

## **CHAPTER 10 GENERAL DISCUSSION**

In the present chapter, I will discuss the main findings of the papers that are presented in this thesis in the context of the three parts of this thesis: (i) the identification of medically unexplained physical symptoms (MUPS), (ii) structuring management of MUPS and (iii) societal aspects of MUPS. Where appropriate, I will also reflect on the methodological considerations and implications for clinical practice and further research in those three areas.

### **Identification of MUPS**

Both in clinical practice and in research, the identification of patients with MUPS is a challenging task. However, the early identification of patients with MUPS and those who are at risk of persisting and debilitating symptoms, may contribute to a timely and appropriate management and thus possibly mitigate the course of MUPS. In the first part of this thesis we tried to tackle the challenge of (early) identification of patients with MUPS from three different angles.

In Chapter 2 and 3, we explored whether it was possible to identify patients with MUPS and those at risk of developing an unfavourable chronic course from routine primary care electronic medical records (EMRs). In current clinical practice and in research this is already applied for other risk populations, such as patients at risk for cardiovascular diseases, patients with diabetes mellitus, frail elderly and patients at risk for the complications of influenza (1–6). However, using EMRs to identify patients at risk for persistent MUPS is not yet common practice.

Regarding the identification of patients with MUPS, first, we validated an EMR screening method to identify patients with MUPS that was previously developed from data from the Utrecht Health Project (Leidsche Rijn Gezondheidsproject) at the Julius Center related to the University Medical Center Utrecht, the Netherlands (Chapter 2). We compared the results of this EMR screening method (i.e. patients with and without MUPS) with the scores of each patient on the patient health questionnaire-15 (PHQ-15), which we used as a reference test (7). We calculated the test characteristics for various PHQ-15 cut-off points. For the PHQ-15 cut-off point 10 (a moderate somatic symptom severity score, which is a commonly used cut-off), we found a high specificity (0.93), but a low sensitivity (0.30). This means that probably many patients with MUPS were missed when using this selection algorithm.

As this EMR screening method seems not able to adequately select patients with MUPS and was not developed for identifying patients at risk for persistent symptoms, we decided to explore other, more advanced, analytical methods for risk assessment. The final goal of the development of our risk

assessment method was to transform the method into a software algorithm, which then can be implemented in daily clinical practice in order to be part of proactive, structured care for patients with MUPS. In a pre-study, we tried to identify patients with MUPS by performing a latent class analysis in an EMR dataset derived from the academic network of GPs in Amsterdam. Unfortunately we did not succeed as we could not detect and validate one or more classes of patients with MUPS. Therefore, we decided to change our direction and to use other, more innovative statistical machine learning techniques to support our risk assessment. For the development of the algorithms we used EMRs from 22 Dutch GP practices from Utrecht, the Netherlands (Chapter 3). Both developed models, developed with logistic regression analysis and decision tree analysis, were able to identify patients at risk for persistent MUPS moderate to good, measured with AUCs of 0.70 and 0.81, respectively. Even after cross-validation, which is a particular strength of this study, the AUCs remained stable.

Our study results contribute to the body of knowledge that already exists on identification of patients with MUPS in EMRs. We also found more or less comparable results (8–10). We can conclude that the (early) identification of patients with MUPS in EMRs is not a trivial task, but we believe that we found a promising perspective for further fine-tuning. Regarding our developed risk assessment models, one of the possible challenges for further fine-tuning could be to include separate *International Classification of Primary Care* (ICPC) symptom codes (1-29) instead of complete ICPC chapters including those and confirmed diagnose codes (70-99) as well (e.g. complete Chapter A).

An important methodological issue in the development of the identification and risk assessment models is the use of EMRs. The completeness and correctness of the data in an EMR dataset strongly depends on the ICPC coding behaviour of GPs and other practice employees. GPs mostly differ in their coding behaviour in coding symptoms (ICPC code 1-29) versus coding diagnoses (ICPC code 70-99). This has to do with the rules of coding on a true level of understanding, which some GPs apply more consistent than others. For example, this means that different GPs can code either constipation (D12), diarrhoea (D11) or irritable bowel syndrome (D93) for the same patient that consults the GP with intestinal complaints. Also, when a patient presents multiple complaints within one consultation, some GPs only code one complaint, often the most severe complaint, while other GPs code all complaints. In the past years the focus on correct and complete coding has increased in clinical practice and research. But it should still receive attention and awareness, for example in forms of structured coding educational activities for GPs in order to further optimise EMRs for use in research as well as for quality management and disease management purposes.

