

Addressing the needs of patients with Medically Unexplained Symptoms (MUS)



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Aim: Providing a guidance for Family Doctors all over the world in the management of patients with Medical Unexplained Symptoms (MUS)

10 key points

1. Medically Unexplained symptoms (MUS) are **physical symptoms** that have existed for **several weeks** and for which adequate medical examination or investigation have **not revealed any medical condition** that sufficiently explains the symptoms.
2. **MUS is an ongoing working hypothesis**, based on the (justified) assumption that somatic or psychiatric pathology have been adequately detected and treated but the clinical condition presented by the patient was not adequately resolved. Any change in symptoms could be a reason to revise the working hypothesis of MUS.
3. **MUS can be seen as a continuum** ranging from self-limiting symptoms, to recurrent and/or persisting symptoms and symptom disorders.
4. Factors that play a role in understanding the causes of MUS can be categorized into **predisposing, precipitating and perpetuating factors** and can be linked to the biopsychosocial model.
5. Family doctors can set a working hypothesis of MUS after a broad **biopsychosocial exploration** of the symptoms, extensive exploration of psychosocial contributing factors, and an evaluation of the severity of MUS.
6. Family doctors should focus on the **doctor-patient relationship** and **doctor-patient communication** as these are essential elements in the management of MUS, and in themselves are strong therapeutic agents within patient-centered care.
7. Family doctors should provide a **targeted and tangible explanation** in the patient's language and cultural models about what is causing the symptoms, based on the information obtained during the structured exploration of the symptoms.
8. In the initial phase family doctors should focused on creating a **safe environment** for patients to talk about (the context of) their symptoms, aiming at **symptom management**, self-management strategies and **self-care** in order to offer support to the patient and reach symptomatic relief.
9. Family doctors should deliver **proactive** care, aiming at **one coordinating care provider**, and deliver care in a **stepped-care approach** in which the stages of severity of MUS are connected to the (intensity of the) management.

10. As MUS are perceived very differently across cultures, family doctors should develop '**cultural competence**' when dealing with migrants with MUS or patients with MUS from culturally heterogeneous populations.

Definition of MUS

Medically Unexplained Symptoms are physical symptoms that have existed for several weeks and for which adequate medical examination or investigation have not revealed any condition that sufficiently explains the symptoms.

MUS is a **working hypothesis** based on the (justified) assumption that somatic or psychiatric pathology have been adequately detected and treated but the clinical condition presented by the patient was not adequately resolved. Any change in symptoms could be a reason to revise the working hypothesis of MUS.[olde Hartman 2013]

For some patients with physical symptoms a somatic or psychiatric condition may be present, but if the physical symptoms are more severe or more persistent or limit functioning to a greater extent than expected based on the condition in question, they too are referred to as MUS.

MUS can be seen as a continuum ranging from self-limiting symptoms, to recurrent and/or persisting symptoms and symptom disorders.

Causes of MUS

In 1977 George Engel introduced the biopsychosocial model. This model implies that in order to give patients a sense of being understood, clinicians have to understand and respond adequately to patients' suffering. In order to reach this, clinicians must attend simultaneously to the biological, psychological, and social dimensions of illness. This biopsychosocial model is fully integrated in the philosophy of primary care.

The term MUS implies there is no clear explanation for the origin of the symptoms. However, factors that play a role in MUS can be categorized into predisposing, precipitating (i.e. exacerbating) and perpetuating (i.e. maintaining) factors. These factors can be linked to the biopsychosocial model. The different elements of the biopsychosocial model and the predisposing, precipitating and perpetuating factors can play a role in varying degrees in understanding the causes of MUS. Furthermore, they can be used in the explanation of MUS during the clinical encounter.

Table 1. predisposing, precipitating, perpetuating factors and the biopsychosocial model in MUS

Predisposing factors		
<i>Biological</i>	<i>Psychological</i>	<i>Social</i>
Genetics Chronic health problems Serious childhood illness	Current life stresses Psychological trauma Adverse childhood experiences Physical, sexual or emotional abuse (in childhood) Unsafe parental bonding Depression Anxiety disorders Post-traumatic Stress Other psychiatric disorders Personality characteristics (alexithymia, neuroticism)	Illness experience in family Illness behavior in family Neglecting self-care of personal needs Cultural beliefs and expectations Health systems characteristics

Precipitating factors		
<i>Biological</i>	<i>Psychological</i>	<i>Social</i>
Infectious diseases Accident / trauma Surgery	Stress overload Depression Anxiety disorders Other psychiatric disorders Recent life event linked to past trauma Ongoing contact with abusive important others	Negative life-events (loss of a beloved one, impending resignation) Difficult living conditions High workload Limited social support on work Mass media reports on health issues/concerns

