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The 8-item Morisky Medication Adherence Scale translated in German and validated against objective and subjective polypharmacy adherence measures in cardiovascular patients

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Abstract

Rationale, aims and objectives To translate in German the 8-item Morisky Medication Adherence Scale (MMAS-8D). To validate it against objective and subjective measures of adherence in cardiovascular patients with polypharmacy.
Methods A standard forward-backward procedure was used to translate the MMAS-8 into German. Validation took place on a convenience sample of ambulatory patients on chronic antiplatelet therapy between June 2010 and June 2011. Objective adherence was obtained from electronically monitored multi-drug punch cards. Internal consistency was assessed using Cronbach's alpha coefficient, construct validity using exploratory factor analyses and correlations between MMAS-8D and related measures. Convergent validity was assessed with a subjective questionnaire about beliefs about medicines (BMQ Specific, two sub-scales).
Results A total of 70 patients were included (mean age 65.7 ± 9.9 years; 31.4% women). The mean score of the MMAS-8D was 7.5 (SD 0.8; range 4.5–8). Moderate internal consistency (alpha = 0.31) was observed due to multidimensionality of the scale. Factor analysis yielded four components that accounted for 71.7% of the total variance. Convergent validity was supported by significant correlations with BMQ Necessity ($r = 0.31$, $P < 0.01$), BMQ Concerns ($r = -0.16$, $P < 0.05$) and with electronic adherence reports (U-values 44 and 471, $P < 0.05$). Platelet aggregation values were within therapeutic range for 80% of the patients. Blood values of the antiplatelet agent within therapeutic range were associated with a higher MMAS-8D score (U-value 125, $P < 0.05$).
Conclusions The German MMAS-8 appears to be a reliable instrument to catch medication adherence in cardiovascular patients. It may be useful in patients with chronic therapy for detecting non-adherence.

Introduction

The assessment of medication adherence in patients is crucial as non-conformity with prescribed drug regimen poses a substantial risk for therapeutic failure, regardless of the underlying disease [1]. Various adherence assessment methods have been used over the past decades, either direct (i.e. with detection of the substance in a biological fluid, thus proving that a dose of a drug was

ingested) or indirect (i.e. which do not demonstrate drug ingestion). From the indirect measures (such as self-reporting, medication diaries, residual pill counting, pharmacy records, clinician opinion, electronic devices with remote control), questionnaires remain the most commonly used type because of major advantages (mainly they are simple, practical, cheap, non-invasive, unobtrusive) [2], whereas electronic monitoring represents the most objective measure [3].

Among self-reported questionnaires, the 8-item Morisky Medication Adherence Scale (MMAS-8) [4] is one of the most widely used scale to measure self-reported adherence mainly because of the simplicity of its administration and scoring. It consists of seven yes/no questions and one 5-point Likert scale. The scale has demonstrated high internal consistency and good sensitivity and specificity; it was shown to be valid and reliable [4]. The questionnaire was shown to be an effective screening tool in clinical practice to identify non-adherent patients at risk of uncontrolled blood pressure [5]. The MMAS-8 has been translated into more than 50 languages, for example, French, Malay, Portuguese and Thai [6–9], and used in long-term medical conditions, across different settings and various cultural contexts. The scale has also been translated into Chinese and analysed with hypertensive and myocardial infarction patients [10,11].

Numerous adherence studies have been conducted in a German-speaking setting, most of them with self-developed questionnaires [12] or scales [13]. Parts of the MMAS-8 have been translated in German and used in specific investigations [14] or larger trials [15], but the German scale was never validated. Consequently, one can assume that several German versions of the psychometric instrument are available, rendering comparison of results questionable. Further, the lack of validation might lead to biased results. Adherence to antiplatelet therapy has been estimated in many studies and appears to be high. Of the 2640 patients surveyed in the German Stroke Database, 96% reported to be still on any antiplatelet therapy (mostly aspirin) for prevention 1 year after their stroke [16]. In a retrospective analysis using administrative claims data of 9635 US veterans with established cardiovascular disease, 84% had sufficient antiplatelet medicine dispensed over 5 years to cover 80–120% of the treatment duration [17]. Considering that interventions aimed at optimizing adherence will be more effective if they are tailored to a patient's needs, health professionals will need, on the one hand, overall adherence measurement tools and, on the other hand, single items assessing pre-existing behaviours and habits. Because of the foreseeable use of the MMAS-8 as an adherence measurement and assessment tool in German-speaking countries including Switzerland, we were interested in establishing a German version of the MMAS-8, the MMAS-8D (Deutsch).

