A Comparison Between Antihypertensive Medication Adherence and Treatment Intensification as Potential Clinical Performance Measures

Rebecca Vigen, MD, MPA; Susan Shetterly, MS; David J. Magid, MD, MPH; Patrick J. O’Connor, MD, MA, MPH; Karen L. Margolis, MD, MPH; Julie Schmittied, PhD; P. Michael Ho, MD, PhD

Background—Medication adherence and treatment intensification have been advocated as performance measures to assess the quality of care provided. Whereas previous studies have shown that adherence and treatment intensification (TI) of antihypertensive medications is associated with blood pressure (BP) control at the patient level, less is known about whether adherence and TI is associated with BP control at the clinic level.

Methods and Results—We included 162,879 patients among 89 clinics in the Cardiovascular Research Network Hypertension Registry with incident hypertension who were started on antihypertensive medications. Adherence was measured by the proportion of days covered (PDC). TI was defined by the standard based method with scores ranging between −1 to 1 and categorized as: −1 indicated no TI occurred when BP was elevated; 0 indicated TI occurred when BP was elevated; and 1 indicated that TI was made at all visits, even when BP was not elevated. Logistic regression models assessed the association between adherence and TI with blood pressure control (BP ≤140/90 at the clinic visit closest to 12 months after study entry) at the patient and clinic levels. Mean adherence was 0.77±0.28 (PDC±SD) at the patient level and 0.78±0.05 at the clinic level. Mean TI was 0.026±0.23 at the patient level and 0.01±0.04 at the clinic level. At the patient level, for each 0.25 increase in adherence and TI, the odds (OR) of achieving blood pressure control increased by 28% and 55%, respectively [OR for adherence, 1.28 (1.26–1.29), and for TI, 1.55 (1.53–1.57)]. At the clinic level, each 0.04 increment increase in treatment intensification was associated with a 25% increased odds of achieving blood pressure control (OR, 1.24; 95% CI, 1.21–1.27). In contrast, there was an inverse association between increasing adherence and BP control (OR, 0.93; 95% confidence interval, 0.90–0.95).

Conclusions—Patient adherence to antihypertensive medications is not associated with BP control at the clinic level and may not be suitable as a performance measure. TI is associated with BP control, but its use as a performance measure may be constrained by challenges in measuring it and by concerns about unintended consequences of aggressive hypertension treatment in some subgroups of patients. (Circ Cardiovasc Qual Outcomes. 2012;5:276-282.)

Key Words: hypertension ■ performance measures ■ medication adherence ■ treatment intensification ■ quality of care

Performance measures have been developed and adopted by many professional organizations and are often used to guide quality improvement initiatives. Medication adherence and treatment intensification (TI) as performance measures are controversial. In 2009, the National Quality Forum endorsed a performance measure for adherence to chronic medications (ie, angiotensin-converting enzyme inhibitors) and lipid-lowering agents.1 In contrast, a 2011 statement from the American College of Cardiology/American Heart Association (ACC/AHA) decided against adoption of medication adherence as a performance measure reasoning that adherence is not under full control of the provider and can be difficult to measure without access to pharmacy records.2 Further, several studies3–5 have advocated for TI or therapy modifications for patients with poor risk factor control to be considered as quality measures; but, to our
knowledge to date, TI has not been adopted by any organizations. Thus, whether medication adherence and/or TI should be used as a performance measure remains under debate.

Medication nonadherence is a significant barrier to achieving blood pressure control among hypertensive adults. Individuals who are adherent to their antihypertensive medications are more likely to achieve blood pressure control than those who are partially adherent or completely nonadherent. Additionally, TI has been shown to improve blood pressure control among patients. Previous work has demonstrated an association between treatment intensification and risk factor control both at the patient level and across different facilities. However, prior studies have not assessed the association between adherence with blood pressure control at the clinic level, nor the impact of adherence and treatment intensification together on blood pressure control beyond a patient-level analysis.

