

PRedicting Out-of-Office Blood Pressure (PROOF-BP) in the clinic for the diagnosis of hypertension in Primary Care: an economic evaluation

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Abstract

Background: Clinical guidelines in the UK recommend that individuals with suspected hypertension should have ambulatory blood pressure monitoring (ABPM) for confirmatory diagnosis. This approach excludes people with masked hypertension who may benefit from treatment and results in some patients with white-coat hypertension needlessly incurring ABPM. The Predicting Out-of-Office Blood Pressure (PROOF-BP) risk algorithm predicts masked and white coat hypertension based on patient characteristics and clinic blood pressure. This study assessed the cost-effectiveness of using this clinical decision rule in the diagnosis of hypertension in primary care.

Methods: A Markov cost-utility cohort model was developed to compared different diagnostic strategies for hypertensive in a Primary care setting. The model adopted a lifetime horizon with a three month time cycle, taking a UK National Health Service/Personal Social Services perspective. BP diagnostic comparators comprised Clinical Blood Pressure Monitoring, Home Blood Pressure Monitoring, PROOF-BP algorithm and with ABPM as reference. Results were presented in terms of cost per Quality Adjusted Life Year (QALY) gained compared to next best alternative comparator.

Findings: The PROOF-BP risk algorithm was cost-effective in all patients with clinic BP $\geq 120/70$ mmHg for all age and gender groups if healthcare providers were willing to pay up to £20,000/QALY gained, when compared with ABPM only for patients with a clinic BP of $\geq 140/90$ mmHg. Modelling suggested that use of the PROOF-BP risk algorithm would result in total of 14,623 additional people being detected with hypertension per 100,000 population and 9,548 additional cardiovascular events prevented compared to current recommendations. Deterministic and probabilistic sensitivity analyses supported the base case findings.

Conclusions: The PROOF-BP risk algorithm appears to be cost-effective compared to the conventional BP diagnostic options in Primary Care and would lead to reduced death and disability.

Introduction

Hypertension is one of the most important modifiable risk factors for cardiovascular morbidity and mortality.¹ Accurate measurement of blood pressure (BP) is essential to ensure that treatment is targeted appropriately. In the UK, the National Institute for Health and Care Excellence (NICE) published guidelines on the diagnosis of hypertension in Primary Care in 2011.² These recommended that all individuals with persistently high BP readings in the clinic should be referred for ambulatory blood pressure monitoring (ABPM) to confirm a diagnosis of hypertension, before initiating treatment. This recommendation was based on a Markov model-based cost-utility analysis comparing the different BP monitoring methods (clinic [CBPM], self-monitoring at home [HBPM] and ABPM) for diagnosing hypertension in individuals with a screening clinic BP measurement equal to or above 140/90mmHg.^{3,4} ABPM was found to be the most cost-effective option across all age and gender subgroups: despite ABPM being more expensive in terms of diagnostic costs, better targeting of treatment meant that it saved money in the long term by treating fewer individuals with white coat hypertension. Similar arguments have since been used in North America where out of office measurement has also been recommended.^{5,6}

White coat hypertension is the term used to describe when an individual has raised clinic BP ($\geq 140/90$ mmHg) but is normotensive on ABPM ($\leq 135/85$ mmHg).⁷ Individuals with white coat hypertension are considered to be at lower cardiovascular disease risk compared to individuals with sustained hypertension. Conversely, individuals with normotensive clinic BP measurements ($< 140/90$ mmHg) but hypertensive ambulatory BP measurements ($> 135/85$ mmHg) are referred to as having masked hypertension and have an increased risk of cardiovascular events which approaches that of overt hypertension.^{8,9} Individuals with potential masked hypertension were not included in the original health economics analysis for NICE guidelines as their screening clinic BP measurement would have been less than 140/90mmHg.

The Predicting Out-of-Office Blood Pressure (PROOF-BP) risk algorithm calculates an adjusted clinic BP based on individuals characteristics (age, body mass index, past diagnosis of hypertension and/or cardiovascular disease, and antihypertensive prescription), to guide utilisation of ABPM. It has been shown to improve the accuracy of diagnosis of hypertension without appreciably increasing use of ABPM.¹⁰ This study aimed to assess the cost-effectiveness of a strategy of targeted use of ABPM using the PROOF-BP risk algorithm in the diagnosis of hypertension in a primary care setting.

Methods

The full methods of the original model undertaken for the NICE guidelines have been described elsewhere.^{3,4} The original model was developed in Microsoft Excel to assess the cost-effectiveness of each BP monitoring method (CBPM, HBPM & ABPM) with suspected hypertension (clinic BP $\geq 140/90$ mmHg). This model was modified by adding the PROOF-BP risk algorithm as a comparator and expanding the base case model entry population to men and women aged 40 to 75 years with a screening clinic BP of 130/80mmHg and above.

Model comparators

The model compared four methods of BP monitoring in the diagnosis of hypertension. Those approaches examined in the original model - CBPM, HBPM and ABPM - were compared to the new PROOF-BP diagnostic strategy (figure 1):

- If the individual had an adjusted clinic BP $< 130/80$ mmHg, no further action was required and they were measured again at the next check-up period

- If the individual had an adjusted clinic BP between 130/80-144/89mmHg, they received ABPM for confirmatory diagnosis
- If the individual had an adjusted clinic BP $\geq 145/90$ mmHg, treatment was offered without confirmatory ABPM diagnosis.

Study population

The patient population mix by clinic BP and adjusted clinic BP (see table 1) was taken from the Health Survey for England¹¹ and the original PROOF-BP paper.¹⁰ In the original model, the entry population was individuals suspected of hypertension based on a clinic BP measurement of 140/90mmHg and above. The new model population was broadened to include individuals with a clinic BP measurement of 130/80mmHg and above. Individuals were not considered for diagnosis by the CBPM, HBPM, or ABPM strategies if their screening clinic BP was less than 140/90mmHg whereas PROOF BP strategy did.

Model structure

A simplified Markov model diagram of the health states and the movements between states allowed occur in a cycle are shown in figure 2. In keeping with the original model, the model cycle length of 3 months was chosen that equalled the average length of time for a complete CBPM diagnosis.² HBPM, ABPM and the PROOF-BP risk algorithm were assumed to take one month for a complete diagnosis. In the suspected and diagnosed stages of the model, individuals could suffer a fatal or non-fatal cardiovascular event (stable angina, unstable angina, stroke, myocardial infarction [MI], and transient ischemic attack [TIA]). After suffering a non-fatal cardiovascular event, repeat clinical events were not modelled and individuals remained in a post-cardiovascular event state until they die.

In the model, individuals could become hypertensive over time, so false positives could become true positives and true negatives could become false negatives. For model simplification purposes, it was assumed individuals cannot become hypertensive during the diagnostic cycle. Individuals not diagnosed with hypertension (true negatives and false negatives) were assumed to have a BP check-up with CBPM every 5 years. In common with the original model, a failure rate was incorporated into ABPM; if ABPM failed, individuals were assumed to be put on HBPM. In the PROOF-BP risk algorithm strategy, if individuals had a screening clinic BP of less than 140/90mmHg and ABPM failed, it was assumed they remained undiagnosed (as in the HBPM strategy where these individuals were not considered for hypertension diagnosis) and their BP was rechecked every five years.

Clinical model parameters are detailed in table 2. Correct diagnosis of hypertension depended on the sensitivity and specificity of the test strategy used. Test characteristics for CBPM and HBPM were taken from a meta-analysis¹² with ABPM assumed to be the reference standard (100% sensitivity & 100% specificity). The test characteristics of the PROOF-BP risk algorithm with respect to their clinic BP and adjusted clinic BP categories are shown in Appendix table 1.

Model outcomes

Risk of coronary heart disease and stroke were calculated using the Framingham risk equations along with general population prevalence risk factors in the Health Survey for England.¹¹ Non-cardiovascular mortality was based on UK life tables¹³ subtracted by the proportion of cardiovascular related deaths.¹⁴ Individuals with masked hypertensives were assumed to have the same higher risk of cardiovascular events as sustained hypertensives. A hypertensive diagnosis put individuals on antihypertensive drug therapy and

true hypertensive individuals received benefit in terms of cardiovascular risk reduction from treatment. The risk reduction from antihypertensive treatment depended on a person's age and gender.¹⁵ True normotensive individuals were assumed to receive no risk reduction from treatment. The proportion of individuals on different antihypertensive drug classes was based on treatment guidelines.²

Quality of life and cost data are shown in table 4. Baseline gender and age specific general population quality of life (utility) weights were taken from the Health Survey of England¹⁶ and applied to the cohorts. In the base case, Individuals were assumed not to suffer any quality of life reductions (disutility) as a result of antihypertensive treatment.

Model costs

Costs were updated where necessary to 2013-2014 prices using the Health & Community health Services (HCHS) index.¹⁷ Resource usage by diagnostic method and device usage assumptions were in line with the original model.⁴ The costs and consequences of individuals with an earlier diagnosis and treatment in the HBPM, ABPM and PROOF-BP compared to CBPM were taken into account. A more detailed description of costs is given in the extended methods in the Appendix.

Analysis

Results were presented as the total costs and effects of each diagnostic strategy. Effectiveness was measured in quality adjusted life years (QALYs). Total costs and outcomes of each strategy were ordered by increasing cost. Incremental cost-effectiveness ratios (ICERs) were calculated from the difference in costs and effects between two options. Cost-effectiveness was assessed in relation to the NICE lower threshold of £20,000 per QALY.¹⁸ Options that were more costly and less effective (dominated) were excluded from consideration, as were those options where extended dominance was present. Extended dominance occurred when an option was dominated compared to a combination of two other strategies. The analysis adopted a lifetime horizon (60 years) and all costs and outcomes were discounted at the standard 3.5% rate.¹⁹ Costs and outcomes were considered from a UK National Health Service (NHS) /Personal Social Services (PSS) perspective.

Sensitivity analyses

Uncertainty was explored via sensitivity analyses. Additional model runs were undertaken to determine the impact of changing key parameters on the model results. The following univariate sensitivity analysis was undertaken on all cohorts: the model entry was expanded to a screening clinic BP $\geq 120/70$ mmHg population (see Appendix Table 2 for cohort split) and the model entry was then restricted to a screening clinic BP $\geq 140/90$ mmHg population (see Appendix Table 3). In line with the original model, sensitivity analysis for Males aged 60 was undertaken under the following scenarios:

- (i) A treatment disutility of 1% was assumed. This was equivalent to a quarter of the individuals suffering a quality of life reduction of 4% and everyone else suffering no ill effects of treatment.
- (ii) A treatment disutility of 2% was assumed. This was equivalent to a quarter of the individuals suffering a quality of life reduction of 8% and everyone else suffering no ill effects of treatment;
- (iii) Antihypertensive treatment risk reduction was based on half doses of medication;
- (iv) Higher hypertension treatment costs;
- (v) ABPM strategy included a base case screening clinic BP $\geq 130/80$ mmHg population;
- (vi) The prevalence of masked hypertension was increased and decreased by 25% respectively;
- (vii) Antihypertensive treatment risk reduction for masked hypertension was based on half doses;

- (viii) Antihypertensive treatment risk reduction for all treated people
- (ix) Antihypertensive treatment risk reduction assumed to be same as intensive treatment from the SPRINT trial²⁰

Where available, data were inputted into the model as distributions in order to fully incorporate the uncertainty around parameter values for a probabilistic sensitivity analysis (PSA). The PSA ran for 1000 iterations across all cohorts for the three different model entries respectively (screening clinic BP of $\geq 130/80$ mmHg, $\geq 120/70$ mmHg, and $\geq 140/90$ mmHg respectively). The number of times a strategy was the most cost-effective diagnostic option for each simulation (i.e. produced the highest net benefit) was expressed as a percentage for all cohorts. Positive count data from the PROOF-BP risk algorithm test characteristics (True positives, True negatives, False positives, False negatives) formed the parameters for a Dirichlet distribution (see Appendix table 2).

Results

In the base-case analysis, using the PROOF-BP risk algorithm was cost-effective in all cohorts compared to the ABPM strategy and dominated the other comparators (saved costs and increased QALYs) (table 4). For example, in a cohort of 1000 males aged 60, with a screening BP of 130/80mmHg or above, using the PROOF-BP risk algorithm would result in 134 more true hypertension cases detected, 9 more CVD events prevented, 48 QALYs gained and increased total costs by £54,000 compared to ABPM.

The PROOF-BP risk algorithm was also cost-effective when the model entry was widened to individuals with a screening BP $\geq 120/70$ mmHg (Appendix table 4). The PSA results also indicated for the base-case and $\geq 120/70$ mmHg model populations that PROOF-BP was the most cost-effective option (100% probability of being cost-effective at a £20,000 threshold). When the screening BP was restricted to individuals with a screening BP $\geq 140/90$ mmHg (Appendix Table 5), the most cost-effective option was dependant on the underlying population: in the 40 year female old cohort, ABPM was more cost-effective compared to PROOF-BP whereas the opposite was true for women aged 60 and over. Univariate sensitivity analysis (Table 5) demonstrated that the model was sensitive to the assumption of quality of life reduction from treatment. For example, if a quarter of the individuals suffered a quality of life reduction of 8% and everyone else suffered no ill effects of treatment, PROOF-BP was dominated (more costly, less health gain) by the ABPM strategy. Use of the PROOF-BP risk algorithm was also cost-effective compared to a strategy of utilising ABPM in all individuals with a screening BP of $\geq 130/80$ mmHg, which was cheaper, but resulted in less QALYs gained.

Discussion

This represents the first economic evaluation to examine the cost-effectiveness of strategies to diagnose hypertension, which includes the consideration of individuals with potential masked hypertension. Targeted use of ABPM, using the PROOF-BP risk algorithm was the most cost-effective diagnostic option for individuals presenting with a screening clinic BP of 130/80mmHg or above. The increased quality of life arising from use of the PROOF-BP risk algorithm was mainly due to identification and treatment of masked hypertension which was ignored by the other strategies. The results were robust to several sensitivity analyses examining treatment disutility caused by side effects to medication, adjusting the masked hypertension prevalence, higher treatment costs and increased use of ABPM in individuals with apparently normal screening BPs ($<140/90$ mmHg). The findings suggest that a strategy of targeted use of ABPM in individuals with high or normal screening BP is likely to be cost-effective at a willingness to pay of £20,000 per QALY gained, and result in increased quality of life for individuals with hypertension.

Strengths and weaknesses

The major strength of this work is that it represents a direct update of the cost-effectiveness model developed by NICE which currently underpins the use of ABPM in routine clinical practice in the UK. This means that this new strategy of targeted use of ABPM using the PROOF-BP risk algorithm can be directly compared to the current gold standard approach for diagnosis of hypertension. A large number of sensitivity analyses were considered to test the robustness of assumptions in the model and consistently supported the base case findings.

One limitation of the model is that it assumed that individuals derived the same benefit from treatment of masked hypertension as applies to those with sustained hypertension. Although this has been alluded to in a number of observational studies,^{21,22} there is yet to be a randomised trial of treatment versus no treatment in individuals with masked hypertension. One previous study did examine the efficacy of treatment based on ABPM rather than clinic readings and reported similar levels of BP control at follow-up but less treatment in the intervention arm.²³ However, this study did not include any individuals with masked hypertension. There is a trial of treatment of masked hypertension currently underway in the US,²⁴ however this plans to enrol individuals with existing hypertension who are apparently controlled according to clinic BP so the findings will not be directly relevant in the diagnostic scenario examined here. Until a randomised clinical trial of treatment in drug naïve individuals with masked hypertension is conducted, the true benefits of treatment will remain unknown.

The present study assumed a prevalence of masked hypertension in the screening population of 15%. In fact, due to the difficulty recognising masked hypertension in routine clinical practice, the true prevalence is unclear, with estimates ranging from 8.5 to 16.6%.^{21,25} We examined the impact of this in a sensitivity analysis and the PROOF-BP risk algorithm remained cost-effective.

As with the previous model developed for NICE,⁴ the present analysis assumed that there was no benefit from treatment in individuals who were truly normotensive (i.e. individuals with sustained normotension or white coat hypertension). This assumption has been challenged by the meta-analysis by Law and colleagues¹⁵ and more recently the SPRINT trial²⁶ which supports the prescription of treatment to those with BP levels of 130/80 mmHg and above. However, SPRINT was a trial of individuals at high risk and less than 10% were treatment naïve at baseline, limiting the applicability of those results to a modelled population of undiagnosed individuals undergoing screening for hypertension.

Findings in the context of existing literature

There are a number of economic analyses examining the cost-effectiveness and cost benefit of different BP monitoring strategies in the diagnosis of hypertension. Previous studies from Australia, USA and Europe have compared ABPM with CBPM²⁷⁻³⁰ and further studies from Japan and the USA have compared HBPM with CBPM.^{31,32} The original cost-effectiveness model developed for NICE,² which formed the basis for the present analyses, was the first to compare all three strategies. All previous analyses found out-of-office monitoring to be cost-effective, but only examined individuals with a high screening BP and examined strategies which targeted the use of ABPM or HBPM monitoring at those most likely to benefit. A recent analysis compared the cost-effectiveness of central BP monitoring with CBPM and found the former to be cost-effective, although they did not compare it with ABPM or HBPM.³³

The present analysis examined the cost-effectiveness of a new strategy designed to target the use of ABPM at those displaying a potential white coat or masked effect, something which has not been attempted before. Utilisation of the PROOF-BP risk algorithm was found to be cost-effective at all ages and in males

and females, primarily due to treatment of masked hypertension. Some variation by gender was observed, which may be attributable to the varying Framingham risk profile between genders: females had a lower cardiovascular risk which limited the benefits of antihypertensive treatment.

The model was most sensitive to adjustments in treatment disutility. All strategies which put more normotensive individuals on unnecessary treatment were disadvantaged when quality of life decrement penalties due to treatment side-effects were assumed. The level of treatment disutility associated with antihypertension medication is a matter of debate and may vary with age. The non-inclusion of disutility in the present analysis base-case was consistent with previous modelling which argued that where side effects exist, individuals can switch to alternative drugs.⁴ In addition, most drug trials, including the recent SPRINT trial, suggest that the prevalence of side effects with antihypertensive treatment was relatively low, even with intensive treatment.²⁶

Implications for clinical practice

The present analyses suggest that using the PROOF-BP risk algorithm was likely to result in slightly higher healthcare costs (due to increased utilisation of treatment in masked hypertensives) but improved quality of life in individuals with hypertension. The PROOF-BP risk algorithm is not currently utilised in routine clinical practice but implementation would be possible with relative ease: automated blood pressure monitors which take up to three consecutive readings (required for the decision tool) are now cheap and routinely available and the prediction algorithm is already available as an online calculator and could easily be incorporated into general practice computer systems or built into smartphones linked to blood pressure monitors. This strategy has the potential for individuals with apparently normal clinic blood pressure to end up on treatment (if they have masked hypertension), which represents a notable shift from the current practice model and therefore would require some 'buy in' from both patients and practitioners. Presenting the evidence and treatment options clearly, perhaps through formal patient and practitioner education may be required, in much the same way that it accompanied the adoption of ABPM into routine Primary Care.

Conclusions

This is the first analysis to examine the cost-effectiveness of targeted use of ABPM in the diagnosis of hypertension. The PROOF-BP risk algorithm appears to be cost-effective compared to the conventional BP diagnostic options in Primary Care and would lead to reduced death and disability. Limitations of the model include the lack of data on the assumed efficacy of antihypertensive treatment for masked hypertension and assumptions regarding the true prevalence of masked hypertension in routine clinical practice, both of which require further investigation.

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Tables

Table 1. Cohort split of 1000 patients with a clinic Blood Pressure (BP) \geq 130/80mmHg

Patients screening clinic BP by age and gender			PROOF-BP risk algorithm			
Age	Sex	Clinic BP >140/90mmHg	Clinic BP between 130/80mmHg & 140/90mmHg	Ignored (adjusted clinic BP <130/80mmHg)	Put on ABPM (adjusted clinic BP between 130/80mmHg & 144/89mmHg)	Offered Treatment (adjusted clinic BP \geq 145/90mmHg)
40	Male	586	414	29	627	344
40	Female	620	380	27	613	361
50	Male	680	320	22	587	390
50	Female	659	341	24	596	380
60	Male	763	237	17	552	431
60	Female	847	153	11	517	472
70	Male	849	151	11	516	473
70	Female	821	179	13	528	460
75	Male	895	105	7	497	495
75	Female	943	57	4	477	519

BP=blood pressure; PROOF-BP=Predicting out-of-office blood pressure; ABPM=Ambulatory blood pressure monitoring

Table 2. Clinical data inputs for the model

Clinical data for the model	Clinical data for the model	Clinical data for the model
Prevalence of true hypertension in population suspected of having hypertension*	17-64% (age and sex dependent)	Estimated with meta-analysis by Hodgkinson and colleagues ¹² and HSE 2013 ¹¹
Diagnosis inputs		
Clinic BP \geq 140/90mmHg Sensitivity	CBPM 85.6% (95% CI 81.0-89.2); HBPM 85.7% (95% CI 78.0-91.0); ABPM 100.0%; PROOF-BP 100.0%	Meta-analysis sensitivity analysis by Hodgkinson and colleagues ¹² (excluding populations with low mean blood pressure); ABPM was assumed to be reference standard with 100% sensitivity and specificity. Test characteristics taken from Sheppard and colleagues ³⁴
Clinic BP \geq 140/90mmHg Specificity	CBPM 45.9% (95% CI 33.0-59.3); HBPM 62.4% (95% CI 48.0-75.0) ABPM 100.0%; PROOF-BP 65.5%	As above
PROOF-BP Clinic BP between 130/80mmHg & 140/90mmHg Sensitivity	97.3%	Sheppard and colleagues ³⁴
PROOF-BP Clinic BP between 130/80mmHg & 140/90mmHg Specificity	96.2%	Sheppard and colleagues ³⁴
PROOF-BP Clinic BP between 120/80mmHg & 140/90mmHg Sensitivity	82.9%	Sheppard and colleagues ³⁴
Clinic BP between 120/80mmHg & 140/90mmHg Specificity	97.3%	Sheppard and colleagues ³⁴
Proportion of masked hypertension that progress to sustained hypertension by 5 years	34.9%	Trudel and colleagues ³⁵
Time until diagnosis complete	CBPM 3 months; HBPM 1 month; ABPM 1 month	Assumption based on guideline recommendations
Diagnostic device failure rate	ABPM 17%	Wood and colleagues ³⁶
Mortality and risk of cardiovascular disease		
Probability of non-cardiovascular death	Age and sex dependent	England and Wales 2011-2013 lifetables with circulatory death ^{13,14}
Probability of coronary heart disease event if truly normotensive within 10 years	0.8-14.9% (age and sex dependent)	Calculated with Framingham coronary heart disease and stroke risk equations ³⁷ and risk factor profile based on HSE 2013 ¹¹
Probability of coronary heart disease event if truly hypertensive within 10 years	1.7-22.2% (age and sex dependent)	As above
Probability of stroke event if truly normotensive within 10 years	0.3-4.8% (age and sex dependent)	As above
Probability of stroke event if truly hypertensive within 10 years	0.8-14.8% (age and sex dependent)	As above
Coronary heart disease event distribution (age and sex dependent)	MI 14.3-37.8%; unstable angina 10.4-20.9%; stable angina 37.7-62.9%; coronary heart disease death 6.6-17.8%	Ward and colleagues ³⁸
Stroke event distribution (age and sex dependent)	Stroke 51.7-70.1%; TIA 13.4-36.1%; stroke death 12.2-16.5%	Ward and colleagues ³⁸
Relative Risk of coronary heart events on treatment—true positives	0.639-0.721 (age and sex dependent)	Calculated with meta-analysis by Law and colleagues ¹⁵ and HSE distribution of people on 1-3 drugs ¹¹
Relative Risk of coronary heart events on treatment—false positives	1	Assumption that people without raised blood pressure get no treatment benefit
Relative Risk of stroke events on treatment—true positives	0.533-0.721 (age and sex dependent)	Calculated with meta-analysis by Law and colleagues ¹⁵ and HSE distribution of people on 1-3 drugs ¹¹
Relative Risk of stroke events on treatment—false positives	1	Assumption that people without raised blood pressure get no treatment benefit
Standardized Mortality Rate (SMR) after myocardial infarction	2.68 (95% CI 2.48-2.91)	Brønnum-Hansen and colleagues ³⁹
SMR after unstable angina	2.19 (95% CI 2.05-2.33)	NICE guideline in unstable angina and non-ST-segment-elevation myocardial infarction (REF)
SMR after stable angina	1.95 (95% CI 1.65-2.31)	Rosengren and colleagues ⁴⁰
SMR after stroke	2.72 (95% CI 2.59-2.85)	Brønnum-Hansen and colleagues ³⁹
SMR after transient ischaemic attack	1.40 (95% CI 1.1-1.8)	Oxfordshire Community Stroke Project ⁴¹
Blood pressure over time and ongoing monitoring		
Probability of blood pressure raised (true positive and false positive)	13-34% (age and sex dependent)	Calculated based on HSE 2013 ¹¹
Check-up frequency if diagnosed not hypertensive	Every 5 years	Assumption based on present UK practice
Diagnosis method following check-up	Same as initial diagnosis method	

CBPM= Clinic Blood Pressure Monitoring. HBPM= Home Blood Pressure monitoring. ABPM= Ambulatory Blood Pressure Monitoring. PROOF-BP=Predicting out-of-office blood pressure. TIA= Transient Ischaemic

Attack. MI= Myocardial infarction. NICE= National Institute for Health and Care Excellence. HSE= Health Survey for England. CI= Confidence Interval

* Left ventricular hypertrophy risk input assumed to be 0%

Table 3. Quality of life and cost data inputs for the model

Quality of life weights (utilities)	Data	Source
No cardiovascular event	0.737-0.905 (age and sex dependent)	General population utilities from analysis of EQ-5D (UK tariff) from HSE 2012 ¹⁶
Quality of life multipliers		
Stroke	0.629	Ward and colleagues. ³⁸ Applied multiplicatively to general population age-dependent and sex-dependent utilities
Myocardial infarction	0.760	As above
Unstable Angina	0.770	As above
Stable Angina	0.808	As above
Transient Ischaemic Attack	1	As above
On hypertension treatment	1	Assumption that no quality of life loss to treatment in base case
Costs		
Cost of diagnosis CBPM	£46.37	Calculated based on resource-use assumptions from Lovibond and colleagues ⁴ and UK unit costs below
Cost of diagnosis HBPM	£47.59	As above
Cost of diagnosis ABPM	£63.61	As above
Practice nurse consultation	£11.37	PSSRU 2014 unit costs ¹⁷
General practitioner consultation	£35.00	PSSRU 2014 unit costs ¹⁷
HBPM device	£46.00	Median price of approved HBPM devices from NHS supply chain catalogue; only monitors also on the British Hypertension Society list of validated devices suitable for home use were used
ABPM device	£1,105	Median price from NHS supply chain catalogue
HBPM calibration/services per year	£10.00	Data on File at Greenridge Surgery, South Birmingham primary-care trust (McManus, unpublished)
ABPM calibration/service/parts per year	£413	Mean of two estimates (£460.00 and £300.00) updated to 2013-14 ¹⁷
Battery (1.5 volt size AA/LR6 high power alkaline)	£0.29	NHS supply chain catalogue
Adult cuff	£17.41	Median price in NHS supply chain catalogue
Nurse practitioner consultation	£22.00	PSSRU 2014 unit costs ¹⁷
Annual hypertension treatment cost	£58.01-64.90	Calculated based on recommended treatment and UK unit costs ^{2,11,17}
Initial stroke costs (3 months)	£8,390	Luengo-Fernandez and colleagues ⁴²
Post-stroke costs (3 months)	£336	Luengo-Fernandez and colleagues ⁴²
Initial cost of Transient Ischaemic Attack (3 months)	£1,045	Diagnostic tests and procedures: Ward and colleagues inflated to 2013-14 ¹⁷ ; drug costs: relevant NICE guidance ^{43,44} and British National Formulary 69 ⁴⁵
Costs after Transient Ischaemic Attack (3 months)	£19.56	Relevant NICE guidance ^{43,44} and British National Formulary 69 ⁴⁵
Initial myocardial infarction costs (3 months)	£5,183	Palmer and colleagues inflated to 2013-14 ¹⁷
Costs after myocardial infarction (3 months)	£152	Taylor and colleagues ⁴⁶
Initial unstable angina costs (3 months)	£3,110	Assumed to be 60% of initial costs of myocardial infarction
Costs after unstable angina (3 months)	£91	Assumed to be 60% of costs after myocardial infarction
Initial stable angina cost (3 months)	£397	An outpatient cardiology assessment (service code 320) plus non-invasive imaging SPECT scan (service code RA37Z) ⁴⁷
Costs after stable angina (3 months)	£8	NICE cg 126 ⁴⁸ and British National Formulary 69 ⁴⁵
Check-up	£35	PSSRU 2014 unit costs ¹⁷

CBPM= Clinic Blood Pressure Monitoring. HBPM= Home Blood Pressure monitoring. ABPM= Ambulatory Blood Pressure Monitoring. PROOF-BP=Predicting out-of-office blood pressure. NICE= National Institute of Health and Care Excellence. PSSRU= Personal Social Services Research Unit

Table 4. Base case model results when entry is restricted to clinic BP \geq 130/80mmHg

