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Rating scales for medication adherence in Parkinson’s disease: a systematic review for critique and recommendations

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Abstract

Background: Behaviors interfering with medication adherence (MA) are common and often complex in Parkinson's disease (PD), negatively affecting quality of life and undermining the value of clinical trials. The Clinical Outcome Assessments (COA) Scientific Evaluation Committee of the International Parkinson and Movement Disorder Society (MDS) commissioned the assessment of MA rating scales to recommend the use in PD.

Objective: Critically review the measurement properties of rating scales used to assess MA in PD and to issue recommendations.

Methods: We conducted systematic review across seven databases to identify structured scales to assess MA in PD. Eligible studies were critically appraised for methodological quality using the Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) Risk of Bias checklist. Standards for good measurement properties of the selected scales were summarized narratively using the COSMIN, the MDS-COA Committee methodology, the World Health Organization concepts, and the Ascertaining Barriers to Compliance taxonomy. The certainty of the evidence was determined using the modified Grades of Recommendation, Assessment, Development and Evaluation approach with final assessments (highest to lowest) of “Recommended”, “Suggested” and “Listed”.

Results: Of the nine reviewed scales, none met the designation “Recommended”. The Morisky Medication Adherence Scale (MMAS-8); Beliefs Related to Medications Adherence questionnaire, Beliefs about Medication Questionnaire, Medication Adherence Rating Scale, and Satisfaction with Information on Medicines Scale were rated “Suggested”.

Conclusions: We suggest further work focusing on resolving the problems of the suggested scales or developing a new scale meeting all required criteria.
According to the latest Global Burden of Disease Study (GBD) report, among the 14 neurological disorders that are quantified as part of GBD, Parkinson's disease (PD) was the fifth most burdensome in terms of adjusted life-years and the fifth leading cause of death worldwide. Although many of PD motor and nonmotor symptoms are controlled by medication, as disease progresses its severity inevitably evolves, moving from forms of mild motor predominance to intermediate and diffuse malignant. Therefore, the continuous symptoms assessment and their responsiveness to drug therapy is essential throughout the course of the disease. Continual assessment supports appropriate use of medication therapies and delivery systems from oral, transdermal, and infused as along the continuum of PD. In PD patients, successful therapy is achieved when drug treatments are implemented with expected levels of adherence, which can be particularly difficult to achieve given the complexity of PD treatment, often marked by high frequency and variation of drugs and dosages (prescribed for use every 3-4 hours with different fractions each time).

Medication adherence (MA) is a multidimensional domain, defined as the extent to which a person's behavior when taking medication corresponds to the recommendations provided by a healthcare professional. According to the World Health Organization (WHO) and the Ascertaining Barriers to Compliance (ABC) taxonomy, a person's behavior can be influenced by interrelated components of MA such as: five dimensions (patient, health system/health care, social/economic, therapy and health condition), two factors (intentional and unintentional), and four phases (initiation, implementation, discontinuation, and persistence).

Detailed adherence assessments ought to provide a standard for therapeutic decision-making with a comprehensive examination covering the most relevant adherence dimensions, factors, and phases, preferably using more than one test per dimension to increase sensitivity. This approach may increase the accuracy of testing but is time consuming and not readily available in all settings. Therefore, a
measurement instrument covering multiple domains of MA would provide a global assessment of adherence performance with less burden and greater clinical and research engagement, providing accuracy to clinical trials. The current review aims to critically assess the measurement properties of available MA rating scales (RS) that have been used in people with PD to issue recommendations for their utilization.

Methods
We conducted a systematic review according to the Joanna Briggs Institute (JBI) methodology (7). We registered the study protocol in the International Prospective Register of Systematic Reviews (PROSPERO: CRD42021211099) and published the detailed review steps elsewhere (8).

Administrative Organization and Critique Process
The International Parkinson and Movement Disorders Society (MDS) Clinical Outcome Assessments (COA) Scientific Evaluation Committee (SEC) supported the creation of the Medication Adherence Rating Scale Review Subcommittee. This subcommittee is composed by a group of six international investigators specialists in PD, MA and/or measurement properties assessment from South America (MHST, BGRBO), North America (CGG, GTS, DM), and Oceania (VM), who participated in the various phases of this study. The final report from this subcommittee was reviewed and approved by MDS-COA-SEC.

Literature search
In the first step, conducted on May 4, 2021, we performed an initial limited search of MEDLINE (PubMed) to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles, and the index terms used to describe the articles were used to develop a full search strategy for MEDLINE (PubMed). In the second step, conducted on June 26, 2021, we expanded the search strategy by including all identified keywords and index terms found in step 1 and adapting them for each included database: MEDLINE (PubMed), LILACS (BVS Portal), PsycINFO (APA PsycNet), CINAHL
EBSCO), Web of Science (Clarivate Analytics), Embase and Scopus (Elsevier) (see Supplemental 1). In the third step, conducted on June 29, 2021, we reviewed the reference lists of all selected studies to identify potential additional studies.

During the search process, we did not apply any year or language restrictions, and we included all studies published until June 26, 2021. However, during the full texts analysis we identified three studies in languages other than English and Portuguese (two in Spanish \(^9,10\) and one in Japanese \(^11\), and we excluded them for feasibility reasons (translation costs). For the same reason, four studies developed by German investigators who used the original German version of the Stendal Adherence to Medication Score (SAMS) to measure medication adherence in PD were also excluded, as this scale, as well as their measurement properties studies are all published in German \(^12-15\). The results of the search, study selection and inclusion process were reported in full and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram \(^16\).

From the selected studies, we included RS that have been used to assess any of the components (dimensions, factors, and phases) related to MA in PD patients. We then screened the reference lists for original studies describing the development and validation of each rating scale so that additional measurement properties could be assessed, regardless of the format in which they were presented (e.g., journal article, book chapter and user guide) and the patient population involved.

We evaluated the RS according to the standards for good measurement properties recommended by the Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) and the standards of the MDS-COA-SEC \(^17,18\), including: reliability (such as: Intraclass Correlation Coefficient (ICC) and Cronbach’s alpha (\(\alpha\))), validity (such as: criterion, convergent, and construct validity), responsiveness, feasibility, acceptability, parameters for cross-cultural validity and measurement invariance. We evaluated the components of MA assessed by the items of each rating scale according to
the WHO and the ABC Taxonomy of MA\textsuperscript{(4,5)}, a successful approach previously used by our study group\textsuperscript{(19)}.

