Effective Health Care Program

Future Research Needs Paper
Number 16

# Self-Measured Blood Pressure: Future Research Needs

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*Future Research Needs Paper*

**Number 16**

# Self-Measured Blood Pressure: Future Research Needs

**Identification of Future Research Needs From Comparative Effectiveness Review No. 45**

**Prepared for:**
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
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www.ahrq.gov

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**Prepared by:**
Tuft Evidence-based Practice Center, Tufts Medical Center
Boston, MA

**Investigators:**
Katrin Uhlig, M.D., M.S.
Kamal Patel, M.P.H., M.B.A.
Thomas W. Concannon, Ph.D.
Ethan M. Balk, M.D., M.P.H.
Sara J. Ratichek, M.A.
Lina Kong Win Chang, B.S.
Ramon Iovin, Ph.D.

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The information in this report is intended to help health care researchers and funders of research make well-informed decisions in designing and funding research and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of scientific judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical research and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances.



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None of the investigators has any affiliation or financial involvement that conflicts with the material presented in this report.

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# Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

An important part of evidence reports is to not only synthesize the evidence, but also to identify the gaps in evidence that limited the ability to answer the systematic review questions. AHRQ supports EPCs to work with various stakeholders to identify and prioritize the future research that are needed by decisionmakers. This information is provided for researchers and funders of research in these Future Research Needs papers. These papers are made available for public comment and use and may be revised.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality. The evidence reports undergo public comment prior to their release as a final report.

We welcome comments on this Future Research Needs document. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.


Carolyn M. Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.
Director, Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Stephanie Chang M.D., M.P.H.
Director, EPC Program
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Elisabeth U. Kato, M.D., M.R.P.
Task Order Officer
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

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The authors gratefully acknowledge the stakeholders for their contributions to this project.

## Contributors

Hayden B. Bosworth, Ph.D.
Associate Director
Center for Health Services Research in Primary Care
Durham Veterans Affairs Medical Center
Durham, NC

Research Professor
Department of Medicine
Department of Psychiatry and Behavioral Sciences
School of Nursing
Duke University Medical Center
Durham, NC

Jonathan P. Curtin, M.D.
Medical Director
Division of OHIP Operations
Office of Health Insurance Programs
New York State Department of Health
Albany, NY

Beverly Green, M.D., M.P.H.
Affiliate Investigator, Group Health Research Institute
Family Physician, Group Health Cooperative
Assistant Clinical Professor, University of Washington School of Medicine
Seattle, WA

Michael R. Martin, M.D., FACP
Regional Medical Director
Arkansas Blue Cross and Blue Shield
Texarkana, AR

Debbie Mitchell-Dozier, R.N., B.S.N.
Staff Nurse – Division of Nephrology
Kidney & Blood Pressure Center
Tufts Medical Center
Boston, MA

Quyen Ngo-Metzger, M.D., M.P.H.
U.S. Department of Health and Human Services
Health Resources and Services Administration
Chief, Data Branch
Office of Quality and Data, 6A-55
Bureau of Primary Health Care
Rockville, MD

David Shakespeare
Boston, MA

Gary Snyder
Boston, MA

Jennifer Trigano, PA-C, M.S.
Physician Assistant – Division of Nephrology
Tufts Medical Center,
Kidney & Blood Pressure Center
Boston, MA

Anthony Viera, M.D., M.P.H.
Associate Professor, Department of Family Medicine
University of North Carolina at Chapel Hill School of Medicine
Chapel Hill, NC

Richard W. Whitten, M.D., M.B.A., FACP
Contractor Medical Director, DME MAC D
Noridian Administrative Services
Fargo, ND

# Self-Measured Blood Pressure: Future Research Needs

## Structured Abstract

**Background.** Hypertension is an important public health issue. Self Measured Blood Pressure Monitoring (SMBP), the self measurement of blood pressure (BP) outside of the health care setting may be an effective tool to facilitate BP control.

**Purpose.** Generate prioritized topics for future research on SMBP, building on evidence gaps identified in a prior comparative effectiveness review and following an explicit a stakeholder-driven nomination and prioritization process.

**Methods.** Building on evidence gaps identified in a previous CER on SMBP, a preliminary list of future research needs (FRN) was supplemented and refined through input from stakeholders. Stakeholders were asked to indicate their top five priority topics considering the following dimensions in prioritization: (1) importance, (2) desirability of research/avoidance of unnecessary duplication, (3) feasibility, and (4) potential impact. The five topics with the highest number of stakeholder endorsements were identified as the prioritized FRN topics.

**Future Research Needs Topics.** Four priority topics pertain to interrelated evidence gaps such as the lack of longer term studies which show persistence of BP control or clinical benefit from SMBP, uncertainty regarding who is likely to benefit from SMBP, lack of standardization in prescription of SMBP, and uncertainty regarding the most effective additional support. The fifth topic relates to the inability to assess cost-effectiveness of SMBP, due to the deficiencies in evidence identified in the first four gaps.

To address these gaps, longer term randomized controlled trials are needed to examine clinical outcomes; exploration of treatment heterogeneity may identify those groups more likely to benefit from SMPB. Different prescriptions of SMBP should be compared in trials examining SMBP adherence and BP control. Additional support that shows promise for future study should be further refined by expert panels. Filling these evidence gaps will inform future modeling of cost-effectiveness.

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# Executive Summary

## Background

Hypertension is a common, long-term health condition that leads to increased cardiovascular morbidity and mortality, as well as increased consumption of health care resources. Effective treatments for hypertension are available; however, long-term adherence to medication and lifestyle modification remains a challenge. Self-measured blood pressure monitoring (SMBP) has been suggested as one method that may improve adherence to blood pressure (BP) treatment and consequently improve outcomes. SMBP refers to the regular self-measurement of a patient's BP at home or otherwise outside the office or clinic, as a supplement or alternative to those obtained in a health care setting. While patient self-participation in chronic disease management appears a promising means of improving adherence, the sustainability and clinical impact of this strategy, as well as its impact on health care utilization, remain uncertain.

The current Future Research Needs (FRN) project was launched upon the completion of an Agency for Healthcare Research and Quality (AHRQ) Comparative Effectiveness Review (CER) on SMBP, and builds on the evidence gaps identified in that review. The SMBP CER reviewed pertinent publications through July 2011 and identified 47 comparative studies of at least 8 weeks duration, and one observational study. For the comparison of SMBP alone versus usual care, the strength of evidence was moderate, supporting a lower BP with SMBP (SBP/DBP [systolic BP/diastolic BP] –3.1 / –2.0 mmHg at 6 months). For SMBP plus additional support versus usual care, the strength of evidence was high, supporting a lower BP with SMBP use (SBP/DBP –3.4 to –8.9 / –1.9 to –4.4 mmHg) at up to 12 months. For SMBP plus additional support versus SMBP alone or with less intense additional support, the strength of evidence was low, failing to support a difference in BP. For all comparisons, evidence for clinical outcomes was insufficient; for all other non-BP outcomes (surrogate and intermediate outcomes, and health care encounters) strength of evidence was low, failing to support a difference. No trials compared different SMBP devices or provided evidence on the relationship between BP control and clinical or surrogate outcomes. There was insufficient evidence concerning predictors of SMBP adherence. No studies in children were identified for the review.

The evidence gaps identified in the SMBP CER are summarized in Table A, organized and labeled by Key Question and PICOD (Population, Intervention, Comparator, Outcome, study Design) category. These gaps limited the conclusions that could be drawn in the original CER, and thus became the initial list of priority topics for the present FRN project. Figure A depicts the analytic framework used to guide the Key Questions for the CER of SMBP, with the addition of annotations indicating evidence gaps. Although the evidence gap in children was noted, it was determined that the current project proceed with a focus on adults only, as refinement of the future research agenda in children would require a specially composed stakeholder group.

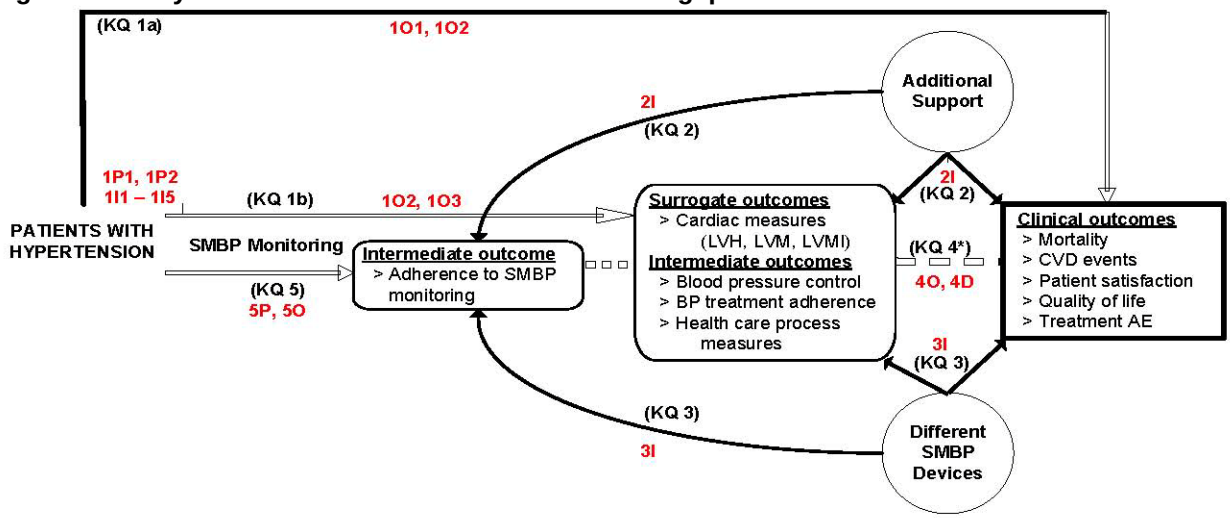
**Table A. Identified evidence gaps organized by relevant Key Question and PICOD element**