Perpetuating factors		
<i>Biological</i>	<i>Psychological</i>	<i>Social</i>
Decrease ability to exercise Decreased capacity and resilience Increased sensitivity and perception (sensitization, hypervigilance)	Inability to modify current worries and anxiety Depression Dysfunctional illness cognitions Low self-esteem False attributions Catastrophizing thoughts Role and behavior of the clinician	Lack of social support Illness gain Learned behavior Family dynamics

Diagnosing MUS

MUS *always* remains a working hypothesis, as in a limited number of cases it could become clear over time that the symptoms were in fact caused by somatic pathology [Morris et al, 2007]. In case of alarming symptoms (according to the family doctor) or changes in the pattern of symptoms (according to the patient), the working hypothesis MUS should be reconsidered and physical re-examination or additional investigations might be needed.[olde Hartman 2013]

Exploration of symptoms

The biopsychosocial model proposes illness to be viewed as a result of interacting mechanisms at the biomedical, interpersonal and environmental or contextual levels. Therefore the exploration of symptoms in patients with MUS should focus on the exact chronology of the symptoms themselves, including where and when the symptoms appear (context of the symptoms), which potential causes of MUS are present, patients' ideas, concerns and expectations (i.e. ICE), and patients' illness behaviour and in a patient's life and on the social environment of the patient.

This exploration results in a better understanding of the patient and the nature of the symptoms.[olde Hartman 2017]

A list of symptom dimensions with sample questions follows:

1. Symptom focus. Which specific symptoms are bothering you at the moment? (location, duration, severity, pattern, accompanying symptoms, use of medication).
2. Ideas. What are your own ideas and thoughts about these symptoms? (origin and persistence of the symptoms (including chronological aspects and when symptoms are present), contributing factors to the symptoms, patient's own influence on the symptoms, what aspects of their lives the patients considered to be associated with the symptoms).
3. Concerns. Do you have any concerns or worries about these symptoms? (anxiety or panic for what exactly, uncertainty, depressed, despair).
4. Effects. What effect do these symptoms have on you? (absence of work, avoidance of physical activity, ignoring the symptoms, other behaviour that inhibit recovery). Do these symptoms interfere with your daily life and social activities?
5. Reaction of others. How do other people react to your symptoms (relationship, friendships, work).
6. Expectations. What do you expect will happen with your symptoms in the future? What do you expect from treatments for your symptoms?

Exploration of potential psychosocial contributing factors

As MUS often (but not always) can be linked to psychosocial stress, the family doctor needs to pay attention to these issues. Important in this regard is to listen very carefully to what patients communicate. In 95% of the MUS consultations patients present psychosocial cues or hints. However, it is important that Family doctors do not ignore these cues. Picking up these cues and exploring them in depth by using open ended questions ("What do you mean by [...]") often results in a deeper understanding of the patients' symptoms. When psychosocial stress is present, discussing and treating these issues often leads to symptomatic improvement. A list of these psychosocial problems (with sample questions) follows:

1. Current life stresses – Are you experiencing stress at the moment? Did you have a stressful experience just before the start of your symptoms?
2. Limited Self-Care Skills – Do you care for others but have difficulty putting yourself on the list of people for whom you care?
3. Adverse Childhood Experiences (ACEs) – Were you under stress as a child? Would you feel sad or angry if a child you care about was growing up just as you did? Do you still interact with anyone who mistreated you as a child?

4. High workload – What work do you do at the moment? Do you like your job? How are your working times? Do you take work with you at home?
5. Problems in interpersonal relationships – Do you face problems in relationships with important others?

Identifying comorbid psychiatric disorders

As patients with anxiety disorder, depression or PTSD can present with physical symptoms, for example fatigue or palpitations, it is important to explore whether there is a comorbid anxiety disorder, depression or PTSD (see also above). Furthermore, the presence of a comorbid psychiatric disorder can be a predisposing or precipitating factor in MUS. In case such a comorbid psychiatric disorder is present the clinician first has to treat the comorbid psychiatric disorder according to the existing guidelines (see for example the WHO mhGAP intervention guide 2.0). For diagnosing and treating anxiety disorder, depression or PTSD we refer to existing disease specific guidelines. When this treatment proceeds the working hypothesis MUS can be reconsidered based on the remaining symptoms.

