Medication adherence and its relationship to the therapeutic alliance: Results from an innovative pilot study within a community pharmacy MTM practice

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ABSTRACT
Objectives: *To determine whether patients who received Medication Therapy Management (MTM) from community pharmacists using a brief scale to measure Therapeutic Alliance (i.e., MTM + TA) would show better medication adherence than patients who received MTM without use of the TA scale (MTM only).* ***Design:*** *Quasi-experimental, using a direct intervention group (MTM + TA) and a comparison group of randomly selected claims records from patients who received only the MTM service (MTM only). We used a doubly robust propensity score approach to estimate the average effect of therapeutic alliance on medication adherence. The analysis was limited to the following broad medication categories: antihypertensives, antidiabetic agents, and antihyperlipidemics.* ***Setting:*** *The direct intervention group included patients receiving MTM services from pharmacists in a community pharmacy chain setting.* ***Participants:*** *After matching with claims data, the direct intervention group was n=117, with an average age of 76.4. The comparison group was n=146, with an average age of 76.2.* ***Intervention:*** *Administration of two brief scales designed to measure general health outcomes and TA within the context of MTM (with focus on TA scale administration).* ***Main Outcome Measures*** *Proportion of Days Covered (PDC) and PDC80.* ***Results:*** *Using the therapeutic alliance scales in the context of community pharmacist-provided MTM was associated with a 3.1 percentage point increase in patients' overall PDC (p<.001) and an increase of 4.6 percentage points in PDC80 (p=.02) as compared to patients receiving MTM without use of the therapeutic alliance scales.* ***Conclusion:*** *Measuring therapeutic alliance in the context of MTM is associated with improved medication adherence and represents one strategy for enhancing the effectiveness of MTM encounters. Furthermore, administration of the therapeutic alliance scales used very little time; therefore it is likely feasible for pharmacists to routinely use the scales in their practice.*

Introduction

Medication non-adherence, or deviating from the specific prescription of a physician or other prescribing healthcare provider, is a significant clinical issue.[1] Numerous studies have found a relationship between non-adherence and worse health outcomes. For example, medication non-adherence in patients with diabetes mellitus is associated with greater risks of hospitalization and mortality.[2] Non-adherence to antihypertensives is a contributing factor to persistent elevated blood pressure.[3] Elderly persons have shown significant declines in adherence to statin therapies, which can exacerbate or lead to clinical events associated with cardiovascular disease.[4] Further, it is suggested that medication non-adherence may lead to increased hospital admissions and contribute to upward of 100 billion dollars in annual healthcare costs.[5]

Reasons for medication non-adherence are many and broad [6,7] and there are various types of interventions designed specifically to address non-adherence.[8,9] McDonald and colleagues note, however, that "current methods of improving medication adherence for chronic health problems are mostly complex, labor-intensive, and not predictably effective."[10]

Therapeutic alliance is a concept that was described originally in the context of psychotherapy, but has since spread

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throughout the healthcare community. Therapeutic alliance is broadly defined as a "collaborative bond" between a patient and a therapist[11] although one no longer needs to be a therapist to develop this particular relationship with a patient. The therapeutic alliance is based on the premise that the healthcare provider and his or her patients are equals, with both parties making decisions and acting together toward common goals. Studies of therapeutic alliance in psychotherapy suggest that therapeutic alliance is predictive of better clinical outcomes.[12]

With regard to therapeutic alliance in pharmacy practice, Berger emphasizes its importance and writes that "pharmaceutical care requires a much more intimate and intensive relationship between the pharmacist and patient than simple pharmaceutical dispensing."[13] Berger notes that pharmacist competence, trustworthiness, and caring are core of the therapeutic alliance between a pharmacist and his/her patients. More importantly, he notes that patients will be less likely to discuss medication problems with their pharmacist if patients perceive they will be judged or scolded for non-adherence.[14] Thus, pharmacists must appreciate their role is extending beyond dispensation and that therapeutic relationships with patients is both desirable and achievable. An indication of pharmacists' positive attitudes towards therapeutic alliance is observed in one study that suggested 80% of pharmacists believed that establishment of a therapeutic alliance was the highest priority in counseling, and 76% believed that "enhanced health outcomes would follow from mutual and cooperative interactions."[15]

The practice of pharmacy is indeed moving beyond mere dispensing of medications. Routinely, pharmacists are providing medication therapy management (MTM) services.[16] MTM refers to a range of pharmacist provided services that include the assessment of patients' medications in order to achieve optimal medication regimens, improve adherence, enhance therapeutic outcomes, and reduce costs. MTM gives pharmacists the opportunity to identify and discuss medication-related problems, including medication non-adherence and its numerous causes.

