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Using a generic quality of life measure to determine adherence thresholds: a cross-sectional study on older adults with neurological disorders in Germany

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ABSTRACT

Objectives Measuring the degree of adherence to medication is essential in healthcare However, the cut-offs provided for adherence scales are often arbitrary and disease-specific, and need to be validated against a clinical outcome. Here, we used health-related quality of life (QoL) to determine cut-offs for a self-report adherence questionnaire in patients with neurological diagnoses.

Design Cross-sectional study.

Participants 910 patients (age 70±8.6 years) with neurological disorders were recruited from the wards of neurology at a local university hospital. All patients received a comprehensive geriatric assessment, including assessments of adherence (Stendal Adherence to Medication Score, SAMS) and QoL (Short Form Survey SF-36).

Outcome measures The main aim of the study was to define a cut-off for non-adherence at which QoL is significantly impaired. Thus, we used Spearman's rank correlation, multivariate and univariate analyses of variance to test the impact of different adherence levels on QoL. Receiver operating characteristics and area under curve measures were then used to determine cut-off scores for adherence based on significant differences in QoL.

Results Correlations between SAMS and SF-36 domains were weak (ranging between r=−0.205 for emotional well-being and r=−0.094 for pain) and the effect of non-adherence on QoL disappeared in the multivariate analysis of variance (p=0.522) after adjusting for demographical and clinical factors. SAMS cut-offs in terms of SF-36 domains varied greatly, so that an overall SAMS cut-off for this cohort could not be defined.

Conclusions QoL as measured by the SF-36 is not suitable as a single outcome parameter to study the impact of non-adherence on QoL in a mixed neurological cohort. Since both QoL and adherence are heterogeneous, multifaceted constructs, it is unlikely to find an overarching cut-off applicable for all patients. Thus, it may be necessary to use disease or cohort-specific external outcome parameters to measure the indirect effect of interventions to enhance adherence.

Trial registration number DRKS00016774.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We used a commonly applied quality of life questionnaire to define clinically relevant cut-off scores for non-adherence using receiver operating characteristic (ROC) and area under curve analysis.
⇒ Our comprehensive data on 910 older adults provides ample information on adherence and its influence of quality of life when controlling for relevant covariates such as depression, cognition and health.
⇒ Our data and results are limited to the cohort of older adults with neurological disorders; however, in this particular cohort, the problem of non-adherence is particularly relevant.

BACKGROUND

Adherence describes the extent to which a person's behaviours correspond with agreed recommendations from their healthcare provider. However, many people cannot or do not want to take medications as prescribed. This non-adherence contributes to poorer health outcomes, higher healthcare costs and lower quality of life (QoL).[1 2] Measuring adherence is important for several reasons, for example, determining the influence of non-adherence on outcome parameters in clinical trials, identifying patients' needs or determining the effect of interventions to improve adherence and thus health. Non-adherence can be detected with objective and subjective methods, which both have their drawbacks.[3] Objective measures include methods such as dose counts, pharmacy records, electronic monitoring of medication administration (eg, the Medication Event Monitoring System) and drug concentrations in plasma. Subjective measures of adherence include patient interviews and self-report adherence scales. These subjective measures are simple to use and can identify personal reasons for non-adherence.[3 4] In addition to the question of which instrument to use, another issue with measuring adherence is the question

of an appropriate cut-off to determine non-adherence. Most subjective adherence scales provide cut-offs for identifying non-adherence. However, the arbitrary nature of the cut-offs provided for most self-report adherence scales needs to be kept in mind.[5] Oftentimes, the cut-off point to identify non-adherence is based on the respective distribution of scores, or determined in comparison to objective measures, such as the score that corresponds to patients that took 80% of their medication as ascertained by an objective measure of adherence. However, these cut-off scores do not necessarily determine whether the identified level of non-adherence is clinically relevant. A small number of scales have assessed the sensitivity and specificity of their cut-off against an external clinical parameter.[6 7] These external clinical outcomes are oftentimes disease-specific (eg, blood pressure, cardiovascular events). However, to define an adherence cut-off in mixed cohorts with more than one disorders is challenging. This is especially true in older adults, where multimorbidity is common[8] and one single clinical endpoint is not feasible. Given that non-adherence was also found to be associated with poor health-related QoL,[1 9 10] we aimed to test if a generic QoL measure can be used to determine adherence cut-off in a cohort of older patients with mixed neurological diagnoses.

