Medically unexplained conditions considered by patients in general practice

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Abstract

Background. Patients frequently present with multiple and 'unexplained' symptoms, often resulting in complex consultations. To better understand these patients is a challenge to health care professionals, in general, and GPs, in particular.

Objectives. In our research on symptom reporting, we wanted to explore whether patients consider that they may suffer from conditions commonly regarded as unexplained, and we explored associations between these concerns and symptom load, life stressors and socio-demographic factors.

Methods. Consecutive, unselected patients in general practice completed questionnaires addressing eight conditions commonly regarded as unexplained (amalgam poisoning, Candida syndrome, fibromyalgia, food intolerance, electromagnetic hypersensitivity, burnout syndrome, chronic fatigue syndrome and irritable bowel syndrome). With logistic regression, we analysed associations with symptom load, burden of life stressors with negative impact on present health and socio-demographic variables.

Results. Out of the 909 respondents (response rate = 88.8%), 863 had complete data. In total, 39.6% of patients had considered that they may suffer from one or more unexplained conditions (UCs). These concerns were strongly and positively associated with recent symptom load and number of life stressors. If we excluded burnout and food intolerance, corresponding associations were found.

Conclusion. Patients frequently considered that they may suffer from UCs. The likelihood of such concerns strongly increased with an increasing symptom load and with the number of life stressors with negative impact on present health. Hence, the number of symptoms may be a strong indicator of whether patients consider their symptoms part of such often controversial multisymptom conditions.

Key words: Causal attribution, general practice, medically unexplained symptoms, multisymptomatology, symptom reporting.

Introduction

Multisymptomatology, the reporting of multiple symptoms, is a frequent phenomenon both in population and primary care samples and is established as a relevant indicator of individual health status (1–7). In general practice, ~50% of patients present with symptoms rather than established diagnoses (8). As a consequence, knowledge about the integrated symptom profile of patients should be acknowledged and is especially important to GPs who face all symptoms and conditions.

For a substantial number of the symptoms presented in general practice, there are no objective findings (9–11). Such

symptoms are commonly labelled medically unexplained symptoms (MUS) (12). GPs struggle with symptoms and conditions, which do not fit into a diagnostic manual (13,14). This is reflected in the low status of symptom conditions and research is consequently traditionally oriented towards predefined illness categories with a high level of prestige (8,15,16). Each medical specialty seems to have its own 'unexplained' condition [irritable bowel syndrome (IBS) in gastroenterology and fibromyalgia (FM) in rheumatology, etc.]; using criteria with substantial overlap, making diagnostics complicated in primary care (17–19). However, although GPs disclose that they feel ill-equipped to handle consultations regarding MUS, they tend to agree that these patients are best handled in general practice (20). Despite the clear relevance to primary care, research on symptomatology has mainly been conducted within psychiatry to identify so-called 'somatoform' symptoms (21).

Although traditional causal frameworks for the development of multisymptomatology and MUS focus on psychological factors, there is increasing evidence of disturbances in various biophysiological pathways, e.g. within the hypothalamus–pituitary–adrenal cortex axis, neurological and immunological systems (22–27). Modern multifactorial theories describe how these pathways adapt and interact in response to internal and external stressors (23,24). Life stressors, or adverse life events, may be one of many factors contributing to illness development (28–31). However, although many patients present clues to psychosocial issues, GPs commonly ignore them (32).

Patients' symptom accounts may provide more diagnostic information than the physical examination (8). One deciding factor in whether patients consult a physician with their symptoms is whether they perceive them as 'abnormal' or part of an illness. Hence, causes to which they attribute their symptoms may influence the way in which symptoms are presented and the way in which physicians perceive them and act upon them. Furthermore, illness perception and causal attribution influence health outcomes, also in 'purely physical' conditions (33–35). Exploration of causal attributions may assure the patient that their symptoms are acknowledged as real and may guide the GP in providing acceptable explanatory frameworks. Evidence supports that patients are not biased towards simple, biomedical explanations but rather endorse multicausal perspectives and acknowledge that medicine is not clear cut (36,37).