Another methodological issue related to the identification of MUPS is the operationalization of the MUPS outcome variable. In literature there is an on-going discussion about definitions and classifications(11,12). Differentiation is mainly based on the number of complaints and the severity of symptoms, the impact of symptoms on patient's daily life or symptoms from different organ clusters. In the development of our risk assessment models, we chose to operationalize persistent MUPS with the use of the three ICPC codes for MUPS related chronic syndromes (irritable bowel syndrome (D93), fibromyalgia (L18.01) and chronic fatigue syndrome (A04.01)) and chronic or recurrent low back pain without radiation (L03), one of the most common MUPS. Hereby we aimed to capture the largest group of MUPS patients at risk for one of these persistent outcomes. It must be noted that other studies have made other choices when operationalizing persistent MUPS, for example by using the duration of MUPS.

Next to the development of the risk assessment models, we performed a qualitative focus group study (Chapter 4). In this study we explored how GPs thought they recognized patients with MUPS during consultations, as little is known about this process. More insight into how GPs recognize patients with MUPS and how GPs code these patients in EMRs could contribute to further fine-tuning and improvement of identification and risk assessment methods. In addition, we asked the GPs participating in the focus groups sessions whether they could recognize different subgroups of patients with MUPS. This might not only contribute to improved identification, but also to a more tailored management because it is possible that different subgroups of patients have different needs in their management.

In the first part of our analysis, which was related to recognition in general, it became clear that most GPs use the core values of family practice in recognizing MUPS. These core values are generalist, personalized and continuous care for patients. Knowledge of the patient and his/her history and context made it easier to recognize them early in the consultation. Not only frequent and long consultations with frequent questions for referrals, but also subjective feelings such as irritability and frustration were clues for recognition. These findings are in line with the findings of previous studies (13–17). Regarding the differentiation of patients in subgroups, we were able to distinguish five different subgroups of patients with MUPS: the anxious MUPS patient, the unhappy MUPS patient, the distressed MUPS patient, the passive or dependent MUPS patient and the puzzling MUPS patient. Although the subgroups showed overlapping features, they were based on the predominance of specific characteristics of patients. We did not see these five subgroups with their characteristics back in our quantitative risk assessment models.

Two main methodological considerations regarding this qualitative study are important. First, our results only give insight into perceptions of GPs and not into their actual behaviour. It is possible that GPs recognize individual patients with MUPS in clinical practice differently than how they believe they do. Second, we have not yet validated the subgroups. This has to be done in future studies. It is possible that patients do not recognize themselves in the subgroup that they are assigned to by the GP. This could result in a mismatch or struggle between the GP and patient during the consultation. Also because the subgroups show overlapping features this could contribute to the fact that patients do not recognize themselves in the assigned subgroup. When the subgroups are validated in both qualitative and quantitative research, they can support GPs and patients in providing guidance in management and the treatment can be more personalized and tailored to the patient.

### **Structuring management of MUPS**

In general, MUPS management can be divided in different phases. After the first diagnostic phase follows the explanation phase of the consultation. Most patients need an explanation to effectively handle his or her symptoms. Unfortunately, most GPs are trained to specifically provide explanations for symptoms with an underlying cause. They are often not well equipped to explain symptoms without an underlying cause (18). In Scotland the Symptom Clinic Intervention (SCI) was developed, a communication intervention study in primary care where explanations for MUPS were the central element (19). The intervention was taught to Scottish GPs. The study results are presented elsewhere (20). In our qualitative study, we analysed the dialogues between the GP and the patient with MUPS and the responses of the patients in relation to these symptom explanations (Chapter 7). Based on these analyses, we described a range of dialogue types and patients' responses and we presented a classification structure in our paper. This classification can be applied in teaching, evaluation of practice, and research after further validation. We found that deliberative dialogue types(21,22), dialogues with engagement between the GP and patient with both contributing ideas, were associated with acceptance of the explanation by the patient and that explanations were often not directly rejected. For future research, what further needs to be explored is which elements of the explanation are effective for which patients or for which symptoms and which are not.