**Quality assessment and data extraction**

Eligible studies were evaluated for methodological quality using the COSMIN Risk of Bias checklist, a standardized instrument for the critical appraisal of measurement properties\textsuperscript{(20)(21)}. Authors of papers were contacted to request missing or additional data for clarification, where required. All studies, regardless of the results of their methodological quality, underwent data extraction and synthesis. Once the data was quantitatively synthesized, we qualitatively summarized them using the criteria for good measurement properties suggested by COSMIN\textsuperscript{(20)(21)} classifying the measurement properties of each scale as of the percentage of items of the scale, or subscale that fulfill the criteria:

- **Sufficient [+]:** $\geq 85\%$.
- **Insufficient [-]:** $< 85\%$.
- **Indeterminate [?]:** No or not enough information available or quality of or part of the study inadequate.

The same classification criteria were applied to assess components of MA measured by the individual items of each scale.

Based on the reviews of the scale development studies, on the scale measurement properties, and on the reviewer’s own rating of the components of MA measured by the individual items of each scale, we determined the quality of the evidence using the modified GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach\textsuperscript{(22)}. Each criterion was rated to determine whether the quality of the evidence is:

- **High:** there is confidence that the true measurement property is close to that of the measurement property estimate.
- Moderate: there is moderate confidence in the measurement property estimate, as the true measurement property is likely to be close to the measurement property estimate, but there is a possibility that it is substantially different.
- Low: there is confidence that the measurement property estimate is limited, and the true measurement property can be substantially different from the measurement property estimate.
- Very low: there is very little confidence in the measurement property estimate, as the true measurement property is likely to be substantially different from the measurement property estimate.

We assumed that all evidence was high, and we downgraded the evidence with one or two levels for each criterion: 1) Risk of bias of the studies; 2) Inconsistency of the measurement properties results of the overall ratings for the subgroups of studies related to each scale; 3) Imprecision in the results of the available studies; 4) Indirectness of scales that measure MA in populations other than PD; and 5) Inaccuracy of scales in measuring the components of MA. We downgraded the evidence to moderate, low, or very low when there was risk of bias (low study quality), (unexplained) inconsistency in results, or indirect results.

**Data synthesis**

The extracted data were pooled in tables using descriptive statistics to synthesize the characteristics of: the studies (such as: study location, year of publication, language, design, setting), the sample (such as: sample size, sex, age, disease duration) and the RS (such as: development year, type, construct assessed, original language), as well as the criteria for good measurement properties of the RS being used to assess the components of MA. We used descriptive statistics to present means, median, range and percentage (%).

Ultimately, we determined the level of recommendation using an adaptation of the MDS-COA Committee criteria (17)(22), classifying each scale as:
- **Recommended**: if it had been used in patients with PD **AND** by investigators other than the original developers, **AND** it was found to be reliable (e.g., ICC and $\alpha \geq 75$), valid (at least one parameter tested), and sensitive to change in PD samples.

- **Suggested**: if it had been used in patients with PD, but only one of the other criteria applies.

- **Listed**: if it was used in PD samples, but none of the other criteria was met **OR** if data on reliability were poor or absent.

**Results**

*Study selection and characteristics*

We screened 559 studies, removed 241 duplicates, excluded 27 that did not meet the eligibility criteria, retrieved 291 for full-text assessment, and selected 20 studies using nine RS, all characterized as Patient-Reported Outcome (PRO), to measure MA in PD patients. We added 10 studies, identified through the reference list, that presented evidence on the measurement properties of each of the nine PRO included. Thus, we analyzed 20 studies using a total of nine PRO to measure MA in PD patients and 10 original studies describing the development and validation of each PRO (Figure 1). One of the studies was classified in both categories, as it was a study for the development and validation of a MA-PRO in patients with PD (23).

From the sample of studies assessing MA in patients with PD (n=20), we identified that the majority were conducted by researchers from Europe and America (40.0% each), published between 2006 and 2015 (55.0%), in English (100.0%). 60.0% were observational studies and 75.0% were implemented in outpatient settings. The MGL-MAQ, MMAS-8 and BMQ-H are the most used RS, both in number of studies and in sample size of patients with PD: MGL-MAQ - 8 studies with a total of 2403 patients with PD; MMAS-8 - 6 studies with a total of 1341 patients with PD; BMQ-H - 3 studies with a total of 300 patients with PD (Table 1).

*Quality of PRO development studies and measurement properties of the included PRO*
We analyzed the general design requirements of the 11 PRO development studies and evidenced that all of them had very good clarity of the construct and its origin, the target population, and the context of use of the PRO. However, most of them failed in the development phases because no patients were involved in the development of the instrument’s items and/or to comment on the PRO readability, comprehensiveness, applicability, relevance, and missing themes (See Supplemental 2). The Parkinson’s Disease Medication Beliefs Scale (PD-RX)\(^{23}\) and Morisky, Green, Levine (MGL-MAQ)\(^{24,25}\) development studies mentioned that a sample representing the target population for which the PRO was developed was involved in reviewing the items of the developed instrument. However, no further details regarding the methods were provided and it was not possible to determine whether the approach was appropriate, leading us to classify them as doubtful.

When combining the analysis of the general design requirements and the measurement properties of the PRO development studies, we evidenced that their overall rating, according to COSMIN standard, was inconsistent or unsatisfactory. These results contributed to very low-quality GRADE criteria of evidence for most of PRO (Table 2).

**Criteria ratings**

No scale met the required criteria to be ranked as “Recommended”. The Morisky Medication Adherence Scale (MMAS-8)\(^{26–31}\), The Beliefs Related to Medications Adherence questionnaire (BERMA)\(^{32,33}\), the Beliefs about Medication Questionnaire (BMQ-H)\(^{30,34–36}\), The Satisfaction with Information on Medicines Scale (SIMS)\(^{37,38}\), and the Medication Adherence Rating Scale (MARS)\(^{35,39,40}\) met the criteria of “Suggested”; and the MGL-MAQ\(^{24,25,34,41–47}\), the Brief Medication Questionnaire (BMQ-S)\(^{23,48,49}\), the Malaysian Medication Adherence Scale (MALMAS)\(^{50–52}\), and the PD-RX\(^{23}\) met the criteria of “Listed” (Table 3). The PD-RX\(^{23}\) it is the only scale developed specifically for the population with PD, but in addition to its clinimetric weakness, it has not been used by any investigator other than the original developers.
Suggested

Morisky Medication Adherence Scale (MMAS-8)

Scale description: The MMAS-8 provides a bi-dimensional assessment of eight unintentional and intentional medication-taking behavior items, covering eight components of MA. This PRO was developed in 2008 targeting patients with hypertension. It requires 5 minutes for the assessment of the seven items of this dichotomous (yes/no) instrument and the one 5-point Likert item (total score ranging from 0 to 8), that captures the current MA behaviors. The MMAS-8 was the most cross-culturally validated rating scale (80 languages) (53), including a cross-cultural validation study for the use of the Italian version in PD patients (29). The MMAS-8 is protected by copyright and users must contact the author for pricing and licensing (Table 4) (26).

