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IS TREATMENT ADHERENCE CONSISTENT ACROSS TIME, ACROSS DIFFERENT TREATMENTS, AND ACROSS DIAGNOSES?

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Abstract

Objective—Examine consistency of adherence across depression treatments and consistency of adherence between depression treatments and treatments for chronic medical illness.

Methods—For 25,456 health plan members beginning psychotherapy for depression between 2003 and 2008, health plan records were used to examine adherence to all episodes of psychotherapy, antidepressant medication, antihypertensive medication, and lipid-lowering medication.

Results—Within treatments, adherence to psychotherapy in one episode predicted approximately 20% greater likelihood of subsequent psychotherapy adherence (OR 2.20, 95% CI 1.83 to 2.64). Similarly, adherence to antidepressant medication in one episode predicted approximately 20% greater likelihood of subsequent antidepressant adherence (OR 1.99, 95% CI 1.74 to 2.28). Across treatments, adherence to antidepressant medication predicted approximately 10% greater likelihood of concurrent or subsequent adherence to psychotherapy (OR 1.52, 95% CI 1.42 to 1.63), a 4% greater likelihood of adherence to antihypertensive medication (OR 1.24, 95% CI 1.14 to 1.37) and a 3% greater likelihood of adherence to lipid-lowering medication (OR 1.16, 95% CI 1.03 to 1.32). Adherence to psychotherapy predicted a 2% greater likelihood of concurrent or subsequent adherence to antihypertensive medication (OR 1.11, 95% CI 1.04 to 1.19) and was not a significant predictor of adherence to lipid-lowering medication (OR 0.99, 95% CI 0.90 to 1.18).

Conclusions—Adherence is moderately consistent across episodes of depression treatment. Depression treatment adherence is a statistically significant, but relatively weak, predictor of adherence to antihypertensive or lipid-lowering medication.

Keywords

depression; adherence; antidepressant; psychotherapy; hypertension; cholesterol

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Consistent evidence supports the efficacy of both antidepressant medications and structured psychotherapies for treatment of depression (1–3). When either treatment is delivered as intended, half or more of outpatients experience significant improvement.

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Unfortunately, poor adherence to depression treatment - both medication and psychotherapy - frequently interferes with treatment effectiveness. Among outpatients starting antidepressant treatment for depression, fewer than half continue medication through 12 weeks of acute-phase treatment (4–6). Among outpatients making an initial psychotherapy visit for depression, one third do not return for a second visit and fewer than half continue for four or more visits (7, 8). Increasing adherence to treatment is a central component of most successful depression care improvement programs (9–11).

Poor adherence is certainly not unique to treatment of depression. Non-adherence is consistently identified as a major barrier to management of most chronic health conditions, responsible for as many as 89,000 premature deaths and as much as \$290 billion in avoidable medical spending each year (12, 13).

Given the importance of non-adherence in the management of depression and other chronic health conditions, surprisingly little is known about the consistency of adherence behavior across time or across different treatments. Previous research has identified predictors of adherence to antidepressants, including higher income or educational attainment, white race, non-Hispanic ethnicity, lower out-of-pocket costs, and history of previous antidepressant treatment (4, 14, 15). Regarding adherence to psychotherapy for depression, previous research typically finds higher rates of treatment continuation associated with older age, greater educational attainment, history of previous psychotherapy, and lower out-of-pocket costs (7, 16–20). Previous research consistently finds that depression is associated with poorer adherence to concomitant treatments for chronic medical conditions (21, 22). But we can identify no previous research examining whether adherence to different depression treatments is consistent within individuals across different episodes of treatment (e.g. consistency of adherence between two episodes of antidepressant treatment OR consistency of adherence between medication and psychotherapy treatments). One previous study examined consistency of adherence to depression and HIV treatment, finding that antidepressant adherence did predict adherence to antiretroviral medication (23). We can identify no other research examining whether adherence to depression treatment is consistent with adherence to medication treatment for other co-occurring medical conditions.

