

Chapter 1 : Medication Adherence Report Scale (MARS) – “Spoonful of Sugar”

1. Introduction. Adherence to medication is a crucial part of patient care and indispensable for reaching clinical goals. The WHO, in its report on medication adherence, states that "increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment" [1].

This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. This is recognized as a significant public health issue, since medication nonadherence leads to poor health outcomes and increased healthcare costs. Improving medication adherence is, therefore, crucial and revealed on many studies, suggesting interventions can improve medication adherence. One significant aspect of the strategies to improve medication adherence is to understand its magnitude. However, there is a lack of general guidance for researchers and healthcare professionals to choose the appropriate tools that can explore the extent of medication adherence and the reasons behind this problem in order to orchestrate subsequent interventions. This paper reviews both subjective and objective medication adherence measures, including direct measures, those involving secondary database analysis, electronic medication packaging EMP devices, pill count, and clinician assessments and self-report. While choosing a suitable approach, researchers and healthcare professionals should balance the reliability and practicality, especially cost effectiveness, for their purpose. Meanwhile, because a perfect measure does not exist, a multimeasure approach seems to be the best solution currently.

Introduction Adherence to medication is a crucial part of patient care and indispensable for reaching clinical goals. By opposition, nonadherence leads to poor clinical outcomes, increase in morbidity and death rates, and unnecessary healthcare expenditure [2, 3]. It includes the initiation of the treatment, implementation of the prescribed regime, and discontinuation of the pharmacotherapy [8]. Meanwhile, some studies classify adherence as either primary or secondary. Primary nonadherence is the frequency with which patients fail to fill prescriptions when new medications are started so it is related to refilling and initiation of the medication therapy [9]. Secondary nonadherence is defined as the medication being not taken as prescribed when prescriptions are filled. It does not only affect the clinical outcome but also affect the financial outcome of the health system [10]. Often, compliance is also used and the two can be used interchangeably in research and clinical practice [11]. Therefore, in this paper, adherence will mainly be used. Poor medication adherence has multifactorial causes that need to be understood before interventions can be designed to improve medication adherence [2]. According to WHO, there are multiple factors leading to poor medication adherence, normally classified into five categories: With an understanding of whether the nonadherence is primary initiation of pharmacotherapy or secondary implementation of the prescribed regime, and what factors have led to it, a proper intervention can then be tailored individually to improve the medication-taking behavior of each patient. Measuring adherence is, therefore, important to both researchers and clinicians. Inaccurate estimation of medication adherence can lead to several problems which are potentially costly and dangerous in both settings. Effective treatments may be judged as ineffective, expensive diagnostic procedures may be ordered, and therapy may be unnecessary and dangerously intensified. In addition, results of clinical trials cannot be realistically interpreted without adherence information [15, 16]: Nevertheless, measurement of medication adherence can be quite challenging since and parameters of acceptable adherence need to be carefully delineated and appropriated for individual situations [17]. There are numerous tools available for these measurements, but these need to prove to be valid, reliable, and sensitive to change [13, 17]. Currently none of the available methods can be considered as a gold standard and the combination of methods is recommended [15]. However, even after decades of research, there is very little guidance for healthcare professionals and researchers to choose the most suitable adherence measures. The aim of this paper is to give an overview of validated and commonly used medication adherence measures and a general scope for identifying nonadherence in common situations. Overview For more than four decades, numerous researches on how to properly measure and quantify medication adherence have been conducted but none of them can be counted as the gold standard. Different tools have been designed and

validated for different conditions, in different circumstances. Generally, measurements of medication adherence are categorized by the WHO as subjective and objective measurements [1]. Self-report and healthcare professional assessments are the most common tools used to rate adherence to medication [18]. The most common drawback is that patients tend to underreport nonadherence to avoid disapproval from their healthcare providers [19]. Objective measures include pill counts, electronic monitoring, secondary database analysis and biochemical measures and are thought to represent an improvement over subjective measures [13 , 18]. As such, objective measures should be used to validate and correlate the subjective ones. However, a meta-analysis on adherence outcomes states that a multi-subjective-measure approach may have higher sensitivity, but not accuracy, over employing a single objective measure [20]. In summary, subjective and objective measures have both advantages and disadvantages and should be used in combination. Further details will be individually discussed below.