The validity of electronic devices (i.e. systems that record date and time of each dispensing of medication) in measuring adherence was demonstrated in many studies, either for container caps with single drug [18] or for weekly pill boxes with polypharmacy [19]. Recently, electronic monitoring was recommended as a method of choice in research on adherence [20]. A meta-analysis demonstrated a high to moderate correlation between self-reported questionnaires and medication adherence measured using monitoring devices [21]. Thus, we performed a validation against electronic measures of adherence and the Beliefs about Medicines Questionnaire (BMQ) [22], a validated subjective questionnaire that showed a significant relationship with adherence to medication in substantial different social, cultural, economic and health care system contexts [3]. Further, the association did not differ if objective or subjective adherence measures were used. This article reports the validation of the German MMAS-8 against objective and subjective measures of adherence in ambulatory patients with antiplatelet therapy.

Method

Participants and setting

A convenience sample of 19 general practitioners in Solothurn, Switzerland, invited patients with chronic antiplatelet treatment to participate in a cross-sectional study on drug resistance between June 2010 and June 2011. The study is described elsewhere [23]. In brief, 82 outpatients older than 18 years with ongoing prescriptions for aspirin and/or clopidogrel accepted participation. They obtained their entire oral solid medication (polypharmacy) for 7 days in a punch card equipped with electronic adherence monitoring. Blood samples were collected after adherence monitoring to measure platelet aggregation and to determine polymorphism of the *CYP2C19* gene. The patients were aware of the purpose and function of the electronic system prior to study. They were advised to take their medicine at the time they were normally used to by just pushing out all the pills contained in one cavity. Filling of the questionnaires was performed at the study centre; questions were answered on site by the study investigator. This observational cross-sectional study obtained ethical approval from the Swiss local Ethics Committee of Aargau and has been registered at ClinicalTrials.gov ID NCT01039480. All patients provided written informed consent before participation.

Translation of the instrument

Translation in German was performed according to the 'Principles of Good Practice' for the translation and cultural adaptation process for patient-reported outcomes measures [24]. The back-translation technique was performed by two translators: one conducting the forward translation and the other one conducting the back translation. Equality of sense rather than equality of word was favoured. The source language versions were compared and discrepancies lead to modifications in the target language version until both translators were satisfied with semantic and conceptual equivalence between source and target languages. The developer of the MMAS-8 approved the German version. The corrected target language version was validated with three monolingual subjects for comprehensiveness, appropriateness, acceptability and feasibility.

Subjective adherence measure

The MMAS-8 [4] consists of seven yes/no questions and one 5-point Likert scale. Patients answering 'no' to all questions but 'yes' to item 5 (reverse coding) and 'never/rarely' to item 8 obtain the maximal 8 points and are classified as 'high adherence'. Patients answering differently obtain a lower score that indicates lower adherence and are classified as 'medium' (6–<8) or 'low' (<6) adherence. The questionnaire takes about 5 minutes to complete. The term '[health concern]' medication was not specified in our questionnaire in order to steer for polypharmacy.

Beliefs about medicines

The BMQ [22] is an instrument that assesses the cognitive representation of medication and consists of two sections (BMQ-Specific and BMQ-General). Many studies demonstrated a high correlation between BMQ scales and self-reported adherence in several chronic diseases, including asthma [25], hypertension [26], HIV [27] and diabetes [28]. We selected this questionnaire as it targets beliefs about medicine in general, that is, polypharmacy, and not a single drug. The German version has been validated in chronically ill patients and showed good internal consistency (Cronbach's alpha 0.79–0.83) [29]. We used the BMQ-Specific that assesses patients' beliefs about the particular medication prescribed for them and consists of a 5-item Necessity scale (necessity of taking medications for maintaining present and future health) and a 5-item Concerns scale (concerns about the potential adverse consequences of taking medicine). Responses are given on a 5-point Likert scale ranging from strongly agree (scored 5) to strongly disagree (scored 1). Scores are summed and range from 5 to 25 for each sub-scale, with high scores indicating strong beliefs in the concept. The Necessity-Concerns differential is calculated by subtracting concerns scores from necessity scores (scores range from −20 to +20). This score represents a crude indicator of the way a person rates his/her perceived need for the treatment relative to his/her concerns about following it. If the differential is positive, the person notes that the benefits of medication outweigh the costs. Contrarily, if negative, the person perceives heavier cost than benefit [22].

Objective adherence measures

Polypharmacy electronic monitoring system (POEMS) technology [2] was used to asses adherence to the reference medication. In brief, POEMS consists of a polymer film with imprinted electronic components that measure the electrical resistance and record the time of its changes when a loop is broken, that is, when a cavity is emptied. The patient's entire oral solid medication is filled in a disposable multi-drug punch card with 7×4 cavities, equipped with the film on its backside. For a given patient, we calculated two established adherence rates to the antiplatelet agent, that is, to the drug of interest within the prescribed polypharmacy: taking adherence (number of days with performed intakes divided by number of days with prescribed intakes) and timing adherence with the strictest grace interval of 25% [30] (number of doses taken at 24 ± 6 hours for a once-daily regimen or 12 ± 3 hours for a twice daily regimen). In addition, we calculated for each patient the mean drug intake time of the antiplatelet agent. The timing variability in drug intake was defined as variance of the mean drug intake time [31] and indicates the timeliness of the intakes.

