ARIC Manuscript Proposal #2443

PC Reviewed: 9/9/14	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Psychometric Properties of the 4-item Morisky Medication Adherence Scale among the Atherosclerosis Risk in Communities Study visit-5 participants

b. Abbreviated Title (Length 26 characters): Morisky Psychometric Properties

2. Writing Group:

Writing group members: Hadi Beyhaghi, Bryce Reeve, Sally Stearns, Jo Ellen Rodgers, others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __HB__ **[please confirm with your initials electronically or in writing]**

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3. Timeline: 3 months for draft; 1 years for publication (assuming revisions)

4. Rationale:

Medication adherence, which is defined as "the extent to which a person's behavior with regard to taking medication corresponds with agreed recommendations from a health care provider" [1], has been the subject of extensive research for the past few decades [2,3]. The World Health Organization (WHO) estimates that on average only 50% of patients with chronic diseases are adherent to their medications in developed countries [4]. Studies have shown that medication nonadherence is associated with worse clinical outcome [5,6], including higher hospitalization rates [7], higher risk of preventable drugs-related hospital admissions [8], and a higher mortality rate [9]. Despite the widespread prevalence and cost of poor adherence, medication nonadherence remains underdiagnosed and undertreated in a significant portion of patients across different care settings. Marcum and colleagues suggested that medication nonadherence should be viewed as a diagnosable and treatable medical condition [10]. In this framework, accurate diagnosis and the determination of causal factors associated with medication nonadherence are two essential components.

Nonadherence may be measured directly or indirectly. Direct measures detect the presence of the drug in a person's body using assays for the drug, its metabolites, or other markers in blood, urine, or other bodily fluids. High cost of implementation and inability to provide feedback at the point of care results in infrequent use of direct measures in medical practice large observational studies and clinical trials. Indirect methods measure medication adherence behavior using electronic drug monitoring, pill counts, pharmacy refills, medical record review, directly observed therapy, clinician assessment, and self-report [11]. Although no single measure has been recognized as a "gold standard" for measuring adherence [12-15], self-report measures have several advantages over other methods, including being brief, inexpensive, applicable in various settings, and able to provide feedback at the point of care. Furthermore, self-reporting can detect underlying reasons contributing to nonadherence.

Despite these advantages, self-report measures are criticized for inadequate reliability and poor distributional properties (i.e. restricted range and skewness) [16]. As a result of various biases, e.g. social desirability and recall bias, self-report methods usually underestimate the rate of medication nonadherence by10-20% compared to other methods [12, 17-19].

The most commonly used multi-item measure of medication nonadherence is the four-item Morisky Medication Adherence Scale (MMAS), which asks whether people miss doses because of forgetting, being careless, feeling better, or feeling worse [20]. Although MMAS is designed for measuring medication nonadherence, Voils and colleagues believe that MMAS only contains the items that identify respondents' reasons for nonadherence, therefore it cannot be appropriately classified as a measure of extent of medication nonadherence (effect indicator model) and more appropriately falls into measures of causes of medication nonadherence (causal indicator model) [11]. These two models have divergent implications for measure validation [12]. Since, to the best of our knowledge, the ARIC cohort provides the largest sample that has responded to MMAS,

assessing psychometric properties of MMAS in this population can inform future selection of measures for assessing medication nonadherence.

5. Main Hypothesis/Study Questions:

This study aims to evaluate the psychometric properties of MMAS as a measure of medication nonadherence among ARIC study visit-5 exam participants. Three questions will be addressed:

1. Does the ARIC data support the factorial validity of the MMAS as a single factor?
2. Is the MMAS a reliable measure of nonadherence in the ARIC data?
3. How does MMAS perform in comparison with other measure of medication adherence (measures of extent and measures of reason for non-adherence) used in ARIC Visit 5 data collection?

If any deficiencies in the measures are detected, the results could be useful in informing medication adherence measures to be used in future assessments.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodological limitations or challenges if present).

