Ambulatory BP Monitoring: Getting the Diagnosis of Hypertension Right

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Professor and Chair
Objectives

• Review limitations of office BP in making a correct diagnosis of hypertension
• Describe most recent USPSTF recommendation
• Discuss the role of ABPM as the gold standard for accurate diagnosis
• Illustrate the clinical importance of ABPM while noting practical limitations
Office BP

• BP measurement is basis for the most common diagnosis in adult primary care
• Accurate measurement of BP is challenging, especially in busy office practices
• Mercury no longer used
• Oscillometric devices predominate
Limitations of Office BP

• Poor quality control due to technique
  – Wrong cuff size
  – Improper patient position (e.g. feet not on floor, arm not at heart level)
  – Failure to allow 5 minutes rest
  – If manual sphygmomanometer used
    • Letting air out of cuff too rapidly
    • Digit bias (rounding to nearest 5 or 10 mmHg)
    • Other observer biases
Limitations of Office BP

Even when done correctly...

- Limited reliability due to the small number of readings
- Substantial variability
Blood Pressure Varies

• Inherent variability
• Influenced by external factors
• Usual practice is to base diagnosis of hypertension on office measurements
  – Ideally, repeated measurements at same visit and over different visits
  – Repeat measurement protocols rarely followed
BP is also a Moving Target

• Even when a measurement is accurate, it may not reflect a person’s usual, or “true,” blood pressure
Case 1: 42 y/o woman with elevated BPs X 2 visits

- Office BPs: 160s/80s mmHg
- No signs of target organ damage
- LDL 106 mg/dl
- HDL 53 mg/dl
- Not diabetic, not on OCP
- No family history of early CVD
- About to start medications…
Clinical Questions

• Are her office BPs accurate?
• Assuming they are accurate, do they represent the patient’s usual BP?
• Do you make the diagnosis of hypertension (and start medications)?
Misclassification

• Clinic BP can overestimate usual BP
  – White-coat hypertension may be misclassified as (sustained) hypertension

• Misdiagnosis → overtreatment → harms

• Out-of-office BP: home BP & ambulatory BP monitoring → how do they compare?
RESEARCH

Relative effectiveness of clinic and home blood pressure monitoring compared with ambulatory blood pressure monitoring in diagnosis of hypertension: systematic review

J Hodgkinson research fellow¹, J Mant professor², U Martin clinical reader in clinical pharmacology³, B Guo research fellow⁴, F D R Hobbs professor¹, J J Deeks professor⁴, C Heneghan reader in evidence based medicine⁵, N Roberts information specialist⁶, R J McManus professor¹
BMJ Systematic Review 2011

- Compared clinic and home to ABPM
- 7 studies compared clinic and 3 studies compared home measurements
- Sensitivity and specificity range 62-86%
- Conclusion: neither clinic nor home adequate as a single diagnostic test

BMJ 2011;342:d3621 doi: 10.1136/bmj.d3621
Cost-effectiveness of options for the diagnosis of high blood pressure in primary care: a modelling study

Kate Lovibond, Sue Jowett, Pelham Barton, Mark Caulfield, Carl Heneghan, F.D Richard Hobbs, James Hodgkinson, Jonathan Mant, Una Martin, Bryan Williams, David Wonderling, Richard J McManus

Summary

Background The diagnosis of hypertension has traditionally been based on blood-pressure measurements in the clinic, but home and ambulatory measurements better correlate with cardiovascular outcome, and ambulatory monitoring is more accurate than both clinic and home monitoring in diagnosing hypertension. We aimed to compare the cost-effectiveness of different diagnostic strategies for hypertension.

Methods We did a Markov model-based probabilistic cost-effectiveness analysis. We used a hypothetical primary-care population aged 40 years or older with a screening blood-pressure measurement greater than 140/90 mm Hg and risk-factor prevalence equivalent to the general population. We compared three diagnostic strategies—further blood pressure measurement in the clinic, at home, and with an ambulatory monitor—in terms of lifetime costs, quality-adjusted life years, and cost-effectiveness.