METHODS

Setting and participants

This paper reports explorative analyses of the cross-sectional dataset from the NeuroGerAd study,[11] which is a longitudinal observational study in older hospitalised adults with neurological disorders (registered in the German Clinical Trials Register DRKS00016774; registered on 19 February 2019).[12 13] Briefly, from February 2019 to March 2020, elderly patients with neurological disorders received a comprehensive geriatric assessment during their stay in the Department of Neurology at the Jena University Hospital. We included patients (age>55 with multimorbidity or age>60) with a common neurological disorder (cerebrovascular disorders, movement disorders, epilepsy and neuromuscular or peripheral neurological disorders). Patients with dementia, acute psychotic symptoms and delirium were excluded.

Detailed information on the study can be found in the corresponding data descriptor.[13] In short, 2021 patients aged 55 years and above were admitted to the department during the data collection phase, of which 113 could not be approached before discharge. Of the remaining 1908 patients, 997 were excluded because they did not meet the inclusion criteria, were physically unable or declined to participate. A total of 995 patients were deemed eligible, and 910 patients completed the assessments. The following assessments were used for this analysis: age, gender, main neurological diagnosis, medication regime at admission and discharge, marital status (single/divorced/widowed or married), living condition (alone, not alone), level of education (high, middle, low), number of medications per day, medical diagnoses, depression (Beck's Depression Inventory II, BDI,[14] personality (Big Five Inventory, BFI,[15] Healthcare Climate Questionnaire (HCCQ),[16] QOL (SF-36),[17] adherence (Stendal Adherence to Medication Score, SAMS),[18] Timed-Up-and-Go Test (TuG),[19] and Montreal Cognitive Assessment (MoCA).[20]

The Short Form Survey (SF-36) is a general health-related QoL questionnaire with eight different domains: problems regarding both physical and social activity due to health, limitations in daily life due to physical or emotional problems, pain, mental health, vitality and general health perception. Each domain is summarised as the weighted sum of the respective items, with lower scores indicating less disability. A physical and mental compound score as well subscores can be calculated.[17]

The SAMS is a questionnaire with 18 items summed up in a cumulative adherence score, with 0 indicating complete adherence and 72 complete non-adherence.[21] One if its advantages is that different facets of adherence are included, namely modification of medication, lack of knowledge and forgetting to take medication.[18 22] The SAMS has previously been validated in neurological patients, patients with chronic pain and patients with kidney transplants, and has been used in a variety of studies since.[18 23–27]

All self-report questionnaires were checked for completeness by study staff, which was available in case of questions. The face-to-face approach allowed us to assess if patients were cognitively able to participate and give valid information.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Statistical analysis

Descriptive statistics (mean and SD for continuous data, absolute and relative frequencies for categorical data) were used to describe the overall study population. Spearman's rank correlation coefficient was calculated to assess the association between SAMS and the SF-36 domains. In order to adjust for sociodemographic factors and clinical parameters, multivariate analysis of variance (MANOVA) was performed. Here, the SF-36 domains served as dependent variables and the SAMS as well as the following covariates were included as independent variables: gender, living condition, diagnosis, personality according to BFI, number of daily medication, HCCQ, MoCA and TuG in seconds. The mean difference in the SF-36 domains was analysed for different cut-offs of the SAMS score and area under curve (AUC) with 95% CI was calculated to evaluate the discrimination between the groups defined by the cut-off value. The significance level was set at 0.05 for all statistical tests.