Evaluation

Based on the exploration of symptoms (and with it the identification of predisposing, precipitating and perpetuating factors), the clinician is able to evaluate the severity of MUS. MUS can be considered on a severity scale from mild via moderate to severe. The greater the number and the longer the duration of symptoms presented, the more number of bodily systems affected (for example gastro-intestinal, cardio-pulmonary, musculoskeletal), the more number of consultations with the physicians and the more the level of functioning is impaired, the greater the severity of MUS is. The severity established by the physician guides the stepped care approach described below. [olde Hartman 2013]

Management of MUS

Important elements in the management of MUS

We distinguish a number of important elements in the management of MUS. Most of these elements and its content are described in and extracted from a recent review of national guidelines and Cochrane reviews. [olde Hartman 2017]

Importance of doctor-patient relationship

Patients with MUS evoke difficulties in the family doctor encounter and challenge the doctor-patient relationship. A good doctor-patient relationship is associated with patient satisfaction and improved health outcomes and is an important condition for a good treatment course. Furthermore, the doctor-patient relationship can be strengthened by recognizing the patient's illness, taking the patient and his/her symptoms seriously, showing empathy and interest in the patients' life context and problems that are related to the presence of MUS. The family doctor should take an open, empathic, active supporting attitude to the symptoms and their management, in order to build a sustainable and equal working relationship. The physician needs to convey to the patient that the impact of the symptoms is understood and the physician acts with sensitivity to the difficulties that the patient experiences. The management of patients with MUS is most successful when there is a continuing and warm doctor-patient relationship. [olde Hartman 2017]

Importance of doctor-patient communication

Doctor-patient communication is essential for the treatment of MUS, as patients seek understanding for their symptoms. To achieve this, the family doctor has to focus on consultations skills: (1) a structured exploration of the symptoms, (2) paying attention to cues and hints, (3) providing a summary and (4) explicit communication about expected results of biomedical investigations.

So, family doctors should *explore* the patient's reasons for encounter, ideas, concerns and expectations (ICE) about the symptoms, and assess for potential predisposing, precipitating and perpetuating in a structured way using open questions. This exploration validates the patient's sense of suffering and provides a detailed insight into the bio-psycho-social background of the symptoms which is needed for a shared understanding of the symptoms. Paying attention to *cues and hints* in the story of the patients (i.e. psychosocial background of the symptoms) can be reached to listen attentively and very carefully for what the patient is telling you and by asking open questions in order to reach understanding of the cues and hints provided. Provision of a *summary* by the family doctor is a tool in the communication with these patients. Such a summary should include the topics that have been discussed in the consultation. It gives the patient the opportunity to check whether the doctor understands the problem and to complement deficits. Explicit *communication about expected results* of biomedical investigations is essential. When discussing treatment, the doctor should communicate with the patient in an open and accommodating dialogue in which the advantages and disadvantages of further testing and treatment can be discussed.[olde Hartman 2017]

Importance of explanation

Family doctors should provide a targeted and tangible explanation in the patient's language and cultural models about what is causing the symptoms. Information obtained during the structured exploration of the symptoms should be incorporated in this explanation. Patients benefit from "explanation that makes sense, removes any blame from the patient, and generates ideas about how to manage the symptoms". [Burton 2015] Recent research on explanations provides suggestions for constructing plausible and acceptable explanations for symptoms. Patients need to be able to exchange ideas with their doctors on the explanatory models they have and build up a common understanding on how these symptoms develop within explanatory models that are culturally acceptable, especially when the biological links between problems, emotions and symptoms are clarified. Explanations that are co-created by patient and family doctor are most likely to be accepted by patients.[den Boeft et al. 2017] However, although evidence for the effectiveness of those explanatory models in reassuring patients is limited, a patient-centered approach is always the best model to improve self-management and patient empowerment. According to existing consensus targeted and tangible explanations in the patient's language and cultural models are necessary to reassure patients with MUS about the absence of a somatic disease.

One general explanation that most patients can comprehend is that "when a person's stress level is too high or persists for too long, this can lead to physical symptoms very much like tension can lead to headache, fearful situations can cause a 'knot' in the abdomen or embarrassment can cause blushing."

Here are some examples of explanatory models that could be used in daily primary care (adapted from Olde Hartman 2013).