The complexity of the MUS phenomenon has led to controversy regarding conceptual frameworks in research and diagnostic criteria in clinical contexts. It is unlikely that a uniform definition of the 'unexplained' will emerge. Most research instruments to capture MUS ultimately measure multisymptomatology, regardless of whether the symptoms are explained or not. As the field of multisymptomatology and MUS remains unresolved, descriptive, explorative studies based on unselected patient samples should be conducted, where assumptions regarding causal relationships are avoided. There is also evidence to support that multisymptomatology and MUS are closely related constructs according to GPs' evaluations (7). Multisymptomatology may be a descriptive, pragmatic and more feasible alternative to MUS. In this study, we wanted to explore whether patients seen in general practice have at least considered that they may suffer from conditions commonly regarded as unexplained [unexplained conditions (UCs)], and we have analysed how these reports are associated with symptom load, the burden of life stressors and socio-demographic factors.

Methods

Study design and sample

Consecutive adult patients (>18) were recruited by 47 GPs in the Norwegian counties of Oslo and Akershus. They were asked to anonymously fill in a questionnaire after the consultation, irrespective of reason for encounter. Questionnaires were returned in pre-stamped envelopes. The recruitment period was from June 2010 to January 2012.

Outcome variable

To record whether the patients suffered from or had considered that they may be suffering from UCs, the following question was posed: 'Do you suffer from, or have you considered whether you suffer from, one or more of the following conditions? (i) amalgam poisoning, (ii) Candida syndrome, (iii) electromagnetic hypersensitivity syndrome, (iv) fibromyalgia (FM), (v) chronic fatigue syndrome/myalgic encephalopathy (CFS/ME), (vi) food intolerance, (vii) burnout syndrome and (viii) irritable bowel syndrome (IBS)'. The conditions were not further defined or explained. We did not define a time window but included any consideration, present or past. We wanted to explore whether patients reported at least one UC, hence we dichotomized a sum score of UCs into the categories 0 (the patient does not report any of the conditions) and 1 (the patient reports at least one condition).

Independent variables

The symptom list consisted of 38 common symptoms experienced during the previous 7 days. Pain/discomfort in 10 body regions were covered by the validated Standardised Nordic Questionnaire (SNQ) (38): head, neck, shoulder, elbow, hands/wrists, upper back, lower back, hip, knee and ankles/feet. Twenty-eight symptoms not covered by the SNQ were based on the Subjective Health Complaints (SHC) Inventory (39): infection/cold, palpitations, chest pain, breathing difficulties, heartburn/stomach discomfort, constipation, bowel gas/ feeling bloated, diarrhoea, nausea/vomiting, sweating/hot flushes, cold hands/feet, problems concentrating, reduced memory, tiredness/

exhaustion, dizziness, anxiety/unease, depression, sleep problems, eczema/skin problems/itching, allergies, urinary problems, leg cramps, muscle twitching, visual impairment, dry eyes/mouth, oedema/feeling swollen, tinnitus and fainting. We calculated a sum score of symptoms (0–38) to assess total symptom load.

We addressed life stressors with the following question: 'Do you experience that any of the following issues have had a negative influence on your present health?': (i) work situation, (ii) experiences in childhood/adolescence, (iii) family issues, (iv) economic issues and (v) other serious life events. To assess the total burden of life stressors, we calculated a sum score of life stressors (0–5).

Patients recorded the following socio-demographic factors: sex; year of birth; marital status ('married/cohabiting', 'separated/ divorced', 'widow/widower' and 'single'); educational level ('10 years or less', '11–13 years', 'university or university college 4 years or less' and 'university or university college >4 years'); employment status (clustered into 'employed': 'employed', 'home worker' and 'student') and out of work ('sick leave', 'disability pensioning', 'under rehabilitation' and 'unemployed' and 'retired').

Statistical analysis

All analyses were based on questionnaires with complete data for the outcome variable and the independent variables.

The study population is described by frequencies and percentages. To explore the contribution of the individual variables in the outcome variable, we performed logistic regression analyses. In the bivariate models, all independent variables were entered separately and in the main multivariate model, all independent variables were entered simultaneously. To assess the importance of each of the five life stressors, we performed five multivariate regression analyses exchanging number of life stressors with individual life stressors. Odds ratios (ORs) with 95% confidence intervals (CIs) and *P* values are presented.

We also performed analyses where we excluded burnout syndrome and food intolerance, as these may in some cases have plausible explanations. Finally, we performed analyses where the listed conditions were divided into three groups. Group 1 consisted of CFS/ME, FM and IBS, Group 2 consisted of electromagnetic hypersensitivity, Candida syndrome and amalgam poisoning, whereas Group 3 included food intolerance and burnout syndrome.

We used the software SPSS for Windows (PASW version 20) and R software.

Results

A total of 909 patient questionnaires were returned (reflecting a patient response rate of 88.8%). Of these, 863 provided the complete data needed for this paper. More of the participants were female (64.5%). The distribution in age groups is presented in Table 1.

