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The Difficulties in Developing and Implementing Fibromyalgia Guidelines

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1. Introduction

Fibromyalgia syndrome (FMS) is increasing in prevalence both in Europe and the rest of the developed world. In 1995 the prevalence was estimated in the USA as roughly 1 in 50 with a female to male ratio of 6:1 (Wolfe F. et al, 1995). In 1998 the German health survey identified similar figures. In 2010 a survey of five European countries estimated it to be now as high as 1 in 30 (Branco et al, 2010), with a sex ratio of 2 to 1. This ratio varies widely in different countries being as high as forty to one in Brazil (Senna et al, 2004). The presence of the sex ratio and its variability is one of many hotly debated areas in FMS. Why prevalence of the syndrome should be increasing is another area under discussion, although it is not as controversial as to how such a subjective condition should be accurately diagnosed and effectively treated; there have been many guidelines constructed by experts to assist in these two domains and this is the focus of the following chapter.

2. Guidelines

It might be useful before beginning to focus on fibromyalgia to simply ask the question, why do we have guidelines? In Britain alone, there are thousands of guidelines and protocols, some of which are formulated within a particular clinic, some for the wider region and some nationally; many give little more than general advice such as antibiotic guidelines in urinary tract infections, whereas others are expected to be adhered to more strongly, such as deep venous thrombosis protocols. Is it possible for a doctor to even be aware of the existence of every one of these guidelines? Indeed, it could be asked whether our obsession with guidelines is encouraging our healthcare practitioners to simply learn to follow stepwise instructions rather than to think for themselves? In the future will doctors be replaced by robots who are quicker, more accurate and likely to follow protocols better? The answer is surely "No!" if only because the doctor themselves exerts a great healing effect simply through their own person, that is through the interaction of the doctor-patient relationship (Balint, 1957).

It is also hard to imagine how any computer algorithm would be able to adapt guidelines to the benefit of the patient in front of them; this is where guidelines and protocols differ of

course; a protocol must be followed and if it isn't one is open to legal challenge in the event of future problems. They are well suited to complex drug regimens such as the setting up of chemotherapy; such repetitive tasks benefit from protocols to assist practitioners in not missing important steps. But this is different to the role of guidelines. The Institute of Medicine defines guidelines as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances." (Field and Lohr, 1990). In other words they are devised in order to help clinicians make better decisions. When reading any guideline it is this that the physician should ask him or herself.

2.1 Why are guidelines useful to doctors?

A good guideline helps the physician by addressing only the major decisions and making the evidence clear at each stage (Jackson and Feder, 1998). Ideally it should be as concise as possible for obvious reasons. This is why NICE (the National Institute of Clinical Excellence, in the UK) publishes 'long' guideline versions and 'short' versions. Moreover, good guidelines help doctors in their continuing professional development (CPD) by providing clinical overviews and identifying knowledge gaps. However, despite their apparent usefulness, research has shown that guidelines are not very effective at changing physician practice (Woolf S.W., et al 1999). Other important benefits to guidelines are empowering patients and informing health policy. Even the existence of a guideline will give publicity to a condition and bring it to the attention of politicians.

It has been shown that guidelines can improve medical care (Grimshaw and Russell, 1993) but this naturally pre-supposes they are of high quality. Even with the best intentions however, guideline committees can miss evidence, and they can allow their subjective opinions to override what might be good evidence. This also extends to their recommendations. Attempts to minimise this by having large committees ameliorate this to a degree but are themselves open to "group-think", whereby a subtle peer pressure leads group members to agree with each other and advocate ideas that may not be right. This is the great danger with guidelines that are based on 'group consensus' but it is reduced by having members from as wide and different backgrounds as possible. Finally guidelines often have conflicting interests. Good guidelines have any potential conflicts of interest (normally financial) stated at the end. However, some guidelines are specifically constructed to address matters such as cost. This raises such thorny issues as the value of a life, or the value of an extra healthy year (Sassi, 2006). Finally, doctors also may be influenced even unwittingly by other priorities or special interests.

Guidelines are supposed to encourage more consistent practice and reduced variation (both geographical and between doctors) but where does this leave individualised medicine, which is the bedrock of modern primary care (Schuster et al, 2006)? Even guidelines that are accurate, up-to-date, well-evidenced and patient-centred may conflict with other guidelines and may undermine the years of training physicians have undertaken.

It has been said that guidelines are only useful when scientific evidence can provide an answer; given this, it is arguable that there is not a great deal of point in publishing guidelines in the absence of useful evidence. Such guidelines would only really be able to give recommendations based on consensus opinion, that is, the opinion of people who have

not met our patients, but only their own. It is this which is the main problem in the construction of guidelines for fibromyalgia syndrome.

3. Guidelines for diagnosis

In response to the huge amount of published work concerning FMS over the decades there have been a number of attempts to elucidate the best ways to diagnose and treat it. Thus far, there have proven no physical tests that are consistently positive in people who complain of the symptoms characteristic of the disorder. In other words, there is no “gold standard” that enables physicians to rule in or rule out the diagnosis.

3.1 There are no useful diagnostic tests

In actual fact, there has been only one biochemical marker that research has shown to be commonly raised (as much as threefold) in the condition and that is substance P, a neurotransmitter, thought to be involved in pain perception, as measured in cerebrospinal fluid (Russell et al, 1994). However, there are a number of reasons why this is not likely to prove a useful test: firstly there is the sheer practicality of measuring the level of a neurotransmitter, as it would need invasive testing - there is no peripheral blood correlate; secondly it does not always appear to be raised and the levels do not correlate with subjective pain - so whilst there is an apparent relationship any test is not likely to be specific or sensitive enough to be useful. It might be theorised that actually what the raised biochemical marker is telling us is the same as what the patient is saying, that is to say that they are suffering pain. Any subjective feeling should have a neurochemical correlate, if we can but find it.

3.1.2 Altered central nervous system processing

Indeed functional magnetic resonance imaging scans of patients suffering with FMS shows that areas of the brain correlating with pain perception (such as the primary and secondary somatosensory cortices) are more greatly activated than in normal controls (Gracely et al, 2002). In this study similar subjective pain perception resulted in similar cortical activation in FMS patients compared with controls, whereas similar pressure application led to far greater cortical activation in the FMS patients. But what does this actually tell us? It tells us that the patient is truly perceiving pain; it tells us that are not lying to their doctors. But even doctors who question the validity of the entire syndrome would surely never suggest that patients are making up their symptoms; exaggerating, misinterpreting, misunderstanding, perhaps, but our thoughts and feelings need a physical medium to function; if we measure the workings of that medium we ought to see correlative changes.

This is given further weight by work which suggests that the threshold for perceiving pain is lower at a spinal level in certain chronic pain conditions, such as chronic knee pain, whiplash, and fibromyalgia (Lim et al, 2011). In other words, patients with chronic pain conditions are more sensitive, a description which would hopefully not generate offence.

3.2 Diagnostic guidelines

In the absence of any tests there have been other attempts to create useful diagnostic guidelines. The first widely accepted ones were those constructed by the American College

of Rheumatology (ACR), originally to enable consistent research, ironically (Wolfe et al, 1990).

3.2.1 ACR criteria 1990

These guidelines were simple to use in that they defined FMS as widespread persistent pain of more than 3 months duration in three out of four body quadrants, as well as the axis (spine or sternum). Moreover, physical examination was included, namely concerning pressure points, of which 11 of 18 needed to be positive for a diagnosis. Physicians were also supposed to exclude other causes; whilst this is obviously wise, it is now recognised that other diseases can trigger FMS, although the links are weak; only 10% of lupus sufferers fulfil FMS criteria for example (Taylor et al, 2000). Despite its simplicity however, it was not widely used by primary care doctors and many patients who were given diagnoses of FMS did not fulfil the 1990 ACR criteria. Even primary care doctors who did perform tender point examinations often did so incorrectly, for reasons which are likely to be manifold, although a scepticism with the 1990 guidelines is probably part of it. Such scepticism was formalised by a study which showed that sham points were nearly as discriminative as 'ACR points' and that pain at three 'ACR points' was equivalent to any greater number for diagnostic accuracy (Harden et al, 2007).