Direct Measures In addition to the classification of adherence measures as subjective and objective, many other studies labeled them as direct and indirect [7 , 15 , 21 , 22]. These measures can be made randomly or at specific intervals [15]. Even though direct measures are considered to be the most accurate and can be used as a physical evidence to prove that the patient has taken the medication, there are many drawbacks regarding their use. Tests themselves can also be very intrusive which may cause pressure and anxiety in patients. Drug metabolism should be taken into account while considering using these methods. For instance, traces of neuroleptic and psychiatric medications can be detected in the blood even long after stopping the medication. Since individuals vary in physiological state and metabolic rate, drug plasma levels also differ after different individuals take the same dose of the same medicine. Moreover, the quantification itself can be difficult. For instance riboflavin, a biological marker, is simply nonquantitative for detection [23]. Therefore, these direct methods are generally unsuitable for psychiatric patients and those under multidrug regimes, even when they are hospitalized. Furthermore, direct measures are very expensive and difficult to perform as many technicians and professionals are required to monitor the process and carry out the tests. Using direct observation as an example, patients can hide their medicines under tongue and discard them afterwards, making routine inspection impractical. Therefore, these measures are mostly used for patients under single-dose therapy or intermittent administration and hospitalized [13]. Bias can also be introduced if patients take the medication only before the upcoming tests. White coat adherence [7 , 22] is a phenomenon that cannot be ignored in any study involving direct measures or visits from healthcare professionals. This suggests that a false adherence may occur and should be considered while carrying these measures.

Measures Involving Secondary Database Analysis The data of secondary database includes the sequences and patterns derived from the curated primary data in systems such as electronic prescription service or pharmacy insurance claim. Such data allows quantification of medication adherence to various refill adherence measures. Refill adherence assumes that prescription-refilling patterns correspond to the patient medication-taking behavior. This assumption has been considered as an acceptable estimate [29]. Furthermore, these measures also assume that the medication is taken exactly as prescribed [27]. As a result, partial adherence where patients only take a part of the medication in that interval cannot be revealed using these measures. Farmer has divided refill adherence into 3 types: However, this tool is a measure of persistence to the medication therapy, instead of adherence. Reviewing prescription refill records requires a centralized computerized system along with a consistency among prescribers and dispensers to collect a complete dataset over that designated period [15]. This allows an analysis of a large population and results in the popularity of this method in research. Moreover, this method is able to assess multidrug adherence and to identify patients at risk for treatment failure [30]. Even though barriers, such as demographic features, can be compared and pinpointed as nonadherence factors, this method does not give many clues to the researcher or the health professionals concerning the barriers involved in the detected nonadherence in terms of individual patient [31]. To avoid errors from inaccurate data input, administrative datasets compiling billing information for healthcare service [28] and insurance claims are often used in research, as this complete dataset, including all prescription activities, is verified by insurance companies or prescription benefit managers PBMs in the United States [15]. Therefore, utilizing the database for refill adherence is intended for consistent, nondiscretionary use. Table 1 presents the equation of each method

described below. Equations of medication adherence measures involving secondary database analysis and pill count [15 , 19 , 27 , 28]. The former is used in the case such as patients with depression or HIV whereas the latter is generally used for assessing seasonal use of medication, asthma or allergies, and so forth [29]. The denominator variation makes MPR impossible to use on a large population analysis. Hence, appropriate correlation and average would be necessary to adjust for overall adherence values [28]. Consequently, overestimated adherence values are found while using this method. Dichotomous Variable This measure requires a cutoff value to distinguish adherence and nonadherence or adherence from partial adherence [15 , 27]. Compared to the continuous variable, it has lower sensitivity probably due to its general lack of pharmacological basis for deciding the cutoff value [15]. These drawbacks made some authors to recommend the use of continuous variable measures instead, since they show higher reliability and power [34].

Continuous, Multiple Interval Measure of Medication Gaps CMG CMG measures are obtained dividing the total number of days in treatment gaps by the duration of the time period of interest in order to recognize any time intervals without drug exposure [27]. Any negative value would be set to 0. It calculates nonadherence values for cumulative periods without considering the possibility of early refill or overfill. If any surplus is included, CMOS should be used to adjust for oversupplies obtained during earlier prescription intervals to incorporate any excess medication within the time period [28]. Bias occurs when the patient gets more than one refill a day or when refill is close to the day of completion [28]. It is calculated by the number of days without any medication over number of days in the interval. Similar to CSA, CSG is more suitable for short-term drug exposure, such as the patients with only one prescription and the short-term drug usage is related to clinical outcome [27]. The popularity of above features that appear in devices is ranked in descending order. Even though not all such features are available in all devices, recording adherence performance is essential for analysis and to tailor suitable interventions.