Of the 863 consecutive patients in general practice, 39.6% had at least considered that they may suffer from a UC, (women = 43.8%, men = 32.0%). The most commonly reported UCs were burnout syndrome and IBS, both reported by approximately a sixth of the patients. The least frequently reported conditions were electromagnetic hypersensitivity, Candida

Table 1. Consecutive, unselected general practice patients (*n* = 863) described by socio-demographic variables, individual life stressors, number of life stressors and number of symptoms reported in the previous 7 days

	Women % (*n* = 557)	Men % (*n* = 306)	Total % (*n* = 863)
Sex	64.5	35.5	
Age			
18–39	39.5	25.8	34.6
40–59	32.9	40.8	35.7
60+	27.6	33.3	29.7
Marital status			
Married/cohabiting	61.8	75.5	66.6
Separated/divorced	13.1	5.6	10.4
Widow/widower	6.6	2.6	5.2
Single	18.5	16.3	17.7
Educational level			
10 years or less	15.8	19.0	16.9
11–13 years	38.2	35.9	37.4
University/college 1–4 years	28.0	27.5	27.8
University/college 4 years+	18.0	17.6	17.8
Employment status			
Employed/student/homeworker	51.7	53.9	52.5
Out of work[a]	31.2	26.1	29.4
Retired	17.1	19.9	18.1
Individual life stressors			
Work situation	28.0	28.1	28.0
Experiences childhood/adolescence	13.8	7.5	11.6
Family situation	21.7	10.1	17.6
Economic situation	12.2	13.7	12.7
Other serious life events	11.1	8.8	10.3
Number of life stressors			
0	49.0	59.5	52.7
1	27.6	24.2	26.4
2	14.0	8.5	12.3
3+	9.0	7.8	8.6
Number of symptoms			
0	2.2	4.6	3.0
1–4	29.6	35.9	31.9
5–9	35.5	36.6	35.9
10–14	20.1	15.4	18.4
15+	12.6	7.5	10.8

[a]Out of work = on short- or long-term sick leave, disability pensioning or unemployed.

syndrome and amalgam poisoning. Women reported most of the UCs more often than men, except for burnout syndrome and amalgam poisoning, which were more frequently reported by men. Several patients reported more than one UC, the mean number of conditions among those reporting at least one UC being 1.8 (CI: 1.6–1.9).

The patients reported a mean number of 7.5 symptoms (CI: 7.2–7.9), women = 8.1 (CI: 7.6–8.6) and men = 6.5 (5.9–7.1). Only 3.0% did not report any symptoms (women = 4.6%, men = 2.2%) (Table 2).

Almost half (47.3%) of the patients (women = 51.0% and men = 40.5%, *P* < 0.003) reported to have experienced at least one life stressor with negative impact on present health, work and family situation being the most frequent (Table 3). Those reporting at least one UC reported to have experienced a mean of 1.3 (1.1–1.4) of the listed life stressors, whereas non-reporters had a mean of 0.5 (0.4–0.6) life stressors.

In those reporting at least one UC, the mean number of symptoms was 10.6 (CI: 9.9–11.2), compared to 5.6 (CI: 5.2–5.9) among non-reporters. In females, the proportion reporting at least one UC increased from 0% with no symptoms to 85.7% with 15 symptoms or more. Correspondingly, in men, the proportion increased from 7.1% to 60.9%.

Bivariate logistic regression models revealed that women and patients who were separated/divorced or out of work had a higher likelihood of reporting a UC, compared to men, those who were married or employed. For each increase in the number of symptoms (from 0 to 38), the likelihood of reporting a UC increased by an OR of 1.21 (CI: 1.17–1.25) (*P* < 0.001) (Fig. 1).

Table 2. Proportion (%) of consecutive unselected general practice patients (*n* = 863) who reported having been diagnosed with or having personally considered suffering from predefined UCs, by sex

	Women (%) (*n* = 555)	Men (%) (*n* = 306)	Total (%)
Individual conditions			
Burnout syndrome	16.9	18.6	17.5
Irritable bowel syndrome	19.2	11.1	16.3
Food intolerance	15.3	4.2	11.4
Fibromyalgia	13.3	2.0	9.3
Chronic fatigue syndrome/ myalgic encephalopathy	9.0	5.2	7.6
Amalgam poisoning	2.9	3.9	3.2
Candida syndrome	4.5	0.3	3.0
Electromagnetic hypersensibility	2.2	0.3	1.5
Number of conditions			
0	56.2	67.6	60.3
1	23.9	22.5	23.4
2	10.1	7.2	9.0
3+	9.9	2.6	7.3