The ACR paper built on previous work, of course, the most foundational being that of Yunus, often known as the father of fibromyalgia. It was he who first applied the term "primary fibromyalgia" in a systematic way to a syndrome of muscular aches, tiredness, anxiety, poor sleep and subjective swelling. Before him the term "fibrositis" had been used for nearly a century (Gowers, 1904). This referred unsystematically to patients with hard to define muscular pains, although it was Hench, in 1976, who suggested the term 'fibromyalgia' was more appropriate as there was no evidence of inflammation (implied by the suffix '-itis'). It was Yunus who then adopted it (Yunus, 1981) and formally applied it the condition under discussion.

As Wolfe elaborates in the 2010 paper (Wolfe et al, 2010) the original 11/18 tender points from the 1990 ACR criteria have not been used consistently as a diagnostic tool. Indeed he was one of the first authors to say they should actually not be (Wolfe, 2003). At least 25% of patients with a diagnosis of FMS have never satisfied the 1990 list, and hence new criteria were proposed which examine a wider range of symptoms, and are quantifiable using two parameters: the wide-spread pain index (WPI) and the symptom severity scale (SS).

3.2.2 Proposed new criteria from 2010

The chosen symptoms are these: fatigue, waking unrefreshed, cognitive symptoms and somatic symptoms. The minimum duration is again three months, and must not be explained by another physical disease process. Experienced General Practitioners (GPs) and rheumatologists will know well the huge variety of potential symptoms the last two categories comprise. It is immediately obvious that such fluid and subjective measures are likely to mean that some patients will slip in and out of a diagnosis of fibromyalgia, but this is, of course, what is actually seen, as patients move from good to bad phases and back again. Usefully, as Wolfe pertinently observes at the end of his 2010 editorial (Wolfe, 2010), these new criteria now enable us to "study fibromyalgia syndrome ... without the requirement for belief in its existence."

This table summarises the two diagnostic strategies:

Guideline	Pain	Regions	Other symptoms	Other conditions
1990 ACR	11 out of 18 tender-points	3 out of 4 quadrants +axis	Not diagnostic	Exclude diagnosis
Proposed 2010 - Criteria 1	WPI ≥ 7 in the last week	Any of 19 areas.	SS scale ≥ 5	Concurrent diagnosis acceptable.
- Criteria 2	WPI ≥ 3 in the last week	Any of 19 areas.	SS scale ≥ 9	Concurrent diagnosis acceptable.

Table 1.

The new criteria obviate the need for a physical examination, which seems sensible, as there is not actually anything physical to find. The WPI roughly correlates to the tender points notion except that patients are *asked* if particular areas have been painful over the last week. A score of 7 (out of 19) or more is diagnostic if accompanied by a SS score of 5 or greater; alternatively an SS greater than or equal to 9 with a WPI of 3-6 also qualifies; it will be noted that the second scale has much overlap with chronic fatigue. Each of the four symptom categories is scored 0-3, giving a potential score of 12. It is worth noting that these new provisional criteria classify nearly 90% of patients as having FMS who fulfilled the original tender point criterion. The new criteria also enable easier longitudinal patient assessment and make it simpler for GPs to assess patients. At this stage the new criteria are still provisional depending on feedback and validation through research, but the improvement they offer is clear and they are likely to be official before too long. There are voices of concern however; Smythe (Smythe 2011) for example, suggests that in discarding the 'objective measure' of tender points, the scope and hence number of those diagnosed is likely to rise even further. Diagnosis is now based purely upon subjective feelings with the huge potential for disease mongering that this creates (see below). Also the diagnostic strategies will include different types of patient. He also questions the validity of allowing overlap with other conditions and symptom constellations; in essence, the new criteria push us to think of FMS no longer as simply a pain condition with associated symptoms. This has implications for many of the guidelines below whose emphasis was actually upon pain rather than these other subjective disturbances.

3.3 Part of the somatoform spectrum

The lack of abnormalities on physical examination, and the absence of objective diagnostic tests lead many physicians to question whether FMS should have its own diagnostic category or whether it should simply be categorised in the spectrum of somatoform illnesses (Ciccone and Natelson, 2003). Even Wolfe, the lead author of the paper defining the 1990 ACR fibromyalgia classification criteria, having first in 2003, questioned the use of the tender points classification he helped to devise, now feels that FMS should not be recognised as a disease at all but as a greater than normal physical response to stress, depression, and anxiety; he has written that it should be recognised simply as part of the

human condition (Wolfe 2010), although most authors would argue that it is, at the very least, at the far end of the spectrum. Indeed many of the opponents of the FMS diagnostic category feel that the label may legitimise sickness behaviour and can slow recovery (Payer, 1992).

Whilst some authors question the validity of the diagnosis at all, preferring to class it within the wider “functional somatic syndromes set” (Kanaan et al, 2007) there have also, conversely, been attempts to actually sub-divide FMS. For example Mueller in 2007 (Mueller et al, 2007) advocated the following four sub-divisions:

- extreme sensitivity to pain but no associated psychiatric conditions
- fibromyalgia and comorbid, pain-related depression
- depression with concomitant fibromyalgia syndrome
- fibromyalgia due to somatization

They even suggest that these sub-divisions may (“may” being the operative word) respond to different therapies; this will require a great deal of further research to refute or deny. Perhaps the most logical position is that FMS is an 'illness' ie a constellation of symptoms, rather than a disease, which is normally understood as being based on a pathophysiological disorder (Wilke, 1999).

3.4 The value of receiving a diagnosis is controversial

Whilst anecdotally, many GPs might agree that labels appear to legitimise sickness behaviour, there is little evidence that the presence or absence of the fibromyalgia label has any effect on the course of the disease over the years (White et al, 2002). Indeed there is little which does alter the course of FMS, leading to the observation that most cases of FMS are 'resistant' cases! (Wilke, 1995). Neither inpatient rehabilitation nor early retirement seem to affect it. Indeed most patients are physically able to work full-time in jobs requiring light activities (Raspe et al, 1994). What does appear to improve is patient satisfaction with their health status once they receive the diagnosis; it seems that, whilst the label might not help people recover or function better, most are happy to at least “know” what the problem is, something that is consistently observed across a range of conditions, whether improvement then follows or not (Choy et al, 2010).

Indeed this reflects the fact that prognostication has historically been a very important physician skill, although it is less so these days (perhaps naturally enough, when many diseases can actually be cured rather than simply observed); prognosis is still highly valued by patients, though (Christakis, 1999). However, with FMS patients it appears this satisfaction is short-lived; in the UK it has been found that visits to the doctor, for any reason, are reduced for about two years following diagnosis, but that they rise to even higher levels after that, typically over twice that of controls ie all other patients (Hughes et al, 2006).

3.5 Aetiology is controversial

Another element which contributes to the difficulty in creating diagnostic guidelines is the unknown aetiology, indeed the absence of any plausible mechanism. What appears to be true is that psychosocial factors predominate (both in the causality and also in effective treatment) but this is very hard to investigate. The long-term, refractive nature of the condition makes comparative studies very hard to achieve. Patients also tend to have strong beliefs regarding their diagnosis, treatment and prognosis which creates resistance to many

proffered treatments and difficulties with blinding studies. In particular patients are very resistant to psychological explanations or solutions and for the most part reject them. Indeed it is notoriously easy to offend patients with FMS; the notion of number needed to offend (NNO) is useful here: 40% of patients with medically unexplained symptoms find the terms 'psychosomatic' or 'medically unexplained' offensive in the UK, which is an NNO of 2-3; this is less than those offended by the term 'hysterical' but more than the mere 12% (NNO 9) who object to the term 'functional' (Stone et al, 2002).