| Key Question | Category | Evidence Gaps (Code*) |
|---|---|---|
| **Key Question 1.** In people with hypertension (adults and children), does SMBP, compared to usual care or other interventions without SMBP, have an effect on clinically important outcomes?<br><br>**Key Question 1a.** How does SMBP monitoring compare to usual care or other interventions without SMBP in its effect on relevant clinical outcomes (cardiovascular events, mortality, patient satisfaction, quality of life, and adverse events related to antihypertensive agents)?<br><br>**Key Question 1b.** How does SMBP compare to usual care or other interventions without SMBP in its effect on relevant surrogate outcomes (cardiac measures: LVH, LVM, LVMI)* and intermediate outcomes BP control, BP treatment adherence, or health care process measures)? | Population | Unclear if treatments or treatment goals differ if a patient has uncontrolled hypertension, white coat hypertension, or masked hypertension (1P1)<br>Unclear if effects from SMBP differ in subgroups, for example older patients, those with comorbidities, and minorities (1P2) |
| | Intervention/ Comparator | Unclear what the BP treatment goals should be for home BP in relation to clinic BP (1I1)<br>Unclear how to compare findings across studies, as different studies use different protocols for SMBP, different additional support and different care in the control groups (1I2)<br>Unclear what the best practice protocol would be for SMBP (1I3)<br>Unclear what the adherence is to SMBP protocols or devices in the long-term (1I4)<br>Unclear how the effect of SMBP can be enhanced by particular additional support (1I5) |
| | Outcomes | Unclear what the effects are of SMBP on clinical event outcomes, i.e., after longer followup periods (1O1)<br>Unclear if the effect of SMBP is sustained beyond 1-2 years (1O2)<br>Unclear what the effect of SMBP is on patient understanding of disease, and how this correlates with attitudes towards and participation in disease management, medication adherence and BP control (1O3) |
| | Design | N/A |
| **Key Question 2.** In trials of SMBP monitoring, how do clinical, surrogate, and intermediate outcomes (including SMBP adherence) vary by the type of additional support provided? | Population | N/A |
| | Intervention/ Comparator | Unclear what the optimal additional support is for facilitating patient-provider interaction, and medication management including telemedicine (2I) |
| | Outcomes | N/A |
| | Design | N/A |
| **Key Question 3.** How do different devices for SMBP monitoring compare with each other (specifically semiautomatic or automatic versus manual) in their effects on clinical, surrogate, and intermediate outcomes (including SMBP adherence)? | Population | N/A |
| | Intervention/ Comparator | Unclear if the device type impacts adherence, BP control and outcomes (3I) |
| | Outcomes | N/A |
| | Design | N/A |
| **Key Question 4.** In trials of SMBP monitoring, how does achieving BP control relate to clinical and surrogate outcomes? | Population | N/A |
| | Intervention/ Comparator | N/A |
| | Outcomes | Unclear what the link is between achieving BP control and clinical outcomes (4O) |
| | Design | Need for longer term follow up (4D) |
| **Key Question 5.** How does adherence with SMBP vary by patient factors? | Population | N/A |
| | Predictor | Unclear how patient characteristics, such as demographic and psychosocial variables, affect adherence to SMBP (5P) |
| | Outcomes | Need for validated outcome measures of adherence with SMBP (5O) |
| | Design | N/A |

**Abbreviations:** BP=blood pressure; N/A=not applicable; SMBP=self-measured blood pressure monitoring

* The parenthetical alphanumeric code is used to label each evidence gap on the analytic framework (Figure A). The first number of the alphanumeric code corresponds to the Key Question, the following letter to the PICOD category, and the final numeral to distinguish among multiple gaps within the same Key Question and Domain (if applicable). Where there is only one gap identified, the last number is dropped.

**Figure A. Analytic framework for SMBP with evidence gaps***




**Abbreviations:** AE=adverse events; BP=blood pressure; CVD=cardiovascular disease; KQ=Key Question; LVH=left ventricular hypertrophy; LVM=left ventricular mass; LVMI=left ventricular mass index; SMBP=self-measured blood pressure
* Each gap is indicated with an alphanumeric code, where the first number of the alphanumeric code corresponds to the Key Question, the following letter to the PICOD category, and the final numeral to distinguish among multiple gaps within the same Key Question and category (if applicable). Where there is only one gap identified, the last number is dropped.

# Methods

## Identifying and Engaging a Stakeholder Panel

We followed a recently developed taxonomy that was designed to aid researchers in the identification, recruitment, and engagement of stakeholders.[1] Based on an *a priori* categorization of stakeholders according to type, we convened a panel consisting of 2 patients, 3 providers, 3 payers, 1 policymaker, and 2 researchers. Product-makers were invited to nominate topics but did not participate in the panel. The stakeholders were provided with the executive summary of the SMBP CER and went through a formal orientation process.

## Identifying Evidence Gaps and Developing PICOD for Each Gap

As the authors of the SMBP CER, we generated the initial list of FRN topics based on the Research Needs section of the report, and then organized the list of evidence gaps according to key questions and PICOD elements. Participating panelists reviewed the preliminary topics and used an iterative process to identify additional FRN topics through Webinars and emails.

## Criteria for Prioritizing Evidence Gaps

Stakeholders were asked to consider four dimensions of need. These four dimensions are outlined in the Effective Health Care (EHC) Program Selection Criteria and consist of: (1) importance, (2) desirability of research/avoidance of unnecessary duplication, (3) feasibility, and (4) potential impact. The fifth dimension of the EHC program selection criteria, appropriateness, was not evaluated by the stakeholders, as AHRQ had already deemed the topic of SMBP to adequately meet this criterion.

## Approach to Prioritization

Following two rounds of Webinar discussions and email communication, the topic list was finalized. Stakeholders were asked to indicate their top five priority FRN topics according to the pertinent EHC Program criteria. The five topics with the highest number of stakeholder endorsements were identified as the five prioritized FRN topics.

## Developing Research Questions

We transformed the final list of FRN topics into research questions using standard PICOD criteria. Stakeholders were not utilized during this process. We discussed various alternatives for future research efforts aimed at answering each question, specifically considering the feasibility of addressing the research questions with respect to potential sample size, the time required, recruitment and ethical issues.

# Results

Based on the SMBP CER and our discussion with stakeholders, 16 future research needs topics were nominated. The topics chosen as the highest priority future research needs are listed in Table B.

**Table B. The top five priority future research needs as indicated by participating stakeholders**

| Topic | Topic Description |
|---|---|
| 1 | What are the effects of SMBP on BP, medication adherence rates, satisfaction, and clinical event outcomes, after longer followup periods of 2 to 5 years or longer? |
| 2 | Which patients may be more likely to benefit from using SMBP? |
| 3 | What is the best prescription or protocol for SMBP (when, how often, and how frequently)? How do different prescriptions for SMBP compare regarding acceptance by patients, adherence with SMBP, and effect on BP control? |
| 4 | What is the role of additional support? What particular components of additional support should be further evaluated? |
| 5* | What is the effect of SMBP on resource utilization? What is the cost-effectiveness of SMBP? |

**Abbreviations:** BP=blood pressure; SMBP=self-measured blood pressure monitoring
* Topic was not covered by the SMBP CER.

The first four topics pertain to interrelated evidence gaps such as the lack of longer term studies which show persistence of BP control or clinical benefit from SMBP, uncertainty regarding who is likely to benefit from SMBP, lack of standardization in prescription of SMBP, and uncertainty regarding the most effective additional support. The fifth topic relates to the inability to assess cost-effectiveness of SMBP, due to the deficiencies in evidence identified in the first four gaps.

Hypertension is a long-term condition and BP changes with age, acute illness, and comorbidities achieving optimal control requires long-term monitoring. The benefits of long-term BP control are presumed to include a reduction in clinical cardiovascular outcomes; therefore, the need to demonstrate that SMBP has long-term benefit is paramount to establishing a justification for SMBP. This is particularly pertinent, since SMBP requires long-term patient participation. Thus, the first topic (Topic 1) is focused on the need for longer term studies and plays a central role also for the remaining topics. At the same time, since long-term effects of SMBP may be modulated by patient and disease factors, SMBP prescription, and types of additional support, considerations for Topics 2, 3, and 4 affect research design deliberations for Topic 1.

Longer term trials are necessary in order to address FRN Topic 1. Clinical outcome trials, while providing the most rigorous information on comparative effectiveness, do not appear feasible given the large sample sizes necessary. Embedding the study of SMBP in another large trial of a CVD (cardiovascular disease) risk reduction strategy, however, might be a viable alternative. Also, it may be possible to extrapolate from a large body of experimental evidence that links BP reduction with improved clinical outcomes to SMBP. However, longer term clinical trials of SMBP that assess adherence with SMBP, adherence with prescribed medications, BP control, and patient satisfaction are feasible and necessary to address the question of whether the SMBP effect is durable. Observational studies comparing outcomes in SMBP users versus nonusers are confounded, and this bias cannot be satisfactorily overcome.

For FRN Topic 2, modeling can be used to explore the heterogeneity of treatment effects, using individual patient data from trials or observational studies to develop and validate predictive instruments for SMBP adherence or BP control. Candidate predictor variables include sex, age, race/ethnicity, socioeconomic status, disease characteristics, and cardiovascular disease risk factors, as well as attitudes regarding participation in disease management. Using these instruments prospectively may circumvent the problem of multiple subgroup comparisons in future trials.

With regards to FRN Topic 3, SMBP prescriptions ought to be standardized based on randomized controlled trials comparing different prescriptions and their effect on adherence to SMBP, adherence to BP medication and BP control.

For FRN Topic 4, an expert panel should be employed to prioritize what elements of additional support should be chosen for future comparative studies of SMBP. The panel should include pharmacists, experts in telemedicine and bioinformatics, and authorities in adherence and chronic disease management.

To address FRN Topic 5, which was outside the scope of the SMBP CER, a systematic review of the existing cost-effectiveness analyses would be the first step. Longer term SMBP studies of BP outcomes and resource use (and possibly clinical outcomes and subgroup effects) are needed to assess the overall balance of costs and benefits of SMBP.

## Discussion

The prioritization of topics for future research was generated based on a stakeholder-driven nomination and prioritization process. Our stakeholder panel represented a broad range of perspectives, across major stakeholder categories identified in this taxonomy. We were able to obtain input from all panel members, and the final ranking showed a clear separation of the top priorities.

Nevertheless, the process was not without limitations. The total number of stakeholders recruited was restricted, thus limiting representation. Also, despite formal planning, the selection of stakeholders, solicitation of contributions, facilitation of discussion, and synthesis of suggestions remain, to some degree, idiosyncratic.

One additional crosscutting methodological issue outside of the scope of the SMBP CER relates to the challenge of translating BP readings obtained at home, in the clinic, or by ambulatory BP monitoring. Once it is possible to convert between home BP, clinic BP, and ambulatory BP readings, BP can be assessed comprehensively across different settings, and consistent targets can be set.

## Conclusions

This report identifies five high-priority future research needs with regards to SMBP, as determined by a stakeholder panel. They are:

1. What are the effects of SMBP on BP, medication adherence rates, satisfaction, and clinical event outcomes, after longer followup periods of 2 to 5 years or longer?
2. Which patients may be more likely to benefit from using SMBP?
3. What is the best prescription or protocol for SMBP (when, how often, and how frequently)? How do different prescriptions for SMBP compare regarding acceptance by patients, adherence with SMBP, and effect on BP control?
4. What is the role of additional support? What particular components of additional support should be further evaluated?
5. What is the effect of SMBP on resource utilization? What is the cost-effectiveness of SMBP?

In summary, to address these gaps: longer term randomized controlled trials that examine SMBP's effects on BP control and resource utilization are needed; the impact of SMBP on CVD outcomes may be gleaned from embedding SMBP in other CVD outcome trials; the exploration of treatment heterogeneity may identify those groups more likely to benefit from SMPB. When, how often, and how frequently to use SMBP, and what additional support to employ, should be further refined. Finally, filling these evidence gaps will inform future modeling of cost-effectiveness.

# Background

Hypertension is a common, long-term health condition, particularly prevalent among older adults. Untreated or undertreated hypertension leads to increased cardiovascular morbidity and mortality, as well as increased consumption of health care resources; however, long-term adherence to lifestyle modification and medication remains a challenge. Self-measured blood pressure monitoring (SMBP) has been suggested as one method that may improve adherence to blood pressure (BP) treatment and consequently improve outcomes. SMBP refers to the regular self-measurement of a patient's BP at home or otherwise outside the office or clinic, as a supplement or alternative to those obtained in a health care setting. While patient self-participation in chronic disease management appears to be a promising means of improving adherence, the sustainability and clinical effect of this strategy, as well as its impact on health care utilization, remain uncertain.