Methods
The CVRN Hypertension Registry includes adult patients with hypertension in 3 integrated healthcare delivery systems including Kaiser Permanente Colorado, Kaiser Permanente Northern California, and HealthPartners of Minnesota. In 2009, Kaiser Permanente Colorado had more than 450,000 enrollees among 17 clinics in the Denver, CO, metropolitan area. Health Partners served more than 620,000 members in the Minneapolis, MN, metropolitan area in 22 clinics. Kaiser Permanente Northern California provided care to more than 3.2 million members in 50 clinics. Members choose the primary clinic location where they receive their medical care, typically based on geographic proximity. Once the member chose their clinic, they were assigned to a primary care provider at that clinic. Only members who were assigned to a specific clinic were retained in these analyses. Members who are not assigned to a clinic most often reflect new members of the health plan who have not yet identified a clinic for their primary care. Providers for the most part were nested within clinics. The small number of providers who occasionally saw patients at a second location were nested under the clinic where they primarily practiced. Electronic data on longitudinal blood pressure measurements and medication dispensings, diagnoses, and healthcare utilization was available from electronic health records and administrative databases at all sites dating back to January 2000. Data from each of the health plans were restructured into a common, standardized format with identical variable names, formats, and specifications and identical variable definitions, labels, and coding.

Patients with hypertension were identified based on diagnostic codes, blood pressure measurements in the electronic medical record, or pharmacy dispensing for antihypertensive medications, using criteria from a published algorithm developed at one of the sites. Patients were included in the registry if they were aged 18 years or older, and met 1 or more of the following criteria: (1) 2 consecutive elevated blood pressure measurements on different days at outpatient office visits (ie, >140/90 mm Hg or >130/80 mm Hg in the presence of diabetes or chronic kidney disease); (2) 2 ICD-9 code diagnoses of hypertension on separate dates; (3) at least 1 pharmacy dispensing for an antihypertensive medication and 1 ICD-9 code diagnosis of hypertension; (4) 1 elevated blood pressure measurement and 1 hypertension ICD-9 code diagnosis. The cohort entry date was defined by the date of the first ICD-9 diagnosis of hypertension for those who entered the registry due to 2 diagnosis codes, or the date of the 2nd elevated blood pressure for those who entered the registry due to 2 consecutive elevated blood pressure measurements. Diabetes mellitus was considered present if any of the following occurred: 2 outpatient visits or 1 inpatient primary discharge diagnosis of diabetes, prescription of an antidiabetic medication, 2 elevated fasting blood glucose measurements (≥126 mg/dL), or an elevated hemoglobin A1c measurement (≥7%). Chronic kidney disease was indicated by diagnosis of chronic kidney disease or 2 consecutive serum creatinine values with associated estimated glomerular filtration rates <60 mL/min, using the Modification of Diet in Renal Disease Study Group equation. Additional comorbidity adjustment variables were defined using ICD-9 diagnosis codes from medical care visits.

The main analysis included patients with incident hypertension being started on antihypertensive medication. Incident hypertension was defined as being a member of the health plan for at least 1 year before meeting criteria for the registry, without any diagnosis of hypertension and without any prior pharmacy dispensing for antihypertensive medications (eg, diuretics, beta-blockers, angiotensin-converting enzyme inhibitors) during that prior 1-year period. Individuals included in the analyses were also required to have at least 1 year of membership after their first prescription dispensing and have data on at least 1 of the 3 measures of interest: blood pressure control, medication adherence, and TI (described below). Based on these criteria, the analytic cohort for the study comprised 162,879 patients with incident hypertension from 2002 to 2006.

Medication adherence was calculated by the proportion of days covered (PDC) for 5 classes of antihypertensive medications, including beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, dihydropyridine calcium channel blockers, nondihydropyridine calcium channel blockers, and diuretics. The PDC was calculated based on the number of days of blood pressure medications that were supplied divided by the observation time...
interval. The PDC in this study ranges from 0 to 1.2 because patients can have overlaps in their supplies of medications, based on when their refills are requested. For patients who were prescribed multiple medications, a summary PDC measure was estimated based on the average PDC of all medications during the same time period.