It is probably true that many patients fear not being taken seriously by the doctor, or adjudged to be abusing their time. Every day, patients apologise to their GPs for wasting their valuable time (to which the conscientious GP replies "but without you I would be unemployed!"). When someone with fibromyalgia, who experiences daily pain is told their problem is "all in the mind" and they can solve it by simply "pulling yourself together" it is unsurprising that they would both disagree and be offended; of course, few GPs would phrase it like this, but it is this that patients with FMS often hear.

The most widely accepted hypothesis of causality is that of increased brain sensitivity to pain stimuli. However, this is not really a explanation at all, as it is just another way of stating what patients tell us. The question is, of course, how could such a sensitivity change arise? Numerous associations have been noted as statistically significant, such as pre-morbid anxiety (Netter and Hennig, 1998), abuse (Haeuser et al, 2011), negative life events (Anderberg et al, 2000), genetics (Rapael et al, 2004), and neck trauma (Buskila et al, 1997). Levels of dopamine and serotonin have also been observed to be deranged in some studies, although inconsistently; once again this raises the question of what is actually being measured: cause or effect (or neurological substrate)?

So, diagnosis and causality are controversial. There are no tests. There are no objective signs. All the symptoms are subjective. However, anyone who feels that great controversy has thus far been demonstrated 'ain't seen nothing yet'.

4. Treatment guidelines

In 1987 Goldenberg prophesied that fibromyalgia was "emerging but controversial condition" (Goldenberg, 1987). He was proved quickly right. Attempts at making guidelines for FMS were made even before Goldenberg's prophetic comments. Indeed, in 1986, Hench created an early incarnation of guidelines (Hench, 1986) and suggested that treatment should include physical, behavioural, psychological, and pharmacological means. Moreover he observed that no drug therapy had proved particularly successful, the tendency being only to provide temporary relief from pain. He suggested that studies aimed at defining the cause have linked it to sleep disorders, neurogenic mediators, immune mechanisms, muscle disease, and psychological disturbances. His final conclusion was that after the establishment of an initial therapy program, patients should assume the major responsibility for management.

Nowadays, the phrase 'responsibility for management' would be put differently but the attitude that patients should be listened to, their preferences taken into account and that they should be fully involved in their management plan is a very vogue attitude that is unlikely to change (Woolf S.H., 1997). In so far as it aids compliance or even advances concordance this stance is admirable in many conditions (Bissell et al, 2004). For example, there are numerous anti-hypertensives for which an important part of the treatment plan is how a particular person feels about side-effects and overall efficacy; hence advocating

choice is very valid in this condition. Moreover different patients will respond differently to different drugs; indeed the placebo effect itself is likely to be different with different medications and different patients (Zhang et al, 2008). However, there is sadly no evidence that advocating patient choice or encouraging patients to seek therapies with which they are happier has any effect in improving outcomes in FMS. It is likely that this reflects the absence of truly effective options. This raises the question of whether it is sensible, or even ethical, to offer our patients a choice between cognitive behavioural therapy and reflexology, between an exercise program and homeopathy?

4.1 Guideline for the management of fibromyalgia syndrome pain in adults and children 2005

Goldenberg himself, in late 2004, (Goldenberg et al, 2004) observed that despite there being in existence papers concerning treatment for decades, stepwise guidelines were absent in the medical literature. This was following the otherwise well received American Pain Society (Buckhardt et al, 2005), to which Goldenberg himself had just contributed. A patient version of the guidelines was also produced, aimed at improving patients' knowledge on the aetiology and effective treatment options available, thus promoting self-management. The guidance graded the diagnostic and treatment evidence-base according to the well-recognised Oxford Centre for Evidence-based medicine system (Oxford University, 2009), that is 1-5 for evidence levels and A-D for Grades of Recommendation.

The guideline presented six diagnostic recommendations (four according to panel consensus), nineteen broad treatment recommendations for adults (including ten consistent with Grade A level) and ten for children (all according to panel consensus, but logically extrapolated from the adult evidence). This guideline was first formulated in 2004 and has since been updated in 2007, in response to new pharmacological research concerning antidepressants (Guideline central, 2007). It appears at first glance very impressive but the lack of useful treatments is laid bare by the fact that two of the level A recommendations are 'do not's (steroids and non-steroidal anti-inflammatories) and two are appeals to use many different strategies. This leaves the following A graded advice: gentle exercise, balneotherapy, sedatives, tricyclics, education and cognitive behavioural therapy. It is no wonder that physicians responded to such advice with frustration.

4.1.1 Goldenberg's stepwise guideline 2005

Doctors, particularly general (or family) practitioners often like to think in terms of stepwise management plans. This has the advantage of encouraging recognised 'best practice', simplifying treatment decisions and making the treatment journey easier for patients to understand. A good example of such stepwise treatment plans is the British Thoracic Societies guideline for asthma which is so useful for GPs in the United Kingdom (BTS, 2011). Presumably partly as a consequence of the perceived flaws in the guideline above, Goldenberg and two of the other authors constructed a step-wise treatment algorithms in an effort to guide doctors (particularly family practitioners) and patients more clearly along a treatment path, a journey which most research suggests is inevitable. It delineated a three step process. The first step should involve diagnosis, education and treatment of any co-morbid conditions; this is followed by tricyclic antidepressants (TCAs), exercise and cognitive behavioural therapy (CBT); thirdly, the following drugs were suggested as second-line: tramadol, selective serotonin uptake inhibitors (SSRIs), anti-convulsants or a

combination of medications. If all else fails then refer to rheumatology, the pain team or a psychiatrist; their guidance does not extend to suggesting what might then subsequently be done, although most wily primary care doctors will already have a fairly shrewd idea.

4.2 Arnold's stepwise guidelines 2006

The theme of a stepwise approach was taken up by Arnold following the APS guidelines (Arnold L.M., 2006). She was critical that the guidelines took little consideration of post-morbid conditions leading her to feel other, newer antidepressants may often be more appropriate. She was also critical of the emphasis placed on exercise, pointing out that for such patients there are many barriers to this such as pain, stress, depression and support. Given that compliance with exercise advice is very low, she advises that any barriers should be addressed first in order to enable exercise to be better pursued; indeed she suggests CBT as one means of boosting self-efficacy to achieve this.

The down-side of this advice is that whilst psychosocial issues are recognised to contribute to aetiology, most GPs will also recognise them as exacerbating factors and often even excuses; this can contribute to the sad state of affairs where patients suffering from FMS are perceived as 'yes-but's, a type of heart-sink patient more formally known as 'manipulative health rejecters', by their doctors (O' Dowd, 1988). The term 'heart-sink' has now entered the English language and the World English Dictionary defines it thus: "a patient who repeatedly visits his or her doctor's surgery often with multiple or non-specific symptoms, and whose complaints are impossible to treat". This description will sound very familiar to those caring for patients with FMS; indeed one of the reasons for trying to define the disease, and ease the route to diagnosis, was to shorten the distressing period during which patients lived in the limbo time of non-diagnosis. This is true of any condition of course, but particularly FMS.

Thus Arnold's stepwise approach starts in the same way as the Goldenberg et al's above. In essence, she then switches steps 2 and 3, advising antidepressants and/or anti-convulsants following this, particularly an SSRI +/- pregabalin +/- low dose TCA. Only following this does she recommend using CBT and exercise. To a degree, this change in emphasis reflects the fact that even well-informed doctors, relying on the evidence, will have different opinions as to what is the best treatment, a situation magnified, of course, by orders of magnitude in our patients.