Medication Events Monitoring System MEMS Even though various models have been designed over decades, the basic principle of this system is that whenever the medication is removed from the container, a microprocessor embedded would record the time and date, assuming that the patient has taken that specific dose at that particular time [5 , 15 , 23]. This objective measure is being highly accurate in several studies [5]. It helps identify whether the nonadherence is sporadic or consistent or any other abnormal medication-taking pattern and it is able to detail the number of daily doses on any partial adherence situation. These features make MEMS more useful than biochemical and self-report measures [15]. As a result, it is always used as a reference standard for validating other adherence measures. Despite the fact that more effort is needed to create the false impression of adherence, there is no assurance that patient would not do it. Apart from purposefully misleading the system, patients may accidentally actuate the container without taking the medication [15]. This can lead to medication adherence overestimation. The bulkiness of the container is also an obstacle, which can make patients transfer the medication into another container or not carry the medication when they go out [15 , 23]. Furthermore, the presence of the container alone may keep reminding the patient that they are under surveillance. This has been reported to result in anxiety, stress, and somatic complaints in some cases [15]. Although the accuracy of MEMS is undeniable, its lack of interest for studies with large populations, such as clinical trials, or routine use is related to high costs and the amount of support required [5 , 15 , 23 , 35].

Chapter 2 : Medication Adherence Rating Scale (MARS) Calculator

The MARSâ„¢ measures adherence in a non-threatening manner to minimize social pressure which leads to under reporting of non-adherence. Respondents indicate their agreement with statements about their medicine use on a 5 point Likert scale.

This study determines the following for a hypertensive patient population: Members from patient panels in the UK, Germany, Italy, and Spain were invited to participate in an online survey that included the Medication Adherence Report Scale-5 MARS-5 adherence instrument and a patient segmentation instrument developed by CoMac Analytics, Inc, based on a linguistic analysis of patient talk. Subjects were screened to have a diagnosis of hypertension and treatment with at least one antihypertensive agent. The proportion of patients defined as perfectly adherent scored 25 on MARS-5 varied sharply across the segments: Side effects, being employed, and stopping medicine because the patient got better were all significant determinants of adherence in a probit regression model. By categorizing patients into worldview clusters, we identified wide differences in adherence that can be used to prioritize interventions and to customize adherence messages. Also, the predictive power of segments was greater than that for variables measuring concerns over cost, side effects, and efficacy. Logically, the set of variables used to predict adherence should guide the interventions to improve adherence. However, simply identifying the main variables related to adherence is not sufficient, because many of these variables do not point to effective interventions. Immutable characteristics of the patient, such as their age and sex, although clearly related to adherence, provide little guidance on which interventions might alter behavior or clues as to the messages that might move the patient. Indeed, messages aimed at such immutable characteristics could be counterproductive. Interventions that address the specific concerns and worldviews of each patient, ie, patient-centered solutions, are more likely to increase long-term adherence than generic interventions. An example of a patient-centered solution is tailored messaging, defined as: Any combination of strategies and information intended to reach one specific person, based on characteristics that are unique to that person, related to the outcome of interest, and derived from an individual assessment. The survey instrument used in the current research, the CoMac Analytics Descriptor CAD , identifies psycho-socio linguistic characteristics of patients with hypertension and examines the association of these characteristics with self-reported adherence. In these cases, however, if the behavioral model that underlies an intervention is not accurate, then the interventions will not induce real and sustainable changes. Similarly, even if the games and prizes in an intervention were attractive, a patient with an underlying reason to avoid her medication could refill her prescriptions and claim that she was adherent solely to qualify for a prize. If a patient believes that the side effects of a medication outweigh its benefits, then the logical interventions are to find a medication with fewer side effects or to convince the patient that their assessment of the net benefits is mistaken. There are similar logical interventions for the two other causes of low adherence in this instrument: The key questions with this instrument are the extent to which beliefs about cost, efficacy, and side effects determine adherence and the extent to which those beliefs can be altered. Again, the payoff for these interventions depends on knowledge, skill, and confidence, being the main drivers of adherence, and whether interventions can change those factors. The CoMac Analytics, Inc survey instrument is aimed at better identifying the behavioral determinants of adherence. For example, while a question may appear to be about the efficacy of a medication, the response a patient chooses can provide insight into their locus of control. An advantage of relying on linguistic clues is that it is much harder for a patient to adjust their responses so as to appear better or to please the interviewer. A further advance is the use of three constructs control orientation, emotion, and agency in one survey. To be salient to the patient, the questions must reflect their daily lives, eg, for patients with diabetes, the CoMac diabetes instrument has questions about situations in which they must make choices about sugar-laden foods. For patients with hypertension, the instrument has questions about salt-laden foods. This specificity and relevance necessitates a longer instrument. The version for hypertension used in the current study has 25 questions. For example, in order to fashion the appropriate messages, it is not enough to identify a patient as having negative emotions. To address a patient, the source of their negative