Platelet aggregation was measured in venous blood samples and is described elsewhere [23]. In brief, values below the cut-off of 30 arbitrary units (AU) for the ASPItest (aspirin) and 53 AU for the ADPtest (clopidogrel) were considered as in the therapeutic range, and consequently, the patient as fully adherent. Pharmacogenetic analysis of the *CYP2C19* gene was performed for clopidogrel values outside therapeutic range. Polymorphism (*CYP2C19**2, *2C19**4, *2C19**17) is associated with insufficient platelet inhibition in clopidogrel-treated persons [32]. Laboratory signs of inflammation were defined by C-reactive protein >5 mg L^{-1} and is associated with resistance to aspirin [33].

Statistical analysis

Where appropriate, mean and standard deviations, median and interquartile ranges are presented. Internal consistency or reliability of the MMAS-8D was assessed using Cronbach's coefficient alpha, which indicates whether each item of a scale is appropriate for assessing the underlying concept of its scale. Values for Cronbach's alpha range between 0 and 1; the closer they are to 0, the less the items are related to one another. Values above 0.7 are generally considered to indicate satisfactory internal consistency [34]. However, opinions differ regarding acceptable cut-offs [35].

Construct validity, that is, the degree to which an instrument reflects the underlying construct that it was designed to assess, was performed with exploratory factor analysis [principal component analysis (PCA) extraction method], followed by varimax rotation. Factors with Kaiser's eigenvalues of >1 were selected, that is, factors that accounted for more of the total variance than any single original item. Factor loadings greater than 0.4 were used for defining items associated with a given factor. Results are given in terms of percentage of variance in the score explained by the principal factor.

Convergent validity, that is, the degree to which an instrument is related to measures of similar constructs, was performed with the non-parametric Spearman's rho test as self-reported values (MMAS-8D and BMQ-Specific) and objective measure (electronic punch cards) were skewed towards high scores. Differences in adherence rates were compared using the Mann–Whitney *U*-test for continuous variables; comparison of categorical variables was performed with chi-square test. Correlations were interpreted with the following criteria: 0–0.25 = little or no correlation; 0.26–0.50 = small correlation; 0.51–0.75 = moderate to good correlation; and greater than 0.75 = very good to excellent correlation. Data were entered and analysed using SPSS statistical package version 21.0 (SPSS Inc., Chicago, IL, USA), and *P*-values <0.05 were considered significant.

Results

From 82 enrolled patients, 12 were excluded because of missing data due to deficiency in the recording technology. Of the remaining 70 patients [mean age 65.7 ± 9.9 years; 31.4% women, mean age 67.9 ± 9.7 years and 68.6% men, mean age 64.7 ± 9.9 years; non-significant (ns)], full sets of data were available. The study sample consisted of patients with a prescription of antiplatelet agents for primary (42.9%) or secondary prevention (57.1%). Mean number of prescribed drugs per patient was 5.2 ± 2.3 (range 1–13), which were to be taken once daily (37.1%; all but one in the morning), twice daily (48.7%, all but four in the morning and the evening), thrice daily (11.5%) or fourth daily (2.9%). With one exception, all antiplatelet agents were lodged with the morning medication (98.6%). All doses of the antiplatelet agents were taken (100% taking adherence) and all but four patients had intake times within the grace interval of ±3 hours (91.4% timing adherence). A stricter grace interval of ±1.5 hours was observed in 39 patients. The variance of the mean intake times averaged 1.4 hours^2 ± 4.3 hours^2, with a median of 0.5 hours^2 and an interquartile range (IQR) of 0.8 (25th percentile of 0.2 hours^2; 75th percentile of 1.0

hours[2]). The variance was not associated with the number of drugs ($r = 0.19$, $P = 0.06$; ns) nor with the number of intake times ($r = 0.17$, $P = 0.08$; ns). Platelet aggregation values were within therapeutic range for 74% of the patients taking aspirin, 75% of those with clopidogrel and 95% of those on dual therapy, yielding a total of 56 patients (80%) with optimal platelet aggregation. For further seven patients (10%), genetic mutation (three patients with clopidogrel) or underlying inflammation factors (four patients with aspirin) were detected.