Findings Ambulatory monitoring was the most cost-effective strategy for the diagnosis of hypertension for men and women of all ages. It was cost-saving for all groups (from £56 [95% CI −105 to −10] in men aged 75 years to £323 [95% CI −220 to −123] in women aged 60 years).
Cost-Effectiveness Study

• Markov model-based; hypothetical primary-care population ≥40 years with a screening BP >140/90 mm Hg and risk-factor prevalence equivalent to the general population

• ABPM most cost-effective strategy for the diagnosis of hypertension
  – Based on not treating white-coat hypertension

• Cost-saving for all groups and resulted in more QALYs for men & women older than 50 years

NICE (UK) Guidelines 2011

• Largely based on the *BMJ* SR and the *Lancet* modeling cost-effectiveness study

• “If clinic blood pressure is 140/90 mm Hg or higher, use ambulatory blood pressure monitoring to confirm the diagnosis of hypertension.”
Ambulatory BP Monitoring

- Multiple readings over the course of 24 hours
- Superior to office BP in predicting outcomes
- Much evidence accumulated in past decade
  - >10,000 articles on PubMed
- Considered to be the noninvasive gold standard
Ambulatory BP Monitoring

• Several kinds of devices available
• Trained nurse or MA provides instructions and fits the monitor
  – Instructions include not to remove the cuff, to avoid strenuous activity, to try to relax arm when device is taking a reading
• Person wears monitor (usually) 24-hours
• Programmed for automatic readings at desired intervals (e.g., every 30 minutes)
Normal ABPM

Systolic BP

Diastolic BP

Heart rate

“White coat” period

Awake period

Sleep time period

Awake period

Nocturnal dip

Morning surge
Definitions

• “Cut-offs” for ABPM:

<table>
<thead>
<tr>
<th></th>
<th>Cut-off (mmHg)</th>
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</thead>
<tbody>
<tr>
<td>Awake average</td>
<td>135/85</td>
</tr>
<tr>
<td>Nighttime (sleep) average</td>
<td>120/70</td>
</tr>
<tr>
<td>24-hour average</td>
<td>130/80</td>
</tr>
</tbody>
</table>
BP Dip and BP Load

• Nocturnal dip
  – Normal is 10% to 20%
  – <10% is nondipper; >20% extreme dipper
  – Some are risers (reverse dippers)

• BP load
  – % of BP readings above threshold
  – <25% considered normal
  – >50% abnormal or higher risk
Diagnostic and Predictive Accuracy of Blood Pressure Screening Methods With Consideration of Rescreening Intervals: A Systematic Review for the U.S. Preventive Services Task Force

Margaret A. Piper, PhD, MPH; Corinne V. Evans, MPP; Brittany U. Burda, MPH; Karen L. Margolis, MD, MPH; Elizabeth O’Connor, PhD; and Evelyn P. Whitlock, MD, MPH

**Background:** Elevated blood pressure (BP) is the largest contributing risk factor to all-cause and cardiovascular mortality.

**Purpose:** To update a systematic review on the benefits and harms of screening for high BP in adults and to summarize evidence on rescreening intervals and diagnostic and predictive accuracy of different BP methods for cardiovascular events.

**Data Sources:** Selected databases searched through 24 February 2014.

**Study Selection:** Fair- and good-quality trials and diagnostic accuracy and cohort studies conducted in adults and published in English.

**Data Extraction:** One investigator abstracted data, and a second checked for accuracy. Study quality was dual-reviewed.

**Data Synthesis:** Ambulatory BP monitoring (ABPM) predicted long-term cardiovascular outcomes independently of office BP (hazard ratio range, 1.28 to 1.40, in 11 studies). Across 27 studies, 35% to 95% of persons with an elevated BP at screening remained hypertensive after nonoffice confirmatory testing. Cardiovascular outcomes in persons who were normotensive after confirmatory testing (isolated clinic hypertension) were similar to outcomes in those who were normotensive at screening. In 40 studies, hypertension incidence after rescreening varied considerably at each yearly interval up to 6 years. Instrastudy comparisons showed at least 2-fold higher incidence in older adults, those with high-normal BP, overweight and obese persons, and African Americans.

