal complaints, palpitations, and dizziness. Most people do not seek medical attention for these symptoms (3), unless they are severe, persistent, or alarming (4). In primary care, 20 to 35% of presented physical symptoms remain medically unexplained (5-7). In these cases, physical examination, laboratory tests, and/or diagnostic imaging do not show abnormalities and the symptoms do not match a known medical condition. In secondary care, 30 to 50% of symptoms cannot be (fully) explained by organic pathology (8-10).

Troublesome for Patients, Doctors and Society

Although 50 to 75% of medically unexplained symptoms (MUS) improve or recover within one year; 10 to 30% deteriorate or become chronic (11). Persistent MUS not only place a burden on patients, but also on healthcare providers and society. For patients, MUS considerably reduce health-related quality of life (HRQoL) (12-14). The symptoms can affect many aspects of life, including physical, psychological, and social functioning. For healthcare providers, patients with MUS are difficult to help (15-17), because their problems do not fit the biomedical model of disease (18). Since most doctors consider diagnosing and treating disease as their fundamental tasks, patients with symptoms in the absence of objectifiable disease pose a significant challenge. For society, MUS are associated with extensive costs due to increased use of healthcare resources (13, 19, 20), work absenteeism, and disability (21, 22).

Etiology: a Multifactorial Origin

Reflections on the etiology of MUS are hampered by dualistic and reductionist views, wherein symptoms are attributed to a single cause, which can be either physical (i.e. a virus) or psychological (i.e. stress). This perspective is neither helpful nor realistic. It is much more likely that symptoms arise as the result of a complex interplay between physical, psychological, and social factors (23-26). In this so called biopsychosocial model, etiological factors can also be divided into predisposing, precipitating, and perpetuating factors (see table 1). Predisposing factors make a person vulnerable or at risk for developing MUS, precipitating factors trigger the onset of symptoms, and perpetuating or maintaining factors hinder recovery.

Apart from the fact that the etiology of MUS is likely to be multifactorial, contributing factors may also vary greatly between persons. This is illustrated by the two cases in box 1.

Table 1. Types of etiological factors with examples (24-28).

	Physical	Psychological	Social
Predisposing	Genetic predisposition	Personality traits, such as neuroticism	Childhood traumatic events, such as sexual or physical abuse
Precipitating	Acute (inflammatory) illness or injury	Negative life events, such as bereavement, divorce, loss of work	
Perpetuating	Reduced physical fitness Sleep disturbance	Illness anxiety Catastrophizing Avoidance behavior	Lack of acknowledgement and support at home, at work, or in healthcare

In case 1, there is probably a familial predisposition for irritable bowel syndrome, since multiple family members are affected (*predisposing factor*). The patient's symptoms worsened after she was forced to take care of her sick mother while also starting a new job (*precipitating factors*). Feelings of shame, experiencing a lack of control, all-or-nothing behavior, and a lack of social support are potential perpetuating factors in this case. In case 2, symptoms started after a sports injury (*precipitating factor*). The patient's fearful cognitions, inactive/avoidant behavior, and (in the long term) reduced physical fitness might maintain his symptoms (*perpetuating factors*).

Box 1. Two cases, describing the history of patients with MUS.

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

A 41-year-old single mother of two visits her general practitioner (GP), because she is increasingly bothered by gastrointestinal complaints. She was diagnosed with irritable bowel syndrome ten years ago, which runs in her family. The symptoms had been manageable for years, but recently she has been frequently experiencing diarrhea, flatulence, bloating, and fatigue. Even though the patient feels very embarrassed of the gastrointestinal symptoms, the fatigue is bothering her the most. She has no idea why the symptoms have worsened and doesn't know what to do about it. With the responsibility of her two children, taking on the care of her sick mother and her new job as a nurse, her way of dealing with the symptoms is to just keep going until she is no longer able to. She then stays in bed for a couple of days. The patient feels like it is difficult to cope, because she has little help and support.

Box 1 (continued). Two cases, describing the history of patients with MUS.

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

A 22-year-old student presents with fatigue, headache, and cognitive symptoms at a neurology clinic. The symptoms had started three months earlier after he had been hit on the head by a baseball. He had been unconscious for five minutes and described feeling as if he were “in a bubble” and having a severe headache afterwards. He was taken to the emergency department where physical examination and a CT scan were normal. In the weeks following the accident, he experienced extreme tiredness, general weakness, dizziness, and headaches. He spent most of his time in bed, at home with his parents. He was unable to read or watch TV because he had difficulty concentrating. His parents noticed that at times he was struggling to find the right words and that he had become rather irritable. The patient was worried that the accident might have caused permanent damage to his brain and he feared he would not be able to finish his studies.