Responses of the MMAS-8D were coded analogue to the English version. With the recommended scoring method, the mean score of the MMAS-8D was 7.5 (SD 0.8; range 4.5–8), with a median of 8 and an IQR of 1 (25th percentile of 7; 75th percentile of 8). With the recommended cut-offs, the majority of patients were in the high adherence group (64.3%), whereas 30.1% and 5.7% were in the medium and low adherence groups, respectively. Only two patients indicated that they did not take their medication the day before (item 5), whereas nine patients (12.9%) declared to forget sometimes to take their medication (item 1). The mean BMQ scores were 19.7 (SD 4.1; range 6–25; median 20) for the Necessity scale and 9.5 (SD 3.9; range 5–20; median 9) for the Concerns scale. With a Necessity-Concerns differential of 10.1 (SD 5.6; range –2 to +20), participants noted that the benefits of medication outweigh the costs.

Internal consistency/reliability

Cronbach's alpha was 0.31 for the eight items of the German version MMAS-8D and slightly higher when item 1 was not used for computation (0.40). Overall standardized Cronbach's alpha was 0.41. The item-to-total correlations ranged from –0.015 to +0.530 (Table 1).

Table 1 Reliability test ($n = 70$)

	Corrected item-total correlation	Cronbach's alpha if item deleted
Item 1	–0.015	0.401
Item 2	0.287	0.161
Item 3	0.127	0.282
Item 4	0.064	0.309
Item 5	0.009	0.328
Item 6	0.038	0.317
Item 7	0.247	0.219
Item 8	0.530	0.202

Construct validity

The PCA was used to show the dimensionality of the scale. On the basis of eigenvalues greater than 1, four components were retained, which explained 71.7% of the total variance. The items that contributed to the first component involved forgetfulness and remembering (items 1, 2 and 8) and explained 24.4% of the variance. The items that contributed to the second component (17.3% of the variance) concerned stopping medication when one feels better and feeling hassled about one's treatment plan (items 6 and 7). The items that contributed to the third component concerned stopping medication when one feels worse and taking the medication the day before (items 3 and 5). Item 4 concerning travelling situation contributed to the fourth component (13.5%). Table 2 shows the moderate to strong loading (>0.4) of all items, after varimax rotation with Kaiser normalization.

Convergent validity

Convergent validity of the MMAS-8D was demonstrated through correlations with objective and subjective measures (Table 3). Patients with intake times within a grace interval of ±3 or 1.5 hours had a significant higher MMAS-8D score (U-values 44 and 471, $P < 0.05$). Adherence measured as timeliness of the intakes correlated moderately with MMAS-8D scores ($r = –0.15$) and in the expected direction, without reaching statistical significance ($P = 0.11$; ns). There was a statistically significant relationship between items 6 and 7 and the recorded intake times (chi-square values 34 and 22, $P < 0.01$), with patients not stopping their medicine when they feel like their health is under control (item 6) and not feeling hassled about sticking to their treatment plan (item 7) taking their medication more often within the 3-hour grace period. The MMAS-8D scores were significantly correlated with the Necessity ($r = 0.31$, $P < 0.01$) and the Concerns sub-scores of the BMQ ($r = –0.16$, $P < 0.05$). The correlations were small to moderate, and in the expected directions, that is, patient who self-reported higher adherence to their medication with the MMAS-8D had significantly higher sense of necessity of medication and lower

Table 2 Items, patients' answers and maximal value of factor loading of the MMAS-8D in German ($n = 70$)

Item No.	Patients' response to be considered adherent	Number (%)	Factor loading (component)*
1	No	61 (87.1%)	0.692 (1)
2	No	64 (91.4%)	0.179 (1)
3	No	64 (91.4%)	0.748 (3)
4	No	67 (95.7%)	0.875 (4)
5	Yes	69 (98.6%)	0.795 (3)
6	No	68 (97.1%)	0.782 (2)
7	No	67 (95.7%)	0.824 (2)
8	Never/rarely; once in a while; sometimes; usually; all the time	Never: 62 (88.6%) Once: 7 (10%) Sometime: 1 (1.4%)	0.773 (1)

*First, second, third or fourth component obtained with principal component analysis after varimax rotation with Kaiser normalization.

Table 3 Convergent validity: Spearman correlations and Mann–Whitney *U*-values of the MMAS-8D with objective adherence measures (electronic monitoring and blood values of antiplatelet agent) and beliefs about medicine scores

Measures [numbers of patients]	MMAS-8D		
	Correlation	*U*-value	*P*-value
BMQ necessity [70]	0.31		<0.01
BMQ concerns [70]	–0.16		<0.05
Adherence as timeliness of intake [70]	–0.15		0.11 (ns)
Adherence as variability ± 3 hours [70]		44	<0.05
Adherence as variability ± 1.5 hours [70]		471	<0.05
Platelet aggregation in the range [63]		125	<0.05

BMQ, Beliefs about Medicines Questionnaire; ns, non-significant.

concerns about it. After exclusion of the seven patients with inflammation or genetic polymorphism, blood values of the antiplatelet agent within therapeutic range correlated highly with MMAS-8D score (*U*-value 125, $P < 0.05$). A subgroup analysis was performed according to indication of antiplatelet therapy. Patients with an antiplatelet agent for secondary prevention showed a statistically significant higher MMAS-8D score than patients in the primary prevention group (median 8 vs. 7; *U*-value 407, $P < 0.01$).