**Limitation:** Few diagnostic accuracy studies of office BP methods and protocols in untreated adults.

**Conclusion:** Evidence supports ABPM as the reference standard for confirming elevated office BP screening results to avoid misdiagnosis and overtreatment of persons with isolated clinic hypertension. Persons with BP in the high-normal range, older persons, those with an above-normal body mass index, and African Americans are at higher risk for hypertension on rescreening within 6 years than are persons without these risk factors.

**Primary Funding Source:** Agency for Healthcare Research and Quality.
Systematic Review for USPSTF

• Summarize evidence on...diagnostic and predictive accuracy of different BP methods for cardiovascular events

• Key questions:
  – Diagnostic accuracy of office BP
  – Prediction of CVD events by BP method and diagnostic accuracy of nonoffice measurements

Ann Intern Med. 2015 Feb 3;162(3):192-204.
Systematic Review for USPSTF

• 9 studies that evaluated the predictive value of 24-hour ABPM on long-term health outcomes
  – Studies followed a cohort of patients over time and reported hazard or risk ratio
  – At least 2 BP measurement methods at baseline
  – Outcomes: overall mortality or CVD events

Ann Intern Med. 2015 Feb 3;162(3):192-204.
Ambulatory BP and CVD Outcomes

• 4 studies found that each 10-mm Hg increase in ambulatory BP (adjusted for office BP) was significantly associated with increased risk for fatal and nonfatal stroke
• 6 studies found that each 10-mm Hg increase was associated with increased risk for fatal and nonfatal cardiovascular events, with hazard ratios ranging from 1.11 to 1.42
<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Outcome</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac events or mortality</td>
<td>Cardiac events (fatal and nonfatal)</td>
<td>1.11 (0.93–1.31)</td>
</tr>
<tr>
<td>Staessen et al, 1999 (39)</td>
<td>Cardiac mortality (fatal HF, MI, or sudden death)</td>
<td>1.16 (1.07–1.25)</td>
</tr>
<tr>
<td>Dolan et al, 2005 (41)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CV events or mortality</td>
<td>CV mortality</td>
<td>1.19 (1.13–1.27)</td>
</tr>
<tr>
<td>Dolan et al, 2005 (41)</td>
<td>CV mortality</td>
<td>1.42 (1.14–1.77)</td>
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<tr>
<td>Gasowski et al, 2008 (43)</td>
<td>CV mortality</td>
<td>1.27 (1.04–1.55)</td>
</tr>
<tr>
<td>Ohkubo et al, 2005 (38)</td>
<td>CV mortality</td>
<td>1.11 (0.88–1.40)</td>
</tr>
<tr>
<td>Staessen et al, 1999 (39)</td>
<td>CV mortality</td>
<td>1.30 (1.10–1.55)</td>
</tr>
<tr>
<td>Clement et al, 2003 (34)</td>
<td>MI or stroke (fatal and nonfatal)</td>
<td>1.33 (1.17–1.52)</td>
</tr>
<tr>
<td>Hermida et al, 2011 (36)</td>
<td>Major CV events (CV death, MI, or stroke)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>Stroke (fatal)</td>
<td>1.28 (1.15–1.43)</td>
</tr>
<tr>
<td>Dolan et al, 2005 (41)</td>
<td>Stroke (fatal or nonfatal)</td>
<td>1.37 (1.20–1.56)</td>
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<tr>
<td>Mesquita-Bastos et al, 2010 (44)</td>
<td>Stroke (fatal or nonfatal)</td>
<td>1.40 (1.21–1.62)</td>
</tr>
<tr>
<td>Ohkubo et al, 2005 (38)</td>
<td>Stroke (fatal or nonfatal)</td>
<td>1.36 (1.04–1.79)</td>
</tr>
<tr>
<td>Staessen et al, 1999 (39)</td>
<td>Stroke (fatal or nonfatal)</td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>All-cause mortality</td>
<td>1.02 (0.86–1.20)</td>
</tr>
<tr>
<td>Clement et al, 2003 (34)</td>
<td>All-cause mortality</td>
<td>1.13 (1.08–1.19)</td>
</tr>
<tr>
<td>Dolan et al, 2005 (41)</td>
<td>All-cause mortality</td>
<td>1.09 (0.92–1.29)</td>
</tr>
</tbody>
</table>
Conclusion about predicting CVD outcomes