Note. Second case derived from: Stone J, Hoeritzauer I, Gelauff J, Lehn A, Gardiner P, van Gils A & Carson A (2016). Functional Disorders in Neurology: Case Studies (29).

Terminology and Classification: an Ongoing Subject of Discussion

The phenomenon of physical symptoms in the absence of underlying organic pathology has been given many names throughout the years. They have been referred to as hysteria, somatization, psychogenic symptoms, psychosomatic symptoms, subjective health complaints, functional somatic symptoms (FSS), and, more recently, MUS, and bodily distress syndrome. There is no consensus on what is the most appropriate term (30). In recent years, the term ‘medically unexplained symptoms’ has gained popularity, especially amongst primary care practitioners. This resembles the Dutch term ‘Somatisch Onvoldoende verklaarde Lichamelijke Klachten’ (SOLK), used by the Dutch College of General Practitioners (31). A major disadvantage of ‘MUS’ is that it defines the symptoms by what they are not, rather than by what they are. Also, it perpetuates dualistic thinking; regarding symptoms as either organic (physical) or non-organic (psychological) (32). The term ‘functional symptoms’ is commonly used in scientific literature and clinical practice, because it is neutral and least offensive to patients (33). Both ‘MUS’ and ‘FSS’ are used in the published chapters of this thesis. The different use of terms between chapters reflects the different customs of the fields in which these chapters were published.

In addition to these terms, clusters of persistent MUS have been described by so called ‘functional somatic syndromes’ in virtually all medical specialties. Some of these are irritable bowel syndrome in gastroenterology, fibromyalgia in rheumatology, and chronic fatigue syndrome in internal medicine. Since there is considerable diagnostic and clinical overlap between these syndromes, there is an ongoing debate on whether they should be considered

distinct conditions or artefacts of Western medicine with all of its specialties (34). A recent PhD thesis on this subject concludes that functional syndromes may reflect different subtypes of the same underlying syndrome (35).

In psychiatry, persistent MUS have been classified using the Diagnostic and Statistical Manual of Mental Disorders (DSM). The previous edition (DSM-IV-TR) contained a chapter called 'somatoform disorders', which included classifications such as somatization disorder and pain disorder (36). One of its main criticisms was that these diagnoses were largely based on negative criteria (37). Merely establishing that symptoms cannot be explained by a known medical condition does not justify classifying them as a mental disorder. In the current edition of the DSM (DSM-5), the chapter of somatoform disorders has been replaced by 'somatic symptom disorders'. Diagnostic criteria strongly emphasize maladaptive cognitive, emotional, and behavioral reactions to physical symptoms and the distinction between medically explained and unexplained symptoms has been abandoned (38).

Evidence-Based Treatments are Limited

Since the pathophysiology of MUS remains unclear, most treatments are aimed at creating the optimal conditions for recovery by targeting perpetuating factors (see table 1). In line with recommendations by experts in the field (24), the Dutch multidisciplinary guideline on MUS proposes a stepped-care approach. Patients with mild MUS (one or few symptoms, mildly impaired) are managed by their GP, who is expected to explore different symptom dimensions (physical, cognitive, emotional, behavioral, and social), and provide education, advice and regular check-ups. Patients with moderate MUS (multiple symptoms, moderately impaired) should be referred to a general practice mental health worker (GP-MHW), physiotherapist, or psychologist. Patients with severe MUS (multiple, persistent symptoms, severely impaired) should be referred for specialized or multidisciplinary treatment in secondary or tertiary care (39). A recent observational study shows that Dutch GPs do not use all of the management strategies that are recommended by this guideline. For example, GPs rarely explore all symptom dimensions and they hardly ever refer patients to a psychologist or psychiatrist (40).

Research on specific types of treatment for MUS is limited and generally of low quality (41, 42). There is little evidence that pharmacological interventions, such as antidepressants or herbal supplements (e.g. St. John's wort), are effective in decreasing MUS. Because side effects are common, pharmacological interventions are generally not recommended (41). Evidence on non-pharmacological interventions is mainly focused on psychological treatments, and cognitive behavioral therapy (CBT) in particular. Meta-analyses show that psychological therapy has a small to medium sized effect in decreasing MUS and improving HRQoL (42, 43).

Obstacles in the Treatment of Medically Unexplained Symptoms

In addition the scarcity of treatment options, there are several other obstacles, preventing patients with MUS from receiving adequate care.