To further explore the relationship between medication adherence and therapeutic alliance in the context of pharmacy practice, we undertook a study to investigate whether the administration of two brief scales, the Outcome Rating Scale (ORS) and the Session Rating Scale (SRS), by pharmacists providing MTM would increase medication adherence among their patients, thereby serving as a potential innovative strategy for enhancing the provision of MTM services by community pharmacists. Thus, we note that the use of the ORS and SRS would be an addition to the services already provided in MTM.

The ORS and the SRS were developed and validated for use in psychotherapy as tools for monitoring and enhancing client outcomes and therapeutic alliance.[17,18] Within this setting, the therapist uses client ratings from both scales to create a "client-directed and outcome- informed" process. Clients provide information on the scales, and therapists use that information to provide feedback both within a session and across sessions. The use of a continuous feedback system based on "practice-based evidence" (i.e., the data from the scales) can increase effectiveness and enhance outcomes. Results from one study where therapists used the ORS and SRS as a means of providing feedback with patients suggested greater and more efficient treatment gains than a "therapy-as-usual" comparison group.[19] Diabetes care managers have also successfully used the ORS and SRS with patients and have demonstrated improved diabetes-associated outcomes.[20]

We believed that the use of the ORS and SRS in pharmacy practice might produce similar results as those shown in psychotherapy and would enhance the effectiveness of pharmacists' clinical services. To implement the scales in the context of MTM, only one minor modification to one scale (SRS) was made: in one question the word "therapist" was changed to "pharmacist." All other questions were not changed, and we believed their reliability and validity was applicable to the clinical context of community pharmacist-provided MTM services.

Objectives

We aimed to examine the relationship between therapeutic alliance and medication adherence in the context of pharmacy practice. The primary hypothesis was that patients who presented for MTM sessions with community pharmacists and received the ORS and SRS during the MTM sessions would show better medication adherence than patients who received MTM sessions but did not receive the ORS and SRS.

Methods

We collaborated with a national leader in MTM services who introduced us to a partnering pharmacy chain, Kerr Drug. Kerr Drug provides MTM services to Medicare Part D patients (per the MTM Core Elements, including services such as comprehensive medication reviews, prescriber consultations, patient compliance consultations, patient education and monitoring, physician collaboration and consultation and over-the-counter consulting). Most of the patients receiving MTM services have chronic conditions such as diabetes,

hypertension, hyperlipidemia. Six pharmacists at Kerr Drug volunteered to participate in the study. The intervention was defined as the use of the two scales in the context of an MTM interaction where pharmacist and patient had the opportunity to communicate (e.g., during a comprehensive medication review or follow-up session). Pharmacists received a one-hour training in the administration and interpretation of the scales prior to project implementation. Patients could receive up to three interventions per the study protocol (to measure responses over time), however there were no criteria used to determine the number of interventions a patient would actually receive.

The study protocol was approved by both the University of Pittsburgh IRB and Western IRB. Pharmacists invited their patients to participate in the study, and the patients were provided with an informational script detailing rights as a study participant. Patients provided consent verbally, as a waiver of signed consent was granted by WIRB. Patients could receive up to three MTM sessions per the study protocol. Based upon initial power calculations, the target enrollment for the intervention group was 200 patients. Study enrollment began in November, 2008, with the target enrollment number met on March 12, 2009. Data collection for the experimental group was completed on July 31, 2009.

The study design called for pharmacists to provide the ORS and SRS within the context of MTM services. As such, scales could be administered "face-to-face" during MTM interactions or via telephone (if desired) during pharmacist- or patient-initiated follow-up sessions. The ORS was to be presented at the beginning of the MTM session and the SRS at the end of the session. Two versions of the ORS and SRS, written and oral, were made available to pharmacists and their patients and the version used was determined by patient preference.[1] For the written version, patients complete a visual analog scale, marking their scores with hash marks along a 10cm line for each of the four questions. There are no numbers on the scale; pharmacists use a ruler to measure the hash marks (from 0- 10cm) and note the score, where 1cm=1, 2cm=2, etc. For the oral version, pharmacists read questions to the patients and patients provide responses on a scale from 1-10.

The four items in the ORS ask patients to mark or rate from 1-10 their quality of life in the following areas: Individually, Interpersonally, Socially, and Overall. The four items on the SRS ask patients to mark or rate from 1-10 the therapeutic alliance with their pharmacist in the following areas: Feeling heard, understood, and respected (Relationship); the patient having the opportunity to talk about or work on what the patient wants to talk about or work on (Goals and Topics), Approach or fit with the pharmacist (Approach and Fit), and the degree to which "something is missing in the session" (Overall).