emotions, eg, family, care providers, physical limitations caused by their disease, etc, has to be identified. That would be difficult if there were three or fewer questions for each domain. The only feasible indirect method for determining how the adherence decision was made is identifying the behavioral variables, as opposed to immutable characteristics of the patients, which best predict adherence. The objectives of the research were: Interested individuals clicked on an email link to access a screener for patients to qualify for the survey. Patients were deemed eligible if they self-reported a condition of hypertension and treatment with at least one antihypertensive medication. The respective country sample sizes were based on the number of participants who responded to the email and met the survey criteria. Questionnaire design The study, including the survey instrument and the informed consent, were approved by an external board of review. Eligible subjects proceeded to complete the online survey deployed in their local language: A drug information pharmacist licensed to practice in each of the study countries translated the US instrument into the local language. Adapting the US version of the instrument to other languages required sensitivity to cultural norms. The hypertension questionnaire includes CAD, which identifies three psychosocial domains related to adherence: First, it was created from lengthy interviews of patients, and second, the actual language of the patients who had been classified as belonging to different domains was used to craft response options in the questions. By treating the three domains as dichotomous variables internal or external control orientation, high or low agency, and positive and negative emotion, the instrument categorizes a patient into one of eight patient segments: The use of these correlations can be problematic on several levels. One problem is that there may not be a single underlying adherence construct that the five questions measure. For example, patients who take less than their prescribed dosage splits pills might be trying to save money and thus might have different motivations than patients who have stopped taking their medication. If that is the case, the Cronbach alpha measure of internal consistency for the instrument could be low, as was found in some of the studies. A third problem, perhaps the most fundamental, is that the health consequences of different percentages of days of missed medication just below perfect adherence are not known. Finally, the variable on the other side of the correlation, typically the medicine possession ratio, may not accurately measure adherence. Except for Italy, in the present study, the hypertension medications were free of charge. When medications are free, there is no immediate financial consequence of skipping doses or throwing medicine away. A binary variable for perfect adherence also avoids the problem of scant evidence on consequences of different percentages of missed days for hypertension medications. It aligns with the goal of having patients take their blood pressure medications daily. This binary variable may even be a better predictor of health outcomes than the medicine possession ratio. For example, McAdam-Marx et al 27 found that for diabetes patients, there was a statistically significant correlation with this binary for weight loss, while the medicine possession ratio was not significant. Data analysis To score the MARS-5, responses to each question were coded from 5 to 1, respectively, for the choices never, rarely, sometimes, often, or very often, and then the codes were added. Assuming that patients have a latent or unobserved propensity to be adherent that follows a normal distribution, we utilized probit regression. Although probit and logit estimation usually yield similar answers except at the tails of the distributions, probit is theoretically preferred whenever an underlying continuous behavior is dichotomized into two categories “ in this case the behavior of being perfectly adherent and the behavior of not being perfectly adherent. Logit is theoretically preferred if the underlying process generates binary results “ such as positive or negative lab results. Logit is more popular because its results can be directly interpreted as the odds ratios. A discussion of probit estimation can be found elsewhere in Sandy. This setup allowed us to compare the predictive power of the concerns versus the CoMac behavioral clusters. The dependent variable for the equation was a binary metric of adherence as measured by the MARS Models with higher predictive power place a higher percentage of the patients in their correct adherence categories. Results A total of individuals responded to the survey, including 50 in the UK, in Italy, 51 in Germany, and in Spain. As with many online research studies, younger patients were overrepresented, primarily due to their greater use of the Internet. There was a broad range of employment status: Figure 1 shows the distribution of the responses to the MARS-5 instrument. A test of whether the proportions of the respondents in the four countries differed in their self-reported perfect adherence failed to reject the null hypothesis that they were the same chi-square, 3.

This Pearson chi-square test was a simple check on whether the adherence results for the four countries could be combined. There were not enough data to run the regression models separately for each country. Table 2 displays the prevalence of patients against the eight behavioral clusters based on the three underlying domains, as well as the distribution of the constituent domains. Figure 2 displays the percentage of perfectly adherent patients by cluster. As seen in Figure 2, there are significant differences in the rates of perfect adherence across the behavioral clusters. The rate of the most adherent cluster, IPH, is 6. Figure 2 Percentage with perfect adherence by cluster. One, two, and three asterisks indicate statistical significance at the 0. The standard errors are in parentheses. As seen in Table 3, while the age variable was always negative meaning the higher the age, the lower the likelihood of being perfectly adherent, it was only significant in the final specification. Being employed was always negative and significant at the 0. Relative to the omitted country, Italy, there was no evidence that the patients in the other three countries differed in their probability of being adherent. Table 3 Probit regression output Notes: Standard error indicated in parentheses. Anticipated side effects may have driven behavior even more than the realized side effects. The last set of variables was composed of the CoMac clusters. Here, statistical significance was measured relative to the omitted category of EPH, the largest segment. The IPL segment was significantly less likely to be adherent than the EPH segment in both the third and fourth specifications, in the last at the 0. The ENL segment was also less likely to be adherent, with significance at the 0. The INL segment was the least likely of the categories to be adherent. The coefficient for that category had the largest absolute value and was significant at the 0. Finally, the ENH segment showed a trend toward significance at the 0. The coefficients in probit regressions do not have an intuitive interpretation, such as for ordinary least squares regression $\hat{\epsilon}$ ” the response of the dependent variable to a unit change in the explanatory variable, while all other variables are constant. The most intuitive way of describing the importance of binary right-hand variables in a probit regression is the marginal effect on the probability of being adherent by changing the right-hand variable from 0 to 1. One question raised was whether the determinants of perfect adherence differed by age and sex. The current dataset does not contain information on sex for all observations, so that variable could not be used. To test whether the coefficients of all of the variables in the third regression in Table 3 varied by age, the sample was split into those above and those below the mean age of A likelihood ratio Chow test indicated whether the coefficients for all variables in the younger and older samples were different. The results were a likelihood chi-square with 14 df of

