Blood Pressure Trajectories and Associations With Treatment Intensification, Medication Adherence, and Outcomes Among Newly Diagnosed Coronary Artery Disease Patients

Thomas M. Maddox, MD, MSc; Colleen Ross, MS; Heather M. Tavel, BS; Ella E. Lyons, MS; Maggie Tillquist, BA; P. Michael Ho, MD, PhD; John S. Rumsfeld, MD, PhD; Karen L. Margolis, MD, MPH; Patrick J. O’Connor, MD, MPH; Joe V. Selby, MD, MPH; David J. Magid, MD, MPH

Background—Blood pressure (BP) control among coronary artery disease patients remains suboptimal in clinical practice, potentially due to gaps in treatment intensification and medication adherence. However, longitudinal studies evaluating these relationships and outcomes are limited.

Methods and Results—We assessed BP trajectories among health maintenance organization patients with hypertension and incident coronary artery disease. BP trajectories were modeled over the year after coronary artery disease diagnosis, stratified by target BP goal. Treatment intensification (increase in BP therapies in the setting of an elevated BP), medication adherence (percentage of days covered with BP therapies), and outcomes (all-cause mortality, myocardial infarction, and revascularization) were evaluated in multivariable models: 9569 patients had a <140/90 mm Hg BP target and 12,861 had a <130/80 mm Hg BP target. Within each group, 4 trajectories were identified: good, borderline, improved, and poor control. After adjustment, increasing BP treatment intensity was significantly associated with better BP trajectories in both groups. Medication adherence had inconsistent effects. There were no significant differences in combined outcomes by BP trajectory, but among the diabetes and renal disease cohort, borderline control patients were less likely to have myocardial infarction (odds ratio, 0.61; 95% confidence interval, 0.40–0.93), and good control patients were less likely to have myocardial infarction (odds ratio, 0.53; 95% confidence interval, 0.34–0.84) or a revascularization procedure (odds ratio, 0.66; 95% confidence interval, 0.47–0.93) compared with poor control patients.

Conclusions—In this health maintenance organization population, treatment intensification but not medication adherence significantly affects BP trajectories in the year after coronary artery disease diagnosis. Better BP trajectories are associated with lower rates of myocardial infarction and revascularization. (Circ Cardiovasc Qual Outcomes. 2010;3:347-357.)

Key Words: hypertension ■ epidemiology ■ health services research ■ myocardial infarction ■ mortality

Among patients with coronary artery disease (CAD), treatment and control of blood pressure (BP) significantly reduces rates of myocardial infarction (MI) and mortality.1 Yet, BP control among CAD patients is suboptimal, with some studies demonstrating that nearly half of eligible patients are not at recommended BP levels.2 Prior studies suggest that factors underlying suboptimal BP control include failure to intensify antihypertensive treatments and failure to adhere to these treatments.3

Editorial see p 335

Most studies analyzing BP control have used discrete, cross-sectional assessments of BP control at arbitrary points in time, which may not accurately reflect BP control. In contrast, clinical decisions regarding BP management are typically based on serial BP measurements, or trajectories, over time. Characterizing BP trajectories over time and their association with treatment intensification and medication control is critical to understanding the impact of treatment strategies on long-term outcomes.

Received April 12, 2010; accepted May 5, 2010.
From the Denver VAMC/University of Colorado Denver (T.M.M., M.H., J.S.R.), Denver Colo; Institute for Health Research (C.R., H.M.T., E.E.L., D.J.M.), Kaiser Permanente Colorado, Denver, Colo; University of Colorado Denver School of Medicine (M.T.), Denver, Colo; Health Partners Research Foundation (K.L.M., P.J.O.), Minneapolis, Minn; and Kaiser Permanente Northern California (J.V.S.), Oakland, Calif.
The online-only Data Supplement is available at http://circoutcomes.ahajournals.org/cgi/content/full/CIRCOUTCOMES.110.957308/DC1.
Guest Editor for this article was Paul Heidenreich, MD.
Correspondence to Thomas M. Maddox, MD, Denver VAMC, Cardiology Section (111B), 1055 Clermont St, Denver, CO 80220. E-mail thomas.maddox@va.gov
© 2010 American Heart Association, Inc.
Circ Cardiovasc Qual Outcomes is available at http://circoutcomes.ahajournals.org
DOI: 10.1161/CIRCOUTCOMES.110.957308
adherence may provide better understanding of the mechanisms underlying suboptimal BP control than cross-sectional assessments. Furthermore, BP trajectories may provide more accurate insights into the relationship between BP and cardiac outcomes than cross-sectional assessments.\textsuperscript{5,6} and may help interventions for improvement.