- “...ABPM consistently and statistically significantly predicted stroke and other cardiovascular outcomes independently of OBPM.”

Ann Intern Med. 2015 Feb 3;162(3):192-204.
## Diagnostic Accuracy of Office BP

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Proportion Confirmed by 24-hr ABPM</th>
<th>95% CI</th>
<th>Screened, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kario, 1993</td>
<td>0.89</td>
<td>0.85-0.93</td>
<td>239</td>
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<tr>
<td>Inden, 1998</td>
<td>0.88</td>
<td>0.83-0.92</td>
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<tr>
<td>Pierdomenico, 1995</td>
<td></td>
<td></td>
<td>255</td>
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<tr>
<td>Khoury, 1992</td>
<td>0.52</td>
<td>0.43-0.60</td>
<td>131</td>
</tr>
<tr>
<td>Hozawa, 2002</td>
<td>0.35</td>
<td>0.27-0.42</td>
<td>150</td>
</tr>
</tbody>
</table>

Got it right 35% to 89% of the time.
The USPSTF recommends screening for high blood pressure in adults age 18 years and older. Ambulatory blood pressure monitoring is recommended to confirm high blood pressure before the diagnosis of hypertension, except in cases for which immediate initiation of therapy is necessary.
**USPSTF Final Recommendation**

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade (What's This?)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults aged 18 years or older</td>
<td>The USPSTF recommends screening for high blood pressure in adults aged 18 years or older. The USPSTF recommends obtaining measurements outside of the clinical setting for diagnostic confirmation before starting treatment (see the Clinical Considerations section).</td>
<td>A</td>
</tr>
</tbody>
</table>

The USPSTF found convincing evidence that ABPM is the best method for diagnosing hypertension. Although the criteria for establishing hypertension varied across studies, there was significant discordance between the office diagnosis of hypertension and 12- and 24-hour average blood pressures using ABPM, with significantly fewer patients requiring treatment based on ABPM (Figure 1). Elevated ambulatory systolic blood pressure was an independent predictor of cardiovascular events, independent of the clinical setting for diagnostic confirmation. ABPM is the best method for diagnosing hypertension. …the USPSTF recommends ABPM as the reference standard for confirming the diagnosis of hypertension.”
Case 1: 42 y/o woman with elevated BPs X 2 visits

• Office BPs: 160s/80s mmHg
• No signs of target organ damage
• LDL 106 mg/dl
• HDL 53 mg/dl
• Not diabetic, not on OCP
• No family history of early CVD
• About to start medications…
Graph of ABPM data

- Systolic BP
- Diastolic BP
- Nocturnal dip
- Heart rate

“White coat” period
Awake period
Sleep time period
Awake period
ABPM Report

• Quality
  – 90% readings overall
  – 32 daytime
  – 8 nighttime

• Mean overall BP: 130/79 mmHg
• Mean awake BP: 134/83 mmHg
• Mean sleep BP: 109/61 mmHg
• Nocturnal dip: 20%/29%
• BP load: 17%

Want at least 70%
Want at least 20 readings
Want at least 7 readings
Interpretation

- Normal ABPM averages
- Normal nocturnal BP
- Normal dipping pattern
- Diagnosis: white-coat hypertension
Management

• BP meds not warranted
• Appropriate lifestyle modifications recommended
• Consider repeat ABPM in 1-2 years
ABPM in Clinical Practice