The current Future Research Needs (FRN) project was launched upon the completion of an Agency for Healthcare Research and Quality (AHRQ) Comparative Effectiveness Review (CER) on SMBP, and builds on the evidence gaps identified in that review. The present report describes the development of a stakeholder-prioritized list of research needs for that topic, along with a measured consideration of the advantages and disadvantages of various potential research designs, in order to help researchers and funders develop future research proposals or solicitations.

## Scope of CER

The January 2012 CER upon which the current FRN report is based, Self-Measured Blood Pressure Monitoring: Comparative Effectiveness, was sponsored by the Agency for Healthcare Research and Quality and conducted by the Tufts Evidence-based Practice Center (EPC).[2] It reviewed pertinent publications through July 2011 and addressed five Key Questions:

1. In people with hypertension (adults and children), does SMBP, compared to usual care or other interventions without SMBP, have an effect on clinically important outcomes?
    a. How does SMBP compare to usual care or other interventions without SMBP in its effect on relevant clinical outcomes (cardiovascular events, mortality, patient satisfaction, quality of life, and adverse events related to antihypertensive agents)?
    b. How does SMBP compare to usual care or other interventions without SMBP in its effect on relevant surrogate outcomes (cardiac measures of left ventricular hypertrophy) and intermediate outcomes (BP control, BP treatment adherence, or health care process measures)?
2. In trials of SMBP, how do clinical, surrogate, and intermediate outcomes (including SMBP adherence) vary by the type of additional support provided?
3. How do different devices for SMBP compare with each other (specifically semiautomatic or automatic versus manual) in their effects on clinical, surrogate, and intermediate outcomes (including SMBP adherence)?
4. In trials of SMBP, how does achieving BP control relate to clinical and surrogate outcomes?
5. How does adherence with SMBP vary by patient factors?

## Findings of the CER

Results and conclusions from the CER are based on 47 comparative studies of at least 8 weeks duration, and one observational study. There were 24 comparisons of SMBP alone versus usual care, 24 of SMBP plus additional support versus usual care, 12 of SMBP plus additional support versus SMBP without additional support or with less intense additional support, and 1 study evaluating predictors of adherence to SMBP. For SMBP alone versus usual care, the strength of evidence was moderate showing a lower BP with SMBP (SBP/DBP [systolic BP/diastolic BP] –3.1/ –2.0 mmHg at 6 months). For SMBP plus additional support versus usual care, the strength of evidence was high showing a lower BP with SMBP use (SBP/DBP –3.4 to –8.9/ –1.9 to –4.4 mmHg) up to 12 months. For SMBP plus additional support versus SMBP alone or with less intense additional support, the strength of evidence was low, and failed to support a difference in BP. For all comparisons, evidence for clinical outcomes was insufficient; for all other non BP outcomes (surrogate and intermediate outcomes, and health care encounters) strength of evidence was low and failed to support a difference. No trials compared different SMBP devices or provided evidence on the relationship between BP control and clinical or surrogate outcomes. There was insufficient evidence concerning predictors of SMBP adherence. None of the studies enrolled children.

## Identification of Evidence Gaps

The 2011 CER on SMBP identified several evidence gaps. Although children were specified as a population of interest, there were no eligible studies conducted in children. Given the rise of hypertension among children, this lack of research represents an important shortcoming in the literature. Refinement of the future research agenda to address this population would require a specially composed stakeholder group with perspectives on the management of hypertension in children. Thus, while the evidence gap in children was noted, it was determined that the current project proceed with a focus on adults only. All other identified evidence gaps are summarized in Table 1, organized and labeled by Key Question and PICOD (Population, Intervention, Comparator, Outcome, study Design) category.

**Table 1. Identified evidence gaps organized by relevant Key Question and PICOD element**

| Key Question | Category | Evidence Gaps (Code*) |
|---|---|---|
| **Key Question 1.** In people with hypertension (adults and children), does SMBP, compared to usual care or other interventions without SMBP, have an effect on clinically important outcomes?<br><br>**Key Question 1a.** How does SMBP monitoring compare to usual care or other interventions without SMBP in its effect on relevant clinical outcomes (cardiovascular events, mortality, patient satisfaction, quality of life, and adverse events related to antihypertensive agents)?<br><br>**Key Question 1b.** How does SMBP compare to usual care or other interventions without SMBP in its effect on relevant surrogate outcomes (cardiac measures: LVH, LVM, LVMI)* and intermediate outcomes BP control, BP treatment adherence, or health care process measures)? | Population | Unclear if treatments or treatment goals differ if a patient has uncontrolled hypertension, white coat hypertension, or masked hypertension (1P1)<br>Unclear if effects from SMBP differ in subgroups, for example older patients, those with comorbidities, and minorities (1P2) |
| | Intervention/ Comparator | Unclear what the BP treatment goals should be for home BP in relation to clinic BP (1I1)<br>Unclear how to compare findings across studies, as different studies use different protocols for SMBP, different additional support and different care in the control groups (1I2)<br>Unclear what the best practice protocol would be for SMBP (1I3)<br>Unclear what the adherence is to SMBP protocols or devices in the long-term (1I4)<br>Unclear how the effect of SMBP can be enhanced by particular additional support (1I5) |
| | Outcomes | Unclear what the effects are of SMBP on clinical event outcomes, i.e., after longer followup periods (1O1)<br>Unclear if the effect of SMBP is sustained beyond 1-2 years (1O2)<br>Unclear what the effect of SMBP is on patient understanding of disease, and how this correlates with attitudes towards and participation in disease management, medication adherence and BP control (1O3) |
| | Design | N/A |
| **Key Question 2.** In trials of SMBP monitoring, how do clinical, surrogate, and intermediate outcomes (including SMBP adherence) vary by the type of additional support provided? | Population | N/A |
| | Intervention/ Comparator | Unclear what the optimal additional support is for facilitating patient-provider interaction, and medication management including telemedicine (2I) |
| | Outcomes | N/A |
| | Design | N/A |
| **Key Question 3.** How do different devices for SMBP monitoring compare with each other (specifically semiautomatic or automatic versus manual) in their effects on clinical, surrogate, and intermediate outcomes (including SMBP adherence)? | Population | N/A |
| | Intervention/ Comparator | Unclear if the device type impacts adherence, BP control and outcomes (3I) |
| | Outcomes | N/A |
| | Design | N/A |
| **Key Question 4.** In trials of SMBP monitoring, how does achieving BP control relate to clinical and surrogate outcomes? | Population | N/A |
| | Intervention/ Comparator | N/A |
| | Outcomes | Unclear what the link is between achieving BP control and clinical outcomes (4O) |
| | Design | Need for longer term follow up (4D) |
| **Key Question 5.** How does adherence with SMBP vary by patient factors? | Population | N/A |
| | Predictor | Unclear how patient characteristics, such as demographic and psychosocial variables, affect adherence to SMBP (5P) |
| | Outcomes | Need for validated outcome measures of adherence with SMBP (5O) |
| | Design | N/A |

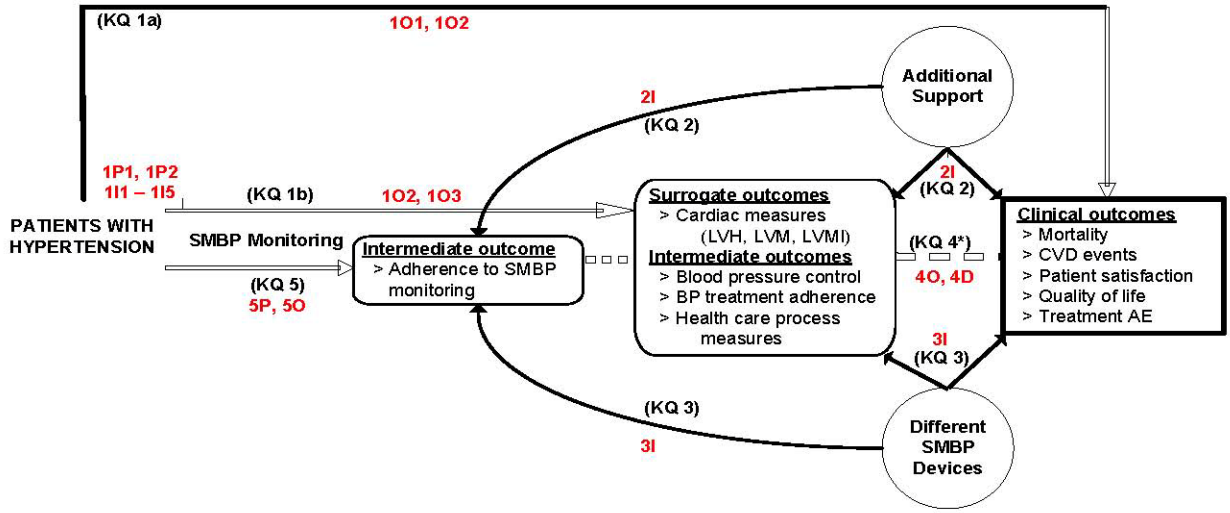
**Abbreviations:** BP=blood pressure; N/A=not applicable; SMBP=self-measured blood pressure monitoring

* The parenthetical alphanumeric code is used to label each evidence gap on the analytic framework (Figure 1). The first number of the alphanumeric code corresponds to the Key Question, the following letter to the PICOD category, and the final numeral to distinguish among multiple gaps within the same Key Question and Domain (if applicable). Where there is only one gap identified, the last number is dropped.

# Analytic Framework

Figure 1 depicts the analytic framework that guided the SMBP CER. It maps the specific linkages associating the populations and subgroups of interest, interventions, and outcomes of interest (intermediate outcomes, health-related outcomes, compliance, and adverse effects) for each Key Question. Specifically, the analytic framework illustrates the chain of logic that the evidence must support to link interventions to improved health outcomes. In addition, we have labeled the figure with each Key Question's identified research gaps.

**Figure 1. Analytic framework for SMBP with evidence gaps***




**Abbreviations:** AE=adverse events; BP=blood pressure; CVD=cardiovascular disease; KQ=Key Question; LVH=left ventricular hypertrophy; LVM=left ventricular mass; LVMI=left ventricular mass index; SMBP=self-measured blood pressure.
* Each gap is indicated with an alphanumeric code, where the first number of the alphanumeric code corresponds to the Key Question, the following letter to the PICOD category, and the final numeral to distinguish among multiple gaps within the same Key Question and category (if applicable). Where there is only one gap identified, the last number is dropped.

# Methods

## Identification of Evidence Gaps

As the original authors of the SMBP CER, we generated the initial list of FRN topics based on the Research Needs section of the report, and then organized the list of evidence gaps according to Key Questions and PICOD elements. We then used an iterative process to identify additional FRN topics through Webinars and emails with a stakeholder panel. We asked the stakeholder panel to prioritize the FRN topics following a formalized schema of prioritization criteria.

