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Clinton IHS Service Unit – 07/11/2013

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| **Annotated Bibliography Table of Contents:** |
| **Articles that review monitor methods:**   1. Evaluating Medication Adherence: Which Measure is Right For Your Program? 2. Persistence With Drug Therapy: A Practical Approach Using Administrative Claims Data 3. A Measurement Model of Medication Adherence to Highly Active Antiretroviral Therapy and Its Relation to Viral Load in HIV-Positive Adult 4. Measuring Strategies Used by Mental Health Providers to Encourage Medication Adherence   **Articles that review an implementation of a monitoring program:**   1. Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review 2. Pharmacist Intervention to Improve Medication Adherence in Heart Failure   **Articles that review positive aspects of adherence assessed through monitoring programs:**   1. Cost-Related Medication Underuse Among Critically Ill Adults: the Treatments People Forgo, How Often, and Who Is at Risk 2. Behavioral and Clinical Factors Associated With Depression Among Individuals With Diabetes 3. Depression and diabetes symptom burden 4. Medication barriers and anti-hypertensive medication adherence: The moderating role of locus of control 5. The role of adherence in mediating the relationship between depression and health outcomes   **Articles that evaluate methods to improve patient adherence:**   1. Adherence to anti-psychotic medications and health behavior theories 2. What Does It Mean When a Patient Says, “My Asthma Medication Is Not Working”   Note about articles not included: Several of the articles reviewed had severe flaws in their methodology, statistical analysis, or both. Because these flaws, these articles were omitted in the bibliography. All reviews are available on the O drive under the folder titled NK Project. |

1. **Fariman, K. and Motheral, B. (2000). “Evaluating Medication Adherence : Which Measure is Right For Your Program?” *Journal of Managed Care Pharmacy,* Vol. 6 (No. 6): 499-504.**

The authors used data from published literature to discuss the strengths and limitations of medication-adherence measurement techniques. To evaluate the adherence measurement techniques, the authors pooled data from areas that included biological markers, pill counts, electronic monitoring devices, patient surveys, and prescription claims data. The authors found the best adherence techniques were dependent on factors unique to the facility, the patient, and the medication type. This implies one single approach is generally no better or worse than another. The critical factor was the selection of the proper adherence measurement technique to insure the data results collected were a true representation of patient compliance. This often meant using multiple adherence measurements to adequately measure the multifaceted medication services of each facility.

The paper discusses dataset preparation and the use of claims data as a way to measure compliance. The author defines length of therapy, persistence, days of coverage, and gaps and subsequently explains their role in analyzing medication adherence from pharmacy claims. One noted downfall of using pharmacy claims to measure adherence is that it is not well fit to measure acute adherence.

Critical analysis: the authors not the potential issues of using pharmacy claims to measure adherence when patients venture outside of their network to fill prescriptions. Without a way to account for this, it could potentially show an adherent patient as being non-adherent. With the current patient chart assess from IHS facility to IHS facility, this could be problematic. Having a universal chart IHS chart that was accessible with ease to any facility for the patient would circumvent polypharmacy, keep the treatment consistent, and give the healthcare providers better insight to the patient’s disease state to allow for more educated treatment.

**Clinton IHS Application:** Installing measures to properly monitor patient compliance could be useful to the IHS should it one day decide to install a more involved patient medication adherence policy. Having an adherence system in place that worked to improve patient compliance at a facility has the potential to greatly reduce facility overhead by giving patients better outcomes of their pharmacologic therapy. Selecting the proper system to monitor patient adherence would be vital in trying to determine if the program is working. This article presents factors that should be understood before any adherence monitoring programs are installed.

1. **Dezii, C. “Persistence With Drug Therapy: A Practical Approach Using Administrative Claims Data” *Managed Care,* February 2001: 42-45.**

The author discusses the Estimated Level of Persistence with Therapy (ELPT) approach to patient compliance and persistence. The author claims the ELPT strategy provides an inexpensive and unobtrusive way to determine the extent to which long term care therapy, for chronic disease states, are being filled on a regular basis.

The ELPT approach does not verify administration of the medication; it does how address the availability of the medication. The author states that if a patient cannot regularly pick up their prescription for chronic disease states, then adherence becomes secondary to the medications availability. The ELPT method of determining patient compliance is simply looking at how many refills a patient should have during a given time frame and comparing them to the number of refills the patient actually acquired.

The researchers required patients to be new to therapy for admittance into the study with at least a six month drug free period. They recorded whether the patient was compliant by persistency thresholds, the previously mentioned method, and analyzed the data using patient-persistent curves. The patient-persistent data curves are then used to compare patient persistence to one agent relative to another. The author states that the data can be used monitor specific patient populations, alert physicians to reasons of non-adherence, and possibly aid a physician when face with choosing between different medications of the same pharmacologic category.

Critical Analysis: The researchers in this study allowed ninety day filling window before classifying a patient as non-persistent. By the researcher’s standards this means that if a patient were prescribed a monthly prescription they would only have to fill the prescription one of every four months to be compliant. If the patient did not meet that threshold, they would be classified as not persistent. The researchers would consider a filling percentage of 25% being compliant. Many medications for chronic disease states require medication compliance rates to be much higher. In a study published in JAMA Internal Medicine titled “Self-reported Medication Adherence and Cardiovascular Events in Patients With Stable Coronary Heart Disease: The Heart and Soul Study”,the definition of compliance was an adherence rate of greater than or equal to 75% for patients taking medication for the chronic coronary heart disease. Another fault of this method is that is does not consider patient goal oriented outcomes when determining medication compliance. For example, a common compliance measure in diabetics is to assess the patient’s glycolated hemoglobin (HbA1C). A patient could theoretically go three months without taking their diabetic medications while simultaneously increasing their HbA1C, and still be considered compliant under the thresholds set forth in this study.

**Clinton IHS application:** The ELPT approach could be utilized by IHS facilities to single out medications with relatively high incompliance rates. Once these drugs are singled out, then measures to address the incompliance. This would require the IHS to implement a drug adherence monitoring software that could generate reports of incompliance generated by lack of patient refills. This information could be used to help shape a facility’s formulary by comparing which pharmacologic alternative is being utilized at a higher percentage and subsequently eliminate the lesser utilized/less adherent medication.

1. **LLabre, M., Weaver, K., Duran, R., Antoni, M., McPherson-Baker, S., and Schneiderman, N. “A Measurement Model of Medication Adherence to Highly Active Antiretroviral Therapy and Its Relation to Viral Load in HIV-Positive Adult” *AIDS Patient Care and STDs,* Vol. 20 (November 2006): 701-711.**

The purpose of this study was to test medication adherence measurement model’s ability to predict adherence. The study incorporates multiple measurements of adherence collected over multiple time frames for HIV patients receiving HAART. The authors emphasized the need for a measurement method with this capability was lacking. The authors believe that this second-order factor model of adherence fit could perform this due to its ability to detect errors uniquely, account for more variability, associated with each particular method used to concurrently.

The methods used were a self report questionnaire, an adherence interview item, and electronic medication monitoring through a medication event monitoring system (electronic caps). Single factor models composed of multiple measurement methods were developed for each of the mentioned adherence methods and then were tested for their ability to forecast viral load. The three adherence methods were then combined in a second order factor measurement model, which was also tested for its ability to measure viral load. The models including one method were, at best, able to explain 24% of variability. Second order factor model explained 45% of variability in the viral load.

The patients were assessed and paid at 3 months, and twice again at 6 month intervals. All patients received medication adherence and treatment information during the first three visits. Venous blood samples were collected from participants and viral load was calculated. The results indicated when measuring adherence over time multiple assessments are needed to obtain a reasonable level of reliability.

Critical Analysis: The study design was flawed in that a lack of viral resistance data was obtained at baseline. This is problematic because the purpose of these tests was to see how well these tests tested the ability of adherence measures to predict viral load. If a patient with a specific drug resistant viral strain were given a medication that did not affect the virus, a patient could have taken 100% of his meds and still had an increased viral load because of incompetent medication. This would have likely lowered the predictability of each measurement method utilized in the study.

**Clinton IHS Application:** This article discussed methodology used to determine which adherence measurement strategies were most indicative of the actual results in patients receiving HAART. The outcome combined several tests, each having a unique way to measure medication adherence to account for the overlapping variance, resulted in a measuring methodology that better reflected patient adherence. The application of this article to the IHS is that when installing a medication monitoring program, a single method to measure compliance is not ideal. Also, attaining more measurements equates to more reliable results. However, the results of this study should be taken with caution due to the methodological flaw in the study design of not obtaining viral resistance information at the beginning of the study.

1. **Angell, B. (2006). “Measuring Strategies Used by Mental Health Providers to Encourage Medication Adherence” *Journal of Behavioral Health Services & Research*: 53-72.**

The author wanted to test the Rasch’s measurement model ability to assess an item measure scale’s ability to assess strategies used to promote adherence that vary on a continuum of pressure or social control. The ability to assess adherence strategies would greatly enhance facilities decision to apply a more patient specific strategy with greater confidence as well as rule out strategies that were not as efficate, therefore saving the time and cost associated with a less then optimal strategy. Also, the ability to apply one test to assess the adherence measures with one test in an unidimensional manner would be greatly useful to avoid the ambiguity of looking over multiple tests and trying to come to a meaningful conclusion.

To evaluate the Rasch measurement system’s ability to measure strategies used by clinicians to promote medication adherence, the author choose mental illness patient providers at that worked in assertive community treatment centers and participated in multisite study of treatment pressures and mandates. Patients with severe mental illness have historically poor medication adherence and the risk and cost associated with medication nonadherence can be considerate, thus clinician interventions to insure medication compliance are often warranted. This patient pool is also well fitted for this study because of the various adherence strategies that are commonly applied to persuade medication adherence.

The author found the Rasch method to be acceptable (relative/comparative to Cronbach’s alpha) when adjusting for non-fitting criteria. The author found the Rasch method to be good when revising the test by removing the misfitting items, making it more facility type specific.

Critical Analysis: The authors evaluated the Rasch method ability to recognize adherence strategies used by mental health providers on a one dimensional scale. One of the complications of the test’s ability to test the effectiveness of particular adherence strategies is the ability to the test to separate adherence measures taken that overlap. For example, discussing the benefits of the medication adherence and pointing out the consequences of not taking the medication properly. After adjustments were made to account for redundancy, the authors found the Rasch method was able to significantly predict adherence measures that were efficient. However, removing the unfitting data to make significant results may result in returning to the initial problem the authors sought to overcome. The authors choose to leave in some unfit items that were due to redundancy (overlapping overly fit items), while throwing out unfit items that were due high infit square values (greater than expected randomness). Throwing out the items with high infit while at the same time leaving in items due to redundancy could improve the Rasch test’s ability to detect significance in relationships. The testing groups had different types of facilities whose endpoint corrective measures varied in intensity. Some of the doctors surveyed had the ability to threaten institutionalization (those at assertive community treatment centers) and other highly pressured measured in response to non-adherence where others did not have the same level of reinforcements.

**Clinton IHS Application:** The resulting measure may be employed in future studies to examine the ways in which clinician behavior relates to medication adherence and to consumer perceptions of treatment alliance, quality of care, and perceived coercion. The authors found that the provider’s perception of compliance often correlated with the pressure applied by the provider to encourage medication adherence. IHS does not currently apply any levels of coercion other than counseling the patients on the benefits of adherence and the hazards of non-adherence. Therefore the application of this study to the IHS facilities in an applicative manner is limited. The ability of IHS policy makers to assess articles that used the Rasch’s measurements would be greatly improved by reading this article.

1. **Connor, J., Rafter, N., and Rodgers, A. “Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review” *Bulletin of the World Health Organization* Volume 82, December issue (2004): 935-939.**

In this article the authors objective was to compare adherence of combination therapy (combined oral or unit of use combinations) with the same medication in their usual presentation. They did this by reviewing all randomized controlled trials in which participants were taking more than one self-administered medication, the intervention consisted of the use of a combination therapy, and the study had at least one pharmacological goal of therapy or cost of therapy. The authors found fifteen suitable studies.

The authors concluded by stating that they found few large reliable trials on the effect of combining medications. Seven of thirteen studies reported statistically significant improvements in medication adherence. Out of seven reporting clinical outcomes, four found significant improvement in patients taking combination therapy and these findings were limited by the methodological shortcomings of the studies. The authors found that self-reporting and pill counting measures overestimate adherence and may underestimate the impact of clinical intervention.

Applicable notes from other studies mentioned in the article:

* Simplicity of dosing regimen and side effects of the regimen had the most influence on medication adherence.
* With increase in drug regimen complexity, or the number of treated disease states in a patient, adherence decreases.
* Many trials in this area had sample sizes that were not greatly sensitive. A trial with 150 patients would only be able to detect a difference in two groups of 25% or larger. Reductions less than 25% have been shown to have clinical relevance. In order to detect a change of 15% or greater, a 500 person patient pool is needed.
* Combination medications have the potential to mitigate the under-treatment of cardiovascular disease.
* Combination medications have been shown to reduce the amount of medication waste costs.

**Clinton IHS Applicability:** This research article could be utilized to set an inclusion standard of any study when its substance could be used to make policy decisions. This article also points out the need for better designed studies. Should the IHS decide to conduct a study, this article could help with the frame work of the study. As the authors pointed out, the findings in the studies they reviewed were limited to small sample sizes or design flaws and therefore using the findings of the most of the trials they reviewed is problematic. The article also points out the self report studies often provide inflated adherence reporting. This would further support the need for more than one adherence monitoring method to be in place.

1. **Murray, M., Young, J., Hoke, S., Tu, W., Weiner., Morrow, D., Stroupe, K., Wu, J., Clark, D., Smith, F., Dradus-Pizlo, I., Weinberger, M., and Brater, C. “Pharmacist Intervention to Improve Medication Adherence in Heart Failure” *Annals of Internal Medicine,* Vol. 146 No. 10 (May 2007): 714-725.**

The purpose of this trial was to evaluate the effect of a pharmacist intervention on patients who are socioeconomically disadvantaged and medically vulnerable. The hypothesis was that pharmacist intervention would result in improved adherence to heart failure medication, reduce exacerbations require emergency room visits or hospitalizations, improve disease-specific quality of life, increase patient satisfaction, and reduce healthcare cost.

The trial was randomized and was twelve months in duration. The groups were divided into two: those who received intervention from pharmacists and those who only spoke with technicians. Patients in the intervention groups received the intervention techniques for the first nine months of the period. Patients in the intervention group were encouraged to visit or call the pharmacist regarding their medications. Pharmacist intervened by using Pharmacist Intervention Protocol table (available at [www.annals.org](http://www.annals.org)). Adherence was measured by electronic monitors and clinical exacerbations that required a hospital visit.

The study showed that patients who received intervention had a higher adherence rate of 78.8% compared to the 67.9% in the control group during the intervention period. After the intervention period, first nine months of participation, there was no significant difference in the group’s medication adherence percentage. The intervention group also reported a statistically higher refill adherence rate. The intervention group had 19.4% fewer exacerbations/hospital visits than the control group. Overall patient satisfaction was statistically significant and greater in the intervention group as well.

The direct cost of implementing this program was $205 dollars/patient. The cost per patient comparison was not statistically significant. The authors accredit this to the large variability in costs for healthcare. The authors report $14 dollar for every dollar spent on the investment.

Critical Analysis: The intervening pharmacist in this study were trained by an interdisciplinary team that would make them specialized. A pharmacist with this expanded training would likely make the study less generalizable due to the uniquely high level of training received by them would separate them professional from the general practice standard that is available at most facilities and experienced by the everyday patient.

The use of Medication Event Monitoring Systems prescription container lids (MEMS lids) could have a reinforcing effect on adherence; this could skew the results to a higher adherence rate in both the control group and the intervention group when compared to the general population. For multiple daily dosing, the MEMS lids recorded non-adherence if the patient did not take the dose within a 1.2 hour window of the previous day’s dose. This could skew the results toward non-adherence.

**Clinton IHS Applicability:** The study groups are relatable to the ISH facility patients in that they had no financial burden for adherence. The cost of medication was not a deterrent to adherence.

* The Pharmacist Intervention Protocol could be utilized at any facility that has a pharmacy practice.
* The researchers in this study used *Statistical Analysis System (SAS)* to perform statistical analysis. This software could be utilized by the IHS to perform statistical analysis of adherence programs it might implement.
* The study demonstrated that more intense intervention by pharmacist showed a statistical improvement in medication adherence. T
* The study also demonstrated the need for ongoing patient medication counseling, as after the intervention was halted the adherence rate of the two groups was not significantly different. This would imply that intervention for chronic medication is an ongoing process that justifies ongoing patient counseling efforts throughout the medication duration.

1. **Piette, J., and Heisler, M. (2004). “Cost-Related Medication Underuse Among Critically Ill Adults: the Treatments People Forgo, How Often, and Who Is at Risk.” American Journal of Public Health Vol. 94, No. 10. 1782-1787.**

The authors sought to gather information about the cost-related underuse of medications. Groups of chronically ill patients that fell into one of sixteen chronically ill designations were used in the trial. The researchers used a large pool of subjects from broad socioeconomic backgrounds to allow them to ascertain any potential differences between these groups. The study focuses on two primary aspects with potential relations to medication underuse: 1) the relationship among global measures of cost-related medication adherence, and 2) variation in the importance of socioeconomic risk factors for underuse across treatment types.

The study showed as the out of pocket cost for the patient increased; the more likely the patient was to display drug underutilization. The study did not find any significant difference of medication cost-underuse due to race, gender, and education attainment. The study did find significant relationship with out of pocket costs and respondents income with cost-related underuse.

**Clinton IHS Applicability:** The main focus of this study, cost cutting measures patients take to cope with the financial pressures of out of pocket medication cost, is not applicable to IHS patients. In the discussion section of the paper the author suggests that depending on the treatment types, treatment adherence varied due to many factors and that it was not solely based on out of pocket expense. Some patients were willing to forgo their medications at low out of pocket expense while others with high out of pocket expense were compliant with certain medications. ***This would suggest that patient perception of the importance of the pharmacologic therapy is a significant factor in patient compliance.*** This in turn stresses the need for quality patient education and counseling over their medications.

1. **Katon, W., Simon, G., Korff, M., Ludman, E., Ciechanowski, P., Walker, E., Russo, J., Bush, T., Lin, E., and Young, B. “Behavioral and Clinical Factors Associated With Depression Among Individuals With Diabetes” *Diabetes Care,* Volume 27, Number 4 (April 2004): 914-920.**

The goal of the study was to determine: 1) Are behavioral factors that increase the risk of developing diabetes are more likely to be present in depressed patients versus non depressed patients, 2) Do patients with adverse clinical side effects of diabetes complications have an increased likelihood of meeting the criteria for depression, and 3) do characteristics associated with age and sex influence whether a person is classified as depressed or not.

The study found:

*Major Depression:*

* Major depression was significantly more likely to occur in younger, female, and the unmarried.
* Patients that fell into the major depression group had a significantly higher occurrence of:
  + Co morbidities,
  + Diabetic complications,
  + Higher HbA1C levels,
  + Obesity,
  + Smoking,
  + Insulin usage,
  + Longer treatment periods.
* For individuals < 65 years old, there is a strong relationship between major depression and HbA1C levels.
* Younger patients (<65 years old) had significantly higher HbA1C levels than older patients.
* The relationship between DM complications and major depression was significant for men only. Male patients with major depression had almost twice the rate of have two or more complications.

*Minor Depression:*

* Patients were younger, less educated, more likely to be non-Caucasian, have BMI>30 kg/m2, to smoke, and to have longer duration of diabetes than those patients with diabetes only.
* Minor depression in patients > 65 years old is associated with the patient having more DM type 2 complications.

Critical Analysis: The study did not separate type 1 diabetes mellitus (DM) patients from type 2 patients. This is a problem because the consequence of non adherence for a DM type 1 patient presents with a direr acute outcome then the often asymptomatic symptoms of DM type 2. The physical characteristics of a DM type 1 patient are often drastically different from DM type 2 patients, in particular the obesity occurrence rate in DM type 2 patients. These differences could present enough social stigma differences to introduce enough variability between the two DM groups to make the two groups incomparable in a study measuring depression.

Co morbidities were determined using Rx Risk, which based medical co morbidities on the prior 12 months prescription drug use. This presents a problem of accuracy if the patient utilized multiple pharmacies. Another problem with this program is the current co morbidity could have been a diagnosis prior to the DM type 2 diagnosis. Claiming this as a complication of DM could demonstrate a stronger relationship than is actually present. Also the study did not seek to find if and underlying condition led to the patient developing the co morbidities that commonly occur with DM and depression. One of the categories tested significantly was duration of diabetes. If the study did not differentiate between DM type 1, a lifelong disease state, and DM type 2 the results could be unnecessarily skewed.

Applicable findings of other studies mentioned in this paper:

* Depression has a significant association with increased HbA1C levels and diabetes complications.

**Clinton IHS applicability:** The study demonstrated an association of depression with higher BMI and smoking. The author references another source in stating obesity is correlated with the development of DM type 2. Other sources the author references associate depression with an increased risk of developing DM type 2 by two fold and increased adverse cardiac out comes, as well as a decrease adherence to a diabetic diet. This study demonstrates that controlling DM and other disease states is not just simply addressing the particular disease state, but a holistic approach that nurtures patients’ mental health is needed. The IHS could potentially use this study to justifiable allocate funding towards the behavioral health division of the facilities. To the point of implementing an adherence monitoring program, this article is not directly applicable.

1. **Ludman, E., Katon, W., Russo, J., Von Korff, M., Simon, G., Ciechanowski, P., Lin, E., Bush, T., Walker, E., Young, B. “Depression and diabetes symptom burden” *General Hospital Psychiatry,* Vol. 26 (2004): 430-436.**

The objective of the study was to assess whether diabetic symptoms are more common and severe among patients with depressive illnesses. The authors had an expectation of a stronger association between depression and diabetic symptoms than poor glycemic control and diabetes complications.

The first statistical test tested the relationship between the number of diabetic symptoms reported in the presence of major depressive disorder. They found that patients with major depressive disorder had reported significantly more diabetic symptoms than those patients who were not depressed.

The second statistical test tested the relationship between the number of diabetic symptoms reported relative to the number of depressive symptoms reported. They found that all of the diabetic symptoms reported correlated with the number of depressive symptoms reported. Each diabetic symptom category had a higher rate of reporting in patients with more depressive symptoms.

Logistic Regression was used to determine strength of association between diabetic symptoms and presence of major depression, patients with HbA1C levels >8, and patients with two or more diabetic symptoms. They found that elevated HbA1C levels were only correlated with the following diabetic symptoms: polyuria, abnormal thirst, blurred vision, and daytime sleepiness.

Another statistical comparison performed was comparing the percentage of patients reporting each diabetic symptom among persons with versus without diabetic complications. They found that having two or more complications was significantly related to higher rates of all diabetic symptoms reported except hunger.

Referenced notes from other studies:

* Twofold higher rate of depression in persons with diabetes than individuals without diabetes.
* Patients with anxiety and depressive disorders are associated with high rates of medical symptoms reporting and health care seeking.
* Patients with psychological distress also report more medical symptoms and more functional impairment.

**Clinton IHS Application:** If the patient is reporting greater diabetic symptoms due to the comorbid psychiatric state, it would benefit medical treatment facilities to treat the psychiatric disease state as aggressively as it treats the diabetic disease state. If the patients are in a healthier mental state, they are less likely to seek un-needed medical attention. The article quotes another source that demonstrated that depression is associated with increased symptom burden, functional disability, and medical costs related to chronic medical conditions such as diabetes. The Clinton IHS’s highest disease state prevalence is diabetes; the second highest disease state prevalence is depression. To the point of implementing an adherence monitoring program in the Clinton IHS, this article is not applicable.

1. **Hong, T., Oddone, E., Dudley., and Bosworth, H. “Medication barriers and anti-hypertensive medication adherence: The moderating role of locus of control” *Psychology, Health & Medicine,* February 2006; 11(1): 20-28.**

Locus of control is the focus of this study (internal versus external). In this study the role of health locus of control as a moderator in the relationship between medication barriers and medication adherence is evaluated. HTN is one of the most common medicated disease states in the United States by the Veteran Affairs hospitals.

Internal health locus of control refers to the degree that an individual believes their health status is influenced by one’s own behavior. Locus of Control of the patients used in this was based on the Health locus of control scale. The determination of internal locus of control was made by using the following three questions: 1) The main thing which affects my blood pressure is what I myself do, 2) If I take the right actions, I can maintain my blood pressure control, and 3) I have control over lowering my blood pressure. The determination of external locus of control was made with the following three questions: 1) Health professionals control my health, 2) My control of high blood pressure is largely a matter of good fortune, and 3) No matter what I do, I’m likely to have poor blood pressure control.

Regression analyses were used to examine the relationship between internal locus of control and medication barriers were tested against medication adherence. Internal locus and medication barriers effects on adherence were tested and statistical significance was found for both categories. Better adherence was associated with a higher internal locus score and adherence decreased with increasing the patient barriers.

The next item was to observe whether an internal locus of control could help moderate patient barriers. They did this by testing the patients based on high, medium, and low levels of internal locus of control patients. Results are summarized in the following table:

|  |  |  |
| --- | --- | --- |
| Level of Internal Locus of Control | Adherence with Low Level of Medication Barriers | Adherence with High Level of Medication Barriers |
| Low | Lowest | Highest |
| Medium |  |  |
| High | Highest | Lowest |

Note- All internal locus of control groups, regardless of level, was associated with a higher adherence rate than external locus of control groups.

The same test were going to be performed for the external locus of control group, however the internal consistency was lacking. The authors chose to examine each of the three questions individually as moderator. Question 1 from this group was not associated with poorer adherence; questions 1 and 2 were associated with poorer performance. Neither of the two questions that were associated with poorer adherence were also significant moderators between medication barriers and adherence.

Critical Analysis: 98% of the patients participating in the study were male. In a study that is examining personality traits, internal versus external locus, it would be important to have gender equality.

The internal consistency of the external locus of control subgroup was not consistent. This could have been a result of poorly worded questions in the survey; it could be a result of poorly chosen questions, or many other factors. Better methods to capture external locus of control patients will be necessary for future studies.

Reference notes of importance mentioned in the study:

* Medication barriers and anti-hypertensive medication adherence. Only 1/3rd of patients have controlled their blood pressure. 30-60% of patients discontinue their HTN medication within the first year and fewer than 20% remain in therapy after 5 years.
* Patients make choices based on barriers and side effects of medication. Problem with HTN being asymptomatic and the pharmacologic therapy making the patient feel worse than the disease state.
* Barriers to adherence referenced in the article- forgetfulness, beliefs, and patient attitude.
* Perceived barriers might be the most influential.