Therefore, in a cohort of hypertensive patients with newly diagnosed CAD, we sought to (1) describe BP trajectories in the year after CAD diagnosis, (2) evaluate the association between treatment intensification, medication adherence, and BP trajectories, and (3) assess the relationship between BP trajectories and outcomes.

**WHAT IS KNOWN**

- Blood pressure (BP) control among patients with coronary artery disease is suboptimal, and prior studies suggest that factors underlying suboptimal BP control include failure to intensify antihypertensive treatments and failure to adhere to these treatments.
- Characterizing BP trajectories over time and their association with treatment intensification and medication adherence may provide better understanding of the mechanisms underlying suboptimal BP control and their associated outcomes than cross-sectional assessments.

**WHAT THE STUDY ADDS**

- In this population of health maintenance organization patients with hypertension and coronary artery disease, we identified 4 distinct SBP trajectories during the year after their initial diagnosis of coronary artery disease: good control, borderline control, improved control, and poor control.
- In this population, treatment intensification of antihypertension medications but not medication adherence was consistently associated with better systolic BP control over the year after an initial coronary artery disease diagnosis.
- Systolic BP trajectories did not demonstrate significant associations with a combined outcome of all-cause mortality, myocardial infarction, and revascularization, but good control patients were less likely to have myocardial infarction or revascularization procedures than poor control patients, and borderline control patients were significantly less likely to have myocardial infarction than poor control patients.

**Methods**

**Study Population and Data Collection**

The study cohort comprised nonpregnant, adult patients with hypertension (HTN) who were newly diagnosed with CAD and derived from the Cardiovascular Research Network (CVRN) HTN registry (Figure 1). Development of the CVRN HTN registry has been described previously.\textsuperscript{6} In brief, patients with HTN being seen at the health maintenance organizations (HMOs) of Kaiser Permanente Northern California, and Health Partners of Minnesota from 2000 to 2007 were identified using a published algorithm.\textsuperscript{7}

From this HTN population, we then identified patients with an initial diagnosis of CAD between 2003 and 2006. We selected patients with an initial diagnosis of CAD because a CAD diagnosis can motivate efforts to improve BP control, and BP control is likely to reduce subsequent events in this population. An initial diagnosis of CAD was defined as the first occurrence of CAD, using ICD-9 or CPT-4 codes for MI, other forms of acute or chronic ischemic heart disease, or receipt of a coronary revascularization procedure (percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)) (see Supplemental Appendix).

We further restricted the cohort to those patients with continuous health plan enrollment and pharmacy coverage for the year preceding and after the initial CAD diagnosis, with at least 1 ambulatory BP measurement recorded before the CAD diagnosis, and with at least 3 ambulatory BP measurements occurring at least 30 days apart from one another after CAD diagnosis. The study cohort was approved by the Kaiser Permanente Colorado Institutional Review Board.

**Blood Pressure**

BP values were obtained from each patient’s electronic medical record. For this analysis, only systolic blood pressures (SBP) were used because SBP has a stronger association with outcomes than diastolic BP.\textsuperscript{7} To avoid spuriously high values, we excluded all measurements that occurred in an inpatient setting on the day of a procedure (where BP medications may have been temporarily held) or during an emergency department visit (where pain or other emergent conditions may cause temporary elevations in BP). Target systolic SBP control was defined as <140 mm Hg and <130 mm Hg in patients with concurrent diabetes (DM) or chronic kidney disease (CKD) (estimated glomerular filtration rate <60 mL/min).\textsuperscript{7}