Study population

ARIC cohort members who participated in the visit-5 exam and completed the Medication Survey Questionnaires concerning medication adherence

Selected questionnaires

This study will use the four-item Morisky Medication Adherence Scale (MMAS). Values of 1+ are considered to be nonadherent, while zero (selecting response "No" for all of the items) is considered as full adherence. The MMAS is typically scored with a single number that represents the aggregate of the 4 items with higher scores reflecting more non-adherence. Thus, it is typically treated as an "effect indicator" model.

In addition to MMAS, we will assess the psychometric properties of other measures of adherence in the Visit 5 exam, including two items that directly asked about the extent of medication adherence and 13 items on the causes of medication nonadherence (causal indicators). Medication adherence measures in Visit 5 are presented in Table 1.

Table 1. Medication adherence questionnaires in ARIC Visit 5 exam	
Item	Measures
	Morisky Medication Adherence Scale
1	Ever forget to take medicines
2	Ever careless about taking medicines
3	Stop taking medicines when feeling better
4	Stop taking medicines if you feel worse
	Frequency of nonadherence in past 4 weeks
5	Frequency of stretching medicines in past 4 weeks
6	Frequency of running out of medicines in past 4 weeks
7	Frequency of missed taking of medicines in past 4 weeks
	Direct measure of the extent of adherence
8	Percent of on-time medication taking
	Causal indicator measure of medication nonadherence ("reasons for nonadherence")
9	Medication not taken on time because could not afford
10	Medication not taken on time because lack of transportation
11	Medication not taken on time because poor memory
12	Medication not taken on time because ran out of it
13	Medication not taken on time because confusing directions
14	Medication not taken on time because felt better
15	Medication not taken on time because felt worse
16	Medication not taken on time because too complicated
17	Medication not taken on time because scared of side effects
18	Medication not taken on time because no belief in effectiveness
19	Medication not taken on time because other reason

Analysis

Classical test theory

The internal consistency reliability will be assessed using Cronbach's Coefficient Alpha. Item analysis including response frequency and Spearman's inter-item correlation matrix will be calculated to assess the reliability of MMAS. The correlation between MMAS items and the two single-item measures directly reflecting the extent of medication adherence will be estimated to test the scale performance across two measures that had face validity for measuring the extent of adherence. We will also examine the association of the MMAS items with the items capturing "reasons for nonadherence". The magnitude of association between the MMAS items and the other measures of nonadherence will allow us to determine if the MMAS should be considered more of an effect indicator model (reflecting extent of nonadherence) or a causal model (reflecting reasons for nonadherence).

Exploratory factor analysis

To identify the number of factors that underlie the MMAS items, an exploratory factor analysis will be conducted. The factor analysis uses standard Pearson correlations to generate the factors, which is primarily appropriate for continuous variables. Since most

of the questionnaire items used in this study have binary or categorical response options, the methods will be modified to account for the scale of measurement. An exploratory factor analysis will also be conducted on the entire set of medication adherence measures used in the survey including MMAS to investigate factor loadings of similar items.

Challenges:

- The sample will be limited to those participants who were willing to participate in Visit 5 and to respond to the medication adherence questions; these participants may be healthier than the general population;
- The data do not provide the opportunity to assess the pre- and post-test reliability as well as other types of validity e.g. known groups validity;

7.a. Will the data be used for non-CVD analysis in this manuscript? __X__ Yes ____ No

b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? __ X __ Yes ____ No
(This file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?
____ Yes __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = "No use/storage DNA"?
____ Yes ____ No

9. **The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.** ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/ARIC/search.php

___X___ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

MS 2043 (Jo Ellen Rodgers is the lead author of 2043, and she is part of the writing group for this manuscript.

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____ Yes __X__ No

11.b. If yes, is the proposal

___ A. primarily the result of an ancillary study (list number* _____)

___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PUBMED Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

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