4.3 The Canadian consensus 2003

By way of contrast in the way of guidelines is the Canadian Consensus document for FMS from 2003 (Jain et al, 2003). It is written in a very different style to most guidelines; it does not grade evidence nor does it reject unproven therapies; the style is that of experienced physicians giving sensible, practical advice. Moreover it does not recommend any therapies above others, or suggest any kind of stepwise approach. Although referred to as a guideline it is more of a review article. As a result their suggestions regarding both aetiology and treatments are great and wide-ranging in number. Most of them are rather circumspect, and often preceded thus: "may occur", "may result", "may reduce", "may protect". The rationale is that all patients are individuals and different causal factors will be present in different people; equally different treatments may be efficacious in different individuals.

This document does, however, they also make the point that studies tend to show FMS persists over decades and most people gradually get worse. Perhaps this is the reason why

subsequent guidelines have restricted themselves to describing only causes and cures with a strong evidence base, whilst acknowledging that patient preference must be considered. The authors of the Canadian Consensus are also firm in their belief that CFS, FMS and depression are completely different disease entities, which is another controversial position. In a way, the title itself illustrates one of the problems of this document: it is a "consensus". To be sure, this illustrates the lack of available evidence, and if we can't rely on the opinion of those with decades of experience then on whose can we rely? However, many authors feel that an overemphasis on expert opinion is dangerous, particularly when constructing guidelines that may be followed at a national or even international level (Herrmann and Klement, 2008).

4.4 German guidelines 2008

In Germany guideline development for FMS was initiated by the Deutschen Interdisziplinäre Vereinigung für Schmerztherapie (DIVS - German interdisciplinary Society for pain therapy) and the Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF - Association of the Scientific Medical Societies in Germany); thirteen different medical and psychological Scientific Societies contributed, including the Deutschen Gesellschaft für Allgemeinmedizin und Familienmedizin (DEGAM - German Society of General Practice and Family Medicine). Two patient self-help groups also partook (Haeuser et al, 2008). Notably absent however was input from public health and societies of social medicine, which is unfortunate as in the case of FMS, these domains are probably more central than with most conditions.

The rationale for the development of the guidelines was as follows (in common with previous guidelines presumably): the high prevalence in the general population, the high associated disease-related costs, and the conflicting data on treatment effectiveness (Schiltenswolf et al, 2008). The hope, as with all guidelines, was that the advice would provide patients and physicians help in selecting among the alternatives available. This it surely does; however, like most other guidelines, the best it can probably hope for is to "help patients live with fibromyalgia syndrome (FMS) pain" (in the words of the "Guide for Adults with Fibromyalgia Syndrome Pain").

A summary of the DIVS/AWMF advice is now presented. The management suggested is stepwise and based on patient preferences and informed decision making. The first step is concerned with diagnosis, education, and treatment of co-morbid conditions (such as depression): first treatments (basic therapy) should be exercise, CBT and amitriptyline. The authors emphasised that they did not feel the ACR criteria of 11/18 tender points were necessary, which is becoming increasingly accepted. Indeed, pain can also be felt in other areas and is known to fluctuate. They also emphasised the importance of fatigue, sleep disturbance, and a feeling of stiffness and swelling in the limbs. These criteria were arrived at by strong consensus (defined as over 95% agreement). FMS is currently a diagnosis of exclusion so consensus is probably the best that could be hoped for here. Although some authors argue for a diagnosis of inclusion (Khasnis and Wilke, 2010), this does not yet appear possible.

Step 2 involves doing many of these things together (multicomponent treatment). Step 3 comprises either giving no further treatment or encouraging self-management (exercise, stress reduction), or further multicomponent therapy. Included in the latter is further pharmacological therapy (duloxetine or SSRI, pregabalin, tramadol +/- paracetamol),

further CBT, psychotherapy, including hypnotherapy, and warm bath treatments. These latter two straddle the border between mainstream and complementary therapies. Further complementary medicine suggestions are homeopathy or vegetarian diet, which take into account the desire patient's generally have for further passive treatments, but which have no evidence for efficacy.

The authors emphasised the difficulty of using or even finding controlled studies on which to base the evidence, for the following reasons. Firstly it is virtually impossible to conduct studies on care coordination of the long term nature needed in FMS. Secondly the healthcare systems of different countries are sufficiently different as to make evidence from international sources of dubious applicability to Germany.

The German guidelines describe the foundations of therapy as being cognitive behavioural therapy, aerobic exercise, antidepressants (such as amitriptyline), and anticonvulsants (such as pregabalin). These are the only treatments with a solid evidence base and it has been shown with controlled-studies that they reduce pain and increase capacity for activities of daily living (Haeuser et al, 2009, Arnold et al, 2011). There is also good evidence that "multimodal therapy" (ie exercise activities with psychotherapeutic input) is effective in the medium term, but this is really just another way of describing the extension of the foundations of treatment. In terms of long term care the guidelines are based purely on consensus opinion as the evidence base is so poor. Other guidelines are constructed in a similar manner ie full of good advice from experts, but little is ever based on good evidence (given that there isn't any). The implication that this advice is factual (even when the process of consensus is transparent) has worrying implications; patients may read such guidelines and not understand the levels of evidence. Harm may follow, not least in potential mistrust that could damage the doctor-patient relationship.

4.4.1 The majority of patients with FMS are cared for by general practitioners

As Herrmann and Klement emphasised in 2008: such a guideline not only will have difficulties being relevant to primary care, given the emphasis of the treatment options, but there is also a great risk of what they call "disease mongering" ie the expansion of the number of people who might spuriously fall into the defined group; this is because FMS has no binding definition, a controversial aetiology and no way of objectively testing for it.

If subjective illness is redefined as disease then it becomes harder to define individual cases according to symptomatology. The DEGAM guidelines above are actually more oriented to this sort of subjectivity anyway (compare their tiredness and back pain guidelines). This principle is known as hermeneutical case-finding. By classifying purely subjective complaints as diseases, the focus switches from a picture of a pathological process to a subjective one, concerned more with disturbances of functionality. In a way the personal needs of an individual are restructured into a disease requiring treatment, the external agency aspect is disease-mongering.

Given this, it is remarkable that most diagnoses are made in primary care and that most rheumatologists normally concur with the diagnosis (Porter, 2009). It would seem wise, given this and the long term nature of the condition that primary care doctors should have overall responsibility for managing patients with the condition. Indeed many rheumatologists refer patients back to GPs after a diagnosis has been made, although whether this is wise is questioned by some who suggest rheumatologists should retain ownership (Shir and Fitzcharles, 2009).

4.5 There are no NHS guidelines in Britain

Particular criticism was levelled at the AWMF guidelines due to the fact they were largely based upon consensus opinion, and not even always strongly concordant opinion either, rather than on scientific evidence. Given the paucity of useful evidence it is difficult to see what the guideline authors could do however, except perhaps take the route the National Institute of Clinical Excellence (NICE) in the UK have chosen, which is not to publish a guideline at all. NICE articulate an oft heard worry concerning FMS, that is, given the paucity of evidence-based treatments, will these guidelines actually help people or will they risk encouraging illness behaviour? This is known as disease mongering in some quarters, which is meant to imply external agencies having an undue influence on the self-perception of disease; this is very different to *malingering* which implies the patient is deliberately fabricating their symptoms for secondary gain.

It should be emphasised here that despite all the criticism of FMS as a real entity, guidelines as being incomplete and the research being flawed, no implication that patients are making up or exaggerating their symptoms is ever intended by researchers. It is always agreed that patients' suffering is real; it is the causes and hence the treatment which cannot be agreed upon. It has been noted that when guidelines are produced for a condition such as fibromyalgia, one whose aetiology is unknown, which has no agreed diagnostic criteria, and where there is a poor evidence base for treatment, then the possibility of over-diagnosing patients is great. It has also been noted that joblessness, sick pay and pension requests are all positively correlated with FMS. The consequent harm of disease mongering to patients' long-term psychological functioning and indeed to society itself is thus potentially very large.