**Medication Adherence**

Medication adherence was calculated as the proportion of days covered (PDC), based on the number of days supplied of BP medication divided by the observation time interval. For patients receiving multiple BP medications, an average PDC was calculated across all medications. Patients were classified as “nonadherent” on the basis of a PDC <0.80.\textsuperscript{9}

**Treatment Intensification**

Treatment intensification (TI) was calculated using a standard-based method score, as characterized by Rose et al.\textsuperscript{9} The TI score assesses the number of times that treatment intensification appropriately occurs. Calculation of the TI score is the number of observed TI minus the number of expected TI divided by the number of clinic visits over the observation period. Observed TI occurred when an antihypertensive was prescribed or a current dose increased in the 4 weeks after the occurrence of an elevated BP. Expected TI occurred when the measured SBP was elevated above the target goal. Accordingly, the TI score could range from −1 to 1, with −1 indicating no treatment intensification at any visit where the SBP was elevated, 0 indicating treatment intensification at every visit where the SBP was elevated, and 1 indicating treatment intensification at every visit regardless of the SBP level.

To account for potential clinical ambiguity in intensifying therapy when the SBP is only a few mm Hg above the target goal, we assessed for treatment intensification only when the measured SBP was 10 mm Hg or more above the JNC VII goal (ie, 140 mm Hg or more for patients with DM or renal disease, 150 mm Hg or more for all others). In addition, we allowed a grace period of 4 weeks after the measurement of an elevated SBP where intensification was not assessed to allow for the clinical scenario when providers may be waiting for any prior treatment intensification to take effect before taking further clinical action.

**Outcomes**

Adverse outcomes of interest were all-cause mortality, MI, or the receipt of a revascularization procedure (PCI or CABG). All-cause mortality was determined by enrollment and state death date within each HMO. MI and
revascularization was determined by ICD-9 or CPT-4 codes. Outcomes were assessed beginning 1 year after the initial CAD diagnosis and continuing during the remainder of the patient follow-up period.

**Statistical Analysis**

The cohort was stratified by target SBP goal, as defined above. For each cohort, SBP trajectories were determined using the PROC TRAJ procedure in SAS, consistent with prior studies evaluating trajectories. This procedure models the conditional distribution of longitudinal SBP measurements, given a discrete latent class assignment. The procedure isolates distinct trajectories of SBP over time (1 for each latent class) and fits a mixture model to calculate the probability of membership in each latent class for each patient. The Bayesian information criterion (BIC) is used to determine the optimal number of trajectories and is analogous to the adjusted $R^2$ in that it balances model complexity and model fit, with smaller BIC values indicating a better fit.

We examined models based on all available SBP data during the year after CAD diagnosis. The model with 4 distinct SBP trajectory groups, based on its BIC value, appeared to provide the best balance between data fit and complexity. Patients were assigned to the group for which the probability of inclusion was the highest, and the average probability of patients being assigned to their group was $72\%$. As a sensitivity analysis, we also examined models with 3 and 5 SBP trajectory groups, but the fit and complexity did not improve compared with the analysis using 4 groups (data not presented).

Once the BP trajectories were determined, the relationship between BP trajectory groups, treatment intensification, and medication adherence was assessed. For each trajectory group, the TI score and medication adherence values were calculated, reported, and compared using $t$ tests for treatment intensification and $\chi^2$ tests for
medication adherence. Then, to assess for independent effects of treatment intensification and medication adherence, generalized logit models were constructed using BP trajectory group as the outcome. In addition to treatment intensification and medication adherence, we entered all of the demographic and clinical variables listed in Table 1 in the models. Socioeconomic stress was measured by geocoding. Those patients who lived in areas with at least 20% of households at below poverty level or at least 25% of the population with no education beyond high school were considered as having socioeconomic stress. In the cohort of patients with DM and/or renal disease, those comorbidities were also included in the model.

Finally, combined and individual outcomes (all-cause mortality, MI, and revascularization) occurring after the first anniversary of the initial CAD diagnosis were assessed for each group, reported as percentages, and compared using the log-rank method. Cox proportional hazard models were used to control for potential confounding by clinical differences between the trajectory groups. Covariates in the model included all of the demographic and clinical variables listed in Table 1. Proportional hazards assumptions were tested using Martingale residuals.