Measurement properties: In a population of 1367 people with hypertension, the MMAS-8 showed moderate overall reliability (Cronbach's alpha 0.83). The sensitivity of the MMAS-8 for identifying low versus higher adherers was estimated to be 93%, and the specificity was 53% (cutoff <6). In PD, the MMAS-8 was validated in Italian in 2013, showing an acceptable linguistic validity when tested in a sample of 49 PD patients participating in two rounds of comprehension test (29). This same study identified, using a sample of 773 PD patients, a significant association between lower MMAS-8 total score and higher disease duration (29). Another observational study conducted with 34 PD patients using the MMAS-8, did not identify a correlation between low adherence and psychosis in this population (28).

Two studies tested correlations between MA and MA app use as an intervention. An observational study conducted with 204 PD patients identified that patients using the MA app had higher MA scores according to the MMAS-8 (27). An open-label multicenter randomized clinical trial assessing the impact of using a smartphone-based Parkinson’s tracker app to promote MA in a sample of 158 PD patients (64% of dropout rate in the treatment arm and 83% in the control arm) showed that, after 16 weeks patients using the app significantly improved MA when compared to treatment as usual (mean difference: 0.39,
95%CI 0.04–0.74; p = 0.0304). This translated into a 6.6% reduction in low MA category in the Parkinson’s tracker app group compared to 1.4% reduction in the treatment-as-usual group (30).

**Conclusions:** The MMAS-8 was used by other investigators beyond the original developers and was shown to be reliable and valid in patients with hypertension (a chronic disease that usually requires concomitant use of medications, as in PD), and valid (linguistic and criterion validity) and responsive in PD patients. Though the eight items of the PRO covers some of the components of MA, and despite having been used in six studies with PD patients (27–31,54), the MMAS-8 has limited clinimetric data available in the PD population. The MMAS-8 is suitable for screening and correlative studies; however, it cannot be recommended for treatment trials until more evidence regarding reliability and sensitivity to change are available for the PD population.

**Beliefs Related to Medications Adherence questionnaire (BERMA)**

**Scale description:** The BERMA provides assessment of three factors or scales (Memory for Medications (20 items), Dealing with Health Professionals (23 items), and Attitudes about Drugs (10 items), with items covering all components of MA (WHO and ABC taxonomy dimensions, factors, phases). This PRO was developed in 2004 targeting older people. There is no description regarding the time required to complete the assessment of the 53 items on this Likert scale (scores ranging from 53 to 265) that capture MA behaviors from a time-interval measurement of one month. It is not clear whether the instrument is protected by copyright, and the PRO is available embedded in its original publication (Table 4) (33).

**Measurement properties:** In a population of 92 older people, BERMA showed excellent overall reliability (Cronbach’s alpha 0.94), as well as excellent reliability of each of the individual subscales (ranging from 0.83 to 0.91). The PRO showed good criterion validity correlating higher efficacy regarding memory for taking medication, with better self-assessment of adherence, and fewer external strategies required to remember to take medications. It also correlated greater effectiveness of communication
between patients and health professionals, increasing self-perception about the influence of adherence on the severity of symptoms. Lastly, more positive attitudes about medications were associated with better self-rated health and fewer reported side effects experienced from medications. In a case-control study with 33 PD patients, the 20-items corresponding from the Memory for Medications of BERMA showed that a decline in prospective memory is correlated with poor self-reported medication management.

Conclusions: The BERMA was used by investigators other than the original developers and was shown to be reliable and valid in a small sample of older adults (a prevalent age group in PD). There is no information regarding its sensitivity to change, and the only validity property tested was that of criterion, which was also tested in PD. Items in this PRO covers all the components of MA but was used only in one study with a small sample of PD patients. The BERMA is suitable for screening and correlative studies; however, it cannot be recommended for treatment trials until evidence on sensitivity to change is available.

Beliefs about Medication Questionnaire (BMQ)

Scale description: The BMQ provides assessment of four factors or scales that are divided into two sections that can be used in combination or separately. The BMQ-Specifics, assesses representations of medication prescribed for personal use, and the BMQ-General, assesses beliefs about medicines in general. Items in this PRO cover ten components of MA, by capturing MA behaviors at the present time. The BMQ was developed in 1996 targeting the general population. There is no description of the time required to administer the assessment of the 18 items of this Likert scale (total score ranging from 18 to 90) (Table 4). The BMQ is protected by copyright and it is available at Online Support for Clinical Outcome Assessments (ePROVIDE): https://eprovide.mapi-trust.org/instruments/beliefs-about-medicines-questionnaire.
Measurement properties: In samples of patients with six diagnostic categories (asthma (n=78), diabetes (n=99), renal failure (n=47), psychiatric (n=89) and cardiac diseases (n=116), and general medical inpatients (n=90)), the BMQH showed satisfactory overall reliability with Cronbach's alpha ≥0.70 (ranging from 0.47 to 0.83) between the six diseases and four subscales. The PRO also showed overall test-retest correlation ≥0.70 (ranging from 0.60 to 0.78), in a subsample of 31 patients with asthma. The subscales were able to distinguish between different diseases group/treatment modalities, different adherence behaviors, and between users of allopathic and complementary therapies (tested in a subsample of 104 patients). The evaluation of the validity of the BMQH was limited by the absence of data testing the predictive validity of the PRO (37).

In the PD population, the BMQH was tested as a secondary outcome measure in two randomized clinical trials. The first investigated whether adherence therapy improves MA and quality of life compared with routine care, in a sample of 76 PD patients evaluated in a 12-week follow-up period (34); the second study assessed the impact of using a smartphone-based Parkinson’s tracker app in a sample of 158 PD patients evaluated in a 16-week follow-up period (30). In both studies, no significant improvement in MA was found according to the overall BMQH score. A similar result was found in another prospective pilot study assessing the effectiveness of the multifaceted pharmacist-led intervention program in improving MA in a sample of 23 PD patients in an 8-week follow-up period (35).