For each scale, there is a "clinical indicator" based on the total score (40) of each scale. A scale score below the clinical indictor (score of 25 on the ORS, score of 36 on the SRS) cues the provider to engage the patient and discuss the score *in toto* or in relation to a notably low item score. For example, on the SRS (the measure of therapeutic alliance), a patient may rate three of the four scale items with a "9", but rate one item a "4". The overall scale score would equal 31 and warrant further discussion, specifically (although not exclusively) to the item where the "4" was rated. So, if a patient rated the pharmacist a "4" in the Relationship category "feeling heard, understood and respected"), it would be necessary for the pharmacist to 1) note the rating at some point in the current or consequent interaction, 2) collaborate with the patient on ways to address and improve the rating and 3) re-measure at the next time point and assess the scores again. This feedback based process is used for both scales and across all 8 items. The main points are that 1) the pharmacist seeks to measure alliance and 2) used patient feedback as a means of improving alliance when applicable.

After administering and interpreting the scores in the context of an MTM interaction, pharmacists then faxed the hard copies of the scales to the data collection center at the University of Pittsburgh. Upon receipt, a confirmation email (including number of surveys received) was sent to pharmacists. Unclear or missing data were clarified or verified through email. Data were then hand-entered into a Microsoft Access database and bimonthly reports were sent electronically to each pharmacist. All data were organized according to patient identification number. Pharmacists were to retain hard copies of the scales in patient charts or refer to the report as basis for follow-up discussion with patients. Patients could be seen for up to a total of three MTM sessions in order to assess scores over time/Again, there were no criteria established for additional sessions, other than pharmacist and patient willingness and/or availability.

At the completion of the study, the list of enrolled patients was delivered to the MTM service provider for linkage of claims data within their system. Using this process, we were able to link 117 of the experimental group with claims data. A selection of comparable and de-identified claims data from

[1] The written versions of the ORS and SRS are copyrighted materials. The oral version of the questions are presented in the Appendix.

MTM service provider served as the comparison group (n=146). Pharmacy claims data for the study period were merged with individual MTM session data for both study groups. Claims data were available from May 1, 2008 through July 31, 2009. We divided these data into two study periods of equal length: before implementation of the project and after, to obtain a pre-scale implementation observation period that matched the follow-up time period.

Our primary outcome measures were Proportion of Days Covered (PDC)[21] and PDC80, where adherence is defined as a PDC of 80% or greater within a given interval.[22] The denominator for the PDC for a particular medication was the total time between the first fill date for the medication within the study period and the end of the study period. The numerator was the total days of supply within this same period. The supply for the last prescription in a study period was capped at the last day of the period so that no PDCs were larger than 1.

There is no a priori theory about therapeutic alliance (TA) having differential effect for adherence to different medications or by patients with different chronic illness. Therefore, our study included patients who were taking medications from at least one of three broad medication categories: antihypertensives (AH), antihyperlipidemics (AL), and antidiabetic (AD) agents (Table 1). We defined our sample in two steps. The first step was subsetting to a sample with specific medication classes. We included these classes of medications because they are associated with chronic diseases states (hypertension, hyperlipidemia, and diabetes) often experienced by patients utilizing community pharmacist-provided MTM. For our analysis, we assumed that any switching between specific medications within the same class was not a reduction in persistence. For example, a switch between atenolol and metoprolol was counted as one continuous prescription for purposes of calculating the PDC. We eliminated medications for which the patient only had one fill during the study period or patients whose claims record in either the baseline or follow-up period was less than 90 days. Excluding these patients reduced our original sample sizes from 159 to 134 in the intervention group and 178 to 156 in the comparison group. Our second step was to focus on a sample that had persistence in study medications in the periods before and after the study. This further reduced the samples of our intervention and comparison groups' numbers of 117 and 146, respectively. Notably, the average PDC for individuals eliminated was above 99% within each study group and regardless of whether their only observation was in the prior or post period. This similarity between the experimental groups implies a limited loss of differential treatment effect due to their exclusion.

Alternative measures

When patients had more than one qualifying medication, we averaged the PDC across the medications to produce an overall PDC and subsequent PDC80. We also include in our analyses several alternative measures. First, we calculated a Least-PDC measure that was the lowest PDC among a patient's medications. This allowed us to estimate the improvement in a patient's least adhered-to medication. We also constructed the Least-PDC80 measure in which the outcome was a dichotomous variable that indicated where the Least-PDC was greater than 80%. An alternative way of thinking of the Least-PDC80 highlights its clinical significance: if a patient's Least-PDC is greater than 80% then the PDC for *each* of that patient's medications is greater than 80%, which is an ideal adherence outcome for these chronic diseases.