## Criteria for Prioritization

Stakeholders (described in the next section) were asked to consider four dimensions of need. These four dimensions are outlined in the Effective Health Care Program Selection Criteria (Appendix A). Briefly, they are:

- Importance
- Desirability of Research/Avoidance of Unnecessary Duplication
- Feasibility
- Potential Impact

The fifth dimension of the Selection Criteria, appropriateness, was not evaluated by the stakeholders, as AHRQ already deemed the topic of SMBP to adequately meet this criterion. The Effective Health Care Program guidance on these criteria was explained in detail at each Webinar encounter with the stakeholders and was also specified on a worksheet that was distributed for discussion.

To inform the selection criterion of Desirability of Research/ Avoidance of Unnecessary Duplication, we conducted an update of the original CER's MEDLINE® search through January 13, 2012 to find new studies that addressed the CER's Key Questions. The full search is provided in Appendix A (Table A1). We also searched the National Library of Medicine Clinical Trial Registry (www.ClinicalTrials.gov) to identify ongoing or recently completed trials relevant to the CER questions (Appendix A, Table A2). Relevant recently completed or registered studies identified in the searches were compared against the nominated FRN topics to assess if they would make future research on any nominated topic redundant, but none appeared to do so.

## Engagement of Stakeholders, Researchers, and Funders

Although researchers and funders of research are the primary audience for future research needs documents, the EPC solicits input from other stakeholders as well when identifying high priority research gaps and future research needs. Stakeholders are selected to provide broad expertise and a breadth of perspectives, as well as input on the kind of information that is helpful in healthcare decisionmaking. These stakeholders are engaged throughout the future research process. Their role is to (1) review the preliminary list of evidence gaps and possible future research topics derived from them, (2) to nominate additional topics to the list, (3) discuss topic nominations, (4) to participate in prioritization of the future research needs topics. Stakeholders are not involved in translating the gaps into research questions and study designs, composing or reviewing the report. The final future research needs document will be released for public

comment. Stakeholders who participated in the future research needs identification process are invited to provide comments on this report during the public posting. Public input may be incorporated into or otherwise reflected in the final report.

We engaged a stakeholder panel representing the stakeholders who use research evidence in health care and public health decisionmaking. To form the panel, we used the Tufts-developed 7Ps model of stakeholder engagement,[1] which identifies seven primary stakeholder categories. The stakeholder categories of the 7Ps model consist of:

1. **Patients and the public:** This group represents current and potential consumers of patient-centered health care and population-focused public health programs. This group also includes caregivers, family members, and patient advocacy organizations, all of whom represent the interests of consumers or patients.
2. **Providers:** This group includes individuals (e.g., nurses, physicians, and other providers of care and support services) and organizations (e.g., hospitals, clinics, community health centers, pharmacies, emergency medical services agencies, schools) that provide care to patients and populations.
3. **Purchasers:** This group includes employers; the self-insured; Federal, state, and local governments; and other entities responsible for underwriting the costs of healthcare.
4. **Payers:** This group represents private insurers, government insurers (e.g., Medicare, Medicaid, the Veterans Administration), and others responsible for reimbursement for care.
5. **Policymakers:** This group includes entities such as the legislative and executive branches of the Federal and state governments, professional associations, and other intermediary groups that collect and distribute information to policymakers.
6. **Principal investigators:** This group consists primarily of researchers, and research funders.
7. **Product makers:** This group consists primarily of manufacturers and device makers.

These categories are not necessarily mutually exclusive, and one stakeholder may belong to more than one category.

We recruited stakeholders representing Patients and the Public, Providers, Payers, Policymakers, and Principal investigators and asked them to provide input foremost according to their designated stakeholder category. We did not specifically recruit stakeholders representing purchasers because their interest in SMBP was not sufficiently different from that of payers. For Product makers, we contacted manufacturers from the list of companies that were sent Scientific Information Packets for the CER. These companies were asked to provide potential FRN topics with rationales, but were not invited to be stakeholders due to the inherent financial conflict of interest.

We identified individuals to serve on the stakeholder panel through several means. We invited some individuals who had previously served in advisory roles on the original SMBP CER. We used our affiliation with the Kidney Disease and Hypertension Outpatient clinic at Tufts Medical Center to identify patients and clinical providers. We used professional contacts to identify public and private payers and a policy maker. Further, our Task Order Officer helped recruit a Medicare representative who represented a payer.

Individuals were selected based on their perceived interest in the topic and their level of previous participation in discussions on the topic, as well as their coverage of a necessary

stakeholder category. Our predetermined goal was to assemble a representative panel of 11 stakeholders across the first 6 stakeholder categories (Table 2).

**Table 2. List of predetermined target stakeholders**

| Category | Subcategory | No. of Stakeholders |
|---|---|---|
| Patients and the public | Patients with hypertension | 2 |
| Providers | Clinician – MD General Practitioner<br>Clinician – Physician assistant in hypertension clinic Clinician – Nurse Practitioner in hypertension clinic | 3 |
| Payers | Medicaid<br>Medicare<br>Private insurer (Blue Cross Blue Shields) | 3 |
| Policymakers | Health Resources and Services Administration | 1 |
| Principal investigators | Clinical research investigators | 2 |
| Total | | 11 |

All individuals involved in the project were required to submit a standard disclosure of interest form. Participation was only confirmed after review of the disclosure form. Stakeholders were asked to disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because they may be called upon to provide unique clinical or content expertise, stakeholders may potentially be retained even when there are potential conflicts. AHRQ's Task Order Officer and the EPC conferred to approve each stakeholder.

Individuals who met the criteria to participate as a stakeholder were contacted by email with a brief description of the project and its purpose, a formal invitation to serve as a stakeholder, and the executive summary of the original SMBP CER. After confirmation of participation, we sent additional instructions and materials to orient stakeholders as to how the project would proceed. We also sent the Future Research section of the original CER and a proposed outline for the future research needs project.

In January 2012, we conducted a first round of Webinars with stakeholders. In these Webinars, we first explained the purpose and process of FRN topic development. Subsequently stakeholders were asked to self-identify as a representative of a particular stakeholder category and directed to provide feedback chiefly with respect to their primary stakeholder category. We also directed stakeholders to restrict their FRN nominations to topics within the scope of the CER, specifically delineating out-of-scope topics, such as the diagnosis of hypertension or the management of hypertension in pregnant women or in chronic dialysis patients (based on the topic and study eligibility criteria of the SMBP CER). We then reviewed the research gaps identified in the CER and explained the criteria for prioritization. After this orientation, the stakeholders were asked to identify additional FRN topics of interest to them and to discuss their or others' topics, the supporting rationale or related research challenges. Stakeholders were also given the option of nominating additional topics by email.

Topics nominated by stakeholders were incorporated into the topic list along with supporting rationale, which we condensed from the discussion and subsequent emails. We combined duplicate or similar FRN topics together and disseminated the revised list of topics, along with Webinar minutes, with an invitation to comment as to whether the nominated topics and supporting rationales were appropriately recorded and accounted for.

We held a second round of Webinars in February 2012, during which we reviewed the refined list of nominated topics. Stakeholders were asked if their nominations were appropriately

captured and accounted for and were able to have additional discussion. We then asked each stakeholder to identify his or her top five priority topics and to provide any justifications based upon the provided criteria for prioritization.

Following this second round, we further edited the topic list based on stakeholder rationale. We also added topic suggestions to the topic list that were made by the product maker representative. We then sent it back to stakeholders. Stakeholders were given one week to provide comments on the revised list by email. Following this commentary period, we finalized the list and asked stakeholders to electronically indicate their top five topic choices using an online application Survey Monkey™ to elicit a structured response. The five topics with the highest number of stakeholder endorsements were designated as the prioritized future research needs topics.

To ensure that input from all stakeholders was heard and considered, great pains were taken to accommodate scheduling restraints for all stakeholders. Composition of each Webinar list of invitees was also carefully planned. In particular, we scheduled a Webinar during the first series for just the two patient representatives to make certain that they had the opportunity to contribute and interact in this way. In total, we were able to almost complete participation of all stakeholders at both Webinars, with one providing input by email in lieu of in-person participation at the second Webinar.

Use of the Effective Health Care Program prioritization criteria was repeatedly emphasized throughout the prioritization process, including during discussion, nomination, and final topic selection. Upon the close of stakeholder prioritization, we identified the top five topics as those most frequently endorsed by stakeholders in their top five selections. The final ranked list was emailed to stakeholders.

## Research Question Development and Research Design Considerations

We transformed the final list of FRN topics into research questions using standard PICOD criteria. (Stakeholders were not utilized during this process.) We discussed various alternatives for future research efforts aimed to answering each question, specifically considering the feasibility of addressing the research questions with respect to potential sample size, the time required, recruitment and ethical issues. In particular, we evaluated the advantages and disadvantages of various potential research designs with regards to:

- Value of study design
- Resource use, size, and duration
- Ability to recruit
- Ethical issues

When randomized trials were deemed to be the most appropriate study design to address a FRN topic, we performed sample size calculations using standard formulae for a two-sided chi-squared test at the 0.05 level of significance. We also examined the literature for estimates of the relative effect between intervention and control. We assumed an allocation ratio of 1:1, no loss to followup, no crossover between treatments, and no sequential monitoring.

# Results

## Research Needs

The FRN identification process led to the nomination of 16 topics (Table 3). The five topics with the highest number of stakeholder endorsements constitute the highest priority FRN topics. The first four are based directly on evidence gaps identified in the CER. These topics pertain to interrelated issues such as the lack of longer term studies to evaluate persistence of BP control or clinical benefit from SMBP, uncertainty regarding what populations are likely to benefit from SMBP, lack of standardization in the prescription of SMBP, and uncertainty regarding the most effective additional support. The fifth prioritized topic, the cost-effectiveness of SMBP, was not included in the CER; it pulls together the issues raised in the top four topics, and, thus, is hindered by the lack of adequate evidence regarding the other research topics.

SMBP requires patient participation to assess and improve BP control. Since hypertension is a long-term condition and BP changes with age, acute illness, and comorbidities, achieving optimal control requires long-term monitoring. The benefits of long-term BP control are presumed to include a reduction in clinical cardiovascular outcomes; therefore, the need to demonstrate that SMBP has long-term benefit is paramount to establishing a justification for SMBP. Thus, the first topic (Topic 1) is focused on the need for longer term studies and plays a central role also for the remaining topics. At the same time, since long-term effects of SMBP may be modulated by patient and disease factors, SMBP prescription, and types of additional support, considerations for Topics 2, 3, and 4 affect research design deliberations for Topic 1.