Conclusions: The BMQH was used by investigators beyond the original developers of the scale and was shown to be reliable and valid in a population of patients with different chronic diseases. The PRO covers most of the components of MA, but despite having been used in three studies with PD patients, only the criterion validity data is available in the PD population. The BMQH is suitable for screening and correlative studies; however, it cannot be recommended for treatment trials until evidence on reliability and sensitivity to change is available in PD population.

Medication Adherence Rating Scale (MARS)
**Scale description:** The MARS provides a unidimensional assessment of factors of subjective positive attitudes to medication, subjective negative attitudes, and a more general illness control factor. The MARS scale incorporates features of both the Drug Attitude Inventory (DAI) and the MGL-MAQ. The 10 items of this PRO cover eight components of MA, capturing MA behaviors from the past week. The MARS was developed in 2000 for use in psychiatric patients. There is no description of the time required to administer this Likert scale (total score ranging from 0 to 10). Copyright for this PRO is held by the journal in which it was first published (Elsevier) (Table 4). The MARS is available in its original publication and at Online Support for Clinical Outcome Assessments (ePROVIDETM): https://eprovide.mapi-trust.org/instruments/medication-adherence-rating-scale.

**Measurement properties:** In a population of 66 patients with psychiatric illness, the MARS showed satisfactory overall reliability with Cronbach’s alpha ≥0.75. The PRO also showed overall test-retest correlation ≥0.72 after a 2-week interval. The MARS showed good internal, convergent, and construct validity, when compared with DAI and MGL-MAQ instruments. It also showed positive correlations between MARS scores and blood levels of lithium and carbamazepine. In the PD population, MARS was used in two observational prospective cohorts. The first pilot study aimed to evaluate a community pharmacy scheme in which 145 PD patients could contact local specialist pharmacists about their medications, however, no changes were found on MARS scores. Another pilot study assessing the effectiveness of the multifaceted pharmacist-led intervention program in improving MA in a sample of 23 PD patients in an 8-week follow-up period, showed that if nonadherent patients were selected (MARS score, <23 at baseline; n=11), a significant improvement in ON time was seen after the combination of all 3 interventions (unit dose packaging, Parkinson KinetiGraph alarm, and pharmacist-led medication review).

**Conclusions:** The MARS was used by investigators beyond the original developers and was shown to be reliable and valid in a population of psychiatric patients. The PRO covers some of the
components of MA, and it was used in two studies with PD patients. However, the MARS only the
criterion validity data is available in this population, making it suitable for screening and correlative
studies; As such, it cannot be recommended for treatment trials until evidence on reliability and
sensitivity to change is available in the PD population.

The Satisfaction with Information on Medicines Scale (SIMS)

Scale description: The SIMS provides a bidimensional assessment of factors identifying patients’
satisfaction with information about the action and usage of medication (items 1 to 9), and the potential
problems of medication (items 10 to 17). Items in this PRO cover nine components of MA, capturing
current MA behaviors. The SIMS was developed in 2001 targeting the general population. There is no
description of the time required for the administration of the 17 items on this Likert scale (total score
ranging from 0 to 17), and it is not clear whether the instrument is protected by copyright. The SIMS is
available in its original publication (Table 4) (37).

Measurement properties: In samples of patients with eight diagnostic categories (anticoagulant
sample (n=150), asthma (n=153), diabetic- insulin treated (n=65), diabetic on oral antihyperglycemic
agent treatment (n=112), cardiac rehabilitation (n=44), cardiac sample (n=120), general medical sample
(n=91), oncology sample (n=91)), the SIMS showed satisfactory overall reliability with Cronbach’s alpha
≥0.70 (ranging from 0.61 to 0.91) between the eight diseases and two subscales. The PRO also showed
overall test-retest correlation ≥0.60 (ranging from 0.40 to 0.76) in a subsample of 72 patients treated
with anticoagulant therapy. Criterion validity was demonstrated by significant correlations between
SIMS scores and patients’ reports of beliefs and adherence to their medications, confirming the
prediction that higher levels of satisfaction were related to greater reported adherence to medication.
In addition, lower levels of information satisfaction were associated with greater concern about adverse
drug effects (37). In the PD population, the SIMS was tested in a pilot study aiming to evaluate a
community pharmacy scheme in which 145 PD patients could contact local specialist pharmacists about
their medications \(^{(38)}\). PD patients who indicated satisfaction with information about what the medication does and about the possible impact on their sex life, had statistically significant improvements in SIMS scores. Additionally, a significant improvement was found in the SIMS summary score of “potential medication problems” when the patients were able to contact a local pharmacist for information \(^{(38)}\).

**Conclusions:** The SIMS was used by investigators beyond the original developers and was shown to be reliable and valid in a population of patients with different chronic diseases. The PRO covers most of the components of MA. It was used in only one study with PD patients. The SIMS has limited clinimetric data available in PD population (criterion validity), making it suitable for screening and correlative studies; however, it cannot be recommended for treatment trials until evidence regarding reliability and sensitivity to change is available in the PD population.

**Discussion**

Growing evidence reporting MA problems in different chronic conditions, including PD, and insufficient evidence on how to improve MA behaviors highlight the need for transformative research \(^{(4)}\). There is a critical need to prioritize the development of research focused on understanding the conditions that contribute to poor MA, as well as developing interventions to improve it \(^{(4)}\).

The results of this research show that this also applies in the context of PD, where the creation of an instrument to specifically measure all the components involved in the MA process, ensuring stakeholder involvement in a standardized methodological plan, could reduce the research gaps of MA. This is especially true today, as industry restarts clinical research trials after two years of disruption caused by the COVID-19 pandemic. We now encounter a golden opportunity to rethink, realign and rebuild around the needs of those who matter most – the patients.

Developing appropriate RS may seem straightforward; however, when analyzing the results of this study in the absence of high-quality evidence or consensus for optimal methods, we identified that rating
scale developers adopt inconsistent approaches, failing in both the initial, and in the late phases of scale development. It was noted that in the initial phases, there was an absence of data, or presentation of incomplete data, regarding the involvement of stakeholders for the creation of the theoretical framework of the identified MA-PRO for PD patients. In the final phases, a scarcity of longitudinal studies testing the instrument's responsiveness was noted.