Table 1 Clinical and demographical characteristics (N=910)

	n	%	Missing
Sex			
Female	389	42.7	0
Male	521	57.3	
Marital			
Single/widowed/divorced	277	30.8	12
Married	621	69.2	
Living situation			
Alone	204	24.1	65
Not alone	641	75.9	
Education			
High	325	36.3	14
Middle	306	34.2	
Low	265	29.6	
Occupation status			
Not working/retired	756	84.0	10
Working	144	16.0	
Diagnosis group			
Movement disorder	303	33.3	0
Cerebrovascular disorder	233	25.6	
Epilepsy	48	5.3	
Neuromuscular	168	18.5	
Others	158	17.4	
	M	**SD**	**Missing**
Age	70.1	8.6	0
Beck Depression Inventory II	9.8	7.6	1
Healthcare Climate Questionnaire	5.6	1.1	79
Montreal cognitive assessment	22.5	4.4	0
Timed-Up-and-Go duration in seconds	10.5	4.3	325*
Stendal Adherence to Medication Score	6.3	7.6	0
No of Medications/day	5.6	3.7	67
SF-36 Physical Component Scale	33.9	11.0	61
SF-36 Mental Component Scale	48.6	11.2	61

*Timed-Up-and-Go not performed in 325 subjects for medical reasons.
M, mean; SF-36, Short Form Survey.

RESULTS

Demographical data of the 910 adults (42.75% or 389 female, 57.25% or 521 male, mean age 70±SD = 8.6 years) are given in table 1. Health-related QoL as measured by the SF-36 was substantially impaired in this sample of older ill adults in comparison with the general German population[28] (figure 1).

There were weak negative correlations between the SAMS and the SF-36 domains physical functioning (r=−0.129, p<0.001), social functioning (r=−0.176, p<0.001), role limitations due to physical health (r =−0.144, p<0.001), role limitations due to emotional problems (r=−0.177, p<0.001), emotional well-being (r=−0.205, p<0.001), energy/fatigue (r=−0.184, p<0.001), pain (r=−0.097, p=0.004), general health (r=−0.191, p<0.001), Physical Component Scale (r=−0.135, p<0.001) and Mental Component Scale (r=−0.200, p<0.001). An MANOVA with the 8 SF-36 domains as dependent variables showed a significant influence of the SAMS on the combined dependent variables, $F(8, 840) = 5.891$, p<0.001, partial Wilk's $\Lambda=0.947$. Post hoc univariate analysis of variances were conducted for every dependent variable. The SAMS was significantly associated with all SF-36 domains except pain: physical functioning (p=0.014), social functioning (p<0.001), role limitations due to physical health (p<0.001), role limitations due to emotional problems (p<0.001), emotional well-being (p<0.001), energy/fatigue (p<0.001), general health (p<0.001), pain (p=0.176). However, after adjustment for sociodemographic and clinical factors, the SAMS was no longer significantly associated with the SF-36 domains (p=0.522) (table 2).

We then explored how the SF-36 domains differed between subjects below and above the possible SAMS cut-offs (ranging from 0 to 72 points). By doing so, we determined how the SF-36 domains change as a function of the SAMS, that is, at which SAMS cut-off the influence on the SF-36 is maximal. For the two compound SF-36 scales, a mixed picture emerges. For the Physical Component Scale, the maximum mean difference was 3.2 points when the SAMS cut-off was set at two points (ie, comparing groups with SAMS ≤2 vs >2). For a SAMS cut-off of 31 or higher, the SF-36 Physical Component Scales were even higher than in the other group, which can certainly be attributed to the small sample with SAMS >31 and the increased sampling error (figure 2).

In contrast, for the SF-36 Mental Component Scale, the differences of the means at all SAMS cut-offs were greater than zero. The maximum difference of 8.4 points in the SF-36 was reached at a SAMS cut-off of 41 points (AUC=0.713, 95% CI: 0.453 to 0.973, p<0.001) (figure 3). The detailed SAMS thresholds for the SF-36 component scales and 8 SF-36 domains are given in figures 2 and 3. All SAMS cut-offs and the corresponding AUCs are detailed in online supplemental tables 1 and 2.