Discussion

In the present study with electronic adherence monitoring as reference standard, we examined the reliability and validity of the 8-item German version of the MMAS. The high adherence scores obtained electronically even with the strictest grace interval for medication intake were indicative of a highly adherent sample of patients. Direct measure of adherence by laboratory tests such as platelet aggregation confirmed drug intake for 80% of patients, whereas reasons for reduced antiplatelet effect such as genetic polymorphism or inflammation were observed for further 10% of the patients. Estimates of adherence obtained with the translated scale were in concordance to all rates calculated from electronic records.

We found low psychometric properties for the German version of the MMAS-8D compared with the original English MMAS-8, especially for internal consistency (Cronbach's alpha 0.31 vs. 0.83 [4]). The small to moderate reliability we observed is similar to that of three other studies that validated the French [9], Malaysian [7] and Thai [8] versions of the MMAS-8. As Cronbach's alpha measures whether each item of a scale is appropriate for assessing the concept of the scale, the internal consistency of the entire scale will be high if all items measure the same phenomenon. In our case, we retained four components after varimax rotation that explained 71.7% of the variance (24.4% for the first component), indicating that the scale is four dimensional. This is in contradiction with the original English scale that was declared one dimensional [4], but in strong concordance with the results of the French and the Thai scales that attributed 55.2% and 57.4% of the variance, respectively, to three components [8,9]. Consequently, the unacceptable low Cronbach's alpha in our study may indicate the multidimensionality of the scale rather than its inconsistency [35]. Further, the MMAS-8 contains items aimed at identifying *reasons* for non-adherence that can be classified as causal indicators rather than effect indicators [36]. Because causal indicators by definition may not be highly intercorrelated, statistics with Cronbach's alpha are inappropriate for these indicators, as high internal consistency depends upon high inter-item correlation [36]. In this sense, some authors urge to indicate supplementary information to evaluate multiple-item measures of a scale [35] as Cronbach's alpha seems to be an inadequate index to describe the internal consistency of a scale.

Although subjective and objective measures of adherence have different strengths, the MMAS-8D demonstrated convergent validity with electronic measures of adherence and with laboratory values. As subjective measures are subject to potential inaccuracy because of patients' memory or reluctancy to report deviant behaviour, and may thus overestimate adherence [37], objective measures with electronic systems were valued as more accurate. However, the correlation between self-related questionnaires and electronic records of adherence was shown to be small to moderate [21], predominantly because different sets of information are collected with different approaches and perspectives. Notwithstanding, the correlation with electronic records, blood values and the significant association with BMQ sub-scores support the validity of the MMAS-8D. The latter is in accordance with findings from a study with women newly treated against osteoporosis with daily or weekly oral bisphosphonates, where the Necessity sub-score of the BMQ showed a significant association with the 8-item Morisky scale [38].

The subgroup analysis showed that patients with antiplatelet therapy for secondary prevention self-reported a higher adherence than patients in primary prevention. This is in line with a recent meta-analysis with 376 162 patients, where two-thirds of the patients with a history of cardiovascular disease (and thus with a prescribed drug to prevent secondary disease progression) were adherent, compared to one-half of the patients with a drug to prevent a first event (primary prevention) [39].

The authors acknowledge some limitations of the study. Firstly, the sample could be prone to selection bias. Motivated patients might have been more likely to accept participation and thereby be more adherent than the general population of outpatients with antiplatet therapy. In a similar perspective, the sample could be prone to social-desirability response bias, that is, patients tending to present themselves in the most favourable manner. This is suggested by the overrepresentation of the maximal MMAS-8D scores, with almost two-thirds of the patients allocated to the high adherence group. This substantial ceiling effect is common in questionnaires [40]. Similar high results were observed in the French validation study (median score of 7; 44% of patients in the high adherence group [9]). Secondly, the modest sample size may have biased our results as small sample sizes can affect the result of the internal consistency. However, our sample size was greater than the study validating the Swedish version of the MMAS-8 (60 respondents in 1998, 53 respondents in 2002 [41]) and than the first study validating a rating scale against electronic monitoring (61 patients with electronic medication's caps [42]). Thirdly, the relatively brief