We improved the accuracy and precision of our estimated effects by utilizing a double robust propensity score matching between our study groups and statistical modeling of improvements in our outcomes over time within patients. We compared baseline characteristics between our two study groups and analyzed their standardized differences[23] in variables with the inclusion of propensity score weights in order to assess balance. Balance assessment determines the degree to which the statistics for covariates of non-random groups have been adjusted to seem more like covariates under randomization. A common heuristic for whether a measure is balanced is if the standardized difference is less than 10.[24] Treatment effects for alternative outcomes were estimated. We also explored how sensitive our analyses were to alternative propensity score matching methods and model specifications as well as sub-samples based on medication groups and trimming based on propensity scores.

Propensity score matching allows us to adjust for observed patient characteristics that might have increased the likelihood of being in the treatment group.[25-27] The propensity score is a patient's probability of being in a specific treatment conditional on observed covariates. Conditioning on the propensity score match replicates some of the characteristics of a randomized controlled trial under certain assumptions.[28] Specifically, we estimated the probability of receiving TA-enhanced MTM using time invariant (age gender, and indicator variables of whether the patient ever had a prescription fitting our three major medication categories) and baseline-only characteristics (PDC, PDC80, Lowest PDC, number of visits to the pharmacy, number of fills for any prescription medication, and number of unique study medications, and length of claims record prior to study implementation) and several alternative specifications with interactions of these variables and squares of the continuous variables. All analyses were conducted using STATA 11 and

the DR and PSMATCH2 routines. We used standardized difference calculations[29] to measure the improvement generated by propensity score matching (sample balance assessment).

Our primary results are based on doubly robust propensity score models which combine standard inverse propensity score weighting and multivariate statistical modeling. This method is particularly useful for circumstances when there is continued imbalance in baseline measures, even after adjusting and re-adjusting balance. With a well-specified model, the method provides unbiased estimates of the effect of a treatment.[30] This approach also overcomes differences in outcomes prior to the intervention. With a simple post-intervention comparison of differences between groups or differences-in-differences estimation of TA's effect could be biased. Model-based estimates of TA's effect that included baseline dependent variables as controls could help reduce the bias but are themselves limited by the range of the outcomes. For example, we observe that the PDC80 is closer to 100% for the MTM group than for the MTM+TA group. Any spurious improvement (e.g., regression to a mean adherence level) will necessarily be smaller for the MTM than the MTM+TA group and would lead to an upward bias on the estimated effect of TA. We report the differences-in-differences results alongside our propensity score model results for comparison. For the binary outcome of PDC80, we employed a generalized linear model with a probit link function. For continuous PDC standard regression is used. In this manner, we gain the benefits of a comparison group, reduce bias from selection into treatment, and control for baseline outcomes and other characteristics. When estimating these models for the subpopulations based on medication group, we include both the specific medication group PDC and the overall PDC measures as baseline covariates in order to control for all the information describing a patients behavior regarding adherence.

Results

Six pharmacists participated in the study. Five (83%) are female and one (17%) is male. Other pharmacist characteristics and location of pharmacies (e.g., urban, suburban, rural) were not recorded. Pharmacists enrolled patients in twenty-eight (28) pharmacies. The mean number of stores covered by pharmacists was approximately 4.7 (range 2-7), and the mean number of patients seen by each pharmacist was 34 (range 5-60). We note the attrition of two participating pharmacists who left their pharmacies for other pursuits during the course of the study. The total number of participants enrolled was 201. Consequently, 134 participants (66.7%) received a second session, and 73 participants received a third session (36.3%). In order to alleviate survey burden, we did not collect any demographic data other than age and gender. More than two-thirds (70%) of the study sample were females. After matching with claims data, the direct intervention group was n=117, with an average age of 76.4. The comparison group was n=146, with an average age of 76.2. Anecdotally, pharmacists reported that patient ethnicity included, primarily, African-Americans, Caucasians, and Native Americans.

Main Outcomes

Propensity Score Adjustment Results

At baseline, demographic differences were minimal between the MTM+TA (N=117) and MTM (N=146) groups. Table 2A shows the unadjusted and inverse propensity-score weighted summary statistics for the two experimental groups. The two groups exhibit little difference in their interactions with the pharmacies during the 9 months prior to the implementation of the intervention. They both had roughly 20 visits and 37 fills for any medication. Likewise, both groups had prescriptions for an average of 3.1 unique study medications, counted by having had at least one fill for a prescription.

The statistics we present here for medications do not correspond directly with the included medications in our key outcome variables (PDC and PDC80), but they help to demonstrate potential differences in our study samples. Thus they are used in our propensity score model and as controls in the multivariate model because they are correlated with unobserved patient characteristics that could bias our estimates of TA's impact. For individual medication categories the two groups were similar. For example, around 89% of patients had at least one fill for an anti-hypertensive medication (not including combination medications that included an anti-hypertensive). There were differences in the prevalence of having filled at least one prescription from more than one medication category, although these were not statistically significantly different. For all of these pre-interventions patient characteristics we note the standardized differences before and after propensity score weighting. With the exception of the number of fills for anti-hypertensive and anti-diabetic medications the differences were less than 10 and for both of these exceptions the differences did decrease with the inclusion of weights.