**Clinton IHS Applicability:** This article could be useful to IHS facilities because the patient pool in this study is similar to the IHS patient pool in that there was a minimum financial burden placed on the patients. The article also focused on a modifiable behavior that can directly affect medication adherence. This is promising because it could potentially mean that a better patient understanding and knowledge about their personal health could have a positive effect on their treatment outcome. Educating patients on the importance of their participation and giving the patient accountability through this process would likely improve patients’ disease state outcome. To the point of implementing an adherence monitoring program, this paper would not be helpful. Once a monitoring program is in place, this paper would be very helpful in developing the most productive provider/patient relationship.

1. **Wing, R., Phelan, S., and Tate, D. “The role of adherence in mediating the relationship between depression and health outcomes” *Journal of Psychosomatic Research* 53 (2002): 877-881.**

The goal of this paper was to explore the relationship between medication adherence and depression. In particular, the authors wanted to explore the possibility of non-adherence causing depression. The authors wanted a better understanding to the well documented poor adherence rates of depressed individuals.

The article discusses following relationships: 1) depressions relationship with adherence, 2) adherence and outcome, and 3) does poor adherence mediate the relationship between the relationship between depression and outcome.

The authors used various studies to explore the relationship between adherence and depression. Many of these studies documented depressed patients having poor adherence compared to non-depressed patients. The authors then used various studies to explore the relationship between adherence and outcome. They found many articles which supported the relationship of poor medication adherence reflected a poorer disease state outcome.

The authors did not find any evidence that non adherence mediated the relationship between depression and outcome.

The authors conclude by stating the correlation between depression symptomology and adherence and giving suggestions for future research to improve the understanding of the relation between the two areas.

Side notes the author references in the article that are relevant to this facility:

* In type 2 diabetes mellitus depressive symptoms were found to be associated with higher cholesterol, triglycerides, and HbA1C
* Increasing exercise is an effective treatment for depression.

**Clinton IHS applicability:** The number one and number two disease state prevalent at the Clinton IHS facility is diabetes mellitus type II and depression. The findings that the authors in this study collected could be used to implement personal trainers and promote healthier lifestyles. To the point of implementing an adherence monitoring program at the IHS facility, the findings

1. **Corrigan, Patrick. “Adherence to anti-psychotic medications and health behavior theories” *Journal of Mental Health* Volume 11, No. 3, (2002): 243-254.**

The authors in this paper attempt to use two factors, value expectancies and social support, from health behavior (HB) theories to explain non adherence to anti-psychotic medication and pose corresponding interventions to ameliorate the problem.

Notes from article:

* Most persons with psychotic disorders benefit from regular administration of anti-psychotic medication.
* More than 40% of persons receiving anti-psychotic medications fail to comply with the regimen.
* Failing to comply with anti-psychotic medications increased re-hospitalization by threefold, accounting for 800 million dollar in hospital cost worldwide.

The author summarizes the Value Expectancy theory by stating that patients are likely to pursue a specific treatment behavior when they believe they suffer symptoms that the treatment will adequately address while not causing undue side effects. The following chart, similar to the one in the article, summarizes remediation directions for value expectancy and adherence barriers due to pyschosis:

|  |  |
| --- | --- |
| ***Adherence Barriers*** | ***Empirically-Validated Strategy to Remedy*** |
| * Lack of Disease Awareness * Cognitive Deficits of the Patient\* * Reactance to Disempowerment | Motivational Interviewing  \*Personal Problem Solving Exercises |
| Medication Side Effects- undermine the perceived value of a medication. Atypical antipsychotics seem to yield less side effects. | |

The author summarizes the Social Support/Action theory by stating that individuals socially relating to persons with psychosis may impede or facilitate adherence to a medication regimen. The following chart, similar to the chart in the article, summarizes remediation directions for inadequate social support for people with living with the disabilities of psychosis:

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| --- | --- |
| ***Adherence Barriers*** | ***Empirically-Validated Strategy to Remedy*** |
| Patient has a poor alliance with healthcare provider. | * Give the patient support from a trained health case manager. * Provide motivational interviewing. |
| Patient with family/friends who do not support medication. | Provide the patients family with motivational interviews. |
| Lack of resources/support to obtain/maintain medication. Patients have trouble acquiring the medication. | * Support from case manager * Working with the patient to solve the problems with obtaining the medication. |
| Insufficient adherence information by the patient or the patient social support group | Obtain refill record from the pharmacy/physician appointment feedback. |

**Clinton IHS Applicability:** A healthcare facility could use this article to justify adding programs that incorporate case managers trained to apply all the aspects of Value Expectancy and Social support to their patients. To the point of implementing an adherence monitoring program, this article is not applicable. After an adherence monitoring program is in place, this article could be used in training case managers/pharmacist in techniques to improve adherence in non adherent patients.

1. **Rubin, B. “What Does It Mean When a Patient Says, “My Asthma Medication Is Not Working”” *Opinions/Hypotheses CHEST,* Volume 126/3 (September 2004): 972-981.**

This article discusses the reasons people report to providers for medication non-adherence and offers suggestions to improve adherence in asthma patients using various inhaled medication. The reasons for non-adherence are categorized into: 1) The patient who does not want to take medication, 2) The patient who does not understand how or when to use medication, 3) The patient who is concerned about medication side effects, 4) The Patient who cannot feel the medication working, 5) the patient with unrealistic expectations, 6) The patient who incorrectly thinks that they are inhaling the medication, 7) The patient who does not really have asthma, and 8)The patient who really needs more medicine.

The patient who does not want to take medication is further subdivided into three categories: 1) I am not really sick, 2) Secondary gain, and 3) Too expensive. The patients that fall under the category one minimize symptoms and often do not understand how the medicine improves lung function long term. Due to high inaccuracies in peak flow monitor recordings in diaries it is hard to determine patient status. Monitored administration may be necessary in these patients. Secondary gain is discussed because in this article because the large portion of children/adolescents that can either gain extra attention or miss school due to the symptoms associated with non-adherence of their asthma medication. The next category of too expensive is not applicable at this facility and therefore will not be discussed any further.

The patient who does not understand how or when to use medication discusses how multiple medications with different delivery devices can exacerbate adherence. This section also discussed how a patient’s inability to comprehend a written medication action plan can exacerbate adherence. This could be due to poor hand writing or poor word choice of the physician in the treatment plan.

The patient who is concerned about medication side effects discusses patients’ perception of medication side effects through various media sources. The article discussed how patients could possibly perceive inhaled corticosteroids as having the same effects as inhaled corticosteroids. Some patients believed that all medications could lead to the same psychological and physiological dependence seen in opioids. The author recommends patient medication education to overcome this non-adherence problem.

The patient that cannot feel the medication working section discusses the false perception of some patients that a new improved dosage form does not work as well due to the lack of negative administration side effects (for example, the negative taste experienced by some inhalers). The patient’s sensory perception of an administered dose may make a difference in a patient’s belief that the medication is effective. An example of this at our facility could be the change from the traditional chlorofluorocarbon (CFC) inhalers to more environmental friendly Respimat inhalers. The CFC inhalers produce a cold sensation during inhalation, the Respimat inhalers do not. The author recommends better patient counseling with clear communication to overcome this problem as well.

The patient who incorrectly thinks they are inhaling medication discusses the amount of patient counseling received by patients on new medications. The article mentions two studies of note. One study stated that 47% of pediatric patients receiving an inhaler did not receive instruction on its usage. The other study stated that inadequate cleaning is associated with a decreased nebulizer output up to 50%. The Center for Disease Control and Prevention recommends cleaning the nebulizer after each use. The article also delves into proper administration techniques associated with nebulizer and inhaler usage to increase medication performance. The article recommends programs that evaluate how patients are using a prescribed device as well as a periodic physician reassessment.

The patient who does not have asthma talks about the misdiagnosis of asthma in pediatrics and how the treatment for the misdiagnosis will not help improve the patient’s medical condition. Once such example is an infant diagnosed with asthma that has a pulmonary viral infection. Many other examples of possible faulty diagnosis are mentioned. The author notes that the younger the child is, the likely hood of a misdiagnosis increases because of a higher frequencies of abnormalities present in younger children.

The patient who really needs more medicine discusses the course of action to determine patients that are compliant with current medications and are still showing a disease state progression. The author recommends first trying to determine if any new allergens have been introduced into the patient’s environment. The author also recommends ruling out other disease states that could cause exacerbations, a respiratory infection for example.

Critical Analyses: This article discusses a particular medication delivery system which makes it less capable of generalization.

**Clinton IHS Applicability:** Combivent has recent changed the delivery device from an inhalation aerosol to an inhalation spray. Some of the reasons stated in the paper for non-adherence, such as the sensory sensation, are likely to be different and this could cause some of the patients to believe it does not work as well. This will be something that our providers need to be aware when counseling the patients on its usage. Explaining to the patient the differences in delivery devices and sensations experienced could prevent patient non-adherence. Most of the advice in the article revolved around enhancing the patients’ disease state/medication knowledge. This article reinforces the positive affects experience by educating patients.

Prepared by Neil Kellogg - Pharmacy JRCOSTEP

Clinton IHS Service Unit – 07/11/2013

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1. **Fariman, K. and Motheral, B. (2000). “Evaluating Medication Adherence: Which Measure is Right For Your Program?” *Journal of Managed Care Pharmacy,* Vol. 6 (No. 6): 499-504.**

The authors used data from published literature to discuss the strengths and limitations of medication-adherence measurement techniques. To evaluate the adherence measurement techniques, the authors pooled data from areas that included biological markers, pill counts, electronic monitoring devices, patient surveys, and prescription claims data. The authors found the best adherence techniques were dependent on factors unique to the facility, the patient, and the medication type. This implies one single approach is generally no better or worse than another. The critical factor was the selection of the proper adherence measurement technique to insure the data results collected were a true representation of patient compliance. This often meant using multiple adherence measurements to adequately measure the multifaceted medication services of each facility.

The paper discusses dataset preparation and the use of claims data as a way to measure compliance. The author defines length of therapy, persistence, days of coverage, and gaps and subsequently explains their role in analyzing medication adherence from pharmacy claims. One noted downfall of using pharmacy claims to measure adherence is that it is not well fit to measure acute adherence.

Critical analysis: the authors not the potential issues of using pharmacy claims to measure adherence when patients venture outside of their network to fill prescriptions. Without a way to account for this, it could potentially show an adherent patient as being non-adherent. With the current patient chart assess from IHS facility to IHS facility, this could be problematic. Having a universal chart IHS chart that was accessible with ease to any facility for the patient would circumvent polypharmacy, keep the treatment consistent, and give the healthcare providers better insight to the patient’s disease state to allow for more educated treatment.

**Clinton IHS Application:** Installing measures to properly monitor patient compliance could be useful to the IHS should it one day decide to install a more involved patient medication adherence policy. Having an adherence system in place that worked to improve patient compliance at a facility has the potential to greatly reduce facility overhead by giving patients better outcomes of their pharmacologic therapy. Selecting the proper system to monitor patient adherence would be vital in trying to determine if the program is working. This article presents factors that should be understood before any adherence monitoring programs are installed.

1. **Dezii, C. “Persistence With Drug Therapy: A Practical Approach Using Administrative Claims Data” *Managed Care,* February 2001: 42-45.**

The author discusses the Estimated Level of Persistence with Therapy (ELPT) approach to patient compliance and persistence. The author claims the ELPT strategy provides an inexpensive and unobtrusive way to determine the extent to which long term care therapy, for chronic disease states, are being filled on a regular basis.

The ELPT approach does not verify administration of the medication; it does how address the availability of the medication. The author states that if a patient cannot regularly pick up their prescription for chronic disease states, then adherence becomes secondary to the medications availability. The ELPT method of determining patient compliance is simply looking at how many refills a patient should have during a given time frame and comparing them to the number of refills the patient actually acquired.

The researchers required patients to be new to therapy for admittance into the study with at least a six month drug free period. They recorded whether the patient was compliant by persistency thresholds, the previously mentioned method, and analyzed the data using patient-persistent curves. The patient-persistent data curves are then used to compare patient persistence to one agent relative to another. The author states that the data can be used monitor specific patient populations, alert physicians to reasons of non-adherence, and possibly aid a physician when face with choosing between different medications of the same pharmacologic category.

Critical Analysis: The researchers in this study allowed ninety day filling window before classifying a patient as non-persistent. By the researcher’s standards this means that if a patient were prescribed a monthly prescription they would only have to fill the prescription one of every four months to be compliant. If the patient did not meet that threshold, they would be classified as not persistent. The researchers would consider a filling percentage of 25% being compliant. Many medications for chronic disease states require medication compliance rates to be much higher. In a study published in JAMA Internal Medicine titled “Self-reported Medication Adherence and Cardiovascular Events in Patients With Stable Coronary Heart Disease: The Heart and Soul Study”,the definition of compliance was an adherence rate of greater than or equal to 75% for patients taking medication for the chronic coronary heart disease. Another fault of this method is that is does not consider patient goal oriented outcomes when determining medication compliance. For example, a common compliance measure in diabetics is to assess the patient’s glycolated hemoglobin (HbA1C). A patient could theoretically go three months without taking their diabetic medications while simultaneously increasing their HbA1C, and still be considered compliant under the thresholds set forth in this study.

**Clinton IHS application:** The ELPT approach could be utilized by IHS facilities to single out medications with relatively high incompliance rates. Once these drugs are singled out, then measures to address the incompliance. This would require the IHS to implement a drug adherence monitoring software that could generate reports of incompliance generated by lack of patient refills. This information could be used to help shape a facility’s formulary by comparing which pharmacologic alternative is being utilized at a higher percentage and subsequently eliminate the lesser utilized/less adherent medication.

1. **LLabre, M., Weaver, K., Duran, R., Antoni, M., McPherson-Baker, S., and Schneiderman, N. “A Measurement Model of Medication Adherence to Highly Active Antiretroviral Therapy and Its Relation to Viral Load in HIV-Positive Adult” *AIDS Patient Care and STDs,* Vol. 20 (November 2006): 701-711.**

The purpose of this study was to test medication adherence measurement model’s ability to predict adherence. The study incorporates multiple measurements of adherence collected over multiple time frames for HIV patients receiving HAART. The authors emphasized the need for a measurement method with this capability was lacking. The authors believe that this second-order factor model of adherence fit could perform this due to its ability to detect errors uniquely, account for more variability, associated with each particular method used to concurrently.

The methods used were a self report questionnaire, an adherence interview item, and electronic medication monitoring through a medication event monitoring system (electronic caps). Single factor models composed of multiple measurement methods were developed for each of the mentioned adherence methods and then were tested for their ability to forecast viral load. The three adherence methods were then combined in a second order factor measurement model, which was also tested for its ability to measure viral load. The models including one method were, at best, able to explain 24% of variability. Second order factor model explained 45% of variability in the viral load.

The patients were assessed and paid at 3 months, and twice again at 6 month intervals. All patients received medication adherence and treatment information during the first three visits. Venous blood samples were collected from participants and viral load was calculated. The results indicated when measuring adherence over time multiple assessments are needed to obtain a reasonable level of reliability.

Critical Analysis: The study design was flawed in that a lack of viral resistance data was obtained at baseline. This is problematic because the purpose of these tests was to see how well these tests tested the ability of adherence measures to predict viral load. If a patient with a specific drug resistant viral strain were given a medication that did not affect the virus, a patient could have taken 100% of his meds and still had an increased viral load because of incompetent medication. This would have likely lowered the predictability of each measurement method utilized in the study.

**Clinton IHS Application:** This article discussed methodology used to determine which adherence measurement strategies were most indicative of the actual results in patients receiving HAART. The outcome combined several tests, each having a unique way to measure medication adherence to account for the overlapping variance, resulted in a measuring methodology that better reflected patient adherence. The application of this article to the IHS is that when installing a medication monitoring program, a single method to measure compliance is not ideal. Also, attaining more measurements equates to more reliable results. However, the results of this study should be taken with caution due to the methodological flaw in the study design of not obtaining viral resistance information at the beginning of the study.

1. **Angell, B. (2006). “Measuring Strategies Used by Mental Health Providers to Encourage Medication Adherence” *Journal of Behavioral Health Services & Research*: 53-72.**

The author wanted to test the Rasch’s measurement model ability to assess an item measure scale’s ability to assess strategies used to promote adherence that vary on a continuum of pressure or social control. The ability to assess adherence strategies would greatly enhance facilities decision to apply a more patient specific strategy with greater confidence as well as rule out strategies that were not as efficate, therefore saving the time and cost associated with a less then optimal strategy. Also, the ability to apply one test to assess the adherence measures with one test in an unidimensional manner would be greatly useful to avoid the ambiguity of looking over multiple tests and trying to come to a meaningful conclusion.

To evaluate the Rasch measurement system’s ability to measure strategies used by clinicians to promote medication adherence, the author choose mental illness patient providers at that worked in assertive community treatment centers and participated in multisite study of treatment pressures and mandates. Patients with severe mental illness have historically poor medication adherence and the risk and cost associated with medication nonadherence can be considerate, thus clinician interventions to insure medication compliance are often warranted. This patient pool is also well fitted for this study because of the various adherence strategies that are commonly applied to persuade medication adherence.

The author found the Rasch method to be acceptable (relative/comparative to Cronbach’s alpha) when adjusting for non-fitting criteria. The author found the Rasch method to be good when revising the test by removing the misfitting items, making it more facility type specific.

Critical Analysis: The authors evaluated the Rasch method ability to recognize adherence strategies used by mental health providers on a one dimensional scale. One of the complications of the test’s ability to test the effectiveness of particular adherence strategies is the ability to the test to separate adherence measures taken that overlap. For example, discussing the benefits of the medication adherence and pointing out the consequences of not taking the medication properly. After adjustments were made to account for redundancy, the authors found the Rasch method was able to significantly predict adherence measures that were efficient. However, removing the unfitting data to make significant results may result in returning to the initial problem the authors sought to overcome. The authors choose to leave in some unfit items that were due to redundancy (overlapping overly fit items), while throwing out unfit items that were due high infit square values (greater than expected randomness). Throwing out the items with high infit while at the same time leaving in items due to redundancy could improve the Rasch test’s ability to detect significance in relationships. The testing groups had different types of facilities whose endpoint corrective measures varied in intensity. Some of the doctors surveyed had the ability to threaten institutionalization (those at assertive community treatment centers) and other highly pressured measured in response to non-adherence where others did not have the same level of reinforcements.

**Clinton IHS Application:** The resulting measure may be employed in future studies to examine the ways in which clinician behavior relates to medication adherence and to consumer perceptions of treatment alliance, quality of care, and perceived coercion. The authors found that the provider’s perception of compliance often correlated with the pressure applied by the provider to encourage medication adherence. IHS does not currently apply any levels of coercion other than counseling the patients on the benefits of adherence and the hazards of non-adherence. Therefore the application of this study to the IHS facilities in an applicative manner is limited. The ability of IHS policy makers to assess articles that used the Rasch’s measurements would be greatly improved by reading this article.

1. **Connor, J., Rafter, N., and Rodgers, A. “Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review” *Bulletin of the World Health Organization* Volume 82, December issue (2004): 935-939.**

In this article the authors objective was to compare adherence of combination therapy (combined oral or unit of use combinations) with the same medication in their usual presentation. They did this by reviewing all randomized controlled trials in which participants were taking more than one self-administered medication, the intervention consisted of the use of a combination therapy, and the study had at least one pharmacological goal of therapy or cost of therapy. The authors found fifteen suitable studies.

The authors concluded by stating that they found few large reliable trials on the effect of combining medications. Seven of thirteen studies reported statistically significant improvements in medication adherence. Out of seven reporting clinical outcomes, four found significant improvement in patients taking combination therapy and these findings were limited by the methodological shortcomings of the studies. The authors found that self-reporting and pill counting measures overestimate adherence and may underestimate the impact of clinical intervention.

Applicable notes from other studies mentioned in the article:

* Simplicity of dosing regimen and side effects of the regimen had the most influence on medication adherence.
* With increase in drug regimen complexity, or the number of treated disease states in a patient, adherence decreases.
* Many trials in this area had sample sizes that were not greatly sensitive. A trial with 150 patients would only be able to detect a difference in two groups of 25% or larger. Reductions less than 25% have been shown to have clinical relevance. In order to detect a change of 15% or greater, a 500 person patient pool is needed.
* Combination medications have the potential to mitigate the under-treatment of cardiovascular disease.
* Combination medications have been shown to reduce the amount of medication waste costs.

**Clinton IHS Applicability:** This research article could be utilized to set an inclusion standard of any study when its substance could be used to make policy decisions. This article also points out the need for better designed studies. Should the IHS decide to conduct a study, this article could help with the frame work of the study. As the authors pointed out, the findings in the studies they reviewed were limited to small sample sizes or design flaws and therefore using the findings of the most of the trials they reviewed is problematic. The article also points out the self report studies often provide inflated adherence reporting. This would further support the need for more than one adherence monitoring method to be in place.

1. **Murray, M., Young, J., Hoke, S., Tu, W., Weiner., Morrow, D., Stroupe, K., Wu, J., Clark, D., Smith, F., Dradus-Pizlo, I., Weinberger, M., and Brater, C. “Pharmacist Intervention to Improve Medication Adherence in Heart Failure” *Annals of Internal Medicine,* Vol. 146 No. 10 (May 2007): 714-725.**

The purpose of this trial was to evaluate the effect of a pharmacist intervention on patients who are socioeconomically disadvantaged and medically vulnerable. The hypothesis was that pharmacist intervention would result in improved adherence to heart failure medication, reduce exacerbations require emergency room visits or hospitalizations, improve disease-specific quality of life, increase patient satisfaction, and reduce healthcare cost.

The trial was randomized and was twelve months in duration. The groups were divided into two: those who received intervention from pharmacists and those who only spoke with technicians. Patients in the intervention groups received the intervention techniques for the first nine months of the period. Patients in the intervention group were encouraged to visit or call the pharmacist regarding their medications. Pharmacist intervened by using Pharmacist Intervention Protocol table (available at [www.annals.org](http://www.annals.org)). Adherence was measured by electronic monitors and clinical exacerbations that required a hospital visit.

The study showed that patients who received intervention had a higher adherence rate of 78.8% compared to the 67.9% in the control group during the intervention period. After the intervention period, first nine months of participation, there was no significant difference in the group’s medication adherence percentage. The intervention group also reported a statistically higher refill adherence rate. The intervention group had 19.4% fewer exacerbations/hospital visits than the control group. Overall patient satisfaction was statistically significant and greater in the intervention group as well.

The direct cost of implementing this program was $205 dollars/patient. The cost per patient comparison was not statistically significant. The authors accredit this to the large variability in costs for healthcare. The authors report $14 dollar for every dollar spent on the investment.

Critical Analysis: The intervening pharmacist in this study were trained by an interdisciplinary team that would make them specialized. A pharmacist with this expanded training would likely make the study less generalizable due to the uniquely high level of training received by them would separate them professional from the general practice standard that is available at most facilities and experienced by the everyday patient.

The use of Medication Event Monitoring Systems prescription container lids (MEMS lids) could have a reinforcing effect on adherence; this could skew the results to a higher adherence rate in both the control group and the intervention group when compared to the general population. For multiple daily dosing, the MEMS lids recorded non-adherence if the patient did not take the dose within a 1.2 hour window of the previous day’s dose. This could skew the results toward non-adherence.

**Clinton IHS Applicability:** The study groups are relatable to the ISH facility patients in that they had no financial burden for adherence. The cost of medication was not a deterrent to adherence.

* The Pharmacist Intervention Protocol could be utilized at any facility that has a pharmacy practice.
* The researchers in this study used *Statistical Analysis System (SAS)* to perform statistical analysis. This software could be utilized by the IHS to perform statistical analysis of adherence programs it might implement.
* The study demonstrated that more intense intervention by pharmacist showed a statistical improvement in medication adherence. T
* The study also demonstrated the need for ongoing patient medication counseling, as after the intervention was halted the adherence rate of the two groups was not significantly different. This would imply that intervention for chronic medication is an ongoing process that justifies ongoing patient counseling efforts throughout the medication duration.

1. **Piette, J., and Heisler, M. (2004). “Cost-Related Medication Underuse Among Critically Ill Adults: the Treatments People Forgo, How Often, and Who Is at Risk.” American Journal of Public Health Vol. 94, No. 10. 1782-1787.**

The authors sought to gather information about the cost-related underuse of medications. Groups of chronically ill patients that fell into one of sixteen chronically ill designations were used in the trial. The researchers used a large pool of subjects from broad socioeconomic backgrounds to allow them to ascertain any potential differences between these groups. The study focuses on two primary aspects with potential relations to medication underuse: 1) the relationship among global measures of cost-related medication adherence, and 2) variation in the importance of socioeconomic risk factors for underuse across treatment types.

The study showed as the out of pocket cost for the patient increased; the more likely the patient was to display drug underutilization. The study did not find any significant difference of medication cost-underuse due to race, gender, and education attainment. The study did find significant relationship with out of pocket costs and respondents income with cost-related underuse.

**Clinton IHS Applicability:** The main focus of this study, cost cutting measures patients take to cope with the financial pressures of out of pocket medication cost, is not applicable to IHS patients. In the discussion section of the paper the author suggests that depending on the treatment types, treatment adherence varied due to many factors and that it was not solely based on out of pocket expense. Some patients were willing to forgo their medications at low out of pocket expense while others with high out of pocket expense were compliant with certain medications. ***This would suggest that patient perception of the importance of the pharmacologic therapy is a significant factor in patient compliance.*** This in turn stresses the need for quality patient education and counseling over their medications.

1. **Katon, W., Simon, G., Korff, M., Ludman, E., Ciechanowski, P., Walker, E., Russo, J., Bush, T., Lin, E., and Young, B. “Behavioral and Clinical Factors Associated With Depression Among Individuals With Diabetes” *Diabetes Care,* Volume 27, Number 4 (April 2004): 914-920.**

The goal of the study was to determine: 1) Are behavioral factors that increase the risk of developing diabetes are more likely to be present in depressed patients versus non depressed patients, 2) Do patients with adverse clinical side effects of diabetes complications have an increased likelihood of meeting the criteria for depression, and 3) do characteristics associated with age and sex influence whether a person is classified as depressed or not.