Chapter 3 : [Full text] Variation in medication adherence across patient behavioral segments: | PPA

CERP Adherence rating scales 3 DAI questionnaire Name Date Question Answer 1 I don't need to take medication once I feel better T / F 2 For me, the good things about medication outweigh the bad T / F.*

The former is used in the case such as patients with depression or HIV whereas the latter is generally used for assessing seasonal use of medication, asthma or allergies, and so forth [29]. The denominator variation makes MPR impossible to use on a large population analysis. Hence, appropriate correlation and average would be necessary to adjust for overall adherence values [28]. Consequently, overestimated adherence values are found while using this method. Dichotomous Variable This measure requires a cutoff value to distinguish adherence and nonadherence or adherence from partial adherence [15 , 27]. Compared to the continuous variable, it has lower sensitivity probably due to its general lack of pharmacological basis for deciding the cutoff value [15]. These drawbacks made some authors to recommend the use of continuous variable measures instead, since they show higher reliability and power [34]. Continuous, Multiple Interval Measure of Medication Gaps CMG CMG measures are obtained dividing the total number of days in treatment gaps by the duration of the time period of interest in order to recognize any time intervals without drug exposure [27]. Any negative value would be set to 0. It calculates nonadherence values for cumulative periods without considering the possibility of early refill or overfill. If any surplus is included, CMOS should be used to adjust for oversupplies obtained during earlier prescription intervals to incorporate any excess medication within the time period [28]. Bias occurs when the patient gets more than one refill a day or when refill is close to the day of completion [28]. It is calculated by the number of days without any medication over number of days in the interval. Similar to CSA, CSG is more suitable for short-term drug exposure, such as the patients with only one prescription and the short-term drug usage is related to clinical outcome [27]. The popularity of above features that appear in devices is ranked in descending order. Even though not all such features are available in all devices, recording adherence performance is essential for analysis and to tailor suitable interventions. Medication Events Monitoring System MEMS Even though various models have been designed over decades, the basic principle of this system is that whenever the medication is removed from the container, a microprocessor embedded would record the time and date, assuming that the patient has taken that specific dose at that particular time [5 , 15 , 23]. This objective measure is being highly accurate in several studies [5]. It helps identify whether the nonadherence is sporadic or consistent or any other abnormal medication-taking pattern and it is able to detail the number of daily doses on any partial adherence situation. These features make MEMS more useful than biochemical and self-report measures [15]. As a result, it is always used as a reference standard for validating other adherence measures. Despite the fact that more effort is needed to create the false impression of adherence, there is no assurance that patient would not do it. Apart from purposefully misleading the system, patients may accidentally actuate the container without taking the medication [15]. This can lead to medication adherence overestimation. The bulkiness of the container is also an obstacle, which can make patients transfer the medication into another container or not carry the medication when they go out [15 , 23]. Furthermore, the presence of the container alone may keep reminding the patient that they are under surveillance. This has been reported to result in anxiety, stress, and somatic complaints in some cases [15]. Although the accuracy of MEMS is undeniable, its lack of interest for studies with large populations, such as clinical trials, or routine use is related to high costs and the amount of support required [5 , 15 , 23 , 35]. The equipment alone is very expensive. With the possibility of equipment loss by patient, rental of hardware and software for data retrieval, staff time, bed days, and the cost to encourage patients to return the cap, MEMS studies require large funds to complete. These authors also mentioned other practical issues, including the difficulty in coordinating refills with outpatient pharmacies and the need to encourage patients for the correct use of the cap [23]. The incorrect use of the MEMS container may lead to false categorization of patients as nonadherent [36]. Pill Count This indirect, objective measure counts the number of dosage units that have been taken between two scheduled appointments or clinic visits. This number would then be compared with the total number of units received by the patient to calculate the adherence ratio [15 ,

19]. Table 1 presents the equation based on the definition. The low cost and simplicity of this method contribute to its popularity. However, several limitations have been identified. First, although it can be used for various formulations, such as tablets, capsules, and actuated inhaler, this approach is unfeasible in assessing those with nondiscrete dosages or Pro re nata prn medication [19]. Moreover, adherence underestimation occurs frequently, since this method simply uses the dispensed date as the denominator of the equation without considering the chance of having surplus medication. Especially for patients with chronic conditions, it is common for them to refill the medication before running out [19]. Moreover, the cutoff value to differentiate adherence and nonadherence, in this case, is generated arbitrarily [15]. Although pill count is based on a similar assumption to MEMS, which is the fact that the removal of the dosage unit is equivalent to taking the medication, pill count does not generate a medication-taking pattern as the latter does. Removing the correct number of dosage units from the container does not necessarily mean the patient follows the dosing regime consistently [36 , 37].

