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Is chronic fatigue syndrome common in Poland ?

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Abstract

Objectives This project considered whether CFS was a condition identifiable in a Polish population. We also set out to define the presence and characteristics of CFS in Poland in order to identify a cohort of those with who could potentially participate in further research studies.

Design observational study

Setting Poland

Participants We evaluated a cohort of 1400 participants, 92 of them complained of at least 6 months of unusual fatigue that was not relieved by rest. During face to face interview with the 92, self-report or record review revealed a medical or psychiatric condition that could have explained the fatigue in 23; 69 (0.05%) participants met Fukuda criteria for CFS.

Main outcome measures Participants completed the following screening symptom assessment tools: Chalder fatigue scale, Hospital anxiety and depression scale (HADS), Epworth sleepiness scale (ESS), COMPASS 31, Quality of life scale (QOLS), Functional assessment of the cardiac and autonomic nervous system.

Results The majority had experienced symptoms for over 2 years with 37% having symptoms for 2-5 years and 21.7% for more than 10 years. Compass 31 scores indicated that 50% have symptoms consistent with orthostatic intolerance. 43/69 (62%) had Epworth sleepiness scores >=10 i.e. consistent with excessive daytime sleepiness, 26/69 (38%) had significant anxiety and 22/69 (32%) depression measured by HADS A & D. Quality of life is signif icantly impaired in those with Fukuda criteria CFS (mean (SD) QOLS score 64 (11)) with significant negative relationships between quality of life and fatigue ($p<0.0001$), anxiety ($p=0.0009$), depression ($p<0.0001$) and autonomic symptoms ($p=0.04$).

Conclusion CFS is a significant previously unrecognized problem in a Polish population.

Strengths and limitations of this study

- This is the first study to summarize illness characteristics of a cohort of Polish CFS/ME patients.
- This study determine whether diagnostic criteria in common use in the UK are identify phenotypically similar cohorts of patients.
- Methodologically robust epidemiological study of fatigue and its consequences in a Polish population are now needed.

INTRODUCTION

Chronic fatigue syndrome (CFS) is considered to be a common condition in countries such as the UK, Australia and the US [1,2]. In the UK, it affects up to 250,000 individuals with frequencies reported of up to 0.2% [3]. These cohorts confirm that CFS can affect any age and is more frequent in females. To date CFS has not been reported in Poland, nor its prevalence defined. There are currently no CFS Clinical services.

This project considered whether CFS was a condition identifiable in a Polish population and to determine whether diagnostic criteria in common use in the UK [4] would identify phenotypically similar cohorts of patients. We also set out to define the presence and characteristics of CFS in Poland in order to identify a cohort of those with who could potentially participate in further research studies.

The study team identified potential CFS patients through a series of radio advertisements inviting individuals who thought they may be affected by this condition to self-present themselves to the research team (supplementary data). Subsequently those who were identified as having symptoms consistent with the Centers for Disease Control and Prevention (Fukuda) criteria were invited to participate in a more extensive research protocol. In this current study we describe the characteristics of this cohort.

METHODS

Process

Over a 2 week period 2 local radio broadcasts & 2 local television interviews were delivered. Over the next 2 weeks after considerable media interest, 2 national newspapers and a national TV station subsequently also ran details. Each of these media interactions included information about chronic fatigue syndrome (CFS) and the fact that Nicolaus Copernicus University, Poland were setting up a research programme. The national television article also included an interview with an eminent US researcher in the field describing their successful research programme. Details of the content of these media campaigns are contained in the supplementary data section.

Initially any individuals willing to participate were directed to a phone line. Within days of setting up the phone line it became clear that this mechanism to identify and recruit potential participants would be overwhelmed. The team therefore directed all potential participants to a website where more information about the study was available and where individuals were invited to self-complete the Fukuda criteria online. If individuals, on completing the online scoring felt that they met the Fukuda criteria [4] they were invited to contact the research team by email.

The research team then completed a series of screening questions which clarified whether the Fukuda criteria was met. Those passing this screening stage were invited to attend the research facility. The identification process is shown in **Figure 1**.

Clinical assessment

Those who fulfilled the eligibility criteria for Centers for Disease Control and Prevention (Fukuda) were invited to attend the research unit at the chronobiology laboratory (windowless and sound-insulated room, temperature 22°C, humidity 60%). They were seen by members of the research team in an assessment that took place over 40 minutes. All assessments took place during the period of March 2014 to July 2016. Individuals participated in a standardized baseline assessment which comprised of a battery of symptom assessment tools. Those screened as fulfilling criteria for CFS [4] were also reviewed clinically by a member of the research team in order to determine whether there symptoms were consistent with this criteria, that there were no psychiatric exclusions or other diagnoses that could be associated with chronic fatigue syndrome or where fatigue was not the primary complaint. 69 individuals subsequently went on to have a further baseline objective assessment.

Symptom assessment tools

Participants completed the following screening symptom assessment tools.

Measure of fatigue - Chalder fatigue scale [5]

The Chalder Fatigue Scale (CFQ) is a self-administered questionnaire for measuring the extent and severity of fatigue within both clinical and non-clinical, epidemiological populations.

The CFQ provides an 11 item brief tool to measure both physical and psychological fatigue. Each items is answered on a 4-point scale ranging from the asymptomatic to maximum symptomology, such as 'Better than usual', 'No worse than usual', 'Worse than usual' and 'Much worse than usual'. For all items, the least symptomatic answers are on the left of the response-set, providing an easy-to-understand checklist for respondents. Using the Likert scoring method, responses on the extreme left receive a score of 0, increasing to 1, 2 or 3 as they become more symptomatic. The respondent's global score ranges from 0 to 33. The global score also spans two dimensions—physical fatigue (measured by items 1–7) and psychological fatigue (measured by items 8–11). The Likert scoring system allows for means and distributions to be calculated for both the global total as well as the two sub-scales.

Reliability coefficients for the CFQ 11 have been high in studies of CFS patients [6]. It has been used widely in studies ascertaining tiredness among working populations as well as

patient groups and consistently fares extremely well against other longer and multidimensional tools [7].

Hospital anxiety and depression scale (HADS)

The HADS [8] is a 14-item measure of current anxiety (HADS-A) and depression (HADS-D). Caseness for anxiety or depression is revealed by subscores greater or equal to 11 on each subscale.

Epworth sleepiness scale (ESS)

In view of the association between excessive daytime sleepiness and fatigue, all subjects completed the ESS questionnaire (possible score range 0–24) [9]. This fully validated tool assesses daytime hypersomnolence, with a score ≥10 being indicative of significant hypersomnolence during the day.

COMPASS 31

Participants completed the Autonomic Symptom Profile [10] as a self-report measure of autonomic symptoms. However, scoring was performed according to the recently abbreviated and psychometrically improved version of this questionnaire, the Composite Autonomic Symptom Score 31 (COMPASS 31) [11]. Scoring consists of 31 items from six domains – orthostatic intolerance, vasomotor, secretomotor, gastrointestinal, bladder, pupillomotor – each weighted according to number of items and clinical relevance. Weighted individual domain scores are totalled to a maximum of 100, which indicates greater symptom load.

Assessment of quality of life

Participants also completed the following quality of life measure:

Quality of life scale (QOLS)

The Quality of Life Scale (QOLS) used in this study has 16 items. The QOLS has been used in studies of healthy adults and patients with rheumatic diseases, fibromyalgia, chronic obstructive pulmonary disease, gastrointestinal disorders, cardiac disease, spinal cord injury, psoriasis, urinary stress incontinence, posttraumatic stress disorder, and diabetes.

The QOLS is scored by adding up the score on each item to yield a total score for the instrument. Scores can range from 16 to 112. There is no automated administration or scoring software for the QOLS. Higher scores medicate better quality of life. The average total for healthy populations is approximately 90 [10-12].

Functional assessment of the cardiac and autonomic nervous system

Apparatus

All participants underwent formal autonomic assessment in the Cardiovascular Laboratory, all measurements were performed with a dedicated high-tech device – Task Force Monitor

(TFM, CNSystems, Medizintechnik, Graz, Austria). The main area of TFM application is as an automated and computed beat-to-beat analysis of heart rate (electrocardiogram (ECG)) oscillometric and non-invasive continuous blood pressure measurements (oscBP, contBP). On the basis of these biological signals source hemodynamic and autonomic parameters are calculated. The TFM facilitates continuous (beat-to-beat), reliable and reproducible measurements of all parameters [15-18]. Basic statistics (mean, median. min, max and SD) of all ameters were calculated automatically for defined periods.

Protocol of autonomic assessment

All subjects were instructed to refrain from smoking, caffeine, alcohol ingestion, and intensive physical activity on the day of investigation and ate a light breakfast only. All investigations were performed at the same time of day, and took place in a neutral ambient temperature, quiet room [19,20].

In all cases TFM measurements were performed during 10 minutes of supine rest (phase 1) and subsequently asked to standing (phase 2) during which changes in heart rate were assessed and where haemodynamic changes were consistent with recognized consensus criteria for a diagnosis of postural tachycardia syndrome made [21].

Assessment of heart rate and blood pressure variability

All cardiovascular assessments were carried out with continuous heart rate and beat-to-beat blood pressure measurement implemented in TFM. The integrity of the autonomic nervous system was assessed using a three-channel ECG and continuous blood pressure monitoring (contBP – with periodically cross-checked oscillometric BP measurements). TFM automatically provides a power spectral analysis for heart rate variability (HRV) and blood pressure variability (BPV). HRV and BPV spectral analysis is conducted using the adaptive autoregressive model (AAR) proposed by Bianchi et al. [22] In addition to total power spectral density (PSD), three frequency bands are calculated with TFM: VLF, LF and HF, but only two of these were taken account of as there were short-term autonomic regulations of HR and BP i.e. LF 0.05-017 Hz (low-frequency band) and HF 0.17-0.4 Hz (high frequency band) in absolute values, and both frequencies were also calculated in normalized units (LFnu-RRI, HFnu-RRI for heart rate variability and LFnu-sBP, HFnu-sBP, LFnu-dBP and HFnu-dBP for systolic and diastolic blood pressure variability). Using only HRV bands when considering autonomic regulation has some limitations, therefore TFM also provides spectral analysis of blood pressure variability, a more reliable tool for sympathetic and parasympathetic autoregulation assessment. For that purpose bands: LFnu-RRI, LF-RRI, LF-sBP, LFnu-sBP, LF-dBP and LFnu-dBP are referred to as sympathetic modulation of sinoatrial (SA) node and

vasomotor function. Whilst HF-RRI and HFnu-RRI bands refer to parasympathetic modulation of cardiovascular activity. Cardiovascular disturbances of the autonomic circulatory regulation cause alternations in spectra and proportion of frequencies in the total spectrum power. Parameters such as PSD, LF and HF are quantitive indicators of autonomic regulation and the ratio between LF and HF band represents the sympatho-vagal balance [23-25].

We classified each individuals autonomic function profile into sympathetic or parasympathetic dominant according to their sympathetico-vagal balance during 10 minutes of supine rest. This was based upon previous studies and assessed using the LF/HF ratio which was considered to suggest a sympathetic dominant pattern if LF/HF was >1 and parasympathetic if the ratio was <1. [26, 27]

RESULTS

Recruitment of the cohort – the prevalence of fatigue in a Polish population

During the media campaign 1400 individuals identified themselves to the research team as fitting, they believed, the criteria for CFS. 1308 of those subsequently were found not to meet the Fukuda criteria for chronic fatigue syndrome.

In the 1308 (93%) individuals who identified themselves as fatigued, recognized chronic conditions were identified. These were conditions associated with the symptom of fatigue and therefore could have been the attributable cause for their fatigue symptoms (and therefore not consistent with the Fukuda diagnostic criteria). These fatigue associated conditions were broadly classified into conditions that were: neurological (n=280, 21.5%), neurodegenerative (n=200, 15%), psychiatric (n=654, 50%) and immunologic (n=174, 13.5%) disorders.

Characteristics of a polish cohort of CFS patients meeting the Fukuda criteria

Of the total group with CFS, 41 were female (59.4%). The majority of individuals had a normal BMI (58%) with 24 (35%) being considered overweight and 3 (4.3%) being obese. Two individuals (2.9%) were considered underweight. The majority of individuals were considered to be of a specialist professional group (engineers).