The study found:

*Major Depression:*

* Major depression was significantly more likely to occur in younger, female, and the unmarried.
* Patients that fell into the major depression group had a significantly higher occurrence of:
  + Co morbidities,
  + Diabetic complications,
  + Higher HbA1C levels,
  + Obesity,
  + Smoking,
  + Insulin usage,
  + Longer treatment periods.
* For individuals < 65 years old, there is a strong relationship between major depression and HbA1C levels.
* Younger patients (<65 years old) had significantly higher HbA1C levels than older patients.
* The relationship between DM complications and major depression was significant for men only. Male patients with major depression had almost twice the rate of have two or more complications.

*Minor Depression:*

* Patients were younger, less educated, more likely to be non-Caucasian, have BMI>30 kg/m2, to smoke, and to have longer duration of diabetes than those patients with diabetes only.
* Minor depression in patients > 65 years old is associated with the patient having more DM type 2 complications.

Critical Analysis: The study did not separate type 1 diabetes mellitus (DM) patients from type 2 patients. This is a problem because the consequence of non adherence for a DM type 1 patient presents with a direr acute outcome then the often asymptomatic symptoms of DM type 2. The physical characteristics of a DM type 1 patient are often drastically different from DM type 2 patients, in particular the obesity occurrence rate in DM type 2 patients. These differences could present enough social stigma differences to introduce enough variability between the two DM groups to make the two groups incomparable in a study measuring depression.

Co morbidities were determined using Rx Risk, which based medical co morbidities on the prior 12 months prescription drug use. This presents a problem of accuracy if the patient utilized multiple pharmacies. Another problem with this program is the current co morbidity could have been a diagnosis prior to the DM type 2 diagnosis. Claiming this as a complication of DM could demonstrate a stronger relationship than is actually present. Also the study did not seek to find if and underlying condition led to the patient developing the co morbidities that commonly occur with DM and depression. One of the categories tested significantly was duration of diabetes. If the study did not differentiate between DM type 1, a lifelong disease state, and DM type 2 the results could be unnecessarily skewed.

Applicable findings of other studies mentioned in this paper:

* Depression has a significant association with increased HbA1C levels and diabetes complications.

**Clinton IHS applicability:** The study demonstrated an association of depression with higher BMI and smoking. The author references another source in stating obesity is correlated with the development of DM type 2. Other sources the author references associate depression with an increased risk of developing DM type 2 by two fold and increased adverse cardiac out comes, as well as a decrease adherence to a diabetic diet. This study demonstrates that controlling DM and other disease states is not just simply addressing the particular disease state, but a holistic approach that nurtures patients’ mental health is needed. The IHS could potentially use this study to justifiable allocate funding towards the behavioral health division of the facilities. To the point of implementing an adherence monitoring program, this article is not directly applicable.

1. **Ludman, E., Katon, W., Russo, J., Von Korff, M., Simon, G., Ciechanowski, P., Lin, E., Bush, T., Walker, E., Young, B. “Depression and diabetes symptom burden” *General Hospital Psychiatry,* Vol. 26 (2004): 430-436.**

The objective of the study was to assess whether diabetic symptoms are more common and severe among patients with depressive illnesses. The authors had an expectation of a stronger association between depression and diabetic symptoms than poor glycemic control and diabetes complications.

The first statistical test tested the relationship between the number of diabetic symptoms reported in the presence of major depressive disorder. They found that patients with major depressive disorder had reported significantly more diabetic symptoms than those patients who were not depressed.

The second statistical test tested the relationship between the number of diabetic symptoms reported relative to the number of depressive symptoms reported. They found that all of the diabetic symptoms reported correlated with the number of depressive symptoms reported. Each diabetic symptom category had a higher rate of reporting in patients with more depressive symptoms.

Logistic Regression was used to determine strength of association between diabetic symptoms and presence of major depression, patients with HbA1C levels >8, and patients with two or more diabetic symptoms. They found that elevated HbA1C levels were only correlated with the following diabetic symptoms: polyuria, abnormal thirst, blurred vision, and daytime sleepiness.

Another statistical comparison performed was comparing the percentage of patients reporting each diabetic symptom among persons with versus without diabetic complications. They found that having two or more complications was significantly related to higher rates of all diabetic symptoms reported except hunger.

Referenced notes from other studies:

* Twofold higher rate of depression in persons with diabetes than individuals without diabetes.
* Patients with anxiety and depressive disorders are associated with high rates of medical symptoms reporting and health care seeking.
* Patients with psychological distress also report more medical symptoms and more functional impairment.

**Clinton IHS Application:** If the patient is reporting greater diabetic symptoms due to the comorbid psychiatric state, it would benefit medical treatment facilities to treat the psychiatric disease state as aggressively as it treats the diabetic disease state. If the patients are in a healthier mental state, they are less likely to seek un-needed medical attention. The article quotes another source that demonstrated that depression is associated with increased symptom burden, functional disability, and medical costs related to chronic medical conditions such as diabetes. The Clinton IHS’s highest disease state prevalence is diabetes; the second highest disease state prevalence is depression. To the point of implementing an adherence monitoring program in the Clinton IHS, this article is not applicable.

1. **Hong, T., Oddone, E., Dudley., and Bosworth, H. “Medication barriers and anti-hypertensive medication adherence: The moderating role of locus of control” *Psychology, Health & Medicine,* February 2006; 11(1): 20-28.**

Locus of control is the focus of this study (internal versus external). In this study the role of health locus of control as a moderator in the relationship between medication barriers and medication adherence is evaluated. HTN is one of the most common medicated disease states in the United States by the Veteran Affairs hospitals.

Internal health locus of control refers to the degree that an individual believes their health status is influenced by one’s own behavior. Locus of Control of the patients used in this was based on the Health locus of control scale. The determination of internal locus of control was made by using the following three questions: 1) The main thing which affects my blood pressure is what I myself do, 2) If I take the right actions, I can maintain my blood pressure control, and 3) I have control over lowering my blood pressure. The determination of external locus of control was made with the following three questions: 1) Health professionals control my health, 2) My control of high blood pressure is largely a matter of good fortune, and 3) No matter what I do, I’m likely to have poor blood pressure control.

Regression analyses were used to examine the relationship between internal locus of control and medication barriers were tested against medication adherence. Internal locus and medication barriers effects on adherence were tested and statistical significance was found for both categories. Better adherence was associated with a higher internal locus score and adherence decreased with increasing the patient barriers.

The next item was to observe whether an internal locus of control could help moderate patient barriers. They did this by testing the patients based on high, medium, and low levels of internal locus of control patients. Results are summarized in the following table:

|  |  |  |
| --- | --- | --- |
| Level of Internal Locus of Control | Adherence with Low Level of Medication Barriers | Adherence with High Level of Medication Barriers |
| Low | Lowest | Highest |
| Medium |  |  |
| High | Highest | Lowest |

Note- All internal locus of control groups, regardless of level, was associated with a higher adherence rate than external locus of control groups.

The same test were going to be performed for the external locus of control group, however the internal consistency was lacking. The authors chose to examine each of the three questions individually as moderator. Question 1 from this group was not associated with poorer adherence; questions 1 and 2 were associated with poorer performance. Neither of the two questions that were associated with poorer adherence were also significant moderators between medication barriers and adherence.

Critical Analysis: 98% of the patients participating in the study were male. In a study that is examining personality traits, internal versus external locus, it would be important to have gender equality.

The internal consistency of the external locus of control subgroup was not consistent. This could have been a result of poorly worded questions in the survey; it could be a result of poorly chosen questions, or many other factors. Better methods to capture external locus of control patients will be necessary for future studies.

Reference notes of importance mentioned in the study:

* Medication barriers and anti-hypertensive medication adherence. Only 1/3rd of patients have controlled their blood pressure. 30-60% of patients discontinue their HTN medication within the first year and fewer than 20% remain in therapy after 5 years.
* Patients make choices based on barriers and side effects of medication. Problem with HTN being asymptomatic and the pharmacologic therapy making the patient feel worse than the disease state.
* Barriers to adherence referenced in the article- forgetfulness, beliefs, and patient attitude.
* Perceived barriers might be the most influential.

**Clinton IHS Applicability:** This article could be useful to IHS facilities because the patient pool in this study is similar to the IHS patient pool in that there was a minimum financial burden placed on the patients. The article also focused on a modifiable behavior that can directly affect medication adherence. This is promising because it could potentially mean that a better patient understanding and knowledge about their personal health could have a positive effect on their treatment outcome. Educating patients on the importance of their participation and giving the patient accountability through this process would likely improve patients’ disease state outcome. To the point of implementing an adherence monitoring program, this paper would not be helpful. Once a monitoring program is in place, this paper would be very helpful in developing the most productive provider/patient relationship.

1. **Wing, R., Phelan, S., and Tate, D. “The role of adherence in mediating the relationship between depression and health outcomes” *Journal of Psychosomatic Research* 53 (2002): 877-881.**

The goal of this paper was to explore the relationship between medication adherence and depression. In particular, the authors wanted to explore the possibility of non-adherence causing depression. The authors wanted a better understanding to the well documented poor adherence rates of depressed individuals.

The article discusses following relationships: 1) depressions relationship with adherence, 2) adherence and outcome, and 3) does poor adherence mediate the relationship between the relationship between depression and outcome.

The authors used various studies to explore the relationship between adherence and depression. Many of these studies documented depressed patients having poor adherence compared to non-depressed patients. The authors then used various studies to explore the relationship between adherence and outcome. They found many articles which supported the relationship of poor medication adherence reflected a poorer disease state outcome.

The authors did not find any evidence that non adherence mediated the relationship between depression and outcome.

The authors conclude by stating the correlation between depression symptomology and adherence and giving suggestions for future research to improve the understanding of the relation between the two areas.

Side notes the author references in the article that are relevant to this facility:

* In type 2 diabetes mellitus depressive symptoms were found to be associated with higher cholesterol, triglycerides, and HbA1C
* Increasing exercise is an effective treatment for depression.

**Clinton IHS applicability:** The number one and number two disease state prevalent at the Clinton IHS facility is diabetes mellitus type II and depression. The findings that the authors in this study collected could be used to implement personal trainers and promote healthier lifestyles. To the point of implementing an adherence monitoring program at the IHS facility, the findings

1. **Corrigan, Patrick. “Adherence to anti-psychotic medications and health behavior theories” *Journal of Mental Health* Volume 11, No. 3, (2002): 243-254.**

The authors in this paper attempt to use two factors, value expectancies and social support, from health behavior (HB) theories to explain non adherence to anti-psychotic medication and pose corresponding interventions to ameliorate the problem.

Notes from article:

* Most persons with psychotic disorders benefit from regular administration of anti-psychotic medication.
* More than 40% of persons receiving anti-psychotic medications fail to comply with the regimen.
* Failing to comply with anti-psychotic medications increased re-hospitalization by threefold, accounting for 800 million dollar in hospital cost worldwide.

The author summarizes the Value Expectancy theory by stating that patients are likely to pursue a specific treatment behavior when they believe they suffer symptoms that the treatment will adequately address while not causing undue side effects. The following chart, similar to the one in the article, summarizes remediation directions for value expectancy and adherence barriers due to pyschosis:

|  |  |
| --- | --- |
| ***Adherence Barriers*** | ***Empirically-Validated Strategy to Remedy*** |
| * Lack of Disease Awareness * Cognitive Deficits of the Patient\* * Reactance to Disempowerment | Motivational Interviewing  \*Personal Problem Solving Exercises |
| Medication Side Effects- undermine the perceived value of a medication. Atypical antipsychotics seem to yield less side effects. | |

The author summarizes the Social Support/Action theory by stating that individuals socially relating to persons with psychosis may impede or facilitate adherence to a medication regimen. The following chart, similar to the chart in the article, summarizes remediation directions for inadequate social support for people with living with the disabilities of psychosis:

|  |  |
| --- | --- |
| ***Adherence Barriers*** | ***Empirically-Validated Strategy to Remedy*** |
| Patient has a poor alliance with healthcare provider. | * Give the patient support from a trained health case manager. * Provide motivational interviewing. |
| Patient with family/friends who do not support medication. | Provide the patients family with motivational interviews. |
| Lack of resources/support to obtain/maintain medication. Patients have trouble acquiring the medication. | * Support from case manager * Working with the patient to solve the problems with obtaining the medication. |
| Insufficient adherence information by the patient or the patient social support group | Obtain refill record from the pharmacy/physician appointment feedback. |

**Clinton IHS Applicability:** A healthcare facility could use this article to justify adding programs that incorporate case managers trained to apply all the aspects of Value Expectancy and Social support to their patients. To the point of implementing an adherence monitoring program, this article is not applicable. After an adherence monitoring program is in place, this article could be used in training case managers/pharmacist in techniques to improve adherence in non adherent patients.

1. **Gryglewska, Barbara. “How can we improve the effectiveness of treatment in elderly hypertensives?” *Blood Pressure* Volume 14 (Suppl 2) (2005): 46-49.**

In this article the author points out only a small number of elderly are treated to goal levels and inconsistencies in treatments, general poor patient adherence, as well as the side effects of anti hypertensive (HTN) drugs as the culprits. The author states that the rate of dissemination of development of recommendations and their implementations in practice is far too slow. The need for a complex and consistent effective strategy to disseminate this information to treat hypertension in elderly that can be utilized by physicians is a focal point of this article. The author discusses several studies that have achieved remarkable results in hypertensive patients.

**CLINTON IHS APPLICABILITY: Studies Referenced and their key findings:**

**ALLHAT (Antihypertensive & Lipid Lowering Treatment to Prevent Heart Attack):** In this study 86% of patients were treated to a goal blood pressure and maintain the blood pressure for over 3 years.

**HOT (Hypertensive Optimal Treatment):** In this study compliance to antihypertensive medication rose from a baseline of 27.4% to 66% five years later.

**EISBERG project:** 90% of uncontrolled HTN patients have uncontrolled systolic blood pressure, where only 50% have uncontrolled diastolic blood pressure. Diastolic blood pressure was more controlled than systolic.

**Do we need drug therapy to manage mild hypertension in the elderly?:** the results of this demonstrated no benefit in treating elderly patients with mild hypertension.

**The rationale for combination versus single-entity therapy in hypertension:** Combining lower doses of antihypertensive drugs with different mechanisms of action, complimentary to each other, provides efficacy with slight side effects as opposed to high doses of single agents.

**Evaluation of computer based clinical decision support system and risk chart for management of hypertension in primary care:** Adequate hypertension guidelines awareness is rather modest even in specialist.

**Physician-pharmacist comanagement of hypertension:** Confirmed blood pressure control improvement and reduction of average visit costs per patient.

**What you need to know about home blood pressure telemonitoring:** Home blood pressure measurements are very useful to increase patient participation in medical care.Telecommunication could be a convenient way to keep in contact with the patient.

1. **Rubin, B. “What Does It Mean When a Patient Says, “My Asthma Medication Is Not Working”” *Opinions/Hypotheses CHEST,* Volume 126/3 (September 2004): 972-981.**

This article discusses the reasons people report to providers for medication non-adherence and offers suggestions to improve adherence in asthma patients using various inhaled medication. The reasons for non-adherence are categorized into: 1) The patient who does not want to take medication, 2) The patient who does not understand how or when to use medication, 3) The patient who is concerned about medication side effects, 4) The Patient who cannot feel the medication working, 5) the patient with unrealistic expectations, 6) The patient who incorrectly thinks that they are inhaling the medication, 7) The patient who does not really have asthma, and 8)The patient who really needs more medicine.

The patient who does not want to take medication is further subdivided into three categories: 1) I am not really sick, 2) Secondary gain, and 3) Too expensive. The patients that fall under the category one minimize symptoms and often do not understand how the medicine improves lung function long term. Due to high inaccuracies in peak flow monitor recordings in diaries it is hard to determine patient status. Monitored administration may be necessary in these patients. Secondary gain is discussed because in this article because the large portion of children/adolescents that can either gain extra attention or miss school due to the symptoms associated with non-adherence of their asthma medication. The next category of too expensive is not applicable at this facility and therefore will not be discussed any further.

The patient who does not understand how or when to use medication discusses how multiple medications with different delivery devices can exacerbate adherence. This section also discussed how a patient’s inability to comprehend a written medication action plan can exacerbate adherence. This could be due to poor hand writing or poor word choice of the physician in the treatment plan.

The patient who is concerned about medication side effects discusses patients’ perception of medication side effects through various media sources. The article discussed how patients could possibly perceive inhaled corticosteroids as having the same effects as inhaled corticosteroids. Some patients believed that all medications could lead to the same psychological and physiological dependence seen in opioids. The author recommends patient medication education to overcome this non-adherence problem.

The patient that cannot feel the medication working section discusses the false perception of some patients that a new improved dosage form does not work as well due to the lack of negative administration side effects (for example, the negative taste experienced by some inhalers). The patient’s sensory perception of an administered dose may make a difference in a patient’s belief that the medication is effective. An example of this at our facility could be the change from the traditional chlorofluorocarbon (CFC) inhalers to more environmental friendly Respimat inhalers. The CFC inhalers produce a cold sensation during inhalation, the Respimat inhalers do not. The author recommends better patient counseling with clear communication to overcome this problem as well.

The patient who incorrectly thinks they are inhaling medication discusses the amount of patient counseling received by patients on new medications. The article mentions two studies of note. One study stated that 47% of pediatric patients receiving an inhaler did not receive instruction on its usage. The other study stated that inadequate cleaning is associated with a decreased nebulizer output up to 50%. The Center for Disease Control and Prevention recommends cleaning the nebulizer after each use. The article also delves into proper administration techniques associated with nebulizer and inhaler usage to increase medication performance. The article recommends programs that evaluate how patients are using a prescribed device as well as a periodic physician reassessment.

The patient who does not have asthma talks about the misdiagnosis of asthma in pediatrics and how the treatment for the misdiagnosis will not help improve the patient’s medical condition. Once such example is an infant diagnosed with asthma that has a pulmonary viral infection. Many other examples of possible faulty diagnosis are mentioned. The author notes that the younger the child is, the likely hood of a misdiagnosis increases because of a higher frequencies of abnormalities present in younger children.

The patient who really needs more medicine discusses the course of action to determine patients that are compliant with current medications and are still showing a disease state progression. The author recommends first trying to determine if any new allergens have been introduced into the patient’s environment. The author also recommends ruling out other disease states that could cause exacerbations, a respiratory infection for example.

Critical Analyses: This article discusses a particular medication delivery system which makes it less capable of generalization.

**Clinton IHS Applicability:** Combivent has recent changed the delivery device from an inhalation aerosol to an inhalation spray. Some of the reasons stated in the paper for non-adherence, such as the sensory sensation, are likely to be different and this could cause some of the patients to believe it does not work as well. This will be something that our providers need to be aware when counseling the patients on its usage. Explaining to the patient the differences in delivery devices and sensations experienced could prevent patient non-adherence. Most of the advice in the article revolved around enhancing the patients’ disease state/medication knowledge. This article reinforces the positive affects experience by educating patients.

1. **Ruoff, G. “A method that dramatically improves patient adherence to depression treatment” *The Journal of Family Practice,* Vol. 54, No. 6 (2005): 846-851.**

The author implemented a treatment flow sheet for patients that were depressed or had depressive symptoms to 15 family physicians practices in the Midwest region of the United States. The author’s goal was to show increased patient adherence through the use of the flow sheet.

Diagnostically depressed patients were first asked to complete a self-administered 9-item diagnostic survey to confirm the severity of depressive symptoms in patients. Subsequently, the physicians participating in the study implemented the flow sheet in the patient’s chart. The patients’ charts were audited throughout the study to record adherence and non-adherence and the reason for the latter. The flow sheet treatment duration of nine months reflected the National Institute of Health Mental Health’s current guidelines for the treatment of depression.

The flow sheet, for the qualified patients, first gave the patients information about the disease state and the importance of the nine month duration, as well as an initial adherence education by the attending physician. Each patient was encouraged to schedule follow up appointments at four weeks, four to nine months, and at one year. The purpose of the follow up appointments was to stress the importance of continuing the treatment for the full nine month duration. Patients that did not make their scheduled appointments were contacted by nurse, at which point they scheduled an appointment, they then confirmed that they were still on the regimen, or had discontinued their medication.

The author claimed in the study that the use of the depression flow sheet, in conjunction with suitable instructions to both physicians and patients, lead to better patient adherence and therefore alleviation of depressive symptoms regardless of outcomes. The author claims a patient adherence rate of 66%, doubling that from the national database he used as a comparison. The author attributes the apparent success of the flow sheet to not only the frequent patient reminders, but also to the physician reminders.

Critical Analysis: The study did not have a control. The author used data gathered from an article titled “Discontinuation of use and switching of anti-depressants: Influence of patient-physician communication” as the control group for his study groups statistical comparison. The study had outcome directed study design and lacked a null hypothesis as a result of not having a control. The author stated in the Method section of the paper that no exclusion criteria were applied. However, the Patient Health Questionnaire that the patients in the study filled out did include exclusion criteria. Therefore trying to determine if the author used exclusion criteria is ambiguous. The author did not include age, gender, and race stratification. Race is important- studies have shown that non-white patients are less likely to adhere to pharmacologic treatment for depression according to an article by Brown, Schulberg, Sacco, Perel, and Houck titled “Effectiveness of Treatment for Major Depression in Primary Medical Care Practice: A Post Hoc Analysis of Outcomes for African Americans and White Patients”. The paper stated that demographics were included periodically through the study period and stated that the stratified data show significant improvements in patient compliance across the demographic board when compared to the national averages. The author did not provide these statistics.

**IHS Application:** The ability to implement applications of this study is greatly weakened by the poor design of the study. A takeaway from the study that is applicable to any healthcare facility is a better understanding and ownership/accountability of role responsibilities of all the parties involved in patient medication adherence. Patient medication compliance does not rest solely on the patient’s shoulders, and it is also a duty of healthcare providers to remain persistent in reinforcing the importance of medication compliance. If providers fail to communicate effectively the importance of the patient’s medication, the patient is less likely to understand the importance of taking their medications as instructed. Currently the IHS only counsels new prescriptions. Implementing periodic counseling sessions after the initial counseling session on the importance of medication adherence, for patients taking medications chronically, would be positive step towards improved patient medication compliance.

1. **Steiner, J., Koepsell, T., Fihn, S., and Inui, T. “A Generalized Method of Compliance Assessment Using Centralized Pharmacy Records” *Medical Care,* Vol. 26 No. 8 (August 1988): 814-823.**

This study demonstrates a general method of adherence measurement which, the authors claim, can incorporate changes in drugs or dosages, variable refill intervals, and regimens with multiple medications. Adherence was based on the amount of medication received over a set period of time relative to the amount of medication that should had been received if the patient were completely adherent. The study used to classes of patients with definitive physiologic measures to test medication adherence against. The use of phenytoin levels in an anticonvulsant group to measure compliance, and the diastolic blood pressure measurements in a hypertensive group.

The authors found a correlation between the patients that were adherent by their statistical model and phenytoin levels. The authors reported a lower diastolic blood pressure with better compliance according to their statistical model, although the finding was not statistically significant.

Critical Analysis: The authors’ method of recording compliance does not account for legitimate gaps in medication therapy, such as hospitalization. Another problem with the authors’ method is the rigidity of the time scale. It is simply defined as number of days prescribed divided by the number of days elapsed. If a patient’s medication schedule is put off track by a hospital stay in which the hospital supplied the patient medication, the patient will be late on every refill thereafter regardless of their actual compliance rates. In this method this will reflect as periods of non-adherence, even if the patient is completely compliant. The sample sizes for the groups were not optimal for the test to have much statistical power. Using blood pressure as a definitive measure of compliance is problematic. If a patient develops tolerance to a particular medication, even if the patient is completely compliant, a blood pressure measurement alone would indicate otherwise. Phenytoin is a [CYP3A4](http://en.wikipedia.org/wiki/CYP3A4) and [CYP2C19](http://en.wikipedia.org/wiki/CYP2C19) families of the [P450](http://en.wikipedia.org/wiki/P450) enzyme, and therefore its plasma concentration could be easily affected by a number of medications (prescribed or over the counter). Since this study does not take into account possible drug interactions, the possibility of a patient starting a new medication and it altering the plasma concentration is there.

**IHS Applicability:** The method used by these authors to test adherence versus physiologic outcomes was flawed by the external measures the authors choose to compare their model against. The use of phenytoin levels to measure compliance is problematic because the number of drug interactions that can alter phenytoin levels and monitoring is only performed once a year. The blood pressure group did not show statistical significance, so that group would lean towards the statistical method not working. This test would need to be repeated with more definitive physiologic measures of compliance, such as diabetic HbA1C levels, to determine if it is a reasonable application the IHS facilities.

1. **Dezii, C., “A Retrospective Study of Persistence With Single-Pill Combination Therapy Vs. Concurrent Two-Pill Therapy In Patients With Hypertension” *Managed Care (Suppl),* Volume 9(9) (September 2000): S2-S6.**

The author sought out to discover if single pill combination products would lead to better compliance than multi-pill combinations of the same drugs in hypertensive patients. He sought to do this by comparing newly diagnosed patients receiving combination (lisinopril or enalapril + hydrochlorothiazide (HCTZ)) pill therapy versus patients that with a known diagnosis who were currently taking linsinopril or enalapril and HCTZ as individual doses. The author found that the groups with the combination pill therapy demonstrated a statistically significant higher rate of compliance. The author only compared compliance rates; no disease state markers were tested.

**Critical Analyses:** The author works for BMS, a company that currently has four combination drugs. This is problematic because BMS would benefit from results stating that combination products are superior to multiple single doses.

The study was retrospective; this would allow the author to hand pick studies that could potentially used to formulate favorable results. Another problem with retrospective studies is the control of variables across different studies. All studies are not equal and to compare two equally is not always conducive to finding reliable results that can be generalized.

The author compared newly diagnosed patients receiving combination (lisinopril or enalapril + hydrochlorothiazide (HCTZ)) pill therapy versus patients that with a known diagnosis who were currently taking linsinopril or enalapril and HCTZ as individual doses. This is problematic because the patients were at different stages of the disease and the dynamics of each stage would make the two patient pools unequal and therefore incomparable to the point of discerning any useful information.

IHS applicability: I do not believe the information presented in this article should be generalized due to the inherent flaws of the study design. There are multiple studies demonstrating the inverse relationship of medication adherence and the number of medications that are prescribed. In lieu of the inherent flaws, this study is redundant in its efforts to show taking fewer medications per day will lead to better adherence.

1. **Goicoechea, M., Best, B., Seefried, E., Wagner, G., Capparelli, E., and Haubrich, R. “Failure of Modified Directly Observed Therapy Combined with Therapeutic Drug Monitoring to Enhance Antiretroviral Adherence in a Patient with Major Depression” *Aids Patient Care and STDs* Volume 20, No. 4 (2006): 233-237.**

The authors of this article sought to report the findings of short course of modified directly observed therapy (mDOT) combined with therapeutic drug monitoring (TDM) as an adherence intervention. The authors sought to explore some of the short comings of mDOT and TDM by writing a case report on a 43 year old woman with severe depression and persistent virologic failure. The study found that even with mDOT and TDM adherence waned after time.

References from the article:

* Patients suffering from depressive symptoms are at risk for medication non adherence and treatment failure.
* Increasing depressive symptoms are associated with decreased medication adherence.

**Critical Analysis- Clinton IHS Applicability:** The study is not applicable to the Clinton IHS facility due to the following reasons: 1) the facility does not currently have any patients on antiretroviral therapy, 2) the facility does not perform mDOT or TDM current, and 3) the article is a case study over a single individual and is hard to generalize. Not only are the findings of this study statistically inadequate, the health care provided to this patient is unrealistically impractical to provide in any ordinary health care setting.

1. **Wagner, G., and Rabkin, J. “Measuring medication adherence: are missed doses reported more accurately than perfect adherence?”**

The authors’ goal was to compare self reported adherence versus a microelectronic cap reported dosing with the goal of exploring the reliability of self reporting. The regimen used was similar to a highly active antiretroviral therapy.

The study found that self reporting adherence in the self reporting was found to be 20-25% higher than what was measured by the electronic monitoring. They reported that self report is not more accurate in people that report missed doses than in those that report perfect adherence, although the finding was statistically insignificant.

Critical Analysis: The patient pool in this study was too small to have much power statistically, 30 patients. The patient pool was did not have a patient pool that was representative of the general population: the patients were predominantly male, non-white, and most had a history of drug abuse. Patients participating in this study were informed that they were taking a placebo when they entered the study. Another weakness of the test is the duration of two weeks. Most studies on adherence are tested on patients that are taking medications chronically. Therefore generalizing the finding of this self report study to self reports in studies that lasted, in some cases, years, is not justifiable.

**IHS applicability:** This study should not be generalized due it being statistically insignificant. A test with an adequate testing group size and an appropriate duration is needed. The information found by such a test would be very useful to any clinics monitoring adherence through self reporting.

1. **Hosek, S., Harper, G., and Domanico, R. “Predictors of medication adherence among HIV-infected youth” *Psychology, Health & Medicine,* Vol. 10(2) (May 2005): 166-179.**

The goal of this study was to better understand adherence among HIV infected youth. The patients were given a Time-Line Follow-Back to determine medication adherence, which used a temporal ordering cue to help participants piece together their adherence rates over the two weeks prior to the interview. An adherence percentage rate was calculated based on those two weeks. The patients were given a AIDS Clinical Trial Group Adherence Follow-up Questionnaire to examine the reasons for missing medications over the previous month. The patients’ cognitive ability was assessed by using an abbreviated version of the Arlin Test of Formal Reasoning, a vocabulary test, and a Block Design test. Negative affective states were tested by the Center for Epidemiological Studies Depression Scale, a State-Trait Anxiety Inventory, and the Beck Hopelessness Scale. Substance use was tested by the Addiction Severity Index.

The most common reasons reported for not taking antiretroviral medications among HIV infected youth were the side effects, inconvenience of regimen, and constant reminder of disease state. This study explored the negative affect, cognitive function, and substance abuse effects on medication adherence.

Depression and anxiety, negative affective states, have been associated with medication non-adherence in a range of illnesses. In this study patients that reported hopelessness about their disease state also reported difficulties with taking their medications. Affective responses affect drug adherence. The statistical results did not show significance in the correlation between depression/anxiety and medication adherence.

The adherence and cognitive function statistical correlation results did not show any significant relationship. The adherence and substance abuse statistical correlation did not show any significant results.

Critical Anaylsis: The sample size was far too small to draw any statistically significant conclusions from the results. The patient’s comprehension was based on a single interviewer’s interpretation over a one hour interview. Drawing conclusions from the interpretation of a single interviewer whose attention span, receptivity, body language, and mood could fluctuate from patient to patient for various reasons outside reasons not necessarily associated with the interview could be problematic as well. The Time-Line Follow-Back method of determining adherence is problematic. Relying on patients’ memory to recall a missed/taken dosage is likely to produce results is probably not the most accurate method to determine adherence. Studies have demonstrated this method tends to overestimate compliance. Studies have also shown that using multiple compliance measures would result in more accurate results. Adding a pill count would have over the same time frame would have better enforced the reported adherence rates.

Substance abuse was only test by the Addiction Severity Index, a survey. Having urine analysis performed could have been a measure taken to better assess the accuracy of drug abuse reporting.

The average number of medications per day was six. Making an inclusion criteria based on the type of HIV therapy, for example Highly Active Antiretroviral Therapy which requires a three drug regimen, would have been a measure to ensure the difficulty of maintaining treatment was equal across patients.

**IHS Applicability:** Due to the lack of statistically significant findings and the small sample size, this article is not applicable to the IHS facilities. A test with a larger patient pool and a more selective inclusion criterion could be beneficial to the IHS. One of the paper’s focal point was the issue of non-adherence creating drug resistant HIV strains. This is not a huge issue in our local clinics; not having proper medication adherence can create medication resistant bacterial strains as well so the subject of non-adherence is applicable.

1. **Russell, C., Conn, Vicki., and Jantarakupt, P. “Older Adult Medication Compliance: Integrated Review of Randomized Controlled Trials” *American Journal Of Health Behavior,* 2006;30(6):636-650.**

The authors used a compilation of 57 randomized controlled trials that examined interventions and outcomes of medication compliance studies in older adults. The intention of the study was to conduct an integrated review of these trials to improve older adult medication compliance. Compared to the control groups, 54% of these articles found greater medication compliance in the subjects.

This integrative review included studies whose subjects were sixty years of age or older. The data collected covered study designed, intervention techniques, and outcome data. The primary reason for exclusion of a study was a lack of the study having a control group. The authors used software that is designed to connect relational associations that proceed or connect to a central point to combine the data to formulate the results. Most studies did not include the ethnicity and the medical diagnosis of the subjects in the studies.

The dominant themes that the software detected for intervention are summarized in the following schematic:

|  |  |  |  |
| --- | --- | --- | --- |
| **Dominant Themes** | | | |
| **Cues and Organizers** | **Self Medication Programs** | **Dosing Frequency** | **Counseling and Education** |
| **Cues: 11 studies:** Reminders (calling daily to remind, etc) to take and refill medications  **Organizers:**  pillboxes unit dosing, and calendar packing.  **Finding:**  55% of the treatment groups scored better than the controls. | **Fewest: 2 studies.**  These involved clinical pharmacist and nurses that started a patient on the program prior to discharge from the hospital. Patients were put on a progressively independent regimen and then tested for compliance 10 days after discharge. | **Few: 3 studies.**  All studies in this group found that the treatment group scored better than the control.  -This group examined once daily, twice daily, and three times daily dosing.  **Finding:**  All treatment groups scored better than the control groups when the dosing frequency was lowered. | **Most common: 41 studies**  Gives: When, why, and how to take medication. Gives common side effects and places emphasis on adherence.  -Further divided into intervention duration and interventionist used.  **Intervention Duration:**  Brief (<3days in length, 56% of studies reported in this group), Extensive (>3days in length, 41% of the studies), Not Stated. (Number of days in which interventions were delivered)  **Interventionist Used:**  Clinical Pharmacists, Other Health Care Provider, None Stated  **Finding:**  The authors choose to only use 16 of the 41 articles; these were the articles that measured compliance immediately after completion of intervention. Only seven found a significant effect. The authors also found that the more days until between the end of intervention and the assessment, the more often a statistical significance was reported. They also found that extensive treatment did not significantly differ from studies that did not significantly improve compliance. |

Four of the articles used in this integrated review examined gender roles and found no significant difference between males and females in medication compliance.

Reports used often provided little details about intervention activities, so diverse activities used fall under counseling and education. Counseling and education intervention were often combined with other strategies and rarely used alone. The duration of the counseling and education sessions was not recorded; this would have been a nice indicator of quality of the counseling session. There was a wide variation in the outcome assessment in these studies (from 0 days -2 years). These variations often lead to significant differences in the review.

The authors claim that this review will help improve medication compliance in older adults and stated that this review was more extensive than the existing reviews because it included more diverse studies. They then proceeded to talk about the shortcomings of the study and suggested changes in the research field that need to happen. One factor they mentioned is that studies are increasing each year and assessment of the quality of studies is not on the same pace. They also recognized problems with methodological practicalities (I.e. large variations in samples sizes, widely diverse medication compliance measures used in the studies, each study not providing a theoretical foundation, not reporting the patient diagnosis, etc.) to make these studies more comparable to each other.

**IHS Applicability:** The study did not have a uniform standard of compliance, and the only exclusion used was the lack of a control group. This is a problem because some studies have relative lenient compliance thresholds, were others can be relatively strict. Therefore, without consistent standards of compliance throughout the research field drawing a conclusion from data with consistency issues is problematic. For instance, a study with lenient standards might label a patient compliant were as a more stringent study design would not. Therefore trying to draw usable conclusions from this would be nearly impossible. The authors also used unpublished studies which could possibly weaken the results further. The applicability of the results of this study to the IHS facilities is limited because of the author recognized limitations of the results. A possible take away from this article is that a standard methodology that can be widely used and produce statistically compatible results is direly needed and before policy decisions based on these types of papers should be produced.

1. **Hill, Z., Kendall, C., and Fernandez, M. “Patterns of Adherence to Antiretrovirals: Why Adherence Has No Simple Measure” *AIDS Patient Care and STDs,* Vol. 17 (November 2003): 499-504.**

In HIV patients, medication adherence is crucial because of the ability of a virus to rapidly mutate and develop resistant strains if even a few doses are missed. Although several factors have been associated with poor adherence, no consistent predictors of non-adherence have been provided. The authors indicate one possible explanation to the lack of consistent predictors is that many adherence studies use incomparable measures of adherence. There are several tools to measure patient adherence, but most studies classify the patient as adherers or non-adherers. This general classification without distinguishing it further makes it difficult to ascertain, this study takes into account the definition of adherence and the different patterns of adherence. Without the ability to understand patterns or predictors of adherence it would be difficult to devise effective interventions.

The authors used data gathered during interviews with patients attending and HIV Clinic in New Orleans, Louisiana, to whom combination therapy had been prescribed to explore adherence patterns and explanations of antiretroviral therapies from the patient’s perspective. More specifically these interviews explored the patients’ beliefs about consequences of non-adherence, their current and past adherence behavior, and contextual issues. The data collected from these interviews was analyzed using dtSearch 5.0 and distinct patterns of adherence during emerged. The analysis then focused on identifying patterns of adherence and exploring patients’ perception of non-adherence consequences.

The authors found that the respondents in the study perceived that different patterns of non-adherence had different health consequences, some being more severe than others. For example, most respondents viewed going long periods of a time without taking medication as worse than taking self reduce the dose of their medication or skipping doses.

The article stated that the level of the patient understanding seemed to be linked with the type of relationship the patient had with their provider. Although most patients felt they had a good relationship with their provider, providers that worked with patients to devise a care planned seemed to fare better in educating patients on the importance of adherence than those who simply gave instructions and re-enforced non-adherence consequences.

Patients usually viewed the consequences of non-adherence as simply causing side effects rather than adherence being an important function of the medication. The authors found that the respondents that rarely took their medication or went long periods between taking medication were the patients having difficulty accepting their disease state. Acceptance and the attitude the patient had toward the disease were significant to the patient’s medication adherence.

Critical Analysis: Interviews were performed by two different people and were in an open-ended and semi-structured format. Open ended interviews could vary from interview to interview, and be problematic if one would like to repeat the study. Also, in open ended interviews the interviewer could willingly or subconsciously fish for information that fit what they believe to be the reasons for non-adherence. The data collected in this study was taken from only one clinic with a small patient pool. Making applicable generalities at this point is problematic.

The authors sought out a solution to non-comparable studies. In doing so they contributed to the problem. The interview format was open and likely varied from patient to patient. While this approach will give a more patient specific approach, I do not believe it can be duplicated in its current format on more broad bases.

**IHS Application:** The authors found that a patient’s perceived importance of medication adherence had a direct effect on medication adherence. This reinforces the value of quality counseling and communication between the providers and the patient to properly educate the patient on the necessity of the pharmacologic intervention as well as the importance of medication adherence. If the patient is adequately educated through provider interaction, medication adherence will likely be enhanced. However, due to the small sample size this study is not should not be generalized.

1. **Osterberg, L., and Blaschke, T. “Adherence to Medication” *The New England Journal of Medicine* Volume 353 (5) (2005): 487-497.**

The authors gathered various studies to discuss various issues of medication adherence. The following were topics of discussion included in the article: measurement of adherence, epidemiology of medication-taking behavior, identifying poor adherence, barriers to adherence, interventions, and examples of challenges to adherence.

Important notes from study:

* Pill counts are not a good measure of compliance.
* Rate of refilling prescriptions have been shown to be an accurate method to monitor compliance in closed system pharmacy.
* Electronic adherence measuring devices are the most accurate. They still have downfalls, and are costly. They are best when used in research programs.
* Patients generally improve their medication taking behavior 5 days before and after an appointment with a healthcare provider. White Coat Adherence.
* Simple dosing, one dose per day versus two, improves compliance. Adherence is inversely proportional to frequency of dose. Lantus versus Levemir.
* Race, sex, and socioeconomic status have not been consistently linked with poor adherence. Therefore, the most practical way to identify poor adherence is to ask the patient in a non-judgmental way if they have been taking their medication.
* The most common reason a dose is missed is forgetfulness.
* Two applicable barriers to adherence relevant to IHS facilities mentioned in this article are: 1) using a restrictive formulary, and 2) switching to a different formulary.
* Four categorical ways to improve compliance the study noted from various other studies: 1) patient education, 2) improved dosing schedule, 3) increased clinical hours, and 4) creating shorter clinical wait times.
* Adherence is enhanced when patients are involved in their medical plan. Authoritative attitudes should be avoided by the healthcare providers.
* To improve adherence in hypertensive drugs that are concentration dependent the physician should choose the drug with the longest half life to allow more flexibility to the dosing regimen. Some class examples are calcium channel blockers, angiotension-converting enzymes inhibitors, angiotensin II type 1 receptor antagonist, alpha blockers, and direct vasodilators.
* Newer antidepressant drugs and antipsychotic agents have fewer side effects than older medications which, consequently, resulted in higher adherence rates.
* Cues, such as pill boxes and sending reminder messages to the patients through cell phones and other media devices, are helpful in getting patients maintain compliance with their regimen.

**IHS applicability:** Incorporating software that monitors rate of refilling prescriptions to measure adherence has been shown to be an accurate in a closed system pharmacy. Should the IHS facilities implement an adherence monitoring program, refill monitoring software would be ideal.

The recent switch of the Clinton IHS facility made from Lantus to Levemir as a cost saving measure could be problematic in that it will negatively affect adherence, according to this study. Adherence negatively in two ways: 1) many patients will have to go to a once a day dose to a two dose regimen, and 2) switching compliant patients to a drug that they are unfamiliar with could possibly discourage the patient, causing further incompliance. Possibly switching patients who went from once a day dosing with Lantus to twice a day dosing with Levemir would be a step to take to mitigate the cost of Lantus and limit the adherence issues with Levemir.

Newer antidepressant drugs and antipsychotic agents result in higher compliance rates. This is applicable because the current agents utilized by the Clinton IHS could be considered older agents. The adherence of depressed patients is poor, and the poor adherence is not specific to their antidepressant drugs alone. In a facility where diabetes mellitus is the number one disease state and depression is the number two, it would behoove the facility to move to antidepressant agents with fewer side effects and thus improve compliance in patients’ entire medication regimen.

1. **Morgan, Thomas. (2001). “The Economic Impact of Wasted prescription Medication in an Outpatient Population of Older Adults.” The Journal of Family Practice Vol. 50, No. 9: 779-781.**

The author, MD from Dartmoth Medical School’s Department of Community and Family Medicine, used collected data from 73 New Hampshire retirement communities to assess the occurrence, costs, and reasons for medication waste in a population of adults greater than or equal to 65 years old. All of the patients in the study had full prescription benefits without any out of pocket charges. The study showed that increasing age correlated with an increase in drug waste. The most frequently wasted medications in the study were antibiotics, benzodiazepines, and antihypertensives. Many of the wasted medication reported were medications that were taking episodically versus chronically. The patients’ perspective of usefulness/efficacy of the medication accounted for more than half of the waste cost. If the patient did not view the medication as being of importance, they were less likely to take the medication.

Critical Analysis: The authors recognized that the study size was probably too small to make any generalizations that could be implemented in practice.

**IHS Application:** The paper demonstrated that the most frequently wasted medications were medications that were taken episodically, with the exception of antihypertensives. While benzodiazepines, antidepressants, and antihypertensives accounted for 1/3rd of the total cost waste in this study. The study also found that smaller prescriptions that require multiple pharmacy visits are not effective in cost reducing measures. Research on optimal prescribing quantities would benefit the IHS.

The next highest percentage of medication waste occurred as a result of the patient’s perceived ineffectiveness of the drugs. All the subjects in this study had their medications completely covered, the patients had no out of pocket cost. This mirrors the situation of the patients that receive care from the IHS facilities across the country. Perceived effectiveness of the pharmacologic treatment is an area in which the health care providers can take some accountability. This stresses the need for quality counseling sessions to ensure the patients have an adequate understanding of their disease state and the importance of medication adherence. Ensuring patient understanding and adherence would likely produce better patient outcomes while potentially saving money in overhead cost due to improved disease states in patients.

1. **Heisler, M., Wagner, T., and Piette, J. (2004). “Patient Strategies to Cope With High Prescription Medication Costs: Who is Cutting Back on Necessities, Increasing Debt, or Underusing Medications?” *Journal of Behavioral Medicine,* Vol. 28, No. 1: 43-51.**

The authors sought out coping mechanism strategies for the financial burden imposed by medication costs other than coping by medication underuse, they term it “cutting back.” They also wanted ascertain whether patients coping with the cost of medications use many coping strategies or just a single primary coping strategy. The researchers used survey that recorded the frequency at which the patients responded to medication cost by cutting back on necessities (Ie-food and utilities), or increasing debt to attain medications, or restricting medication use or any combination of these methods. The socio-demographic and clinical characteristics of the subjects in the study were also collected to determine if these were contributable.

The study found that 31% of all patients involved used one of the previously mention strategies to cope with their medication costs. 22% of the subjects reported cutting back on necessities, 16% reported increasing their financial debt, and 18% report cost related medication underuse. The study also found that women were more likely than men to use to use one of the cut back strategies. Non-white participants were twice as likely to use a non-medication restrictive coping strategy. Lower household income subjects more frequently utilized the coping strategies. However, the study found that regardless of income, the subjects were more likely to use one of the strategies if the out of pocket cost exceeded 100 dollars. Conversely, the majority of patients regardless of income did not utilize any of the coping strategies.

Among patients that reported using the coping strategies the most common coping strategies used were cutting necessities and increasing debt. The research found that the 65 and older group was more likely to cut necessities or increase debt while restricting medication usage. The 65 and older group was also less likely to pursue all three coping strategies when compared to their younger counterparts. Having a household income of less than 20,000 dollars a year and an out of pocket fee of 100 dollars or greater were associated with greater odds of pursuing each of the three coping strategies. Monthly out of pocket fees of 100 dollars or more meant an eightfold increase in using one of the coping strategies when compare to the less than 50 dollar per month out of pocket group.

The study found that 15% of patients that did not report cost related medications restrictions also reporting using a coping strategy. This is a potential under appreciation of the negative impact of medication cost demonstrated in this study.

**IHS application:** This study’s focus was on the coping mechanisms people on chronic medication utilize to deal with the cost of acquiring the medication. Patients that utilize IHS facilities do not have direct out of cost expenses for chronic disease state prescriptions. The only out of cost fees IHS patients incur are for over the counter medications that might be needed. Due to the acute nature of most disease states that are treated with over the counter medications, this does not seem to be a significant cost relative to the cost represented in this study.

A potential area of cost that an IHS patient might incur is the lost of generated income from missing work to go to the health clinic. This loss of work hours would likely only occur during a new diagnosis situation as refills can be attained at no cost via the IHS mailing system. However, this was not a focus of the study and therefore it would be inappropriate to speculate how this might affect patient compliance.

1. **Slack, M., McEwen, M., Carter, J., and Brueckner, R. “Case management delivery model for pharmacy” *American Journal of Health-System Pharmacy* Volume 53 (December 1996): 2860-2867.**

In this article the author identifies key characteristics and components of case management, explains the difference between the case management delivery model and pharmacy delivery model, describes why case management is an important delivery model in managed care, and discusses the implications of case management on pharmacists.

The author states, that regardless of a specific model, the goal of case management is to identify and deliver services so that the care provided is appropriate for a particular patient so that an optimal response is seen. The important characteristics of case management the author discusses in the article are appropriateness, collaboration, consultation, prevention, and outcomes. Components of case management are: 1) procedures for identifying appropriate case management, 2) a comprehensive patient assessment procedure, 3) a problem list, 4) care plan based from the problem list, 5) implementation of the plan, and 6) evaluations and intervention.

Criteria for patient admission into case management include, but are not limited to, social, psychological, and environmental factors. Assessment is a multifactorial (health status, emotional status, cognitive ability, functional level, home environment, the patient’s perspective of treatment, etc.) process that occurs after a patient is found to be in need of case management and its purpose is to provide the means for adapting health care interventions to the needs of the patient. After an assessment is made, a problem list and care plan should be developed in collaboration with the patient. The next step is implementing the plan, which is crucial and dependent on the case manager. Evaluation documents the assessment, problem list, and care plan.

The author suggest pharmacist take a case manager/consultant role in case management in delivery model care. This could include pharmacists acting as case managers and pharmacist as consultants to case managers. The author states the importance of marketing to promote a pharmacists ability to be a case manager. The stated purpose of case management model is to prevent poor medication management. A pharmacist in the role of case management would have the knowledge to proactively suggest regimen changes to the physicians.

**IHS applicability/critical analysis:** Mainly, the paper is just not applicable to IHS facilities because the amount of individual care that is given to patients, that have a case manager, is not practical or affordable in a clinical setting without case workers. The article suggests that pharmacist assume the role of case manager in the clinical setting. This would mean the pharmacist would need to cover the essential components of case management. This means the development of a problem list and a care plan by pharmacists. The doctors at the IHS are currently the only health care team members allowed to do this at the facility, major policy changes would be necessary to implement the suggestions made by the author of this article. Another problem is the author talks of pharmacist in the role of case managers in retail pharmacy settings. While the theory of a pharmacist in the retail setting is promising, the reality of hectic pace of a retail pharmacy would not be conducive to case management in that environment.

1. **Blazer, D., Moody-Ayers, S., Craft-Morgan., and Bruchett, B. “Depression in diabetes and obesity Racial/ethnic/gender issues in older adults” *Journal of Psychosomatic Research*, 53 (2002): 913-916.**

The purpose of this study was to explore the risk for comorbid depression/diabetes and depression/higher BMI by race, gender, and various control variables relationships. To do this the research team conducted three in person interviews and telephone follow ups over the following data: age, gender, race, marital status, education, urban versus rural residence, presence of arthritis, health status, cognitive status, depressive symptomology and functional status. These traits were then tested for correlation with diabetes.

The authors claim that factors associated with the comorbid condition of depression and diabetes are the following: younger age, female gender, lower education, and functional impairment resulting from diabetes. The frequency of comorbidity for both conditions combined was approximately 5% and the authors state these patients should be considered at an increased risk for adverse health outcomes. They assume that the functional and cognitive impairment are the result of the comorbid conditions of depression and diabetes.

Critical Analysis: The question to determine if a person was diabetic was “Have you ever been told by a doctor, nurse, therapist or medical assistant that you had diabetes or sugar in the urine or high blood pressure?”. This line of questioning could lead to a patient pool of diabetics and hypertensives. This could inflate the amount of diabetic subjects reported by the study and possible weaken claims made from the statistical results of the study.

In “An odd measure of risk: use and misuse of the odds ratio”, the author found that 26% of articles that use odds ratios incorrectly interpret the results as a risk ratio equivalent [1]. The authors of this article appear to have committed this error. However, I am no statistician.

**CLINTON IHS APPLICABILITY: The healthcare providers can use this study to take preemptive measures to better control comorbid conditions in diabetic patients.**

Prepared by Liz Peters - Pharmacy JRCOSTEP

Clinton IHS Service Unit - 6/15/2012

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1. Martin, Michelle Y., et al. "Taking Less Than Prescribed: Medication Nonadherence and Provider-

Patient Relationships in Lower-Income, Rural Minority Adults With Hypertension." *Journal of Clinical Hypertension* 12 (Sept. 2010): 706-713. Print.

This study looked at reasons for medication nonadherence in African American, lower-income, rural adults receiving medications at no personal cost. The most frequently endorsed reasons for taking less medication than prescribed were not having blood pressure medicine when it was time to take a dose (36%), running out of medicine (35%), bothered by side effects (29%), and a change in one’s daily routine (27%). Nonadherent individuals were significantly more likely to report discomfort with asking the health provider questions (74% vs 63%), were more likely to report that health care visits were stressful (25% vs 16%), and exhibited more depressive symptoms (58% vs 45%).

Suggestions for improvement:

* Health care providers should routinely explore barriers to medication adherence, including reasons that are primarily logistical or emotional.
* Minimize the stressful aspect of appointments and make them more conducive to patients having information needs met. (Despite the fact that almost all patients believed their providers cared about them as individuals and found it easy to talk with their providers, almost 70% were uncomfortable asking questions.)
* Allocating time in appointments for questions
* Providing patients with question prompt sheets
* Acknowledge patients who successfully manage their medication-taking behavior and high BP in spite of difficult life circumstances

1. Bell, Ronny A., et al. "Depressive Symptoms and Diabetes Self-Management among Rural Older

Adults." *Am J Health Behav.* 34.1 (2010): 36–44. Print.

Data from 696 rural older African Americans, American Indians and whites were used to assess depressive symptoms (modified CES-D) and diabetes self-management (physical activity, blood glucose self-monitoring, self foot checks, following a healthful eating plan, and medication adherence). Participation in the study involved a 1.5 hour face-to-face interview. Older adults with diabetes and depression are less likely to adhere to self management, increasing their risk of complications. Race was not as important of an indicator for adherence as age and depression in this study.

Health care provider recommendation is the most significant correlate of blood glucose self monitoring in this population. Thus, more aggressive assessment and encouragement by health care providers to self-monitor among those dealing with depression is warranted. Efforts to improve physical activity and dietary adherence could be encouraged by the management team, such as participation in exercise sessions in group settings (eg, churches and senior centers) or education of caregivers and health care providers regarding the importance of dietary adherence and physical activity.

1. Le, Tao T., et al. "Do Asthma Medication Beliefs Mediate the Relationship Between Minority Status

and Adherence to Therapy?" *Journal of Asthma* 45 (2008): 33–37. Print.

86 adults with asthma on inhaled corticosteroid therapy completed surveys regarding selected beliefs about asthma medications. Medication adherence for 1 month was electronically measured. Adherence was significantly lower among the primarily inner-city African-American minority patients (29% vs. 51% for Caucasians, *p <*.001) and women (31% vs. 42% for men, *p* = *.*05). Multiple negative asthma medication beliefs were associated with lower adherence (*p*’s *<* .05). Minorities had a 7-fold adjusted odds of having a high negative medication beliefs score. African-Americans have been noted to have more fear of ICS, higher depression scores, and lower ICS knowledge scores. In addition, there are racial and ethnic disparities in regards to healthcare access.

Survey Questions Asked: (0 = strongly disagree; 4 = strongly agree):

1. “I have not needed to take as much of my inhaled steroid as the doctor prescribed.”

2. “My inhaled steroid is safe to use every day, even when I’m not having problems.”

3. “If I use my inhaled steroid every day, it won’t work as well when I really need it.”

4. “I don’t like the idea of using an inhaled steroid medicine.”

5. “Using an inhaled steroid every single day may cause longterm side effects and problems.”

1. Piette, John D., et al. "Beliefs about Prescription Medications among Patients with Diabetes:.

"*Journal of Health Care for the Poor and Underserved* 21 (Feb. 2010): 349-361. Print.

806 African American and White diabetes patients were surveyed about their beliefs regarding medications, cost-related adherence problems, socioeconomic status and communication about treatments with their clinicians.

Nearly twice as many African Americans agreed that “people who take prescription medications should stop their treatments for a while every now and again” (20% vs. 11%, p5.0005), substantially more African American than White patients agreed that most prescription medications are addictive (40% vs. 28%, p5.0003), and more African American than White patients agreed that prescription medications do more harm than good (25% vs. 17%, p5.003). Racial differences in patients’ beliefs about their medications were particularly pronounced with respect to the efficacy and safety of generic drugs. For example, nearly three times as many African American patients as White patients agreed that generic medications contain dangerous additives (21% vs. 8%, p,.0001). African Americans expressed more negative attitudes than White patients and were more likely than White patients to report cost-related medication underuse (19% versus 13%; p5.02). Some African Americans perceive racial discrimination in their health care and may be more likely than White patients to mistrust their providers.

1. Schoenberg, Nancy E., et al. "Diabetes Self-care among a Multiethnic Sample of Older Adults." *J*

*Cross Cult Gerontol* 23 (2008): 361–376. Print.

This study had 80 diabetes patients that were African-American, Native American, Mexican American, or rural dwellers. Half of Mexican American participants, 20% of African Americans, 15% of Native Americans, and 15% of rural Whites had used unconventional treatments at some point, including herbal remedies (15% of total sample), dietary remedies (9%), and teas, spiritual interventions, and other approaches (5% each). Most participants (68%) indicated that their physician or other allopathic health care provider (nurse, pharmacist) was their primary source for diabetes information. Other primary sources of information included media (25% of overall sample); friends and family (4%) and other or common sense (3%). Participants revealed a considerable commitment to certain conventional diabetes self-care practices (medication taking and, to a lesser degree, diet and foot care) with less commitment to checking blood sugar and exercise.

Themes:

* Respect for the authority of the physician
* Although medications and medical devices were provided, some patients had a hard time affording test strips or healthy food
* Living in a resource strapped environment elicited stress and eroded optimal self-care

1. Rothman, Russell L., et al. "Self-Management Behaviors, Racial Disparities, and Glycemic Control Among Adolescents With Type 2 Diabetes." *Pediatrics* 121.4 (2008): 912-919. Print.

Adolescents with T2DM are often faced with the new diagnosis of a chronic disease at the exact same time they are transitioning from dependent relationships to autonomy. This study was conducted via telephone interviews on 103 adolescents with Type 2 Diabetes.

Nonwhite patients had higher glycated hemoglobin and hospitalizations per year compared with white patients. In multivariable analyses, nonwhite race remained significantly associated with higher glycated hemoglobin even after adjusting for age, gender, BMI, insurance status, and other factors. Nonwhite patients were more likely to watch ≥2 hours of television per day (78% vs 56%), to report exercising ≤1 time per week (35% vs 21%), and to drink ≥1 sugary drink daily (27% vs 13%).

Previous studies have stated that minority children may not have the family support, financial resources, or access needed to participate in rigorous exercise programs or to eat healthily. Another possible explanation for disparities in glycemic control could relate to physiologic differences, because previous studies have suggested that nonwhites may have higher insulin resistance, which may contribute to their worse glycemic control.

1. Duru, O. Kenrik, et al. "Identifying Risk Factors for Racial Disparities in Diabetes Outcomes - The

Translating Research Into Action for Diabetes Study." *Medical Care* 47.6 (2009): 700-706. Print.

In this case-control study, 764 blacks and whites with diabetes were studied. Versus whites, blacks with diabetes have poorer control of hemoglobin A1c (HbA1c), higher systolic blood pressure (SBP), and higher low-density lipoprotein (LDL) cholesterol as well as higher rates of morbidity and microvascular complications. This study found that depression and missing medication doses are more strongly associated with poor diabetes control among blacks than in whites. These 2 risk factors may represent important targets for patient-level interventions to address racial disparities in diabetes outcomes. They did not find evidence to support hypotheses that running out of medications, low self-efficacy for reducing cardiovascular risk, or poor provider communication skills was disproportionately associated with inadequate control for blacks.

1. Fernandez, Senaida, et al. "A Senior Center–Based Pilot Trial of the Effect of Lifestyle Intervention on

Blood Pressure in Minority Elderly People with Hypertension." *JAGS* 56.10 (2008): 1860–1866. Print.

This study involved therapeutic lifestyle classes with 65 primarily African-American seniors with hypertension in New York City. Minority older adults may particularly benefit from interventions targeting lifestyle factors, because they may underestimate the importance of these factors in controlling BP. For example, recent data suggest that older African-American and Latino adults are more likely than their Caucasian peers to think that medications are the only way to treat HTN. This senior center–based lifestyle intervention was associated with a significant reduction in SBP and adherence to prescribed antihypertensive medications and diet in the intervention group.

Examples of the class set-up: 6 classes and 2 booster classes

* Week 1 education about HTN and overview of therapeutic lifestyle changes;
* Week 2 education about antihypertensive medications & strategies for promoting adherence;
* Weeks 3 and 4 information on the DASH diet, training in reading food labels, & food monitoring;
* Week 5 promoting and increasing physical activity and training in physical activity monitoring;
* Week 6 review of previous sessions and wrap-up;
* Monthly Boosters 1 & 2 progress in adopting and maintaining TLC & problem solving for barriers

1. Babamoto, Kenneth S., et al. "Improving Diabetes Care and Health Measures Among Hispanics Using

Community Health Workers: Results From a Randomized Controlled Trial." *Health Educ Behav* 36 (2009): 113-126. Print.

189 Hispanic patients newly diagnosed with type 2 diabetes were randomly assigned to one of three 6-month diabetes management approaches—Community Health Workers (CHW), case management, and standard provider care—and assessed for diabetes-related health measures and clinical indicators at baseline and postintervention. Participants in the CHW group achieved greater improvements than did the controls in program measures: health status, emergency department utilization, dietary habits, physical activity, and medication adherence. They also had 2.9 times greater odds of decreasing body mass index.

As members residing within the community, CHWs have a greater understanding and knowledge of the local cultural values, such as health beliefs and behaviors, access issues to health services, social and environmental influences, and language barriers. Besides having an understanding of community life, CHWs can provide additional assistance in retention and follow-up, helping patients to appropriately engage and utilize the health care system and local community resources, thus resulting in informed, activated patients and family members. Health care professionals can support CHWs by establishing specific roles and responsibilities for CHWs within clinics, ensuring adequate CHW training, and continuing to provide medical management of diabetes patients.

1. Cooper, Lisa A, et al. "A randomized controlled trial of interventions to enhance patient-physician

partnership, patient adherence and high blood pressure control among ethnic minorities and poor persons: study protocol NCT00123045 ." *Implementation Science* 4.7 (2009): n. pag. Print.

This study was unusual in that I could not find the results mentioned. It mainly represented a detailed methodology that a study could use in providing care for minorities. The study proposed a patient-centered, culturally tailored, education and activation intervention for patients with active follow-up delivered by a community health worker in the clinic. It also included a computerized, self-study communication skills training program for physicians, delivered via an interactive CD-ROM, with tailored feedback to address their individual communication skills needs.

They propose the use of multifaceted (educational, behavioral, and affective) intervention approaches, incorporating culturally and linguistically appropriate methods tailored to individuals' needs (*e.g*., the use of community health workers as interventionists to address common cultural beliefs and practices, the development of a participatory photonovel that is engaging and user-friendly) to support the therapeutic partnership from both the patient and physician perspective.

1. Manias, Elizabeth, and Allison Williams. "Medication Adherence in People of Culturally and

Linguistically Diverse Backgrounds: A Meta-Analysis." *The Annals of Pharmacotherapy* 44 (June 2010): 964-982. Print.

Studies included in this meta-analysis used interventions that were either multifaceted programs, testing the role of education in combination with psychosocial or behavioral initiatives, or provider-directed strategies such as the implementation of medication reviews. Methods of delivery included pictorial instructions, handouts, DVDs, medication timer devices, telephone contacts, home visits, and group and individual discussion sessions.

The study concludes that relatively little high-quality work has been conducted on adherence-enhancing interventions for people of culturally and linguistically diverse (CALD) backgrounds. Greater attention needs to be given to examining the needs of specific CALD population groups.

1. Adams, Alyce S., et al. "Medication Adherence and Racial Differences in A1C Control." *Diabetes Care*

31.5 (2008): 916-921. Print.

This was a retrospective, longitudinal study involving 1,806 black and white patients. Although blacks typically had lower adherence rates and higher A1cs, there were racial differences found in A1C that could not be explained by differences in medication adherence. These findings suggest that targeting medication adherence alone is unlikely to reduce disparities in glycemic control in this setting. Further research is needed to explore possible genetic and environmental determinants of higher A1C among blacks at diagnosis, which may represent a critical period for more intensive intervention.

1. B., Peeters, et al. "Factors associated with medication adherence to oral hypoglycaemic agents in

different ethnic groups suffering from Type 2 diabetes: a systematic literature review and suggestions for further research." *Diabetic Medicine* 28 (2011): 262-275. Print.

This article could be useful if we wanted to design a research project on this topic. Thirteen databases were searched and 1201 articles were screened for this review article. It discussed several methodological challenges with respect to measuring medication adherence, measuring ethnicity and study designs that need to be resolved to make future studies comparable.

1. Medication Adherence: WHO Cares?
2. Using Arrays to Calculate Medication Utilization
3. Ingredients of Successful Interventions to Improve Medication Adherence
4. Trouble Getting Started: Predictors of Primary Medication Nonadherence
5. Psychosocial Considerations in the Management of Diabetes

Brown M, Bussell J. Medication adherence: WHO cares?. Mayo Clinic Proceedings. Mayo Clinic [serial online]. April 2011;86(4):304-314.

This article was written with the aim of reviewing factors associated with medication adherence in the treatment of chronic illnesses and to provide strategies and resources for improving medication adherence in patients. As part of their methods, a MEDLINE database literature search was conducted resulting in 127 articles published between January 1, 1990 and March 31, 2010 with specified search terms included in the abstract. The following search terms were used for the literature search: *cardiovascular disease, health literacy, medication adherence, and pharmacotherapy*.   
Cardiovascular disease was chosen due to the amount of data available regarding medication adherence in CVD, and the approximation of adherence via the measurement of surrogate markers such as blood pressure and lipid levels.

Researchers note the challenge of measuring patient adherence due to adherence being an individual patient behavior. Approaches listed for measuring medication adherence include subjective, objective, and biochemical measurements. The reported incidence of adherence in developed countries averages about 50%. Poor adherence to medication leads to increased morbidity, mortality, and increased incurred costs of approximately $100 billion per year. Factors associated with decreased compliance fall into 5 categories: socioeconomic factors, factors associated with the health care team and system in place, disease-related factors, therapy-related factors, and patient-related factors.

The authors focused on patient, physician, and health-system related factors to provide strategies for improving medication adherence. Patient-related strategies to improve medication adherence included patient education, actively involving patients in treatment decisions when possible, “shame-free” approaches to addressing inadequate health literacy, recognition and treatment of mental illness, and condisderation of patients’ economic status. Physician-related strategies to improve adherence included communicating effectively, avoiding complex drug regimens, and providing effective communication about adverse effects. Health-system related strategies aimed at improving adherence included implementing team-based approaches to address office vist time restraints, increased implementation of electronic medical records and electronic prescribing, initiating long-term medication for an acute event during hospitalization rather than after discharge, and medication reconciliation.

**CRITICAL ANALYSIS/LIMITATIONS:** When looking at approaches to medication adherence studies have found that no one simple intervention and few complex intervention are effective at improving long-term medication adherence and health outcomes, highlighting the difficulty of improving medication adherence. The literature review focused on adherence related to cardiovascular disease, noting most reasearch is disease-specific and not focused on medication adherence alone.

R. Scott Leslie. Using Arrays to Calculate Medication Utilization. MedImpact Healthcare Systems.

The purpose of the article is to offer a code that calculates a patient’s medication utilization as the proportion of days medication is supplied over a time period. The paper offers an example of the steps involved in the coding. By utilizing dummy variables to specify treatment for each day of a review period, various outcomes can be identified such as compliance, adherence, persistence, and discontinuation to therapy.

Zullig L, Peterson E, Bosworth H. Ingredients of successful interventions to improve medication adherence. Jama [serial online]. December 25, 2013;310(24):2611-2612.

This article was written with the purpose of identifying interventions effective in promoting both overall and condition-specific medication adherence based on evidence reviews. The author identifies there is no universal formula that will improve adherence in all settings, and that utilizing several interventions is essential for improving medication adherence.

Interventions discussed in the article include patient knowledge, counseling and accountability, self-monitoring, costs, and personalizing the program. The article reports that patients’ knowledge must be understood for interventions to be effective. Educational content must appropriately match the patient’s level of health literacy and align the patient’s readiness to change. Patient education can be delivered and reinforced by several members of the clinical care team n a collaborative care model. Longitudinal patient counseling and accountability interventions are critical to reinforce understanding and ensure sustained improvement. Self- monitoring through a variety of measures (eg. Prescription renewal data, BP or glucose levels, and symptoms or functional status) is an essential intervention to improve adherence and to inform the health care team about a patient’s behavior and health needs. Prescription medication may be prohibitively expensive for the patient so cost reductions that can be accomplished in a variety of ways may be necessary to facilitate adherence. Personaliing the program by matching intervention delivery and intensity with a specific patient’s needs is a goal to establish successful medication adherence programs.

**CRITICAL ANALYSIS/LIMITATIONS:** There is a suggested need for more information on how to develop scalable and sustainable interventions for medication adherence. Interventions should be continually evaluated and assessed in phases for effectiveness. The challenge now faced is how to create and sustain large-scale programs that ensure patient adherence on a national scale.

Fischer M, Choudhry N, Shrank W, et al. Trouble getting started: predictors of primary medication nonadherence. *The American Journal Of Medicine* [serial online]. November 2011;124(11):1081.e9-22.

This purpose of this study was to analyze e-prescribing data to evaluate the rate of primary nonadherence to newly prescribed medications across multiple characteristics of patients, prescribers, and prescriptions and to develop multivariable models to identify predictors of nonadherence. The study analyzed e-prescribing data and filled claims from a pharmacy benefit management company with CVS Caremark drug coverage who received e-prescriptions from the iScribe e-prescribing system in 2008. E-prescriptions were matched with filled claims by utilizing data on the drug name, date of e-prescription, and date of filled claims. Patients were allowed up to 180 days to fill e-prescriptions.

The study identified 423,616 e-prescriptions for new medications, with 3,634 prescribers and 280,081 patients. The primary nonadherence rate was 24%. Factors that were found to be associated with nonadherence to e-prescriptions included: nonformulary status of medications (OR 1.31 compared with preferred medications (*P* <.001) and residence in low-income ZIP code (OR 1.23 compared with high-income ZIP code; *P* <.001). Nonadherence was also found to occur less often when e-prescriptions were transmitted directly to the pharmacy rather than printed and given directly to the patients (OR 0.54; *P* <.001).

Results from the study concluded that 24% of e-prescriptions for new medications were not filled suggesting the need for interventions to address economic barriers and an increase in electronic integration into the healthcare system to provide approaches to improve medication adherence.

**CRITICAL ANALYSIS/LIMITATIONS:** Matching of e-prescriptions to filled claims to determine primary adherence was performed by text matching medication names. The process was imprecise and misclassification of some e-prescriptions as unfilled could have occurred leading to overestimation of nonadherence. Underestimation of nonadherence could have occurred by conservative assumptions presumed in the study such as: not including e-prescriptions reissued before a filled claim appeared and allowing up to 180 days for a filled claim to appear allowing for a subsequent handwritten or called prescription to the pharmacy. Allowing for the exclusion from the study the population with no filled prescriptions at all who could have had other sources of coverage may have led to underestimation of nonadherence. If patients filled prescriptions by paying cash without generating PBM claims, then they would have been misclassified as unfilled.

Dang D. Psychosocial considerations in the management of diabetes. *Drug Topics.* February 2013; 50-59

The purpose of the article is to identify psychosocial barriers to treatment adherence in patients with diabetes mellitus, discuss the impact of diabetes-related distress and comorbid depression on the management and control of diabetes mellitus, and discuss management considerations for geriatric patients with diabetes mellitus.

The article identified medication nonadherence has been correlated with worse glycemic control and health outcomes. Patient-related adherence barriers include: fears, lack of understanding about the rationale for a medication regimen, lack of skills to manage a medication regimen, personal health beliefs, depression and/or other medical conditions, poor health literacy, poor patient-prescriber relationship, adverse family dynamics, and lack of confidence in the immediate or future benefits of the medication. Medication-related adherence barriers identified in the article include complex regimens, frequency of dosing, cost, and adverse effects. Prescriber and system-related factors include the lack of time available to fully educate patients about their medication regimen, address concerns, and appropriate follow-up. It is important for the pharmacist to look for warning signs that may indicate poor treatment adherence.

The article identifies perceptions patients may have that differ from those of the treating clinician such as: medication as a benefit versus penalty, medication intensification versus de-intensification as a goal, and long-term versus short-term perspective. Interventions to improve adherence include: improving the patient-prescriber relationship and communication, providing more education on the medication and medical condition, and simplifying the medication regimen. Strategies that pharmacist can recommend to enhance medication adherence include simplifying the medication regimen, changing to a different formulation or different medication with a lower risk of side effects, using medication adherence aids, employing strategies specific to insulin administration, and reducing medication cost. Identifying the best strategy is one that is individualized for a particular patient. The strategy to enhance diabetes medication adherence by managing comorbid depression and diabetes-related distress is to include combination therapy with psychotherapy along with antidepressant treatment.

The article includes therapy consideration in geriatric patient due to increased number of comorbid conditions and a larger number of prescribed medications compared to younger patients. A conservative approach to the initiation and titration of doses is prudent as well as consideration of reduced renal and hepatic function and the increased risk of adverse drug reactions. Older patients have been reported to be more reluctant to discuss concerns about their medication regiment to their physician, so pharmacist can play an important role by engaging these patients in conversation about their attitude toward the medication regimen and collaborate with prescribers to identify and resolve medication-related problems in geriatric patients.

Prepared November 2013

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| **Annotated Bibliography Table of Contents by Subject:** |
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| \*\* Hyperlinks **on the articles** within the document link to .PDF files located within system folders |
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1. [Matza, Louis Yu Isenberg, Kristina Coyne, Karin Park, Jinhee Wakefield, Jessica Skinner,Elizabeth Wolever, Ruth. Further testing of the reliability and validity of the ASK-20 adherence barrier questionnaire in a medical center outpatient population .](C:\\Users\\yur3\\Desktop\\Questionnaire\\ASK-20.pdf)*[Current Medical Research and Opinion](C:\\Users\\yur3\\Desktop\\Questionnaire\\ASK-20.pdf)*[. 2008;24:3197-3206.](C:\\Users\\yur3\\Desktop\\Questionnaire\\ASK-20.pdf)

The ASK-20 questionnaire (Adherence Starts with Knowledge) was developed to assess both potential barriers and adherence behavior as it relates to medication adherence regardless of the medical condition of the patient. Previous studies described the process of developing the questionnaire, internal consistency, and concurrent validity. The purpose of this study was to analyze its psychometric properties along with a more extensive analysis of reliability, internal consistency, and test-retest reliability. Furthermore, validity was also examined in relation to other patient-report measures (e.g the Morisky Medication Adherence Scale and the general self-report adherence questions), objective measures of adherence, and proportion of days covered.

In regards to internal consistency, the ASK-20 questionnaire had a Cronbach’s alpha of 0.76 and good test-retest reliability with an intraclass correlation of 0.80. For concurrent validity, they used correlations with Morisky Medication Adherence Scale (r = -0.61, p < 0.001), condition-specific measures, and the SF-12 Mental Component Summary score (r = 0.40, p < 0.001). The correlation between ASK-20 and proportion of days covered (PDC) for 6 months was weak (r = -0.13). Overall, findings provide support for the reliability and validity of the ASK-20 for assessing patients’ perceptions of potential barriers to medication adherence and adherence-related behavior.

**LIMITATIONS/CRITICAL ANALYSIS:** It was noted that 6 out of 20 of the items seemed to demonstrate floor effects which may limit how responsive the instrument is and therefore it may prove to be beneficial to drop some of these items. Since the correlation with PDC was weak, it can mean that the barriers that the questionnaire assesses do not necessarily result in lower medication adherence. The authors also attribute this low correlation to how difficult it is to assess adherence in general.

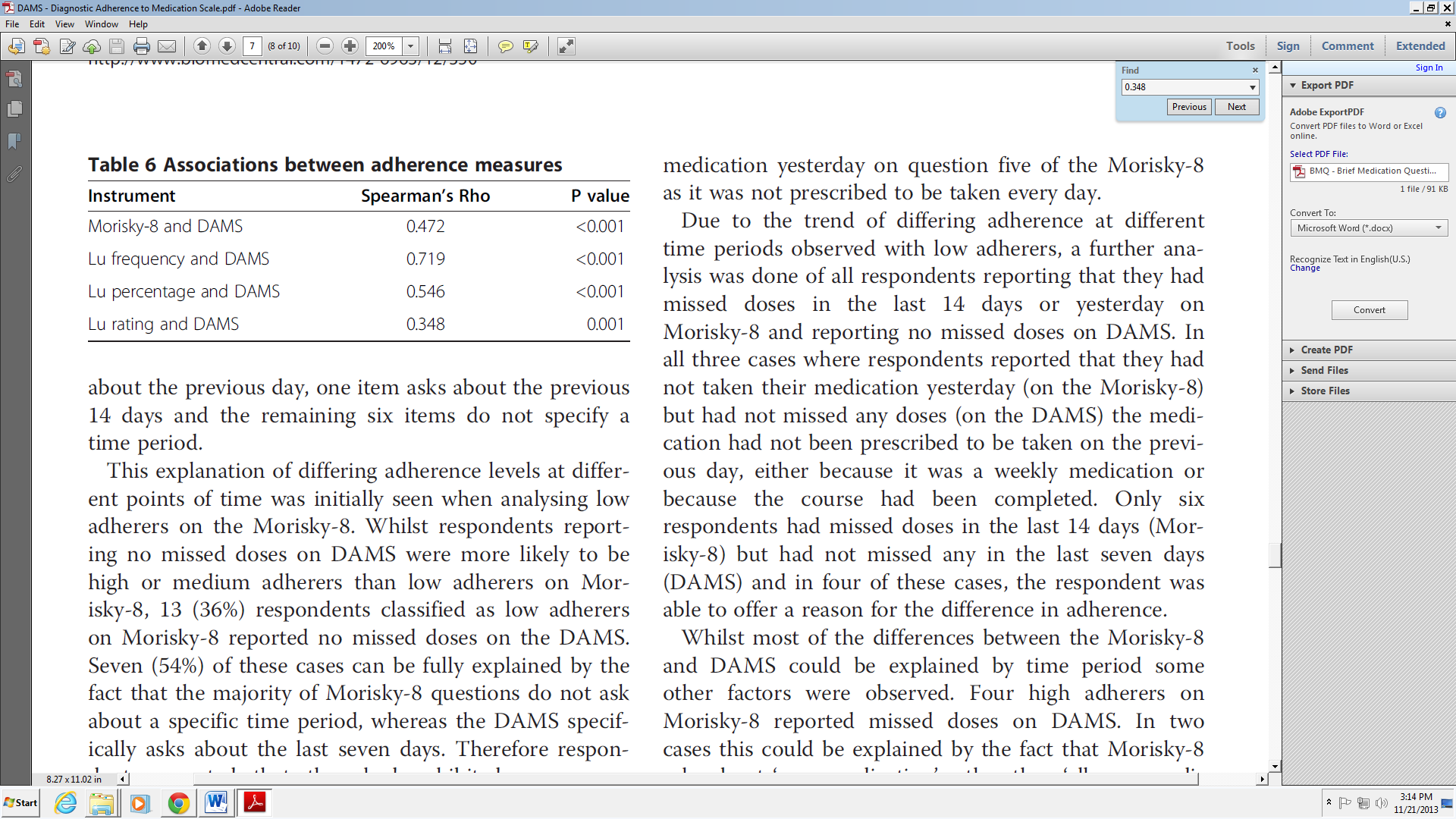
Further studies are suggested to focus on further refinement and validation as well as determining its usefulness across different settings and patient populations.

1. [Garfield, Sara Eliasson, Lina Clifford, Sarah Willson,Alan Barber, Nick. Developing the Diagnostic Adherence to Medication Scale (the DAMS) for use in clinical practice.](C:\\Users\\yur3\\Desktop\\Questionnaire\\DAMS - Diagnostic Adherence to Medication Scale.pdf)*[BMC Health Services Research](C:\\Users\\yur3\\Desktop\\Questionnaire\\DAMS - Diagnostic Adherence to Medication Scale.pdf)*[. 2012;12:350-350.](C:\\Users\\yur3\\Desktop\\Questionnaire\\DAMS - Diagnostic Adherence to Medication Scale.pdf)

The Diagnostic Adherence to Medication Scale (DAMS) was developed in collaboration between a multidisciplinary team of pharmacists and psychologists. It is designed, along with a version for caregivers, to be a short recall questionnaire on taking prescribed medication doses during a 7 day period for all medications a patient is taking and for multiple conditions. The framework for the questionnaire is designed in the “accident causation framework” which looks at non-adherence as a systemic issue rather than an issue of personal blame. It was designed to track a patient’s adherence in a clinical practice as well as evaluate interventions that are made. Also, it aims to distinguish between intentional and unintentional non-adherence so that the appropriate approach may be used in addressing the issue.

The objective of the study was to establish face and content validity and preliminary content validity in comparison to other self-report measures.

The DAMS was compared to the Morisky-8 and to the questionnaire developed by Lu et al with a Spearman Rho ranging from 0.348 to 0.719 the details of which are in the following table. The measures were all done in a short amount of time with the DAMS being the longest at an average of 1 minute 28 seconds with a correlation between the number of medications taken and time to completion.



**LIMITATIONS/CRITICAL ANALYSIS:** It was noted that the Morisky-8 and Lu questionnaires were not able to distinguish between low and zero adherence. The DAMS was not applicable to patients that were prescribed “as needed” medications because adherence scores could not be calculated. Out of the 100 patients in the study, only 20 had verified medication records. Adherence in the DAMS was calculated according to self-reports but were not compared to actual records. Further investigation needs to be done in comparison to objective measures, reliability, and the caregiver version.

1. [Cameron, Kenzie Ross, Emily Clayman, Marla Bergeron, Ashley Federman, Alex Bailey, Stacy Davis,Terry Wolf, Michael. Measuring patients' self-efficacy in understanding and using prescription medication.](C:\\Users\\yur3\\Desktop\\Questionnaire\\MUSE - Measuring patients’ self-efficacy in understanding and using prescription medication - 2009.pdf)*[Patient Education and Counseling](C:\\Users\\yur3\\Desktop\\Questionnaire\\MUSE - Measuring patients’ self-efficacy in understanding and using prescription medication - 2009.pdf)*[. 2010;80:372-376.](C:\\Users\\yur3\\Desktop\\Questionnaire\\MUSE - Measuring patients’ self-efficacy in understanding and using prescription medication - 2009.pdf)

The Medication Understanding and Use Self-Efficacy Scale (MUSE) was designed to assess self-efficacy in relation to the individuals perceived ability in understanding and using prescription medications. Initially, there were 18 items written at a 6th grade reading level but through factor analysis they were able to remove some of the items and ultimately shorten the scale to 8 items (4 associated with taking medication, 4 associated with learning about medication). For their participants they conducted literacy tests and had them demonstrate understanding of appropriate medication use to assess functional understanding of medication instructions.

Their results for Cronbach’s alpha was 0.77 for items associated with taking medications and 0.68 for items associated with learning about medication. Scores varied depending on literacy level, however, multivariate analysis did not detect an interaction between literacy level and MUSE score.

The authors cite that while many scales in regards to self-efficacy focus on specific barriers or conditions or are specific for certain health conditions, self-efficacy applies to a wide variety of health behaviors and not just specific situations. As a result, they wanted to develop a more generalized scale for use not only in research but clinical practice that included not only the act of taking a medication, but also the understanding of medication regimens.

**LIMITATIONS/CRITICAL ANALYSIS:** This instrument is useful in determining barriers and guiding interventions to assist individuals in understanding and using their medications which may translate to improved adherence. The authors, however, have not determined any correlations in the scale to actual objective numbers for medication adherence. Also, they looked only at the understanding of written prescription instructions, which they provided, and not actual behaviors of actual medications. As such, at this point it is hard to determine how well the scale actually translates to actual medication adherence.

They do cite studies about how their subscale relating to learning about medications strongly influences patient-reported adherence and the need for further research to further validate the tool.

1. [Kripalani, Sunil Risser, Jessica Gatti,Margaret Jacobson, Terry. Development and evaluation of the Adherence to Refills and Medications Scale (ARMS) among low-literacy patients with chronic disease.](C:\\Users\\yur3\\Desktop\\Questionnaire\\ARMS - Development and evaluation of the Adherence to Refills and Medications Scale (ARMS) among low-literacy patients with chronic disease 2008.pdf)*[Value in Health](C:\\Users\\yur3\\Desktop\\Questionnaire\\ARMS - Development and evaluation of the Adherence to Refills and Medications Scale (ARMS) among low-literacy patients with chronic disease 2008.pdf)*[. 2009;12:118-123.](C:\\Users\\yur3\\Desktop\\Questionnaire\\ARMS - Development and evaluation of the Adherence to Refills and Medications Scale (ARMS) among low-literacy patients with chronic disease 2008.pdf)

The purpose of this study was to develop a medication adherence scale that would be well suited for patients with low literacy levels in order to limit such things as misunderstanding and variations in interpretation. The researchers cite the possible connection between literacy levels and medication adherence but current research has not yet shown a clear relationship.

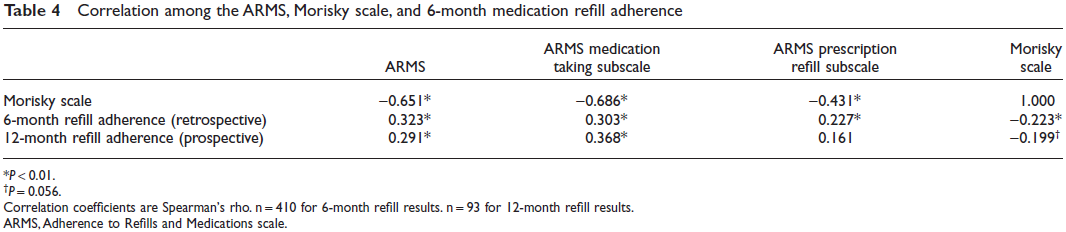
The scale was developed by a multidisciplinary team with generalizability for a multitude of medical conditions. Using the Morisky scale and the Hill-Bone Compliance Scale as their starting points, they then further expanded it to include more diseases, simplify any wording if necessary, and added more items. They ended up with 2 subscales: one for the adherence of medication, the other for the filling/refilling of medications. Responses structured along the Likert scale and questions were written where lower scores indicated better adherence.

The scale was administered orally as part of another study, the Improving Medication Adherence through Graphically Enhanced interventions in Coronary Heart Disease (IMAGE-CHD) study. Along with the ARMS questionnaire at baseline, participants’ literacy skills were also assessed, and the Morisky scale was administered. The patients were then randomized to 4 study groups; “an illustrated daily medication schedule, postcard refill reminders, both interventions, or usual care (control).” Follow-up questionnaires were administered at a later date which included ARMS. This allowed for assessment of test-retest reliability. A Lexile analysis was also conducted on the items to help determine reading difficulty and their aim was for an eighth grade or lower reading level (i.e. less than 1000L). To assess validity of the scale they did; (1) comparisons to the Morisky scale, (2) correlated ARMS with pharmacy records for medications refills at 6 months with a cumulative medication gap, (3) looked at predictive validity with refill adherence at 12 months compared to the control, and (4) split participants into 2 groups with the median ARMS score as the cutoff point to compare percentage of patients with controlled blood pressure.

They initially developed the scale with 14 items which had a Cronbach’s alpha of 0.816. Subsequently, they dropped 2 items because they did not have very good interitem correlations and this gave them a Cronbach’s alpha of 0.814.

The Lexile score for the 12-item scale was 920L which is compared to the Hill-Bone scale at 850L and the Morisky scale at 650L. For those they considered to have inadequate literacy skills, the Cronbach’s alpha was still high at 0.792 compared with those considered to have marginal/adequate literacy skills at 0.828.

A summary of the correlations the researchers found are listed on the table below. Of significance, it correlated well with the Morisky scale which is commonly used. Additionally, ARMS had a stronger correlation than Morisky to refill adherence. There were 429 out of 435 patients that hypertension with 46.9% of patients with overall controlled blood pressure. The researchers found that patients having an ARMS score below the median of 16 were found to have a statistically significant percentage of patients with controlled diastolic blood pressure (81.3% vs. 73.2%, P < 0.05). This trend was seen for controlled systolic (52.2% vs. 46.3%) and overall (50.4% vs. 42.9%) blood pressure, however, these were not determined to be statistically significant.



Patient demographics showed that many patients had other comorbidities other than coronary heart disease including hypertension, diabetes, etc. which translates to applicability across a variety of patient populations.

LIMITATIONS/CRITICAL ANALYSIS: The refill subscale (4 items) had a lower correlation with refill adherence compared to medication taking subscale (8-items), the reasons for which are unclear and need further study and evaluation. Limitations include:

* The study may not be generalizable because it was conducted at one location with predominately African American patients.
* Patients had 6 medications on average which may lead to different results for patients taking less medication.
* There was a 3 month gap between retesting and if shorter, the reliability may have been higher.
* Because data was collected during scheduled appointments, this behavior (i.e. keeping appointments) may translate to patients being more comparatively adherent.
* The ARMS score distribution was skewed towards being more adherent which they indicate with being common in self-report scales due to where the scale was administered (i.e. at a clinic appointment) and wanting to give desirable answers.

1. [Risser, Jessica Jacobson,Terry Kripalani, Sunil. Development and psychometric evaluation of the Self-efficacy for Appropriate Medication Use Scale (SEAMS) in low-literacy patients with chronic disease.](C:\\Users\\yur3\\Desktop\\Questionnaire\\SEAMS - Self-Efficacy for Appropriate Medication Use Scale.pdf)*[Journal of Nursing Measurement](C:\\Users\\yur3\\Desktop\\Questionnaire\\SEAMS - Self-Efficacy for Appropriate Medication Use Scale.pdf)*[. 2007;15:203-219.](C:\\Users\\yur3\\Desktop\\Questionnaire\\SEAMS - Self-Efficacy for Appropriate Medication Use Scale.pdf)

The Self-Efficacy for Appropriate Medication Use Scale (SEAMS) was developed to help understand and address medication adherence in patients with low literacy skills. The scale was also developed with the framework of addressing the issue of self-efficacy, which they attribute to behavior changes required for disease management and medication adherence. An additional aim was to develop the scale in order to be applicable across a variety of medical conditions and situations.

The scale was developed by a multidisciplinary team into an initial 21-item instrument. The items are scored on a 3-point scale that addresses their level of confidence about taking medications correctly. Higher scores indicate better self-efficacy. SEAMS was administered orally as part of the Improving Medication Adherence Through Graphically Enhanced Interventions in Coronary Heart Disease (IMAGE-CHD) study.

Patients were randomized into one of 4 groups: intervention A, intervention B, interventions A and B, or usual care (control). A baseline SEAMS score was recorded for patients with follow-up interviews approximately 3 months after enrollment. In addition, patients were also given the Morisky’s self-report measure of adherence and the Rapid Estimate of Adult Literacy in Medicine for literacy.

The study population had a total of 436 subjects with 91% African American, 53% completing high school, and 45% with inadequate literacy skills. Many patients had chronic, comorbid diseases, and took an average of 9 medications. Average blood pressure was 136/75 for all patients, of which 46% of patients were considered adequately controlled. Average blood glucose was 173 for diabetic patients.

Mean interitem correlation of the items was 0.32 and Cronbach’s alpha for the overall scale was 0.90. Test-retest reliability of the 21-item scale was moderate (Spearman’s ρ = 0.62). There were 4 factors found during the factor analysis which all together explained 54.61% of the variance.

The final developed scale was then narrowed down to 13 items (Cronbach’s alpha = 0.89) representing 2 dimensions of self-efficacy: taking medications under difficult situations (Cronbach’s alpha = 0.86), and continuing medications during situations where medication-taking is uncertain (Cronbach’s alpha = 0.79). The test-retest reliability of the 13-item scale was adequate (Spearman’s ρ = 0.57). In regards to correlation to the Morisky scale, it had a Spearman’s ρ of 0.51.

There was good internal consistency in the psychometric analysis between low and higher literacy patients. For low literacy patients, the Cronbach’s alpha for the 13-item scale was 0.89, with a mean interitem correlation of 0.40 compared to those with higher literacy skills with a Cronbach’s alpha of 0.88 and a mean interitem correlation of 0.36.

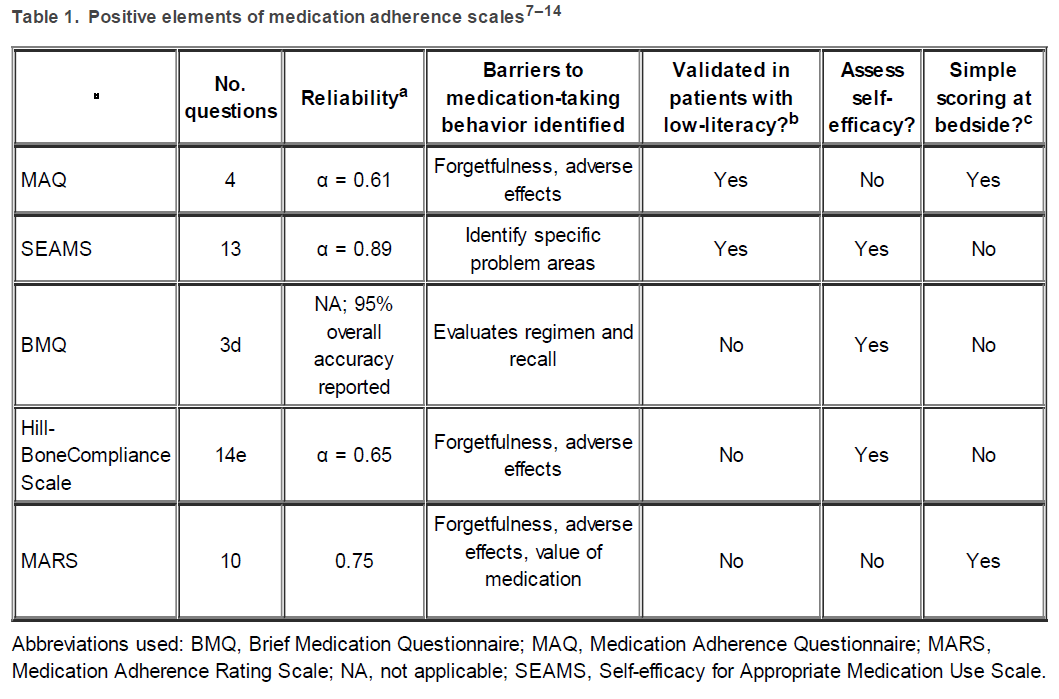
**CRITICAL ANALYSIS/LIMITATIONS:** When looking at patients with controlled hypertension or blood glucose, there was no statistically significant difference comparing those with high self-efficacy versus low self-efficacy. This may be due to other factors that can influence the complex interactions between self-efficacy, medication adherence, and health outcomes. Due to the design of the parent study (IMAGE-CHD) with a follow-up for retest at 3 months, this could have led to a lower correlation between test-retest scores. Generalizability may be limited as well due to the majority of patients being predominately African American and only using one study site.

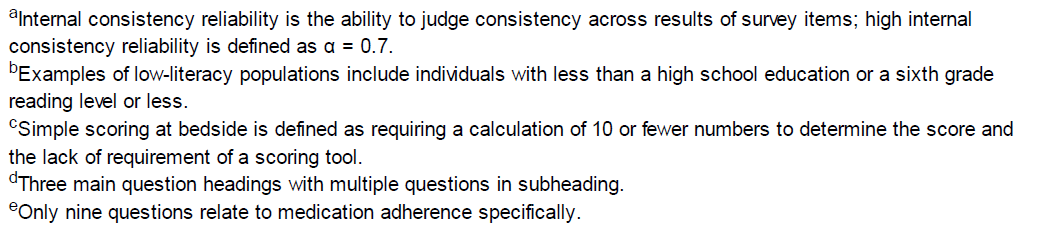
1. [Lavsa, Stacey Holzworth,Ashley Ansani, Nicole. Selection of a validated scale for measuring medication adherence.](C:\\Users\\yur3\\Desktop\\Resources & Information\\Selection of a Validated Scale for Measuring Medication Adherence 2011.pdf)*[Journal of the American Pharmacists Association](C:\\Users\\yur3\\Desktop\\Resources & Information\\Selection of a Validated Scale for Measuring Medication Adherence 2011.pdf)*[. 2011;51:90-94.](C:\\Users\\yur3\\Desktop\\Resources & Information\\Selection of a Validated Scale for Measuring Medication Adherence 2011.pdf)

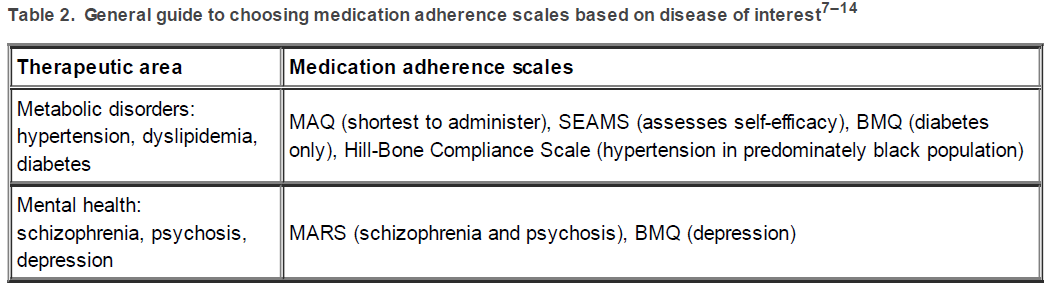
The objective of this article was to compare the variety of medication adherence surveys/scales in order to help clinicians choose the most appropriate one for their particular practice. This was done because at the moment, there is no gold-standard in regards to which scale to use.

A literature search was conducted and scales had to meet the criteria of “English language, generalizability to practice (validated in at least two diseases) and ease of administration (scale containing ≤30 questions).” They were able to identify the following scales that met the criteria: the Medication Adherence Questionnaire (MAQ; also known as Morisky 4), the Self-efficacy for Appropriate Medication Use Scale (SEAMS), the Brief Medication Questionnaire (BMQ), the Hill-Bone Compliance Scale, and the Medication Adherence Rating Scale (MARS).

After identifying the scales, the researchers then went on to look at the pros and cons of each scale which are summarized in the table below.







The following sensitivities and specificities were indicated for the following scales:

|  |  |  |
| --- | --- | --- |
| Scale | Sensitivity | Specificity |
| MAQ | 0.81 | 0.44 |
| BMQ | 1.0 | 0.8 |
| BMQ – recall screen | 0.4 | 0.4 |

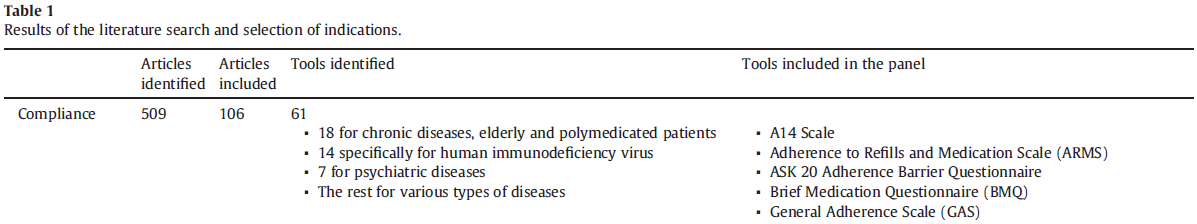
Additionally, in regards to the MAQ, it was noted that with a higher score in regards to medication adherence, a higher predictive value was seen compared with low medication adherence. The authors noted that SEAMS would be useful in a clinical setting which provides medication management that is able to focus on medication adherence. The BMQ requires the patient to list their specific medication regimens while also assuming that this list is comprehensive and so may be more useful in dedicated pharmacy clinics as well. The Hill-Bone Compliance Scale is limited in generalizability and so is more specifically geared towards cardiovascular patients. The MARS was geared towards mental health patients.

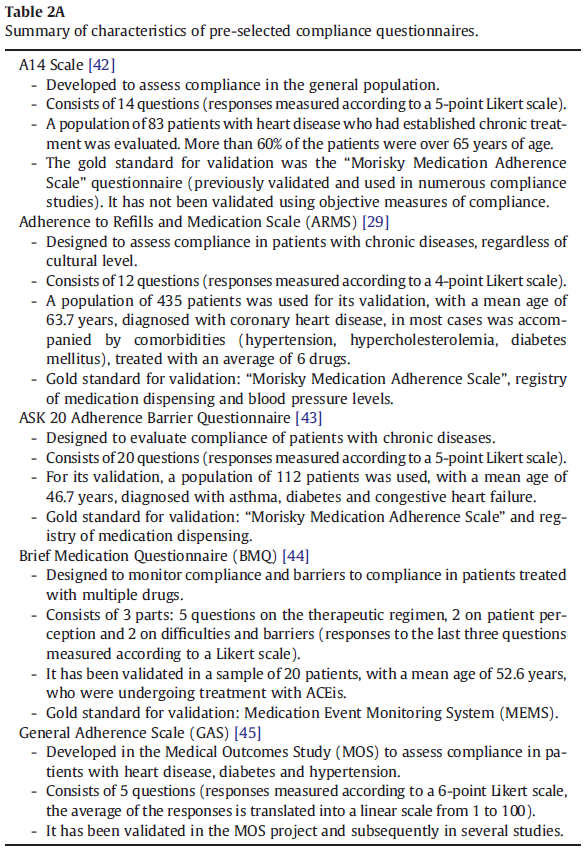
1. [Alfaro Lara, Eva Vega Coca, Maria Galván Banqueri, Mercedes Marín Gil, Roberto Nieto Martín, María Pérez Guerrero, Concepción Ollero Baturone,Manuel Santos Ramos, Bernardo. Selection of tools for reconciliation, compliance and appropriateness of treatment in patients with multiple chronic conditions.](C:\\Users\\yur3\\Desktop\\Resources & Information\\Selection of tools for reconciliation, compliance and appropriateness of treatment in patients with multiple chronic conditions 2012.pdf)*[European Journal of Internal Medicine](C:\\Users\\yur3\\Desktop\\Resources & Information\\Selection of tools for reconciliation, compliance and appropriateness of treatment in patients with multiple chronic conditions 2012.pdf)*[. 2012;23:506-512.](C:\\Users\\yur3\\Desktop\\Resources & Information\\Selection of tools for reconciliation, compliance and appropriateness of treatment in patients with multiple chronic conditions 2012.pdf)

This article was written by researchers in Spain with the aim of selecting what they deemed to be the best tool to use for determining medication compliance, appropriateness, and reconciliation in patients with multiple chronic diseases. Since the purpose of this annotated bibliography is focused primarily on medication adherence, I will be concentrating primarily on their results dealing with medication compliance.

As part of their methods, they conducted a literature search on various databases. They selected documents that were developed for patients with multiple chronic diseases or had similar attributes (chronic, multiple medications, comorbid elderly, etc.), validated or widely used with “quality fieldwork study,” and allowed for quantitative estimate or assessment of items according to a Likert scale (to help determine an estimated rate of compliance). The selected documents were reviewed by a group of 11 experts independently whose background and characteristics were noted in the article. They were instructed to take into account certain aspects of the selected article such as usefulness in patients with chronic illnesses, strength of evidence in the use of the tool, ability to detect causes of low compliance, etc.

The result of the literature search yielded 61 compliance questionnaires but none were validated specifically for patients with multiple chronic diseases. Ultimately, they were able to select 5 articles meeting the inclusion criteria of chronically ill and elderly patients. Details on reasons for rejections of questionnaires are noted in the article.





The “Adherence to Refills and Medication Scale” (ARMS) questionnaire was ultimately considered to be the best tool with a high degree of agreement between the expert reviewers. The ARMS questionnaire was considered easy to use and well designed. It contained 2 subscales (getting medications and proper administration of medications) which they attributed with better understanding of obstacles to compliance. This would lead to personalized interventions to address these obstacles. Though this scale does not consider patients with patients with chronic multiple diseases, the patients did have coronary artery diseases which they associated with also having other comorbidities.

Comments on considerations on the other tools are summarized below:

* A14-Scale
  + May be useful for detecting causes of non-compliance.
  + Was considered to be feasible for implementation in clinical practice.
* ASK 20 Adherence Barrier Questionnaire
  + Agreement was not reached by the expert panel
  + Considered to be excessively long and only validated for much younger and less complex patients and so not feasible to be implemented
* General Adherence Scale (GAS)
  + Initially considered due to feasibility of implementation
  + Scale included more than just compliance which could lead to errors
* Brief Medication Questionnaire (BMQ)
  + For certain aspects considered, there were doubts about the appropriateness
  + Tested on few patients who were younger

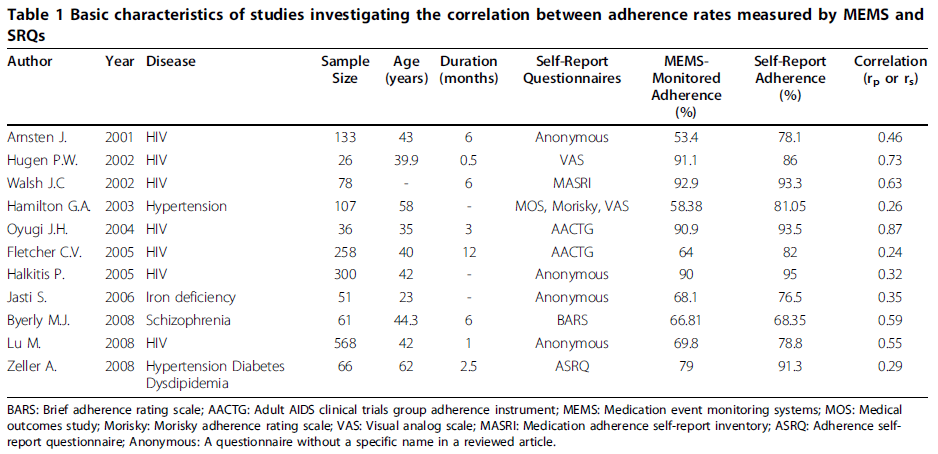
The researchers mention the Morisky scale and how it is widely used but not included because it did not meet their defined criteria of being able to estimate compliance quantitatively or semiquantitatively. This is because the Morisky scale is dichotomous in regards to the responses to items.

**LIMITATIONS/CRITICAL ANALYSIS:** Literature search was only up until December 2009. Compliance tools found did not fulfill their main qualification of being specifically in patients with chronic multiple diseases.

1. [Shi, Lizheng Liu, Jinan Fonseca, Vivian Walker, Philip Kalsekar,Anupama Pawaskar, Manjiri. Correlation between adherence rates measured by MEMS and self-reported questionnaires: a meta-analysis.](C:\\Users\\yur3\\Desktop\\Resources & Information\\Correlation between adherence rates measured by MEMS and self-reported questionnaires - a meta-analysis.pdf)*[Health and Quality of Life Outcomes](C:\\Users\\yur3\\Desktop\\Resources & Information\\Correlation between adherence rates measured by MEMS and self-reported questionnaires - a meta-analysis.pdf)*[. 2010;8:99-99.](C:\\Users\\yur3\\Desktop\\Resources & Information\\Correlation between adherence rates measured by MEMS and self-reported questionnaires - a meta-analysis.pdf)

The authors sought to examine the correlation, if any, between medication event monitoring systems (MEMS) and self-reported questionnaires (SRQs) through the use of literature searches over a variety of databases. MEMS was stated to be a “imperfect gold standard” because it has the drawbacks of being expensive to implement, not applicable for some medications/formulations, using up large resources, and being time consuming. This is in comparison to SRQs which are convenient but are prone to measurement bias (e.g. recall and response bias, etc.) which can cause inaccuracies in actual medication adherence measures. They cite that other literature reviews have looked at the correlation between SRQs and measures such as pharmacy refill records and that they were taking it one step further by comparing it to the higher standard with MEMS as the comparison.

A summary of the 11 articles used in the meta-analysis is as follows:



The researchers found a pooled correlation coefficient of 0.45 (p = 0.001, 95% CI: 0.34-0.56), therefore, showing a moderate correlation between MEMS and SRQs. This, they cite, follows other studies that show moderate-to-high correlation between SRQs and other adherence measures.

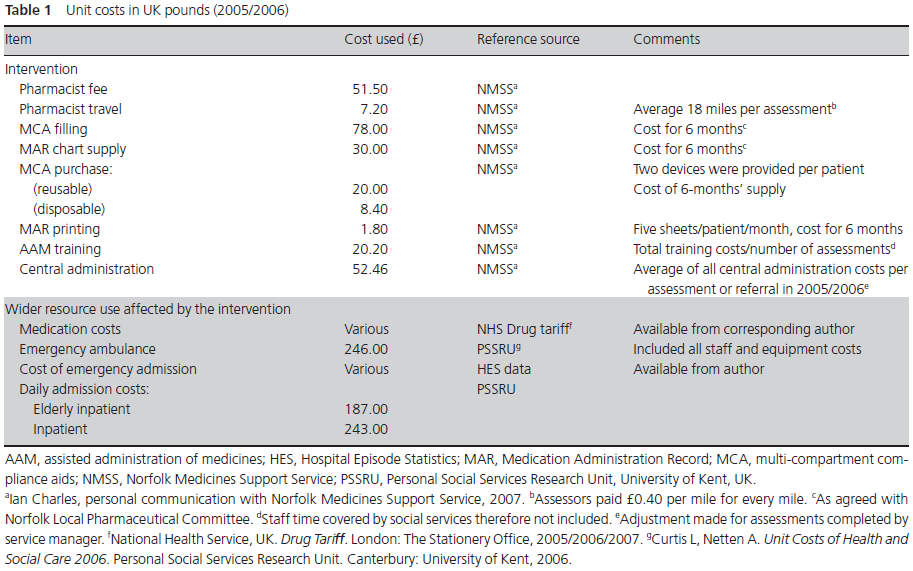
**LIMITATIONS/CRITICAL ANALYSIS:** Compared to some of the more well-known questionnaires, some of the studies that used questionnaires that were labeled “Anonymous” showed lower correlations as well. This could translate to meaning lower validity in these questionnaires and therefore unsatisfactory to be developed further (i.e. poor questionnaires that did not effectively translate to actual medication adherence) and possibly contributing to a lower pooled correlation. One of the notable weaknesses noted was that the number of studies included was limited and they were not very consistent to another (e.g. different definitions for adherence, diseases states, duration of the study, etc.)

**APPLICATION/IMPLICATION:** In regards to further research in the area of medication adherence and evaluating the effectiveness of any medication adherence program implemented, multiple measures would be able to provide a more complete picture than either alone. As far as the implementation of programs, SRQs may prove to be less costly to implement and use in the beginning compared to MEMS, which are not currently covered by insurance and so are costly. In addition, SRQs provide insight into such things patient behaviors, barriers, and self-efficacy which can help in guiding interventions.

1. [Desborough, James Sach, Tracey Bhattacharya, Debi Holland,Richard Wright, David. A cost-consequences analysis of an adherence focused pharmacist-led medication review service.](C:\\Users\\yur3\\Desktop\\Cost-Benefit & Effectiveness Analysis\\A cost-consequences analysis of an adherence focused pharmacist-led medication review service.pdf)*[The International Journal of Pharmacy Practice](C:\\Users\\yur3\\Desktop\\Cost-Benefit & Effectiveness Analysis\\A cost-consequences analysis of an adherence focused pharmacist-led medication review service.pdf)*[. 2012;20:41-49.](C:\\Users\\yur3\\Desktop\\Cost-Benefit & Effectiveness Analysis\\A cost-consequences analysis of an adherence focused pharmacist-led medication review service.pdf)

This study comes from the UK and is aimed with conducting an economic evaluation of a pharmacist-led medication review service for patients identified in primary care as non-adherent. The study was designed as a before and after quasi-experiment. The intervention was conducted in the home of the patient. The only costs included were those of providing the service, implications on secondary care emergency hospital admissions, and prescribing costs.

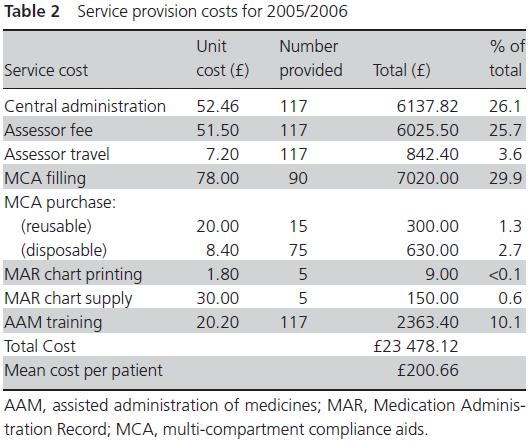
The table below represents the items used in the service and the items likely to change as a result of the service. Pharmacists were paid a set fee regardless of the time spent and this fee was included in the analysis. Mean costs per patient in the 6 months prior to assessment compared to mean costs 6 months after assessment. Also included in the analysis was the mean difference in cost per patient.

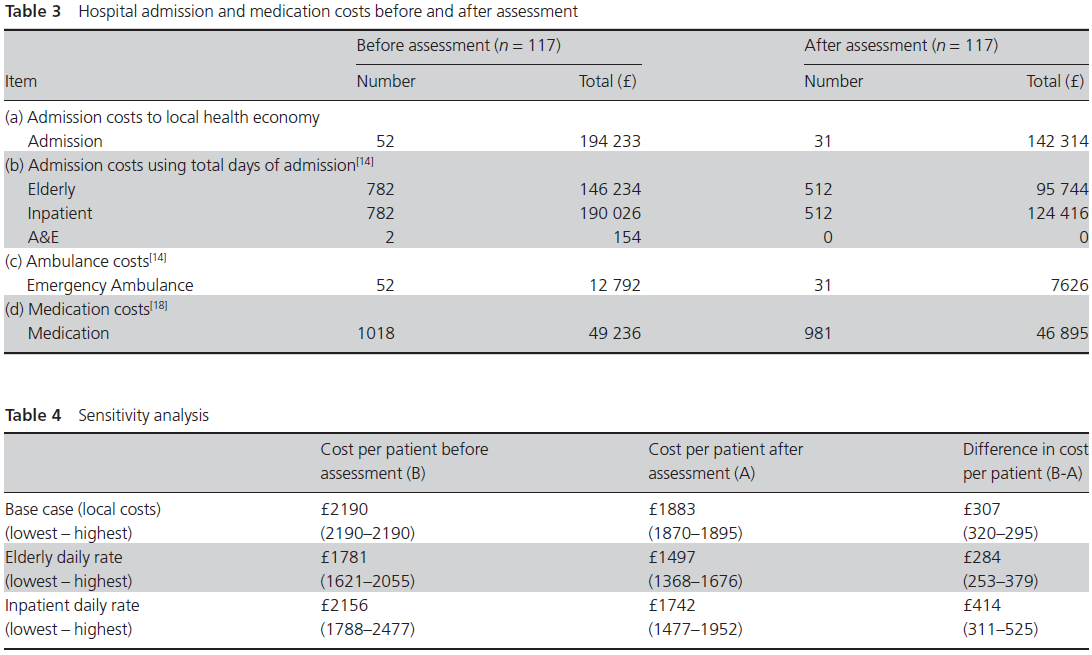


Baseline measurements were done before the initial review. These included self-reported adherence (Medication Adherence Report Scale; MARS), and health-related quality of life (HRQOL) using the EQ-5D descriptive system. Follow-ups were then done at 6 weeks and 6 months after the initial review.

A total of 117 elderly patients received interventions of which 16 were lost to follow-up for questionnaire data (hospital admission data was collected) and nine died (all data collected prior to mortality were included).

Table 2 shows the total costs for providing the service. Table 3 shows resource use of patients before and after intervention. Table 4 shows the difference in costs of daily rates and maximum and minimum cost estimates.





Self-reported adherence significantly increased at 6 months from a (mean score of 22.12 to 23.15). The proportion of patients classified as adherent rose from 19 to 29 and was also significant. HRQOL from the EQ-5D was reduced but not determined to be significant and may be explained by overall deteriorating health. The cost at 6 months was £201 per patient but was offset by the reduction in hospital admissions saving £307 per assessed patient.

**CRITICAL ANALYSIS/LIMITATIONS:** Most noticeable was the lack of a control group and this was due to the fact that evaluation of this service was done when the service was already started, hence the quasi-experimental design. Resource constraints were also noted in the collection of data. In turn, they are not able to determine a causal relationship in the findings. This is because other interventions, as part of a package of interventions along with the medication review service, may have contributed to any positive result seen. Additionally, the researchers state that the reduction in hospital admissions may be due to regression towards the mean. These patients may have been referred to the service because of an admission and so admission rates may have dropped regardless of the intervention.

The researchers did not reach their planned sample size of 326 contributing to large confidence intervals. The confidence intervals for the mean difference in cost per patient were also large and crossed zero. This means that while the intervention could decrease costs it could also increase costs. The authors note that “few studies are powered to detect statistically significant differences for economic costs or outcomes.” Since decisions need to be made, they state that this study should be used to guide such decisions until more research is done in this area.

Additionally, the cost analysis also did not take into account attributed to primary care, social services or the patient. They cite other studies looking at medication review services that demonstrated more positive prescribing outcomes, and so better clinical outcomes, when there were a small number of pharmacists working with a patient’s primary care physician and vice versa. In their particular study however, they had a large number of pharmacists (n = 30) that showed positive clinical outcomes. They attribute this to the patients being referred to the service, who actually needed it, from a wide spectrum of people involved in the active care of the patient. This is compared to other studies where other researchers would look at demographic information (e.g. number of medications) to then give interventions. Another attribute that may have contributed to positive outcomes is the established relationships between a service manager at a medical office and a central link at the service center.

**APPLICATION/IMPLICATION:** Without personally knowing the finances of the Clinton Service Unit, it would be hard to conduct a cost-benefit analysis on pharmacist improvement of medication adherence, especially one where the pharmacist travels to the patient’s home. Additionally, the healthcare system in the UK may not be relatable to the healthcare system here in the US. What is notable about this study is the environment in which the intervention was conducted. Since the service unit has a collaborative practice agreement between clinical pharmacists and physicians, and those relationships and trust are continually being established and solidified, a greater improvement in clinical outcomes may be seen as a product of improving medication adherence. The various caregivers (e.g. physicians, social services, clinical pharmacists) that are actively involved in their routine care may be able to identify and refer those patients which may benefit the most from a medication review service such as the one in the study. This may be a better way to begin initiating the program and choosing patients to enroll than just looking at demographic information.

1. [Chapman, R H Ferrufino, C P Kowal, S L Classi, P Roberts,C S. The cost and effectiveness of adherence-improving interventions for antihypertensive and lipid-lowering drugs\*.](C:\\Users\\yur3\\Desktop\\Cost-Benefit & Effectiveness Analysis\\The cost and effectiveness of adherence-improving interventions for antihypertensive and lipid-lowering drugs.pdf)*[International Journal of Clinical Practice](C:\\Users\\yur3\\Desktop\\Cost-Benefit & Effectiveness Analysis\\The cost and effectiveness of adherence-improving interventions for antihypertensive and lipid-lowering drugs.pdf)*[. 2010;64:169-181.](C:\\Users\\yur3\\Desktop\\Cost-Benefit & Effectiveness Analysis\\The cost and effectiveness of adherence-improving interventions for antihypertensive and lipid-lowering drugs.pdf)

Anticipated or actual costs of large scale medication adherence programs are a possible barrier to their implementation. This particular study wanted to address the issue and so it dealt with looking at a variety of interventions to improve medication adherence in cardiovascular disease therapies with antihypertensive and lipid-lowering drugs. The study did so in the context of effectiveness and costs of such interventions. As part of their methods, article reviews were done and the data used in order to complete the study. There were 18 interventions from one study were used as the basis for their information and an additional literature search and screening found another 5 interventions for a total of 23 interventions. The data used for analysis included effectiveness (measured in relative improvement) and costs of interventions (estimations done by an informal panel with assumptions) with various elements included.

Their results showed that relative improvement (adherence outcome in intervention group divided by control group) ranged from 1.11 for monthly mailed prescription reminders to 4.65 for pharmacist management programs. The researchers set 6-months as the standard for follow-up time and costs ranged from $9.59 per patient for mailed prescription reminders to $142.22 per patient for pharmacist management programs which included patient diaries and educational materials. A full table of the studies detailing relative improvement, costs, and the type of intervention is included in the article but not added here due to its size.

Article titles and abstracts were first screened to remove studies that did not report an adherence intervention or were not published in English. A second screen was undertaken to ensure each study used at least one generalizable intervention to improve adherence to antihypertensive or

The researchers found that overall, as a program increased medication adherence among patients, the cost in implementing the program also increased. The most effective interventions were those that addressed adherence from multiple angles (e.g. personalized intervention sessions). The researchers noted the use of MEMS in one of the studies they looked and found that it was costly when pharmacist monitoring was included. In one of the studies regarding MEMS that was notable, 31% more patients with hypertension had normalized blood pressure but only gained 0.003 more quality-adjusted life-years using the experimental strategy compared to usual care. Most of the recommended interventions they suggested were noted to be initiated in the early stages when the patient was just starting drug therapy. The suggestion is that this would the optimal time to begin so that patients establish appropriate behaviors, attitudes, and beliefs so that they persist long-term.

**CRITICAL ANALYSIS/LIMITATIONS:** The study, since it was a review of information from other articles, may be prone to publication bias (i.e. positive findings more likely to be published). This is compounded by the fact that they only screened for studies which showed a positive improvement, removing negative studies from the beginning. In addition, other screening criteria may have removed highly efficacious interventions due to the design of the study.

Since 6 months was their standardized follow-up time, and since some studies had longer study times, those interventions which included a fixed cost may have an overestimated average cost. Costs associated with training, initializing the program, and indirect costs were not included.

Many of the studies also differed from one another in regards to the interventions studied, study designs, study population, and the method of how adherence was measured, calculated, and reported. This adds to the difficulty in comparing the various interventions.

Future studies should include information on standard measures of adherence including persistence. These would be such things as medication possession ratio, proportion of days covered, and proportion of patients who reached a set threshold for adherence. This would aid in comparing interventions more effectively which can translate to applying more cost-effective programs. Lastly, the study only dealt with cardiovascular disease therapies and therefore costs for other disease states may differ and therefore the result may not be as generalizable.

**APPLICATION/IMPLICATION:** Even with all the unknowns in this study, it seems to provide a good estimate during the planning process of designing an adherence program. It also provides a gauge in which to compare how any IHS program implemented compares to others.

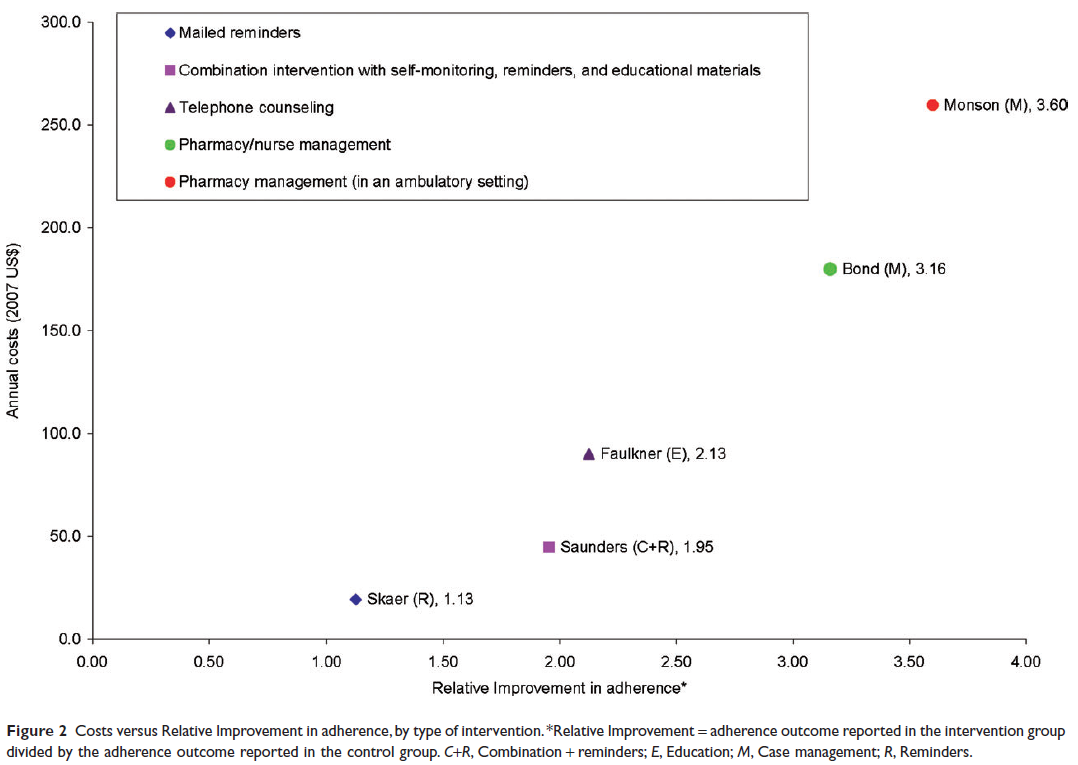
1. [Chapman, Richard Kowal, Stacey Cherry, Spencer Ferrufino, Cheryl Roberts,Craig Chen, Linda. The modeled lifetime cost-effectiveness of published adherence-improving interventions for antihypertensive and lipid-lowering medications.](C:\\Users\\yur3\\Desktop\\Cost-Benefit & Effectiveness Analysis\\The Modeled Lifetime Cost-Effectiveness of Published Adherence-Improving Interventions.pdf) *[Value in health](C:\\Users\\yur3\\Desktop\\Cost-Benefit & Effectiveness Analysis\\The Modeled Lifetime Cost-Effectiveness of Published Adherence-Improving Interventions.pdf)*[. 2010;13:685-694.](C:\\Users\\yur3\\Desktop\\Cost-Benefit & Effectiveness Analysis\\The Modeled Lifetime Cost-Effectiveness of Published Adherence-Improving Interventions.pdf)

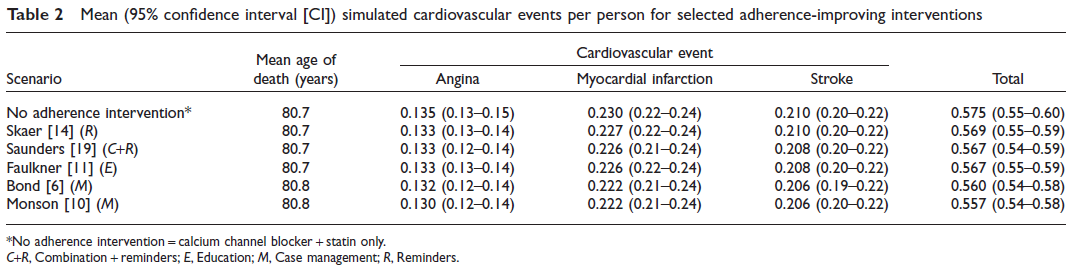
This article builds upon the work done in article 10 (conducted by the same main author) but adding in the effect of different levels of non-adherence and its burden. Use of this model, the researchers say, would simulate real-world clinical settings where patients’ adherence and persistence levels are well short of the optimal adherence stated in many trials. Similar to their previous study, they did a cost-effectiveness analysis for the variety of interventions from the point-of-view of payers.

The researchers used the same 23 interventions as in the last study and these were classified according to their primary method of delivery. Effectiveness was also assessed as relative improvement. Eligible studies had cost-effectiveness assessments done taking into account a variety of factors which are detailed in the article. As part of developing the model to simulate the burden that non-adherence has, the following were taken into consideration:

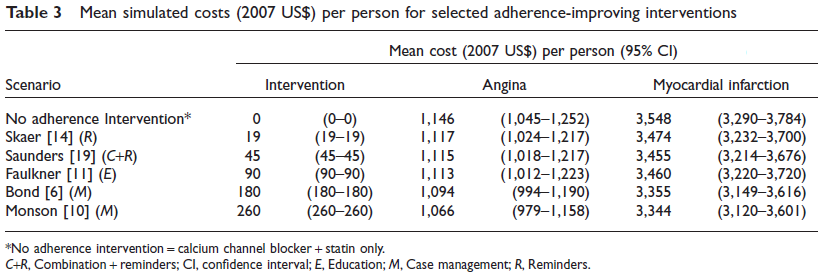
1. Patient characteristics were modeled after the Anglo-Scandinavian Cardiac Outcomes Trial–Lipid Lowering Arm (ASCOT-LLA),
2. The Monte Carlo microsimulation model estimated lifetime costs, morbidity, and mortality associated with adherence improvements from each intervention
3. Various models took into account variances between no treatment to ideal adherence
4. Relative improvement from each intervention study was applied to each patient’s baseline adherence
5. Proportion of days covered were used
6. Patients were allowed to transition between various levels of adherence and these were modeled after adherence patterns found in a representative population
7. Adherence distributions were modeled for each study.

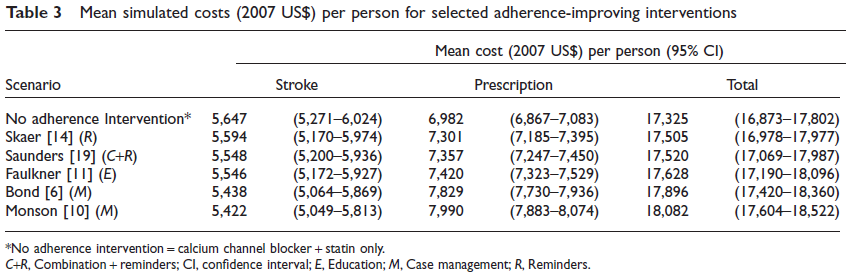
Of the 23 interventions, 5 of those were identified to be eligible for analysis. Improvement in adherence, measured in relative improvement, ranged from 1.13 (mailed reminders) to 3.60 (pharmacist management in an ambulatory setting). Annual costs for the interventions ranged from $19.18 per patient for mailed reminders to $259.56 per patient for pharmacist management in an ambulatory setting. A combination program involving self-monitoring, reminders, and educational materials was $25.46 more costly per patient than reminders alone. Pharmacist management in an ambulatory setting was $79.76 more expensive per patient than a combined pharmacist and nurse management program of compliance.



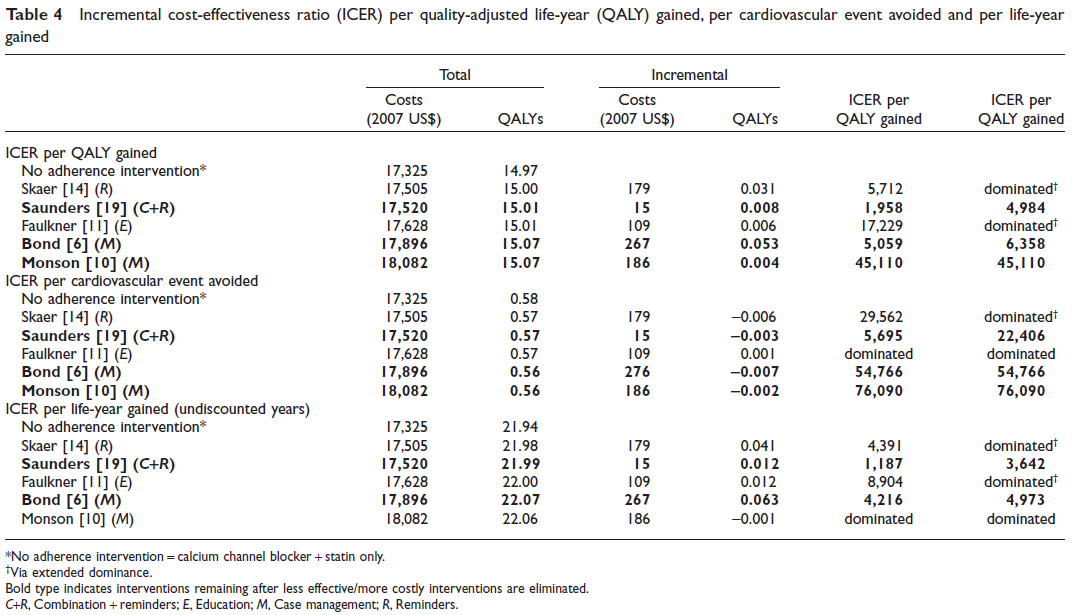


From their modeled simulations, costs ranged from $17,325 with no adherence interventions to $18,082 for pharmacist management in an ambulatory setting. Prescription costs contributed most to overall costs.





After eliminating less effective/more costly interventions, two interventions remained: self-monitoring, reminders, and educational materials (Saunders et al.); and a pharmacist/nurse management program (Bond and Monson). A summary of the findings are in Table 4 below.