Measures Involving Clinician Assessments and Self-Report Many authors believe that these subjective methods are the least reliable among all. Nevertheless, their low cost, simplicity, and real-time feedback have contributed to their popularity in clinical practice [4 , 38 , 39]. They can be administered as structured interviews, online assessments, written questionnaires, voice response system, and so forth. Additionally, due to their practicality and flexibility, these questionnaires are able to identify individual patient concerns and subsequently tailor appropriate intervention [5]. Surely, the drawbacks of such approaches should not be undermined. The relatively poor sensitivity and specificity can occur due to false data input by patients, purposefully or accidentally [21 , 38], or faulty communication skills and questions constructed by the interviewers as well as the design of survey [15 , 23]. Negativity in questions, suggesting blaming the patients for not fulfilling their prescribed regime, may lead to bias [15].

Patient-Kept Diaries This is the only self-report tool that is consistently documented with how the patient follows their prescribed regime. Patients can be asked to estimate their own medication-taking behavior, namely, which percentage of dose that they may miss within a designated period or the frequency that they are unable to follow the medication regime. Healthcare professionals then evaluate their response to determine the level of adherence. Apart from the traditional approach described above, motivational interview has an increased popularity in clinical practice. This combines the adherence measuring and subsequent intervention into one tool. It does not only measure and evaluate medication adherence, but it intervenes if there is any case of medication nonadherence. Miller and Rollnick defined it as a direct patient-centered approach to help patients understand and resolve ambivalence so as to encourage behavioral changes [41]. In a meta-analysis, Rubak et al.

Questionnaires and Scales These subjective approaches were first designed to minimize the limitations of other self-report methods by standardizing the measurement of adherence to a specific medication regime [15]. These questionnaires are generally validated against other measures, both subjective and objective, and with numerous versions to accommodate various conditions, such as for a broad-ranged or single diseased population, or in different languages. Self-report questionnaires should be completed by patients themselves or their caretakers. However, questionnaires can be difficult for patients with low literacy levels [44]. In a systematic review, Nguyen et al. Furthermore, the authors categorized the scales into 5 main groups that evaluate the following: Beliefs associated with adherence are related to personal concerns on the medication safety or the need of following the prescribed regime. In terms of determining nonadherence, these authors summarized the methodology for those scales. Most analyzed scales have a recommended cutoff value. As many scales were identified, this paper will focus on those that are considered as the most useful covering the concept of medication-taking behaviors, barriers to adherence, and belief associated with adherence. It consists of three different screens, a 5-item Regime screen, a 2-item Belief screen, and a 2-item Recall screen. These screens assess how patients took each of their medications in the past week, on drug efficacy and bothersome features and remembering difficulties, respectively. Thus, the entire process may be more time-consuming comparatively to other questionnaires, which makes it difficult to be scored at the point of care [4]. The test consists of 3 subscales, medication-taking behavior, ability to keep appointment, and sodium intake, and is rated on a four-point Likert-type scale. The number of items available for testing varies among population types. When first designed, it has showed high internal consistency [45] and so it did when