For all analyses, SAS version 9 was used. Probability values <0.05 were considered to be statistically significant.

### Table 1. Baseline Characteristics of the No Diabetes or Chronic Kidney Disease Cohort

<table>
<thead>
<tr>
<th>HMO site</th>
<th>All Subjects (n=9569)</th>
<th>Good Control (n=3955)</th>
<th>Borderline Control (n=4633)</th>
<th>Improved Control (n=408)</th>
<th>Poor Control (n=573)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, y</strong></td>
<td>66.9 ± 11.6</td>
<td>65.2 ± 11.8</td>
<td>67.6 ± 11.4</td>
<td>70.5 ± 11.0</td>
<td>70.6 ± 11.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Male sex</strong></td>
<td>5333 (55.7)</td>
<td>2482 (62.8)</td>
<td>2437 (52.6)</td>
<td>168 (41.2)</td>
<td>246 (42.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>6275 (65.6)</td>
<td>2557 (64.7)</td>
<td>3085 (66.6)</td>
<td>267 (65.4)</td>
<td>366 (63.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>728 (7.6)</td>
<td>305 (7.7)</td>
<td>354 (7.6)</td>
<td>21 (5.1)</td>
<td>48 (8.4)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>640 (6.7)</td>
<td>210 (5.3)</td>
<td>338 (7.3)</td>
<td>33 (8.1)</td>
<td>59 (10.3)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1056 (11.0)</td>
<td>481 (12.2)</td>
<td>476 (10.3)</td>
<td>54 (13.2)</td>
<td>45 (7.9)</td>
<td></td>
</tr>
<tr>
<td>Unknown/missing</td>
<td>870 (8.9)</td>
<td>402 (10.2)</td>
<td>380 (8.2)</td>
<td>33 (8.1)</td>
<td>55 (9.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Socioeconomic stress</strong></td>
<td>1796 (18.8)</td>
<td>694 (17.5)</td>
<td>889 (19.2)</td>
<td>76 (18.6)</td>
<td>137 (23.9)</td>
<td>0.0009</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>6129 (64.1)</td>
<td>2581 (65.3)</td>
<td>2976 (64.2)</td>
<td>237 (58.1)</td>
<td>335 (58.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Current tobacco use</td>
<td>2170 (22.7)</td>
<td>926 (23.4)</td>
<td>1023 (22.1)</td>
<td>84 (20.6)</td>
<td>137 (23.9)</td>
<td>0.299</td>
</tr>
<tr>
<td>Former tobacco use</td>
<td>3040 (31.8)</td>
<td>1297 (32.8)</td>
<td>1481 (32.0)</td>
<td>107 (26.2)</td>
<td>155 (27.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>1075 (11.2)</td>
<td>480 (12.1)</td>
<td>517 (11.2)</td>
<td>40 (9.8)</td>
<td>38 (6.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>CHF</td>
<td>1508 (15.8)</td>
<td>733 (18.5)</td>
<td>611 (13.2)</td>
<td>65 (15.9)</td>
<td>99 (17.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CVA</td>
<td>777 (8.1)</td>
<td>301 (7.6)</td>
<td>387 (8.4)</td>
<td>24 (5.9)</td>
<td>65 (11.3)</td>
<td>0.006</td>
</tr>
<tr>
<td>PVD</td>
<td>936 (9.8)</td>
<td>373 (9.4)</td>
<td>451 (9.7)</td>
<td>51 (12.5)</td>
<td>61 (10.6)</td>
<td>0.216</td>
</tr>
<tr>
<td>Depression</td>
<td>2217 (23.2)</td>
<td>937 (23.7)</td>
<td>1066 (23.0)</td>
<td>95 (23.3)</td>
<td>119 (20.8)</td>
<td>0.469</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>3247 (33.9)</td>
<td>1337 (33.8)</td>
<td>1592 (34.4)</td>
<td>125 (30.6)</td>
<td>193 (33.7)</td>
<td>0.493</td>
</tr>
<tr>
<td>OSA</td>
<td>603 (6.3)</td>
<td>269 (6.8)</td>
<td>292 (6.3)</td>
<td>19 (4.7)</td>
<td>23 (4.0)</td>
<td>0.035</td>
</tr>
</tbody>
</table>