Therefore, based on the results of this review, some aspects will need to be considered when selecting one of the MA-PRO currently available and used in people with PD, including:

1. Most PRO measure patients' current behaviors, while other functional RS (e.g., the MDS-UPDRS) generally assess a longer period, such as the last week or month. As these PRO capture patients' current behaviors, the PD patient's motor status and fluctuations in alertness and cognition can influence adherence outcomes \(^{(14)}\). Additionally, these tests do not necessarily measure the decline that PD patients may experience in their adherence behaviors, which will require support from family members and care partners. Therefore, it is highly recommended to measure patient’s motor and/or functional condition, recorded uniformly in ON/OFF periods, to correlate with MA measures, including the level of participation of family members/care partners in this process. This should enable better stability and reproducibility of findings in time and across studies, especially those including patients with motor fluctuations as this will provide important data on the long-term association between MA and motor fluctuations.

2. The presence of other common non-motor symptoms of PD, such as severe depression, severe apathy, excessive daytime sleepiness, or concomitant psychosis and cognitive impairment, may also influence adherence behaviors \(^{(14)}\). These other factors should be considered as potential confounding influences on MA test results. However, discussion of these other factors and their effects on MA, is beyond the scope of this article and like previous MDS recommendations, an inclusive approach is recommended. In this approach, symptoms should be scored if they are
present, regardless of whether they can be attributed to the presence of other confounding factors.

3. Variables such as age, gender, and educational level often have an impact on adherence behaviors – for example, adherence tests may be less sensitive for detecting low MA in highly educated individuals \(^{(13)}\). Therefore, MA-PRO scores and specific cut-off points for what is determined to be normal, need to be adjusted for these variables as appropriate and available depending on the specific scale.

4. Different modes of drug delivery can also influence adherence behaviors \(^{(41,55)}\). Therefore, differentiating levels of adherence behavior according to different drug prescriptions (e.g., oral versus patch medications, fractionated versus single-dose medications) is important to determine adherence levels more accurately. This is particularly important in PD patients using other device-assisted medical therapies – such as apomorphine pens, subcutaneous and enteral pumps – for whom research data on MA are lacking in the scientific literature.

Conclusion

We recommend conducting further validation studies before using the instruments presented. Preferably, we recommend the development of a new scale that is developed specifically to measure MA behavior in people with PD, so that not only the problems and deficits of the scales identified in this review, but also specific aspects of PD, such as capturing the measurement time that best aligns with the functional PD scales, are addressed. However, being aware of the challenges inherent to the development of a new scale, making it difficult to reach this objective in the short/medium terms, we emphasize that the currently “suggested” scales may become "recommended" if large field validation show acceptable measurement properties in PD.
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1. Research project: A. Conception, B. Organization, C. Execution.

M.H.S. Tosin: 1A, 1B, 1C, 2A, 2B, 2C, 3A.
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MHST: received grants and research from: Coordination for the Improvement of Higher Education Personnel (CAPES), International Parkinson and Movement Disorder Society. MHST Reports consulting with honoraria from Rush University Medical Center.

BGRBO: received grants and research from: National Council for Scientific and Technological Development (CNPq) and Research Support Foundation of the State of Rio de Janeiro (FAPERJ). BGRBO also receive salary from Fluminense Federal University.

CGG: reports funding from Rush University Medical Center from the National Institutes of Health, Department of Defense, and Michael J. Fox Foundation for research conducted by Dr. Goetz. During the reporting time, Dr. Goetz directed the Rush Parkinson's Disease Research Center supported by the Parkinson's Foundation and some of these funds supported Dr. Goetz's salary as well as his research efforts. He also reports faculty stipends from the International Parkinson and Movement Disorder Society and the American Academy of Neurology, guest professorship honorarium provided by NorthShore University Health System, royalties from Oxford University Press and Wolters Kluwer Publishers, and a salary from Rush University Medical Center.

DM: Morisky is the developer and owner of the copyrighted and trademarked MMAS-8 diagnostic adherence assessment instrument and receives license fees for the use of the MMAS-8 scale. Dr. Morisky was not involved in evaluating the data from the scales he developed. Licenses can be obtained through MMAR, LLC, donald.morisky@moriskyscale.com.

VM: No disclosures. Victor McConvey is employed as the Manager of Health, Clinical and Community services at Fight Parkinson's Australia. Fight Parkinson's has received small grants from ABBVIE, SERQIURS, PFIZER and STADA to support delivery of clinical initiatives.

MS: received speakers’ honoraria and/or consultation fees from AbbVie, Biogen, Boston Scientific, Ever Pharma, Krka, Medtronic, Sandoz and STADA, he received grant support from the IBM, from Slovak
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**AS:** consultancy funding from Abbvie, royalties from Oxford University Press, and grant funding from the
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for Health Research ULCH Biomedical Research Centre.

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**GTS:** reports consulting and advisory board membership with honoraria from: Acadia, Pharmaceuticals,
Adamas Pharmaceuticals, Inc., Biogen, Inc., Ceregene, Inc., CHDI Management, Inc., Cleveland Clinic
Foundation, Ingenix Pharmaceutical Services (i3 Research), MedGenesis Therapeutix, Inc., Neurocrine
Biosciences, Inc., Pfizer, Inc., Tools-4-Patients, Ultragenyx, Inc., and the Sunshine Care Foundation. GTS
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Foundation for Parkinson’s Research, Dystonia Coalition, CHDI, Cleveland Clinic Foundation,
International Parkinson and Movement Disorder Society, and CBD Solutions. GTS reports honoraria
from: International Parkinson and Movement Disorder Society, American Academy of Neurology,
Michael J. Fox Foundation for Parkinson’s Research, Food and Drug Administration, National Institutes of
Health, and the Alzheimer’s Association. GTS received salary from Rush University Medical Center.

**Ethical Compliance Statement**

The authors confirm that the approval of an institutional review board and patient consent was not
required for this work. We confirm that we have read the Journal’s position on issues involved in ethical
publication and affirm that this work is consistent with those guidelines.
References


45. Valldeoriola F, Coronell C, Pont C, Buongiorno MT, Câmara A, Gaig C, et al. Socio-demographic and clinical factors influencing the adherence to treatment in Parkinson’s disease: the ADHESON


Legends

Figure 1. Search results and study selection and inclusion process.

Table 1. Characteristics of studies assessing medication adherence in patients with Parkinson’s Disease.

Table 2. Quality of studies on PRO development and measurement properties of the included rating scales.

Table 3. Summary of “use recommendations” of Medication Adherence Rating Scales used in Parkinson’s Disease.

Table 4. Characteristics of the reviewed medication adherence rating scales.


Supplemental 2. Quality of the PRO development.

Supplemental 3. Studies excluded for not addressing the topic (presented in alphabetical order).

Table 1. Characteristics of studies assessing medication adherence in patients with Parkinson’s Disease

<table>
<thead>
<tr>
<th>Variables</th>
<th>N (%)</th>
<th>Mean/Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Characteristics (n=20)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Country (each)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GBR, USA</td>
<td>4 (20.0)</td>
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</tr>
<tr>
<td>BRA</td>
<td>3 (15.0)</td>
<td>-</td>
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<tr>
<td>SVK, MYS, MEX, CHN, SAU, DEU, ESP, ITA, HKG</td>
<td>1 (5.0)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Year of publication</strong></td>
<td></td>
<td></td>
</tr>
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<td>2006 to 2015</td>
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<td>1.6 (1 to 3)</td>
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<td>2016 to 2021</td>
<td>9 (45.0)</td>
<td>1.5 (1 to 2)</td>
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<td>English</td>
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</tr>
<tr>
<td>English &amp; Portuguese</td>
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<td>-</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td></td>
<td></td>
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<td>Observational</td>
<td>12 (60.0)</td>
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<tr>
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<td>5 (25.0)</td>
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<td>Quasi-experimental</td>
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<tr>
<td>Interventional</td>
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<td><strong>Setting</strong></td>
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<td></td>
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<td>Outpatient clinic</td>
<td>15 (75.0)</td>
<td>-</td>
</tr>
<tr>
<td>Hospital</td>
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<td>-</td>
</tr>
<tr>
<td>Primary care</td>
<td>1 (5.0)</td>
<td>-</td>
</tr>
<tr>
<td>Community pharmacy</td>
<td>1 (5.0)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Medication adherence rating scales used in the studies (each)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MGL-MAQ</td>
<td>8 (40.0)</td>
<td>-</td>
</tr>
<tr>
<td>MMAS-8</td>
<td>6 (30.0)</td>
<td>-</td>
</tr>
<tr>
<td>BMQ-H</td>
<td>3 (15.0)</td>
<td>-</td>
</tr>
<tr>
<td>BMQ-S, MARS</td>
<td>2 (10.0)</td>
<td>-</td>
</tr>
<tr>
<td>SIMS, PD-RX, MALMAS, BERMA</td>
<td>1 (5.0)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Distribution of PD sample size by scale across all studies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MGL-MAQ</td>
<td>2403</td>
<td>300±106.7 (57 to 943)</td>
</tr>
<tr>
<td>MMAS-8</td>
<td>1341</td>
<td>223.5±115.4 (3 to 775)</td>
</tr>
<tr>
<td>BMQ-H</td>
<td>300</td>
<td>100±52.8 (23 to 201)</td>
</tr>
<tr>
<td>BMQ-S</td>
<td>187</td>
<td>93.5±18.5 (75 to 112)</td>
</tr>
<tr>
<td>MARS</td>
<td>168</td>
<td>84±61 (23 to 145)</td>
</tr>
<tr>
<td>SIMS</td>
<td>145</td>
<td>-</td>
</tr>
<tr>
<td>PD-RX</td>
<td>75</td>
<td>-</td>
</tr>
<tr>
<td>MALMAS</td>
<td>58</td>
<td>-</td>
</tr>
<tr>
<td>BERMA</td>
<td>33</td>
<td>-</td>
</tr>
</tbody>
</table>

Legend: Country codes according to the Online Browsing Platform (OBP) from International Organization for Standardization (ISO)
GBR: United Kingdom of Great Britain and Northern Ireland, USA: United States of America, BRA: Brazil, SVK: Slovakia, MYS: Malaysia, MEX: Mexico, CHN: China, SAU: Saudi Arabia, DEU: Germany, ESP: Spain, ITA: Italy, HKG: Hong Kong | PD: Parkinson’s Disease
Table 2. Quality of studies on patient report outcome development and measurement properties of the included rating scales

<table>
<thead>
<tr>
<th>PRO (ref)</th>
<th>PRO development</th>
<th>Content validity</th>
<th>Structural validity</th>
<th>Cross-cultural validity</th>
<th>Criterion validity</th>
<th>Construct validity</th>
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<tr>
<td></td>
<td></td>
<td>Relevance OR QE</td>
<td>Comprehensiveness OR QE</td>
<td>Comprehensibility OR QE</td>
<td>OR QE</td>
<td>OR QE</td>
</tr>
<tr>
<td>MGL-MAQ(25)</td>
<td>Doubtful</td>
<td>− VL ± VL − VL ± VL</td>
<td>− VL NA NA</td>
<td>+ VL + VL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Q(36)</td>
<td>Inadequate</td>
<td>− VL − VL − VL + VL</td>
<td>NA NA</td>
<td>+ H + VL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMQ(48)</td>
<td>Inadequate</td>
<td>− VL − VL − VL ? VL</td>
<td>NA NA</td>
<td>− VL + VL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MARS(59)</td>
<td>Inadequate</td>
<td>− VL − VL − VL − VL</td>
<td>NA NA</td>
<td>± VL ± VL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIMS(37)</td>
<td>Inadequate</td>
<td>− VL − VL − VL − VL</td>
<td>NA NA</td>
<td>? VL − VL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BERMA(33)</td>
<td>Inadequate</td>
<td>− VL − VL − VL − VL</td>
<td>NA NA</td>
<td>+ L ± VL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMAS-B(56)</td>
<td>Inadequate</td>
<td>− VL − VL − VL − VL</td>
<td>NA NA</td>
<td>± L ± VL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALMAS(50,51)</td>
<td>Inadequate</td>
<td>± L ± L ± L ± L</td>
<td>± L NA NA</td>
<td>+ L ± L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-RX(23)</td>
<td>Doubtful</td>
<td>± VL ± VL − VL − VL</td>
<td>NA NA</td>
<td>− VL ± VL</td>
<td></td>
<td></td>
</tr>
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</table>

Table 2. Continuation

<table>
<thead>
<tr>
<th>PRO (ref)</th>
<th>Internal consistency</th>
<th>Reliability</th>
<th>Measurement error</th>
<th>Responsiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR QE</td>
<td>OR QE</td>
<td>OR QE</td>
<td>OR QE</td>
</tr>
<tr>
<td>MGL-MAQ(25)</td>
<td>− VL</td>
<td>− VL</td>
<td>? VL</td>
<td>+ VL</td>
</tr>
<tr>
<td>□ Q(36)</td>
<td>+ VL</td>
<td>± VL</td>
<td>? VL</td>
<td>− VL</td>
</tr>
<tr>
<td>BMQ(48)</td>
<td>− VL</td>
<td>? VL</td>
<td>− VL</td>
<td>− VL</td>
</tr>
<tr>
<td>MARS(59)</td>
<td>− VL</td>
<td>− VL</td>
<td>? VL</td>
<td>± L</td>
</tr>
<tr>
<td>SIMS(37)</td>
<td>− VL</td>
<td>− VL</td>
<td>? VL</td>
<td>± L</td>
</tr>
<tr>
<td>BERMA(33)</td>
<td>− VL</td>
<td>− VL</td>
<td>L*</td>
<td>? VL</td>
</tr>
<tr>
<td>BMAS-B(56)</td>
<td>+ VL</td>
<td>− VL</td>
<td>? VL</td>
<td>± VL</td>
</tr>
<tr>
<td>MALMAS(50,51)</td>
<td>− VL</td>
<td>− VL</td>
<td>? L</td>
<td>± L</td>
</tr>
<tr>
<td>PD-RX(23)</td>
<td>− VL</td>
<td>± VL</td>
<td>? VL</td>
<td>± VL</td>
</tr>
</tbody>
</table>

Legend: PRO: Patient Report Outcome | OR: Overall rating (COSMIN) | QE: Quality of evidence (GRADE) | (+): satisfactory results | (±): inconsistent results | (−): unsatisfactory results | (?) indeterminate | H: High (as there is one very good study available) | L: Low | VL: Very Low | NA: Not applicable | *Downgraded due to small sample size.
Table 3. Summary of “use recommendations” of Medication Adherence Rating Scales used in Parkinson’s Disease (ordered by recommendation level and year of development)

<table>
<thead>
<tr>
<th>Scale</th>
<th>(ref)</th>
<th>Used in PD</th>
<th>Used beyond original developers</th>
<th>Reliability</th>
<th>Validity</th>
<th>Responsiveness</th>
<th>Recommendation</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMAS-8</td>
<td>(26–31)</td>
<td>Yes</td>
<td>Yes</td>
<td>α: 0.83 a</td>
<td>1-factor structure, sensitivity 93%, specificity 53%, RMSEA &lt; 0.01 a</td>
<td>Low adherence to PD medication correlated with disease duration, use of three and more daily doses of PD drugs, sex (male), QoL, depression, frequency, and severity of NMS, motor and NMS complications, frequency, and severity of NMS (excessive daytime sleepiness, anhedonia, and forgetfulness) predicted lower levels of adherence, acceptable Italian linguistic validity for use in PD patients b</td>
<td>↓ Results in accordance with the hypothesis. However, small sample with the limitation of high dropout rate b</td>
<td>Suggested</td>
</tr>
<tr>
<td>BERMA</td>
<td>(32,33)</td>
<td>Yes</td>
<td>Yes</td>
<td>Overall α: 0.94 for 3 subscales a</td>
<td>3-factor structure, results in accordance with the hypothesis a</td>
<td>Decline in PD prospective memory is correlated with poor self-reported medication management b</td>
<td>↓ Responsiveness not tested a</td>
<td>Suggested</td>
</tr>
<tr>
<td>BMQ-H</td>
<td>(30,34-36)</td>
<td>Yes</td>
<td>Yes</td>
<td>Overall α: ≥0.70 (ranging from 0.47 to 0.83) &amp; ICC: ≥0.70 (ranging from 0.60 to 0.78) between the 6 diseases and 4 subscales a</td>
<td>4-factor structure, CFA: &gt;0.95 a</td>
<td>Good criterion-related and discriminant validity data</td>
<td>↓ Responsiveness not tested in the development study a</td>
<td>Suggested</td>
</tr>
<tr>
<td>MARS</td>
<td>(35,39,40)</td>
<td>Yes</td>
<td>Yes</td>
<td>α: 0.75 a</td>
<td>3-factor structure, results in accordance with the hypothesis a</td>
<td>Results in accordance with the hypothesis a</td>
<td>Suggested</td>
<td>Low use in PD, used by investigators other than the original developers, moderate measurement properties in psychiatric population (clinimetrics not tested in PD)</td>
</tr>
<tr>
<td>Tool</td>
<td>Use in PD</td>
<td>Use by Original Developers</td>
<td>Overall α: ≥0.70 for 2 subscales</td>
<td>2-factor structure, results in accordance with the hypothesis</td>
<td>Overall ICC: &lt;0.70 for 2 subscales</td>
<td>1-factor structure, results in accordance with the hypothesis</td>
<td>Low adherence to PD medication positively correlated with forgetfulness, % of drug taken daily, patients at risk for depression (GDS score ≥5) were more likely to have unsatisfactory adherence. Low adherence to PD medication correlated with cognitive deterioration and psychiatric pathology</td>
<td>Results in accordance with the hypothesis</td>
</tr>
<tr>
<td>------</td>
<td>----------</td>
<td>---------------------------</td>
<td>-------------------------------</td>
<td>-----------------------------------</td>
<td>---------------------------</td>
<td>-----------------------------------</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>SIMS (37,38)</td>
<td>Yes Yes</td>
<td>Overall α: ≥0.70 for 2 subscales</td>
<td>2-factor structure, results in accordance with the hypothesis</td>
<td>Overall ICC: &lt;0.70 for 2 subscales</td>
<td>1-factor structure, results in accordance with the hypothesis</td>
<td>Low adherence to PD medication positively correlated with forgetfulness, % of drug taken daily, patients at risk for depression (GDS score ≥5) were more likely to have unsatisfactory adherence. Low adherence to PD medication correlated with cognitive deterioration and psychiatric pathology</td>
<td>Results in accordance with the hypothesis</td>
<td>Suggested Uses</td>
</tr>
<tr>
<td>MGL-MAQ (24, 25,34,41–47)</td>
<td>Yes Yes</td>
<td>↓α: 0.61a ↓ICC: 0.40a</td>
<td>3-factor structure, sensitivity, specificity &amp; overall accuracy &gt;80%</td>
<td>Insensitive in detecting suboptimal PD medication intake, but it was highly specific, and it also quantified underuse</td>
<td>1-factor structure, sensitivity 88.9%, specificity 29.6%, results in accordance with the hypothesis</td>
<td>3-factor structure, negative beliefs about PD medication correlated with poorer QoL</td>
<td>Results in accordance with the hypothesis</td>
<td>Listed Uses</td>
</tr>
<tr>
<td>N-AQ-S (24,44,49)</td>
<td>Yes Yes</td>
<td>↓Data not available</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>MALMAS (50-52)</td>
<td>Yes Yes</td>
<td>↓α: 0.69 a** ↓ICC: 0.71 a** ↓α: 0.56 a*** ↓ICC: 0.41 a***</td>
<td>1-factor structure, sensitivity 88.9%, specificity 29.6%, results in accordance with the hypothesis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-RX (23)</td>
<td>Yes</td>
<td>↓No</td>
<td>↓α: 0.67 b ↓ICC: 0.47 b</td>
<td>3-factor structure, negative beliefs about PD medication correlated with poorer QoL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Legend:** PRO: Patient Report Outcome | PD: Parkinson’s Disease | MA: Medication Adherence | *: according to the World Health Organization and the Ascertaining Barriers to Compliance (ABC) Taxonomy of MA | ↓: downgraded according to the COSMIN, GRADE and MDS criteria | ICC: Intraclass Correlation Coefficient | α: Cronbach’s alpha (0.5 indicate poor reliability, between 0.5 and 0.75 moderate reliability, between 0.75 and 0.9 good reliability, and any value above 0.9 indicates excellent reliability) | CFA: Confirmatory Factor Analysis | a: Clinimetric data not available from studies in PD | b: Clinimetric data available from studies in PD | a**: Malaysian version of MALMAS | a***: English version of MALMAS | HBP: High Blood Pressure | DM: Diabetes Mellitus | QoL: Quality of Life | NMS: Nonmotor symptoms
Table 4. Characteristics of the reviewed medication adherence rating scales (ordered by year of development)

<table>
<thead>
<tr>
<th>Scales Characteristics</th>
<th>MGL-MAQ</th>
<th>BMQ-H</th>
<th>BMQ-S</th>
<th>MARS</th>
<th>SIMS</th>
<th>BERMA</th>
<th>MMAS-8</th>
<th>MALMAS</th>
<th>PD-RX</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
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<td></td>
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<td>BM</td>
<td>MA</td>
<td>MA</td>
<td>IM</td>
<td>MA</td>
<td>MA</td>
<td>MA</td>
<td>BM</td>
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<td>No</td>
<td>No</td>
<td>No</td>
<td>No (29)</td>
<td>No</td>
<td>No</td>
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</tr>
<tr>
<td>Number of items</td>
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<td>18</td>
<td>10</td>
<td>10</td>
<td>17</td>
<td>53</td>
<td>8</td>
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</tr>
<tr>
<td>Measurement time</td>
<td>Present</td>
<td>Present</td>
<td>Past week</td>
<td>Past week</td>
<td>Present</td>
<td>Past 1 month</td>
<td>Present</td>
<td>Past 1 month</td>
<td>Present</td>
</tr>
<tr>
<td>Type of scaling</td>
<td>Dichotomic</td>
<td>Likert</td>
<td>Dichotomic, Likert &amp; Qualitative</td>
<td>Dichotomic</td>
<td>Likert</td>
<td>Likert</td>
<td>Dichotomic &amp; Likert</td>
<td>Dichotomic, Likert &amp; Qualitative</td>
<td>Likert</td>
</tr>
<tr>
<td>Time to administer</td>
<td>NM</td>
<td>NM</td>
<td>NM</td>
<td>NM</td>
<td>NM</td>
<td>5 minutes</td>
<td>10 minutes</td>
<td>NM</td>
<td></td>
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<tr>
<td>Total score range</td>
<td>0 to 4</td>
<td>18 to 90</td>
<td>-</td>
<td>0 to 10</td>
<td>0 to 17</td>
<td>53 to 265</td>
<td>0 to 8</td>
<td>0-100%</td>
<td>11 to 55</td>
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<td>Scale direction*</td>
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<td>↑S ↑BM</td>
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Legend: MGL-MAQ, MMAS-8: Morisky Medication Adherence Scales | BMQ-H: Beliefs about Medication Questionnaire | BMQ-S: Brief Medication Questionnaire | MARS: Medication Adherence Rating Scale | SIMS: The satisfaction with information on medicines scale | BERMA: Beliefs Related to Medications Adherence questionnaire | MALMAS: Malaysian Medication Adherence Scale | PD-RX: Parkinson’s Disease Medication Beliefs Scale | PRO: Patient Reported Outcome | S: Score of the scale | MA: Medication adherence | BM: Beliefs about medication | IM: Information about Medication | WHO: World Health Organization | HS/HC: Health system/ Health care | ABC: Ascertaining Barriers to Compliance | *↑S ↑MA/BM/IM: the higher the total score of the scale, the higher the medication adherence/ Beliefs about medication/ Information about Medication
Studies identified from databases (n=559):
- SCOPUS=193
- WOS=170
- MEDLINE=79
- EMBASE=69
- CINAHL=30
- PsycNET=17
- LILACS=1

Studies removed before screening:
Duplicate records removed=241

Studies screened (n=318)

Studies sought for retrieval (n=291)

Studies excluded (n=27)
- Review=21
- Study Protocol=4
- Letter=1
- Conference Paper=1

Studies assessed for eligibility (n=291)
- Rating Scales assessed for eligibility=10

Studies excluded (n=271)
- Not addressing the topic=229*
- No scale used=23
- Wrong population=10
- RS and its development studies available only in German=4
- No data available for PD=2
- Japanese=1
- Spanish=2
- Rating Scales excluded (n=1, SAMS)

Studies included in review (n=30)
- Rating Scales identified in the included studies (n=9)
  - MGL-MAQ, MMAS-8, BMQ-H, BMQ-S, MARS, SIMS, PD-RX, MALMAS, BERMA

Original studies describing the development and validation of each Rating Scales (n=10)