used in a primary healthcare setting from a study in South Africa [46]. The authors also described that Hill-Bone has a higher performance for black than nonblack populations despite its high cultural sensitivity [47]. Meanwhile, the study with community-dwelling population also proved its high internal consistency in outpatient settings [48]. Therefore, this scale has been suggested as suitable for use in studies specific for hypertension in a predominantly black population. The additional items focus on medication-taking behaviors, especially related to underuse, such as forgetfulness, so barriers to adherence can be identified more clearly [44]. MMAS was also validated with outstanding validity and reliability in patients with other chronic diseases [44]. As a result, it is probably the most accepted self-report measure for adherence to medication. Along with blood pressure control data, MMAS should be able to identify medication nonadherence and help control blood pressure [39]. Therefore, it is recommended to serve as a screening tool for validated conditions in the clinic setting. This questionnaire is the quickest to administer and score and is only able to identify barriers to adherence due to its length [4]. Since it has been validated in the broadest range of diseases and in patients with low literacy, it is the most widely used scale for research [49]. In a study on factor structure and validity of MAQ for cigarette smokers, it was reported that the coefficient alpha reliability of MAQ varied among studies as well as validity estimates [50]. It may be difficult to carry out at the point of care because of its length. However, this scale has been validated in various chronic conditions [4 , 49]. Reliability of this scale was measured by its internal consistency. With coefficient alpha reliability at 0. As a result, it is able to examine medication-taking behaviors and attitudes toward medication with higher validity and reliability values. The internal consistency reliability of MARS is unclear [4]. Still, Thompson et al. It was designed and first validated for patients with schizophrenia [52]. Hence, this scale is limited to use in patients with chronic mental illness. Choosing a Suitable Medication Adherence Measure An ideal medication adherence measure should present low cost and be user friendly, easy to carry out, highly reliable, flexible, and practical [13 , 15]. However, there is no single measure that can meet all these gold standards since each has its own drawbacks as described above. In a broad sense, subjective and objective measures are preferred in clinical and research settings, respectively, mainly due to cost effectiveness ratios. Self-report questionnaires, which have a reasonable predictive power, are more useful in a busy, resource-limited clinical setting with moderate to high literacy population. Although pill count is an objective measure, the needs of staff and time have made it primarily used in routine clinical practice instead.

Chapter 4 : Medication Adherence Measures: An Overview

Medication Adherence Rating Scale (MARS) Click here for Medication Adherence Rating Scale (MARS) - page 7 The total score ranges from with a higher score indicating better adherence.

The authors state that although several methods are available for the assessment of adherence, accurate measurement continues to be difficult. At present there is no generally accepted "Gold Standard" for measuring adherence. Biological Assays Biological assays measure the concentration of a drug, its metabolites, or tracer compounds in the blood or urine of a patient. These measures are intrusive and often costly to administer. Patients who know that they will be tested may consciously take medication that they had been skipping so the tests will not detect individuals who have been nonadherent. Drug or food interactions, physiological differences, dosing schedules, and the half-life of the drugs may influence the results. Biological tracers that have known half lives and do not interfere with the medication may be used, but there are ethical concerns. All of these methods have high costs for the assays that limit the feasibility of these techniques. Some data indicate that this technique may underestimate adherence in older populations Grymonpre et al. Patterns of non-adherence are often difficult to discern with a simple count of pills on a certain date weeks to months after the prescription was filled. Because pill counts are often based upon the date a prescription is filled, patients who get prescriptions refilled prior to their first one running out and then combining pills into a single and possibly non-original bottle presents complications. Loss of data is common among many studies. When compared with patient log books of daily medication use, weight estimates of adherence were considerably lower than patient log estimates. They recommend that clinical trials involving topical applications incorporate medication weights as the primary measure of adherence. In a comparison of methods to measure adherence, Carroll et al. The system electronically monitors when the pill bottle is opened, and the researcher can periodically download the information to a computer. The availability and cost of this system could limit the feasibility of its use. Pharmacy Records and Prescription Claims This method can be used primarily for medications that are taken for chronic illnesses such as hypertension. Concerns regarding the completeness and reliability of these records have been expressed Vik et al. These records provide only an indirect measure of drugs consumed. Patterns of over and under consumption for periods less than that between refills cannot be assessed. Interviewing patients to assess their knowledge of the medications they have been prescribed and the dosing schedule provide little information as to whether the patient is adherent with the actual dosing schedule. Subjective assessments by interviewers can bias adherence estimates. This method is rarely used in medical research to assess adherence Vik et al. Patient Estimates of Adherence Direct questioning of patients to assess adherence can be an effective method. Patients who admit to nonadherence are generally accurate in their assessment. However, patients who claim adherence may be underreporting their nonadherence to avoid caregiver disapproval Vik et al. Other methods may need to be employed to detect these patients. Scaled Questionnaires Morisky et al. Thier scale demonstrated acceptable psychometric properties. Their measures are culturally sensitive and demonstrate good reliability. The Hill-Bone Compliance to High Blood Pressure Therapy Scale includes 14 items, 8 of which are directed at assessing medication taking behavior in hypertensive patients Hill et al. Not only is this method relatively simple and economically feasible to use, but it has the added advantage of soliciting information regarding situational factors that interfere with medication adherence e. The Compliance-Questionnaire-Rheumatology CQR is a item questionnaire that has been favorably compared with electronic medication event monitoring de Klerk et al. This instrument has good validity and reliability. The purpose of the MASE scale is so clinicians and researchers can identify situations in which patients have low self-efficacy in adhering to prescribed medications. Journal of the American Academy of Dermatology. Cancer Epidemiol Biomarkers Prev Prog Cardiovasc Nurs Current Opinion in Cardiology. Annals of Pharmacotherapy 38,

Chapter 5 : Measuring Medication Adherence

Background: Self-report is considered most suitable to measure medication adherence in routine clinical practice. However, accuracy of self-report as a quantitative measure of adherence is not well documented.

