

CHAPTER 1 GENERAL INTRODUCTION

Medically unexplained physical symptoms in primary care

Experiencing physical symptoms is a part of the daily life of people. Most of these physical symptoms are transient and people usually do not seek medical care (1,2). When symptoms persist the general practitioner (GP) is often consulted. Up to thirty per cent of all physical symptoms presented to the GP appear to be so called medically unexplained physical symptoms (MUPS)(3,4), physical symptoms for which no sufficient explanation or evidence for an underlying physical disease can be found after adequate medical examination (5,6). Therefore, MUPS are a common phenomenon in primary care. Also in specialist care, MUPS are a frequent reason for encounter with percentages up to 70 per cent depending on the speciality (7,8). In this thesis we especially focus on MUPS in primary care.

MUPS represent a broad spectrum of symptoms in varying degrees of severity (9,10). Examples of MUPS are pain, fatigue, dizziness, stomach complaints and musculoskeletal complaints. Sometimes several of the presented symptoms seem to cluster. In that case we can speak of functional somatic syndromes, such as irritable bowel syndrome, chronic fatigue syndrome and fibromyalgia (11–13). Most MUPS are transient and mild, with little impediments for daily life (2). In 2.5% of the patients MUPS become severe and persistent, which may have negative consequences in many domains of daily life. Most patients with persistent MUPS are functionally impaired, have high levels of psychological distress and report a reduced quality of life (14–16). Also they are at risk for additional unnecessary examinations and treatments that may be potentially harmful (14–16). Furthermore, persistent MUPS put a burden on the doctor-patient relationship. Patients with MUPS are often dissatisfied with the medical care they receive (17). They feel that their doctors do not take them seriously and that their symptoms are unfairly psychologized (17,18). They often feel the need to fight to gain acknowledgement of their symptoms by their GPs. On the other hand, doctors may feel or are frustrated and indicate that effective treatments to manage patients with MUPS adequately are lacking (18–20). Also they struggle to provide symptom explanations for MUPS (21). They only use a limited repertoire in clinical practice (22). When explanations are provided, they often follow psychosocial models of causality (23), which are mostly rejected by patients and can even be felt as threatening (24,25).

In addition, persistent MUPS may have major impact on society due to high healthcare costs (26,27). Several studies show that patients with (persistent) MUPS use disproportionately large amounts of both somatic and mental healthcare services (28–31). This high healthcare use is often attributed to patients pressurizing their GPs for a somatic treatment, while several studies suggest that patients

mostly want support and acknowledgement of the reality of their symptoms, but receive interventions initiated by the GP instead (32). Moreover, MUPS can interfere with work functioning, both in terms of disability at work and long-term and short-term absenteeism from work (33–35). Not being able to work or not performing optimally at work is not only a burden for patients and their direct environment, but also leads to an increase in healthcare costs.

Rationale for this thesis

Although much research already has been performed on the subject of MUPS, our knowledge on several aspects needs to be increased to address and constrain the consequences of MUPS for patients, for doctors and for the society as I described above. One of the possibilities to improve care especially for patients with MUPS developing towards persistent MUPS is to offer structured care proactively, coordinated by the GP. By attentively exploring MUPS and their impact on the daily life of patients and by discussing interventions in an early stage, persistent MUPS may be prevented. The GP, or multidisciplinary organized primary care centres in which GPs are in the lead, eminently come into sight as the right place from which to coordinate this kind of proactive care as the GP knows his/her patients and usually has a long-term relationship with them within their context. Also the GP is in the position to check on his/her patients regularly and can offer continuity of care.

The first step in structured care is to identify patients with MUPS evolving towards a chronic condition in an early stage. Early identification of patients with MUPS could lead to more attention for better communication during the consultations and providing explanations for patients' symptoms. Also it urges GPs to consider and discuss possible treatment strategies in an earlier stage, taking into account the wishes and needs of the patient. This kind of proactive care, based on risk assessment followed by identification of care gaps among subpopulations of patient who share predefined risks is called panel management. Specific MUPS guidelines provide tools for organizing structured care in clinical practice in this process (5,6).

This thesis is divided into three parts, each focusing on a different part of structured care.