Symptom burden of a polish cohort of CFS patients meeting the Fukuda criteria

The majority of those with CFS had had symptoms for over 2 years with 37% having symptoms for 2-5 years and 21.7% having symptoms for more than 10 years. The vast majority described unrefreshing sleep with impaired short memory and concentration (91.3%), post-exertional malaise 89%, multi-joint pain without swelling or redness 72.5%, headaches 62.3%, muscle pain 66.7%, sore throat 39.1% and tender cervical or axillary lymph nodes 30.4%.

Table 1 shows the prevalence of other symptoms identified in those found to have Fukuda CFS. This illustrates the fact that many clinical specialists may come into contact with individuals who may subsequently be identified as having chronic fatigue syndrome. When COMPASS 31 scores were considered these are shown in **Table 2** with 50% of individuals with CFS/ME having symptoms consistent with orthostatic intolerance. HAD scores were high for both anxiety and depression. 43/69 (62%) were found to have ESS scores >=10 i.e. consistent with excessive daytime sleepiness. Considering scores from HADS A & D, 26/69 (38%) had scores consistent with significant anxiety and 22/69 (32%) depression.

Quality of life of a polish cohort of CFS patients meeting the Fukuda criteria

Quality of life scores assessed using the QOLS were mean (SD) 64 (11). This confirmed that quality of life is significantly impaired in those with Fukuda criteria CFS and well below the expected for a healthy population. When we considered the relationship between quality of life and the other symptoms frequently seen in those with CFS, there were strong significant negative relationships between quality of life and fatigue ($p<0.0001$), anxiety ($p=0.0009$), depression ($p<0.0001$) and autonomic symptoms ($p=0.04$). There were no significant relationships between age or daytime sleepiness.

Autonomic function in a polish cohort of CFS patients meeting the Fukuda criteria

When we classified the cohort according to predominance of sympathetic or parasympathetic function, 44/69 (64%) were found to be sympathetic predominant and 25 parasympathetic. When we considered symptom burden between these two phenotypes, there were no significant differences in symptoms or impact upon quality of life between the groups (**Table 3**). At rest, the sympathetic predominant group had significantly higher heart rate, ER and LF HRV and reduced LVET, PEP and HF HRV compared to the parasympathetic group. The total PSD was comparable between groups however sympatheticovagal balance was different between the phenotypes with increased LF BPV in both diastolic and systolic blood pressure, reduced baroreflex sensitivity in those with the sympathetic dominant phenotype (**Table 4**).

Those with the parasympathetic predominant phenotype were more likely to have had the disease for between 5-10 years (**table 5**).

Prevalence of postural tachycardia syndrome in a Polish cohort of CFS patients

The presence of postural tachycardia syndrome is frequently seen in those with CFS [28,29]. A total of 35 (51%) of the CFS group had haemodynamic responses to standing consistent with a diagnosis of PoTS. There was no difference in the proportion of those with PoTS in the sympathetic or parasympathetic groups (**Table 5**).

DISCUSSION

This study has confirmed for the first time that fatigue is a common symptom experienced by the Polish population and that CFS is an under recognized syndrome in this group. When CFS is identified and studied, it is clear that, as in other European and US studies, it is a condition associated with a large symptom burden and impaired quality of life.

We believe that the numbers of patients we have identified in this cohort are a huge under estimate of the true prevalence of fatigue. We chose to publicise our project via radio and television adverts using both national and local media. The response was overwhelming and our initial plans to respond to by telephone proved to be impossible due to the sheer number of responses. We therefore were forced to change our identification strategy to invite respondants to self present via email, then being directed to a web portal. We believe therefore that our findings represent a significant under estimate of fatigue and its impact in Poland and would suggest that formal epidemiological studies are required.

Our study confirms that fatigue is very common in a Polish population but that this is frequently related to other conditions rather than to chronic fatigue syndrome. Of the cohort of 1400 who self-presented with fatigue only 69 subsequently were confirmed as having CFS using the Fukuda criteria. This suggests that in Poland there is significant amounts of fatigue related to other conditions, with only a small percentage of those experiencing fatigue having chronic fatigue syndrome (69/1400; 5%).

From the initial responses, we rigorously identified those who met with Fukuda criteria for CFS. We did this by asking individuals to complete the tool, but also using face to face sessions with trained clinicians. We believe therefore, that our cohort represents a well characterized group who we are confident fulfil one of the recognised diagnostic criteria for CFS. When we compared this Polish cohort with CFS to other national cohorts there were some similarities, but also some differences.

Compared to the UK cohort [30] with in excess of 6500 individuals collected from the UK NHS Clinical CFS services, the Polish cohort appeared to be of a similar age to the UK cohort with comparable levels of fatigue and illness duration, have similar levels of sleep and cognitive symptoms but less post exertional malaise, muscle pain and headaches. The Polish cohort appeared to have more males than was seen in the UK cohort.

These differences might arise because of the self report nature of the Polish cohort and that the UK cohort was recruited from the national health service clinical services which were specifically set up to identify and manage CFS [3]. A comprehensive review of the prevalence of CFS/ME in three regions of England involving 143000 subjects suggested an older cohort with longer disease duration than that seen in the UK clinical services

An Australian cohort [31] was established using similar identification strategies to our Polish cohort with self-report in response to adverts inviting individuals to participate in a research database. Individuals in this cohort were included if they had received the diagnosis from a primary care physician. Again the proportion of females in the Australian cohort was higher than in the Polish cohort

As in previous national cohorts [3, 30, 31], the presence of fatigue in the Polish population was associated with impaired quality of life. As has been seen previously impaired quality of life associates with the severity of symptoms such as fatigue and autonomic dysfunction, but in contrast to other studies not daytime sleepiness. Impaired quality of life is also associated with increased anxiety and more depression. As in other series, we would suggest that this association is a secondary phenomena i.e. arising as a consequence of the condition rather than a cause. The fact that we rigorously excluded depression and psychiatric disorders when determining the criteria would be consistent with this.

Our study has also confirmed a high prevalence of the condition postural tachycardia syndrome (PoTS). This form of dysautonomia [21] has been recognized as occurring frequently in those with CFS [28,29], and represents a potential therapeutic target in those with CFS. It is important that clinicians and researchers are aware of the overlap and trained to identify and manage this condition.

This study has a number of limitations. The case ascertainment process used self report as the means of identifying those with CFS. It became clear during the radio and television campaign that there was considerable interest, and as a result our recruitment process needed to be changed to facilitate timely screening of those self presenting with fatigue. It is clear that a thorough, methodologically robust epidemiological study of fatigue and its consequences in a Polish population are now needed.

Our study has confirmed that fatigue is a common and under recognised symptom affecting the Polish population. It impacts upon quality of life and is associated with a range of other symptoms that have been previously recognised in other cohort studies. Despite this, there are no clinical services for fatigue or CFS in Poland and it is poorly understood and infrequently diagnosed. Our research programme now aims to consider the effect of interventions upon fatigue in a Polish CFS population.

Contributorships: JS and PZ were involved in writing of the manuscript. JS, PZ, JJK and MTF conceived and supervised the study. SK provided statistical advice. JS, PZ, JN contributed

conceived, designed and performed the experiments, collected and analyzed the data, revising it critically for important intellectual content and final approval of the version to be submitted.

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TABLE 1: OTHER SYMPTOMS REPORTED AT INITIAL ASSESSMENT, N=69

Specific symptom	No	%
IBS	12	17.7
Migraine	17	24.6
seasonal allergy	8	11.6
slight food intolerance / nausea / alcohol intolerance	40	58.1
back pain	13	18.8
Tinnitus	9	13.0
palpitations with no cardiac history	9	13.0
periodical fever	8	11.6
sensory disturbances	0	0
chest symptoms with no medical history	15	21.7
mood fluctuations	30	43.5
chronic stress	41	59.4
overworked / work stress	34	49.3
shift work	0	0
care work	3	4.3
newborn care	7	10.1
frequent infections	9	13.0
night hyperhidrosis	22	31.9
sleep disturbance / hypersomnia	28	40.6
unexplained anxiety	3	4.3
sensory disturbance	10	14.5

TABLE 2: COMPASS 31 - AUTONOMIC SYMPTOMS, N=69

Specific symptom	No	%
orthostatic intolerance	40	50.0
dizziness / headaches	41	59.4
sudden paleness	25	36.2
arrhythmia	29	42.0
dryness eyes mouth	45	65.2
vasomotor	24	34.8
secretomotor	30	43.5
upper gastro. tract symptoms	38	55.1
unknown gastro. pain	26	37.7
constipation	21	30.4
diarrhea	28	40.6
urinary	21	30.4
sexual failure	19	27.5
sleep	68	98.5
pupilomotor	28	40.6
anxiety	34	49.3

TABLE 3: BASELINE QUALITY OF LIFE SCORES, N=69

	Total Group		Sympathetic dominant (n=44)		parasympathetic dominant (n=25)		
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Chalder Fatigue Scale	25.3	3.7	25.5	3.8	25.0	3.8	p>0.05
Fatigue Severity Scale	48.8	8.7	48.0	8.5	50.2	9.1	p>0.05
Fatigue Impact Scale	92.2	26.2	92.6	24.6	91.6	29.2	p>0.05
HADS_A	9.6	3.4	9.3	3.1	10.1	3.9	p>0.05
HADS_D	8.5	3.1	8.5	3.0	8.6	3.4	p>0.05
BDI	17.6	8.1	18.3	8.3	16.4	7.9	p>0.05
Epworth Sleepiness Scale	10.3	5.6	10.6	5.3	9.8	6.2	p>0.05
Quality of Life Scale	63.5	10.9	62.1	11.9	65.9	8.8	p>0.05
Orthostatic Grading Scale	8.4	3.1	3.5	3.4	3.4	2.5	p>0.05

TABLE 4 CARDIOVASCULAR / AUTONOMIC PARAMETERS

	Variable	Total group (n=69)		Sympathetic dominant (n=44)		parasympathetic dominant (n=25)		
		Mean	SD	Mean	SD	Mean	SD	
Haemodynamics	**HR**	67.6	9.2	70.1	8.4	63.2	9.0	0.0017
	Sbp	117.3	13.3	118.5	11.3	115.2	16.2	p>0.05
	Dbp	79.3	10.6	79.6	9.7	78.8	12.1	p>0.05
	mBP	95.9	11.1	96.0	9.9	95.7	13.2	p>0.05
Cardiac Impedance	**SI**	52.3	12.4	50.8	12.5	54.9	12.1	p>0.05
	CI	3.5	0.8	3.5	0.8	3.4	0.8	p>0.05
	TPRI	2304.7	747.3	2285.2	684.3	2339.0	861.1	p>0.05
	EDI	85.0	19.9	82.3	19.9	89.7	19.5	p>0.05
	IC	62.8	21.2	59.7	20.6	68.2	21.5	p>0.05
	ACI	85.7	34.4	80.4	33.8	95.0	34.3	p>0.05
	LVWI	4.4	1.1	4.5	1.1	4.4	1.2	p>0.05
	LVET	318.2	17.3	313.2	18.2	327.0	11.1	0.0005
	TFC	31.3	4.5	30.8	4.7	32.3	4.0	p>0.05
	PEP	110.2	12.1	107.1	11.3	115.7	11.6	0.0040
	STR	34.9	4.3	34.6	4.7	35.5	3.4	p>0.05
	ER	35.5	3.3	36.3	2.6	34.2	3.9	0.0092
	MSER	300.8	68.9	306.2	72.5	291.4	62.4	p>0.05
	REP	77.8	16.8	79.7	19.8	74.5	9.1	p>0.05
	HI	0.3	0.1	0.3	0.1	0.4	0.1	p>0.05
	RZ	187.1	12.2	185.3	11.1	190.4	13.6	p>0.05
	TAC	2.6	0.7	2.5	0.7	2.8	0.8	p>0.05
Heart rate variability	**LFnu-RRI**	54.2	17.2	62.2	14.0	40.1	12.7	0.0000
	HFnu-RRI	45.8	17.2	37.8	14.0	59.9	12.7	0.0000
	PSD-RRI	1684.1	1993.7	1604.9	2166.9	1823.4	1678.7	p>0.05
	LF/HF-RRI	1.7	1.6	2.3	1.8	0.8	0.4	0.0000
Diastolic Blood pressure variability	**LFnu-Dbp**	52.2	14.7	59.7	10.2	38.9	11.7	0.0000
	HFnu-dBP	14.0	10.4	11.0	7.5	19.3	12.7	0.0004
	PSD-dBP	13.6	16.5	15.2	19.3	10.8	9.5	p>0.05
	LF/HF-dBP	6.6	6.2	8.7	6.8	2.8	1.8	0.0000
Systolic Blood pressure variability	**LFnu-sBP**	42.1	13.5	47.5	10.7	32.6	12.9	0.0000
	HFnu-sBP	16.5	10.8	15.6	11.0	18.2	10.4	p>0.05
	PSD-sBP	20.2	30.2	17.5	16.3	25.0	45.5	p>0.05
	LF/HF-sBP	3.8	2.8	4.5	3.0	2.5	1.7	0.0019
Baroreflex parameters	**Total Event Count**	17.4	13.6	21.5	14.4	10.2	8.4	0.0006
	Total Slope Mean	19.6	13.0	16.7	8.9	24.8	17.2	0.0114
	Total BEI	70.5	15.1	72.4	14.2	67.0	16.4	p>0.05