Medication TI scores were calculated using the standard-based method, which has been previously validated with a higher threshold for expected TI for reasons described below. The standard-based TI scores provide a ranking of the appropriateness of TI (dosage increase or new medication) and is calculated as the number of observed medication intensifications minus the number of expected medication intensifications divided by the number of clinic visits in the observation period. Treatment intensification is expected whenever measured blood pressure during a clinic visit is higher than the blood pressure goal. The TI score range is between -1 to 1. A score of -1 indicates that no TI occurred when the blood pressure was elevated. A score of 0 indicates TI was made when the blood pressure was elevated but not when blood pressure was normal. Finally, a score of 1 indicates that TI was made at all visits, even when the blood pressure was not elevated. For this study, the intensity score only used clinic visits to departments most likely to manage hypertension: primary care, cardiology, and nephrology clinics. Because clinicians may be reluctant to intensify blood pressure medications when blood pressures levels are minimally above goal or when intensification has occurred at a recent visit, we only expected intensifications if blood pressure was 10 mm Hg or more above JNC VII goals and if intensification had not occurred in the prior 2 weeks.

Outcome Variables

The primary outcome of interest was blood pressure control at 12 months after the initial antihypertensive drug dispensing. We selected the closest blood pressure measurement to the 12-month date from blood pressures measured between 6 and 18 months. Blood pressure was considered to be uncontrolled if blood pressure $>140/90$ (or $>130/80$ in patients with diabetes mellitus or chronic kidney disease).

Statistical Methods

To describe clinic groups, we first divided the 89 clinics into quintiles, based on the average level of blood pressure control. Patient-level characteristics and clinic-level average adherence and intensification were described overall and within clinic quintiles. Statistical comparisons between quintiles used $\chi^2$ tests for categorical variables and Wilcoxon rank sum tests for continuous variables.

We estimated odds ratio (OR) associations for medication adherence and TI with blood pressure control at 1 year for individual patient-level data using multilevel logistic regression models. In the primary analyses, medication adherence and intensification variables were entered as continuous variables and ORs estimated for an increment of 0.25, which approximated the standard deviations for adherence and TI distributions at the patient level. These models nested patients within provider and clinic random-effect variables, resulting in a within-clinic provider effect and a between-clinic effect. Adjustment variables such as age, baseline blood pressure, and comorbidities were included as fixed-effect variables. Secondary analyses evaluated intensification as a categorical variable to facilitate interpretation by categorizing TI scores into 3 groups: TI $<$ 0 (no TI when blood pressure was elevated), TI = 0 (intensification occurred when blood pressure was elevated), and TI $>$ 0 (intensification occurred when blood pressure was not elevated). Using TI $<$ 0 as the reference group, we calculated ORs for TI = 0 versus TI $<$ 0 and TI $>$ 0 versus TI $<$ 0.

Next, we used these multilevel hierarchal logistic regression models to estimate the association between clinic adherence and clinic TI with blood pressure control. In these hierarchical models, the average adherence or intensification for a clinic was calculated using the MIX procedure in SAS 9.2. Models were estimated using the GLIMMIX procedure in SAS 9.2.

For clinic-level comparisons of performance measures, patient-level data may not be available for hierarchical modeling. Typically, only summary data such as counts of hypertensive patients, the number in control and average patient characteristics are provided. For this reason, we also modeled summary data, using the number of patients with hypertension and the number in control to define hypertension control at the clinic level. Similarly, averages at the clinic level were used for exposures of particular interest (adherence and medication intensification) and potential adjustment variables (average age, smoking, and comorbidities). Clinic-level logistic regression models used events per trials syntax for the outcome of blood pressure control were estimated using SAS version 9.2. ORs were estimated for an increment of 0.05 for adherence at the clinic level and 0.04 for TI at the clinic level.

Results

Of the 162 879 patients included in the study, the average age was 56 years, and 48.9% were male (Table 1). Among these patients, 13.6% had diabetes, 1.0% had previous MI, 3.8% had chronic kidney disease, 1.7% had a previous ischemic stroke, and 0.9% had congestive heart failure. The average adherence as measured by PDC±SD was 0.77±0.28 and the average TI score was 0.026±0.23. Of the 162 879 patients in the registry, 126 629 had complete data on adherence and blood pressure control and 128 006 had
Table 2. Multivariable Adjusted* Odds Ratios Between Adherence and Blood Pressure Control and Treatment Intensification and Blood Pressure Control Among Individuals† and Clinics‡

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherence and blood pressure control (n=126 629)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual-level adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Univariate</td>
<td>1.23 (1.22–1.25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted</td>
<td>1.28 (1.26–1.29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinic-level adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Univariate</td>
<td>0.93 (0.91–0.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted</td>
<td>0.93 (0.90–0.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TI and blood pressure control (n=128 006)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual-level TI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Univariate</td>
<td>1.75 (1.73–1.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted</td>
<td>1.55 (1.53–1.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinic-level TI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Univariate</td>
<td>1.25 (1.22–1.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted</td>
<td>1.24 (1.21–1.27)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

TI indicates treatment intensification.