First, I will focus on different methods to identify patients with MUPS and specifically those at risk for persistent MUPS. Second, I will outline the existing treatments and potential gaps in research and practice. Third, I will bring more insight into the relevance of societal consequences of MUPS over time.

Identification of MUPS

Early identification of patients with MUPS

The identification of patients with MUPS and especially those patients at risk for persistent MUPS is a difficult task both in research and in clinical practice. The biggest challenges for the identification are the lack of knowledge how doctors identify patients with MUPS during consultations, the different MUPS definitions used in literature (11), the heterogeneity among patients with MUPS (9,10) and, although inherent to the definition problem, the lack of a generic MUPS code in GP coding systems like the International Classification of Primary Care (ICPC)(36).

One of the methods for the identification of various patient populations or populations at risk, which is currently increasingly and often used in primary care research, is risk assessment based on advanced analysis of routine electronic medical records (EMRs). Routine EMRs refer to the systematized registration of medical information of patients and populations that are stored electronically during daily practice. They include a broad range of data, namely demographic information, characteristics such as age and gender, medical history, medications, allergies, additional diagnostics and referral correspondence. These EMRs can be used in scientific research when data are anonymised and their use in earlier research has proved to be effective and feasible in various risk populations such as frail elderly and chronically diseased patients (37–40). The advantages of using EMRs are that patient data are directly available, that often no additional data collection is needed and that data of patients usually not being able or willing to agree with analyses in identifiable datasets can also be used. Also, once reliable algorithms become available, individual data can be used for proactive periodical screening purposes as it can provide a quick overview of populations at risk. Regarding MUPS, only a few studies used EMRs for identification. Unfortunately, in these studies either the method was not directly suitable for primary care purposes or it was not useful for screening purposes (41,42). Therefore, better models are needed and should be developed. In this thesis we aimed:

- To validate a recently developed EMR screening method from Utrecht, the Netherlands, to identify patients with MUPS (Chapter 2)
- To develop risk assessment models using different (advanced) statistical techniques applied to routine primary care EMRs to identify patients at risk for persistent MUPS (Chapter 3)

How do doctors identify the heterogeneous group of patients with MUPS?

It is known that patients with MUPS constitute a heterogeneous group of patients. Not only due to the broad range of clinical symptoms, but also due to the variety in sociodemographic characteristics such as age, employment status, educational level and mental health comorbidity (9,10). Therefore they are coded in the routine EMRs by GPs in different ways. The heterogeneity of MUPS and their

registration not only impedes the process of identification but also the fine-tuning of treatment. It may well be possible that the varying and disappointing treatment outcomes are partly due to this heterogeneity, as different groups of patients may benefit from different types of treatment. In previous studies this point was underlined. In patients with fibromyalgia, the authors identified two subgroups: patients with pain avoidance and patients with pain persistence. They concluded that these subgroups benefitted from a different treatment approach (43–45). Two other studies highlighted the relevance of the heterogeneity among patients with chronic fatigue syndrome for their treatment response and the need to explore this heterogeneity more in to depth (46,47). In the light of these previous studies and the scarcity of effective treatments for patients with MUPS (48), more insight should be gained into how doctors identify patients with MUPS during consultations and which subgroups they distinguish. This could help to develop more targeted interventions and is of additional value for research to include the correct population. In this thesis we aimed:

- To examine how GPs recognize MUPS in their patients during consultations and which subgroups of patients with MUPS can be recognized (Chapter 4)

Structuring management of MUPS

How to structure management of patients identified with MUPS?

In the past decades, many strategies for the approach of treatment for MUPS were developed and studied. Up to now, effective treatment strategies in primary care are still lacking and many aspects of the treatments, such as the optimal duration and deliverer of treatment, are still unclear.