TABLE 5: POTS (SYMPATHETIC, N=44; PARASYMPATHETIC, N=25)

		sympathetic dominant		parasympathetic dominant		
		No	%	No	%	p
PoTS		22	45.5	12	48	p>0.05
Fatigue period	6 month - 2 years	8	22.9	8	23.5	p>0.05
	2-5 years	14	40.0	12	35.3	p>0.05
	5-10 years	4	11.4	8	23.5	0.0492
	more than 10 years	9	25.7	6	17.6	p>0.05
Fatigue period IQR		2-5 years		6 month - 2 years		
Fatigue period in years IQR		8		2.5		

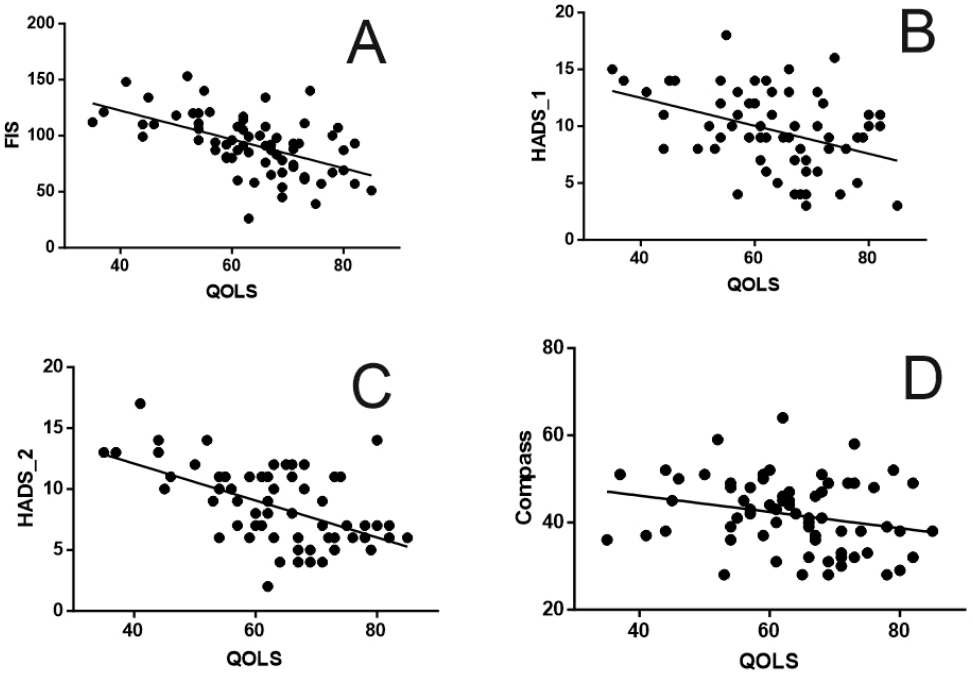

Figure 2: The relationship between quality of life measured using the QOLS scale and a) fatigue severity assessed using the fatigue impact scale b) anxiety measured using the HADS Anxiety scale (HADS -1) c) depression measured using the HADS Depression Scale (HADS – 2) and d) autonomic symptom burden measured using the COMPASS 31

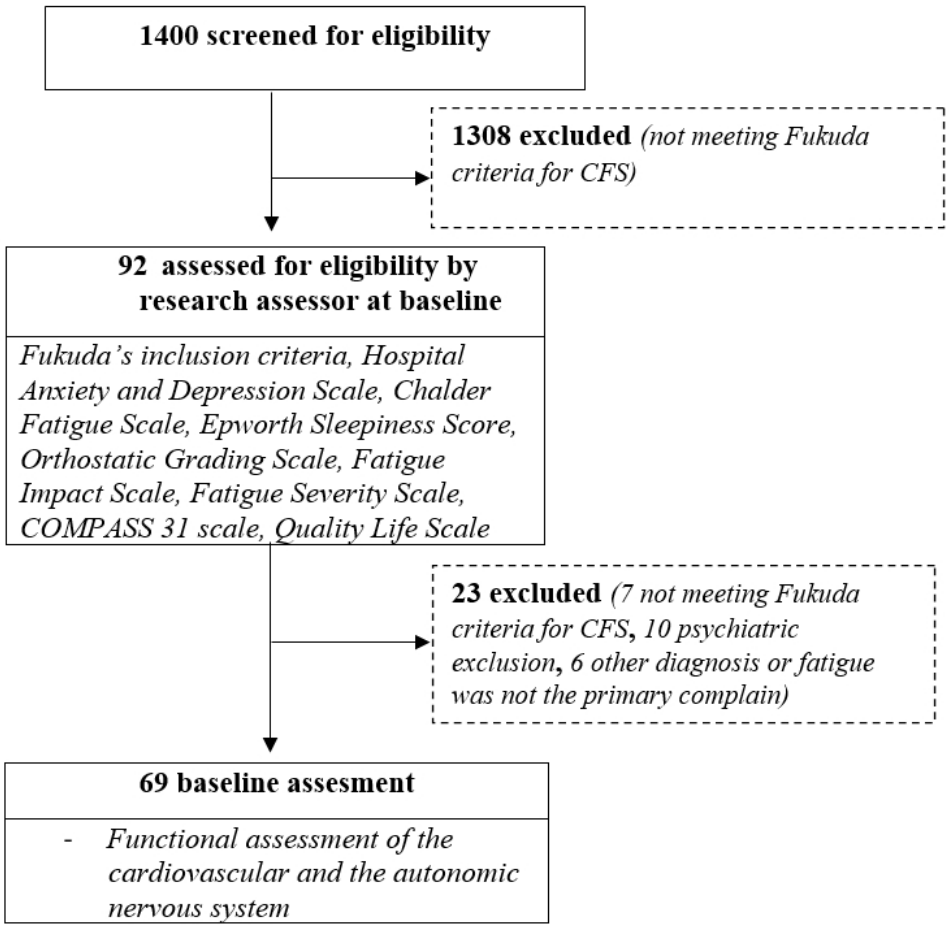

Figure 1: Study protocol

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Chronic fatigue syndrome/Myalgic encephalomyelitis (CFS/ME) is common in Poland and associated with significant symptoms and impairment in quality of life – a cross sectional study of the prevalence of CFS/ME in Polish population

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Chronic fatigue syndrome/Myalgic encephalomyelitis (CFS/ME) is common in Poland and associated with significant symptoms and impairment in quality of life – a cross sectional study of the prevalence of CFS/ME in Polish population

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Abstract

Objectives: The aim of this study was to estimate the prevalence of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and describe illness characteristics in a community population in Poland.Design: cross-sectional study

Setting: Poland

Participants: Of the cohort of 1400 who self-presented with fatigue only 69 subsequently were confirmed as having CFS/ME using the Fukuda criteria.

Main outcome measures: Participants completed the following screening symptom assessment tools: Chalder fatigue scale, Hospital anxiety and depression scale (HADS), Epworth sleepiness scale (ESS), COMPASS 31, Quality of life scale (QOLS). Hemodynamic and autonomic parameters were automatically measured at rest with a Task Force Monitor.

Results: In 1308 from 1400 (93%) individuals who identified themselves as fatigued, recognized chronic conditions were identified e.g. neurological (n=280, 21.5%), neurodegenerative (n=200, 15%), psychiatric (n=654, 50%) and immunologic (n=174, 13.5%) disorders. The remaining 69 participants (mean age 38.3±8.5) met the Fukuda defintion for CFS/ME and had baseline objective assessment. The majority had experienced symptoms for over 2 years with 37% having symptoms for 2-5 years and 21.7% for more than 10 years. The Composite Autonomic Symptom Score 31 (COMPASS 31) indicated that 50% have symptoms consistent with orthostatic intolerance. 43/69 (62%) had Epworth sleepiness scores >=10 i.e. consistent with excessive daytime sleepiness, 26/69 (38%) had significant anxiety and 22/69 (32%) depression measured by HADS A & D. Quality of life is significantly impaired in those with Fukuda criteria CFS (QLS score 64±11) with significant negative relationships between quality of life and fatigue ($p<0.0001$), anxiety ($p=0.0009$), depression ($p<0.0001$) and autonomic symptoms ($p=0.04$).

Conclusion: This is the first study to summarize illness characteristics of Polish CFS/ME patients. Our study has confirmed that fatigue is a common and under-recognised symptom affecting the Polish population.

Key words: chronic fatigue, epidemiology, prevalence, quality of life

Strengths and limitations of this study

- This is the first study to summarize illness characteristics of a cohort of Polish CFS/ME patients.

- We used Fukuda criteria to indicate patients with CFS/ME. An identified cohort was examined in a comprehensive manner.
- The main potential limitation could be the manner in which patients were identified. However the alternative approach of identification through primary care may have yielded very few patients, because there is little recognition of the chronic fatigue syndrome in Poland.
- Methodologically more robust epidemiological studies of fatigue and its consequences in the Polish population are now needed.

Introduction

Diagnostics and treatment of the Chronic Fatigue Syndrome/Myalgic encephalomyelitis (CFS/ME) present a challenge to specialists as this syndrome is not a clearly identified, uniform disease but a set of symptoms resembling those occurring in other diseases, in which a sense of chronic fatigue predominates. In some countries (e.g Poland), CFS/ME is diagnosed very rarely, which may be associated with the fact that the aetiology of the disease is still poorly known, and with diagnostic problems resulting from a lack of detailed and uniform guidelines allowing an unambiguous diagnosis and initiation of effective treatment in CFS/ME patients.

The available studies provide several diagnostic criteria based on a definition of the American Centers for Disease Control (CDC), the Oxford Criteria, or the Canadian Guidelines. Criteria proposed by CDC (Fukuda et al. 1994) are most commonly used as acceptable diagnostic criteria when recruiting CFS/ME patients for scientific studies. However, they are encumbered by several disadvantages (e.g. fatigue experienced for at least 6 months), which – from the point of view of clinical practice – may delay a diagnosis in patients who do not meet this criterion precisely. The Oxford criteria propose a new diagnostic approach, focusing mainly on an aspect of mental rather than somatic fatigue. The Canadian criteria (CDC) expand the CFS/ME definition with additional diagnostic criteria, i.e. post-exertional malaise and presence of neurological, endocrine, cognitive and autonomic (orthostatic intolerance) disorders. The proposed CFS/ME definition, including malaise and symptoms exacerbation after exercise, allows differentiating CFS/ME patients from patients with depression or fibromyalgia. Alternative criteria, such as the International Consensus Criteria (ICC), disclose a further range of symptoms pertaining to the neurological, immunological, gastrointestinal, and autonomic systems.