Those in favour of NICE producing guidelines point to many other NICE guidelines that also only suggest cheap, low technology treatments such as Chronic Fatigue Syndrome and Low Back Pain (NICE, 2007). One of the functions of NICE, after all, is to *reject* treatments that may appear attractive but that are actually too expensive and/or ineffective. A NICE guideline would surely help primary care doctors become up-to-date with this difficult condition, even if no new treatments were suggested. Indeed this is one of the chief aims of the German DIVS guidelines, although whether they achieved this is questionable.

4.6 Primary care is best placed to care for patients with FMS

The DEGAM, as Germany's pre-eminent GP organisation, was ideally placed to contribute to primary care guidelines for FMS. DEGAM is an opinion leader in primary care and emphasises the following aspects of primary care, with particular relevance to Germany:

- GPs are experts in first contact health care.
- As such they perform a filtering and steering function for all their patients' medical problems.
- GPs look at patients holistically: social, psychological, spiritual, ecological and physical aspects, and all these aspects may be involved in their treatment.
- GPs are involved in emergency, acute and long-term care as well as prevention and education.
- The basis of good GP care is the long-term relationship with the patient.

From this short but lucid description of the essence of general practice, which applies to anywhere that primary care is pursued, it can be seen that GPs are ideally placed to care for patients with FMS. Indeed it is hard to imagine how a specialist could manage the task,

except in an advisory role. As such FMS guidelines ought to be principally aimed at GPs, but a continual criticism is the lack of applicability to primary care.

4.7 EULAR guidelines 2007

Other organisations have published guidelines with similar aims to those above. In 2007, the European League Against Rheumatism (EULAR) published a well-researched report, basing their guidance on 39 pharmacological and 59 non-pharmacological studies, following which they gave ten broad recommendations. These recommendations were specifically not weighted in terms of order and there was no step-wise advice for a treatment plan, which for many physicians limits their usefulness. They were as follows:

1. Recognition of FMS as a complex condition requiring good understanding of psychosocial context and daily functioning as well as pain levels.
2. A multidisciplinary approach is recommended according to symptoms and discussion with the patient.
3. Exercise: aerobic/strength
4. Heated pool treatment
5. Relaxation/Rehabilitation/Physiotherapy
6. Cognitive Behavioural Therapy
7. Tramadol
8. Antidepressants
9. Tropicsetron, pramipexole or pregabalin
10. Other analgesics such as paracetamol but not opiates.

The pharmacological recommendations 7-9 were based upon randomised controlled double-blind trials. Recommendations 1,2,6 and 10 were purely on the basis of consensus expert opinion. Recommendations 3,4 and 5 were based on randomised, blinded, crossover trials of varying quality. This list illustrates well the lack of evidence for diagnosis and treatment and how most is purely based on the opinion of 'experts'; this is presumably better informed than that of 'non-experts', but of course expert opinion has a notoriously poor track record. 'Experts' have naturally always listened to other 'experts' opinions and historically speaking this has led to the perpetuation of either useless or even harmful treatments for centuries or more. More pertinently, it often leads to the rejection of new ideas, although hopefully physicians are more open minded these days.

This advice was formulated at about the same time as the German AWMF advice and it can be seen that it is similar, especially in the broad lack of evidence-based advice and the over-reliance on expert consensus.

4.8 Guidelines differ

It has been noted that guidelines tend to differ. Haeuser attributes this (unsurprisingly) to the composition of the panels among other things (Haeuser et al, 2010). The EULAR guidelines were predominantly formulated by rheumatologists and have an emphasis on pharmacological treatments; this is probably also partly because they placed the highest credence on randomised controlled trials. The APS and the AWMF also considered these (especially looking at meta-analyses) but also placed great importance on systematic reviews, since many treatments are less easily assessable using RCTs; as such they emphasise CBT and exercise more.

4.9 Overlap with chronic fatigue and depression

In the UK, as already stated although there is no specific FMS guideline, NICE have, however, published guidance for dealing with chronic fatigue syndrome (NICE, 2007). Whilst superficially different from FMS the epidemiology is very similar. For those with an FMS diagnosis, the presence of extreme fatigue is almost always present, as would be expected with a condition where sleep disorder is a major component. For those with CFS, studies show a co-morbidity of 33-75% with FMS (some studies quote an increased odds ratio of twenty to one – Aaron et al, 2001). In FMS the annual prevalence of depression approaches 25% (Offenbaecher et al, 1998), and with CFS it is even higher. Many people, particularly patients themselves maintain their FMS or CFS caused their depression, rather than vice versa. However, many doctors now believe that FMS, CFS and major depression have much overlapping aetiology and risk factors, as well as symptomatology. This is illustrated by the fact the first degree relatives of those with FMS have as high a risk of developing major depression as if their relatives had depression instead of FMS (Raphael et al, 2004). This is consistent with the hypothesis that FMS is a depression spectrum disorder. Indeed there are some physicians who even feel the term itself is redundant and only serves to legitimise sickness behaviour. This depends on how the label is used however. If it serves to help explain to patients their illness is not progressive and that withdrawal from normal activities will not promote healing, it may be useful (Goldenberg, 1995). In that respect it is no more a label than particular psychosocial issues or personality traits are.

4.10 Alternative and complementary medical options

Another criticism of most guidelines is the notable absence of suggested alternative medical therapeutic options. Whilst there is also little demonstrable evidence for these other treatments, patients themselves are normally keen to pursue them, so at the very least 'harmless' (is any treatment truly harmless?) or popular therapies could be discussed.

There have indeed been huge numbers of studies of complementary and alternative medical therapies in FMS; some guidelines have mentioned these. Indeed, the Canadian consensus was particularly voluble in its listing of such treatments; unfortunately the best they could say was that they “may” help. Given that patients themselves are so keen to pursue these avenues, it does seem wise not to ignore them in guidelines. Indeed some studies put the usage of CAM among FMS patients at over 50% (Sarac and Gur, 2006). A study in Washington in 2007 found that FMS users who used CAM actually had worse symptoms than those who didn't (Lind et al, 2007). Whether this is cause or effect, is, of course, hard to ascertain. The economic study did, however, find that CAM users did not have higher health expenditures than the non-CAM users, because, although they visited healthcare practitioners more often, they saw their actual doctors (who are more expensive) less. This finding, already intuitive to many doctors, could be expected to be one reason why CAM in FMS might be advocated by the medical profession. Any doctors who feel it is unethical can take heart from a study in another psychosomatic condition (IBS) which showed that even telling patients they are receiving a placebo does not negate the actual placebo effect (Kaptchuk et al, 2010). *Indeed this likely reflects the fact that good medical care is more than simply supplying medications (or other interventions); time, concern for the person and a relationship with the practitioner are also essential parts of the healing process.*

Countless claims for alternative therapies have been made over the years, one of the most persistent being for guaifenesin. It has been strongly advocated by St. Amand and has been

widely believed by many in the FMS community for decades. At the very least, a strong belief is likely to have a powerful placebo effect and that, given the few treatment options with known benefit, might be useful part of a physician's armoury against FMS. Bennett conducted a year-long RCT investigating the claims of guaifenesin (Bennett and Clark, 1996). The results were negative. Disgracefully, this led to the study being unpublished, which is inexplicable given the importance, although Bennett reported on it himself in a review editorial in "Arthritis and Rheumatism" (Bennett, 1996). (This illustrates well the dangers of positive publication bias). Guaifenesin is actually still very popular among FMS patients and indeed still strongly advocated by St. Amand himself who gives many excuses for why the original trial failed (despite actually being an external advisor throughout). Bennett's concluding comment tells us a lot about how many complementary medical techniques work: "We have shown the placebo is just as effective as the placebo!"