DISCUSSION

According to the SF-36, the studied cohort showed poorer health-related QoL in all domains in comparison to a German reference cohort, the German Health Interview and Examination Survey for Adults.[28] This is in line with other studies linking chronic illness and multimorbidity to worse functional status, disability and thus reduced QoL,[29] indicating that the SF-36 measured our cohort's

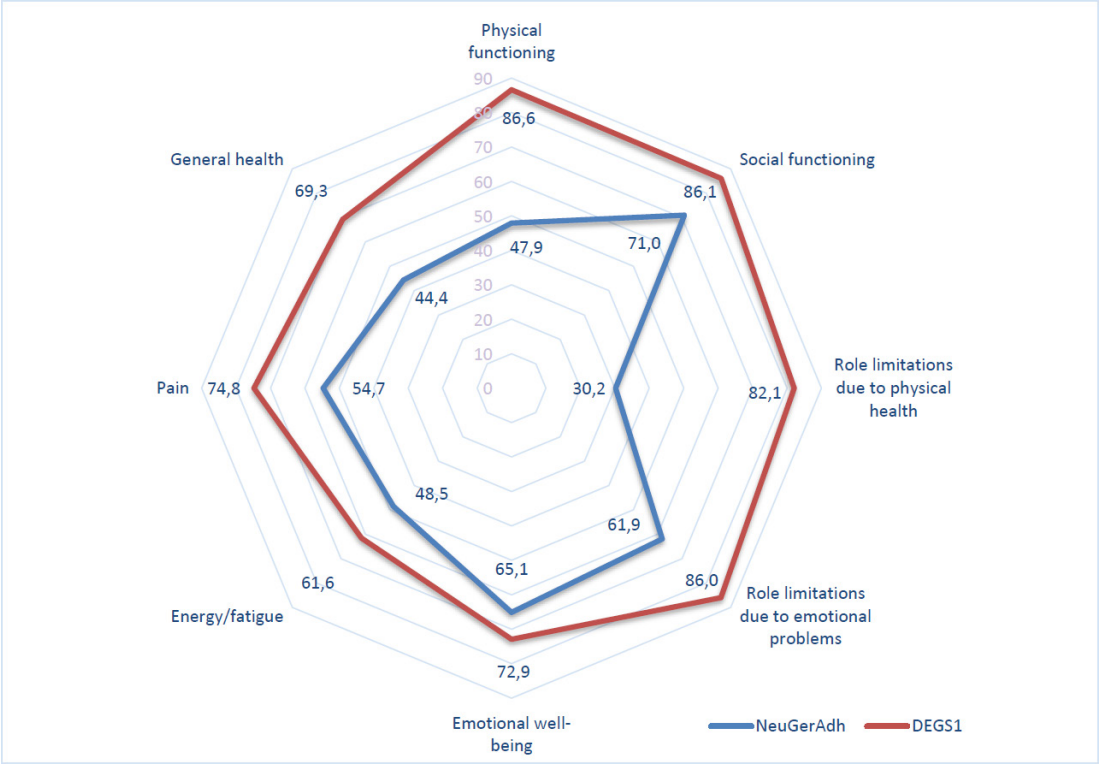

Figure 1 Comparison of mean health-related quality of life as measured in the Short-Form Survey (SF-36) domains between the NeurGerAdh cohort and German reference cohort (DEGS1). DEGS1, German Health Interview and Examination Survey for Adults.

QoL somewhat accurately. Despite a well-documented link between non-adherence and QoL,[30–32] some studies found only weak univariate associations between adherence and QoL domains[9 10] that match our own results. This weak association is also the reason why some of the cut-offs for the SAMS found are so variable and high. The difficulty in finding a concrete connection between adherence and QoL may stem from the heterogeneity of the two constructs themselves. The factors associated with adherence are numerous, complex and vary between patients.[1 33] Similarly, as health-related QoL is essentially a patients' interpretation of the current health status, it is a highly individual construct with varying factors, leading to different scales measuring different concepts without covering all aspects of QoL.[34 35] Therefore, for each patient, different aspects may influence both QoL and non-adherence, leading to heterogeneity in the association between both constructs. Therefore, our results contradict our initial hypothesis and instead suggest that QoL as an overarching and relevant clinical endpoint is

Table 2 Results from the MANOVA with the eight SF-36 domains as dependent variables