This report uses health plan electronic medical records and claims records to examine three questions regarding consistency of adherence behavior:

- Is adherence to depression treatment (either psychotherapy or medication) consistent within individuals across different treatment episodes (i.e. state vs. trait effects)?
- Is adherence to depression treatment consistent within individuals across medication and psychotherapy?
- Does adherence to depression treatment predict an individual's concurrent or subsequent adherence to medication treatment for general medical conditions?

Regarding general medical conditions, we focus on antihypertensive and lipid-lowering medications because these are the long-term medications (other than antidepressants) most often prescribed to people with depression.

METHODS

Data were extracted from the electronic medical records and claims data of Group Health Cooperative, a prepaid health system providing general medical and mental health care to approximately 650,000 members in Washington and Idaho. Group Health members are

generally similar to the area population in distribution of sex, age, race/ethnicity, and educational attainment. At the time of this study, members were insured through private employers (53%), public employers (22%), individual insurance plans (5%), capitated Medicare plans (12%), and capitated plans through Medicaid or other subsidized insurance for low-income residents (8%). Group Health provides both general medical and mental health care through plan-owned clinics and contracted external providers. Antidepressant medications are prescribed by both primary care physicians (approximately 75% of new prescriptions) and psychiatrists (approximately 25% of new prescriptions). Psychotherapy is provided by an internal staff of approximately 65 psychotherapists and an external network of approximately 250 contracted psychotherapists. Both internal and external therapists include a mix of masters-prepared therapists and doctoral-level psychologists. Group Health's guidelines for depression treatment recommend either pharmacotherapy or psychotherapy (per patient's choice) for treatment of moderate depression and combined treatment (medication and psychotherapy) for severe or treatment-resistant depression. Electronic medical records are available for all visits at plan-owned clinics and all prescriptions filled at plan-owned pharmacies. Insurance claims data are available for all visits to external network providers and all prescriptions filled at external pharmacies. Data available for each outpatient visit include member identifier, date, provider identifier, all procedure codes billed, and all diagnoses assigned. Data available for each outpatient prescription include member identifier, date, National Drug Code, number of pills dispensed, and days supply dispensed.

These data were collected for a larger study examining predictors of adherence to psychotherapy for depression (7). The study population included all members aged 13 and older requesting an initial psychotherapy visit for a chief complaint of depression between 1/1/2003 and 12/31/2008. During this period, Group Health insurance plans all allowed self-referral for psychotherapy with no requirement for physician referral or other authorization. Copayment levels for psychotherapy visits varied between insurance contracts with approximately 40% having copayments of \$10 or less, 50% having copayments of \$15 or \$20, and 10% having copayments of more than \$20. During the study period, some plans did include annual visit limits or requirements for re-authorization, but none had annual limits lower than 10 sessions and none required re-authorization prior to the sixth visit.

All members requesting initial psychotherapy appointments call a central triage center. All provider referrals are routed to this center, and triage specialists initiate outgoing calls for triage. The triage call includes a brief assessment of presenting problem or complaint, recent treatment history, substance use, and indicators of urgent need (e.g. risk of self-harm). For patients requesting psychotherapy and not needing urgent care, the triage call typically ends with the offer of a specific appointment for the initial visit (for those living in areas served by plan-owned clinics) or an authorization and referral to one or more external providers (for those living outside areas served by network providers).

To limit the sample to new episodes of treatment, we excluded treatment requests with any request for psychotherapy or any psychotherapy visit in the prior 180 days. An individual could contribute multiple new treatment requests to the sample, as long as this 180-day requirement was met. The sample of psychotherapy episodes was limited to episodes for which the member was enrolled in Group Health for at least 180 days following the initial request for service.

For each member of the study sample, electronic medical records and claims data were used to identify all psychotherapy visits attended between 1/1/2003 and 12/31/2008. The same records were used to identify all filled prescriptions for antidepressant drugs, antihypertensive drugs, or lipid-lowering drugs between 1/1/2003 and 12/31/2008.