*Multivariable models were adjusted for age, sex, smoking status, diabetes, history of myocardial infarction, chronic kidney disease, ischemic stroke, and congestive heart failure.
†For the individual models, delta was 0.25.
‡For the clinic adherence model, delta was 0.05 and clinic treatment intensification model, delta was 0.04.

Table 3. Baseline Clinic Characteristics

<table>
<thead>
<tr>
<th>Clinic Characteristics</th>
<th>Total</th>
<th>Q1 &lt;55% Controlled</th>
<th>Q2 55% to 58% Controlled</th>
<th>Q3 59% to 60% Controlled</th>
<th>Q4 61% to 65% Controlled</th>
<th>Q5 &gt;65% Controlled</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of clinics</td>
<td>89</td>
<td>17</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>No. of members</td>
<td>162 879</td>
<td>12 219</td>
<td>18 960</td>
<td>64 231</td>
<td>35 676</td>
<td>31 793</td>
<td></td>
</tr>
<tr>
<td>Average clinic adherence</td>
<td>0.78±0.05</td>
<td>0.81±0.08</td>
<td>0.79±0.05</td>
<td>0.77±0.04</td>
<td>0.78±0.03</td>
<td>0.77±0.08</td>
<td>0.09</td>
</tr>
<tr>
<td>Average clinic TI</td>
<td>0.01±0.04</td>
<td>-0.05±0.02</td>
<td>-0.01±0.02</td>
<td>0.02±0.02</td>
<td>0.02±0.02</td>
<td>0.02±0.02</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

TI indicates treatment intensification.

Figure 1. Box-and-whisker plot of blood pressure (BP) control among clinics, based on quintiles of adherence.

Of the 89 clinics included in the study, 50 were from Kaiser Permanente Northern California, with 141 710 patients; 17 were from Kaiser Permanente Colorado, with 13 830 patients; and 22 were from HealthPartners of Minnesota with 7339 patients. The size of clinics included in this study was variable ranging from 62 to 7493 patients, with a mean size of 1830 patients per clinic (STD±1998) and median size of 1077 patients. The average clinic adherence as measured by PDC was 0.78±0.05 (Table 3). Next, we categorized clinics into quintiles of medication adherence to evaluate the association between clinic-level adherence and blood pressure control. There was not much variation in adherence across the quintiles, with average adherence level of <0.75 in quintile 1 (ie, lowest adherence) and average adherence of >0.81 in quintile 5 (highest adherence) (Figure 1).

At the clinic level, adherence was associated with blood pressure control in univariate (OR, 0.93; 95% CI, 0.91–0.95) and multivariable analysis (OR, 0.93; 95% CI, 0.90–0.95) (Table 2). Therefore, for every 0.05 increase in medication adherence, patients had 7% decrease in the odds of blood pressure control, an association not in the expected direction.
In secondary analysis in which clinic-level averages were used for all data, similar results were seen. At the clinic level, adherence was associated with blood pressure control in univariate (OR, 0.93; 95% CI, 0.91–0.94) but not in multivariable analysis (OR, 1.01; 95% CI, 0.98–1.04), again demonstrating that at the clinic level, increases in adherence are not associated with improved blood pressure control.

The mean clinic TI score was 0.01 ± 0.04. To assess the association between TI and blood pressure control, we categorized clinics into quintiles of TI where the average TI in quintile 1 was ~0.02 and the average TI in quintile 5 was 0.04 (Figure 2). Clinic TI was associated with blood pressure control in univariate (OR, 1.25; 95% CI, 1.22–1.27) and multivariable analysis (OR, 1.24; 95% CI, 1.21–1.27) (Table 2). Therefore, an increase of 0.04 in TI increased the odds of achieving blood pressure control by 24%. When TI was treated as a categorical variable, clinics more likely to intensify treatment when blood pressure was elevated ≥150/90 were associated with improvements in blood pressure control (OR, 1.17; 95% CI, 1.11–1.23), compared with clinics less likely to intensify treatment when blood pressure was elevated. Similarly, clinics more likely to intensify treatment when the blood pressure was <150/90 were associated with better blood pressure control (OR, 1.30; 95% CI, 1.23–1.36). In secondary analysis using clinic averages for all variables, the same results were obtained and average clinic TI was associated with blood pressure control in univariate (OR, 1.23; 95% CI, 1.22–1.25) and multivariable analyses (OR, 1.21; 95% CI, 1.17–1.25).

Discussion

The objective of this study was to assess the association between adherence and TI with blood pressure control at the patient and clinic levels. Both adherence and TI at the patient level were significantly associated with blood pressure control. At the level of the clinic, the association between adherence and blood pressure control was not in the expected direction, whereas TI was associated with blood pressure control. These findings raise the question of whether adherence when aggregated to the clinic level can be used to distinguish between high- versus low-performing clinics, as commonly done with performance measurement.11

Our findings are consistent with previous studies that have evaluated the association between medication adherence and blood pressure control among individual patients. In one study that was limited to patients on antihypertensive monotherapy, high-adherence individuals were 45% more likely to have blood pressure control than those with medium or low adherence.12 In another study of patients with coronary artery disease, the odds of having uncontrolled blood pressure among individuals who were nonadherent were 73% higher than adherent patients.13 The size of the association between adherence and blood pressure control in this study is somewhat more modest although consistent with previous literature. The association between adherence and blood pressure control in our study expands on this previous work as it includes all individuals with incident hypertension as well as those on multiple medications.

Treatment intensification, calculated with a higher threshold than the original standard-based method, was associated with improvements in blood pressure control at the patient and clinic levels. The higher threshold used in the current study resulted in fewer clinic visits in which blood pressure was considered above goal and eligible for TI. A previous study of patients with coronary artery disease showed that patients who had appropriate TI had increased odds of achieving blood pressure control.14 Among that cohort, the association between TI and blood pressure control was stronger than adherence and blood pressure control. Consistent with this study, a previous study among clinics from Kaiser Permanente Northern California demonstrated an association between blood pressure control rates and TI at the facility level.15

The ACC/AHA Task Force on Performance Measures has adopted a methodology for creating performance measures that notes the importance of identifying the “reporting unit.” The report emphasizes that “aggregating individual provider data will be needed to both assess the performance of systems of care and to monitor changes in performance over time.”11 Additionally, to improve healthcare quality, performance measures should allow for comparisons between different institutions or providers.15 In the present study, we aggregated patient adherence to a given provider and clinic to assess the association between adherence to antihypertensive medications and blood pressure control. We found that adherence measured at the clinic level was not associated with blood pressure control, suggesting that medication adherence may not be a useful performance measure. There are several potential explanations for why adherence is not associated with blood pressure control when measured at the clinic level in our study. By averaging adherence levels among all clinic patients, the variability in adherence levels among individual patients is decreased, which may explain the lack of association between adherence and blood pressure control at the clinic level. Additionally, there was a small amount of variability in adherence across clinics in our study, and it is possible that if this analysis was done among clinics with greater variability in adherence levels, an association between adherence and blood pressure control may have been observed.
Consistent with a previous study, we found that TI at the level of the clinic was associated with better blood pressure control. Treatment intensification may retain its association with blood pressure control at the clinic level because it measures provider behavior rather than patient behavior in the case of adherence. In addition, the association between TI and blood pressure control at the clinic level may persist despite averaging of the scores given that TI has a stronger association with blood pressure control at the patient level than adherence. In this analysis, the association between TI and blood pressure control increased as providers intensified therapies beyond a blood pressure of 150/90. This may be the result of provider intention to lower blood pressure beyond the threshold of 140/90 or provider decision-making that may be based on home blood pressure measurements. Finally, it is not unexpected that TI in patients who have blood pressures that are already closer to goal would result in improved blood pressure control.

Treatment intensification may be considered a performance measure in the evaluation of the quality of hypertension care but has several important caveats. First, the measurement of TI among clinics that are not part of an integrated healthcare system and do not have pharmacy records may be difficult. Yet, the results from this and previous studies demonstrate the feasibility of measuring TI within integrated healthcare systems, which may be a possible starting point. Second, providers may be hesitant to intensify treatment among patients who are nonadherent, although a previous study has shown that TI is associated with similar improvements in blood pressure among patients with suboptimal adherence. Finally, providers may elect not to intensify treatment among select patient groups in which they may fear adverse side effects from treatment, such as in older patients or those with diabetes. Future studies that evaluate the role of TI in adherent patients and the long-term outcomes of TI in selected subgroups are needed.

Several potential limitations of this study should be noted. First, the 3 healthcare systems that we studied are integrated, nonprofit, managed-care organizations whose composition may not be similar to other healthcare settings. Despite this, these 3 systems care for a large number of patients in geographically and demographically distinct areas. Second, the patients in this study had higher levels of adherence than those included in previous studies and therefore their adherence may have reached a threshold whereby further improvements in adherence are not associated with improvements in blood pressure control. It is possible that among patients and clinics where there is more variability in adherence, the aggregate clinic or provider level associations between adherence and blood pressure control may be stronger. Third, our outcome is a single blood pressure measurement which may not reflect the patients’ overall blood pressure trend, yet performance measurement will probably rely on similar methods. Finally, in this study, we defined an expected TI threshold of >150/90 and demonstrated that TI was associated with blood pressure control in the TI ranges of −1 to 0 and 0 to 1 when evaluated as a categorical variable. TI is clearly indicated when the score is 0, but we are unable to assess the appropriateness of TI for scores of 0 to 1 as providers may be attempting to improve blood pressure beyond the targets chosen in this study and/or may have based treatment decisions on home blood pressure measurements. Future studies should assess adherence at the clinic level in more diverse healthcare systems in which there may be more variability in adherence and whether there is an association with important outcomes as a result of better adherence.

In conclusion, we found that adherence measured at the levels of the clinic is not associated with blood pressure control. In contrast, TI measured at the clinic level is associated with blood pressure control. These findings raise the question of whether adherence to chronic medications can be used as a performance measure. Whether TI is suitable as a performance measure will depend on ability to measure it accurately in various care systems, and on demonstration that such a measure would not lead to unintended harms related to overtreatment of hypertension in some subgroups of patients.

Sources of Funding

Dr Vigen was supported by a Cardiovascular Outcomes Research Fellowship through a Department of Veterans Affairs Graduate Medical Education Enhancement Grant.

Disclosures

Dr O’Connor was supported by Research Grants HL 089471, HL 093345, DK 079861, and HL 02144. Dr Margolis was supported by Research Grants NIH/R01HL09345-01; Berman Center/HHSN268201100027C; KPNC/U19 HL091179; NHLBI/1RO1HL089451-01A1; NHLBI/R01 HL09065-01; NHLBI/N01-WH-3-2101; NIA/UFAG029824; NHLBI/1RO1HL102144-01; A12-046 Assessing Accuracy of Blood Pressure Measurement in HealthPartners Usual Clinical Care.

References


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Circ Cardiovasc Qual Outcomes. published online May 10, 2012;
Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-7705. Online ISSN: 1941-7713

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SUPPLEMENTAL MATERIAL

In this Appendix, we provide additional details to our multivariable analyses of the association between adherence and treatment intensification with BP control. Further, we have conducted additional analyses on treatment intensification. First, we have constructed scatterplots to illustrate the relationship between TI and BP control. Then, we increased the number of categories of treatment intensification from 3 as outlined in the paper to 5 to further explore the relationship between TI and BP control.

Supplemental methods:

This paper used multilevel logistic models and we describe models that include patients’ adherence as a continuous predictor variable (level 1 predictor) and a model that additionally includes the average clinic adherence as a level 2 predictor.

The outcome variable \( y_{ijk} \) is blood pressure control; a 0,1 variable that is modeled for the \( i^{th} \) patient nested within the \( j^{th} \) physician, nested within the \( k^{th} \) clinics using the logit link function \[ g(E(y_{ijk}))=g(\mu_{ijk})=\text{logit}(\mu_{ijk})=\Gamma_{ijk} \].