Obstacle I: Inadequate Communication between Patients and Healthcare Providers

Communication problems between patients and healthcare providers are an important, but often overlooked, perpetuating factor for MUS (44). In general, there seems to be a discrepancy between patients' needs and doctors' responses to patients with MUS. Studies on patients' perspectives show that, above all, patients with MUS want to be taken seriously. More than other patients, they seek emotional support (45). Yet, the prevailing response of doctors is to propose somatic interventions, such as diagnostic procedures and pharmacological treatments, which are often unnecessary and ineffective (46). When these do not lead to the desired result, patients commonly perceive their doctors as skeptical or dismissive (47) (see box 2, case 1).

Box 2. Treatment obstacles, as encountered in the two cases.

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 proposes to prescribe psyllium fibers to regulate her bowel movements.

After three weeks, the patient returns to the GP. Her symptoms did not improve. The GP then suggests to refer her to a psychologist in order to "talk about the problems at home and at work". This upsets the patient. She doesn't see what this has to do with her symptoms. She feels like the GP doesn't understand the severity of her symptoms.

Considerations:

- 1) A qualitative study shows that GPs often miss 'psychosocial cues' that are given by patients with MUS (56). In this case, the patient has indicated that she feels embarrassed and that she feels overwhelmed by her tasks and responsibilities. Instead of acknowledging and addressing these issues, the GP prescribed medication. This is a missed opportunity, since psychosocial factors can be important perpetuating factors.
- 2) Even though this patient might benefit from psychological therapy, the way in which the GP proposes it is inadequate. He should either explain the possible link between the psychosocial problems and the symptoms, or he could simply explain there are effective 'talking therapies' for irritable bowel syndrome, teaching patients how to cope with their symptoms.

Box 2 (continued). Treatment obstacles, as encountered in the two cases.

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 concludes that the patient has suffered a mild traumatic brain injury. The neurologist explains that not much can be done; the symptoms will probably improve over time.

In the weeks following this visit, the patient starts to worry even more. Since his neurologist used the term 'brain injury', he googles this term and finds all kinds of stories from people with serious and long-lasting consequences of brain injuries.

Considerations:

- 1) In this consultation, the patient's worries have not been adequately addressed. His fearful cognitions and their behavioral consequences are important perpetuating factors.
- 2) Complementary to reassuring the patient by disputing or challenging his fearful cognitions, the neurologist could have given the patient some practical advice on resuming his daily activities. In addition to targeting his inactive coping behavior, this would have probably given the patient hope and a sense of control.

Obstacle II: Limited Use of Effective Psychological Treatments

Even though psychological treatment is an effective way to decrease symptoms and improve HRQoL in patients with MUS, only a small proportion of patients benefits from this type of treatment. As mentioned previously, Dutch GPs rarely refer patients with MUS to a psychologist or psychiatrist. Many patients with MUS are not willing to visit a mental healthcare facility for treatment, because it makes them feel stigmatized (48). Misconceptions and miscommunication in healthcare providers (*obstacle 1*) reinforce this stigmatization (see box 2, case 1). Furthermore, because psychotherapy is relatively time-consuming, costly, and requires highly trained professionals, it is scarce and usually offered exclusively to patients with multiple, severe and chronic symptoms.

Obstacle III: Heterogeneity: One Size Does Not Fit All

When psychological treatment is offered to patients with MUS, the effect might be limited due to an inadequate match between the patients' problems and the interventions offered. The group of patients with MUS is heterogeneous in many aspects. First, there are differences in type, number, duration, and severity of symptoms. Some patients experience one specific symptom, such as low back pain. Others present with a broad range of symptoms, varying from problems sleeping to involuntary movements and blackouts. For some, their symptoms represent a minor inconvenience. Others are bedbound or in a wheelchair and need daily care. Apart from these symptom characteristics, etiological factors also vary greatly between

persons. This especially applies to perpetuating factors, which are the intervention targets in psychological therapies. In some patients, symptoms evoke fearful thoughts about the origin of the symptoms. Others catastrophize about the course and consequences of their symptoms (see box 2, case 2). Some patients become very cautious, avoiding rigorous movements or physical exertion, because they fear this will increase their symptoms or harm their body (see box 2, case 2). Others tend to ignore their symptoms and continue their activities, until they are no longer able to, resulting in an all-or-nothing behavior pattern (see box 2, case 1). Because of this heterogeneity, it is unlikely that a ‘one-size-fits-all’ approach to treatment will suffice (49). This might partly explain the relatively low effect sizes of psychological therapies for MUS, compared to other disorders. Most therapies that were studied in randomized controlled trials were manual- or protocol-based, leaving little room for customization.