Much research has been conducted about the effects of different MUPS interventions. Unfortunately intervention effects are often varying and disappointing. Several systematic reviews exist on different forms of MUPS interventions (23,24), but a complete overview for non-pharmacological interventions was missing. For that reason we conducted a Cochrane review, in which we investigated the effects of non-pharmacological interventions for somatoform disorders and chronic MUPS (Chapter 5). We concluded that only cognitive behavioural therapy (CBT) had a small positive

effect on the severity of MUPS. When we summarised the main findings of the four currently existing Cochrane reviews about MUPS (i.e. (non-) pharmacological interventions, enhanced care and consultation letters (25–27)), we again concluded that apart from CBT there is no effective evidence-based treatment available and specifically not in primary care (Chapter 6). Furthermore for CBT, there are many gaps in knowledge regarding the specifics of this treatment. This means that it is not yet clear what the ideal duration of the treatment is, who should provide the therapy and what the content should by all means include. In future research, these issues should be further explored. Also attention should be paid to the quality of the evidence as in all four Cochrane reviews, the quality of the studies was rated very low to moderate.

In order to incorporate the above-mentioned management elements into the concept of proactive, structured care or panel management and implications for clinical practice for patients with MUPS and those at risk for persistent MUPS, GPs should move away from the definition discussion in research literature and should more focus on the patient in the consultation room. First, either by a software reminder or by specific awareness, GPs should identify the patient with MUPS in an early stage in order to prevent persistent symptoms. Just like with every patient, but maybe more specifically for patients with MUPS, in the diagnostic phase GPs should attentively listen with an emphatic attitude to the story of the patient. They have to look for possible clues that arise during this phase and explore the five symptom dimensions according to the Dutch GP Guideline for MUPS and the multidisciplinary guideline for MUPS (28,29). These dimensions are the somatic, cognitive, emotional, behavioural and social dimension. Second, GPs should perform a targeted physical examination and provide a personalized explanation with the classification, when validated, of the different dialogue types and patients' responses in mind. Third, as we know that the heterogeneous group of MUPS patients may be divided into subgroups, personalized and tailored interventions should be discussed with the patient, depending on the impact of the symptoms, possible other characteristics from the subgroups, and wishes of the patient. For example, with a patient with multiple MUPS and predominant anxiety, attention should be paid to effective reassurance(30). With an inactive patient with MUPS, for example with low back pain, the explanation could involve the vicious circle theory (i.e. low back pain leads to inactivity and inactivity leads to stiffness and therefore to more pain, etc.) and this patient should be activated. This was also underlined by van Koulik et al, who differentiated and treated two groups of fibromyalgia patients (31–33). For a patient with physical complaints related to distress or burn-out, attention must be given to decrease the number of stressful activities and/or a reorganisation of the patients personal life (34). An additional advantage of this personalized subgroup approach is that effective strategies from other guidelines, such as the guidelines for depression, anxiety and chronic pain, can be used(35,36).

Patients with severe MUPS or somatoform disorders can be referred to secondary health care for instance for CBT (37).

As the GP, compared to other specialists, has the advantage of knowledge about the patient and his or her context and history and also has a continuous and reliable doctor-patient relationship, the GP is eminently the professional who should coordinate care for patients with MUPS. This means that the GP invites the patient for consultations in a proactive, structured manner, whether or not reminded by EMR alerts and that the GP sees to it if the patient improves. Tasks can also be delegated to mental health practice nurses or psychosomatic physiotherapists. Together with the patient, the medical professionals should try to find the best following steps to improve, to prevent worsening and to prevent that the patient gets lost in the medical circuit.

### **Societal aspects of MUPS**

In the last part of this chapter, I will focus on the societal aspects of MUPS. These societal aspects become more and more important, because in the last decades costs related to healthcare use are steadily rising. Causes of these costs lie among other things in the consequences of MUPS. Therefore, in Chapter 8 and 9, we investigated the association between MUPS and two important societal aspects: healthcare use and work functioning, thereby highlighting the relevance of the problem of MUPS. We used data collected in the Netherlands Study of Depression and Anxiety (NESDA), a longitudinal cohort study investigating depression and anxiety. In the NESDA dataset, of which we could use three repeated measurements, there was information on MUPS and on the outcomes healthcare use and work functioning. Besides the association between MUPS and healthcare use and work functioning, we also investigated the role of influencing factors, such as depression, anxiety, personality characteristics and, specifically for work functioning, job characteristics. In our analyses, we found that MUPS were significantly and independently related to increased healthcare use and decreased work functioning. These results that are comparable with previously conducted studies. This underlines the importance of good MUPS management.

