Chapter 4: Conclusions

Summary of Findings

❑ **Key question 1. Comparison of clinic BP, SMBP, and ABP readings.**

- ***Question 1a. Distribution of BP differences***.
  A total of 18 studies addressed the distribution of BP differences. BP levels measured outside the clinic setting differed from those obtained in the clinic. For both systolic and diastolic BP, clinic measurements exceeded SMBP, daytime ABP, nighttime ABP and 24 hour ABP. In the few studies that compared SMBP and ABP, daytime ABP and SMBP appeared similar, while nighttime ABP was consistently lower than SMBP. The literature was insufficient to determine whether these BP differences are reproducible.
- ***Question 1b. Prevalence of WCH based on SMBP***.
  A total of four studies addressed this issue. Hence, the literature was insufficient to determine the prevalence of WCH by SMBP.
- ***Question 1c. Prevalence of WCH based on ABP***.
  A total of 16 studies addressed this issue. Prevalence varied by WCH definition and study population. Overall, the prevalence was approximately 20 percent among patients with hypertension. Only two studies addressed the reproducibility of WCH. Hence, the literature was insufficient to determine whether WCH based on ABP is reproducible.

❑ **Key question 2. The relationship of SMBP levels and WCH based on SMBP with target organ damage and clinical outcomes.**

- ***Question 2a. Cross-sectional associations of SMBP with target organ damage.***
  Only one study addressed this issue. Hence, the literature was insufficient to determine the associations of absolute SMBP levels or WCH as determined by SMBP with left ventricular mass or proteinuria.
- ***Question 2b. Associations of SMBP with clinical outcomes in prospective studies.***
  Only one study addressed this issue. Hence, the literature was insufficient to determine whether absolute SMBP levels or WCH based on SMBP predicts subsequent CVD.
- ***Question 2c. Comparison of risk prediction from SMBP and clinic BP.***
  Only one study addressed this issue. The dearth of studies combined with the poor or uncertain quality of clinic BP measurements precluded an answer to this question.
- ***Question 2d. Effect of treatment guided by SMBP.***
  Twelve trials addressed this issue, but the evidence was inconsistent. In half of these trials, interventions that included SMBP led to reduced BP. Two trials used contemporary SMBP technology which can store and synthesize SMBP measurements and which can generate BP reports. In both of these trials, the SMBP intervention led to reduced BP.

- **Key question 3. The relationship of ABP levels and WCH based on ABP with target organ damage and clinical outcomes.**

- ***Question 3a. Cross-sectional associations of ABP with target organ damage.***
  A total of 25 studies addressed these issues. Left ventricular mass and albuminuria were positively associated with ABP.
- ***Question 3b. Associations of ABP with clinical events in prospective studies.***
  A total of 10 studies addressed this issue. In each study, at least one dimension of ABP predicted subsequent clinical events, primarily CVD. In two of these studies, WCH was associated with a reduced risk of CVD relative to the risk associated with sustained hypertension. No prospective study adequately compared the risk associated with WCH relative to the risk associated with non-hypertension. In four of five studies, a non-dipping or inverse dipping pattern predicted an increased risk of adverse events.
- ***Question 3c. Comparison of risk prediction from ABP and clinic BP.***
  A total of nine prospective studies addressed this issue, but only two studies assessed 'incremental' gain, that is, whether ABP provided additional information that was predictive of risk beyond that of clinic BP. However, the poor or uncertain quality of clinic BP measurements precluded a satisfactory comparison of risk prediction from ABP and clinic BP.
- ***Question 3d. Effect of treatment guided by ABP.***
  Only two trials addressed this issue. Hence, the literature was insufficient to determine the effects of treatment guided by ABP.

- **Key question 4. Findings to research questions 1-3 in subgroups.**
  The vast majority of studies included both men and women, but few studies reported results separately by gender. Few studies reported enrollment African-Americans, and race-stratified data were rarely presented. The only notable subgroup finding was a higher prevalence of WCH in women than men.

In summary, ABP levels and ABP patterns were associated with BP-related target organ damage in cross-sectional studies. Likewise, in prospective studies, higher ABP, sustained BP and a non-dipping ABP pattern were associated with an increased risk of subsequent CVD events. Few studies examined corresponding relationships for SMBP. The poor or uncertain quality of clinic BP measurements precluded satisfactory comparisons of risk prediction based on ABP or SMBP with risk prediction based on clinic BP. In aggregate, these findings provide some support for use of ABP monitoring in evaluating prognosis. However, evidence was insufficient to determine whether the risks associated with WCH are sufficiently low to consider withholding drug therapy in this large subgroup of hypertensive patients. For SMBP, available evidence from several trials suggested that use of SMBP can improve BP control; however, further trials are needed.

Limitations of Report

The potential scope of the project was beyond available resources. Hence, the EPC team made considerable efforts to focus on the most critical research questions, the most relevant populations, and the most important data collection items. In the process, certain research issues were not covered in this report, for example, the prevalence of non-dipping and its cross-sectional associations. By necessity, the EPC team focused on study populations that are now considered candidates for ABP and SMBP monitoring, that is, non-pregnant adults with hypertension.

The literature review was limited to articles published in English, thus increasing the potential for publication bias. The exclusion of articles not published in the English language reflects the practical realities of obtaining and reviewing non-English articles within the time frame and budget of this project.

The evaluation of diagnostic technologies is complex and often does not lend itself well to the traditional table-based format of an evidence report that synthesizes data from large numbers of basically similar studies, often clinical trials. Furthermore, technologies under evaluation rapidly change such that research is often dated by the time it is completed. In the case of SMBP, only two studies tested contemporary technologies that are capable of storing and transmitting data and generating reports. Finally, it is often unclear whether findings from studies of specific devices can be extrapolated to an entire class of devices.

Another set of issues pertain to the reference technology or 'gold standard' against which new technologies are compared. For this report, a critical issue was whether the standard should be clinic BP as recommended in guidelines or clinic BP as commonly (and sub-optimally) obtained in routine medical practice. In the end, most publications provided little information about clinic BP measurements; hence, it is doubtful that ABP and SMBP were compared to high quality clinic measurements. However, the uncertain or poor quality of clinic BP in these studies may actually parallel its routine use in medical practice.

Limitations of Literature

The ABP and SMBP literature is vast, heterogeneous and poorly indexed. These aspects of the literature created enormous logistic challenges at each point in the process, including the review of 4,852 abstracts, review of 596 articles, the design of appropriate data collection instruments, the abstraction of data, and the construction of evidence tables. In several instances, summary statistics had to be recalculated in order to present data in a common format. Because of heterogeneity in study design and data presentation, results from prospective observational studies and clinical trials were entered directly into separate databases or spreadsheets and into open fields rather than as fixed pre-coded fields.

The quality of publications and presentation of data were often suboptimal. In many instances, core methods and basic descriptive information were presented in an unusual fashion that complicated data abstraction. Likewise, statistical analyses were often suboptimal. In the end, several studies that addressed our research questions could not be included because data were not presented in an abstractable format.

Most studies were single center studies, often with small sample size and without government support. Despite the vital importance of accurate BP measurement, governments have sponsored relatively little research that compares the utility of different techniques.

In most papers, the methods sections provided an incomplete description of clinic measurements. Often the type and training of the manual observer, the type of device, the number of measurement days, the number of BP readings per day, and the use (or non-use) of standard measurement techniques was not reported. When standard BP technique was reported, the measurement was often the average of a few readings, sometimes just one or two from a single visit. Training of manual observers was rarely mentioned. Despite this limitation, it should be recognized that the poor and uncertain quality of clinic measurements likely reflects actual clinical practice, in which high quality clinic BP measurements may never be routinely obtained. In contrast, ABP measurement technique in clinic practice is likely to be similar to that of the research setting.

Other limitations of the literature were evident, including the following:

- Of the available prospective observational studies, most were comparatively small. ABP and SMBP have not been used in the major observational studies that documented the relation between BP and CVD risk.
- Few studies assessed the relation between SMBP and either prevalent BP-related target organ damage (cross-sectional studies) or clinical outcomes (longitudinal studies).
- Few trials assessed the utility of ABP to guide BP therapy.
- Few studies assessed the reproducibility of the diagnosis of WCH or the reproducibility of differences between clinic BP and either ABP or SMBP.
- In the trials that evaluated the utility of SMBP measurements, it is unclear how SMBP data were used to guide BP therapy.
- Few studies have compared SMBP and ABP as predictors of outcomes or as tools to guide BP management.
- Definitions of ABP variables, such as WCH, were exceedingly variable.
- Few studies tested for incremental gain from use of ABP, that is, the gain from concomitant use of ABP with clinic BP beyond that of clinic BP alone. The appropriate analytic model would be simultaneous inclusion of both ABP and clinic BP in regression models rather than stepwise analyses. This proposed analytic strategy would actually parallel the intended use of ABP in clinic practice because ABP would likely be used with clinic BP, not by itself. Specifically, the decision to use ABP and the interpretation of subsequent data is contingent upon clinic BP readings.
- Adjustment procedures were often inadequate leading to the potential for residual confounding

Use of Evidence Report

This report synthesizes evidence that should facilitate clinical decision making and inform policy makers about the utility of BP measurements outside of the clinic setting. The importance of this report is heightened by concurrent concerns and uncertainties over standard clinic measurements. The EPC team intends to disseminate this report through several venues. The

full report will be available through AHRQ's Publications Clearinghouse and its Web Site. Condensed versions of key components will be submitted for publication in peer-reviewed publications that are widely read by physicians and other health care providers who manage patients with hypertension. The NHBPEP will also assist in dissemination of this report through its ongoing activities and meetings. Key findings will also be presented at national meetings of major professional organizations, including the American Society of Hypertension and the American Heart Association. The EPC team anticipates that this report will be used by policy makers who are presently evaluating alternative strategies to measure BP and considering an appropriate research agenda. This report might also stimulate development and dissemination of guidelines for better reporting of ABP and SMBP studies.