Overcoming Treatment Obstacles

The projects that will be described in this thesis were aimed to improve care for patients with MUS by developing solutions to the previously mentioned obstacles (see table 2).

Table 2. Obstacles in the treatment of MUS with potential solutions.

	I	II	III
Obstacle	Inadequate communication between patients and healthcare providers	Limited use of effective psychological treatments	Heterogeneity; inadequate match between problems and interventions
Solution	Education & training for healthcare providers	Increasing reach and acceptability of psychological interventions with self-help	Personalizing explanation and treatment

Solution I: Educating and Training Healthcare Providers

A clear explanation of the symptoms, effective reassurance, and patient-centered communication can positively influence health outcomes of patients with MUS (50). A good explanation can create common ground that allows both the patient and the doctor to address psychosocial as well as physical issues and to avoid unnecessary somatic interventions (44). Since healthcare providers generally feel insufficiently able to manage patients with MUS (51), a first step in improving patient-doctor communication is educating and training healthcare providers. Enhancing healthcare providers’ knowledge on MUS and communication skills might also reduce the stigma, associated with psychological treatment (*obstacle II*) and improve their skills to match interventions to the specific problems of individual patients (*obstacle III*).

Solution II: Increasing the Reach and Acceptability of Psychological Interventions with Self-help

Self-help interventions can be defined as therapeutic interventions, administered through text (printed or online), audio, or video, and conducted (largely) independently of a healthcare professional. Such interventions have the potential to overcome some of the barriers, associated with psychological treatment for MUS. First, self-help interventions do not have to be offered in the mental healthcare setting, which decreases the associated stigma. Second, self-help interventions do not require guidance of trained professionals, making them available to a much larger group of patients. Consequently, self-help can provide a widely available and acceptable treatment option for patients with MUS.

Solution III: Personalizing Explanation and Treatment

In addition to the stepped-care model, which considers the number, duration, and severity of symptoms, specific treatments will have to reflect the nature of the symptoms and their etiological factors. In order to tailor treatment to the individual patient, offering an explanation and treatment plan that match the individuals' symptoms and etiological factors is crucial (52). Previous studies suggest that tailoring treatment to the characteristics and needs of individual patients increases treatment motivation, adherence, satisfaction, and effectiveness (53-55).

Aims and Outline of this Thesis

In line with the three previously described obstacles and potential solutions, this thesis is divided into three parts. The aims and outline of these three parts will now be discussed.

Aim I: Developing an Online Course for Healthcare Providers on MUS

The first part of this thesis is focused on the development of an online, interprofessional course, which aims to teach healthcare providers the knowledge, skills, and attitude they need to diagnose and treat MUS in a patient-centered manner. The course content and results of a pilot study, assessing healthcare provider satisfaction and self-reported learning gains, will be presented (*Chapter 2*).

Aim II: Developing Self-help Interventions for MUS and Examining their Effectiveness

In the second part of this thesis, we will study the effectiveness of self-help interventions for MUS by performing a systematic review and meta-analysis of the literature (*Chapter 3*). Subsequently, the development and content of two online self-help interventions will be described. The first is a self-help website for patients with minor head injuries, the occurrence of which is a common precipitating factor of MUS (*Chapter 4*). The second is a web-based, personalized, guided self-help intervention for MUS in primary care (*Chapter 5*). This part ends with the protocol of a randomized controlled trial, studying the effectiveness of the latter (*Chapter 6*).

Aim III: Exploring the Effects of Psychosocial Factors on MUS and Identifying Potential Targets for Personalized Treatment

A first step in personalizing treatment for patients with MUS is identifying which etiological factors might play a role. In the third part of this thesis, we will explore the effects of psychosocial factors on the development and maintenance of MUS. First, we will examine the influence of parental divorce, parental death (*Chapter 7*), and childhood sexual abuse (*Chapter 8*) on the development of MUS in a large prospective population cohort of Dutch adolescents. Subsequently, we will study the influence of stress (*Chapter 9*), worry, and anxiety (*Chapter 10*) on MUS in daily life by analyzing individual diary data from patients with MUS (*Chapter 9*) and individuals from the Dutch general population (*Chapter 10*). Studying these potential perpetuating factors within individuals hold a promise for the identification of personalized treatment targets.

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PART I



**Development of an online course
for healthcare providers.**