Its global prevalence, ranging between 0.4% and 2.5%, is growing; most commonly, it is observed in the group of 20–40-year-olds, more frequently in professionally active women. CFS/ME is considered to be a common condition in countries such as the UK, Australia and the US [1,2]. In the UK, it affects up to 250,000 individuals with frequencies reported of up to 0.2% [3]. In the UK, Fukuda-defined cases have a prevalence of 0.2%. In the US, the prevalence of Fukuda-defined cases has been reported between 0.2%5 and 0.4%. Finding from the Australian cohort showed that from 535 patients diagnosed with CFS/ME by a primary care physician, 30.28% met Fukuda criteria. To date CFS/ME has not been reported in Poland, nor its prevalence defined. There are currently no CFS/ME Clinical services.

The aim of this study was to summarize sociodemographic and illness characteristics in those reporting CFS/ME symptoms in a Polish population. We set out to define the presence and characteristics of CFS/ME in Poland in order to identify a cohort of those patients who could potentially participate in further research studies.

METHODS

Setting

This study took place from March 2014 till July 2016 and was approved by the Ethics Committee, Ludwik Rydygier Memorial Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University, Toruń. Written informed consent was obtained from all of the participants.

Participants

Recruitment was based on self-identification in response to an advertisement in CFS/ME community support networks across Poland, as well as a general advertisement on local radio and social media.

Initially any individuals willing to participate were directed to a phone line. Within days of setting up the phone line it became clear that this mechanism to identify and recruit potential participants would be overwhelmed. The team therefore directed all potential participants to a website where more information about the study was available and where individuals were invited to self-complete the Fukuda criteria online. If individuals, on completing the online scoring, felt that they met the Fukuda criteria [4] within 7 days they were invited to attend the research facility. To be eligible for this study, participants were required to 1) meet Fukuda criteria, 2) be between 25 and 65 years of age, and 3) be a resident of Poland. The identification process is shown in **Figure 1**.

Patient and public involvement

Patients were not involved in the design of this study. Results from the current study will be disseminated to participants through newsletters in layman terms. We will also communicate our results through a number of other scientific and non-scientific channels including presentations at relevant congresses or in relevant fora.

Clinical assessment

Those who fulfilled the eligibility criteria for Centers for Disease Control and Prevention (Fukuda) were invited to attend the research unit at the chronobiology laboratory (windowless and sound-insulated room, temperature 22°C, humidity 60%). They were seen by members of the research team in an assessment that took place over 40 minutes. Individuals participated in a standardized baseline assessment which comprised a battery of symptom assessment tools. Those screened as fulfilling criteria for CFS/ME [4] were also reviewed clinically by a member of the research team in order to determine whether their symptoms were consistent with these criteria, that there were no psychiatric exclusions or other diagnoses that could be associated with CFS/ME or where fatigue was not the primary complaint. Sixty nine individuals subsequently went on to have a further baseline objective assessment.

Symptom assessment tools

Participants completed the following screening symptom assessment tools.

Measure of fatigue - Chalder fatigue scale

The Chalder Fatigue Scale (CFQ) is a self-administered questionnaire for measuring the extent and severity of fatigue within both clinical and non-clinical, epidemiological populations [5]. The CFQ provides an 11 item brief tool to measure both physical and psychological fatigue. Each item is answered on a 4-point scale ranging from the asymptomatic to maximum symptomatology, such as 'Better than usual', 'No worse than usual', 'Worse than usual' and 'Much worse than usual'. For all items, the least symptomatic answers are on the left of the response-set, providing an easy-to-understand checklist for respondents. Using the Likert scoring method, responses on the extreme left receive a score of 0, increasing to 1, 2 or 3 as they become more symptomatic. The respondent's global score ranges from 0 to 33. The global score also spans two dimensions—physical fatigue (measured by items 1–7) and psychological fatigue (measured by items 8–11). The Likert scoring system allows for means and distributions to be calculated for both the global total as well as the two sub-scales.

Reliability coefficients for the CFQ 11 have been high in studies of CFS/ME patients [6]. It has been used widely in studies ascertaining tiredness among working populations as well as patient groups and consistently fares extremely well against other longer and multidimensional tools [7].

Hospital anxiety and depression scale (HADS)

The HADS [8] is a 14-item measure of current anxiety (HADS-A) and depression (HADS-D). Caseness for anxiety or depression is revealed by subscores greater or equal to 11 on each subscale.

Epworth sleepiness scale (ESS)

In view of the association between excessive daytime sleepiness and fatigue, all subjects completed the ESS questionnaire (possible score range 0–24) [9]. This fully validated tool assesses daytime hypersomnolence, with a score ≥10 being indicative of significant hypersomnolence during the day.

COMPASS 31

Participants completed the Autonomic Symptom Profile [10] as a self-report measure of autonomic symptoms. However, scoring was performed according to the recently abbreviated and psychometrically improved version of this questionnaire, the Composite Autonomic Symptom Score 31 (COMPASS 31) [11]. Scoring consists of 31 items from six domains – orthostatic intolerance, vasomotor, secretomotor, gastrointestinal, bladder, pupillomotor – each weighted according to number of items and clinical relevance. Weighted individual domain scores are totalled to a maximum of 100, which indicates greater symptom load.

Assessment of quality of life

Participants also completed the following quality of life measure:

Quality of life scale (QOLS)

The Quality of Life Scale (QOLS) used in this study has 16 items. The QOLS has been used in studies of healthy adults and patients with rheumatic diseases, fibromyalgia, chronic obstructive pulmonary disease, gastrointestinal disorders, cardiac disease, spinal cord injury, psoriasis, urinary stress incontinence, posttraumatic stress disorder, and diabetes.

The QOLS is scored by adding up the score on each item to yield a total score for the instrument. Scores can range from 16 to 112. There is no automated administration or scoring software for the QOLS. Higher scores medicate better quality of life. The average total for healthy populations is approximately 90 [10-14].

Functional assessment of the cardiac and autonomic nervous system

Apparatus

All participants underwent formal autonomic assessment in the Cardiovascular Laboratory, all measurements were performed with a dedicated high-tech device – Task Force Monitor (TFM, CNSystems, Medizintechnik, Graz, Austria). The main area of TFM application is as an automated and computed beat-to-beat analysis of heart rate (electrocardiogram (ECG)) oscillometric and non-invasive continuous blood pressure measurements (oscBP, contBP). On the basis of these biological signals source hemodynamic and autonomic parameters are calculated. The TFM facilitates continuous (beat-to-beat), reliable and reproducible measurements of all parameters [15-18]. Basic statistics (mean, median. min, max and SD) of all parameters were calculated automatically for defined periods.

Protocol of autonomic assessment

All subjects were instructed to refrain from smoking, caffeine, alcohol ingestion, and intensive physical activity on the day of investigation and ate a light breakfast only. All investigations were performed at the same time of day, and took place in a neutral ambient temperature, and a quiet room [19,20].

In all cases TFM measurements were performed during 10 minutes of supine rest (phase 1) and subsequently asked to standing (phase 2) during which changes in heart rate were assessed and where haemodynamic changes were consistent with recognized consensus criteria for a diagnosis of postural tachycardia syndrome made [21].

Assessment of heart rate and blood pressure variability

All cardiovascular assessments were carried out with continuous heart rate and beat-to-beat blood pressure measurement implemented in TFM. The integrity of the autonomic nervous system was assessed using a three-channel ECG and continuous blood pressure monitoring (contBP – with periodically cross-checked oscillometric BP measurements). TFM automatically provides a power spectral analysis for heart rate variability (HRV) and blood pressure variability (BPV). HRV and BPV spectral analysis is conducted using the adaptive autoregressive model (AAR) proposed by Bianchi et al. [22]. In addition to total power spectral density (PSD), three frequency bands are calculated with TFM: VLF, LF and HF, but only two of these were taken into account as there were short-term autonomic regulations of HR and BP i.e. LF 0.05-017 Hz (low-frequency band) and HF 0.17-0.4 Hz (high frequency band) in absolute values, and both frequencies were also calculated in normalized units (LFnu-RRI, HFnu-RRI for heart rate variability and LFnu-sBP, HFnu-sBP, LFnu-dBP and HFnu-dBP for systolic and diastolic blood pressure variability). Using only HRV bands when considering autonomic regulation has some limitations, therefore TFM also provides spectral analysis of blood pressure variability, a more reliable tool for sympathetic and parasympathetic autoregulation assessment. For that purpose bands: LFnu-RRI, LF-RRI, LF-sBP, LFnu-sBP, LF-dBP and LFnu-dBP are referred to as sympathetic modulation of sinoatrial (SA) node and vasomotor function. Whilst HF-RRI and HFnu-RRI bands refer to parasympathetic modulation of cardiovascular activity. Cardiovascular disturbances of the autonomic circulatory regulation cause alternations in spectra and proportion of frequencies in the total spectrum power. Parameters such as PSD, LF and HF are quantitive indicators of autonomic regulation and the ratio between LF and HF band represents the sympatho-vagal balance [23-25].

We classified each individual's autonomic function profile into sympathetic or parasympathetic dominant according to their sympathetico-vagal balance during 10 minutes of supine rest. This

was based upon previous studies and assessed using the LF/HF ratio which was considered to suggest a sympathetic dominant pattern if LF/HF was >1 and parasympathetic if the ratio was <1. [26, 27]

Statistical analyses

Statistical characteristics of measured values were presented as arithmetic means and standard deviations (±SD). The normality of continuous variables distribution was evaluated with the *Shapiro–Wilk* test Depending on distribution characteristics of analysed variables, the independent samples Student t-test or the Mann–Whitney U test was used to evaluate significance of differences between measured values obtained in the group of each phenotypes. All calculations were performed with the package *Statistica 13.0* (StatSoft), with the assumed level of statistical significance of $\alpha<0.05$.

RESULTS

Recruitment of the cohort – the prevalence of fatigue in a Polish population

During the media campaign 1400 individuals identified themselves to the research team as fitting, they believed, the criteria for CFS/ME. 1308 of those subsequently were found not to meet the Fukuda criteria for CFS/ME.

In the 1308 (93%) individuals who identified themselves as fatigued, recognized chronic conditions were identified. These were conditions associated with the symptom of fatigue and therefore could have been the attributable cause for their fatigue symptoms (and therefore not consistent with the Fukuda diagnostic criteria). These fatigue associated conditions were broadly classified into conditions that were: neurological (n=280, 21.5%), neurodegenerative (n=200, 15%), psychiatric (n=654, 50%) and immunologic (n=174, 13.5%) disorders.

Characteristics of a polish cohort of CFS/ME patients meeting the Fukuda criteria

Of the total group with CFS/ME, 41 were female (59.4%). The majority of individuals had a normal BMI (58%) with 24 (35%) being considered overweight and 3 (4.3%) being obese. Two individuals (2.9%) were considered underweight. The majority of individuals were considered to be of a specialist professional group (engineers).

Symptom burden of a polish cohort of CFS/ME patients meeting the Fukuda criteria

The majority of those with CFS/ME had had symptoms for over 2 years with 37% having symptoms for 2-5 years and 21.7% having symptoms for more than 10 years. The vast majority described unrefreshing sleep with impaired short-term memory and concentration (91.3%), post-exertional malaise 89%, multi-joint pain without swelling or redness 72.5%, headaches

62.3%, muscle pain 66.7%, sore throat 39.1% and tender cervical or axillary lymph nodes 30.4%.

Table 1 shows the prevalence of other symptoms identified in those found to have Fukuda CFS/ME. This illustrates the fact that many clinical specialists may come into contact with individuals who may subsequently be identified as having CFS/ME. When COMPASS 31 scores were considered these are shown in **Table 2** with 50% of individuals with CFS/ME having symptoms consistent with orthostatic intolerance. HAD scores were high for both anxiety and depression and 43/69 (62%) were found to have ESS scores >=10 i.e. consistent with excessive daytime sleepiness. Considering scores from HADS A & D, 26/69 (38%) had scores consistent with significant anxiety and 22/69 (32%) depression.

Quality of life of a polish cohort of CFS/ME patients meeting the Fukuda criteria

Quality of life scores assessed using the QOLS were mean (SD) 64 (11). This confirmed that quality of life is significantly impaired in those with Fukuda criteria CFS/ME and well below the expected for a healthy population. When we considered the relationship between quality of life and the other symptoms frequently seen in those with CFS/ME, there were strong significant negative relationships between quality of life and fatigue ($p<0.0001$), anxiety ($p=0.0009$), depression ($p<0.0001$) and autonomic symptoms ($p=0.04$), figure 2. There were no significant relationships between age or daytime sleepiness.