**BP and treatment parameters**

<table>
<thead>
<tr>
<th>No. of outpatient BP measurements during the year</th>
<th>6.3 ± 3.0</th>
<th>6.5 ± 3.1</th>
<th>6.2 ± 2.9</th>
<th>6.3 ± 2.7</th>
<th>6.2 ± 2.7</th>
<th>0.002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average SBP, mm Hg</td>
<td>128.9 ± 12.5</td>
<td>117.4 ± 5.6</td>
<td>133.8 ± 5.7</td>
<td>148.7 ± 6.9</td>
<td>154.6 ± 7.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline SBP after initial CAD diagnosis, mm Hg</td>
<td>128.6 ± 14.9</td>
<td>117.1 ± 8.7</td>
<td>133.1 ± 9.8</td>
<td>159.7 ± 8.9</td>
<td>149.3 ± 13.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Average SBP at the end of the year after initial CAD diagnosis, mm Hg</td>
<td>128.7 ± 14.4</td>
<td>118.6 ± 9.2</td>
<td>133.4 ± 10.7</td>
<td>137.1 ± 12.7</td>
<td>155.1 ± 13.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medication adherence value</td>
<td>0.87 ± 0.11</td>
<td>0.87 ± 0.11</td>
<td>0.87 ± 0.12</td>
<td>0.87 ± 0.1</td>
<td>0.86 ± 0.12</td>
<td>0.905</td>
</tr>
<tr>
<td>Treatment intensification score</td>
<td>0.01 ± 0.3</td>
<td>0.16 ± 0.22</td>
<td>-0.05 ± 0.29</td>
<td>-0.2 ± 0.27</td>
<td>-0.32 ± 0.29</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are expressed as n (%) or mean ± SD.

CHF indicates congestive heart failure; CVA, cerebrovascular accident; PVD, peripheral vascular disease; and OSA, obstructive sleep apnea.
Results

BP Trajectories
Our study cohort consisted of 22,430 patients with an initial CAD diagnosis between 2003 and 2006, of which 12,861 (57.3%) had either DM and/or CKD.

Among the cohort without DM or CKD (no DM/CKD), 4 distinct trajectory groups were identified: good control (SBP values persistently around 120 mm Hg; n=3,955; 41.6%), borderline control (SBP values persistently around 130 mm Hg; n=4,633; 45.6%), improved control (initially elevated SBP values that declined to normal levels during the observation period; n=408; 6.3%), and poor control (SBP values persistently at or above 140 mm Hg; n=573; 6.5%) (Figure 2).

Among the cohort with DM and/or CKD (DM/CKD), a similar distribution of trajectory groups was identified: good control (SBP values persistently around 120 mm Hg; n=5,001; 39.7%), borderline control (SBP values persistently around 130 mm Hg; n=6,351; 46.6%), improved control (initially elevated SBP values that declined to near-normal levels during the observation period; n=683; 6.8%), and poor control (SBP values persistently at or above 130 mm Hg; n=826; 6.9%) (Figure 3).

Demographic and clinical characteristics for both cohorts are displayed in Table 1 and Table 2. Approximately three
fourths of patients in both cohorts were members of Kaiser Permanente Northern California. In general, patients with good SBP control in both cohorts were younger, more likely male, and less likely to experience socioeconomic stress than patients with borderline, improved, or poor SBP control. Clinically, they were more likely to have an MI as their initial CAD event and undergo PCI. Other comorbidities were fairly evenly distributed among the various trajectory groups. Among the DM/CKD cohort, the prevalence of DM was evenly distributed among the groups, but patients with poor SBP control were more likely to have CKD than those with good SBP control.
better BP control (Table 4). For each 0.1 increase in TI score BP treatment intensity was significantly associated with control, and poor control groups. After adjustment, increasing intensive BP treatments in the borderline control, improved control group and progressively decreased (indicating less treatment intensification) in the no DM/CKD cohort. The overall TI score was highest in the good control group, compared with the poor control group, increased by 23% (OR of being in the borderline control group and improved control groups were 50% and 17%, respectively (OR for borderline control versus poor control, 1.50; 95% CI, 1.45–1.52; OR for improved control versus poor control, 1.17; 95% CI, 1.12–1.25).