- Assessment of possible white-coat effect (only indication currently reimbursable by Medicare, since 2001)
- Other clinical indications
  - Confirm hypertension in children
  - Resistant hypertension
    - Up to a third of such patients have controlled ABP
  - Labile hypertension
  - Hypotensive episodes
  - Postural hypotension
Case 2: 48 y/o man with resistant hypertension

- Recent office BPs: 158/84, 165/90 mm Hg
- On 3 once-daily drugs including a diuretic
- Pharmacy records show Rx’s being filled and reports taking medications
- 1/3 of resistant HTN patients have controlled BP on ABPM, so a good initial step…
Graph of ABPM data

Nocturnal dip

Morning surge
ABPM Report

- Quality
  - 98% readings overall
- Mean overall: 138/85 mmHg
- Mean awake: 139/86 mmHg
- Mean sleep: 133/80 mmHg
- Nocturnal dip: 4%
- SBP load: 60%
Interpretation & Management

- Awake BP average slightly elevated
- Elevated nocturnal BP & nondipper
  - Does he have sleep apnea?
- Diagnosis: resistant hypertension
- Consider increasing or adding additional BP-lowering medication
  - Consider nighttime dosing
Practical Issues

• ABPM not yet widely available
  – Few providers/clinical staff trained
• Recommended to be worn during a work day
• Limits some physical activity
• While tolerable, it is inconvenient and a bit of a nuisance
• A session of insufficient readings is possible (which would necessitate repeat)
Tolerability

• Most bother is interference with normal sleeping pattern
  – 67% reported that the monitor woke them after falling asleep, and 8.6% removed it at some point during the night

• Adverse effects: discomfort (32%), skin irritation (37%), and bruising (7%)

Manufacturers

• SpaceLabs  
  www.spacelabshealthcare.com
• SunTech  www.suntechmed.com
• Welch Allyn  www.welchallyn.com
Cost & reimbursement

• One monitor costs about $1500-$2600

• Charge for the CPT (93784) is $177
• Diagnosis code: 796.2
• Nurse visit for putting the monitor on
What about manual office BP?

- *Annals* review found 3 studies comparing manual and oscillometric office BP to ABPM

- “Neither manual nor automated systolic OBPM results were clearly favored”
Home BP Monitoring

• Another method to determine misclassification
• Also better predictor of outcome than office BP
• Evidence base not as strong
• Good for ruling in, but not as good for ruling out hypertension
Home BP monitoring

- May be a more feasible method
- Widely available
- Relatively affordable (or could be loaned)
- Systematically performed, home BP averages correlate (reasonably) with daytime ABP average
Home BP Monitoring Problems

- Still relies on proper technique
- Dependent on patient effort / engagement
- Concerns over “trustworthiness” of data
- Still misses large segments of day (and nocturnal)
Home BP monitoring, adjusted for office BP

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<td>CV events or mortality</td>
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<tr>
<td>Fagard et al, 2005 (35)</td>
<td>CV events (stroke, MI, or death)</td>
<td>1.17 (1.02–1.33)</td>
</tr>
<tr>
<td>Ohkubo et al, 1998 (48)</td>
<td>CV mortality</td>
<td>1.23 (1.00–1.51)</td>
</tr>
<tr>
<td></td>
<td>Stroke</td>
<td></td>
</tr>
<tr>
<td>Asayama et al, 2006 (45)</td>
<td>Stroke/TIA (first)</td>
<td>1.39 (1.22–1.59)</td>
</tr>
<tr>
<td></td>
<td>All-cause mortality</td>
<td></td>
</tr>
<tr>
<td>Niiranen et al, 2010 (47)</td>
<td>All-cause mortality (adjusted)</td>
<td>1.22 (1.09–1.37)</td>
</tr>
</tbody>
</table>
Take Home Message

- ABPM is superior to office BP in predicting cardiovascular events
- ABPM, if available, is a valuable complement to office BP measurements
- ABPM (with home BP as alternative) recommended to rule out white-coat hypertension prior to diagnosing hypertension (unless need for therapy is obvious)