5. Future developments

There are a number of important themes that are absent in all the guidelines mentioned above, representing new ideas, as well as old.

It is worth mentioning the new "wonder drug" milnacipran, an SNRI similar to duloxetine. The growth consulting company "Frost and Sullivan" predicted the market would be worth at least four hundred million dollars in Europe alone in 2013 (Frost and Sullivan 2008). It is now licensed in America. A study in 2010 (Haeuser et al, 2010) showed it to be similar in efficacy to duloxetine and pregabalin over a 6 month period with respect to pain reduction (30%); whether it has any useful long term effect remains to be seen.

There is a new concept developing in primary care which is known as quaternary prevention; in essence it refers to the old adage of "do no harm" and has particular relevance to FMS. It is the notion of preventing our patients from becoming over-medicalised; this is for their own benefit, as well as society's (Kuehlein et al, 2010). It was first mentioned, prophetically, by Jamouille in 1986 (Jamouille, 1986) but it is only in recent years that it is becoming more and more apparent as a real risk. Patients with FMS are the paradigmatic example of this: they eternally seek tests and solutions with which it is very tempting for their GPs to collude; future guidelines should emphasise that this is actually harmful, and that GPs should be using their unique relational position with their patients to prevent this over-medicalisation (Jamouille, 2011).

The concept of disease-mongering, which includes the expansion of the diagnostic definitions (see above) as well as the increasing of 'public awareness' is particularly relevant with FMS. The field is ripe for drug companies to exploit by promoting knowledge of the disease as well as new curative drugs. An analogous example is 'metabolic syndrome' a pre-diabetic state which it might be imagined could be a prompt to weight loss and exercise, but of course, offers potentially billions of pounds to drug companies who have thus vigorously promoted in and encouraged 'awareness' amongst doctors and patients.

Finally, the age-old concept of the placebo effect probably needs more emphasis in future guidelines; since most treatments either have no effect or a weak effect, it is tempting to suggest that more emphasis should be placed on the utilization of the placebo. However, it could also be argued that this goes against the concept of quaternary prevention mentioned above, and that it may undermine the only known effective treatments of CBT and exercise.

6. Conclusion

Fibromyalgia Syndrome is a controversial condition whose aetiology is unknown, which has no agreed diagnostic criteria, and for which there is a poor evidence base for treatment. Indeed, even the very existence of it as a condition is questioned by many senior researchers and practitioners in the field. Given this, the production of meaningful and useful guidelines is much more difficult than for most medical conditions, and credit should be given to those who have tried as there is no doubt that, whether we agree with all the recommendations or not, their use can help doctors in their mission to help patients cope with their pain, which is ultimately what our medical care is all about.

Without clear aetiology and with the known strong placebo effect of various therapies, it is difficult to create evidence-based guidelines; it is inevitable that the composition of the guideline group, each with their own unique backgrounds will have a strong influence. For the German guidelines to be valid. Following points had a strong influence on the recommendations of the S3 guideline quality:

- the composition of the interdisciplinary consensus conference mainly by specialists, the methodological structure and the frame of the consensus procedure (structure quality).
- the group consensus process structured by a majority vote concerning by the treatment and evaluation of the meagre evidence

The “interdisciplinarity” of the guideline group masks area-specific interpretations and particular interests. The utilitarian concept effectively ignores the concept of authentication and legitimation. It is essential, not only for the scientific credibility of guidelines but also for the therapeutic process. Each form of mistrust interrupts that process, not only for the development of guidelines but also concerning patient therapy. The outworking of this is, of course, different when considering the treatment process as compared to the guideline debate. It is fragile because it is essentially unconscious and so is easily lost. Conquering this mistrust is something that needs to be repeatedly managed by doctors in their dealings with their patients. Interference from the outside provokes mistrust if recommendations are not evaluated and scientifically legitimized in the best way possible.

There are no guidelines where the interests of the pharmaceutical industry are accurately considered. The relevance of the economic side is very important. Traditionally illnesses of the central nervous system are a great challenge for medicine and research. Fibromyalgia is no exception: so far no effective long-term therapy is available for this chronic pain illness. The interest and the commitment of the pharmaceutical sector is correspondingly great. It is possible that a break-through is being approached, since some active substances in clinical studies of later phases have proved promising. In view of these developments the management consultation company Frost and Sullivan (<http://www.pharma.frost.com>) projected that the European market for Fibromyalgia treatment is possible to be worth 406.3 million dollars in the year 2013, as compared to 73.4 million dollars in the year 2007.¹

The establishment of the milnacipran in the drug market is a good example. Since its introduction in Austria in 1998 milnacipran struggled to achieve an important market share. Consequently, manufacturers and distributors relinquished their market entrance into additional European Union member states, although in principle permission from one

¹ <http://www.ishoof.com/?p=25>: Access 02.12.2011

member country of the EU allows marketing in the entire European Union area. In a second attempt the finance and marketing partners prepared a broad introduction into the market in the USA in 2004. According to stock exchange reports investors made available several hundred million US Dollars to promote milnacipran for the indication of fibromyalgia syndrome. According to reports at the time Forest Cypress supported further development to the region of two hundred and fifty million dollars as advance and milestone payments (finanzen.net)².

7. References

- Aaron L.A., Herrell R., Ashton S., Belcourt M., et al. (2001). Comorbid clinical conditions in chronic fatigue: a co-twin control study. *J Gen Intern Med.* Vol 16(1), (Jan 2001), 24-31
- Anderberg U.M., Marteinsdottir I., Theorell T., von Knorring L. (2000). The impact of life events in female patients with fibromyalgia and in female healthy controls. *Eur Psychiatry*, 15 (5), (Aug 2000), 33-41
- Arnold L. (2006). Biology and therapy of fibromyalgia. New therapies in fibromyalgia. *Arthritis Res Ther* (June 2006) Vol 8(4), 212
- Arnold L., Gergana Z., Sadosky A. et al. (2011). Correlations between fibromyalgia symptom and function domains and patient global impression of change: a pooled analysis of three randomised, placebo-controlled trials of pregabalin. *Pain Medicine* Vol 12(2), (Feb 2011), 260-267
- Balint M (1957). *The doctor, his patient and the illness*. International Universities Press , Michigan
- Bennett R.M. (1996) Review: Fibromyalgia and the Disability Dilemma: A New Era in understanding a Complex, Multidimensional Pain Syndrome. *Arthritis and Rheumatism* Vol39 (10), (Oct 1996), 1627-34.
- Bennett R. and Clark S. (1996). A Randomized, Prospective, 12 Month Study To Compare The Efficacy Of Guaifenesin Versus Placebo In The Management Of Fibromyalgia. *Orlando American College of Rheumatology meeting (unpublished)*
- Bissell P., May C.R., Noyce P.R. (2004). From compliance to concordance: barriers to accomplishing a re-framed model of health care interactions. *Soc Sci Med.* Vol 58(4), (Feb 2004), 851-62
- Branco J.C., Bannwarth B., Failde I., et al (2010). Prevalence of fibromyalgia: a survey in five European countries. *Semin Arthritis Rheum.* Vol 39 (6), (Jun 2010), 448-53
- British Thoracic Society. (May 2011). Asthma Guidelines, In: *British Thoracic Society*, Available from:
<<http://www.brit-thoracic.org.uk/Portals/0/Clinical%20Information/Asthma/Guidelines/sign101%20June%202011.pdf>>
- Buckhardt C.S., Goldenberg D., Crofford L. et al. (2005). *Guideline for the management of fibromyalgia syndrome pain in adults and children*. American Pain Society, Glenview