In the no DM/CKD cohort, overall medication adherence values were 0.87, indicating excellent adherence (Table 1). There was no significant difference in adherence values between trajectory groups. After adjustment, the effect of medication adherence on BP control was inconsistent (Table 3). Increasing medication adherence significantly increased the odds for being in the improved control group, compared with the poor control group, by 56% (OR for improved control versus poor control, 1.56; 95% CI, 1.15–2.13) but did not have significant effects on membership in either the good control or borderline control group (OR for good control versus poor control, 1.16; 95% CI, 0.94–1.43; OR for borderline control versus poor control, 1.14; 95% CI, 0.92–1.40).

Medication adherence results were also inconsistent for the DM/CKD cohort. The overall medication adherence value was 0.86, indicating excellent adherence (Table 2). The adherence values between trajectory groups were clinically similar, despite achieving statistical significance. After adjustment, increasing medication adherence significantly increased the odds of membership in the borderline control group, compared with the poor control group, by 23% (OR of

### Table 3. Odds Ratios and 95% Confidence Intervals of Treatment Intensification and Medication Adherence Among the No Diabetes or CKD Cohort

<table>
<thead>
<tr>
<th></th>
<th>Improved Control</th>
<th>Borderline Control</th>
<th>Good Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unadjusted</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment intensification</td>
<td>1.287 (1.212–1.366)</td>
<td>1.702 (1.628–1.780)</td>
<td>1.831 (1.749–1.916)</td>
</tr>
<tr>
<td>Medication adherence</td>
<td>1.582 (1.164–2.150)</td>
<td>1.139 (0.927–1.398)</td>
<td>1.153 (0.936–1.421)</td>
</tr>
<tr>
<td><strong>Adjusted</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment intensification</td>
<td>1.297 (1.218–1.381)</td>
<td>1.717 (1.637–1.799)</td>
<td>1.819 (1.734–1.909)</td>
</tr>
<tr>
<td>Medication adherence</td>
<td>1.563 (1.147–2.132)</td>
<td>1.138 (0.924–1.403)</td>
<td>1.158 (0.936–1.434)</td>
</tr>
</tbody>
</table>

Referent indicates poor control (n=9519). Covariates included age, sex, race, type of initial CAD event, hyperlipidemia, congestive heart failure, cerebrovascular disease, depression, lung disease, peripheral vascular disease, diabetes, renal disease, sleep apnea, and tobacco use.
borderline control versus poor control, 1.23; 95% CI, 1.03–1.46) but did not have significant effects on membership in either the good control or improved control groups (OR of good control versus poor control, 1.06; 95% CI, 0.88–1.27; OR of improved control versus poor control, 1.25; 95% CI, 0.98–1.57) (Table 4).

### BP Trajectories and Outcomes

Patients in the no DM/CKD cohort (n=9562) were evaluated for the combined and individual outcomes of all-cause mortality, MI, or revascularization occurring after their first year after an initial CAD diagnosis; 834 (8.8%) patients experienced an event during a mean follow-up period of 1.8 years. The event rates were lowest in the borderline control trajectory group (372 events, 8.0%), followed by the good control group (352 events, 8.9%), the improved control group (45 events, 11.0%), and the poor control group (65 events, 11.3%) (Figure 4). However, after adjustment for potential confounders, there were no significant differences in combined event rates between the BP trajectory groups (HR of good control versus poor control, 1.08; 95% CI, 0.83–1.42; HR of borderline control versus poor control, 0.88; 95% CI, 0.68–1.15; HR of improved control versus poor control, 1.05; 95% CI, 0.72–1.54) (Figure 5). Analysis of individual events (all-cause mortality, MI, and revascularization) also demonstrated no significant differences between BP trajectory groups.