Autonomic function in a polish cohort of CFS/ME patients meeting the Fukuda criteria

When we classified the cohort according to predominance of sympathetic or parasympathetic function, 44/69 (64%) were found to be sympathetic predominant and 25 parasympathetic. When we considered symptom burden between these two phenotypes, there were no significant differences in symptoms or impact upon quality of life between the groups (**Table 3**). At rest, the sympathetic predominant group had significantly higher heart rate, ER and LF HRV and reduced LVET, PEP and HF HRV compared to the parasympathetic group. The total PSD was comparable between groups however sympatheticovagal balance was different between the phenotypes with increased LF BPV in both diastolic and systolic blood pressure, reduced baroreflex sensitivity in those with the sympathetic dominant phenotype (**Table 4**).

Those with the parasympathetic predominant phenotype were more likely to have had the disease for between 5-10 years (**table 5**).

Prevalence of postural tachycardia syndrome in a Polish cohort of CFS/ME patients

The presence of postural tachycardia syndrome is frequently seen in those with CFS [28,29]. A total of 35 (51%) of the CFS group had haemodynamic responses to standing consistent with

a diagnosis of PoTS. There was no difference in the proportion of those with PoTS in the sympathetic or parasympathetic groups (**Table 5**).

DISCUSSION

This study has confirmed for the first time that chronic fatigue is a common symptom experienced by the Polish population and that CFS/ME is an under-recognized syndrome in this group. The key finding of this study is that prevalence is similar to reported data in the other countries and is associated with a large symptom burden and impaired quality of life.

Of the cohort of 1400 who self-presented with fatigue only 69 subsequently were confirmed as having CFS/ME using the Fukuda criteria. This suggests that in Poland there are significant amounts of fatigue related to other conditions, with only a small percentage of those experiencing fatigue having CFS/ME *per se* (69/1400; 5%).

From the initial responses, we rigorously identified those who met with Fukuda criteria for CFS/ME. We did this by asking individuals to complete the tool, but also using face to face sessions with trained clinicians. We believe therefore, that our cohort represents a well characterized group who we are confident fulfil one of the recognised diagnostic criteria for CFS/ME. When we compared this Polish cohort with CFS/ME to other national cohorts there were some similarities, but also some differences.

Compared with the UK cohort [30] having in excess of 6500 individuals collected from the UK NHS Clinical CFS services, the Polish cohort appeared to be of a similar age to the UK cohort with comparable levels of fatigue and illness duration, have similar levels of sleep and cognitive symptoms but less post-exertional malaise, muscle pain and headaches. The Polish cohort appeared to have more males than was seen in the UK cohort.

As in previous national cohorts [3, 30, 31], the presence of fatigue in the Polish population was associated with impaired quality of life. As has been seen previously, impaired quality of life associates with the severity of symptoms such as fatigue and autonomic dysfunction, but in contrast to other studies, not daytime sleepiness. Impaired quality of life is also associated with increased anxiety and more depression. As in other series, we would suggest that this association is a secondary phenomenon i.e. arising as a consequence of the condition rather than a cause. The fact that we rigorously excluded depression and psychiatric disorders when determining the criteria would be consistent with this.

Our study has also confirmed a high prevalence of the condition postural tachycardia syndrome (PoTS). This form of dysautonomia [21] has been recognized as occurring frequently in those with CFS/ME [28,29], and represents a potential therapeutic target in those with this illness. It

is important that clinicians and researchers are aware of the overlap and are trained to identify and manage this condition.

All of these differences might arise because of the self-report nature of the Polish cohort and that the UK cohort was recruited from the National Health Service clinical services which were specifically set up to identify and manage CFS/ME [3]. A comprehensive review of the prevalence of CFS/ME in three regions of England involving 143,000 subjects suggested an older cohort with longer disease duration than that seen in the UK clinical services.

An Australian cohort [31] was established using similar identification strategies to our Polish cohort with self-report in response to adverts inviting individuals to participate in a research database. Individuals in this cohort were included if they had received the diagnosis from a primary care physician. Again the proportion of females in the Australian cohort was higher than in the Polish cohort

This study has a number of limitations. The case ascertainment process used self-report as the means of identifying those with CFS/ME. It became clear during the radio and television campaign that there was considerable interest, and as a result our recruitment process needed to be changed to facilitate timely screening of those self-presenting with fatigue. It is clear that a thorough, methodologically robust epidemiological study of fatigue and its consequences in a Polish population are now needed.

Our study has confirmed that fatigue is a common and under-recognised symptom affecting the Polish population. It impacts upon quality of life and is associated with a range of other symptoms that have been previously recognised in other cohort studies. Despite this, there are no clinical services for fatigue or CFS/ME in Poland and it is poorly understood and infrequently diagnosed. Our research programme now aims to consider the effect of interventions upon fatigue in a Polish CFS/ME population.

Figure legends

Figure 1: Study protocol

Figure 2: The relationship between quality of life measured using the QOLS scale and a) fatigue severity assessed using the fatigue impact scale b) anxiety measured using the HADS Anxiety scale (HADS -1) c) depression measured using the HADS Depression Scale (HADS – 2) and d) autonomic symptom burden measured using the COMPASS 31

Contributorship statement

JS, DS, SMG, PZ were involved in writing of the manuscript. JS, PZ, JJK and MTF conceived and supervised the study. SK, PZ provided statistical advice. JS, PZ, JN, DS., SMG contributed conceived, designed and performed the experiments, collected and analyzed the data, revising it critically for important intellectual content and final approval of the version to be submitted.

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TABLE 1: OTHER SYMPTOMS REPORTED AT INITIAL ASSESSMENT, N=69

Specific symptom	No	%
IBS	12	17.7
Migraine	17	24.6
seasonal allergy	8	11.6
slight food intolerance / nausea / alcohol intolerance	40	58.1
back pain	13	18.8
Tinnitus	9	13.0
palpitations with no cardiac history	9	13.0
periodical fever	8	11.6
sensory disturbances	0	0
chest symptoms with no medical history	15	21.7
mood fluctuations	30	43.5
chronic stress	41	59.4
overworked / work stress	34	49.3
shift work	0	0
care work	3	4.3
newborn care	7	10.1
frequent infections	9	13.0
night hyperhidrosis	22	31.9
sleep disturbance / hypersomnia	28	40.6
unexplained anxiety	3	4.3
sensory disturbance	10	14.5

TABLE 2: COMPASS 31 - AUTONOMIC SYMPTOMS, N=69

Specific symptom	No	%
orthostatic intolerance	40	50.0
dizziness / headaches	41	59.4
sudden paleness	25	36.2
arrhythmia	29	42.0
dryness eyes mouth	45	65.2
vasomotor	24	34.8
secretomotor	30	43.5
upper gastro. tract symptoms	38	55.1
unknown gastro. pain	26	37.7
constipation	21	30.4
diarrhea	28	40.6
urinary	21	30.4
sexual failure	19	27.5
sleep	68	98.5
pupilomotor	28	40.6
anxiety	34	49.3

TABLE 3: BASELINE QUALITY OF LIFE SCORES, N=69

	Total Group		Sympathetic dominant (n=44)		parasympathetic dominant (n=25)		
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Chalder Fatigue Scale	25.3	3.7	25.5	3.8	25.0	3.8	p>0.05
Fatigue Severity Scale	48.8	8.7	48.0	8.5	50.2	9.1	p>0.05
Fatigue Impact Scale	92.2	26.2	92.6	24.6	91.6	29.2	p>0.05
HADS_A	9.6	3.4	9.3	3.1	10.1	3.9	p>0.05
HADS_D	8.5	3.1	8.5	3.0	8.6	3.4	p>0.05
BDI	17.6	8.1	18.3	8.3	16.4	7.9	p>0.05
Epworth Sleepiness Scale	10.3	5.6	10.6	5.3	9.8	6.2	p>0.05
Quality of Life Scale	63.5	10.9	62.1	11.9	65.9	8.8	p>0.05
Orthostatic Grading Scale	8.4	3.1	3.5	3.4	3.4	2.5	p>0.05

TABLE 4 CARDIOVASCULAR / AUTONOMIC PARAMETERS

	Variable	Total group (n=69)		Sympathetic dominant (n=44)		parasympathetic dominant (n=25)		
		Mean	SD	Mean	SD	Mean	SD	
Haemodynamics	**HR**	67.6	9.2	70.1	8.4	63.2	9.0	0.0017
	Sbp	117.3	13.3	118.5	11.3	115.2	16.2	p>0.05
	Dbp	79.3	10.6	79.6	9.7	78.8	12.1	p>0.05
	mBP	95.9	11.1	96.0	9.9	95.7	13.2	p>0.05
Cardiac Impedance	**SI**	52.3	12.4	50.8	12.5	54.9	12.1	p>0.05
	CI	3.5	0.8	3.5	0.8	3.4	0.8	p>0.05
	TPRI	2304.7	747.3	2285.2	684.3	2339.0	861.1	p>0.05
	EDI	85.0	19.9	82.3	19.9	89.7	19.5	p>0.05
	IC	62.8	21.2	59.7	20.6	68.2	21.5	p>0.05
	ACI	85.7	34.4	80.4	33.8	95.0	34.3	p>0.05
	LVWI	4.4	1.1	4.5	1.1	4.4	1.2	p>0.05
	LVET	318.2	17.3	313.2	18.2	327.0	11.1	0.0005
	TFC	31.3	4.5	30.8	4.7	32.3	4.0	p>0.05
	PEP	110.2	12.1	107.1	11.3	115.7	11.6	0.0040
	STR	34.9	4.3	34.6	4.7	35.5	3.4	p>0.05
	ER	35.5	3.3	36.3	2.6	34.2	3.9	0.0092
	MSER	300.8	68.9	306.2	72.5	291.4	62.4	p>0.05
	REP	77.8	16.8	79.7	19.8	74.5	9.1	p>0.05
	HI	0.3	0.1	0.3	0.1	0.4	0.1	p>0.05
	RZ	187.1	12.2	185.3	11.1	190.4	13.6	p>0.05
	TAC	2.6	0.7	2.5	0.7	2.8	0.8	p>0.05
Heart rate variability	**LFnu-RRI**	54.2	17.2	62.2	14.0	40.1	12.7	0.0000
	HFnu-RRI	45.8	17.2	37.8	14.0	59.9	12.7	0.0000
	PSD-RRI	1684.1	1993.7	1604.9	2166.9	1823.4	1678.7	p>0.05
	LF/HF-RRI	1.7	1.6	2.3	1.8	0.8	0.4	0.0000
Diastolic Blood pressure variability	**LFnu-Dbp**	52.2	14.7	59.7	10.2	38.9	11.7	0.0000
	HFnu-dBP	14.0	10.4	11.0	7.5	19.3	12.7	0.0004
	PSD-dBP	13.6	16.5	15.2	19.3	10.8	9.5	p>0.05
	LF/HF-dBP	6.6	6.2	8.7	6.8	2.8	1.8	0.0000
Systolic Blood pressure variability	**LFnu-sBP**	42.1	13.5	47.5	10.7	32.6	12.9	0.0000
	HFnu-sBP	16.5	10.8	15.6	11.0	18.2	10.4	p>0.05
	PSD-sBP	20.2	30.2	17.5	16.3	25.0	45.5	p>0.05
	LF/HF-sBP	3.8	2.8	4.5	3.0	2.5	1.7	0.0019
Baroreflex parameters	**Total Event Count**	17.4	13.6	21.5	14.4	10.2	8.4	0.0006
	Total Slope Mean	19.6	13.0	16.7	8.9	24.8	17.2	0.0114
	Total BEI	70.5	15.1	72.4	14.2	67.0	16.4	p>0.05

TABLE 5: POTS (SYMPATHETIC, N=44; PARASYMPATHETIC, N=25)

		sympathetic dominant		parasympathetic dominant		
		No	%	No	%	p
PoTS		22	45.5	12	48	p>0.05
Fatigue period	6 month - 2 years	8	22.9	8	23.5	p>0.05
	2-5 years	14	40.0	12	35.3	p>0.05
	5-10 years	4	11.4	8	23.5	0.0492
	more than 10 years	9	25.7	6	17.6	p>0.05
Fatigue period IQR		2-5 years		6 month - 2 years		
Fatigue period in years IQR		8		2.5		