² <http://www.wallstreet-online.de/diskussion/809332-1-10/cypress-bio-erhaelt-millionenvorschuss-fuer-medikament>; Access 02.12.2011

- Buskila D., Neumann L., Vaisberg G., Alkalay D., Wolfe F. (1997) Increased rates of fibromyalgia following cervical spine injury. A controlled study of 161 cases of traumatic injury. *Arthritis Rheum* Vol 40 (3), (Mar 1997), 446-52
- Carville S.F., Arendt-Nielsen S., Bliddal H. (2008). EULAR evidence based recommendations for the management of fibromyalgia syndrome. *Ann Rheum Dis* Vol 67 (4), (April 2008), 536-4
- Choy E., Perrot S., Leon T. (2010). A patient survey of the impact of fibromyalgia and the journey to diagnosis. *BMC Health Services Research*, Vol 10 (April 2010), 102
- Christakis N., (1999). *Death Foretold: Prophecy and Prognosis in Medical Care*, University of Chicago Press, Chicago
- Ciccone D.S. and Natelson B.H. (2003). Comorbid Illness in Women With Chronic Fatigue Syndrome: A Test of the Single Syndrome Hypothesis. *Psychosomatic Medicine* Vol 65 (2), (April 2003), 268-275
- Field M.J. and Lohr K.N. (Eds.). (1990). *Clinical Practice Guidelines: Directions for a New Program*. National Academy Press, Washington
- Frost and Sullivan (2007). In *Frost.com*, available from <http://www.frost.com/prod/servlet/press-release.pag?docid=148807077>
- Goldenberg D.L. (1987). Fibromyalgia syndrome. An emerging but controversial condition. *JAMA* Vol 257 (20) (May 1987), 2782-7
- Goldenberg D.L. (1995). Fibromyalgia: why such controversy? *Ann Rheum Dis*. Vol 54 (1), (Jan 1995), 3-5
- Goldenberg D.L., Burckhardt C., Crofford L. (2004). Management of Fibromyalgia Syndrome. *JAMA* Vol 292 (19), (Nov 2004), 2388-2395
- Gowers W.R. (1904). Lumbago: it's lessons and analogues. *BMJ* (Jan 1904), 117-121
- Gracely R.H., Petzke F., Wolf J.M., Clauw D.J. (2002). Functional magnetic resonance imaging of pain in patients with primary fibromyalgia. *Arthritis and Rheumatism* Vol 46 (5), (Feb 2002), 1333-43
- Grimshaw J.M. and Russell I.T. (1993). Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet* Vol 342 (8883), (Oct 1993), 1317-1322
- Haeuser W., Arnold B., Eich W., Felde E. et al. (2008). Management of fibromyalgia syndrome--an interdisciplinary evidence-based guideline. [German]. *German medical science GMS eJournal* Vol 6, (Dec 2008)
- Haeuser W., Bernardy K., Uceyler N., Sommer C. (2009) Treatment of Fibromyalgia Symptoms with antidepressants. *JAMA* Vol 301 (2), (Jan, 2009), 198-209
- Haeuser W., Kosseva M., Uceyler N., (2011). Emotional, physical, and sexual abuse in fibromyalgia syndrome: a systematic review with meta-analysis. *Arthritis Care Res* Vol 63 (6), (June 2011), 808-820
- Haeuser W., Petzke F., Sommer C., (2010). Comparative efficacy and harms of duloxetine, milnacipran, and pregabalin in fibromyalgia syndrome. *J Pain* Vol 11 (6), (June 2010), 505-521

- Haeuser W., Thieme K., Turk D.C. (2010). Guidelines on the management of fibromyalgia syndrome - a systematic review. *European journal of pain*, Vol 14 (1)(January 2010), 5-10
- Harden R.N., Revivo G., Song S. et al (2007). A critical analysis of the tender points in fibromyalgia. *Pain Med*. Vol 8 (2), March 2007), 147-56
- Hench P.K. (1976). *Nonarticular rheumatism*. *Arthritis Rheum* Vol 19 (6 suppl), (1976), 1081-1088
- Hench P.K. and Mitler M.M. (1986). Fibromyalgia. Management guidelines and research findings. *Postgraduate medicine* Vol 80 (7), (Nov 1986), 57-64
- Herrmann M. and Klement A. (2008). Limits in Transforming Evidence into Guidelines - Analysis on the Example of the Interdisciplinary Guideline About Fibromyalgia Syndrome [German]. *Z Allg Med* Vol 84 (10), (Oct 2008), 436- 443
- Hughes G., Martinez C., Myon E., et al (2006). The impact of a diagnosis of fibromyalgia on health care resource use by primary care patients in the UK: an observational study based on clinical practice. *Arthritis Rheum* Vol 54 (1), (Jan 2006), 177-183
- Jackson R. and Feder G. (1998). Editorial: Guidelines for clinical guidelines. A simple, pragmatic strategy for guideline development. *British Medical Journal* Vol 317 (7256), (August 1998), 427
- Jain A.K., Carruthers B.M., van de Sande M.I., et al (2003) Fibromyalgia Syndrome: Canadian Clinical Working Case Definition, Diagnostic and Treatment Protocols - A Consensus Document. *Journal of Musculoskeletal Pain* Vol 11 (4), (April 2003), 3 - 107
- Jamouille M., (1986). *Les informa-g-iciens*. Namur University Press , Namur
- Jamouille M., (2011). Quarternary Prevention: first, do no harm. *11th Congress of the Sociedade Brasileira de Medicina de Familia e Comunidade*. (June 2011)
- Janis, I. L. (1982). *Groupthink: Psychological Studies of Policy Decisions and Fiascoes*. (2nd Edition). Houghton Mifflin, New York
- Kanaan R.A., Lepine J.P., Wessely S.C. (2007). The association or otherwise of the functional somatic syndromes. *Psychosom Med* 69 (9), (Dec 2007), 855-9
- Kaptchuk T.J., Friedlander E., Kelley J.M (2010). Placebos without deception: a randomized controlled trial in irritable bowel syndrome. *PLoSone*. Vol 5 (12), (Dec2010), e15591.
- Khasnis A. and Wilke W.S. (2010). Diagnosing fibromyalgia: Moving away from tender points. *J Musculoskel Med* Vol 27, (April 2010), 155-162
- Kuehle T., Sghedoni D., Visentin G., et al (2010). Quarternary prevention: a task of the general practitiner. *Primary Care* Vol 10 (18), (2010), 350-
- Lim E.C., Sterling M., Stone A., Vicenzino B. (2011). Central hyperexcitability as measured with nociceptive flexor reflex threshold in chronic musculoskeletal pain: A systematic review. *Pain*. Vol 152 (8), (Aug, 2011), 1811-20
- Lind B., Lafferty W., Tyree P. et al. (2007). Use of complementary and alternative medicine providers by fibromyalgia patients under insurance coverage. *Arthritis Rheum* Vol 57 (1), (Feb 2007), 71-76