A new episode of antidepressant treatment was defined by any filled prescription for an antidepressant drug (excluding trazodone) that was preceded by an interval of 270 days or more with no filled prescription for any antidepressant drug. An individual could contribute multiple episodes of antidepressant treatment to the sample as long as this 270-day requirement was met. The sample of antidepressant episodes was limited to those for which the member was enrolled in Group Health for at least 180 days following the initial prescription date.

Because antihypertensive and lipid-lowering medications are generally intended for continuous (rather than episodic) use, adherence was calculated for each calendar year rather than for distinct episodes of treatment. An individual was considered a user of antihypertensive or lipid-lowering medication in any calendar year if s/he filled two or more prescriptions for any medication in that class during the year. Consequently, each individual could contribute up to six adherence observations for each type of medication (one for each of the six calendar years between 1/1/2003 and 12/31/2008). The samples of antihypertensive and lipid-lowering medication treatment years were limited to years in which the member was enrolled in Group Health for at least 10 of the 12 months.

Previous research in this (24) and other (25–27) settings generally supports the accuracy of pharmacy refill records for assessment of actual medication consumption (as assessed either by patients' self-report or by biological measures). Dichotomous indicators of adherence were defined for each treatment as follows:

- Psychotherapy - for each episode, a sample member was classified as adherent if s/he attended at least one psychotherapy visit within 45 days of the triage call and a second visit within 45 days of the first (i.e. two visits within 90 days and no gap of greater than 45 days). This threshold is based on our finding in this sample (7) that probability dropout is highest prior to the second visit and much lower thereafter.
- Antidepressant medication - for each episode, a sample member was classified as adherent if s/he received prescriptions totaling at least a 90 day supply of any antidepressant during the 180 days including and following the day of the first prescription. This threshold of 90 days of treatment is consistent with HEDIS/NCQA standards (28) and evidence-based guideline recommendations (3, 29) regarding adequate acute-phase treatment.
- Antihypertensive and lipid-lowering medication – In each calendar year in which s/he used medication, a sample member was defined as adherent if s/he had a medication possession ratio of 80% or more (i.e. refill records indicated that total “days supply” dispensed was equal to at least 80% of the days receiving treatment). Medication possession ratio is a standard measure of adherence to long-term medications (25, 26, 30), and we choose a threshold of 80% to facilitate comparison with previous research (30, 31).

Patients' sex and age (at time of each treatment episode) were extracted from health plan enrollment data. For each patient, residential address was used to calculate median neighborhood income and neighborhood distribution of adult educational attainment at the census block level (32, 33).

Data analyses first examined individual patients' consistency of adherence behavior across episodes for the same type of depression treatment. These analyses examined association between adherence to a specific depression treatment and adherence to that same treatment in a subsequent treatment episode (e.g. How does adherence to treatment in one episode of psychotherapy predict adherence in a subsequent episode of psychotherapy?). The practical significance of these associations was assessed by comparing adherence rates for a specific

treatment when prior episodes of that same treatment were classified as either adherent or non-adherent. The magnitude and precision of these associations were expressed as odds ratios (i.e. relative odds of adherence for those who were adherent vs. non-adherent in a previous episode) with 95% confidence intervals. Given that each individual could contribute multiple pairs of episodes to these analyses, confidence limits for odds ratios were calculated using hierarchical logistic regression models with individual-specific random intercepts to account for within-person correlation. These same logistic regression models were also used to assess how associations between previous and current adherence were influenced by accounting for patient demographic characteristics (age, sex, neighborhood income, and neighborhood educational attainment).

Analyses next examined individual patients' consistency of adherence behavior across different treatments (e.g. How does adherence in an episode of psychotherapy for depression predict adherence to medication treatment for depression – either in the same year or in a subsequent year?). Again, the practical significance of these associations was assessed by comparing adherence rates for a specific treatment when episodes of a different treatment were classified as either adherent or non-adherent. The magnitude and precision of these associations were expressed as odds ratios with 95% confidence intervals, calculated using hierarchical logistic regression models with individual-level random intercepts (with and without accounting for patients' demographic characteristics).