To test the acceptability and reliability of the Swedish translation of the Medication Adherence Report Scale-5 MARS-5 in a sample of patients who use mood stabilising medicines for bipolar disorder. In the study population The face validity resulted in four comments regarding difficulties in answering the MARS The MARS-5 showed good psychometric properties. The psychopathology and treatment of bipolar disorder. *Annu Rev Clin Psychol ;2: Lithium - a continuing story in the treatment of bipolar disorder. Acta Psychiatr Scand Suppl Correlation between drug treatment adherence and lithium treatment attitudes and knowledge by bipolar patients. Prog Neuropsychopharmacol Biol Psychiatry Jan 30;31 1: Scott J, Pope M. Nonadherence with mood stabilizers: J Clin Psychiatry May;63 5: Skeppar P, Adolfsson R. Bipolar II and the bipolar spectrum. Am J Psychiatry May; 5: Adherence to long-term therapies: A Nationwide Cross-Sectional Survey. Assessment of medication adherence in a cohort of patients with bipolar disorder. Pharmacopsychiatry Nov;43 7: Treatment nonadherence and neurocognitive impairment in bipolar disorder. J Clin Psychiatry Jul;70 7: Hassan M, Lage MJ. Risk of rehospitalization among bipolar disorder patients who are nonadherent to antipsychotic therapy after hospital discharge. Twelve-month outcome of adolescents with bipolar disorder following first hospitalization for a manic or mixed episode. Am J Psychiatry Apr; 4: Indirect costs associated with nonadherence to treatment for bipolar disorder. J Occup Environ Med May;52 5: Med Care Mar;42 3: Osterberg L, Blaschke T. N Engl J Med Aug 4; 5: Improving treatment adherence in bipolar disorder: Behav Modif May;32 3: Methodological challenges in psychiatric treatment adherence research. Clin Schizophr Relat Psychoses Apr;4 1: Busby KK, Sajatovic M. Patient, treatment, and systems-level factors in bipolar disorder nonadherence: A summary of the literature. The concordance of self-report with other measures of medication adherence: Med Care Jul;42 7: Medication adherence in outpatients with severe mental disorders: J Clin Psychopharmacol Apr;30 2: Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care Jan;24 1: A patient education program to improve adherence rates with antituberculosis drug regimens. Health Educ Q Fall;17 3: Horne R, Weinman J. Self-regulation and Self-management in Asthma: Beliefs about medicines predict refill adherence to inhaled corticosteroids. J Psychosom Res Jan;64 1: Assessing the validity of self-reported medication adherence among inner-city asthmatic adults: Ann Allergy Asthma Immunol Oct; 4: Psychol Health Jun;26 6: Factors associated with medication nonadherence in patients with COPD. Chest Nov; 5: Measuring compliance with drug regimens after renal transplantation: Transplantation Mar 15;77 5: Secondary prevention of coronary heart disease: J Psychosom Res May;58 5: Measuring beliefs about taking hypoglycaemic medication among people with Type 2 diabetes. Diabet Med Mar;23 3: Predictors of medication adherence in inflammatory bowel disease. Am J Gastroenterol Jul; 7: Assessing reported adherence to pharmacological treatment recommendations. J Eval Clin Pract Jun;16 3: Beliefs about medicines and self-reported adherence among pharmacy clients. Patient Educ Couns Dec;69 Influence of disease features on adherence to prophylactic migraine medication. Acta Neurol Scand Dec; 6: Personality, adherence, asthma control and health-related quality of life in young adult asthmatics. Respir Med Jul; 7: The influence of personality traits on reported adherence to medication in individuals with chronic disease: PLoS One ;6 3: J Affect Disord Jun; Understanding medication non-adherence in bipolar disorders using a Necessity-Concerns Framework. J Affect Disord Jul; Compliance with tricyclic antidepressants: Br J Clin Pharmacol Aug;50 2: Adherence and outcomes associated with copayment burden in schizophrenia: J Med Econ ;13 2: Prevalence and correlates of poor medication adherence amongst psychiatric outpatients in southwestern Nigeria. Gen Hosp Psychiatry Mar-Apr;31 2: Perceived information needs and non-adherence: Health Expect Apr Research methods in health: Open University Press; Practical statistics for medical research. Chapman and Hall; Starting at the beginning: J Pers Assess Feb;80 1: Briggs S, Cheek J. The role of factor analysis in the development and evaluation of personality scales. Journal of Personality ;54 1: Psychological Methods ;1 1: Reproducibility and responsiveness of health status measures. Statistics and*

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strategies for evaluation. Control Clin Trials Aug;12 4 Suppl: Assessing health status and quality-of-life instruments: Qual Life Res May;11 3: