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Review of the four item Morisky Medication Adherence Scale (MMAS-4) and eight item Morisky Medication Adherence Scale (MMAS-8)

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Introduction

Non-adherence to medications is considered as one of the largest drug related issues. WHO states that non-adherence to medications is a "worldwide problem of striking magnitude." [1] Poor medication adherence can cause negative health outcomes such as worsening disease or even death and studies showed that there was an association between poor adherences to medications indicated for chronic diseases with health resources utilization.[2] Poor medication adherence also may result in increased health care cost. There are 33%-69% of drug-related hospital admissions in US are because of poor medication adherence, along with a cost of about $100 billion a year.[3]

So far there is no gold standard method to measure medication taking behavior. Methods of measuring adherence can be classified as direct method and indirect method. Direct methods include directly observed therapy, measurement of drug concentration in blood, and measurement of the biologic marker in the body. Indirect methods include patient self-report, pill counts, pharmacy fill data, electronic medication monitoring, and assessment of patient's clinical response.[3] Patient self-report or questionnaire is one of the important indirect methods of measuring medication adherence and persistence and it's the most commonly used method in the clinical setting. Although it's simple and easy, studies show it can measure medication adherence effectively[4,5] and has moderate to high degree of concordance with electronic medication monitoring device.[6] The problems with patient self-report involve with the distortion of results by patients themselves, misinterpretation of the information in the instrument or potential error increasing in time between visits.[3]

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In 1986, Dr. Morisky and his colleagues published the instrument Morisky Medication Adherence Scale (MMAS) that was first validated in antihypertensive drugs in outpatient settings.[7] The original Morisky scale has four items that have dichotomous response categories with yes or no. The rationale behind the four items was "the drug errors of omission could occur in any or all of several ways: forgetting, carelessness, stopping the drug when feeling better or starting the drug when feeling worse."[7] The original Morisky scale was quite innovative at that time for its capture of the fundamental reasons of medication underuse or omission and its reversing the wording of the questions to utilize the "yes-saying" bias to obtain disclosures of non-adherence. However, it did not show very good psychometric properties. The sensitivity and specificity were 81% and 44%, respectively. Cronbach's alpha reliability is 0.61, which is below the acceptable value of 0.7. Despite fair psychometric properties, it still has been implemented in a large amount of studies and clinical settings. In 2008, a modified eight item Morisky Medication Adherence Scale (MMAS-8) developed from the original four item Morisky scale was published.[8] The first seven items are dichotomous response categories with yes or no and the last item was a five point Likert response. Compared to original Morisky scale, it has the following features: 1) The adding four items are trying to identify and address the circumstances or situations related to adherence behavior; 2) Importantly, it has much better psychometric properties: sensitivity and specificity are 93% and 53%, respectively and Cronbach's alpha value is 0.83 that is above the acceptance threshold.[8] Afterwards, MMAS-8 has become popular and commonly used in various clinical settings and different populations, as well as been translated and validated in foreign countries.

Morisky scale and its derivate hold advantages over other patient self-report instruments such as widespread use in different diseases, populations and countries, higher degree of concordance with pharmacy fill data or electronic monitoring devices, less items resulting in less response burden. However, Morisky scale and its modification have drawbacks such as they attempt to capture only a few

reasons or factors associated with non-adherence and do not conduct a comprehensive assessment of medication adherence, thereby making it difficult to develop interventions targeting these factors based on the results from Morisky scale.[9] It was found that the with-in person change of as or more than 2 scores of MMAS-8 indicated a real change of medication adherence in the hypertensive population.[10] Nevertheless, The measurement of adherence by the Morisky scale and its modification still cannot be quantified very well[9] and this might limit their application.

Medication adherence scales are a subjective measure of medication adherence, used for studies conducted in different patient populations with various disease conditions. Many of the adherence scales are validated and compared against an objective measure of medication adherence. A medication adherence scale should be able to accurately capture the beliefs, barriers and behavior related to medication adherence. It should also be easy to administer, understand and be precise.[11] Given the strengths and weaknesses of MMAS-4 and MMAS-8, we think it necessary to investigate how they are used in the clinical studies, their psychometric properties reported in the studies, issues with the use, and also find out what are the future directions to improve the development and implementation of these self-reported instruments in measuring medication adherence. This study also briefly reviews other popular medication adherence scales available for measuring medication adherence.

Current use of MMAS-4 and MMAS-8 to measure medication adherence
Table 1 attached below listed the studies since 2008 using MMAS-4 and MMAS-8 as adherence measurement.[2,12–22] From the literature review, we have found that Morisky scale and its derivate have moderate to high reliability and criterion validity in some studies, yet there is still some space of improving translational validity including face validity or content validity. Of significance, clinicians or researchers should be cautious before using them as medication measurements and need to think about two key points: 1) whether MMAS is appropriate to be used in order to reach the goal of the study or an intervention; 2) if MMAS is validated in this specific situation which may be distinct from the original setting of validation.