RESULTS

The procedures described above identified 25,456 health plan members requesting psychotherapy for depression during the study period. In this group, 13,153 had at least one episode of antidepressant treatment during the study period, 5436 used antihypertensive medication during at least one year during the study period, and 2937 used lipid-lowering medication during at least one year of the study period. For each type of treatment, each individual could experience up to six treatment episodes during the six-year study period. Consequently, the sample of treatment episodes include 27,388 episodes of psychotherapy, 16,831 episodes of antidepressant treatment, 19,518 episodes of treatment with antihypertensive medication, and 7134 episodes of treatment with lipid-lowering medication.

Demographic characteristics of those using each type of treatment are shown in Table 1. Across all treatments, 60 to 70 percent were female (reflecting the initial selection of people starting psychotherapy for depression). As expected, those receiving depression treatments were predominantly younger while the subgroup also receiving treatment for hypertension or hyperlipidemia were predominantly middle-aged and older. Approximately one fifth resided in lower-income neighborhood (median household income less than \$40,000 per year) and approximately 40 percent resided in neighborhoods where fewer than 20% of residents were college graduates.

Table 1 also displays adherence rates for each type of treatment – overall and stratified by demographic characteristics. For all four treatments, likelihood of adherence did not differ meaningfully between men and women and was modestly lower among those living in lower-income or lower-education neighborhoods. Both depression treatments showed a similar pattern of adherence across age groups: increasing adherence with increasing age except for lower adherence among those aged 65 or older. In contrast, adherence rates for both antihypertensive and lipid-lowering medications increased steadily with age.

Figure 1 illustrates consistency of psychotherapy adherence across time within individuals, stratified by the number of years between treatment episodes. Results were generally similar

for episodes one, two, three, or more years apart – with no clear trend toward more or less consistency with increasing time between episodes. Among those classified as adherent to psychotherapy in a previous episode, the proportion classified as adherent psychotherapy in the current episode was approximately 67%, compared to approximately 46% among those classified as non-adherent in the previous episode. In a logistic regression model predicting adherence to psychotherapy, adherence classification in a previous episode was a significant predictor of current adherence (Odds Ratio = 2.20, 95% CI 1.83 to 2.64). Accounting for patients' demographic characteristics (age, sex, and neighborhood characteristics) slightly weakened the association between prior and current antidepressant adherence (Odds Ratio = 2.03, 95% CI 1.65 to 2.49).

Figure 2 illustrates consistency of antidepressant adherence across time within individuals, stratified by the number of years between treatment episodes. Results were generally similar for episodes one, two, three, or more years apart – with no clear trend toward more or less consistency with increasing time between episodes. Among those classified as adherent to antidepressant medication in a previous episode, the proportion classified as adherent in the current episode was approximately 63%, compared to approximately 45% among those classified as non-adherent in the previous episode (Odds Ratio = 1.99, 95% CI 1.74 to 2.28). Accounting for patients' demographic characteristics (age, sex, and neighborhood characteristics) slightly weakened the association between prior and current psychotherapy adherence (Odds Ratio = 1.91, 95% CI 1.66 to 2.40).

Consistency between adherence to psychotherapy and adherence to other treatments is illustrated in Figure 3. Adherence to psychotherapy was a moderate predictor of adherence to antidepressant medication – either within the same calendar year or in subsequent calendar years. For all time periods combined, those classified as adherent to psychotherapy had a 55% observed rate of adherence to antidepressants compared to 46% among those not adherent to psychotherapy in a concurrent or previous episode (Odds Ratio = 1.52, 95% CI 1.43 to 1.61). Adherence to psychotherapy was a marginal predictor of concurrent or subsequent adherence to antihypertensive medication (observed rate of 77% vs 75%, Odds Ratio = 1.11, 95% CI 1.04 to 1.19). Adherence to psychotherapy was not a significant predictor of adherence to concurrent or subsequent treatment with lipid-lowering medications (observed rate of 74% vs. 74%, Odds Ratio = 0.99, 95% CI 0.90 to 1.18). Accounting for patients' demographic characteristics had no meaningful effect on any of these associations (details available on request).