**Table 3. Prioritized and other nominated topics for future research needs in SMBP research**

| Topic* | Topic Questions | # of Stakeholder Endorsements |
|---|---|---|
| | **Prioritized future research needs topics** | |
| 1 | What are the effects of SMBP on BP, medication adherence rates, satisfaction, and clinical outcomes after followup periods of 2 to 5 years or longer? | 7 |
| 2 | Which patients may be more likely to benefit from using SMBP? | 6 |
| 3 | What is the best prescription or protocol for SMBP (when, how often, and how frequently)? How do different prescriptions for SMBP compare regarding acceptance by patients, adherence with SMBP, and effect on BP control? | 8 |
| 4 | What is the role of additional support? What particular components of additional support should be further evaluated? | 7 |
| 5† | What is the effect of SMBP on resource utilization? What is the cost-effectiveness of SMBP? | 7 |
| | **Other nominated future research needs topics** | |
| 6† | What are the best tools to educate providers regarding use of SMBP? | 3 |
| 7† | What are the best tools to educate patients regarding use of SMBP? | 3 |
| 8† | How should SMBP measurements be aggregated or synthesized? For example as BP means, confidence intervals, range including measures of variability (e.g., episodic highs, standard deviations)? Or as pulse pressure? How do different metrics of aggregated SMBP readings predict risk for cardiovascular disease? | 3 |
| 9† | How can SMBP be integrated into the patient centered medical home or into multifaceted approaches to improve cardiovascular disease risk management? | 3 |
| 10† | How do readings from clinic BP and SMBP compare with each other in their ability to predict CVD risk, and for setting treatment targets? | 2 |
| 11† | What is the effect of different device features to minimize errors on quality and accuracy of reading and to enhance adherence? | 2 |
| 12† | Should SMBP measurements be recorded blindly (i.e., automatically) or not? What is the impact on accuracy and anxiety and BP control? | 1 |
| 13 | What are the best approaches for transmitting the readings? | 1 |
| 14 | What are the potential harms of SMBP? Which patients may be more likely to experience harms? | 1 |
| 15† | How and how often should the accuracy of a SMBP device in a particular patient be checked in the office to ensure its accuracy for the individual patient? | 0 |
| 16 | How does including nocturnal SMBP reading compare with no nocturnal SMBP readings in use of SMBP? | 0 |

**Abbreviations:** BP=blood pressure; CVD=cardiovascular disease; SMBP=self-measured blood pressure monitoring
* Prioritized topics (1–5) are ordered logically by clinical content. Other nominated topics are listed in the order they were prioritized by the stakeholder panel.
† Topic was not covered by the SMBP CER. For Topic 12, only the second question was not addressed by the SMBP CER.

## High-Priority Future Research Needs Topic 1. What Are the Effects of SMBP on BP, Medication Adherence Rates, Satisfaction, and Clinical Outcomes After Followup Periods of 2 to 5 Years or Longer?

# Background

The SMBP CER identified three related evidence gaps pertinent to long-term followup. The followup periods in the comparative studies included in the CER were limited, with most studies not extending beyond 12 months; the comparative studies generally lacked clinical outcomes, with only 1 of 47 studies reporting clinical outcomes; and there were no data linking BP outcomes and clinical outcomes. Therefore, it is currently uncertain if patient adherence to SMBP is sustained beyond 1 to 2 years, whether the effect of SMBP on BP reduction is durable beyond 1 to 2 years, or whether this effect translates into improved clinical or patient reported

outcomes. The stakeholders noted that wide coverage of SMBP devices by payers is unlikely unless there is evidence for longer term efficacy and utility (see Topic 5).

# Proposed Study Designs

## Randomized Controlled Trial

### Value of Study Design

Randomized controlled trials (RCTs) provide the most rigorous study design for examining comparative effectiveness for clinical outcomes. RCTs comparing SMBP alone versus usual care, SMBP with additional support versus usual care, or SMBP with additional support versus SMBP alone would produce the most rigorous comparative data. A reasonable time frame for such studies would be 2 to 3 years to demonstrate prolonged effects. Trials should be pragmatic, with wide eligibility criteria and diverse settings to enhance the relevance of their findings. The most direct evidence corroborating a link between surrogate outcomes of BP control with a composite clinical cardiovascular outcome would be derived from RCTs reporting both surrogate outcomes and clinical endpoints; this would require large groups with 5 to 10 years of followup (See Figure 2 for power calculation).

RCTs would also allow for the examination of the modifying effects of patient and disease characteristics (see Topic 2), of different prescription and administration regimes of SMBP (see Topic 3), and of additional support combined with SMBP (see Topic 4). Longer term RCTs examining resource use are further expected to yield data for modeling the cost-effectiveness and utility of SMBP (see Topic 5).

Alternatively, a comparative trial of SMBP can be embedded into a larger trial of cardiovascular disease (CVD) risk reduction; for example, studies of treatments for hypertension, diabetes, or cardiovascular disease. One such study is the National Heart, Lung, and Blood Institute's Ischemia Trial[3] This study compares medical therapy with more invasive approaches for treatment of patients with stable ischemic heart disease. The study aims to enroll approximately 8000 patients. Followup is approximately 4 years, with the primary study outcome being a composite outcome of cardiovascular death or nonfatal myocardial infarction. SMBP can be compared against usual care by nesting within the medical therapy arm or by using a 2x2 factorial design.

A large body of evidence derived from hypertension trials links BP reduction with antihypertensive treatment to reduced CVD morbidity and mortality. The effect of BP reduction and improvement of CVD may be qualitatively similar between studies of antihypertensive agents and studies of SMBP, since the mechanism through which SMBP would lower CVD (i.e., antihypertensive treatment) is the same. Still, indirect comparisons across different interventions lower our confidence in the strength of evidence. For example, SMBP may lower CVD risk through effects beyond better BP control, such as through lifestyle modification.

Assuming evidence from large hypertension trials can be extrapolated to studies of SMBP, longer term RCTs of SMBP could focus on demonstrating an effect on long-term adherence to SMBP, adherence with antihypertensive medication, achieving BP control and patient satisfaction, to alleviate the concern about loss of efficacy over time. This would require smaller sample sizes than for trials with CVD outcomes as the effect sizes would be larger.

An additional approach to decrease the necessary sample size would be to exclude individuals with a pronounced "white coat effect", that is, individuals with clinic BP readings

that are disproportionately higher than their home averages. In these individuals, if BP is managed based on home BP reading, this will result in higher clinic BPs. Combining individuals with and without a white coat effect in a study and basing BP treatment on home readings could result in opposing actions in medication management and dilution or cancellation of the overall effect on clinic BP.

## Resource Use, Size, and Duration

An RCT, especially one with a long duration and large sample size, is a highly resource-intensive endeavor. The decision to conduct such a trial must be balanced against the value of the information that can be gained from longer followup and wider representation.

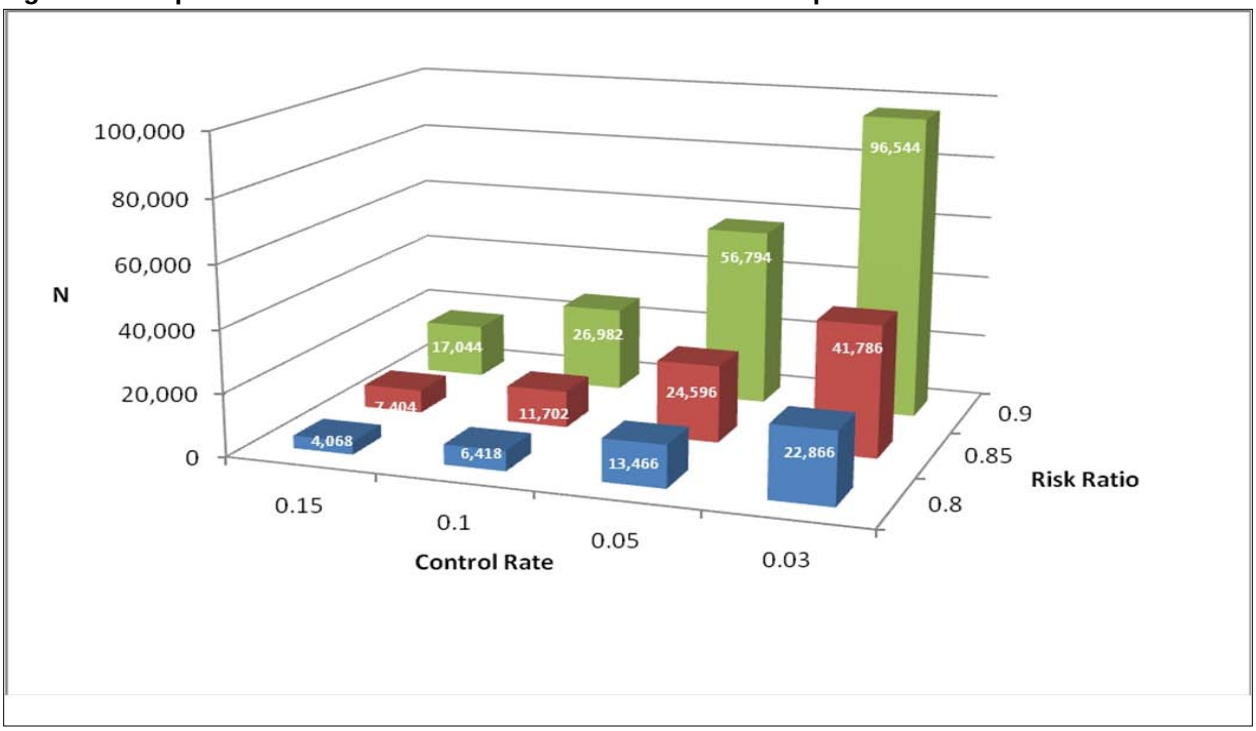
To estimate an appropriate trial sample size, we carried out a power calculation using standard formulas for a two-sided equivalence test. Given the lack of data for the effects of SMBP on a composite cardiovascular outcome, we used data from an existing hypertension trial.[4] This trial, the Heart Outcomes Prevention Evaluation (HOPE) study, compared treatment with the antihypertensive ramipril to placebo in individuals at increased cardiovascular risk, based on the presence of the combination of either vascular disease or diabetes and at least one additional cardiovascular risk factor. In the study, ramipril treatment was reported to reduce SBP by 3 mmHg and DBP by 2 mmHg, with a relative risk of 0.78 for a composite cardiovascular outcome of myocardial infarction, stroke, or death from cardiovascular causes. The event rate in the entire control group over a mean of 5 years was 18 percent. In the smaller subgroup of individuals with diabetes mellitus and one additional cardiovascular risk factor (i.e., those without a history of cardiovascular disease) it was lower at 10 percent. For our calculations, we modeled control rates of 15 percent or less, since individuals with hypertension who do not have clinical cardiovascular disease or diabetes would be expected to have lower risk of cardiovascular disease. Furthermore, trials of lower risk individuals would be more applicable to the general population of patients with hypertension than trials restricted to high-cardiovascular risk patients.

For the estimate of the effect size we reviewed the BP effect in the SMBP CER. Although the BP effect was stronger for the combination of SMBP with additional support, we considered the more modest BP reduction for SMBP alone (approximately 2 mm Hg SBP), which is less than the 3 mmHg change for ramipril in the HOPE study. Also, ramipril may improve CVD outcomes through pathways independent of BP reduction, especially in those with CVD or DM. Therefore we also used lower effect sizes than those achieved in HOPE.

We did not consider loss-to-followup in our estimates. However, loss-to-followup in the trials reviewed for the SMBP CER was as high as 20 percent at 12 months. This would require further increases in sample size to compensate for dropouts as well as decreasing adherence with SMBP and crossover of study participants from one group to another.

Our calculated total sample sizes for relative risk (in a two-arm RCT with a 1:1 ratio between arms, two-sided type I error rate [alpha] of 5 percent, and 80 percent power) for each combination of estimated relative risk and control rate are presented in Figure 2.