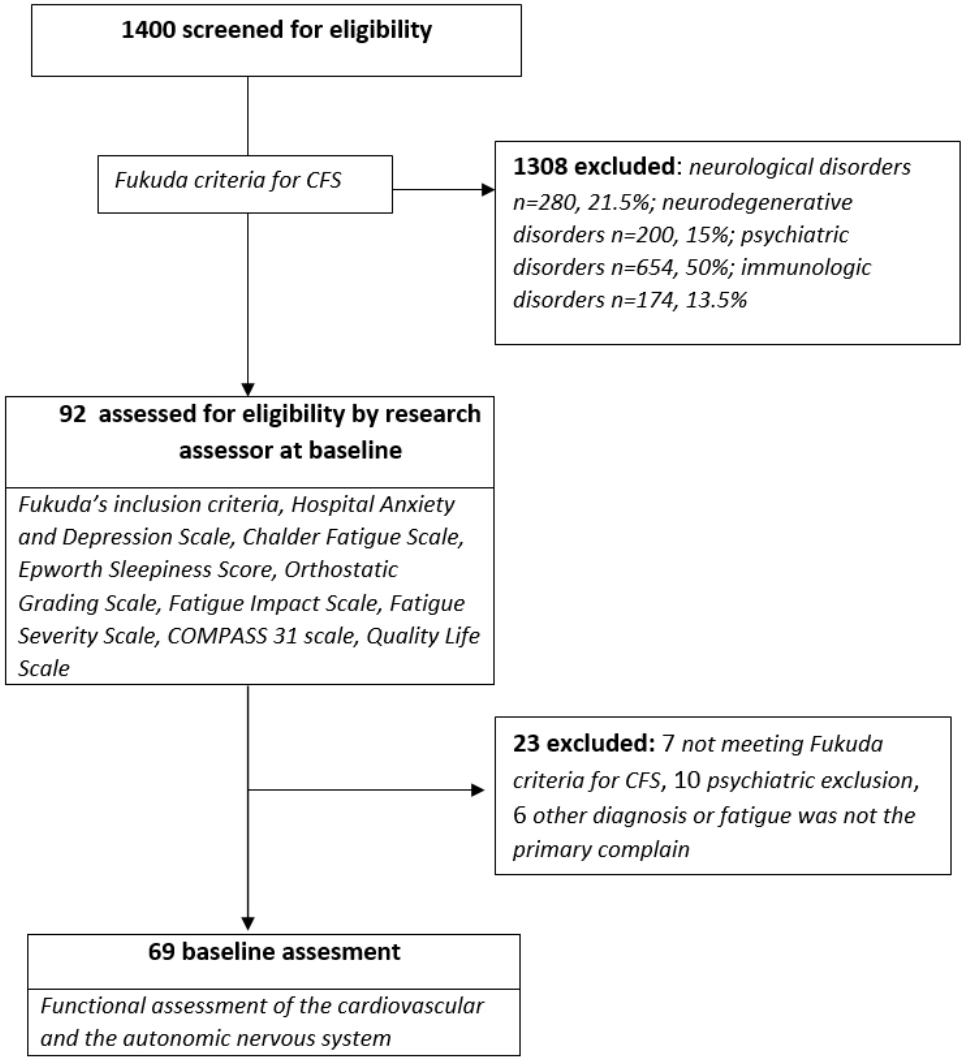

Figure 1. Study protocol

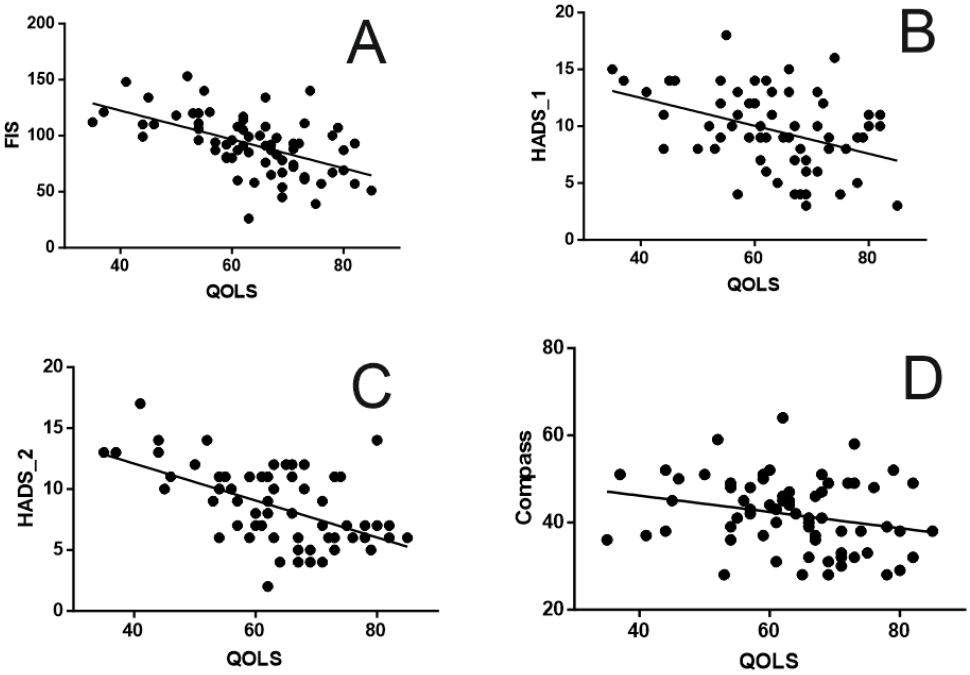

Figure 2: The relationship between quality of life measured using the QOLS scale and a) fatigue severity assessed using the fatigue impact scale b) anxiety measured using the HADS Anxiety scale (HADS -1) c) depression measured using the HADS Depression Scale (HADS – 2) and d) autonomic symptom burden measured using the COMPASS 31

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4, 5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-9*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	Figure
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-11
		(b) Indicate number of participants with missing data for each variable of interest	9-11

Outcome data	15*	Report numbers of outcome events or summary measures	9-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	n/a

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Prevalence and characteristics of Chronic fatigue syndrome/Myalgic encephalomyelitis (CFS/ME) in Poland: A cross-sectional study

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Prevalence and characteristics of Chronic fatigue syndrome/Myalgic encephalomyelitis (CFS/ME) in Poland: A cross-sectional study

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Abstract

Objectives: The aim of this study was to estimate the prevalence of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and describe illness characteristics in a community population in Poland.Design: cross-sectional study

Setting: Poland

Participants: Of the cohort of 1400 who self-presented with fatigue only 69 subsequently were confirmed as having CFS/ME using the Fukuda criteria.

Main outcome measures: Participants completed the following screening symptom assessment tools: Chalder fatigue scale, Hospital anxiety and depression scale (HADS), Epworth sleepiness scale (ESS), COMPASS 31, Quality of life scale (QOLS). Hemodynamic and autonomic parameters were automatically measured at rest with a Task Force Monitor.

Results: In 1308 from 1400 (93%) individuals who identified themselves as fatigued, recognized chronic conditions were identified e.g. neurological (n=280, 21.5%), neurodegenerative (n=200, 15%), psychiatric (n=654, 50%) and immunologic (n=174, 13.5%) disorders. The remaining 69 participants (mean age 38.3±8.5) met the Fukuda defintion for CFS/ME and had baseline objective assessment. The majority had experienced symptoms for over 2 years with 37% having symptoms for 2-5 years and 21.7% for more than 10 years. The Composite Autonomic Symptom Score 31 (COMPASS 31) indicated that 50% have symptoms consistent with orthostatic intolerance. 43/69 (62%) had Epworth sleepiness scores >=10 i.e. consistent with excessive daytime sleepiness, 26/69 (38%) had significant anxiety and 22/69 (32%) depression measured by HADS A & D. Quality of life is significantly impaired in those with Fukuda criteria CFS (QLS score 64±11) with significant negative relationships between quality of life and fatigue ($p<0.0001$), anxiety ($p=0.0009$), depression ($p<0.0001$) and autonomic symptoms ($p=0.04$).

Conclusion: This is the first study to summarize illness characteristics of Polish CFS/ME patients. Our study has confirmed that fatigue is a common and under-recognised symptom affecting the Polish population.

Key words: chronic fatigue, epidemiology, prevalence, quality of life

Strengths and limitations of this study

- This is the first study to summarize illness characteristics of a cohort of Polish CFS/ME patients.
- We used Fukuda criteria to indicate patients with CFS/ME.
- Recruitment was based on self-identification in response to an advertisement in CFS/ME community support networks across Poland.
- Methodologically more robust epidemiological studies of fatigue and its consequences in the Polish population are now needed.

Introduction

Diagnostics and treatment of the Chronic Fatigue Syndrome/Myalgic encephalomyelitis (CFS/ME) present a challenge to specialists as this syndrome is not a clearly identified, uniform disease but a set of symptoms resembling those occurring in other diseases, in which a sense of chronic fatigue predominates. In some countries (e.g Poland), CFS/ME is diagnosed very rarely, which may be associated with the fact that the aetiology of the disease is still poorly known, and with diagnostic problems resulting from a lack of detailed and uniform guidelines allowing an unambiguous diagnosis and initiation of effective treatment in CFS/ME patients.

The available studies provide several diagnostic criteria based on a definition of the American Centers for Disease Control (CDC), the Oxford Criteria, or the Canadian Guidelines. Criteria proposed by CDC (Fukuda et al. 1994) are most commonly used as acceptable diagnostic criteria when recruiting CFS/ME patients for scientific studies. However, they are encumbered by several disadvantages (e.g. fatigue experienced for at least 6 months), which – from the point of view of clinical practice – may delay a diagnosis in patients who do not meet this criterion precisely. The Oxford criteria propose a new diagnostic approach, focusing mainly on an aspect of mental rather than somatic fatigue. The Canadian criteria (CDC) expand the CFS/ME definition with additional diagnostic criteria, i.e. post-exertional malaise and presence of neurological, endocrine, cognitive and autonomic (orthostatic intolerance) disorders. The proposed CFS/ME definition, including malaise and symptoms exacerbation after exercise, allows differentiating CFS/ME patients from patients with depression or fibromyalgia. Alternative criteria, such as the International Consensus Criteria (ICC), disclose a further range of symptoms pertaining to the neurological, immunological, gastrointestinal, and autonomic systems.

Its global prevalence, ranging between 0.4% and 2.5%, is growing; most commonly, it is observed in the group of 20–40-year-olds, more frequently in professionally active women. CFS/ME is considered to be a common condition in countries such as the UK, Australia and the US [1,2]. In the UK, it affects up to 250,000 individuals with frequencies reported of up to 0.2% [3]. In the UK, Fukuda-defined cases have a prevalence of 0.2%. In the US, the prevalence of Fukuda-defined cases has been reported between 0.2%5 and 0.4%. Finding from the Australian cohort showed that from 535 patients diagnosed with CFS/ME by a primary care physician, 30.28% met Fukuda criteria. To date CFS/ME has not been reported in Poland, nor its prevalence defined. There are currently no CFS/ME Clinical services.

The aim of this study was to summarize sociodemographic and illness characteristics in those reporting CFS/ME symptoms in a Polish population. We set out to define the presence and characteristics of CFS/ME in Poland in order to identify a cohort of those patients who could potentially participate in further research studies.

METHODS

Setting

This study took place from March 2014 till July 2016 and was approved by the Ethics Committee, Ludwik Rydygier Memorial Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University, Toruń. Written informed consent was obtained from all of the participants.

Participants

Recruitment was based on self-identification in response to an advertisement in CFS/ME community support networks across Poland, as well as a general advertisement on local radio and social media.