Table 2B continues the comparison of the two study groups and focuses on the key outcomes PDC80 and PDC prior to implementation of TA. There is little difference between the study groups for days in the claims record. This variable represents the total time for which we have a record on a patient during the baseline period and is measured by subtracting the date of their first claim from the date of their

first MTM session during the TA implementation period. It provides a sense of the overall time for which we have data on patients during which we could measure their adherence. It is not necessarily the denominator for PDC calculations since those denominators are medication specific and are defined according to measurement rules defined in the methods section.

Baseline PDC80 is significantly different for the two study groups with the MTM group at 97.3 versus 88.9 for the MTM+TA group. Similarly, the MTM+TA group has a statistically significantly lower PDC, although the difference is much smaller (91.2 versus 94.5). The same pattern of worse baseline outcomes for the MTM+TA group holds for LeastPDC outcomes. The last column of Table 3 provides results for a comparison between the two groups using only their outcomes after the implementation of TA. This calculation ignores baseline values and thus the relative improvement over time. Again, the results are consistent with TA improving outcomes. Only PDC80 is not significant at the p<.1 level, though its magnitude is not small and its sign is positive. This is still suggestive of an effect, since when the groups are already close to PDC80 of 100% there is little room for relative differences. The final column combines the 'within group' and 'across group' differences and thus compares the relative improvements over time and finds large and significant effects for TA for all outcomes. Finally, we note that both the total days in the claims record and the denominators for calculating PDC do not vary significantly across our study groups improving our confidence that any improvement in PDC outcomes is due to improved adherence rather than superficial differences in lengths of medication persistence. Moreover, it is noteworthy that TA did not lead to significant changes in how long patients persisted in medications.

Although Table 3 is suggestive of TA having a positive effect, we feel that the use of the doubly robust approach is well justified and we expect significantly reduces bias due to our quasi-experimental design. Any selection into the TA group is arguably correlated with observable characteristics such as poorer adherence that can be alleviated using propensity score weighting while the doubly robust framework still permits the multivariate model with baseline adherence variables and other controls. Indeed the last three columns of Table 2B show substantial improvement in the balance between the two samples due to propensity score weighting. The PDC80 are closer (94.4 versus 93.7) with a relatively low standardized difference of 3.1. Differences in baseline adherence measures improve for all measures and all standardized differences are less than 10 except for Least-AH-PDC80 and Least-AL-PDC80.

Main effects

Table 4 reports the primary effectiveness results from our double robust model of outcomes. We found that MTM+TA led to a PDC80 rate that was 4.6 percentage points higher than MTM alone (97.0 versus 92.4). The effect was statistically significant at p=.020. Stated alternatively, MTM+TA had an average treatment effect of 4.6 on the rate of PDC80, or a roughly 4.9% improvement over no treatment. This improvement is consistent with the improvement seen for PDC, the continuous latent variable that is used to determine PDC80. PDC increased by 3.1 percentage points from 93.9 to 97.0 (p<.01).

We next report the average treatment effect for each patient's lowest PDC medication. The LeastPDC80 improved by 13.2 percentage points (17.6%, 88.5 versus 75.2) and was statistically significant (p<.01). The alternative interpretation of this is that TA yields 13.2 percentage points more patients who achieved a PDC of 80% for all study medications. The average treatment effect on the underlying PDC was 5.9 percentage points (p<.001; 93.2 versus 87.3).

Discussion

Our findings support the notion that pharmacists and patients do indeed enter into a therapeutic relationship, similar to those found in relationships between patients and other types of healthcare professionals (e.g., psychotherapists or physicians) and that enhancing this relationship can result in significant improvements in patient health behavior and consequently, improvements in the overall effectiveness of MTM encounters. While the evaluation of some clinical pharmacy programs has found improvements in medication adherence,[31] it is encouraging that we found further improvements in adherence in our intervention sample, as compared to when pharmacists delivered MTM per usual practice. This points to the importance of the pharmacist-patient relationship.

Specifically, our findings demonstrate that providing community pharmacists with a method of measuring their therapeutic alliance with patients throughout the course of MTM services is associated with a significant improvement in patient medication adherence. We believe this is because measuring therapeutic alliance enables the pharmacist to appropriately focus his or her interventions to ensure that they are provided from the perspective of what the patient may need; that is, the focus of the intervention is both client-directed and outcome-informed. Based on this study, we believe that measurement of the therapeutic alliance enabled the pharmacist to more effectively understand and respond to patients' medication-related needs and, as a result, successfully promote patient adherence to medications.

Our findings are also important because they demonstrate the utility of a "low intensive" intervention, in terms of time and resources required. Pharmacists in the study were able to implement use of the ORS and SRS scales in their MTM practice after only about one hour of training, and administration of the scales required only about two minutes per visit. This ease of implementation may contribute to improved sustainability of this approach to enhancing MTM practice as compared to other interventions that may be proposed. The implementation of the ORS and SRS scales in MTM practice may also benefit from a "clinical supervision" model, via a management structure that supports its application by all clinical staff. As an example, a clinical supervisor, via a review of the pharmacist's ORS/SRS scores for specific patients and across patients, may suggest ways that the pharmacist might improve his/her alliance with any given patient or might even suggest that a specific patient be transferred to another pharmacist within the practice when the alliance fails to develop. Evaluation of this clinical supervision model (i.e., using the ORS/SRS scores to make practice changes for the pharmacist) could be another fruitful area for further research.

As noted earlier, using the ORS and SRS may also improve the effectiveness and efficiency of a patient's MTM visit. For example, discussions around the ORS and SRS may reveal the "real" reasons for a patient's non-adherence sooner and may allow the pharmacist to respond to the individual needs of the patient at an earlier visit, rather than first trying an intervention because it is what is assumed that the patient needs. This may result in more immediate improvements in adherence. During informal interviews that we conducted with the participating pharmacists, it was noted that the scales helped differentiate the perceived reasons for patient non-adherence and other medication-related problems from the actual cause. As one pharmacist said:

> "I found that using these instruments helped me focus on what the patient needs instead of a medication list or what I think they need. It has caused me to think 'out of the box' in ways that I did not realize I could."[32]

An example of this that pharmacists might see in their practice would be if one makes the assumption that nonadherence is due to patient forgetfulness but it was actually a result of patient concerns regarding medication side effects, psychosocial problems that were overwhelming the patient, duplicative prescribing of specific medications by different physicians or an inability to afford the cost of the medication. The same pharmacist said:

> "One patient told me she was very tired…I found this out when I questioned her from the ORS…it turns out she is taking 4 sedatives throughout the day prescribed by three physicians…much more than she should be…I spoke with her PCP [primary care physician] and we changed her regimen."

Another pharmacist reported that using the scales allowed her to change her practice through actively listening to her patients.[33] The use of the ORS and SRS focuses on the measurement of patient outcomes and therapeutic alliance, although it is clear from these examples that the simple act of measurement lends itself in the short term to opening up a productive dialogue between pharmacists and patients. Pharmacists can use the information from the ORS to inquire and guide their interactions with patients to address patient outcomes, and then use the information from the SRS to ensure that they are doing so in a manner the patient perceives as beneficial. While adherence was an important outcome measure for the purpose of this study, the use of the scales is indeed flexible to address any number of MTM-related issues that may appear.

It is also clear from pharmacist responses that there is a great potential for pharmacy practice change. Given the empirical foundation for the use of the scales, as well as their clinical utility and real world feasibility, we believe teaching the use of the scales in pharmacy schools could avail future generations of pharmacists with the necessary skills to reliably and effectively address patient needs and concerns.

Limitations

There are a few limitations to the study. First, we note administration variations described in the protocol were not recorded and may have had some bearing on the results. Specifically, pharmacists could provide the scales during face-to-face MTM sessions or they could administer the scales via telephone calls. We did not track which scales were administered in person or via the telephone so this variable was not included in our analyses. Further research is warranted to better understand the impact that the care delivery method has on the use of these scales and related changes in medication adherence.

Second, we did not collect any participant demographic information other than gender and age so generalizability of our findings across patient populations is limited. The average age of the study sample was ~75 years old and the majority of participants were female. The results of our study should be considered specific to this particular sample of participants, although future studies would investigate the use of these scales with participants from a wider age range. Anecdotally, pharmacists reported that patient race included African-American, Caucasian, and Native American, but future studies would include participant self-report of comprehensive demographic information, including race and ethnicity, level

of education, and socio-economic status, to name a few. At this time, any variation in adherence changes due to these demographic factors is unknown.

Third, the random selection of comparison group data did not include any information about pharmacist characteristics. Therefore, we were unable to assess similarities or variations in pharmacist characteristics as variables for consideration in the analysis. We also did not examine differences in adherence among patients seen by different providers and we did not determine the impact of changing providers, as for the purposes of this study, patients were seen by the same pharmacist at each of their study-related MTM visits. As described earlier, a model that includes feedback to facilitate adjustments in provider-patient pairing may be useful and the use of these scales should be further evaluated in this type of setting.