Model 1: Estimate the patient level adherence association with blood pressure outcome

Level 1 equation:
\[ \Gamma_{ijk} = b_{0jk} + b_{1jk}\text{adherence} \]

Level 2 equations:
\[ b_{0jk} = \beta_{00} + b^{*}_{0jk} \]
\[ b_{1jk} = \beta_{10} \]
\[ b^{*}_{0jk} \sim N [0, \sigma_{00}^2] \]

Model 2: Estimate the clinic level average adherence association with blood pressure outcome

Level 1 equation:
\[ \Gamma_{ijk} = b_{0jk} + b_{1jk}\text{adherence} \]

Level 2 equations:
\[ b_{0jk} = \beta_{00} + \beta_{0j}\text{MeanAdher} + b^{*}_{0jk} \]
\[ b_{1jk} = \beta_{10} \]
\[ b^{*}_{ijk} \sim N(0, \sigma^2_{00}) \]

MeanAdher=average clinic adherence

Models were run using the GLIMMIX procedure in SAS version 9.2. Example code is shown below for unadjusted models:

Model 1 Estimating patient level adherence association with blood pressure outcome

Proc Glimmix data=Dataset noclprint;
Class clinic_id provider_id;
Model bpcontrol(event='1')= adherence / dist=Binomial Solution ddfm=kr;
Nloptions tech=Nrridg;
Random intercept/ subject=provider_id(clinic_id));
Run;

Model 2 Estimating patient level adherence association with blood pressure outcome

Proc Glimmix data=Dataset noclprint;
Class clinic_id provider_id;
Model bpcontrol(event='1')= adherence MeanAdher/ dist=Binomial Solution ddfm=kr;
Nloptions tech=Nrridg;
Random intercept/ subject=provider_id(clinic_id));
Run;

Additional analyses on treatment intensification:

We used the same models as described above for adherence for our continuous model of treatment intensification. Additionally, we categorized treatment intensification scores into tertiles and quintiles to further explore the relationship between TI and BP control. This data is reported here. First, we plotted the relationship between TI and BP control at the patient level, with TI score on the x-axis, and the proportion of patients with BP control on the y-axis in Figure 1. In this figure, we rounded patient TI scores to the nearest two decimal points. As can be seen from the graph, there is a linear relationship between BP control and treatment intensification from a TI score of -1 to 0, demonstrating that a greater degree of appropriate (i.e., intensification when BP is elevated) TI is associated with better BP control compared to no TI when the BP is elevated. From a TI score of 0 to 1, there appears to be a plateau in the relationship between therapy intensification and BP control, showing that additional TI when the BP is not
significantly elevated (BP<150/90 mm Hg) may not lead to more BP control since the BP is not that elevated to begin with.

Next, we plotted the relationship between TI and BP control at the clinic level with the mean TI score on the x-axis and the proportion of clinics with BP control on the y-axis in Figure 2. Compared to the patient level data, there is less variability in the association between TI and BP control given fewer observations with patients clustered within clinics. There is a linear relationship between BP control and treatment intensification from a TI score of -1 to 0, demonstrating that clinics more likely to intensify treatment when BP is elevated have a greater proportion of patients with BP control.

Next, at the patient level, we categorized TI into 3 levels (data presented in the primary paper) and then 5 levels (Table 1). In the 3 level analysis, treatment intensification, defined by an increase in dosing or addition of an anti-hypertensive medication, as compared to no treatment intensification when BP was elevated (BP >150/90) was associated with blood pressure control (OR 2.87; 95% CI 2.78 – 2.97). As expected, treatment intensification when the BP was <150/90 was also associated with BP control as compared to no treatment intensification when BP was elevated (OR 3.47; 95% CI 3.34 – 3.60). In the 5-level analysis, there was increasing BP control with TI categories closer to 0 from -1. In contrast, there was some increase in BP control with TI categories from 0 to 1 but not to the degree of change seen when the TI score increased from -1 to 0.

Next, we categorized TI at the clinic level into categories (Table 2). The range of Treatment Intensification scores at the clinic level was significantly narrower than at the patient level, and therefore, different values were used to categorized clinic TI in to 3 and 5 groups as compared to the patient level categories. The findings at the clinic level were similar to the patient level analysis with the exception that the hazards ratios were smaller likely due to the smaller range of TI scores at the clinic level. Clinics that were more likely to intensify treatment when BP was elevated were associated with better BP control compared to clinics that were less likely to intensify treatment when the BP was elevated.