Initially any individuals willing to participate were directed to a phone line. Within days of setting up the phone line it became clear that this mechanism to identify and recruit potential participants would be overwhelmed. The team therefore directed all potential participants to a website where more information about the study was available and where individuals were invited to self-complete the Fukuda criteria online. If individuals, on completing the online scoring, felt that they met the Fukuda criteria [4] within 7 days they were invited to attend the research facility. To be eligible for this study, participants were required to 1) meet Fukuda criteria, 2) be between 25 and 65 years of age, and 3) be a resident of Poland. The identification process is shown in **Figure 1**.

Patient and public involvement

Patients were not involved in the design of this study. Results from the current study will be disseminated to participants through newsletters in layman terms. We will also communicate our results through a number of other scientific and non-scientific channels including presentations at relevant congresses or in relevant fora.

Clinical assessment

Those who fulfilled the eligibility criteria for Centers for Disease Control and Prevention (Fukuda) were invited to attend the research unit at the chronobiology laboratory (windowless and sound-insulated room, temperature 22°C, humidity 60%). They were seen by members of

the research team in an assessment that took place over 40 minutes. Individuals participated in a standardized baseline assessment which comprised a battery of symptom assessment tools. Those screened as fulfilling criteria for CFS/ME [4] were also reviewed clinically by a member of the research team in order to determine whether their symptoms were consistent with these criteria, that there were no psychiatric exclusions or other diagnoses that could be associated with CFS/ME or where fatigue was not the primary complaint. Sixty nine individuals subsequently went on to have a further baseline objective assessment.

Symptom assessment tools

Participants completed the following screening symptom assessment tools: Chalder Fatigue Scale (CFQ) [5-7], Hospital anxiety and depression scale (HADS) [8], Epworth sleepiness scale (ESS) [9], Composite Autonomic Symptom Score 31 (COMPASS 31) [10,11], Quality of life scale (QOLS) [10-14].

Functional assessment of the cardiac and autonomic nervous system

Cardiovascular and autonomic nervous system measurements were performed with a dedicated high-tech device – Task Force Monitor (TFM, CNSystems, Medizintechnik, Graz, Austria). The main area of TFM application is beat-to-beat analysis of heart rate (electrocardiogram (ECG)) oscillometric and non-invasive continuous blood pressure measurements (oscBP, contBP) and impendance cardiography. [15-22]. A detailed of study protocol and its methodology have been presented in our previous articles [23,24].

In all cases TFM measurements were performed during 10 minutes of supine rest (phase 1) and subsequently asked to standing (phase 2) during which changes in heart rate were assessed and where haemodynamic changes were consistent with recognized consensus criteria for a diagnosis of postural tachycardia syndrome made [25].

We classified each individual's autonomic function profile into sympathetic or parasympathetic dominant according to their sympathetico-vagal balance during 10 minutes of supine rest. This was based upon previous studies and assessed using the LF/HF ratio which was considered to suggest a sympathetic dominant pattern if LF/HF was >1 and parasympathetic if the ratio was <1. [26, 27]

Statistical analyses

Statistical characteristics of measured values were presented as arithmetic means and standard deviations (±SD). The normality of continuous variables distribution was evaluated with the *Shapiro–Wilk* test Depending on distribution characteristics of analysed variables, the independent samples Student t-test or the Mann–Whitney U test was used to evaluate significance of differences between measured values obtained in the group of each phenotypes.

All calculations were performed with the package *Statistica 13.0* (StatSoft), with the assumed level of statistical significance of $\alpha<0.05$.

RESULTS

Recruitment of the cohort – the prevalence of fatigue in a Polish population

During the media campaign 1400 individuals identified themselves to the research team as fitting, they believed, the criteria for CFS/ME. 1308 of those subsequently were found not to meet the Fukuda criteria for CFS/ME.

In the 1308 (93%) individuals who identified themselves as fatigued, recognized chronic conditions were identified. These were conditions associated with the symptom of fatigue and therefore could have been the attributable cause for their fatigue symptoms (and therefore not consistent with the Fukuda diagnostic criteria). These fatigue associated conditions were broadly classified into conditions that were: neurological (n=280, 21.5%), neurodegenerative (n=200, 15%), psychiatric (n=654, 50%) and immunologic (n=174, 13.5%) disorders.

Characteristics of a polish cohort of CFS/ME patients meeting the Fukuda criteria

Of the total group with CFS/ME, 41 were female (59.4%). The majority of individuals had a normal BMI (58%) with 24 (35%) being considered overweight and 3 (4.3%) being obese. Two individuals (2.9%) were considered underweight. The majority of individuals were considered to be of a specialist professional group (engineers).

Symptom burden of a polish cohort of CFS/ME patients meeting the Fukuda criteria

The majority of those with CFS/ME had had symptoms for over 2 years with 37% having symptoms for 2-5 years and 21.7% having symptoms for more than 10 years. The vast majority described unrefreshing sleep with impaired short-term memory and concentration (91.3%), post-exertional malaise 89%, multi-joint pain without swelling or redness 72.5%, headaches 62.3%, muscle pain 66.7%, sore throat 39.1% and tender cervical or axillary lymph nodes 30.4%.

Table 1 shows the prevalence of other symptoms identified in those found to have Fukuda CFS/ME. This illustrates the fact that many clinical specialists may come into contact with individuals who may subsequently be identified as having CFS/ME. When COMPASS 31 scores were considered these are shown in **Table 2** with 50% of individuals with CFS/ME having symptoms consistent with orthostatic intolerance. HAD scores were high for both anxiety and depression and 43/69 (62%) were found to have ESS scores >=10 i.e. consistent with excessive daytime sleepiness. Considering scores from HADS A & D, 26/69 (38%) had scores consistent with significant anxiety and 22/69 (32%) depression.

Quality of life of a polish cohort of CFS/ME patients meeting the Fukuda criteria

Quality of life scores assessed using the QOLS were mean (SD) 64 (11). This confirmed that quality of life is significantly impaired in those with Fukuda criteria CFS/ME and well below the expected for a healthy population. When we considered the relationship between quality of life and the other symptoms frequently seen in those with CFS/ME, there were strong significant negative relationships between quality of life and fatigue ($p<0.0001$), anxiety ($p=0.0009$), depression ($p<0.0001$) and autonomic symptoms ($p=0.04$), figure 2. There were no significant relationships between age or daytime sleepiness.

Autonomic function in a polish cohort of CFS/ME patients meeting the Fukuda criteria

When we classified the cohort according to predominance of sympathetic or parasympathetic function, 44/69 (64%) were found to be sympathetic predominant and 25 parasympathetic. When we considered symptom burden between these two phenotypes, there were no significant differences in symptoms or impact upon quality of life between the groups (**Table 3**). At rest, the sympathetic predominant group had significantly higher heart rate, ER and LF HRV and reduced LVET, PEP and HF HRV compared to the parasympathetic group. The total PSD was comparable between groups however sympatheticovagal balance was different between the phenotypes with increased LF BPV in both diastolic and systolic blood pressure, reduced baroreflex sensitivity in those with the sympathetic dominant phenotype (**Table 4**).

Those with the parasympathetic predominant phenotype were more likely to have had the disease for between 5-10 years (**table 5**).

Prevalence of postural tachycardia syndrome in a Polish cohort of CFS/ME patients

The presence of postural tachycardia syndrome is frequently seen in those with CFS [28,29]. A total of 35 (51%) of the CFS group had haemodynamic responses to standing consistent with a diagnosis of PoTS. There was no difference in the proportion of those with PoTS in the sympathetic or parasympathetic groups (**Table 5**).

DISCUSSION

This study has confirmed for the first time that chronic fatigue is a common symptom experienced by the Polish population and that CFS/ME is an under-recognized syndrome in this group. The key finding of this study is that prevalence is similar to reported data in the other countries and is associated with a large symptom burden and impaired quality of life.

Of the cohort of 1400 who self-presented with fatigue only 69 subsequently were confirmed as having CFS/ME using the Fukuda criteria. This suggests that in Poland there are significant amounts of fatigue related to other conditions, with only a small percentage of those experiencing fatigue having CFS/ME *per se* (69/1400; 5%).

From the initial responses, we rigorously identified those who met with Fukuda criteria for CFS/ME. We did this by asking individuals to complete the tool, but also using face to face sessions with trained clinicians. We believe therefore, that our cohort represents a well characterized group who we are confident fulfil one of the recognised diagnostic criteria for CFS/ME. When we compared this Polish cohort with CFS/ME to other national cohorts there were some similarities, but also some differences.

Compared with the UK cohort [30] having in excess of 6500 individuals collected from the UK NHS Clinical CFS services, the Polish cohort appeared to be of a similar age to the UK cohort with comparable levels of fatigue and illness duration, have similar levels of sleep and cognitive symptoms but less post-exertional malaise, muscle pain and headaches. The Polish cohort appeared to have more males than was seen in the UK cohort.

As in previous national cohorts [3, 30, 31], the presence of fatigue in the Polish population was associated with impaired quality of life. As has been seen previously, impaired quality of life associates with the severity of symptoms such as fatigue and autonomic dysfunction, but in contrast to other studies, not daytime sleepiness. Impaired quality of life is also associated with increased anxiety and more depression. As in other series, we would suggest that this association is a secondary phenomenon i.e. arising as a consequence of the condition rather than a cause. The fact that we rigorously excluded depression and psychiatric disorders when determining the criteria would be consistent with this.

Our study has also confirmed a high prevalence of the condition postural tachycardia syndrome (PoTS). This form of dysautonomia [21] has been recognized as occurring frequently in those with CFS/ME [28,29], and represents a potential therapeutic target in those with this illness. It is important that clinicians and researchers are aware of the overlap and are trained to identify and manage this condition.

All of these differences might arise because of the self-report nature of the Polish cohort and that the UK cohort was recruited from the National Health Service clinical services which were specifically set up to identify and manage CFS/ME [3]. A comprehensive review of the prevalence of CFS/ME in three regions of England involving 143,000 subjects suggested an older cohort with longer disease duration than that seen in the UK clinical services.

An Australian cohort [31] was established using similar identification strategies to our Polish cohort with self-report in response to adverts inviting individuals to participate in a research database. Individuals in this cohort were included if they had received the diagnosis from a primary care physician. Again the proportion of females in the Australian cohort was higher than in the Polish cohort

This study has a number of limitations. The case ascertainment process used self-report as the means of identifying those with CFS/ME. It became clear during the radio and television campaign that there was considerable interest, and as a result our recruitment process needed to be changed to facilitate timely screening of those self-presenting with fatigue. It is clear that a thorough, methodologically robust epidemiological study of fatigue and its consequences in a Polish population are now needed.

Our study has confirmed that fatigue is a common and under-recognised symptom affecting the Polish population. It impacts upon quality of life and is associated with a range of other symptoms that have been previously recognised in other cohort studies. Despite this, there are no clinical services for fatigue or CFS/ME in Poland and it is poorly understood and infrequently diagnosed. Our research programme now aims to consider the effect of interventions upon fatigue in a Polish CFS/ME population.

Figure legends

Figure 1: Study protocol

Figure 2: The relationship between quality of life measured using the QOLS scale and a) fatigue severity assessed using the fatigue impact scale b) anxiety measured using the HADS Anxiety scale (HADS -1) c) depression measured using the HADS Depression Scale (HADS – 2) and d) autonomic symptom burden measured using the COMPASS 31

Contributorship statement

JS, DS, SMG, PZ were involved in writing of the manuscript. JS, PZ, JJK and MTF conceived and supervised the study. SK, PZ provided statistical advice. JS, PZ, JN, DS., SMG contributed conceived, designed and performed the experiments, collected and analyzed the data, revising it critically for important intellectual content and final approval of the version to be submitted.

Competing interests: none declared.