Consistency between adherence to antidepressants and adherence to other treatments is illustrated in Figure 4. Adherence to antidepressant medication was a moderate predictor of adherence to psychotherapy for depression – either within the same calendar year or in subsequent calendar years. For all time periods combined, those classified as adherent to antidepressants had a 59% observed rate of adherence to psychotherapy compared to 48% among those not adherent to antidepressants in a concurrent or previous episode (Odds Ratio = 1.52, 95% CI 1.42 to 1.63). Adherence to antidepressant medication was also a marginal predictor of concurrent or subsequent adherence both to antihypertensive medication (observed rate of 76% vs 72%, Odds Ratio = 1.24, 95% CI 1.14 to 1.37) and lipid-lowering medications (observed rate of 73% vs 70%, Odds Ratio = 1.16, 95% CI 1.03 to 1.32). Accounting for patients' demographic characteristics had no meaningful effect on any of these associations (details available on request).

DISCUSSION

We found that adherence behavior was most consistent within specific treatments, with less consistency across depression treatments and even less across treatments for different

conditions. Within types of depression treatment (antidepressant medication or psychotherapy), adherence in one treatment episode predicted an absolute difference of approximately 20% in subsequent adherence to that same treatment. Across different types of depression treatment (medication vs. psychotherapy), adherence to one treatment predicted approximately a 10% difference in adherence to the other type of depression treatment. Adherence to medication treatment for depression predicted approximately 3% differences in adherence to medication treatment for hypertension or elevated cholesterol. Adherence to psychotherapy for depression was a marginally significant or non-significant predictor of adherence to medication treatment for hypertension or elevated cholesterol.

Our sample includes adults beginning psychotherapy treatment for depression who also receive medication treatment for depression, hypertension, or hypercholesterolemia. Our findings regarding adherence to medication treatments (especially antihypertensive and lipid-lowering medication) may not generalize to the larger population of people with hypertension or elevated cholesterol who do not also receive treatment for depression.

We should emphasize that health system prescription records may not always accurately reflect medication use. While previous research generally supports the validity of refill records for assessing actual medication use, especially over longer periods (34, 35), misclassification may occur in both directions. Patients may continue to refill prescriptions but not take medication regularly, leading to over-estimation of actual medication use. Or some patients may fill prescriptions through other insurance or pay out-of-pocket, leading to under-estimation of actual medication use. Either type of misclassification would be more likely to cause under-estimation of consistency of adherence behavior.

Our analyses regarding broad classes of drugs may obscure patterns of adherence for individual medications. For example, adherence to a specific antidepressant medication or group of medications might be more consistent across episodes of treatment than is adherence to antidepressant medication in general. Or it is possible that adherence to specific medications is more strongly associated with adherence to psychotherapy or with adherence to treatment for hypertension or elevated cholesterol.

Absent data regarding clinical outcomes, we cannot determine how often non-adherence was associated with adverse clinical outcomes. As we have previously reported for both antidepressant medications (36) and psychotherapy (37), early discontinuation of treatment is associated with both favorable and unfavorable outcomes. In this sample, those classified as non-adherent to depression treatment probably included a mixture of those experiencing unsuccessful treatment (adverse effects or lack of benefit) and those who experienced good outcomes and decided that further treatment was not needed. We might observe more consistency of adherence behavior across treatments if we were able to distinguish those stopping or interrupting treatment for specific reasons. The data needed for that classification are not now available from electronic health system records.