	Wilk's Λ	F	dF	Error df	P value	Partial Eta²
Constant	0.654	28.717	8.000	435.000	0.000	0.346
Sex	0.954	2.636	8.000	435.000	0.008	0.046
Living situation	0.963	2.098	8.000	435.000	0.035	0.037
Diagnosis	0.886	1.674	32.000	1605.796	0.011	0.030
Personality (BFI)	0.879	1.423	40.000	1898.916	0.042	0.025
SAMS	0.984	0.894	8.000	435.000	0.522	0.016
No of medications per day	0.877	7.639	8.000	435.000	0.000	0.123
BDI	0.565	41.866	8.000	435.000	0.000	0.435
HCCQ	0.987	0.740	8.000	435.000	0.656	0.013
MoCA	0.951	2.799	8.000	435.000	0.005	0.049
TuG	0.840	10.376	8.000	435.000	0.000	0.160

BDI, Beck Depression InventoryII; BFI, Big Five Inventory; HCCQ, Healthcare Climate Questionnaire; MANOVA, multivariate analysis of variance; MoCA, Montreal Cognitive Assessment; SAMS, Stendal Adherence to Medication Score; TuG, Timed-Up-and-Go.

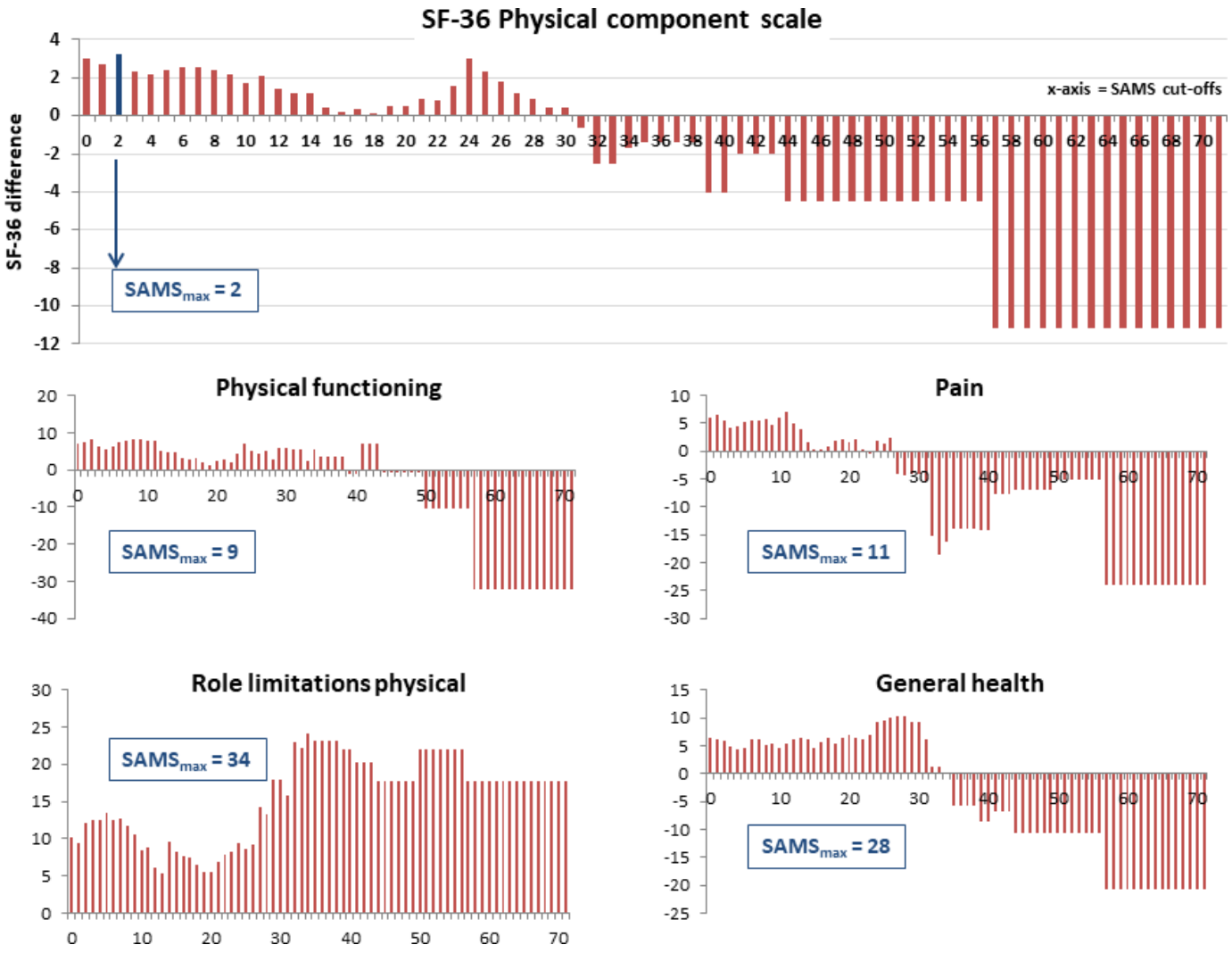

Figure 2 Change of Short-Form Survey (SF-36) domains and component scales as a function of different SAMS cut-offs the Physical Subscale. Note: The x-axis shows the possible SAMS cut-offs based on sum scores ranging from 0 to 72. The y-axis shows how the SF-36 changes depending on the SAMS cut-off. By doing so, we determined at which SAMS cut-off the influence on the SF-36 is maximal. SAMS, Stendal Adherence to Medication Score.

not sufficiently clear-cut to serve as an indicator of non-adherence cut-offs.

While clinical outcomes are the ultimate aim of any intervention to enhance adherence, the use of clinical outcomes as a proxy of adherence can be confounded by disease-specific factors independent of real adherence. The connection between QoL and adherence in our study vanished after controlling for demographical and clinical factors, which all contribute individually to both adherence and QoL.[1] It is possible that measuring such complex constructs with a single questionnaire falls short when each contributing component, such as age, diagnosis or depression, is considered individually. The many dimensions and subscales may interact in individual ways for each patient, thus effectively annihilating any overall effect for wider populations.[36]

As shown in this study, the SF-36 is not suitable as a single external outcome parameter to define a reasonable cut-off of the SAMS in a mixed neurological cohort. Therefore, it is also not possible to determine a general SAMS cut-off that differentiates between adherent and non-adherent patients with respect to QoL. Due to the heterogeneity of both constructs, it seems unlikely to find an overarching cut-off for adherence that is applicable to all patients, and it may be more appropriate to use specific outcome parameters for individual patients or specific cohorts (eg, Unified Parkinon's Disease Rating Scale in Parkinson's disease) to estimate the effect of non-adherence or the effect of interventions to improve adherence.[33]

Limitations

This study has several limitations. This is an explorative study of a dataset, which was intended to study predictors of non-adherence in elderly people with neurological disorders. Therefore, confirmatory statements cannot be made. Another limitation is that we evaluated many symptoms exclusively through self-reports, which are known to be prone to systematic and unsystematic biases.[37] However, the questionnaires used are valid in the clinical