monitoring period may be criticized because it is insufficient to estimate overall adherence to therapy. However, given that, firstly, intake of an antiplatelet agent 7 days is sufficient to influence platelet aggregation and to be detected in blood, and, secondly, MMAS questions span the past 2 weeks, the short study period was estimated satisfactorily in our validation setting and able to deliver the required values of intake pattern. It should be further mentioned that the validity of the MMAS-8D scale might be somewhat compromised when the single medication for the health condition is not specified in the scale item. However, this health concern specified item is not compatible with polypharmacy, and consequently, we generalized the items to target polypharmacy and not a single drug. By doing so, we made the items agree with the electronic monitoring. Finally, any electronic monitoring device can act as intake reminder and temporarily enhance adherence, especially when participants are aware of the purpose of the electronic system as in our study. However, a recent randomized controlled trial with 226 diabetes patients investigated the reactive effect of electronic monitoring over 8 weeks [20]. The authors concluded that using an electronic device may lead to a small increase in adherence compared to standard packaging, however, without reaching significance and without changing over time. As a consequence, a slightly higher adherence is inevitable in a patient's population equipped with any reminder packaging.

Because the German language is the official language in Germany, Switzerland and Austria, with identical grammar and orthography, our questionnaire can be used in the three German-speaking countries without further adaptation. We could not find any negative comments in the literature when a questionnaire in German is used in several German-speaking countries. A recent survey was developed in Switzerland in German language and was sent simultaneously to nurses in Switzerland, Germany and Austria through their respective societies [43]. The authors did not mention any comment on the language of the questionnaire. Much more, an international multi-centre validation of a newly translated questionnaire in German was approved by ethic committees in Switzerland, Germany and Austria and was a strength for the recruitment of patients in primary care [44]. Cultural differences between the German-speaking countries may concern the health system, which however is not a topic in the MMAS.

To conclude, the German MMAS-8D was able to categorize 94.4% of the patients as good adherer, which was confirmed by established measures of adherence obtained from electronic data. It appears to be a reliable instrument to catch medication adherence in cardiovascular patients, despite a low internal consistency. Further, it is endowed with simplicity and quickness of administration and scoring, which facilitates its use in several pathologies.

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Author contributions

The work presented here was carried out in collaboration between all authors. IA and KEH defined the research topic. PNW and IA designed the methods and the instruments. PNW carried out the study. CM analysed the data. IA interpreted the results and wrote the first draft of the manuscript. DEM discussed the analyses and the interpretation. All authors have contributed to, reviewed and approved the manuscript.

References

1. DiMatteo, M. (2004) Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Medical Care*, 42 (3), 200–209.
2. Arnet, I., Walter, P. N. & Hersberger, K. E. (2013) Polymedication electronic monitoring system (POEMS) – a new technology for measuring adherence. *Frontiers in Pharmacology*, 4, 26.
3. Horne, R., Chapman, S., Parham, R., Freemantle, N., Forbes, A. & Cooper, V. (2013) Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the Necessity-Concerns framework. *PLoS ONE*, 8 (12), e80633.
4. Morisky, D. E., Ang, A., Krousel-Wood, M. & Ward, H. J. (2008) Predictive validity of a medication adherence measure in an outpatient setting. *Journal of Clinical Hypertension (Greenwich, Conn.)*, 10 (5), 348–354.
5. de Oliveira-Filho, A., Barreto-Filho, J., Neves, S. & Lyra Junior, D. (2012) Association between the 8-item Morisky Medication Adherence Scale (MMAS-8) and blood pressure control. *Arquivos Brasileiros de Cardiologia*, 99 (1), 649–658.
6. de Oliveira-Filho, A. D., Morisky, D. E., Neves, S. J. F., Costa, F. A. & de Lyra, D. P. Jr (2013) The 8-item Morisky Medication Adherence Scale: validation of a Brazilian–Portuguese version in hypertensive adults. *Research in Social and Administrative Pharmacy*, 10 (3), 554–561.
7. Al-Qazaz, H., Hassali, M. A., Shafie, A. A., Sulaiman, S. A., Sundram, S. & Morisky, D. E. (2010) The eight-item Morisky Medication Adherence Scale MMAS: translation and validation of the Malaysian version. *Diabetes Research and Clinical Practice*, 90 (2), 216–221.
8. Sakthong, P., Chabunthom, R. & Charoenvisuthiwongs, R. (2009) Psychometric properties of the Thai version of the 8-item Morisky Medication Adherence Scale in patients with type 2 diabetes. *The Annals of Pharmacotherapy*, 43 (5), 950–957.
9. Korb-Savoldelli, V., Gillaizeau, F., Pouchot, J., Lenain, E., Postel-Vinay, N., Plouin, P.-F., Durieux, P. & Sabatier, B. (2012) Validation of a French version of the 8-item Morisky Medication Adherence Scale in hypertensive adults. *Journal of Clinical Hypertension (Greenwich, Conn.)*, 14 (7), 429–434.
10. Lee, G., Wang, H., Liu, K., Cheung, Y., Morisky, D. & Wong, M. (2013) Determinants of medication adherence to antihypertensive medications among a Chinese population using Morisky Medication Adherence Scale. *PLoS ONE*, 8 (4), e62775.
11. Yan, J., You, L., Yang, Q., Liu, B., Jin, S., Zhou, J., Lin, C. & Morisky, D. (2014) Translation and validation of a Chinese version of the 8-item Morisky medication adherence scale in myocardial infarction patients. *Journal of Evaluation in Clinical Practice*, 20 (4), 311–317.
12. Ude, M., Leuner, K., Schüssel, K., Schulz, M. & Müller, W. E. (2013) Adherence to antihypertensives: feasibility of two self-report instruments to investigate medication-taking behaviour in German community pharmacies. *The International Journal of Pharmacy Practice*, 21 (3), 169–177.
13. Jank, S., Bertsche, T., Schellberg, D., Herzog, W. & Haefeli, W. (2009) The A14-scale: development and evaluation of a questionnaire for assessment of adherence and individual barriers. *Pharmacy World and Science*, 31 (4), 426–431.
14. Zok, K. (2012) Einstellungen älterer Menschen zur Arzneimitteltherapie [article in German]. WIdO-Monitor, 1.
15. Petersen, J. J., König, J., Paulitsch, M. A., Mergenthal, K., Rauck, S., Pagitz, M., Schmidt, K., Haase, L., Gerlach, F. M. & Gensichen, J.