1. Capacity – burden model:
The balance between four factors (i.e. support, stress, strength and vulnerability) is of importance. If vulnerability and strength are unbalanced in a person, this can lead to symptoms.
2. Stress model:
High levels of stress is correlated with fatigue, pain and somatoform disorders. Psychological distress plays an important role in this relationship. That means that certain psychosocial factors combined with a chronically high level of stress can result in MUS.
3. Somato-sensory amplification model:
Focusing attention on physical sensations leads to more physical sensations (for example: thinking of itching results in itching). Furthermore, this might result in concerns or anxiety in patients. Consequently a vicious circle of maintaining and amplifying the physical symptoms is started.
4. Neurobiological model:
There exists a complex interaction between neurobiological processes (autonomic nervous system, HPA axis and the immune system), environmental factors, attention and behavior. Activation of the autonomic nervous systems generates symptoms, as well as activation of the HPA axis does (for example adrenalin gives an increase in heartrate and breathing frequency). Activation of the immune system can result in a sickness response.
5. Vicious circles:
Vicious circles play an important role in maintaining symptoms, irrespective of the origin of the symptoms. This is a result of the interpretation of symptoms and resulting disease behavior and/or help-seeking behavior.
6. Sensitization:
Previous and repeated stimuli of pain and other symptoms in the past make the central nervous system more susceptible to these stimuli. Benign stimuli are interpreted as malign.
7. Cultural way of understanding:
All explanatory models must be culturally meaningful. It is important for health professionals to be culturally humble, respecting and understanding how different cultures explain the many ways emotional distress relates to physical symptoms. One example is the “nerves” complaints among Latinos’ patients that associate “shaken nerves” as a major mechanism causing MUS.

Symptom management

Many patients with MUS improve without specific treatment. Although around 30% of the symptoms that patients present to their family doctor are unexplained (in specialist care this is even higher, up to 70%) only a minority of these MUS become persistent and disabling. [Verhaak et al, 2006]

When symptoms persist for more than several weeks, the physician may decide to prescribe medications addressing the specific symptom(s) presented, for example analgesics for pain, tricyclic antidepressants for neuropathic pain, or beta blockers for disturbing tachycardia. This symptom management aiming at symptomatic relief via physiological means is advisable especially in the initial phase. When considering pain management, short term analgesia with for example acetaminophen or NSAID (if no contraindication) can be prescribed. In all cases Family doctors have to balance symptomatic treatment with potential adverse effects or risks. [Chitnis et al, 2014]

A Cochrane review on pharmacological treatments for patients with MUS concluded that there is little evidence for the effectiveness of medication (tricyclic antidepressants, new-generation antidepressants (i.e. SSRI's and SNRI's) and natural products (i.e. different herbs and St. John's wort)) in the treatment of patients with MUS. [Kleinstaub 2014]

Self-care and self-management

The physician can advise patients on self-management strategies and self-care. The physician can empower the patient to carry on with (or return to) their normal daily activities as much as possible despite experiencing symptoms. The physician can suggest scheduling activities and exercises, practicing a regular sleep pattern, practicing a regular and healthy diet and relaxation exercises. [van Gils 2016; Henningsen 2007]

Self-help and behavioural activation can reduce symptoms and improve quality of life of patients with MUS. Engagement in pleasurable activities such as regular exercise, pursuit of a hobby or social activities can counteract the discomfort or suffering from MUS and reduce stress. See also WWPMH guidance on non-drug interventions for common mental health problems (<http://www.globalfamilydoctor.com/News/MentalHealthresourceGPFPRoleinnondruginterventions.aspx>).

A stepped-care approach

Family doctors should deliver proactive care and make regular follow-up appointments during the course of treatment based on the patient's need. Furthermore, it is important that one care provider, preferably the family doctor keeps control and coordination of the care process. However, this care provider could also be a community psychiatric nurse, psychologist or occupational health physician. The stages of severity of the symptoms can be connected to management options in a stepped-care approach. Family doctors should assess the patient's risk profile on the basis of severity of MUS and complexity of the disorder (number and duration of symptoms, level of functional impairment, psychosocial stress, psychological comorbidity and experienced difficulties in the doctor-patient relationship). In table 1 the stepped care approach as described in several primary care guidelines is shown (adapted from Olde Hartman 2017).¹⁰

The more severe or complex the symptoms and limitations are, the more intense and complex is the treatment needed for the recovery of the patient. For example when in a patient with mild MUS stress has been uncovered during the exploration of the symptoms, stress relieve is often the only treatment needed to relieve MUS. This can be done by (1) asking patients to compile a list of significant life stresses both present and past and search together how to reduce one or more stresses, (2) recommending 2 to 5 hours of self-care time (purely for personal enjoyment) every week, and/or (3) suggesting relaxation techniques and/or mindfulness medication. In patients with moderate to severe MUS referral to mental health care could be indicated. The most severely affected patients need a close collaboration between professionals with a divergent range of skills and expertise in secondary or tertiary care (i.e. the final step in the stepped care approach).