When interpreting the results, a few important methodological issues must be kept in mind. First, we used the number of consumed medical services and the number of contacts with the medical services as an indicator for healthcare use. However, no information was available about the reason for consultations. Therefore it is possible that the encounters were not related to MUPS but to other health complaints. Also, we only examined the frequency of healthcare use but we cannot determine whether the healthcare consumption was adequate or inadequate (with inadequate defined as the 'infinite' search for physical explanations for the symptoms or reassurance). Second, we did not

calculate the costs that accompanied high healthcare use or decreased work functioning. This has to be examined in future research, as the actual costs are important for health care policies. Third, in the NESDA study, the four dimensional symptom questionnaire (4DSQ) (38) that we used to measure MUPS, refers to complaints one week before the measurement, while the outcome variables were measured over a longer period of time before the measurement. Therefore it is difficult to draw strong conclusions about causality. But the stability of the 4DSQ score over time was moderate to high (correlations between 0.7 and 0.8) and the sensitivity analyses that we performed showed comparable results. Therefore we believe that the results of our analyses give sufficient reliable information about the influence of MUPS on health care use and work functioning. Fourth, the NESDA cohort is not representative for the Dutch general population, because patients with depressive and/or anxiety disorders are highly oversampled. This means that it is questionable whether the results of our analyses hold for the general population. To investigate that, we analysed the associations both in the patients with depressive and/or anxiety disorders and in the patients without those disorders. Based on the results of those analyses, i.e. the relationships between MUPS and the societal outcomes, were stronger in the population without depressive and/or anxiety disorders, we believe that also in the general population MUPS are related to increased healthcare use and decreased work functioning. Specifically for the association between MUPS and work functioning, it was interesting to find the influence of job characteristics (i.e. job control and job support) on the association between MUPS and short-term absenteeism. After adjusting for job control and job support, the association between MUPS and short-term absenteeism became weaker. This suggests that improvement of working conditions may reduce the influence of MUPS on this unfavourable outcome. Future research can address this issue.

As an implication for clinical practice, we believe that it is worthwhile to pay attention to MUPS and their relation with work functioning, both by the GP during consultations (i.e. GPs should ask how work is going in the social dimension) and more directly by employers on the working floor. In addition, future research should be directed at developing preventive and treatment strategies, for example by assessing how optimization of job characteristics can reduce the influence of MUPS on work functioning. Health care insurances companies could play a role in this.

## Conclusion

In this thesis we have summarized our findings and elements that can be incorporated in proactive, structured care: identification of patients with MUPS (and those at risk for persistent symptoms), explanations and treatment of patients with MUPS. Also we paid attention to two important pillars of society: healthcare use and work functioning and how MUPS relate to them.

To conclude this thesis, I would like to add a personal experience from my own clinical practice about patients with MUPS. Even though I strongly believe that the GP is the best physician to manage MUPS patients and has the best position to structure care, I must sadly admit that in the beginning of my GP career a few years ago, I often found myself frustrated and irritated by this group of patients. I explored all symptom dimensions but following that I struggled with providing a decent explanation and with finding common ground with my patient. More than once my patient left the consultation room and I felt desperate and unsatisfied that both my patient and I were probably (very) unhappy. With time I learned that my feelings of irritation decreased when I got more experienced and I could add different tools to my tool-box. I learned how to apply different tools for different patients and in different situations. But the most important thing that helped me was a thing that one other doctor once had said during my traineeship when he also found me not amused. He told me the following:

*“Every patient has his own unique story. And there is no patient in the world that consults you with the purpose to annoy you or make you feel bad. Each patient just want your attentive listening, your empathic attitude to see life from his perspective and your devoted time to explain maybe the unexplainable. For you it might be the hundredth time. But for him, it could be his first time. Do not forget that they have to live with their symptoms, without all the knowledge that you have. So replace irritation with a feeling or a thought of wonder. And then you can be the best physician to guide your patient with his MUPS. And I will reassure you that you will like, or even love it.”*

...And after quite some years, I still totally agree with him.

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