MMAS-4 and MMAS-8 are designed to describe the medication taking behavior of patients but they seem not to be able to comprehensively assess the reasons or predictors of medication adherence. They can be regards as good estimates of the medication taking behavior, yet not good explanatory tools of figuring out why patients are not

adherent, which may lead to poor relationship between the Morisky scale and objective clinical outcome measures. For instance, study of medication adherence in Thailand diabetic population found that blood glucose levels were not associated with Morisky scale scores.[18] In addition, they are good screening and monitoring tools to identify those patients who might have medication adherence problems. However, if health care providers would like to develop some strategies or interventions to improve the adherence, these instruments cannot provide adequate informative support since they are lack of data or information regarding the reasons or predictors of medication adherence.

It is important to test the psychometric properties in a specific situation before choosing the instrument to measure medication adherence. Nina van de Steeg et al. showed that MMAS-4 was not valid for patients taking antihypertensive medications in Germany.[16] Although not many similar results have been found (probably due to publication bias), these studies can still be regarded as red flags to emphasize the importance and necessity to validate MMAS in such situations distinct from the original setting of validation before using MMAS as medication measurement. Face validity is to determine whether the measurement of the overall instrument and its items congruent with the underlying construct, and it is usually based on personal judgment.[23] Although it is a qualitative and subjective assessment of the instrument, it is good to be used to refine or evaluate the instrument. With the increasing applications of Morisky scale and advances in medication adherence research, we are equipped with more theoretical knowledge, empirical evidence, and a broader range of perspectives to help us to further refine and evaluate the wording, phrasing, and construct. In terms of content validity, there are two dimensions in MMAS-4 if we consider whether the non-adherence is intentional or unintentional. The first two items are assessing the unintentional non-adherence due to forgetfulness and carelessness. The last two items are measuring the intentional non-adherence --- stopping medications when feeling better or worse.[10] In the studies developing MMAS-4 and MMAS-8, psychometric properties were tested in the hypertensive population and found that all items were unidimensional.[8,9] However, another study testing the psychometric properties of MMAS-8 in diabetic patients in Thailand found that MMAS-8 had three dimensions including forgetting to take medications, stopping medications when feeling better or worse, and the complexity of the drug regimen.[18] Given the existing inconsistency in content validity, further research on testing the content validity in different disease and population using robust study design and methods are warranted.

Other medication adherence scales

Beliefs about Medicines Questionnaires (BMQ): There are 2 sections of Beliefs about Medicines Questionnaires (BMQ): a two 4 item factor BMQ-General section and a two 5 item factor BMQ-Specific section. BMQ-Specific looks at beliefs associated with medications that the patient is on whereas BMQ-General looks at beliefs associated with medications in general. The two factors of BMQ-General section assess the beliefs associated with harm caused by medications (General-Harm) and the overuse of medications (General-Overuse). The two factors of BMQ-Specific section assess the beliefs associated with the need to take medications (Specific-Necessity) and the long term effects of medications (Specific-Concerns). When the scale was first developed, it was used by patients admitted in departments such as asthma, diabetes, renal disease, cardiac disorders, psychiatric disorders and general medicine. Overall, the four factors of the BMQ scale showed good to acceptable internal consistencies. In case of BMQ-General harm factor, the internal consistency was quite low for asthma (0.47), cardiac (0.51) and general medicine (0.51) patients respectively.[23,24] The BMQ scale has displayed satisfactory validity and reliability when used in patients residing in different countries and for different disease conditions.[25,26] However, when the BMQ-Specific scale was translated to Scandinavian languages such as Norwegian, Swedish and Danish; the content validity was found to be weak. The meanings of certain questions were unclear or totally different after translation. Also, the endpoints of the Likert scale extended at one end-point for the Swedish version and at both endpoints for the Danish version.[27] In another study, when the BMQ-General scale was translated in Spanish language and administered to psychiatric outpatients, medical students, and psychology students to study the medication beliefs associated with psychiatric medications, medium low internal consistency was found. Also, when the 3 population samples were analyzed separately, the BMQ-General scale identified 3 different structures for each of the two factors.[28]

The Medication Adherence Rating Scale (MARS): The Medication Adherence Rating Scale (MARS) is a measure of medication adherence developed from Medication Adherence Questionnaire and Drug Attitude Inventory.[29] MARS consists of 10 items represented by 3 factors: medication adherence behavior, attitude towards medication and general illness control.[30] MARS was first administered in psychosis patients. The reliability of MARS is adequate and validity is moderate. The internal consistency of MARS has been shown to vary from moderate to very good. Some of the format related reasons for this might be the binary response choice, less items and scale multidimensionality.[30,31] The medication adherence behavior factor correlates better with

medication adherence compared to attitude towards medication factor. In larger samples, the attitude towards medication factor is not a very good predictor of medication adherence.[30,31] One of the advantages of using MARS is that the scale takes in account patient behavior of not regularly taking medications by not considering them non-compliant.[31]