**Figure 2. Sample size for a randomized controlled trial for a composite CVD outcome**




Total sample size for an RCT with a 1:1 ratio between 2 arms, 80 percent power, two-sided type I error rate (alpha) of 5 percent, and no loss to followup.

Depending on the specific control rate and relative risk, the total number of subjects required would range from 4,000 to 97,000 subjects per study. Thus, the feasibility of a trial of cardiovascular end-points in individuals with hypertension without other CVD risk factors is limited.

For trials examining the outcome of BP control, that is, achievement of a BP below a specific BP target, the duration of followup can be shorter and the sample size smaller, such as was the case for a recent 24-month SMBP trial.[5] To detect a 10 percent improvement in BP control rates at 24 months with 80 percent power, a type I error rate of 5 percent, the study calculated 570 patients were needed (across 4 arms). However to account for an estimated 24-month dropout rate of 15 percent, the study enrolled 636 individuals divided into 4 arms (159 per arm) and it was in fact adequately powered to show a significant difference of 11 percent. For studies of categorical BP outcomes (i.e., achievement of BP target), sample size needs may vary depending on the discrepancy between the baseline BP and the BP target.

## Ability To Recruit

There should be no major barriers to recruitment for RCTs addressing this evidence gap. The intervention (SMBP) is low-risk, pain-free, unlikely to be a substantial burden for people interested in controlling their BP, and encourages people to be more involved in their health care.

## Ethical Issues

There is sufficient equipoise to continue conducting trials of SMBP. It is unlikely that patients would be unduly coerced to participate in such a trial. Confidentiality is presumed.

## Observational Studies

### Value of Study Design

Observational studies can compare outcomes for SMBP users versus nonusers. However, observational studies are subject to biases due to the lack of randomization. Established methodological approaches such as matching and regression analysis, including propensity score analyses, may be used to reduce biases from known imbalances at baseline. In addition, sensitivity analyses may be used to explore the robustness of findings for nonrandomized comparisons. However, SMBP depends on patient participation, which is subject to complex and poorly measurable or hidden factors, making it unlikely that confounding by selection bias could be adequately overcome. Thus, findings gleaned from cohort studies should be considered as hypothesis-generating rather than confirmatory.

On the other hand, observational studies have the benefit of wider generalizability when data collection occurs in real-life clinical settings and without restrictive inclusion criteria. As an example, in the Veterans Administration (VA) hospital system, SMBP is provided freely to individuals with hypertension. The VA medical system also contains electronic medical and administrative data systems, which reduces the burden for new data collection.

### Ability To Recruit

There should be no barriers to recruitment for observational studies addressing SMBP.

### Resource Use, Size, and Duration

The reliance on observational data substantially reduces resource use and increases feasibility in addressing this evidence gap. Post hoc analyses of existing observational studies can be done quickly and with modest resources. Generally, given the ease of retrospective data analysis, care should be taken to avoid biases from exploratory data-mining. Use of existing databases may be incomplete for some variables.

Prospective observational studies allow for purposeful planning to answer hypotheses and more complete collection of relevant data, which can increase validity compared to post hoc observational using existing data. However, prospective planning and data collection consume a greater amount of resources.

### Ethical Issues

There should be no ethical barriers to the analysis of existing databases or to conducting prospective trials in the investigation of this evidence gap.

## High-Priority Future Research Needs Topic 2. Which Patients May Be More Likely To Benefit From Using SMBP?

# Background

In the studies eligible for the SMBP CER, subgroup analyses in RCTs studies were few and of low quality. Further, subgroups were defined according to various different characteristics. Overall, subgroup analyses did not exhibit clear signals as to what populations might differentially benefit from SMBP. One study included in the CER addressed how adherence with SMBP monitoring varied by patient factors. Stakeholders agreed that future research to

determine which patients would be most likely to benefit from SMBP was important, as it would allow to target SMBP appropriately to those who are likely to benefit.

A number of factors could influence whether a patient derives benefit from SMBP. These include patient demographics, disease characteristics, and CVD risk factors. In addition, the patient's attitude and predisposition toward participation in disease management may impact adherence with SMBP, adherence with medication, BP control, and overall effectiveness. The large number of possible effect modifiers poses a challenge when exploring the heterogeneity of treatment effects.[6]

# Proposed Study Designs

## Randomized Controlled Trial

### Value of Study Design

The ideal study design for rigorous exploration of treatment effects in a particular group is an RCT. To definitively examine treatment effects for subgroups would require even larger sample sizes than for overall group effects. For example, to determine that both women and men benefit from SMBP, a trial would have to be powered for both groups. To enhance the rigor of subgroup analyses, subgroups must be pre-specified and may require enrollment stratified by the characteristic to ensure adequate sample size per subgroup. Examining the effects of SMBP in the context of a larger RCT of cardiovascular disease risk reduction is an alternative, less resource-intensive option that would also allow for the exploration of subgroup effects, provided that the relevant sample sizes were sufficient.

### Resource Use, Size, and Duration

An RCT to examine subgroups is a resource intensive endeavor. Examining SMBP in a larger CVD risk reduction trial could reduce this resource requirement.

### Ability To Recruit

Exploration of subgroups in an RCT may require stratified enrollment. The ability to recruit may depend on how wide a representation is sought for specific characteristics. For example, if a wide range is desired for race, socioeconomic status, and/or specific comorbidities, recruitment would have to recruit populations often underrepresented in clinical trials.

### Ethical Issues

There should be no ethical issues in conducting subgroup analyses.

## Observational Studies

### Value of Study Design

Cohort studies with large sample sizes and diverse populations are suitable to analysis. As a first step, they may serve to compare characteristics of individuals who use or adhere to SMBP. As a second step, candidate predictor variables including sex, age, race/ethnicity, socioeconomic status, disease characteristics, and CVD risk factors, as well as attitudes towards participation in disease management, may be examined as predictors for surrogate and clinical outcomes. Such a cohort could easily allow for multivariable regression analyses that could test multiple potential

subgroup characteristics. However, any such analysis would be subject to spurious associations (false positive results) and should be considered to be hypothesis-generating only.

### Resource Use, Size, and Duration

Use of existing observational data substantially reduces resource use and increases feasibility. Conducting prospective observational studies requires more resources.

### Ability To Recruit

Exploration of subgroup effects across a wide range of characteristics requires an effort to identify and include a heterogeneous population.

### Ethical Issues

There should be no ethical barriers to the analysis of existing databases or to conducting prospective trials in the investigation of this evidence gap.

## Predictive Modeling of Existing Individual Patient Data From RCTs or Observational Cohort Studies

### Value of Study Design

Applying the results of clinical trials to individual patients can be problematic due to the wide variety of possible patient characteristics, and the misapplication of results to specific subgroups.[6] Therefore, when an effect modifier can be captured in a continuous score (as in the Framingham risk score for cardiovascular disease), sample size requirements can be lowered and different thresholds explored. Along with scores for disease severity or risk, predictive scores that capture likelihood of adherence with SMBP or likelihood to achieve BP control. If such scores can be validated to differentiate those likely to use SMBP or achieve BP control and interact with outcomes, they may be used in re-analyses of individual patient trial data to explore the heterogeneity of treatment effects. Development and validation of predictive models in future RCTs would allow exploration of treatment heterogeneity, thus obviating the problem of multiple comparisons for subgroup analyses.

### Resource Use, Size, and Duration

Resource use for the analysis of existing data is relatively low. Additional data collection may be needed to develop measures that capture self-reported attitudes towards SMBP, or adherence with SMBP, along with the necessary predictors to explore in modeling.

### Ability To Recruit

Exploration of a predictor for adherence requires inclusion of individuals with clinical diversity including those with lower affinity or ability to participate in a research study.

### Ethical Issues

There should be no ethical issues involved in reanalyzing existing study data.

# High-Priority Future Research Needs Topic 3. What Is the Best Prescription or Protocol for SMBP? How Do Different Prescriptions for SMBP Compare Regarding Acceptance by Patients, Adherence With SMBP, and Effect on BP Control?

## Background

The CER on SMBP indicated a wide variability in protocols and prescriptions for SMBP across trials. This highlights a fundamental uncertainty regarding how frequently and at what times BP should be measured, and how reading should be aggregated within or across measurement episodes. A recent consensus statement recommends a prescription for how to implement SMBP measurements. To provide adequate data for making clinical decisions, it recommends taking 2 to 3 BP readings per measurement episode, and measuring twice daily, in the morning and at night, over a period of 1 week to obtain a total of at least 12 readings per week.[7] Current guideline recommendations also specify that BP should be measured in a standardized environment, with the patient resting in the seated position, but do not mention how to time measurements in relation to with food intake, exercise, coffee, alcohol.[8,9] However, there is no specific guidance on how to adjust measurement frequency based on how well or for how long BP has been controlled.

The stakeholder panel agreed that patients needed evidence-based guidance on how and when to take measurements. There are a large number of possible variations, and variability in the circadian rhythms or lifestyles of patients further requires customization. In narrowing down options of different measurement approaches, convenience and acceptability to patients, as well as value of information derived from the measurements, must be taken into account.

## Proposed Study Designs

### Randomized Controlled Trial

#### Value of Study Design

The ideal study would compare different prescriptions and approaches to aggregating readings and examine their effect on adherence to SMBP and BP control. Measuring adherence to SMBP requires standardization for the SMBP frequency prescribed. However, an RCT could compare only a small number of specific SMBP prescriptions or protocols, potentially limiting the applicability of any trial. To be of value, the different SMBP protocols would have to be easily replicable by providers and patients, and preferably should be protocols that are already in common use.

#### Resource Use, Size, and Duration

Resource use depends on the number of comparisons. Any trial would have the same issues regarding required large sample sizes discussed for Topic 1.

#### Ability To Recruit

There should be no barriers to recruitment for RCTs addressing this evidence gap.

### Ethical Issues

There should be no ethical barriers in using RCTs to investigate this evidence gap.

## Observational Studies

### Value of Study Design

The issues regarding the value of observational studies to address this topic would be very similar to those discussed for Topic 1. Observational studies can be used to explore the effect of using different prescriptions and approaches to aggregating readings. Accurate ascertainment of measurement exposure may be challenging. It may have to be evaluated in real time, for example via electronic transmission or storage, rather than retrospectively due to recall bias.

### Resource Use, Size, and Duration

Resource use would be less than in conducting an RCT.

### Ability To Recruit

There should be no barriers to recruitment for observational studies addressing this evidence gap.

### Ethical Issues

There should be no ethical barriers in using observational studies to investigate this evidence gap.

# High-Priority Future Research Needs Topic 4. What Is the Role of Additional Support? What Particular Components of Additional Support Should Be Further Evaluated?

## Background

The SMBP CER included studies examining SMBP in combination with many forms of additional support. These additional support modalities include education, counseling by a clinician, telemedicine with automatic reminders, electronic data transmission, and integration with medication management. In looking across studies that compared SMBP alone against usual care, and studies that compared SMBP with additional support against usual care, the findings of the CER appeared to indicate that additional support may be synergistic with SMBP in lowering BP. However, it was unclear which specific component of additional support is most synergistic with SMBP. Recent systematic reviews of trials using telemedicine along with SMBP showed greater BP effects when compared with those reported for SMBP with a mix of additional support in the SMBP CER.[10,11]

Due to the variety in modalities, comparative studies examining every unique combination of SMBP and additional support are not feasible. We specifically asked our stakeholder panel to identify promising types of additional support for future study. The stakeholder panel expressed interest in researching how SMBP may be integrated with electronic health care systems. In addition, the panel was interested in exploring the effectiveness of different means of data transmission as well as feedback to the patient by devices or providers. Furthermore, there was discussion about the merits of telemedicine versus low resource modalities that can be used by patients with a low level of technical literacy.

