Time at blood pressure target and the risk of cardiovascular diseases and mortality

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On behave of S-C Chung and co-authors
**Introduction**

- Effective long term lifestyle and pharmacological interventions to lower blood pressure (BP) in reducing cardiovascular morbidity and mortality
- Suboptimal BP control is common (19-50%)
- The time a patient spends with BP at target level might be an important measure of hypertension care effectiveness
- However, this has not been evaluated in the general population
Study aims

• To describe the average Time per year spent by newly identified hypertensive patients at BP care TaRgEt (TITRE)
• To investigate factors associated with TITRE
• To assess the relationship between TITRE and cardiovascular outcomes
Methods (I)

• **Design:** Population record-linkage cohort of patients newly identified with high BP in CALIBER, England

• **Study period:** Jan 1997 – March 2010

• **Primary endpoints:**
  – **CVD composite:** incident cardiovascular death, acute myocardial infarction and stroke
  – **incident heart failure**
  – **composite of any incident CVD and death**

• **Secondary endpoints:** incident stable angina, peripheral arterial disease and all-cause mortality
Methods (II)

Inclusion criteria:
• $\geq 18$ years old
• $\geq 1$ year CPRD registered
• No prior CVD or hypertension
• $\geq 6$ months follow-up

Study entry

Study end
Methods (II)

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High BP: ≥140/90mmHg
(≥150/90 if ≥60 years without diabetes and CKD)
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On target BP: <140 & 90 mmHg
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High BP: ≥140/90mmHg
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On target BP: <140 & 90mmHg

TITRE: Annual % time, averaged over years of follow-up
Methods (III)

- **Baseline covariates:**
  - **Demographic:** age, sex, year of study entry, ethnicity, index of multiple deprivation
  - **Cardiovascular:** smoking, BMI, diabetes mellitus, total cholesterol, renal dysfunction (eGFR < 60 mL/min/1.73m²)
  - **Hypertension severity:** stage 2 (SBP ≥ 160 or DBP ≥ 100 mmHg)
  - **Treatment:** statin, aspirin

**Covariates during follow-up:**

- **Lifestyle interventions:** nutritional and smoking cessation
- **Treatment:** initial BP lowering drug class
CALIBER patients
2.68M

Study population
169,082

BP reads during study period
1.93M

Time at BP target (TITRE)
1.64M BP readings from 150,130 patients

Incident fatal & non-fatal CVDs: 5684 (3.4%)
CVD composite: 409
Heart failure: 318
Fatal CVD composite: 332

Median follow-up: 5 yr (IQR 3-7)
Median BP reading: 7 (IQR 3-16)
# Patient characteristics

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>N=169,082</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (years)</td>
<td>52</td>
</tr>
<tr>
<td>Women</td>
<td>56%</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>38%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristics during follow-up</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>BP lowering medication</td>
<td>46%</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>16%</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>15%</td>
</tr>
<tr>
<td>Dietary advice</td>
<td>29%</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>2%</td>
</tr>
<tr>
<td>Snapshot ‘control’ during the first year</td>
<td>47%</td>
</tr>
</tbody>
</table>
Time at target (TITRE) distribution (N=150,130)

Median TITRE: 2.8 (IQR 0.3 – 5.6) mths per year
Distribution of study patients by TITRE category

- 0 mths: 25,866 (15%)
- <3 mths: 7,557 (5%)
- 3-6 mths: 25,237 (15%)
- 6-9 mths: 18,952 (11%)
- 9-12 mths: 21,952 (13%)
- BP missing: 7,557 (5%)
- Total: 51,819 (31%)
Associations between patient characteristics & greater TITRE categories (6-8 mths vs. 3-5.9 mths)

<table>
<thead>
<tr>
<th>Hypertension state</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Snapshot 'control' in first year vs. no</td>
<td>2.22</td>
<td>(2.18–2.25)</td>
</tr>
<tr>
<td>Stage 2 vs. stage 1</td>
<td>0.91</td>
<td>(0.90–0.92)</td>
</tr>
<tr>
<td>Treatment during follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiazide diuretics vs. no drug</td>
<td>1.26</td>
<td>(1.23–1.28)</td>
</tr>
<tr>
<td>Calcium channel blocker vs. no drug</td>
<td>0.92</td>
<td>(0.89–0.94)</td>
</tr>
<tr>
<td>Dietary advice</td>
<td>1.10</td>
<td>(1.08–1.12)</td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women vs. men</td>
<td>1.12</td>
<td>(1.11–1.14)</td>
</tr>
<tr>
<td>Age ≥60 vs. &lt;60 years</td>
<td>1.38</td>
<td>(1.36–1.41)</td>
</tr>
<tr>
<td>Black vs. white</td>
<td>0.79</td>
<td>(0.73–0.84)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.20</td>
<td>(1.16–1.23)</td>
</tr>
</tbody>
</table>