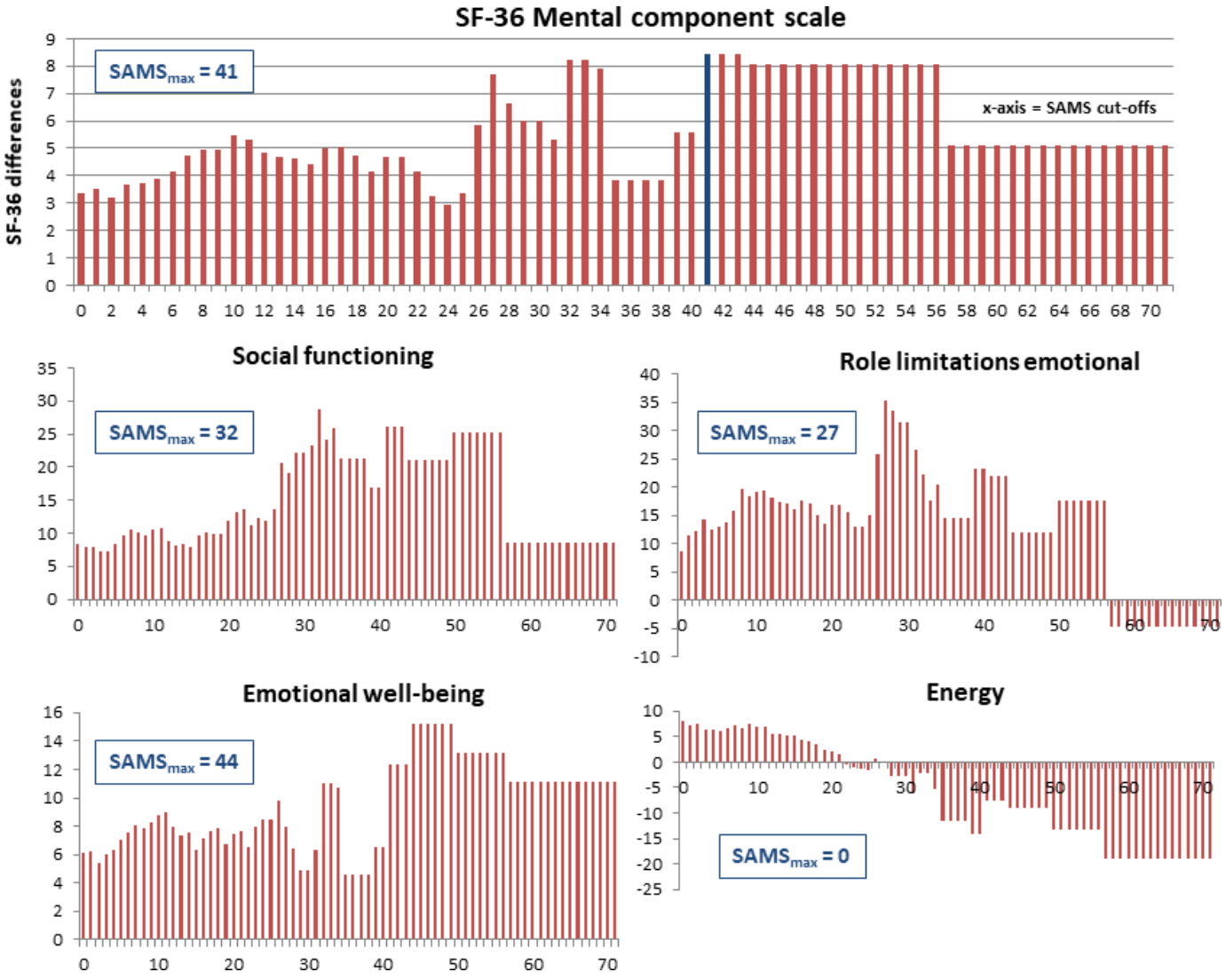

Figure 3 Change of Short-Form Survey (SF-36) domains and component scales as a function of different SAMS cut-offs the Mental Subscale. Note: The x-axis shows the possible SAMS cut-offs based on sum scores ranging from 0 to 72. The y-axis shows how the SF-36 changes depending on the SAMS cut-off. By doing so, we determined at which SAMS cut-off the influence on the SF-36 is maximal. SAMS, Stendal Adherence to Medication Score.

literature.[22 35 38] Furthermore, we only used one measure for adherence and QoL each, and several others exist which were not used in this study. There are more than 40 different self-report scales for measuring adherence, and while those scales differ greatly, none of them perform appropriately in all aspects.[5]

Although research suggests that there are no best practice instruments available that cover all important aspects of adherence and QoL,[5] a general statement about QoL and adherence using different scales cannot be made and further research is needed to validate our results in different groups of patients and using different adherence measures.

Conclusion

Our data suggest that using a general QoL-measurement to determine cut-off scores for adherence levels is not feasible in a mixed patient group, as the multiple dimensions and subscales of the two complex constructs may interact individually for each patient. Therefore, to determine adherence scores that are clinically relevant, disease-specific and patient-specific aspects must be determined to identify clinically relevant adherence.

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Contributors Design of the study: TP. Collection of data: AS and HMM. Analysis: TP, TL. Writing of the paper: TP and HMM. Writing—editing and revision: AS. All authors read and approved the final manuscript. TP is the guarantor for this study.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (ethics committee of the Jena University Hospital, 4572-10/15) and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The study was approved by the local ethics committee (approval number 5290-10/17) of Jena University Hospital. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. The anonymous data from the study can be freely requested from: Prell, T., Schönenberg, A., Mühlhammer, H.M. &Teschner, U (2022). *Data on Medication Adherence in Adults with Neurological Disorders: The NeuroGerAd Study* [Data Collection]. Colchester, Essex: UK Data Service. 10.5255/UKDA-SN-856032

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