(2014) Long-term effects of a collaborative care intervention on process of care in family practices in Germany: a 24-month follow-up study of a cluster randomized controlled trial. *General Hospital Psychiatry*, 36 (6), 570–574.
16. Hamann, G. F., Weimar, C., Glahn, J., Busse, O. & Diener, H. C. (2003) Adherence to secondary stroke prevention strategies – results from the German Stroke Data Bank. *Cardiovascular Diseases*, 15 (4), 282–288.
17. Roughead, E. E., Vitry, A. I., Preiss, A. K., Barratt, J. D., Gilbert, A. L. & Ryan, P. (2010) Assessing overall duration of cardiovascular medicines in veterans with established cardiovascular disease. *European Journal of Cardiovascular Prevention and Rehabilitation*, 17 (1), 71–76.
18. Lehmann, A., Aslani, P., Ahmed, R., Celio, J., Gauchet, A., Bedouch, P., Bugnon, O., Allenet, B. & Schneider, M. (2014) Assessing medication adherence: options to consider. *International Journal of Clinical Pharmacy*, 36 (1), 55–69.
19. Stip, E., Vincent, P., Sablier, J., Guevremont, C., Zhornitsky, S. & Tranulis, C. (2013) A randomized controlled trial with a Canadian electronic pill dispenser used to measure and improve medication adherence in patients with schizophrenia. *Frontiers in Pharmacology*, 4, 100.
20. Sutton, S., Kinmonth, A.-L., Hardeman, W., Hughes, D., Boase, S., Prevost, A. T., Kellar, I., Graffy, J., Griffin, S. & Farmer, A. (2014) Does electronic monitoring influence adherence to medication? Randomized controlled trial of measurement reactivity. *Annals of Behavioral Medicine*, 48 (3), 293–299.
21. Shi, L., Liu, J., Koleva, Y., Fonseca, V., Kalsekar, A. & Pawaskar, M. (2010) Concordance of adherence measurement using self-reported adherence questionnaires and medication monitoring devices. *Pharmacoeconomics*, 28 (12), 1097–1107.
22. Horne, R., Weinman, J. & Hankins, M. (1999) The beliefs about medicines questionnaire (BMQ): the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*, 14 (1), 1–24.
23. Walter, P. N., Tsakiris, D., Romanens, M., Arnet, I. & Hersberger, K. E. (2014) Antiplatelet resistance in outpatients with monitored adherence. *Platelets*, 25 (7), 532–538.
24. Wild, D., Grove, A., Martin, M., Eremenco, S., McElroy, S., Verjee-Lorenz, A. & Erikson, P. (2005) Principles of Good Practice for the translation and cultural adaptation process for Patient-Reported Outcomes (PRO) measures: report of the ISPOR Task Force for translation and cultural adaptation. *Value in Health*, 8 (2), 94–104.
25. Byer, B. & Myers, L. (2000) Psychological correlates of adherence to medication in asthma. *Psychology, Health and Medicine*, 5 (4), 389–393.
26. Ross, S., Walker, A. & MacLeod, M. J. (2004) Patient compliance in hypertension: role of illness perceptions and treatment beliefs. *Journal of Human Hypertension*, 18 (9), 607–613.
27. Gauchet, A., Tarquinio, C. & Fischer, G. (2007) Psychosocial predictors of medication adherence among persons living with HIV. *International Journal of Behavioral Medicine*, 14 (3), 141–150.
28. Broadbent, E., Donkin, L. & Stroh, J. C. (2011) Illness and treatment perceptions are associated with adherence to medications, diet, and exercise in diabetic patients. *Diabetes Care*, 34 (2), 338–340.
29. Mahler, C., Hermann, K., Horne, R., Jank, S., Haefeli, W. E. & Szecsenyi, J. (2012) Patients' beliefs about medicines in a primary care setting in Germany. *Journal of Evaluation in Clinical Practice*, 18 (2), 409–413.