In a Cochrane review on enhanced care (where the GP provides cognitive behavioural techniques), the authors concluded that current evidence does not answer the question whether enhanced care delivered by front line primary care professionals has an effect on the outcome of patients with MUPS (49). Another Cochrane review studied the effectiveness of pharmacological interventions, such as antidepressants, anti-epileptic drugs and natural products (50). Although some positive effects were found, caution is needed because of frequently occurring side effects. There are studies investigating the effect of non-pharmacological interventions regarding MUPS (51-55), including two reviews (56,57), but a comprehensive overview of the whole spectrum is missing. In this thesis we aimed:

- To perform a Cochrane review in which we will assess the effects of non-pharmacological interventions for somatoform disorders and chronic MUPS to assist health care providers to make optimal treatment decisions and to highlight current gaps in research literature (Chapter 5)

- To outline how doctors should manage patients with persistent MUPS in the light of the existing uncertainties (Chapter 6)

Providing symptom explanations

A specific part of MUPS management is providing acceptable explanations to patients. The explanation phase of the consultation is essential because this builds a bridge between the story of the patient, physical examination and treatment. It is known that most patients seek explanations for their symptoms (58,59), but they often find that their doctors are unable to deliver them (21). Commonly used explanations often follow psychosocial models of causality. An example is reattribution, where symptoms are linked to psychological distress (23). However, these explanations are not fully compatible with current models of symptom persistence (60,61) and are commonly resisted by patients (24,25). Therefore more explanation tools are necessary, as well as insight into how the dialogue between patients and doctors surrounding explanations evolves and how patients subsequently react. In this thesis we aimed:

- To carry out detailed analysis of dialogues structure of symptom explanations between patients with MUPS and GPs and reactions of patients (Chapter 7).

Societal consequences of MUPS

In an era where healthcare costs are steadily rising, it is important to acknowledge that persistent MUPS have a major contribution on these costs due to high healthcare use. In addition persistent MUPS also have a negative influence on work functioning (26,27). Therefore, persistent MUPS should be prevented or limit their societal consequences as much as possible. In order to do so, more insight is needed into the associations between MUPS and healthcare use and work functioning over time and into potential influencing factors.

There are already several studies exploring these associations, but they are mostly cross-sectional or retrospective (28,29,34,35,62), which limits the interpretability of the results.

We already know that MUPS frequently co-occur with mental health disorders such as depressive and anxiety disorders and that these mental health disorders also have impact on healthcare use and costs (63–66). Therefore it has to be explored what the extent is of mental health disorders on the association between MUPS and healthcare use and work functioning. Finally, specifically regarding work functioning, studies have shown that unfavourable job characteristics such as long working hours and a low occupational status may have a negative influence on someone's work functioning in general. It is yet not know in which extent this also contributes to patients with MUPS. More insight

in these relationships including the influencing factors can play a major role in the development of prevention and management strategies for MUPS. In this thesis we aimed:

- To examine the association between MUPS and healthcare use over two years and the influence of depressive and anxiety disorders and personality traits on this association (Chapter 8)
- To assess the association between MUPS and work functioning over two years and the influence of job characteristics and depressive and anxiety disorders on this association (Chapter 9)

Outline of this thesis

In **Chapter 2** we show the results from a validation study in which we explored the test characteristics of an EMR screening method, developed in Utrecht, the Netherlands, to identify patients with MUPS in routine primary care EMRs. We compared the identified patients with MUPS from the screening method with their scores on the patient health questionnaire-15, which we used as a reference test.

In **Chapter 3** we show the results of two risk assessment models that we developed by using data mining and different (advanced) statistical techniques in primary care EMRs with the purpose to identify those patients at risk for persistent MUPS.

In **Chapter 4** we present the results of a focus group study among GPs who were asked how they recognize patients with MUPS and which subgroups of patients they distinguished.

Chapter 5 is a concise version of a Cochrane review about the effects of non-pharmacological interventions for somatoform disorders and chronic MUPS in adults.

Chapter 6 contains our recommendations based on the four Cochrane reviews about MUPS on how to manage these patients in the light of the existing uncertainties.

Chapter 7 provides insight into how GPs and patients discuss explanations for MUPS.

For this study we analysed audiotaped consultations that were held in Scotland.

In **Chapter 8** we present the results of the study where we explored the association between MUPS and healthcare use over two years and the influence of depressive and anxiety disorders and specific personality traits on this association. We used data from the Netherlands Study of Depression and Anxiety.

In **Chapter 9** we present the results of the study where we explored the association between MUPS and work functioning over two years and the influence of depressive and anxiety disorders and job characteristics. Again we used data from the Netherlands Study of Depression and Anxiety.

In **Chapter 10** I provide a critical appraisal of our study results and methodological considerations. Also I give recommendations for daily clinical practice and future research.

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