Fourth, we also only examined adherence data for a few specific classes of medications. It is unknown if the use of the scales is related to improvements in adherence to other medications. Further, the actual indication of prescribed medications in this study is unknown; therefore, while we expect that improvements in this study would be related to improvements in clinical outcomes such blood pressure, LDL-cholesterol, and blood glucose, this is unknown as some medications indicated for hypertension, hyperlipidemia, and diabetes are also commonly used to treat other conditions. Future studies that examine the impact of therapeutic alliance measurement on clinical outcomes are needed. In addition to relevant clinical markers listed above, these evaluations should examine whether the use of these scales positively impacts long-term outcomes, including emergency room visits and hospitalizations associated with common chronic diseases addressed in MTM sessions. While our qualitative comments suggest this is the case, future research efforts could also examine whether the use of the ORS and SRS improve patient satisfaction with pharmacist-provided MTM and whether pharmacists using these scales are more confident in their ability to provide MTM and respond to their patients' medication-related needs. Each outcome would provide further argument for the routine use of these scales in pharmaceutical care.

Finally, limitations of pharmacy refill records as the data source for adherence assessments have been described.[34] Therefore, while our findings demonstrate improved adherence as measured by claims data, further assessments of MTM programs using the therapeutic alliance scales that include alternate methods for adherence measurement may be warranted. Examining medication adherence at sustained intervals beyond that measured in the current study (e.g., at one or more years post implementation of the scales by the pharmacists) is also warranted.

Conclusions

Providing pharmacists with a mechanism for measuring their therapeutic alliance with patients receiving MTM services was associated with improvements in medication adherence. Implementing the study intervention required relatively little resources, suggesting that the use of these scales may be a feasible and effective strategy for enhancing the impact of community pharmacist-provided MTM services. Additional research is needed to examine the impact of these scales in different patient populations and in various care settings and future studies would include a randomized clinical trial to test the efficacy of this intervention with a larger sample. In addition to considering the impact of the scales on adherence, these evaluations could include measurements of both clinical outcomes (e.g., hospitalizations) and humanistic outcomes such as patient satisfaction with MTM and pharmacists' confidence in providing MTM services in ways that address patients' medication-related needs.

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Appendix

Outcome Rating Scale Items

On a scale from 1 to 10, where 1 is "bad" and 10 is "good":

1. How have you been doing personally?
2. How have things been going in your relationships?
3. How have things been going for you socially?
4. How would you rate how things in your life are going overall?

Session Rating Scale Items

1. On a scale of 1-10, to what degree did you feel heard and understood today, 10 being completely and 1 being not at all?
2. On a scale of 1-10, to what degree did we work on the issues that you wanted to work on today, 10 being completely and 1 being not at all?
3. On a scale of 1-10, how well did my approach, the way I worked, make sense and fit for you?
4. So, given your answers on these specific areas, how would you rate how things were in today's session overall, with 10 meaning that the session was right for you and 1 meaning that something important that was missing from the visit?

TABLES

Table 1. Medication Classes Included in Adherence Analyses

Antihypertensives	Antidiabetics	Antihyperlipidemics
ACE-inhibitors	Biguanides	Bile acid sequestrants
Calcium-Channel Blockers	Thiazolidinediones	HMG Co-enzyme-A-Reductase Inhibitors
Beta-Blockers	Sulfonylureas	Fibric Acid Derivatives
Thiazide Diuretics	Meglitinides	Niacin
Angiotensin-Receptor Antagonists	DPP-IV Inhibitors	Ezetimibe
Potassium-Sparing Diuretics	Incretin Mimetics	Omega 3
Loop Diuretics	Insulins	VCPs
Renin Inhibitors	VCPs	
Alpha-2 Agonists		
Vasodilators		
Alpha-Blockers		
Mixed Alpha/Beta Blockers		
Various combination products (VCPs)		

Table 2A. Baseline Characteristics of Patients Who Were Observed Before and After the Implementation of Therapeutic Alliance: By Experimental Group