30. Zeller, A., Schroeder, K. & Peters, T. J. (2008) An adherence self-report questionnaire facilitated the differentiation between nonadherence and nonresponse to antihypertensive treatment. *Journal of Clinical Epidemiology*, 61 (3), 282–288.
31. Vrijens, B. & Goetghebeur, E. (1997) Comparing compliance patterns between randomized treatments. *Controlled Clinical Trials*, 18 (3), 187–203.
32. Mega, J. L., Close, S. L., Wiviott, S. D., *et al*. (2009) Cytochrome P-450 polymorphisms and response to clopidogrel. *The New England Journal of Medicine*, 360 (4), 354–362.
33. Larsen, S. B., Grove, E. L., Kristensen, S. D. & Hvas, A. M. (2013) Reduced antiplatelet effect of aspirin is associated with low-grade inflammation in patients with coronary artery disease. *Thrombosis and Haemostasis*, 109 (5), 920–929.
34. Leidy, N. K., Revicki, D. A. & Genesté, B. (1999) Recommendations for evaluating the validity of quality of life claims for labeling and promotion. *Value in Health*, 2 (2), 113–127.
35. Schmitt, N. (1996) Uses and abuses of coefficient alpha. *Psychological Assessment*, 8 (6), 350–353.
36. Voils, C. I., Hoyle, R. H., Thorpe, C. T., Maciejewski, M. L. & Yancy, W. S. Jr (2011) Improving the measurement of self-reported medication nonadherence. *Journal of Clinical Epidemiology*, 64 (3), 250–254.
37. Simoni, J. M., Kurth, A., Pearson, C. R., Pantalone, D. W., Merrill, J. O. & Frick, P. A. (2006) Self-report measures of antiretroviral therapy adherence: a review with recommendations for HIV research and clinical management. *AIDS and Behavior*, 10 (3), 227–245.
38. Reynolds, K., Viswanathan, H. N., O'Malley, C. D., *et al*. (2012) Psychometric properties of the Osteoporosis-specific Morisky Medication Adherence Scale in postmenopausal women with osteoporosis newly treated with bisphosphonates. *The Annals of Pharmacotherapy*, 46 (5), 659–670.
39. Naderi, S. H., Bestwick, J. P. & Wald, D. S. (2012) Adherence to drugs that prevent cardiovascular disease: meta-analysis on 376,162 patients. *The American Journal of Medicine*, 125 (9), 882–887, e1.
40. Wensing, M., Vedsted, P., Kersnik, J., *et al*. (2002) Patient satisfaction with availability of general practice: an international comparison. *International Journal for Quality in Health Care*, 14 (2), 111–118.
41. Södergard, B., Halvarsson, M., Lindbäck, S., Sönnerborg, A., Tully, M. & Lindblad, A. (2006) Differences in adherence and motivation to HIV therapy – two independent assessments in 1998 and 2002. *Pharmacy World & Science*, 28 (4), 248–256.
42. Byerly, M. J., Nakonezny, P. A. & Rush, A. J. (2008) The Brief Adherence Rating Scale (BARS) validated against electronic monitoring in assessing the antipsychotic medication adherence of outpatients with schizophrenia and schizoaffective disorder. *Schizophrenia Research*, 100 (1–3), 60–69.
43. Panfil, E.-M., Zima, K., Lins, S., Köpke, S., Langer, G. & Meyer, G. (2014) Conflict of interest with industry – a survey of nurses in the field of wound care in Germany, Australia and Switzerland [article in German]. *Pflege*, 27 (3), 191–199.
44. Brenk-Franz, K., Hibbard, J. H., Herrmann, W. J., *et al*. (2013) Validation of the German version of the patient activation measure 13 (PAM13-D) in an international multicentre study of primary care patients. *PLoS ONE*, 8 (9), e74786.