Table 3. The bivariate association between socio-demographic variables, individual life stressors, number of life stressors and number of symptoms (experienced during the last 7 days), and report of having considered suffering from at least one UC, in consecutive unselected patients in general practice (*n* = 863)

	OR (95% CI)	*P* value
Sex		0.001[a]
Men	1.0 (ref)	
Women	1.66 (1.24–2.22)	**0.001**
Age		**0.002**
18–39	1.0 (ref)	
40–59	1.35 (0.98–1.86)	0.070
60+	0.73 (0.52–1.04)	0.083
Marital status		**0.007**
Married/cohabitating	1.0 (ref)	
Separated/divorced	2.16 (1.38–3.38)	**0.001**
Widow/widower	0.95 (0.51–1.79)	0.878
Single	1.27 (0.89–1.83)	0.190
Educational level		0.342
10 years or less	1.0 (ref)	
11–13 years	1.30 (0.86–1.96)	0.210
University/college 1–4 years	1.37 (0.89–2.10)	0.154
University/college 4 years+	1.53 (0.95–2.44)	0.078
Employment status		<0.001
Employed/student/homeworker	1.0 (ref)	
Out of work[b]	2.12 (1.55–2.90)	**<0.001**
Retired	0.71 (0.48–1.06)	0.095
Number of symptoms (0–38)	1.21 (1.17–1.25)	**<0.001**
Number of life stressors (0–5)	2.09 (1.80–2.44)	**<0.001**
Individual life stressors		
No life stressors	1.0 (ref)	
Work situation	3.06 (2.25–4.16)	**<0.001**
Experiences childhood/adolescence	4.00 (2.55–6.26)	**<0.001**
Family situation	3.47 (2.41–5.01)	**<0.001**
Economic situation	3.10 (2.04–4.69)	**<0.001**
Other serious life events	2.60 (1.66–4.08)	**<0.001**

Presented as OR with 95% CI and *P* values.
[a]Bold type indicates statistically significant values.
[b]Out of work = on short- or long-term sick leave, disability pensioning or unemployed.

For each increase in the number of life stressors (from 0 to 5), the likelihood of reporting at least one UC increased by an OR of 2.09 (CI: 1.80–2.44). Negative experiences in childhood/adolescence and family issues had the strongest associations with reports of UCs.

In the multivariate logistic regression model (Table 4), the strong association between concerns with UCs and the number of symptoms and number of life stressors remained. For each additional symptom and life stressor reported, the likelihood of considering a UC increased by an adjusted OR of 1.18 (CI: 1.14–1.23) and 1.62 (CI: 1.36–1.94), respectively (both *P* < 0.001). Gender, marital status and employment status were no longer significant, whereas educational level reached significance: those
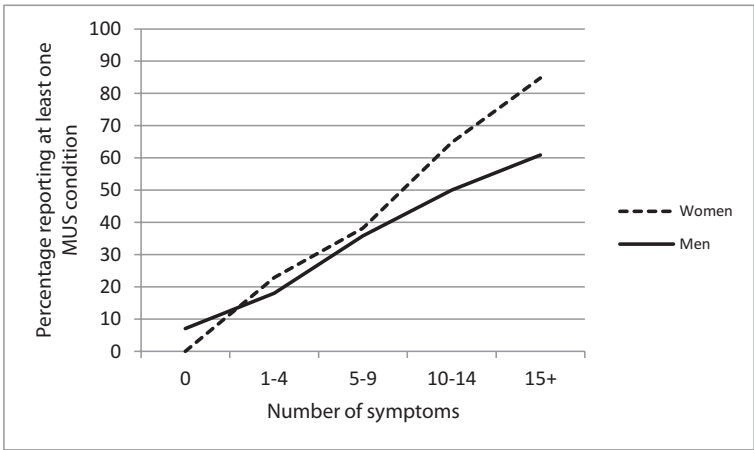
Figure 1. The proportion of unselected, consecutive patients in general practice (*n* = 863) who have considered that they may suffer from at least one UC, by number of reported symptoms (during the last 7 days) and stratified by sex.

with the highest level of education had an increased risk of reporting a UC (OR: 1.94).