Note: Generalised nominal models
## Association between TITRE and endpoints

### CVD composite

<table>
<thead>
<tr>
<th>TITRE</th>
<th>n(%)</th>
<th>OR</th>
<th>95% CI</th>
<th>n(%)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>108 (0.4)</td>
<td>4.51</td>
<td>(3.69–5.52)</td>
<td>59 (0.2)</td>
<td>3.53</td>
<td>(3.09–4.04)</td>
</tr>
<tr>
<td>Missing</td>
<td>39 (0.2)</td>
<td>1.80</td>
<td>(1.19–2.70)</td>
<td>31 (0.2)</td>
<td>2.00</td>
<td>(1.65–2.42)</td>
</tr>
<tr>
<td>&lt;3 months</td>
<td>132 (0.3)</td>
<td>1.74</td>
<td>(1.49–2.04)</td>
<td>107 (0.2)</td>
<td>1.71</td>
<td>(1.58–1.85)</td>
</tr>
<tr>
<td>3-5.9 months</td>
<td>71 (0.2)</td>
<td>1.00</td>
<td>[Reference]</td>
<td>67 (0.2)</td>
<td>1.00</td>
<td>[Reference]</td>
</tr>
<tr>
<td>6-8.9 months</td>
<td>46 (0.2)</td>
<td>0.73</td>
<td>(0.60–0.89)</td>
<td>43 (0.2)</td>
<td>0.70</td>
<td>(0.63–0.77)</td>
</tr>
<tr>
<td>9-11.9 months</td>
<td>13 (0.2)</td>
<td>0.70</td>
<td>(0.50–0.98)</td>
<td>11 (0.1)</td>
<td>0.47</td>
<td>(0.38–0.58)</td>
</tr>
</tbody>
</table>

### Heart failure

Note: \( n(\%) \) indicates the no. of events in each category of TITRE; generalised mixed effects models weighted for duration of follow-up
Association between TITRE and endpoints

Any CVD and death

<table>
<thead>
<tr>
<th>Duration</th>
<th>n(%)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>1228 (4.7)</td>
<td>2.57</td>
<td>(2.43–2.71)</td>
</tr>
<tr>
<td>Missing</td>
<td>561 (3.0)</td>
<td>1.73</td>
<td>(1.58–1.89)</td>
</tr>
<tr>
<td>&lt;3 months</td>
<td>1805 (3.5)</td>
<td>1.46</td>
<td>(1.41–1.51)</td>
</tr>
<tr>
<td>3-5.9 months</td>
<td>1284 (3.2)</td>
<td>1.00</td>
<td>[Reference]</td>
</tr>
<tr>
<td>6-8.9 months</td>
<td>617 (2.4)</td>
<td>0.67</td>
<td>(0.63–0.70)</td>
</tr>
<tr>
<td>9-11.9 months</td>
<td>189 (2.5)</td>
<td>0.42</td>
<td>(0.38–0.46)</td>
</tr>
</tbody>
</table>

Note: n(%) indicates the no. of events in each category of TITRE; generalised mixed effects models weighted for duration of follow-up
Results of sensitivity analyses

• Consistent findings:
  – amongst patients who achieved or not ‘snapshot’ control
  – across groups defined by the average no. of BP readings
  – models additionally adjusted for the no. of BP readings or SBP visit-to-visit variability

• Close to null associations observed when alternative BP measures replaced TITRE:
  – averaged BP value
  – SBP visit-to-visit variability
Summary and conclusions

- Few newly identified hypertensive patients sustained a complete, year-round on-target BP over time
- A higher time at target was associated with a lower risk of incident CVDs, independent of widely used BP control indicators
- Stronger CVD dose-response associations with TITRE than with other BP measures
- Need to compare interventions to increase a person’s time spent at BP target with those aimed at achieving lower BP target