The results of their sensitivity analysis found that QALYs gained increased, and costs decreased, as partial effectiveness increased. Generally speaking, they found that the combination intervention with self-monitoring, reminders, and educational materials (Saunders et al.), pharmacy and nurse management (Bond and Monson), and pharmacist management in an ambulatory setting (Monson et al.) remained relatively cost-effective.

In summary, despite incurring higher costs, they found that a pharmacist/nurse adherence intervention program (Bond and Monson) is cost-effective even when compared to pharmacist management in an ambulatory setting. This was because the design of the pharmacist management program can impact overall cost-effectiveness (e.g. paying additional costs for pharmacists’ time). The intervention by Bond and Monson also found a significant correlation between blood pressure control and compliance (refill patterns). The researchers of this study confirmed their earlier analysis that intensive interventions involving pharmacist management provided the most improvement in adherence. Also, interventions having extensive education improved adherence and those with more than one contact with follow-ups increased relative improvement. The authors note that a number of factors must be taken into account when evaluating cost-effectiveness such as cost of medication resulting from different levels of adherence over a lifetime or reduction in costs resulting from reduced use of health-care services.

**CRITICAL ANALYSIS/LIMITATIONS:** Similar to the last study, publication bias and heterogeneity needs to be considered. Limitations to the cost-effectiveness model were referred to another article which they cite.

Articles Reviewed

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Piette, J., Heisler, M., & Wagner, T. (2004, October). Cost-Related Medication Underuse Among Chronically III Adults: the Treatments People Forgo, How Often, and Who Is at Risk. *American Journal of Public Health*, *94*(10), 1782-1787.

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U.S. Commission on Civil Rights, Broken Promises: Evluating the Native American Health Care System, July 2, 2004.

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Annotated Bibliography

Borger, C., Smith, S., Truffer, C., Keehan, S., Sisko, A., Poisai, J. & Clemens, M.K. (2006). Health Spending Projections Through 2015: Changes On The Horizon. *Health Affairs*, *25*, W61-W73.

*Article Summary*

In this article Borger, Smith, Truffer, et al. provides information on forecasted spending through 2015. The purpose is to give the reader the needed information on the economical impact of past and current spending on the future funding of healthcare. Since 1993, when the national health expenditure was just short of $1 trillion dollars, spending has increased yearly. By 2010, the national health expenditure should reach approximately $3 trillion dollars and by 2015 will reach a $4 trillion dollars. According to Borger et al., the average annual healthcare cost per individual was increase to $9.147 and by 2015 will reach $12,320. This averages out to about a 3.8% growth in healthcare expenditures yearly.

The authors further describe the impact of spending on public funding seems daunting where Medicare will be at a growth rate of 8.8% by 2015. What this means is that with current projection by 2015 the annual cost of Medicare will be $792 billion dollars. The picture looks similar with Medicaid spending will reach $669.7 billion dollars. With the additions to the Medicare program and the changing environment of private payers the outgrowth of economy based upon projects compared to the overall economy growth; the need to reassess public health spending as by 2015 one out of every five dollars spent for healthcare will be require for healthcare.

The authors conclude that there may be dramatic changes in healthcare spending especially with the Medicare Modernization Act and other components of healthcare spending. The challenge to the future funding of healthcare is the quickly expanding Medicaid and Medicare spending. Cost sharing will become an important part of the funding for healthcare over the next decade and will be integral in keeping up with the supply and demand of healthcare spending.

*Critical Analysis of the Article*

This article provides important information on the current and future spending for healthcare. The authors provide graphs and figures that show the spending of healthcare and economic forecast. The impact on the gross domestic product and methods to possibly achieve a balance in the demand for healthcare is described throughout in the article.

The article provides needed information for healthcare providers and organizations in assessing the healthcare spending and planning. The challenge in this article is applying the methods is mainly determinate on federal and state application and intervention. Even so, the article is important in providing an outlook for the future spending of healthcare.

Annotated Bibliography

Catlin, A., Cowan, C., Heffler, S., & Washington, B. (2005). National Health Spending In 2005: The Slowdown Continues. *Health Affairs*, *26*(1), 142-153.

*Article Summary*

Catlin, Cowan, and Heffler provide an overview of spending on healthcare in 2005. The purpose of the article is to give the reader needed information on public spending and the impact of various programs on public spending. The authors initially note that for the general population cost of healthcare is $6,697 per person. This contributed $2 trillion to the overall economy representing 16 percent of the gross domestic product. The public spending on healthcare was over $900 billion and outspent private healthcare spending for healthcare. This spending was mainly reflected in Medicare and Medicaid spending. Each one will be briefly reviewed as the impact and the challenge facing the federal government in keeping up with the increasing demand for healthcare spending.

In 2005, the author note, over $342 billion dollars was spent on Medicare. The spending went toward several services e.g. clinical, physician, hospital, medical supplies. These services have been increased with the introduction of Medicare Part D. The impact of that program on public spending has not been shown as of Catlin’s et al. article however it is expected to increase the amount of spending by Medicare. As of 2005, the overall impact of Medicare on public spending was 30 percent of the overall government spending on health.

During the same time, Medicaid spending was $321 billion dollars. The cost of prescription medication accounted for two-thirds of those costs for public spending on healthcare for Medicaid. While the usage of the Medicaid program seems to have slowed over the past few years it is still a significant part of the overall spending for public health.

Private spending contributed to over $1 trillion dollars for 2005 (Catlin, et al., 2007) Almost $700 billion dollars was from health insurance. Out of pocket expenses for healthcare were $249 billion dollars. Consumer driven health plans and health saving accounts seem to be minimal at this point on the impact of private spending.

The authors conclude that while only 2005 numbers were presented in this section, overall the spending for healthcare has slowed over recent years. This is a positive for healthcare spending and cost containment however more time is needed to understand the impact. What is important about this trend is that healthcare is growing at the same rate as the economy and is not outpacing the economy.

*Critical Analysis of the Article*

This article provided an important overview of current public and private spending on healthcare. The authors provide a thorough perspective on healthcare and add various charts and graphs that affect the healthcare dollar. The authors’, as noted above, analysis demonstrates an environment that is meeting the supply and demand needed to sustain a healthy economy. This is consistent with the information provided by Borger, Smith, Truffer, et al. (2006) regarding the impact of healthcare and the effect on healthcare spending..

While the article provides an important glimpse of the status of healthcare spending, it does not provide needed information on areas that may affect healthcare such as the Medicare Modernization Act. This Act and future funding needs and changes especially with the population aging and living longer has an impact that clearly needs to be addressed. This should not diminish the impact and need for current information on healthcare and the funding needs for public spending which this article provides.

Annotated Bibliography

Dezii, C.M. (2001). Persistence With Drug Therapy: A Practical Approach Using Administrative Claims Data. *Managed Care*, 42-45.

*Article Summary*

Dezii, a senior manager for Bristol-Myers Squibb, provides an interesting to claims data evaluation. The purpose of the paper was to determine compliance by using an approach labeled Estimated level of Persistence with Therapy (ELPT). The approach, as the author states, “…inexpensive, unobtrusive ways to determine the extent to which patients are filling their prescriptions for long-term therapies or treatments for chronic disease on a regular basis (p. 42).”

The author first identifies how a refill history of medication use is critical in identifying who complies with therapy. He further then defines a period of refill of 1.5 times the numbers of day’s supplies as an adherence measure. Further, the author gives some scenarios as to how this ratio works within the approach of ELPT. By using this ELPT approach, the author feels as though non-adherence behavior becomes apparent.

Further explanation to this approach, the author continues to define some terms. Medication possession ratio (MPR) identifies the amount of day’s supply a patient has per prescription and churners or people that are persistent with the medications however take time off at times when taking their medications.

The author concludes that the ELPT measure can be effective in identifying patient adherence. He further discusses that creative efforts are needed in achieving adherence. Finally, the author note that as healthcare organizations are very busy, that finding a time and cost effective method for determining adherence is important in achieving good patient adherence.

*Critical Analysis of the Article*

The article by Dezii and the ELPT method was interesting in the use of having a grace period for adherence while tracking information from pharmacy refill data. The author did, as he also concluded, provide a measure that can look at adherence in patients who he defined as “churners.” The author also made mention of the medication possession ratio, which seemed similar to ELPT in function.

Limitations to this article were the ELPT and finding usefulness to this measure. While the author noted that this should be a time and cost effective measure, understanding how to gather data and utilize seemed confusing with the various scenarios the author provided. The author made a statement about the MPR and its effectiveness beyond that of the ELPT allows the reader to consider the true functionality of the ELPT in adherence.

The author should be commended, as he stated, in trying to come up with a measure for adherence and using creativity in trying to achieve an effective measure. While this measure may not be what will achieve better adherence exploring different measures will be important in identifying and eventually increasing the ability to improve patient adherence to medication.

Annotated Bibliography

Fairman, K. & Motheral, B. (2000). Evaluating Medication Adherence: Which Measure Is Right for Your Program? *Journal of Managed Care Pharmacy*, 6(6), 499-504.

*Article Summary*

The article by Fairman and Metheral describe the impact of patient medication adherence and methods to measure adherence. The purpose of the article was to provide various models for adherence and provide the advantages and disadvantages to the approaches to measure adherence. The authors start out with defining compliance and adherence.

According to the authors, compliance is cited as “the extent to which a person’s behavior coincides with medical or health advice. (p.499)” The term adherence has the same definition. The authors note that adherence seems more palatable than compliance. The article then describes the various methods of adherence study however note that there are no true “gold” standards for measuring. They further note that measures fall into either direct or indirect measures.

Direct measures consist mainly of drug monitoring and direct observe therapy. The advantage to direct measures is that the researcher of provider knows the medication is being taken or not taken. The disadvantage is that this type of measurement is costly and is not necessarily accomplished through the normal healthcare setting.

Indirect measures consist of pill counts, self reports, claims and pharmacy data, and surveys. The advantages to the indirect measure are the potential ease in collecting this type of data. A further advantage is that the information is from the patient perspective. Using claims data is advantageous in that it gives a history of the patient and their medication use. The disadvantage is that the information may be biased from the patient perspective. Diaries may be inaccurate and pill counts can be altered. Claims data may represent patterns but are unable to identify if the patient actually took the medication and was a majority of their focus.

The authors conclude that there may be more than one method needed to determine adherence. The impact of several measures for patients that are suspected of having non-adherence to medication is critical to have effective patient outcomes. They further conclude that pharmacy claims data is useful as an initial starting point for determining patient adherence however should not be the only choice.

*Critical Analysis of the Article*

The authors of this paper described the advantages and disadvantages of adherence strategies. Their focus on claims data was important in that they described various data techniques which would assist in identifying adherence. The impression from the reading is that adherence is challenging to identify without one true “gold” standard.

While the authors provided helpful information and a model for developing datasets, their article could have brought more information on obtaining claims information in order to achieve the datasets. The average healthcare center may have bits and pieces of data but may not be able to achieve data that would reflect a true picture of adherence using claim information.

Annotated Bibliography

Goicoechea, M., Best, B., Seefried, E., Wagner, G., Capparelli, E., & Haubrich, R. (2006, April) Failure of Modified Directly Observed Therapy Combined with Therapeutic Drug Monitoring to Enhance Antiretroviral Adherence in a Patient with Major Depression. *AIDS Patient Care & STDs*, *20*(4), 233-237. Retrieved July 1, 2007, from Academic Search Premier database.

*Article Summary*

In this article, Wagner and Rabkin review and evaluate self reporting compared with objective measures to determine adherence. The purpose of their article is to compare adherence of self reporting and objective measures as they note that self reporting is more accurate among people who report missed doses. The authors choose to review patients with human immunodeficiency virus (HIV) because of the adherence therapy problems because of the complexity of therapy.

As mentioned, the authors selected HIV patients and choose patients not on protease inhibitors and less than three antiretrovirals. Most of the people in the study were male and black. The participants were of various levels of HIV infection including acquired immune deficiency syndrome (AIDS).

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The results from the study showed that self reporting was higher than the objective measure from the electronic measure. The results however did not provide statistical significance or correlation however; the authors note the small sample size as being a factor. They did conclude that overestimation does occur with self reporting and coincides with other reports in the literature.

*Critical Analysis of the Article*

This authors in this article conclude that overestimation occurs when self reporting is compared some a direct measure of adherence. The authors note their own limitations in that placebos may have been an issue with adherence. They further relate the small sample size as well as the social status and impact.

Generalizability is important in studies when reporting in the literature. As in the articles by Fairman and Motheral (2000) as well as Dezii (2001), finding the commonality among adherence will be critical for improving adherence in this country. If the results can not be applied to the general population, it makes it difficult to apply unless you have a similar population which you are assessing. In this study, it is difficult to generalize the results.

While the article has its limitation, the authors do bring up an important aspect of adherence. The ability to determine information from patient reports is critical for assessing patient care and developing healthcare needs and policy. If overestimation occurs, that can affect how healthcare organizations approach adherence. The authors provide a methodology for assessing this issue however the small sample size limits the applicability.

Annotated Bibliography

Hong, T., Oddone, E., Dudley, T., & Bosworth, H. (2006, February). Medication barriers and anti-hypertensive medication adherence: The moderating role of locus of control. *Psychology, Health & Medicine*, *11*(1), 20-28.

*Article Summary*

Hong, Oddone, Dudley, and Bosworth describe the impact of cardiovascular complications and stroke as leading causes of death in the United States. The purpose of their study is determined how the locus of control impact adherence as a perceived barrier. The authors define locus of control for this study as “the degree that an individual believes his or her health status is influenced by one’s own behavior, whereas external health locus of control refers to the belief that other people, chance, fate or luck determines one’s health status.”

The authors enrolled 588 veterans with hypertension and obtained a baseline interview. Most of the participants were male with a majority being white and almost half having a college education. The measure used was a four item Moriskey Self-reported Medication –Taking Scale. The scale uses strongly agree, agree, disagree, and strongly disagree. Barriers identification was use with a nine item measure including side effects, forgetting, confusion, keeping track among others.

The internal locus of control was measured with three questions. The three questions are listed:

“The main thing which affects my high blood pressure is what I myself do.”

“If I take the right actions, I can maintain my blood pressure control.”

I have control over lowering my blood pressure.”

These patient either answered agree or disagree to the questions. The measure was then analyzed using a hierarchal regression analysis.

The authors’ analysis of the study demonstrated that higher scores of locus of control correlated with adherence and perceived barriers to adherence. The regression analysis applied to medication barriers and internal locus confirmed the improved adherence. They displayed this with a graph with a y-axis of adherence and an x-axis of medication barriers that graphed low, medium and high internal locus.

The authors conclude that increased barriers results in poor adherence in veterans. Their results coincide with other finding on internal locus of control. While other studies for locus of control has focused on health outcomes, the authors feel that this is an original research objective that found adherence measures improving with high locus of control. Finally the author note how their research shows that patients may be adherent to medication regimens with low barriers however when barriers increase, adherence decreases.

*Critical Analysis of the Article*

This article provides an important component for healthcare organizations in utilizing strategies for improving medication adherence. The study was conducted to focus in internal locus of control and translated into medication adherence and perceived barriers. This article adds to the current knowledge for adherence strategies and the three questions design for determining locus of control potentially adds to identifying patients with adherence problems.

The article focused on mainly male veterans with almost half having a college education. This does not reflect the general population and applying the locus of control to a more diverse population. The challenge of this article is the consistency knowledge of patient behavior needed to apply the outcomes.

Even with these limitations, the article adds to the literature and provides an important component to the adherence strategies healthcare organizations need in order to improve health outcomes.

Annotated Bibliography

Morgan, T. (2001, September). The Economic Impact of Wasted Prescription Medication in an Outpatient Population of Older Adults. *Journal of Family Practice*, *50*(9), 779-781.

*Article Summary*

In this article, Morgan provided an overview of what the author calls wasted medications. The purpose of the study was to assess the costs, rate, and reasons for medication waste. The author also hopes to determine why patients do not finish their medication regiment.

The study used a cross sectional survey from May 1999 to November 1999. Interviewers reviewed patients’ medication use with home visits and initiated a questionnaire at each visit. The study focused on 73 residents of a community retirement center that were older than 65 years of age. The residents’ prescriptions were fully covered without copay. The demographic profile included varying degrees of education and chronic medical condition status.

The results from the study provided some interesting information regarding most frequently wasted prescriptions and most costly prescriptions. The amount of medication wasted was approximately 2.3% of the cost of the annual cost of prescription medications. This averaged to an annual cost of $1302.78 per participant in the study. The top 10 of medications wasted and most costly prescriptions and are listed.

|  |  |
| --- | --- |
| **Most Frequently Wasted Classes** | **Most Costly Wasted Classes** |
| Antibiotics | Benzodiazepines |
| Benzodiazepines | Antidepressants |
| Antihypertensives | Antihypertensives |
| Antidepressants | Nonsteroidal Anti-inflammatories |
| Glaucoma medications | H2 antagonists |
| Antidiarrheals | Antihistamines |
| Alpha 1 blockers | Anticonvulsants |
| Intranasal steroids | 5 alpha reductase inhibitors |

The authors concluded that the main reasons for wasting medications were resolution of condition and perceived ineffectiveness. The other reasons for wasted medications were prescription change, adverse effects, nonadherence, and medication expired. They recommended that physicians should judiciously prescribe medication and promote medication adherence.

*Critical Analysis of the Article*

The author in this study provides some important information on waste of prescription medication. The identification of classes of waste and costs of waste provide needed information regarding types of medications that may give healthcare organizations the opportunity to improve healthcare funding for medications. Furthermore identifying contributing factors to waste gives further information for improving healthcare.

The limitations to this study are the small sample size. The authors themselves note that the participants in the survey may have had forgotten some components of medication use. Even with these limitations, this study provides some important information and needed follow-up for medication waste within the healthcare setting.

Annotated Bibliography

Osterberg, L. & Blaschke. T. (2005). Adherence to Medication. *New England Journal of Medicine*, 353, 487-497.

*Article Summary*

The article by Osterberg and Blaschke focused on medication adherence and its impact of non-adherence on healthcare costs and outcomes. The purpose of the article was to provide measures for adherence and identify barriers to achieving positive adherence to medications. The authors initiated their discussion citing information regarding the costs of non-adherence to the healthcare costs of approximately $100 billion a year to the system. Because of the increased costs to the healthcare system, identifying non-adherence to medications is critical not only for the patient outcomes but also for sustaining an effective healthcare system. The range of non-adherence is from 0 to 100 percent. The authors provide further ranges which include average adherence of the general population to be in the range of 33 to 69 percent. Within the article they discuss various measures and predictors that may assist the clinicians and healthcare executives in achieving responses that may improve healthcare outcomes and costs.

Within the article, the authors provide a model that represents the factors involved with the patient, provider, and healthcare system interaction. Negative interactions at any of the three vectors can provide the impetus for poor adherence and non-compliance with the regimens. Within each of the vectors there are predictors that the authors provide that affect adherence. These predictors are listed:

Presence of psychological problems

Presence of cognitive impairment

Treatment of asymptomatic disease

Inadequate follow-up or discharge planning

Side effects of medications

Patients lack of belief in benefit of treatment,

Patient’s lack of insight into the illness

Poor provider-patient relationship

Presence of barriers to care or medications

Missed appointments

Complexity of treatment

Costs of medication, co-payment, or both

Identifying the predictors allows healthcare executives and providers to provide interventions in improving adherence rates.

The authors further review ways of measuring adherence, each with advantages and disadvantages. They provide both direct measures and indirect measures in determining adherence rates or effectiveness. The one accurate method for determining adherence is direct observe therapy, however the challenge of witnessing and assuring the patient has taken the medication is not feasible to the healthcare system. The other methods are based upon records or observations that have their own difficulties in assuring adherence.

The authors further describe some disease states that have specific challenges in order to achieve good adherence to medications. The four areas are human immune virus infections, hypertension, psychiatric illness, and pediatric illnesses. These four areas provide some unique challenges, according the authors, which involve identification and presentation of the disease and mental capacity to understand the ramifications of the illnesses.

The authors conclude that their research for validated methods of determining adherence is complex with many different factors involved in why patients do not take their medications. They further conclude that collaboration, education, and regimens that are easy to understand will assist the healthcare system in achieving the outcomes expected. Finally, they recommend a non-judgmental approach to patient medication therapy in order to create an atmosphere of collaboration with the healthcare system, patient, and provider.

*Critical Analysis of the Article*

The author of this paper provided a multitude of information regarding adherence and effort to change adherence rate. Their model of the physician, patient, healthcare system provides an effective method in understanding the relationship and complexity involved with adherence and the patient. The further examples and discussion on barriers to adherence and measures of adherence provide the reader with a basic level of understanding how the model is impacted by these variables in patient care.

While the authors provided a helpful model and some research into the adherence issue, the article was lacking in providing the reader with a more useful method in measuring adherence. They left with the impression that there really is no effective way to determine adherence. The article did provide a valuable reference list which includes many studies and articles regarding adherence for the healthcare provider and system to read or review in order to assist in the healthcare adherence issue.

While the article may have been lacking, it should not reflect on the importance of adherence to the overall costs to the healthcare system. The New England Journal of Medicine is one of the preeminent journals in the nation. Bringing to light the issue of adherence and the impact it has on healthcare dollars is significant especially when becoming a part of the healthcare landscape and thought through a peer reviewed journal like the New England Journal of Medicine.

Annotated Bibliography

Ruoff, G. (2005, October). A method that dramatically improves patient adherence to depression treatment. *Journal of Family Practice*, *54*(10), 846-851.

*Article Summary*

In this article, Ruoff describes the impact that depression may have on adherence to medication therapy. The purpose of this original research is to assess a depression flow sheet and its impact on patient adherence. The authors note that depression can have an adherence rate as low as 33 percent.

The authors conducted the study during 2003 and 2004 in medical practices of urban and suburban patients. They enrolled 153 patients that were newly diagnosed with depression. The patients were administered a 9 question survey with a sensitivity of 73% and specificity of 98 % to determine depression along with differential diagnosis. The flow sheet consisted of demographic information along with various components in assessing depression and documentation of the follow-up for both patient and physician. The study was conducted over one and one-half years and charts were audited for data.

The results from this study demonstrated that those patients whose follow-up was consistent had 66% adherence rate. After reviewing the charts, the authors noted that in the 9 question survey patients score decreased overall with symptoms of depression indicating improved outcomes for resolving depression. The depression scores decreased from 80% with moderate or moderately severe depression to 40 % with moderately or moderately severe depression.

The author concludes that the communication to patients and follow-up of depression symptoms using the flow sheet improved adherence to medication therapy. They further note how communication of adverse effects of medication is also important in the continued adherence to medication therapy. The author further feel there is generalizability may mainly apply to similar practices which are a limitation to their study.

*Critical Analysis of the Article*

The conclusion of a 66% improvement of adherence as compared to the 33% reported in literature is significant based upon the data and information from the authors. The applicability of the flow sheet may be applied to healthcare organizations. The limitation to this, as already stated by the authors, is the applicability to other organizations.

The article provides a method for evaluating and improving adherence. The time and effort to maintain such a tool may not be achieved by many organizations because of the time element involved. Since many of today’s healthcare costs are based upon acute finding and cost minimization, the use of a tool may not be seen as feasible for organizations to implement.

While this may provide a barrier the authors have shown that tools are available and can be utilized to improve patient adherence.

Annotated Bibliography

Wagner, G., & Rabkin, J. (2000, August). Measuring medication adherence: are missed doses reported more accurately then perfect adherence? *AIDS Care*, *12*(4), 405.

*Article Summary*

In this article, Wagner and Rabkin review and evaluate self reporting compared with objective measures to determine adherence. The purpose of their article is to compare adherence of self reporting and objective measures as they note that self reporting is more accurate among people who report missed doses. The authors choose to review patients with human immunodeficiency virus (HIV) because of the adherence therapy problems because of the complexity of therapy.

As mentioned, the authors selected HIV patients and choose patients not on protease inhibitors and less than three antiretroviral. Most of the people in the study were male and black. The participants were of various levels of HIV infection including acquired immune deficiency syndrome (AIDS).

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Annotated Bibliography

Wing, R.R., Phelan, S. & Tate, D. (2002). The Role of Adherence in Mediating the Relationship Between Depression and Health Outcomes. *Journal of Psychosomatic Research*, 53, 877-881.

*Article Summary*

In the article by Wing, Phelan, and Tate, the authors initially review the association of poor health outcomes and the impact of adherence and depression on those outcomes. The authors’ goal for this paper is to examine the relationship between outcomes, adherence, and depression. They provide the definition of adherence as “the partnership between patient and provider in all aspects of medical care” and choose to use this term in place of compliance.

The authors ask two questions in which they review, “does depression affect adherence” and “does adherence affect outcome?” To answer the question about depression and adherence, they cite a meta-analysis of literature from 1968 to 1998. The analysis showed that there is a consistent relationship between depression and adherence. They further review studies that are more recent and reports from those studies indicated a relationship between decreased adherences in the presence of depression.

In the authors’ review of outcome, they reviewed adherence and morbidity and mortality for patients with cardiovascular risk. In their review the authors note that non-adherent patients poorer outcomes than those that were adherent. In this article, they also observed behavior adherence and outcomes but found it difficult to determine the relationship between the two.

The authors finally review the mediation of adherence between depression and health outcomes. In a review of whether the level of adherence is weakened in the presence of depression and outcomes was assessed. In their review the authors found that in the presence, adherence did not diminish the effect of depression on the outcome. They finally conclude after a reviewing other studies that there is no evidence to support mediation between health outcomes and depression.

The authors provide some future direction for research for adherence and outcomes. They first recommend the need for better methods to assess adherence. The issues of self-reporting as well as well as biased answers from those patients that are depressed affect the ability to effectively determine adherence. They further recommend reviewing the adherence strategies of simplifying regimens in patients to improve adherence. This coincides with the improved relationship healthcare organizations, physicians and patients need as partners in their healthcare.

*Critical Analysis of the Article*

The article by Wing et al. provides information regarding the need to explore the relationships between disease, adherence and outcomes. This relationship is important in integrating outcome management for healthcare organizations to effectively treat patients with co-morbid conditions. Even though the authors were not able to provide a mediating effect they did show that adherence does affect depression as well as outcome.

The article provided some important questions for healthcare administrators and providers in achieving good outcomes for patient care. The challenge of this article is applying the results to average patient care. The impact of healthcare decisions is greatly affected by the ability to understand adherence of patients.

While the article did not support the mediation of adherence between depression and health outcomes, the article did incorporate some important concepts with regards to adherence direct impact on disease state management. The suggestions for future research are applicable for many organizations as they look to improve adherence within their patient population.