Adherence Self-Report Questionnaire (ASRQ): Adherence Self-Report Questionnaire (ASRQ) was developed by de Klerk and colleagues and comprises of six different levels of adherence ranging from 'perfect' (level 1) to 'low' (level 6).[32] Generally, ASRQ is administered with medication event monitoring systems (MEMS) cap to measure timing adherence or correct dosing or adherence related to intake of doses. ASRQ is not an optimal tool to measure medication non adherence or poor medication adherence due to low sensitivity or low positive predictive values. ASRQ has been used to monitor anti-hypertensive medication adherence.[33,34]

ASK-20: The ASK-20 adherence barrier survey comprises of 20 questions represented by 11 conceptual areas that focus on medication intake behavior and barriers that are perceived by patients, affecting medication adherence. The 11 conceptual areas are: medication related attitudes and beliefs, awareness and achievement of health goals, harmful effects of taking medications, depression, forgetfulness, cognitive barriers, physical barriers, financial barriers perceived ineffectiveness associated with medication intake, receipt of social support and interpersonal relationship and communication with healthcare providers. The ASK-20 scale has an internal consistency of 0.85. Upon development, ASK-20 was administered among asthma, diabetes and depression patients. Higher scoring of the ASK-20 survey indicates higher medication adherence barriers.[35] A shorter version of ASK-20 is the ASK-12 which has adequate reliability and validity as well.[36]

Hill-Bone compliance scale: Hill-Bone compliance scale primarily focuses on hypertension medication adherence. This scale has 3 sub-scales: reduced sodium intake, appointment timeliness and medication intake. It has a four point Likert scale rating and a very good internal consistency.[37] However; this scale can be used only in hypertension patients so it has limited generalizability. This scale has also demonstrated high internal consistency when used in South Africa[38] or when translated to Turkish.[39] However, when the scale was used in Germany, it showed floor effects and poor ability to predict medication adherence for nearly every third participant. The researchers indicated the need to rethink about the theoretical framework upon which the scale was designed.[40]

Recommendations for future development and research
Based on the review of the development and implementations of Morisky scale and its modification, we believe there is still some space for us to improve these instruments.

First, it is essential to further improve its face validity and content validity to ensure great construct validity. As discussed above, we could integrate more theoretical knowledge, empirical evidence, and different perspectives to further refine and evaluate the wording, phrasing, construct and etc. To achieve a comprehensive assessment of medication adherence, we may add some items addressing more reasons or predictors of non-adherence such as disease and medication knowledge, physician patient communication, treatment satisfaction and medication belief. We can also include more use of other measurement scales such as Likert scale and visual analog scale. In this way, we could enhance the internal consistency reliability by increasing the response choices and lowering the measurement errors.[23] Content validity needs to be tested in different situations to ensure the items and the overall instrument reflect the dimensions of the construct.

Second, although adherence measurements are often reported as dichotomous variables (adherence vs. non-adherence), adherence can actually vary from 0% to over 100%, since patients take more than the prescribed amount of drugs in certain cases.[3] Currently most medication adherence instruments including Morisky scale mainly focus on assessing the medication underuse part, yet the other side of medication non-adherence -- overuse of medications seems to be neglect in the development of these instruments. As the medication overuse issue continues to grow in the United States and attracts more and more attentions, we believe there is an increasing need to take into account the medication overuse issue in developing a general medication use instrument.

Third, patients with multiple comorbidities may hold diverse medication beliefs and medication taking behaviors for different diseases and medications. In other word, patients may be adherent to certain medications but not others. Yet the items of Morisky scale are designed for patients to solely focus on one specific disease state at one time. Future attempt may need to think of this problem from a whole-person care perspective.

Overall, MMAS-4 and MMAS-8 are good screening and monitoring tools in clinical practice to identify and monitor the high-risk non-adherent patients. Further studies of patient-reported instruments are warranted to better assess medication taking behaviors and validate them in different populations and settings.

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Table 1. The studies using MMAS-4 and MMAS-8 as adherence measurement

Study	Population	Country	Method and intervention	Adherence measurement	Outcome measures	Psychometric properties of MMAS reported
Sarah DB et al 2010[2]	Community-dwelling elders	US	Subjects were followed for the occurrence of falls and medication adherence were assessed.	MMAS-4	Falls, medication use and medication adherence	N/A
June MT et al 2011[11]	Community-dwelling people aged ≥75 years	New Zealand	Randomized subjects were interviewed by using a structured questionnaire to assess medication adherence.	MMAS-4	Medication adherence, factors associated with adherence	N/A
Andrea Berni et al 2010[12]	Hypertensive population	Italy	The study was performed to evaluate the predictive value of MMAS for increased AASIs.	MMAS-8	Blood pressure, ambulatory arterial stiffness index(AASI), Medication adherence	Predictive value of MMAS-8: a predictor for both increased AASI (O.R. 0.49, 95% CI 0.31–0.76, Pb0.01) and increased Sym_AASI (O.R. 0.67, 95% CI 0.47–0.95, P=0.026)
CoSMO study 2008[13]	Hypertensive population whose residence damaged by Hurricane Katrina	US	The data from the baseline survey for the Cohort Study of Medication Adherence among Older Adults, were analyzed to assess the effect of Hurricane Katrina on anytihypertensive medication adherence.	MMAS-8	Hurricane-related factors such as PTSD and hurricane coping self-efficacy. Medication adherence	N/A
CoSMO study 2010[14]	Hypertensive population whose residence damaged by Hurricane Katrina	US	Participants were administered questionnaires including Center for Epidemiologic Studies-Depression Scale, the Medical Outcomes Study Social Support Index, and MMAS-8.	MMAS-8	Socio-demographic factors, medication adherence, depressive symptoms, and social support.	N/A
Nina VD Steeg et al 2008[15]	Hypertensive population	Germany	Participants were asked to complete both MMAS-4 and MARS-5. The medication possession ratio (MPR) was used as reference Standard.	MMAS-4 MARS-5	Medication possession ratio(MPR), Psychometric properties of MMAS-4 and MARS-5	<u>Sensitivity:</u> 31.9%, <u>Specificity</u> 72.8% <u>Positive predictive value:</u> 0.405 <u>Negative predictive value:</u> 0.648 <u>Positive likelihood ratio:</u>1.18
Arvind JT et al 2011[16]	Patients suffer from inflammatory bowel diseases (IBDs)	US	Subjects were administered MMAS-8. Prescription claim data was correlated to the MMAS-8 to validate the scale.	MMAS-8	Continuous single interval medication availability (CSA), mean possession ratio (MPR), MMAS score	85% of low adherers identified by MMAS had nonpersistent fill rates compared with 11% of medium and high adherers
Phantipa Sakthong et al 2009[17]	Type 2 diabetic population	Thailand	The cross-sectional study were conducted by using face-to-face interviews which included MMAS, MA-VAS and sociodemographic data to develop and validate a Thai version MMAS-8	MMAS-8 Thai version	MMAS score, HbA1C, psychometric properties of MMAS-8 Thai version	<u>Internal consistency reliability:</u> Cronbach's a = 0.61 <u>Test–retest reliability:</u> intraclass correlation coefficient = 0.83; p < 0.001 <u>Convergent validity:</u> high correlation with the 3-item Morisky scale (r = 0.77; p < 0.01) and a medium correlation with the MA-VAS (r = 0.57; p < 0.01) <u>Known groups</u> <u>Validity:</u> a significant association between MMAS and A1C levels (χ2 = 6.7; p < 0.05) Sensitivity: 51%, Specificity 64% Positive predictive value: 0.71 Negative predictive value: 0.43

Cohen HW et al 2009[18]	Type 2 diabetic population	US	Randomized controlled, behavioural intervention delivered by telephone to assess the concordance of pharmacy claims and self-report data	MMAS-4 SDSCA	HbA1C, medication possession ratio, MMAS and SDSCA scores	There was significant correlation of baseline MPR with Morisky score (r = 0.21, P < 0.001). MMAS score was not significantly associated with HbA1c.
Marie KW et al 2009[19]	Community dwelling seniors with hypertension	US	Subjects were asked to complete a survey that included MMAS-8 and pharmacy records for antihypertensive medications were abstracted to assess the concordance of MMAS-8 with pharmacy fill data.	MMAS-8	Continuous single-interval medication availability (CSA), medication possession ratio (MPR), continuous multiple-interval medication gaps (CMG), MMAS score	Low adherers determined by MMAS-8 were 6.89 times more likely to have non-persistent pharmacy fill rates by CSA and 5.22 times as per MPR. Concordance between MMAS and CSA, MPR, and CMG was >=75%.
Kenneth S Babamoto et al 2009[20]	Newly diagnosed type 2 diabetic population	US	This prospective randomized study evaluated the effectiveness of a trained community health workers (CHW) intervention among Hispanic people with newly diagnosed type 2 diabetes.	MMAS-8	Health status, emergency department utilization, dietary habits, physical activity, and medication adherence	N/A
Fernandez S et al 2008[21]	Minority elderly people with hypertension	US	A pre-post design pilot trial of behavioral counseling for therapeutic lifestyle changes was conducted to evaluate the effectiveness and feasibility of the intervention	MMAS-4	Systolic BP, diastolic BP physical activity, diet, medication adherence	N/A