Table 4. Multivariate logistic regression analysis to ascertain associations between socio-demographic variables, individual life stressors, number of life stressors and number of symptoms (last 7 days) and report of having been diagnosed with or having personally considered suffering from at least one UC in consecutive, unselected general practice patients (*n* = 863)

	OR (95% CI)	*P* value
Sex		0.121
Men	(Ref)	
Women	1.31 (0.93–1.85)	0.121
Age		0.746
18–39	(Ref)	
40–59	1.12 (0.75–1.67)	0.586
60+	1.05 (0.59–1.85)	0.880
Marital status		0.553
Married/cohabiting	(Ref)	
Separated/divorced	1.40 (0.82–2.38)	0.220
Widow/widower	0.97 (0.45–2.07)	0.928
Single	0.86 (0.55–1.35)	0.512
Educational level		0.125
10 years or less	(Ref)	
10–13 years	1.23 (0.76–2.00)	0.397
University/college 1–4 years	1.39 (0.82–2.34)	0.220
University/ college 4 years+	1.94 (1.09–3.43)	**0.023**[a]
Employment status		0.909
Employed/student/home worker	(Ref)	
Out of work[b]	0.97 (0.66–1.44)	0.896
Retired	0.87 (0.46–1.65)	0.662
Number of symptoms	1.18 (1.14–1.23)	**<0.001**
Number of life stressors	1.62 (1.36–1.94)	**<0.001**

Presented as OR with 95% CI and *P* values.
[a]Bold types indicate statistically significant values.
[b]Out of work = on short- or long-term sick leave, disability pensioning or unemployed.

When we modelled the individual life stressors in five multivariate analyses, each of the life stressors, except 'other serious life events', was significant. Work situation had the highest OR of 2.35 (1.63–3.40), followed by experiences in childhood/adolescence [OR: 1.79 (1.02–3.15)].

When burnout syndrome and food intolerance were excluded, the proportion of patients who considered a UC was 28.3%. However, the associations between concerns with UCs and the number of symptoms and the number of life stressors corresponded well with the figures presented above (data not shown). When we divided the conditions into three groups, the number of symptoms remained highly significant (<0.001) in all three groups, for both men and women, with OR for each increase in the number of symptoms of 1.23 (95% CI: 1.19–1.27) for Group 1, 1.13 (1.09–1.18) for Group 2 and 1.16 (1.13–1.19) for Group 3.

Discussion

Summary

Of unselected patients in general practice, almost 40% had at least considered that they might suffer from conditions commonly regarded as medically unexplained (i.e. UCs). The proportion was higher in women and among those who were separated/divorced or were out of work. The likelihood of reporting a UC strongly increased with an increasing symptom load and with the burden of life stressors. The individual life stressors with the strongest associations with UCs were experiences in childhood/adolescence, family situation and work situation.

Strengths and limitations

A strength of this study is that it is based on consecutive, unselected, adult patients. We intended to capture those who had at least considered UCs while striving to find labels and

explanations for their symptoms. The patients were recruited through their GPs. Any selection bias of GPs should be minimal because Norwegian GPs do not select patients on their lists.

We wished to cover a range of conditions commonly regarded as unexplained. The chosen conditions are all based on self-reported constellations of symptoms. For some of the conditions, there are diagnostic categories established by consensus groups. Furthermore, there is a great deal of controversy regarding the causal mechanisms and treatment options for all the conditions. Some conditions can be regarded as more controversial than others (electromagnetic hypersensitivity, Candida syndrome and amalgam poisoning), whereas some are established diagnoses, despite being poorly understood (FM, CFS/ME and IBS). Even though there are plausible causal mechanisms for food intolerance and burnout syndrome, they are still multisymptom conditions characterized by symptom constellation criteria. Despite the differences between the listed UCs, we found corresponding results when we divided the UCs into three groups and excluded burnout syndrome and food intolerance.

Comparison with existing literature

A large number of patients in general practice are willing to consider conditions, which are commonly regarded as unexplained. The high proportion can be considered surprising, as patients with UCs commonly describe their situation as difficult, stigmatizing and socially controversial (40,41).

Female patients had an increased likelihood of reporting UCs, which is consistent with findings in many studies (11,19,42,43). However, a review does not find consistent evidence that female gender predicts worse outcomes (44). Age was not associated with reports of UCs, although one review suggests that the prevalence of MUS is highest in younger age groups (45). The association between being separated/divorced and being out of work and reporting a UC disappeared in adjusted analyses. However, it is established that MUS are a leading cause of sickness absence (46). Our finding that a high level of education was associated with concerns with UCs is noteworthy, because multiple and 'unexplained' symptoms have traditionally been associated with a low educational level (43,47). One possible explanation might be that well-educated patients are more knowledgeable about and more willing to accept the new conditions, for example, through following public debate.