Funding: none

data sharing: no additional data are available**.**

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TABLE 1: OTHER SYMPTOMS REPORTED AT INITIAL ASSESSMENT, N=69

Specific symptom	No	%
IBS	12	17.7
Migraine	17	24.6
seasonal allergy	8	11.6
slight food intolerance / nausea / alcohol intolerance	40	58.1
back pain	13	18.8
Tinnitus	9	13.0
palpitations with no cardiac history	9	13.0
periodical fever	8	11.6
sensory disturbances	0	0
chest symptoms with no medical history	15	21.7
mood fluctuations	30	43.5
chronic stress	41	59.4
overworked / work stress	34	49.3
shift work	0	0
care work	3	4.3
newborn care	7	10.1
frequent infections	9	13.0
night hyperhidrosis	22	31.9
sleep disturbance / hypersomnia	28	40.6
unexplained anxiety	3	4.3
sensory disturbance	10	14.5

TABLE 2: COMPASS 31 - AUTONOMIC SYMPTOMS, N=69

Specific symptom	No	%
orthostatic intolerance	40	50.0
dizziness / headaches	41	59.4
sudden paleness	25	36.2
arrhythmia	29	42.0
dryness eyes mouth	45	65.2
vasomotor	24	34.8
secretomotor	30	43.5
upper gastro. tract symptoms	38	55.1
unknown gastro. pain	26	37.7
constipation	21	30.4
diarrhea	28	40.6
urinary	21	30.4
sexual failure	19	27.5
sleep	68	98.5
pupilomotor	28	40.6
anxiety	34	49.3

TABLE 3: BASELINE QUALITY OF LIFE SCORES, N=69

	Total Group		Sympathetic dominant (n=44)		parasympathetic dominant (n=25)		
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Chalder Fatigue Scale	25.3	3.7	25.5	3.8	25.0	3.8	p>0.05
Fatigue Severity Scale	48.8	8.7	48.0	8.5	50.2	9.1	p>0.05
Fatigue Impact Scale	92.2	26.2	92.6	24.6	91.6	29.2	p>0.05
HADS_A	9.6	3.4	9.3	3.1	10.1	3.9	p>0.05
HADS_D	8.5	3.1	8.5	3.0	8.6	3.4	p>0.05
BDI	17.6	8.1	18.3	8.3	16.4	7.9	p>0.05
Epworth Sleepiness Scale	10.3	5.6	10.6	5.3	9.8	6.2	p>0.05
Quality of Life Scale	63.5	10.9	62.1	11.9	65.9	8.8	p>0.05
Orthostatic Grading Scale	8.4	3.1	3.5	3.4	3.4	2.5	p>0.05

TABLE 4 CARDIOVASCULAR / AUTONOMIC PARAMETERS

	Variable	Total group (n=69)		Sympathetic dominant (n=44)		parasympathetic dominant (n=25)		
		Mean	SD	Mean	SD	Mean	SD	
Haemodynamics	**HR**	67.6	9.2	70.1	8.4	63.2	9.0	0.0017
	Sbp	117.3	13.3	118.5	11.3	115.2	16.2	p>0.05
	Dbp	79.3	10.6	79.6	9.7	78.8	12.1	p>0.05
	mBP	95.9	11.1	96.0	9.9	95.7	13.2	p>0.05
Cardiac Impedance	**SI**	52.3	12.4	50.8	12.5	54.9	12.1	p>0.05
	CI	3.5	0.8	3.5	0.8	3.4	0.8	p>0.05
	TPRI	2304.7	747.3	2285.2	684.3	2339.0	861.1	p>0.05
	EDI	85.0	19.9	82.3	19.9	89.7	19.5	p>0.05
	IC	62.8	21.2	59.7	20.6	68.2	21.5	p>0.05
	ACI	85.7	34.4	80.4	33.8	95.0	34.3	p>0.05
	LVWI	4.4	1.1	4.5	1.1	4.4	1.2	p>0.05
	LVET	318.2	17.3	313.2	18.2	327.0	11.1	0.0005
	TFC	31.3	4.5	30.8	4.7	32.3	4.0	p>0.05
	PEP	110.2	12.1	107.1	11.3	115.7	11.6	0.0040
	STR	34.9	4.3	34.6	4.7	35.5	3.4	p>0.05
	ER	35.5	3.3	36.3	2.6	34.2	3.9	0.0092
	MSER	300.8	68.9	306.2	72.5	291.4	62.4	p>0.05
	REP	77.8	16.8	79.7	19.8	74.5	9.1	p>0.05
	HI	0.3	0.1	0.3	0.1	0.4	0.1	p>0.05
	RZ	187.1	12.2	185.3	11.1	190.4	13.6	p>0.05
	TAC	2.6	0.7	2.5	0.7	2.8	0.8	p>0.05
Heart rate variability	**LFnu-RRI**	54.2	17.2	62.2	14.0	40.1	12.7	0.0000
	HFnu-RRI	45.8	17.2	37.8	14.0	59.9	12.7	0.0000
	PSD-RRI	1684.1	1993.7	1604.9	2166.9	1823.4	1678.7	p>0.05
	LF/HF-RRI	1.7	1.6	2.3	1.8	0.8	0.4	0.0000
Diastolic Blood pressure variability	**LFnu-Dbp**	52.2	14.7	59.7	10.2	38.9	11.7	0.0000
	HFnu-dBP	14.0	10.4	11.0	7.5	19.3	12.7	0.0004
	PSD-dBP	13.6	16.5	15.2	19.3	10.8	9.5	p>0.05
	LF/HF-dBP	6.6	6.2	8.7	6.8	2.8	1.8	0.0000
Systolic Blood pressure variability	**LFnu-sBP**	42.1	13.5	47.5	10.7	32.6	12.9	0.0000
	HFnu-sBP	16.5	10.8	15.6	11.0	18.2	10.4	p>0.05
	PSD-sBP	20.2	30.2	17.5	16.3	25.0	45.5	p>0.05
	LF/HF-sBP	3.8	2.8	4.5	3.0	2.5	1.7	0.0019
Baroreflex parameters	**Total Event Count**	17.4	13.6	21.5	14.4	10.2	8.4	0.0006
	Total Slope Mean	19.6	13.0	16.7	8.9	24.8	17.2	0.0114
	Total BEI	70.5	15.1	72.4	14.2	67.0	16.4	p>0.05

TABLE 5: POTS (SYMPATHETIC, N=44; PARASYMPATHETIC, N=25)

		sympathetic dominant		parasympathetic dominant		
		No	%	No	%	p
PoTS		22	45.5	12	48	p>0.05
Fatigue period	6 month - 2 years	8	22.9	8	23.5	p>0.05
	2-5 years	14	40.0	12	35.3	p>0.05
	5-10 years	4	11.4	8	23.5	0.0492
	more than 10 years	9	25.7	6	17.6	p>0.05
Fatigue period IQR		2-5 years		6 month - 2 years		
Fatigue period in years IQR		8		2.5		

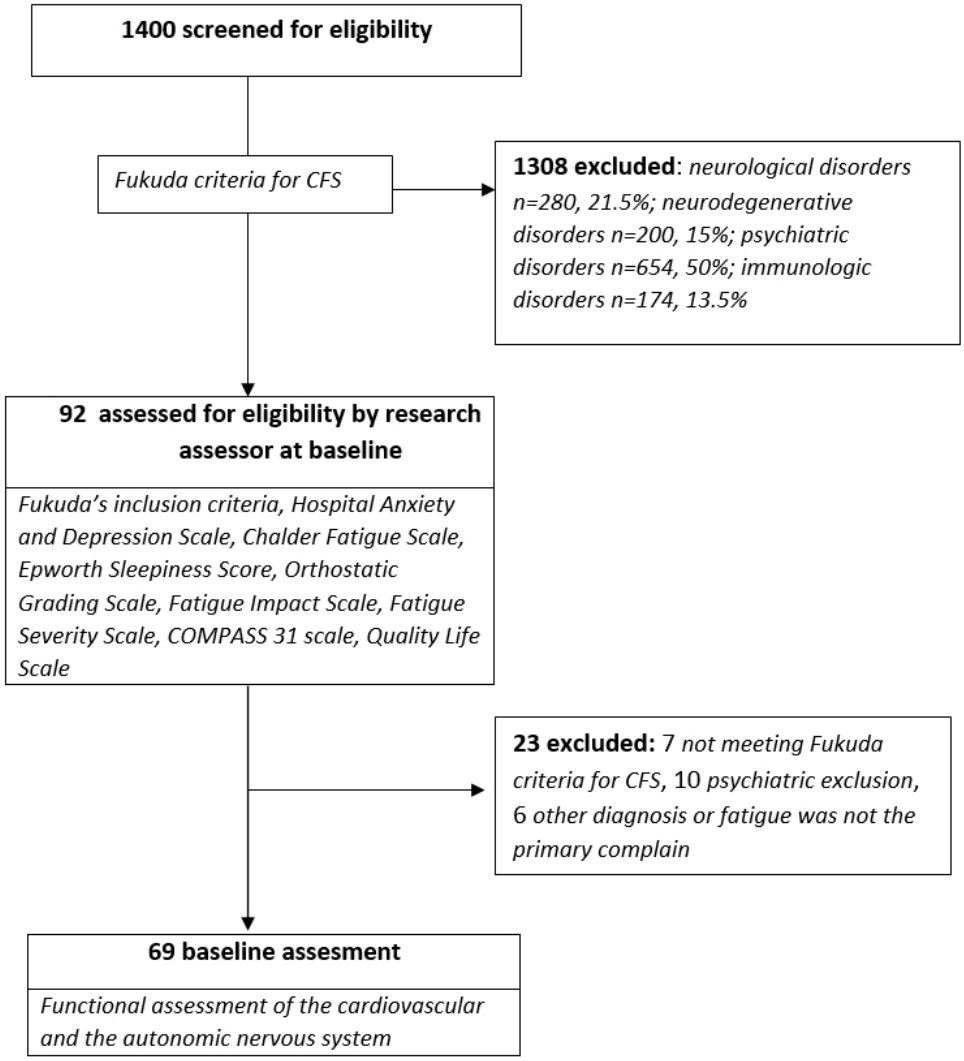

Figure 1. Study protocol

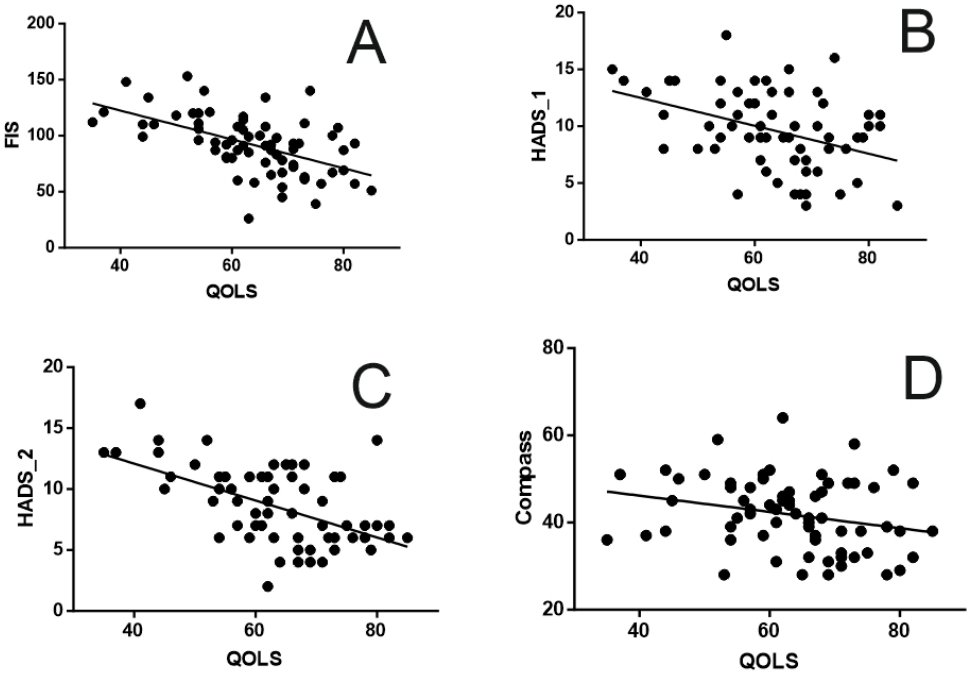

Figure 2: The relationship between quality of life measured using the QOLS scale and a) fatigue severity assessed using the fatigue impact scale b) anxiety measured using the HADS Anxiety scale (HADS -1) c) depression measured using the HADS Depression Scale (HADS – 2) and d) autonomic symptom burden measured using the COMPASS 31

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4, 5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-9*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	Figure
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-11
		(b) Indicate number of participants with missing data for each variable of interest	9-11

Outcome data	15*	Report numbers of outcome events or summary measures	9-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	n/a

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.