# Proposed Study Designs

## Expert Panel

### Value of Study Design

We suggest that prior to conducting new research studies on additional support, an expert panel be convened to determine what specific additional support features appear most promising to explore in future research. In addition to representatives from all stakeholder categories, this panel should specifically include pharmacists, experts in telemedicine and bioinformatics, and authorities in adherence and chronic disease management. The main drawback to this approach would be that stakeholder opinion, rather than evidence per se would dictate the choice of additional support modalities. However, given the resources that would be required to investigate all possible additional support modalities, this tradeoff is likely to be reasonable.

### Resource Use, Size, and Duration

Using an expert panel to identify promising combinations of additional support for future study would be more efficient than large trials comparing many different types of additional support, which would consume a large amount of resources.

### Ability To Recruit

There should be little difficulty recruiting relevant stakeholders.

### Ethical Issues

There should be no ethical issues in using an expert panel to investigate this evidence gap.

## High-Priority Future Research Needs Topic 5. What Is the Effect of SMBP on Resource Utilization? What Is the Cost-Effectiveness of SMBP?

# Background

The SMBP CER did not include cost as an outcome of interest, nor did it address cost-effectiveness. It included resource utilization as an outcome of interest, but the evidence was of low strength. Several stakeholders expressed interest in quantifying how the potential benefits of SMBP (such as improved health outcomes, higher medication adherence, and fewer office visits) weigh against the costs. The use of SMBP requires both an upfront outlay to purchase the device, as well as further costs to the patient and provider in terms of time and resource utilization.

Part of the stakeholder discussion centered on variation in the cost-effectiveness equation for different patients. For example, SMBP monitoring may improve medication adherence for a given patient and lead to fewer office visits to discuss medication issues, but for a different patient, may increase the number of office visits if SMBP leads to more frequent medication adjustments or side effects.

The ability to address Topic 5 hinges on answering Topic 1, as longer term data on medical effectiveness and resource utilization are necessary to estimate the value of SMBP from the societal, payer, and patient perspectives. Similarly, data for Topics 2, 3, and 4 are needed to address the potential value for specific patient subgroups (Topic 2), the comparative value of different SMBP prescriptions or protocols (Topic 3), and the comparative value of additional support (Topic 4).

## Systematic Review

Evidence regarding the cost and cost-effectiveness of SMBP use was beyond the scope of the SMBP CER, and requires exploration in a separate systematic review in order to ascertain the level of existing evidence. This would entail a search of single arm or parallel arm trials using SMBP that have collected information on resource usage, as well as existing cost-effectiveness analyses (CEAs) on SMBP.

## Cost-Effectiveness Analysis

We recommend a quality-adjusted cost-benefit analysis comparing the incremental cost-effectiveness of SMBP to that of medical management in patients with hypertension. The proposed CEAs could be designed to assess the value of SMBP over longer term outcomes, as in Topic 1. The proposed analyses should be designed to address issues relevant to other high priority topic areas, such as patient subgroups (Topic 2), comparisons of the expected value of SMBP following alternative prescription strategies (Topic 3), or comparisons of the effects of SMBP with and without additional support (Topic 4).

Preference should be given to a discrete events analysis. Cost estimates should include: the cost of the device, costs of work absenteeism and presenteeism, additional clinical costs from tracking and responding to SMBP monitoring by providers, costs of antihypertensive treatments (possibly including such costs as gym memberships), and costs of clinical outcomes (e.g., hospitalization due to myocardial infarction, carotid stent placement, and premature death). Effect estimates should include: reductions in mortality and morbidity from improved BP control (including both less under- and less overtreatment), adverse events related to antihypertensive use, and changes in quality-of-life and other patient-relevant outcomes.

The proper outcome measure for such analyses is the quality-adjusted life year (QALY) gained per unit of cost, or the gain in expected life-years with adjustments for morbidity, patient-relevant outcomes, and quality of life. Future QALYs and costs should be discounted over the followup period. For any CEA of SMBP, benefit, utility, and cost estimates are best derived from clinical trial data if available, and from observational data if not. These estimates should include clinical, work-related, and quality-of-life outcomes. Probabilistic sensitivity analyses should be conducted on estimated outcome rates, utilities, and cost estimates. A societal perspective should be assumed in the main analysis. Patients' out-of-pocket costs should be included in the main analysis, and the patient perspective should be assumed in a subanalysis. In the absence of clinical data to support a CEA, sensitivity analyses should also include an assessment of how effective SMBP must be in order to be cost-effective, assuming pre-specified cost-effectiveness threshold(s).

## Value of Study Design

In addition to the expected merit of a simple CEA, sensitivity analyses may be of great value, particularly past the time horizon of 2 years, as clinical data to support a CEA, especially past this time frame, are likely to be very limited.

### Resource Use, Size, and Duration

Because a CEA can draw from previously collected data, the cost of such a study should be low and the duration to complete such an analysis relatively short. It may, however, be challenging to gather relevant data from payers and providers.

## Ability To Recruit

Not applicable.

## Ethical Issues

No new data collection is proposed; therefore, the direct risk to patients is minimal.

# Discussion

Based on the 2011 SMBP CER and our discussion with stakeholders, we identified 16 potential research areas, five of which were ranked as high priority areas of future research. The first four of these high-priority topics pertain to interrelated evidence gaps, such as the lack of longer term studies which show persistence of BP control or clinical benefit from SMBP, uncertainty regarding the populations likely to benefit from SMBP, the lack of standardization in prescription of SMBP, and uncertainty regarding the most effective modality of additional support. The fifth topic relates to the inability to assess the cost-effectiveness of SMBP, due to the deficiencies in evidence identified in the first four future research needs gaps.

The recommendations for priority topics for future research were generated based on a stakeholder-driven nomination and review process. We followed a recently developed taxonomy that was designed to aid researchers in the identification, recruitment and engagement of stakeholders. Our stakeholder panel represented a broad range of perspectives, across all major stakeholder categories identified in this taxonomy. We were able to obtain input from all panel members, and the final ranking showed a clear separation of the top priorities.

Nevertheless, the process was not without limitations. The total number of stakeholders recruited was restricted, thus limiting representation. Also, despite formal planning, the selection of stakeholders, solicitation of contributions, facilitation of discussion, and synthesis of suggestions remain, to some degree, idiosyncratic. There are as of yet no accepted standard methods by which to assess the validity of procedures to synthesize diverse stakeholder viewpoints. We believe that future methods work may be necessary to establish a formal process for validation, certification, or peer review of FRN rankings.

One additional cross-cutting methodological issue merits discussion, namely the challenge of translating BP readings obtained at home, in the clinic, or by ambulatory BP monitoring. This issue was identified as a limitation of the evidence base in the CER, and was also brought up by the stakeholder panel, but did not fall within the scope of the SMBP CER. This problem is relevant to the whole field of hypertension, including diagnosis, management and research, and is not specific to management of hypertension with SMBP.

Generally, SMBP is used in addition to BP monitoring in the health care setting, with readings from ambulatory BP monitoring also available in some patients. Thus, for an accurate assessment of BP, home, clinic, and ambulatory BP measurements must all be integrated in some comprehensive manner. The SMBP CER reported a wide variation across studies in the targets set for home and clinic BP. The need to standardize the integration of BP readings across different settings and modalities, therefore, constitutes an important challenge. Standardization may not be achievable with a constant conversion factor, as different BP patterns, including diurnal variation, must also be considered.

As this question was outside of the scope of the SMBP CER, an updated systematic review of available literature (across the spectrum of hypertension diagnosis and management) is the first step to better understand the existing evidence base. Addressing this gap would require review of observational data comparing concordance of BP levels obtained by SMBP, clinic BP, and ambulatory BP monitoring—possibly aggregated in different ways—as well as the study of risk relationships between BP readings with consideration of different BP patterns and clinical outcomes. In addition, comparative studies may be needed to compare the effectiveness of managing BP according to different approaches to integrate BP readings. Once it is possible to convert between home BP, clinic BP, and ambulatory BP readings, BP can be assessed comprehensively across different settings, and consistent targets can be set.

# Conclusions

This report identifies five high-priority future research needs to study SMBP, which were identified by a stakeholder panel. These are as follows:

1. What are the effects of SMBP on BP, medication adherence rates, satisfaction, and clinical event outcomes, after longer followup periods 2 to5 years or longer?
2. Which patients may be more likely to benefit from using SMBP?
3. What is the best prescription or protocol for SMBP (when, how often, and how frequently)? How do different prescriptions for SMBP compare regarding acceptance by patients, adherence with SMBP, and effect on BP control?
4. What is the role of additional support? What particular components of additional support should be further evaluated?
5. What is the effect of SMBP on resource utilization? What is the cost-effectiveness of SMBP?

In summary, with regards to addressing these gaps: Longer term randomized controlled trials that examine SMBP effects on BP control and resource utilization are needed; the impact of SMBP on CVD outcomes may be gleaned from embedding SMBP in other CVD outcome trials; the exploration of treatment heterogeneity may identify those groups more likely to benefit from SMPB. When, how often, and how frequently to perform SMBP, and what additional support to employ, should be further refined. Finally, filling these evidence gaps will inform future modeling of cost-effectiveness.

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# Abbreviations

| | |
|---|---|
| AHRQ | Agency for Healthcare Research and Quality |
| BP | Blood pressure |
| CEA | Cost-effectiveness analysis |
| CER | Comparative Effectiveness Review |
| CVD | Cardiovascular disease |
| DBP | Diastolic blood pressure |
| EHC | Effective Health Care |
| FRN | Future Research Needs |
| HOPE Study | Heart Outcomes Prevention Evaluation Study |
| PICOD | Population, intervention, comparator, outcome, study design |
| QALY | Quality-adjusted life year |
| RCT | Randomized controlled trial |
| SBP | Systolic blood pressure |
| SMBP | Self-measured blood pressure monitoring |
| VA | Veterans Administration |

# Appendix A. Effective Health Care Program Selection Criteria Literature Search Strategy Yield of Ongoing Studies

## Effective Health Care Program Selection Criteria

**Appropriateness:**

- Represents a health care drug, intervention, device, technology or health care system/setting available (or soon to be available) in the United States.
- Relevant to 1013 enrollees (Medicare, Medicaid, S-CHIP, other federal health care programs.
- Represents one of the priority conditions designated by the U.S. Department of Health and Human Services (HHS).

**Importance:**

- Represents a significant disease burden, large proportion or priority population.
- Is of high public interest; affects health care decision-making, outcomes, or costs for a large proportion of the U.S. population or for a priority population in particular.
- Was nominated/strongly supported by one or more stakeholder groups.
- Represents important uncertainty for decisionmakers.
- Incorporates issues around both clinical benefits and potential clinical harms.
- Represents important variation in clinical care, or controversy in what constitutes appropriate clinical care.
- Represent high costs to consumers, patients, health care systems or payers; due to common use, high unit costs, or high associated costs.