A comprehensive view of adherence behavior must consider factors at the level of the specific treatment offered, the condition being treated, the patient, the provider, and the health system. Using the example of adherence to antidepressant medication, likelihood of adherence during a specific episode of treatment could be influenced by characteristics of the specific medication prescribed, perceived benefits and adverse effects of depression treatment in general, patient characteristics influencing adherence to any treatment (age, social or economic disadvantage), the education and support provided by the prescribing physician, and the generosity of insurance coverage. We find a gradation of increasing consistency of adherence behavior: lowest for consistency across conditions, intermediate for consistency across treatments within depression, and highest for consistency within the

same treatment over time. This pattern suggests that treatment-level or condition-level factors may be more important determinants of adherence behavior than patient-level factors influencing adherence to any treatment.

These analyses do not consider the influence of the treating or prescribing provider on adherence to treatment of depression or other chronic conditions. Our finding of greater consistency of adherence within treatments than across treatments might actually reflect a provider-level effect (more consistency for treatments from the same physician or psychotherapist) rather than a treatment-level effect (more consistency within psychotherapy than between psychotherapy and antidepressant medication). On the other hand, provider-level effects could reduce the observed consistency of adherence within treatments. For example, a patient dropping out of psychotherapy with one provider might select a different provider, and consequently continue treatment, in a subsequent episode of therapy. Examining the relative importance of provider-level and treatment-level influences on adherence is a priority area for future research.

Of interest to clinicians, we find that non-adherence in one episode of pharmacotherapy for depression does predict 20% lower likelihood of adherence in a later episode of antidepressant pharmacotherapy and 10% lower likelihood of adherence to subsequent psychotherapy for depression. Similarly, early dropout in one episode of psychotherapy for depression predicted a 20% lower likelihood of persistent in a subsequent episode of psychotherapy and 10% lower likelihood of adherence to subsequent antidepressant pharmacotherapy. As discussed above, stronger relationships might emerge with examination of specific medications. Clinicians might make specific efforts to assess and enhance treatment motivation in patients who discontinued or interrupted previous depression treatments. But we find that non-adherence in one episode of depression treatment predicts only slightly (0% to 4%) lower likelihood of subsequent adherence to antihypertensive or lipid lowering medication. Consequently, we should not consider some patients to be generally non-adherent across various treatments and chronic conditions.

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Figure 1.
Probability of adherence to psychotherapy for depression depending on adherence to past psychotherapy.

Figure 2. Probability of adherence to antidepressant medication depending on adherence to prior antidepressant treatment.

Figure 3.
Probability of adherence to specific treatments depending on adherence to past or concurrent psychotherapy

Figure 4. Probability of adherence to specific treatments depending on adherence to past or concurrent antidepressant medication.

Table 1

Adherence to specific treatments stratified by patient demographic characteristics.

	Number of Episodes	Number Adherent	Percent Adherent	Number of Episodes	Number Adherent	Percent Adherent	Number of Episodes	Number Adherent	Percent Adherent	Number of Episodes	Number Adherent	Percent Adherent
Total	27388	14772	54%	16831	10091	60%	19518	14839	76%	9616	7134	74%
Sex												
Male	8482	4587	54%	4767	2793	59%	6465	4982	77%	3946	2990	76%
Female	18906	10185	54%	12064	7298	60%	13053	9857	76%	5670	4144	73%
Age												
<30	8666	4456	51%	4902	2618	53%	517	289	56%	41	21	51%
30 to 44	8082	4440	55%	5369	3313	62%	2686	1756	65%	648	395	61%
45 to 64	8655	5030	58%	5293	3415	65%	10561	8104	77%	5815	4252	73%
65+	1985	846	43%	1267	745	59%	5754	4690	82%	3112	2466	79%
Neighborhood Median Income												
<= \$40,000/year	3836	1973	51%	2546	1460	57%	2454	1779	72%	1140	822	72%
>\$40,000/year	21303	11616	55%	12911	7845	61%	15381	11770	76%	7542	5633	75%
Neighborhood Educational Attainment												
<= 20% Coll Grad	8558	4338	51%	5550	3163	57%	6214	4606	74%	2948	2117	72%
> 20% Coll Grad	16581	9251	56%	9907	6142	62%	11621	8943	77%	5734	4338	76%