Supplemental Tables:

Table 1: Three and five-level categorical analyses of patient treatment intensification scores

<table>
<thead>
<tr>
<th>TI Category</th>
<th>n</th>
<th>Percent</th>
<th>MV analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>TI &lt; 0</td>
<td>23,816</td>
<td>18.61%</td>
<td>Referent</td>
</tr>
<tr>
<td>TI = 0</td>
<td>65,469</td>
<td>51.15%</td>
<td>2.87 (2.78 - 2.97)</td>
</tr>
<tr>
<td>TI &gt; 0</td>
<td>38,721</td>
<td>30.25%</td>
<td>3.47 (3.34 – 3.60)</td>
</tr>
</tbody>
</table>

Table 2: Three and five-level categorical analyses of patient treatment intensification scores
Table 2: Three and five-level categorical analyses of clinic treatment intensification scores

<table>
<thead>
<tr>
<th>TI Category</th>
<th>n</th>
<th>Percent</th>
<th>MV analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>TI &lt; -0.25</td>
<td>11,779</td>
<td>9.20%</td>
<td>Referent</td>
</tr>
<tr>
<td>-0.25 ≤ TI &lt; 0</td>
<td>12,037</td>
<td>9.40%</td>
<td>2.34 (2.21 - 2.48)</td>
</tr>
<tr>
<td>TI = 0</td>
<td>65,469</td>
<td>51.15%</td>
<td>4.59 (4.38 - 4.81)</td>
</tr>
<tr>
<td>0 ≤ TI ≤ 0.25</td>
<td>16,247</td>
<td>12.69%</td>
<td>6.46 (6.10 - 6.84)</td>
</tr>
<tr>
<td>TI &gt; 0.25</td>
<td>22,474</td>
<td>17.56%</td>
<td>5.02 (4.76 - 5.29)</td>
</tr>
</tbody>
</table>

Three categories of clinic treatment intensification (n=89)

<table>
<thead>
<tr>
<th>TI Category</th>
<th>n</th>
<th>Percent</th>
<th>MV analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>TI &lt; -0.005</td>
<td>31</td>
<td>34.83%</td>
<td>Referent</td>
</tr>
<tr>
<td>0.005 ≤ TI &lt; 0.03</td>
<td>31</td>
<td>34.83%</td>
<td>1.17 (1.11 – 1.23)</td>
</tr>
<tr>
<td>TI &gt; 0.03</td>
<td>27</td>
<td>30.34%</td>
<td>1.30 (1.23 – 1.36)</td>
</tr>
</tbody>
</table>

Five categories of clinic treatment intensification (n=89)

<table>
<thead>
<tr>
<th>TI Category</th>
<th>n</th>
<th>Percent</th>
<th>MV analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>TI &lt; -0.02407</td>
<td>17</td>
<td>19.10%</td>
<td>Referent</td>
</tr>
<tr>
<td>0.02407 ≤ TI &lt; 0.00485</td>
<td>18</td>
<td>20.22%</td>
<td>1.13 (1.06 - 1.22)</td>
</tr>
<tr>
<td>0.00485 ≤ TI &lt; 0.02113</td>
<td>19</td>
<td>21.35%</td>
<td>1.24 (1.17 - 1.32)</td>
</tr>
<tr>
<td>0.02113 ≤ TI &lt; 0.04066</td>
<td>18</td>
<td>20.22%</td>
<td>1.24 (1.17 - 1.31)</td>
</tr>
<tr>
<td>TI &gt; 0.04066</td>
<td>17</td>
<td>19.10%</td>
<td>1.45 (1.36 - 1.54)</td>
</tr>
</tbody>
</table>

SUPPLEMENTAL FIGURES

Figure 1:
Figure Legend:

Figure 1: Scatterplot depicting patient treatment intensification scores and proportion of patients with blood pressure control. Patient TI scores are rounded to 2 decimal points.

Figure 2: Scatterplot depicting average clinic treatment intensification scores and proportion clinic patients with blood pressure control.