Patients in the DM/CKD cohort (n=12849) were evaluated for the combined and individual outcomes of all-cause mortality, MI, or revascularization occurring after their first year after an initial CAD diagnosis; 1859 (14.5%) patients had an event during a mean follow-up period of 1.7 years. The event rates were lowest in the borderline control trajectory group (848 events, 13.4%), followed by the good control group (723 events, 14.5%), the poor control group (153 events, 18.5%), and the improved control group (135 events, 19.8%) (Figure 6). After adjustment for potential confounders, there were no significant differences in combined event rates between the BP trajectory groups (HR of good control versus poor control, 0.98; 95% CI, 0.82–1.17; HR of borderline control versus poor control, 0.84; 95% CI, 0.71–1.00; HR of improved control versus poor control, 1.10; 95% CI, 0.88–1.40) (Figure 7). However, in the analysis of individual events (all-cause mortality, MI, and revascularization), borderline control patients, compared with poor control patients, were less likely to have an MI (OR, 0.61; 95% CI, 0.40–0.93), and good control patients, compared with poor control patients, were less likely to have an MI (OR, 0.53; 95% CI, 0.34–0.84) and less likely to have a revascularization procedure (OR, 0.66; 95% CI, 0.47–0.93).

### Discussion

In the present population of HMO patients with HTN and CAD, we identified 4 distinct SBP trajectories during the year after their initial diagnosis of CAD: good control, borderline control, improved control, and poor control. Among these trajectories, treatment intensification of anti-HTN medications was associated with better SBP control over the year.
after an initial CAD diagnosis. In contrast, medication adherence had a less consistent association with SBP control. Finally, SBP trajectories did not demonstrate significant associations with a combined outcome of all-cause mortality, MI, and revascularization, but good control patients were less likely to have MIs or revascularization procedures and borderline control patients were significantly less likely to have MIs than poor control patients. These findings suggest that different patterns of SBP control exist in the year after initial CAD diagnosis, appropriate treatment intensification is associated with better control, and better control is associated with individual outcomes of MI and revascularization.

Prior studies have examined various methods of characterizing longitudinal BP patterns and outcomes, but they did not...
evaluate BP trajectories over time.4,5,12,13 Similarly, prior studies demonstrate associations between poor medication adherence, decreased treatment intensification, and outcomes but also did not examine BP trajectories over time.3,14–17

Our group has previously used a trajectory analysis to assess BP patterns over time in a single HMO and found that patients with persistently uncontrolled BP had higher rates of medication nonadherence and treatment intensification compared with those who had controlled BP.3 This association between low treatment intensification and poor BP control is different than the findings of our prior study and may be partly explained by the more specific measure of treatment intensification used in the current study, which has been demonstrated to be superior to a more general measure.9 In addition, we have expanded on the prior findings by evaluating the association between BP trajectories and adverse outcomes.

Our study has important implications for measurement of BP over time and for elucidating the effects of medication adherence and treatment intensification on BP control. Trajectory analysis more accurately represents the clinical reality of BP management. By linking trajectories to outcomes, our study adds credence to this approach to BP management. Furthermore, this method of BP pattern measurement can allow for a more accurate characterization of factors that impact BP control over time, allowing for more effective design of interventions to improve control. Finally, the technique of trajectory analysis has broad application to a variety of serial health measurements, such as symptoms or laboratory values, allowing for better characterization of care and research into its improvement.

Our findings suggest several next steps for investigation. First, our findings should be validated in other populations. Part of the reason why medication adherence was not significantly associated with BP trajectories may be the uniformity of high medication adherence behavior in this HMO population. Medication adherence may play a larger role in BP trajectories in patients in other populations. In addition, one reason why our overall outcome rate was not significantly associated with BP trajectories may be the relatively small numbers of events. Larger studies or studies with longer follow-up times may uncover more significant associations. Interestingly, the reduced rates of MI in the borderline control group is consistent with recent trials, such as the ACCORD study, that indicate that “tight” BP control may not be more beneficial to patients. Although we did not compare good control to borderline control groups directly, future studies should explore these patterns.