**Desirability of New Research/Duplication:**

- Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available evidence.)

**Feasibility:**

- Effectively uses existing research and knowledge by considering adequacy of research for conducting research, and newly available evidence

**Potential Impact:**

- Potential for significant health impact, significant economic impact, potential change, potential risk from inaction, addressing inequities and vulnerable populations, and/or addressing a topic with clear implications for resolving important dilemmas in health and health care decisions made by one or more stakeholder groups.

# Literature Search Strategy

**Databases:** Ovid MEDLINE, MEDLINE(R) In-Process, Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register (CCTR)

**Search conducted:** 1/13/2012

**Table A1. Literature search terms organize**

| # | Searches | Targeting |
|---|---|---|
| 1 | exp Blood Pressure Monitoring, Ambulatory/ | SMBP |
| 2 | exp Blood Pressure Monitors/ | |
| 3 | exp Blood Pressure/ | |
| 4 | exp hypertension/ | |
| 5 | exp Self Care/ | |
| 6 | (3 or 4) and 5 | |
| 7 | ((blood pressure or hypertens$) and self and (measure$ or monitor$ or care or manage$)).mp. | |
| **8** | **1 or 2 or 6 or 7** | |
| 9 | randomized controlled trial.pt. | Comparative Studies (KQ 1-3) |
| 10 | controlled clinical trial.pt. | |
| 11 | randomized controlled trials/ | |
| 12 | Random Allocation/ | |
| 13 | Double-blind Method/ | |
| 14 | Single-Blind Method/ | |
| 15 | clinical trial.pt. | |
| 16 | Clinical Trials.mp. or exp Clinical Trials/ | |
| 17 | (clinic$ adj25 trial$).tw. | |
| 18 | ((singl$ or doubl$ or trebl$ or tripl$) adj (mask$ or blind$)).tw. | |
| 19 | Placebos/ | |
| 20 | placebo$.tw. | |
| 21 | random$.tw. | |
| 22 | trial$.tw. | |
| 23 | (randomized control trial or clinical control trial).sd. | |
| 24 | (latin adj square).tw. | |
| 25 | Comparative Study.tw. or Comparative Study.pt. | |
| 26 | exp Evaluation studies/ | |
| 27 | Follow-Up Studies/ | |
| 28 | Prospective Studies/ | |
| 29 | (control$ or prospectiv$ or volunteer$).tw. | |
| 30 | Cross-Over Studies/ | |
| **31** | **or/9-30** | |
| 32 | exp cohort studies/ or exp prospective studies/ or exp retrospective studies/ or exp epidemiologic studies/ or exp case-control studies/ | Cohorts (KQ 4) |
| 33 | (cohort or retrospective or prospective or longitudinal or observational or follow-up or followup or registry).af. | |
| 34 | case-control.af. or (case adj10 control).tw. | |
| 35 | ep.fs. | |
| **36** | **32 or 33 or 34 or 35** | |
| **37** | **8 and (31 or 36)** | Limits |
| 38 | limit 37 to humans [Limit not valid in CDSR,CCTR; records were retained] | |
| 39 | limit 38 to yr="1888 - 2000" | |
| 40 | remove duplicates from 39 | |
| 41 | limit 37 to yr="2001-2008" | |
| 42 | remove duplicates from 41 | |
| 43 | limit 37 to yr="2009-current" | |

| # | Searches | Targeting |
|---|---|---|
| 44 | remove duplicates from 43 | |
| **45** | **or/40, 42, 44** | |
| **46** | (home adj20 blood pressure).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier] | Added Terms |
| **47** | or/9-45 | |
| **48** | 46 and 47 | |
| **49** | (exp telemedicine/ or exp self-examination/) and (exp Blood pressure/ or exp Hypertension/) | |
| **50** | 47 and 49 | |
| **51** | **45 or 48 or 50** | |
| **52** | (201107$ or 201108$ or 201109$ or 20111$ or 2012$).ed. | Date |
| **53** | **51 and 52** | Final |

# Yield of Ongoing Studies

**Table A2. Ongoing research on SMBP identified through ClinicalTrials.gov**

| NCT ID | Title | Recruitment | Interventions | Enrollment |
|---|---|---|---|---|
| NCT00781365 | Home Blood Pressure Telemonitoring and Case Management to Control Hypertension | Recruiting | *Other:* Telemonitors and pharmacy management | 450 |
| NCT01145742 | Controlling Hypertension in Diabetes- Feasibility Study | Completed | *Behavioral:* home health/primary care collaboration | 56 |
| NCT01300338 | Blood Pressure Telemonitoring and Goal Blood Pressure in Diabetes | Not yet recruiting | *Device:* blood pressure with telemetry<br>*Device:* Home blood pressure monitor without telemetry | 50 |
| NCT01035554 | Behavioral Study to Control Blood Pressure | Recruiting | *Other:* Self-Paced Programmed Instruction (SPPI)<br>*Device:* Home Blood Pressure Monitor<br>*Other:* Usual Care<br>*Other:* Printed Materials | 250 |
| NCT00662753 | A Study in the Use of Home Blood Pressure Monitoring and Telephone Follow-up to Control Blood Pressure | Recruiting | *Device:* Home blood pressure monitor<br>*Other:* monitor and phone call | 150 |
| NCT00334724 | Home Blood Pressure-guided Antihypertensive Intervention for Elderly (HBP-GUIDE) Study | Completed | *Procedure:* Home blood pressure measurement<br>*Procedure:* Office blood pressure measurement | 200 |
| NCT01123577 | Evaluation of Integrating Self Blood Pressure Monitoring Into Urban Primary Care Practices | Enrolling by invitation | *Other:* Home Blood Pressure Monitor Group<br>*Other:* Control Group | 996 |
| NCT00123058 | Comparison of Two Programs to Improve Blood Pressure Treatment Adherence | Active, not recruiting | *Behavioral:* Health Education Program<br>*Device:* BP Monitor | 636 |

| NCT ID | Title | Recruitment | Interventions | Enrollment |
|---|---|---|---|---|
| NCT00514800 | Home Blood Pressure Monitoring Trial | Recruiting | *Behavioral:* Intervention - a validated home BP monitor and support from the specialist nurse<br>*Behavioral:* Control - usual care (BP monitoring by their practice) | 360 |
| NCT00211666 | Improving Hypertension Control in East and Central Harlem | Completed | *Behavioral:* Nurse management, home blood pressure monitors, and a chronic disease self management course. | 480 |
| NCT00968786 | Home Monitoring in the Management of Hypertension and Diabetes Mellitus | Enrolling by invitation | *Device:* Home monitoring | 100 |
| NCT00299468 | The Effect of the Patient Activation Measure on Chronic Care | Completed | *Behavioral:* Patient Activation Measure Intervention Package | 283 |
| NCT01155050 | Louisiana State University Health Care Services Division (LSUHSCD) Tele-Health Projects: Weight Loss in Chronic Disease Patient Population | Completed | *Device:* Tele-health Home Monitoring<br>*Behavioral:* TrestleTree Telephone Coaching<br>*Device:* Tele-health Home Monitoring Plus Trestle Telephone Coaching | 240 |
| NCT01282957 | Way to Health, Healthy Measures | Enrolling by invitation | *Behavioral:* Financial Incentive Group I<br>*Behavioral:* Financial Incentive Group II | 60 |
| NCT01233193 | The Effect of Pharmacist Intervention on Blood Pressure Control | Active, not recruiting | *Behavioral:* Health education, Home blood pressure monitoring | 140 |
| NCT00802152 | Using Health Information Technology (HIT) to Improve Ambulatory Chronic Disease Care: Smart Device Substudy | Completed | *Device:* In-home "smart" diagnostic devices | 108 |
| NCT01167920 | Virtual Hypertension Clinic | Active, not recruiting | *Other:* Virtual Hypertension Clinic | 74 |
| NCT00233220 | Blood Pressure Control in African Americans | Recruiting | *Behavioral:* Multicomponent, multi-level intervention targeted at physicians and patients<br>*Behavioral:* Usual Care | 990 |
| NCT00224861 | Hypertension Telemanagement in African Americans | Completed | *Behavioral*: Self-Management<br>*Behavioral*: Adherence | nd |
| NCT01013857 | Treating to Target for Patients With Hypertension | Active, not recruiting | *Behavioral*: Health coaching<br>*Behavioral*: Health coaching plus home titration | 240 |
| NCT01335984 | Effects of Telemonitoring and Telemedicine Service for Hypertensive Care (Smart-HTN) | Recruiting | *Procedure:* Telemonitoring\|Procedure: Telemonitoring & Telemedicine\|Other: Usual Care | 564 |
| NCT01439256 | Telehealth & Remote Measurement Technologies to Improve Medication Adherence in Hypertension | Not yet recruiting | *Device:* Electronic pill tray direct reporting to physician (Telephone-Linked Care: Hypertension 2-Electronic Pill Tray)<br>*Behavioral:* Patient self reporting of medication adherence | 258 |
| NCT01504022 | Web Based Interactive Treatment and Self- | Recruiting | *Other: Telecare,* selfmonitoring, lifestyl behaviour | 300 |

| NCT ID | Title | Recruitment | Interventions | Enrollment |
|---|---|---|---|---|
| | monitoring in Hypertension (WISH) | | | |
| NCT01416766 | CONtrolling Disease Using Inexpensive IT - Hypertension in Diabetes (CONDUIT-HID) | Recruiting | *Other:* CONDUIT self-monitoring-nurse-primary care provider (PCP) feedback loop | 400 |
| NCT01510301 | Mobile Phone in Hypertension Management | Not yet recruiting | *Device:* Mobile phone-based self-report system, electronic Patient-Reported Outcomes Measure (e-PROM) | 50 |
| NCT01387945 | Pilot Study of Home Blood Pressure Control Program (eBPcontrol) | Recruiting | *Behavioral:* HBPM+website+patient navigator | 30 |
| NCT01402453 | Monetary Incentives and Intrinsic Motivation to Sustain Hypertension Control | Not yet recruiting | *Behavioral:* Monetary Incentives\|Behavioral: Intrinsic Motivation | 262 |
| NCT01484782 | Developing Accessible Telehealth Programs for Hypertensive Patients in Latin America | Active, not recruiting | *Behavioral:* Interactive Voice Response (IVR) automated calls | 200 |
| NCT01390272 | Titrated Disease Management for Patients With Hypertension (TDM) | Not yet recruiting | *Behavioral:* Booster/ low resource<br>*Behavioral:* Booster/ low resource\|Behavioral: Medium/Level 1 resource intensity<br>*Behavioral:* High/Level 2 resource intensity | 400 |
| NCT01425515 | Improving Care for Patients With High Blood Pressure | Not yet recruiting | *Behavioral:* Complex quality improvement intervention | 600 |

**Abbreviations:** BP=blood pressure; CBP=clinic blood pressure; HBP=home blood pressure; HBPM=home blood pressure monitoring; nd=no data.

We used the terms [blood pressure OR hypertension] as a "condition" search string combined with the following search terms for interventions [(home OR ambulatory OR self) AND (monitor* OR telemonitoring OR measure* OR manage*)]