The frequent inclination to consider UCs in our study has several possible explanations. Barsky suggested that the influence of social and cultural factors may result in an increased awareness of bodily functions and an increased concern that even common, transient symptoms may be part of an illness (44). This is reflected in 'The paradox of health', which describes the discrepancy between the steadily improving objective health status in the Western world and the deteriorating subjective health perception over the past decades.

Many of the UCs we studied are related to external or environmental influences, which may potentially affect health. Such concerns have been named modern health worries (MHWs). Rief *et al.* (48) found that the majority of the subjects in their population study had high or extremely high concerns that aspects of modernity (e.g. air pollution, mobile phones, dental fillings, etc.) may have affected their health, and only 6% reported no concerns at all. This is supported by a Norwegian population study, which found that 96% reported at least one MHW (49).

The likelihood of reporting a UC strongly increased with an increasing symptom load, indicating that multisymptom patients tend to consider many alternative labels and explanations for their symptoms. This is consistent with Rief *et al.* (37), who found the number of symptoms to be proportional to the number of causal attributions. Furthermore, a number of studies have established that the likelihood of reporting MHWs increases with an increasing number of symptoms (48–50). Hence, there seems to be a close relationship between reporting multiple symptoms, having concerns about aspects of modern life, and the tendency to consider UCs. However, the direction of the relationship is not established. That is, although individuals who report many symptoms may be more likely to consider them as part of an illness, worries about external health threats may also affect symptom reporting, through an increased awareness of bodily functions.

We found that the burden of life stressors an individual experiences was strongly associated with concerns with UCs. The especially strong association with adverse experiences in childhood/adolescence and family problems are supported by the review by Romans and Cohen (51), which concludes that UCs are associated with interpersonal abuse. UK population studies have reported that patients with UCs are more likely to have experienced recent adverse life events than control groups (19), and that psychological abuse in childhood predicts persistent reporting of multiple symptoms (1). In a German longitudinal study, negative life events were found to be predictors of MUS 1 year later (52).

However, life stressors may not only be associated with 'unexplained' symptoms and conditions, but with illness development in general (24,30,53). The theory of allostatic load suggests that chronic or repeated exposure to stressful events through the life course may result in unfavourable health outcomes. This could be mediated by long-term changes in epigenetic traits and in a wide range of physiological systems as an adaptive response to external and internal stimuli, integrating immunological, endocrinological and neurological pathways (28,30,31). Hence, the evidence supports that experiencing life stressors over the life course affects an individual's susceptibility to disease in general, but that it is also associated with increased symptom reporting and the interpretation of these symptoms.

Patients may or may not report symptoms in studies and may or may not seek health care for them. The deciding factor may be whether the patient perceives their symptoms as normal and transient phenomena or as potential signs of serious disease. In our approach, we included the whole 'symptom iceberg' that the patients had experienced, without limiting symptoms to those which were presented to the GP. In primary care, the reasons for encounter often cover one symptom or diagnosis only and thus overlooks the whole symptom profile. The strong association we found between the number of symptoms and concerns with UCs suggests that even symptoms which are not necessarily presented to the GP may influence whether the patient perceived their symptoms as potentially threatening. Also, it may suggest that symptom reporting in questionnaires does in fact matter, whether or not the symptoms are presented to health care professionals.

Implications for research and practice

GPs should acknowledge that many patients in primary care are concerned with conditions for which there is no clear medical explanation. These concerns may be related to worries about the effects of aspects of modern life (MHWs). Knowledge about the way in which patients perceive their symptoms may help the GP provide acceptable explanatory frameworks through which to discuss the symptoms. The likelihood of perceiving their symptoms as 'abnormal' and part of an illness seems to increase with increasing symptoms load and with the burden of life stressors experienced. GPs should consider assessing a patient's spectrum of experienced symptoms and pursue clues to life stressors, which may contribute to ill-health. This is of special importance as prognosis of localized symptoms worsens with the number of other symptoms experienced. Our findings support the evidence that the number of symptoms is a strong indicator of health and well-being.

The phenomenon of MUS remains unresolved and is difficult to operationalize in research. Hence, a pragmatic way forward may be to abandon the term entirely and focus on symptoms in their own right. We suggest that research should be based on unselected samples and should avoid preconceived assumptions regarding causal relationships, especially through the artificial distinction between 'somatic' and 'mental' causes.

Acknowledgements

Declaration

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