There are several limitations to our study. First, the trajectory groups provide a general trend of BP control over time and may not accurately characterize each individual’s actual BP trajectory. Second, the technique we used to measure treatment intensification accounts for treatment intensification in the setting of a normal BP, which may artificially shift our mean value toward zero (indicating appropriate treatment intensification). However, we attempted to mitigate this effect by entering conditions into our multivariable models that would potentially explain the intensification of BP treatments in the setting of normal BP (eg, β-blocker or ACE inhibitor titration in congestive heart failure, ACE inhibitor titration in CKD). Third, patients had different numbers of BP measurements over the course of the year after their initial CAD diagnosis, which could have resulted in some imprecision in our estimates of treatment intensification. Fourth, our inclusion criteria mandated continuous enrollment and BP measurements in the HMO for at least 1 year before and after CAD diagnosis. Patients without continuous enrollment or BP measurements may be different than those enrolled, so our findings may not generalize to that population. For example, less than 10% of patients in both of our cohorts had persistently elevated SBPs during the year after CAD diagnosis, which is markedly lower than studies in other populations. Similarly, the rates of medication adher-
ence in our population were 86% to 87% of days covered with a prescription, which is markedly higher than studies of other populations. Fifth, our outcomes (all-cause mortality, MI, and revascularization) were based on administrative codes, rather than chart review, which could result in misclassification. Sixth, our method of measuring adherence may underestimate rates by not identifying patients who fail to fill their first and/or second prescription. Finally, as with all observational studies, unmeasured variables may confound our primary findings regarding medication adherence and treatment intensification.

In summary, we found 4 distinct trajectories of SBP control in the year after an initial CAD diagnosis among a patient population from 3 HMOs: good, borderline, improved, and poor control. Increased treatment intensification was associated with better BP control trajectories, and better BP control trajectories were associated with fewer MIs and revascularization procedures. These findings provide evidence that BP trajectories are a useful way to characterize BP patterns over time, improve with greater treatment intensification, and are associated with improved outcomes.

Sources of Funding
This study was supported by a grant made to the Cardiovascular Research Network (CVRN) from the National Heart Lung and Blood Institute under cooperative agreement U19 HL91179-01.

Disclosures
Drs Maddox and Ho are supported by VA Health Services Research and Development Career Development Awards. Dr Ho is a consultant for Wellpoint, Inc.

References
Blood Pressure Trajectories and Associations With Treatment Intensification, Medication Adherence, and Outcomes Among Newly Diagnosed Coronary Artery Disease Patients


Circ Cardiovasc Qual Outcomes. 2010;3:347-357; originally published online May 20, 2010; doi: 10.1161/CIRCOUTCOMES.110.957308

Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7705. Online ISSN: 1941-7713

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circoutcomes.ahajournals.org/content/3/4/347

Data Supplement (unedited) at:
http://circoutcomes.ahajournals.org/content/suppl/2010/05/20/CIRCOUTCOMES.110.957308.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Quality and Outcomes can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Quality and Outcomes is online at:
http://circoutcomes.ahajournals.org//subscriptions/
Appendix: ICD-9 and CPT-4 codes used to identify an initial CAD diagnosis

ICD-9 codes:
- MI 410.xx
- Acute IHD 411.xx
- Chronic IHD 414, 414.0, 414.00, 414.01, 414.2, 414.3, 414.8, and 414.9
- Receipt of PCI 36.0, 36.00, 36.01, 36.02, 36.03, 36.04, 36.05, 36.06, 36.07, 36.09
- Receipt of CABG 36.1, 36.10, 36.11, 36.12, 36.13, 36.14, 36.15, 36.16, 36.17, 36.19, 36.2

CPT-4 codes:
- Receipt of PCI 92973, 92974, 92975, 92977, 92979, 92980, 92981, 92982, 92984, 92987, 92992, 92995, 92996, 92997, 92998
- Receipt of CABG 33510, 33511, 33512, 33513, 33514, 33516, 33517, 33518, 33519, 33521, 33522, 33523, 33530, 33533, 33534, 33535, 33536