Cultural issues in the management of MUS

Physical symptoms are an important part of different “idioms of distress”, which are socially accepted patterns of presenting emotional distress (including anxiety and depressive disorders) that vary due to cultural background. There are several factors that contribute to these patterns, including some previously discussed in this document, but the cultural accepted way to communicate and elaborate emotional suffering is one of the core points, especially when “individualist” or “collectivist” cultures are involved. In the former, personal and subjective ways of expressing emotional distress are valued, while in the latter preserving group cohesion is the most important point and so it is considered inadequate to verbalize feelings and emotions associated with conflicts or negative emotions. But the physical symptoms associated with emotional distress cannot be suppressed, may become quite disturbing and disabling, and represent the most important reason for searching health care.

Trying to build an international cultural background when MUS are concerned may be quite difficult. On one side, it has been found that the most frequent groups of physical symptoms associated with MUS, currently being studied as “Bodily Stress Syndrome”, are universal and similar to those found in previously described “cultural-bound syndromes”, such as “Hwa-Byung” in Korea or as “Nervios” in Latin America. But, on the other hand, functional syndromes are not acknowledged and diagnosed in the same way world-wide. Recognition of chronic fatigue syndrome in Brazil and UK differ dramatically within a similar frequency of core symptoms in general population of the two countries.[Cho 2008] The most important consequence of this problem is the need for primary care physicians to develop “cultural competence” when dealing with migrants or culturally heterogeneous populations. The “Cultural Formulation Interview”^{*} can be used as an instrument to help professionals approaching patients from different backgrounds represents the recognition of the importance of cultural determinants in every day practice in health care. [Kirmayer 2013; Luiz-Fernandez 2017]

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https://www.google.nl/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&cad=rja&uact=8&ved=0ahUK EwibvbjV_JHYAhXQo6QKHeBvCZOQFggwMAA&url=https%3A%2F%2Fwww.psychiatry.org%2Ffile%2520Library%2Fpsychiatrists%2Fpractice%2FDSM%2FAPA_DSM5_Cultural-Formulation-Interview.pdf&usq=A0vVaw0yl4EMDbxmpSbt2uVcjfOL

Recommendations

Every Family doctor encounter patients with MUS. Good consultation and communications skills and building a therapeutic relationship with these patients are prerequisites in high quality management of MUS. Furthermore, collaboration with the patient and with other healthcare professionals is essential. Family doctors have the position to deliver patients with MUS the high quality of care they need.

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Table 1. Stepped-care approach in guidelines (adapted from Olde Hartman et al. 2017)

Dutch family doctor guideline		Danish family doctor guideline		German multidisciplinary guideline		Dutch multidisciplinary guideline	
Mild MUS	<ul style="list-style-type: none"> - Psycho-education - (Self-)management advice - Shared time-contingent plan - Follow-up 	Symptoms and mild functional disorders	<ul style="list-style-type: none"> - Normalization, explanation, biopsychosocial approach - Follow-up 	Step 1	<ul style="list-style-type: none"> - General principals of therapy (empathy, watchful waiting, acknowledgement of the symptoms, explanation) - therapy by family doctor or medical specialist or psychosomatic primary healthcare 	Mild MUS	<ul style="list-style-type: none"> - Biopsychosocial approach by family doctor - Psycho-education - Short-term CBT
Moderate MUS	<ul style="list-style-type: none"> - Psychosomatic physio/exercise therapy - Mental health nurse practitioner - Social psychiatric nurse 	Moderate functional disorders	<ul style="list-style-type: none"> - Explanations and TERM model¹ - Regular consultations - Cooperation with specialist (in charge of assessment, treatment plan, and supervision) 	Step 2	<ul style="list-style-type: none"> - Regular consultations - Therapy by family doctor or medical specialist PLUS psychotherapy - Pain as core symptom: antidepressant - Pain not as core symptom: antidepressant in case of psychiatric comorbidity 	Moderate MUS	<ul style="list-style-type: none"> - case-management by medical specialist, psychiatrist or family doctor - medication (for comorbidity) - CBT
Severe MUS	<ul style="list-style-type: none"> - Multidisciplinary team / treatment centre 	Severe functional disorders	<ul style="list-style-type: none"> - Specialist clinic - Multidisciplinary treatment - CBT² and GET³ - consider pharmacological treatment 	Step 3	<ul style="list-style-type: none"> - Specialist clinic with multidisciplinary treatment 	Severe MUS	<ul style="list-style-type: none"> - CBT - treatment by a multidisciplinary team in tertiary care

1. The Extended Reattribution and Management model

2. Cognitive Behavioural Therapy

3. Graded Exercise Therapy