Variable		Percent/Mean (StDev)		Standardized Difference	P-value[1]		Percent/Mean (StDev)		Standardized Difference
		Unadjusted					Propensity Score Adjusted		
		MTM Only (N=146)	MTM + Therapeutic Alliance (N=117)				MTM Only (N=146)	MTM + Therapeutic Alliance (N=117)	
Female(%)		78.1	70.1	18.26	0.126		76.1	74.8	3.10
		(41.51)	(45.99)				(42.77)	(43.61)	
Age (Years):	All	76.2	76.4	2.87	0.721		76.2	76.1	2.20
		(6.96)	(6.69)				(6.81)	(6.60)	
	Female	75.4	76.6	18.82	0.143		75.9	75.7	2.00
		(6.24)	(6.76)				(6.24)	(6.48)	
	Male	78.9	75.8	41.26	0.094		77.3	77.1	3.72
		(8.62)	(6.58)				(8.37)	(6.98)	
No. of Visits to the Pharmacy		20.5	20.3	1.56	0.944		20.8	20.4	3.33
		(10.86)	(11.98)				(10.84)	(11.81)	
No. of Fills for Any Medication		36.5	37.0	2.64	0.765		37.4	36.7	3.55
		(19.16)	(22.06)				(19.11)	(21.73)	
No. of Study Medications		3.1	3.1	0.12	0.889		3.2	3.1	3.11
		(1.65)	(1.70)				(1.64)	(1.74)	
Any Fills for Hypertension Medications (%)		89.0	89.7	2.27	0.654		90.9	90.4	1.55
		(31.35)	(30.47)				(28.93)	(29.59)	
Any Fills for Hyperlipidemia Medications (%)		56.8	53.8	6.02	0.665		56.9	56.0	1.74
		(49.70)	(50.07)				(49.69)	(49.85)	
Any Fills for Two Medication Categories (%)		41.8	48.7	13.92	0.153		44.4	43.8	1.27
		(49.49)	(50.20)				(49.86)	(49.83)	
Any Fills for All Three Medication Categories (%)		29.5	23.9	12.46	0.428		28.7	27.9	1.68
		(45.74)	(42.85)				(45.40)	(45.07)	

1 - Based on Chi-Squared tests for dichotomous variables and T-tests for continuous variables

2 - Does not include combination medications.

Baseline Characteristics of Patients Who Were Observed Before and After the Implementation of Therapeutic Alliance: By Experimental Group

Table 2B. Baseline Characteristics of Patients Who Were Observed Before and After the Implementation of Therapeutic Alliance: By Experimental Group

Variable	Percent(StDev)		Standardized Difference	P-value[1]		Percent(StDev)		Standardized Difference
	Unadjusted					Propensity Score Adjusted		
	MTM Only (N=146)	MTM + Therapeutic Alliance (N=117)				MTM Only (N=146)	MTM + Therapeutic Alliance (N=117)	
Days in Claims Record	187.3	185.8	5.66	0.605		187.3	186.5	3.21
	(27.75)	(23.60)				(27.58)	(21.86)	
PDC80	97.3	88.9	33.29	0.006		94.4	93.7	3.12
	(16.38)	(31.56)				(23.08)	(24.48)	
PDC	94.5	91.2	40.58	0.000		93.4	93.2	3.18
	(6.30)	(9.68)				(7.50)	(8.03)	
Least-PDC80	79.3	69.6	22.39	0.006		75.2	76.3	2.55
	(40.65)	(46.21)				(43.35)	(42.73)	
Least-PDC	89.2	84.6	34.16	0.006		87.8	87.0	5.83
	(12.15)	(14.85)				(13.19)	(13.63)	

Table 3. Comparison of Study Outcomes Over Time and by Study Group

	MTM			MTM+TA				
	Mean (St. Err.)		Mean, p-value	Mean (St. Err.)		Mean, p-value	Estimate, p-value	
	Before	After	Difference	Before	After	Difference	Post Only Differences	Difference in Differences
PDC80	97.3	96.6	-0.7	88.9	99.1	10.3	2.5	10.9
	(1.4)	(1.5)	.735	(2.9)	(0.9)	.001	.021	.008
PDC	94.5	94.4	-0.1	91.2	96.8	5.6	2.4	5.8
	(0.5)	(0.5)	.854	(0.9)	(0.4)	.000	.000	.000
Least-PDC80	78.8	78.1	-0.7	70.1	88.9	18.8	10.8	19.5
	(3.4)	(3.4)	.887	(4.3)	(2.9)	.000	.001	.001
Least-PDC	89.2	88.0	-1.2	84.6	92.9	8.3	4.9	9.5
	(1.0)	(1.0)	.394	(1.4)	(0.8)	.000	.000	.000
Days in Claims Record	187.3	208.3	21.0	185.8	209.3	23.5	1.0	2.4
	(2.3)	(1.9)	.000	(2.2)	(1.4)	.000	..613	.532
Denominator	181.8	200.1	18.4	179.6	200.3	20.8	.2	2.4
	(2.9)	(2.7)	.000	(2.9)	(2.4)	.000	.466	.363

Notes: p-values were calculated using t-tests for continuous variables and chi-squared tests for binary outcomes. P-values for the difference in differences were calculated within a repeated measures GEE.

Table 4. Doubly Robust Estimates of the Effect of MTM+TA

	Doubly Robust Estimated Outcome (Percent)			Doubly Robust Average Treatment Effect	
	MTM	MTM + TA		Percentage Point Difference, p-value	Percent Difference
PDC80	92.4	97		4.6 0.020	4.98
PDC	93.9	97		3.1 0.000	3.30
Least-PDC80	75.2	88.4		13.2 0.004	17.55
Least-PDC	87.3	93.2		5.9 0.000	6.76