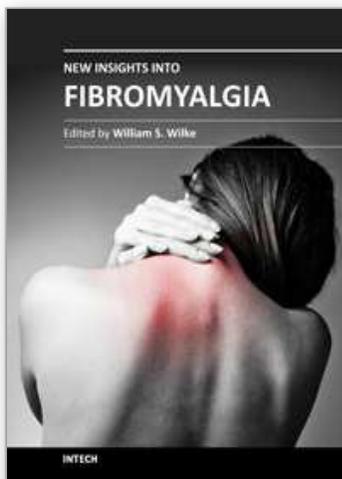
- Mueller W., Schneider E.M., Stratz T. (2007). The classification of fibromyalgia syndrome. *Rheumatol Int.* Vol 27 (11), (Sept 2007), 1005-10
- National Guideline Clearinghouse. (Nov 2007). Guideline for the management of fibromyalgia syndrome pain in adults and children, In: *Guideline Central*, available from:
<http://www.guidelinecentral.com/_webapp_1825321/Guideline_for_the_management_of_fibromyalgia_syndrome_pain_in_adults_and_children>
- National Institute for Health and Clinical Excellence. (Aug 2007). Chronic Fatigue Guidance, In: *NICE*, available from:
<http://www.nice.org.uk/nicemedia/live/11824/36193/36193.pdf>
- Netter P. and Hennig J. (1998) The fibromyalgia syndrome as a manifestation of neuroticism? [German]. *Zeitung fuer Rheumatologie* Vol 57 (2), (1998), 105-8
- O' Dowd T. C. (1988). Five years of heartsink patients in general practice. *BMJ* Vol 297(6647), (Aug 1988), 528-30
- Offenbaecher M., Glatzeder K., Ackenheil M. (1998). Self-reported depression, familial history of depression and fibromyalgia (FM) and psychological distress in patients with FM. *Zeitschrift für Rheumatologie* Vol 57(2), (June 1998), 94-6
- Payer L (1992). *Disease-Mongers: How Doctors, Drug Companies and Insurers Are Making You Feel Sick*. John Wiley, New York
- Porter D., Nelson Hospital (May 2009). Fibromyalgia in Adults. *Diagnosis and Management Advice for GPs*, In: New Zealand Govt Health Files, available from:
<<http://www.nmdhb.govt.nz/filesGallery/New%20Website/03Health%20Concerns/FibromyalgiaMay09.pdf>>
- Raphael K.G., Janal M.N., Nayak S. et al (2004). Familial aggregation of depression in fibromyalgia: a community-based test of alternate hypotheses. *Pain* 110(1), (Jul 2004), 449-60
- Raspe H., Cellarius J., Mau W., Wasmus A., von Gierke S. (1994) *Gesundheitswesen*. 1994 Nov;56(11):596-8. Guidelines for social medicine assessment and evaluation of primary fibromyalgia. [German]
- Russell I.J., Orr M., Littman B., et al (1994). Elevated cerebrospinal fluid levels of Substance p in patients with the fibromyalgia syndrome. *Arthritis and Rheumatism* 37 (Dec 1994) Issue 11, 1593-1601
- St. Amand R. P. (2009). The Guaifenesin Protocol, In: *Fibromyalgia Treatment Centre*. Available from: <<http://www.fibromyalgiatreatment.com/GuaiProtocol.htm>>
- Sarac A.J. and Gur A. (2006). Complementary and alternative medical therapies in fibromyalgia. *Curr Pharm Des* Vol 12(1), (2006), 47-57
- Sassi F (2006). Calculating QALYs, comparing QALY and DALY calculations. *Health Policy Plan* Vol 21 (5), (Sept 2006), 402-408
- Schiltenswolf M., Eich W., Schmale-Grete R., Haeuser W. (2008) Aims of the guidelines for diagnostic and treatment of fibromyalgia syndrome [German]. *Schmerz*, Vol 22 (3), (June 2008), 241-243
- Schuster R.J., Terwoord N.A., Tasosa J. (2006). Changing physician practice behavior to measure and improve clinical outcomes. *Am J Med Qual* Vol 21 (6), (Nov 2006), 394-400

- Senna E.R., De Barros A.L.P., Silva E.O., et al (2004). Prevalence of rheumatic diseases in Brazil: a study using the COPCORD approach. *J Rheumatol* Vol 31 (Nov 2004), 594-7
- Shir Y. and Fitzcharles, M.J. (2009). Should Rheumatologists Retain Ownership of Fibromyalgia? *Rheumatology* Vol 36 (4), (April 2009), 667-670
- Smythe H. (2011). Unhelpful Criteria Sets for "Diagnosis" and "Assessment of Severity" of Fibromyalgia. *J Rheumatol* Vol 38 (June 2011), 975-978
- Stone J., Wojcik W., Durrance D., et al. (2002). What should we say to patients with symptoms unexplained by disease? The "number needed to offend". *BMJ* Vol 325 (7378), 1449-1450
- Taylor J., Skan J., Erb N., et al (2000). Lupus patients with fatigue - is there a link with fibromyalgia syndrome. *Rheumatology* Vol 39 (6), (June 2000), 620-623
- University of Oxford. (March 2009). Levels of Evidence, In: *Centre for Evidence-based Medicine*, Available from: <http://www.cebm.net/index.aspx?o=1025>
- White K.P., Nielson W. R., Harth, M et al (2002). Does the label "fibromyalgia" alter health status, function, and health service utilization? A prospective, within-group comparison in a community cohort of adults with chronic widespread pain. *Arthritis Rheum.* 47 (3), (June 2002), 260-5
- Wilke W.S. (1995). Treatment of "resistant" fibromyalgia. *Rheum Dis Clin North Am.* Vol 21 (1), (Feb 1995), 247-60
- Wilke W.S. (1999). The clinical utility of fibromyalgia. *J Clin Rheumatol* Vol 5 (2), (April 1999), 97-103
- Wolfe F. Editorial (2010). New American College of Rheumatology Criteria for Fibromyalgia: A 20 Year Journey. *Arthritis Care and Research* Vol 62 (5), (May 2010), 583-584
- Wolfe F. (2003). Stop using the American College of Rheumatology criteria in the clinic. *J. Rheumatol* Vol 30 (8), (August 2003), 1671-2
- Wolfe F., Clauw D., Fitzcharles M. et al (2010). The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res*, Vol 62 (5), (May 2010), 600-610
- Wolfe F., Ross K., Anderson J. et al (1995). The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* (Sept 1995), Vol 38 (1), 19-28
- Wolfe F., Smythe H.A., Yunus M. et al (1990). The American college of rheumatology 1990 criteria for the classification of fibromyalgia. *Arthritis and Rheumatism* Vol 33 (2), (Feb 1990), 160-172
- Woolf S.H. (1997). Shared decision-making: the case for letting patients decide which choice is best. *J Fam Pract* Vol 45 (Dec 1997), 205-208
- Woolf S.W., Grol R., Hutchinson A. et al (1999). Education and debate: Clinical guidelines Potential benefits, limitations, and harms of clinical guidelines. *British Medical Journal* Vol 318 (7182), (February 1999), 527-530
- Yunus M. (1981). Primary Fibromyalgia (Fibrositis): Clinical Study of 50 Patients with Matched Normal Controls. *Sem. Arth and Rheum* Vol 11, (Nov 1981), 151-171.

Zhang W., Robertson J., Jones A.C. (2008). The placebo effect and its determinants in osteoarthritis: meta-analysis of randomised controlled trials. *Ann Rheum Dis* Vol 67 (12), (Dec 2008), 1716-1723

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Given the potential problems that can obscure any scientific enterprise, inconsistent results across studies are bound to occur. How are we to decide what is true? Let's turn to philosophy for a reasonable answer. The mathematician-philosopher Bertrand Russell approached a similar problem in his monograph *The Problems of Philosophy* (Russell B, 1912). He addressed the following question: How do we know that anything is "real"? Is the only reality subjective and simply in our minds, as Bishop Berkley challenged, or can we mostly believe the objective reality? His pragmatic answer: All possibilities may be true, but when the preponderance of evidence indicates that objective reality and knowledge are the most probable case, go with it. If the preponderance of all evidence about the clinical description of fibromyalgia and its pathogenic mechanisms and treatment strategies indicate a highly probable interrelated hypothesis, go with it. The direction of the literature on the whole trumps the less likely tangents. At the same time, remember Bertrand Russell and his pragmatic answer, and keep an open mind.

How to reference

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