Strategy	QALYs (95% CI)	Costs (95% CI)	ICER	Most CE strategy probability	Strategy	QALYs (95% CI)	Costs (95% CI)	ICER	Most CE strategy probability
40 years, Male					40 years, Female				
ABPM	18.053 (17.809 to 18.263)	£3323 (£3227 to £3491)		0%	ABPM	17.955 (17.75 to 18.155)	£2096 (£2007 to £2279)		0%
PROOF-BP	18.102 (17.863 to 18.314)	£3440 (£3351 to £3582)	£2,374	100%	PROOF-BP	17.966 (17.762 to 18.166)	£2230 (£2138 to £2397)	£11,895	100%
HBPM	18.051 (17.805 to 18.26)	£3445 (£3349 to £3567)	Dominated	0%	HBPM	17.957 (17.752 to 18.157)	£2315 (£2221 to £2445)	Dominated	0%
CBPM	18.051 (17.804 to 18.263)	£3475 (£3390 to £3588)	Dominated	0%	CBPM	17.958 (17.752 to 18.158)	£2369 (£2285 to £2486)	Dominated	0%
50 years, Male					50 years, Female				
ABPM	15.498 (15.246 to 15.721)	£3457 (£3331 to £3647)		0%	ABPM	15.346 (15.111 to 15.557)	£2358 (£2222 to £2611)		0%
PROOF-BP	15.554 (15.3 to 15.773)	£3511 (£3402 to £3679)	£978	100%	PROOF-BP	15.361 (15.128 to 15.573)	£2437 (£2313 to £2659)	£5,217	100%
HBPM	15.493 (15.237 to 15.718)	£3547 (£3425 to £3696)	Dominated	0%	HBPM	15.346 (15.11 to 15.558)	£2508 (£2385 to £2683)	Dominated	0%
CBPM	15.492 (15.237 to 15.715)	£3570 (£3463 to £3720)	Dominated	0%	CBPM	15.347 (15.111 to 15.558)	£2548 (£2441 to £2715)	Dominated	0%
60 years, Male					60 years, Female				
ABPM	12.694 (12.473 to 12.92)	£3225 (£3041 to £3447)		0%	ABPM	12.403 (12.183 to 12.608)	£2353 (£2168 to £2605)		0%
PROOF-BP	12.742 (12.523 to 12.963)	£3247 (£3084 to £3448)	£447	100%	PROOF-BP	12.422 (12.2 to 12.627)	£2399 (£2229 to £2628)	£2,449	100%
HBPM	12.686 (12.465 to 12.911)	£3303 (£3141 to £3501)	Dominated	0%	HBPM	12.4 (12.179 to 12.605)	£2461 (£2300 to £2667)	Dominated	0%
CBPM	12.684 (12.464 to 12.912)	£3325 (£3174 to £3509)	Dominated	0%	CBPM	12.4 (12.178 to 12.607)	£2492 (£2333 to £2683)	Dominated	0%
70 years, Male					70 years, Female				
ABPM	9.605 (9.393 to 9.81)	£2671 (£2468 to £2930)		0%	ABPM	9.177 (8.942 to 9.382)	£2030 (£1813 to £2316)		0%
PROOF-BP	9.644 (9.431 to 9.85)	£2672 (£2488 to £2914)	£11	100%	PROOF-BP	9.185 (8.95 to 9.389)	£2042 (£1838 to £2309)	£1,419	100%
HBPM	9.597 (9.385 to 9.801)	£2731 (£2543 to £2973)	Dominated	0%	HBPM	9.171 (8.934 to 9.376)	£2102 (£1897 to £2353)	Dominated	0%
CBPM	9.595 (9.385 to 9.8)	£2751 (£2569 to £2991)	Dominated	0%	CBPM	9.17 (8.934 to 9.373)	£2125 (£1934 to £2369)	Dominated	0%
75 years, Male					75 years, Female				
PROOF-BP	7.993 (7.726 to 8.231)	£2367 (£2146 to £2679)	Dominant	100%	ABPM	7.457 (7.158 to 7.696)	£1766 (£1518 to £2119)		0%
ABPM	7.972 (7.704 to 8.213)	£2372 (£2128 to £2705)	Dominated	0%	PROOF-BP	7.46 (7.161 to 7.699)	£1767 (£1529 to £2105)	£228	100%
HBPM	7.965 (7.695 to 8.205)	£2422 (£2189 to £2738)	Dominated	0%	HBPM	7.452 (7.154 to 7.693)	£1826 (£1587 to £2149)	Dominated	0%
CBPM	7.963 (7.692 to 8.206)	£2440 (£2217 to £2749)	Dominated	0%	CBPM	7.451 (7.153 to 7.692)	£1847 (£1618 to £2174)	Dominated	0%

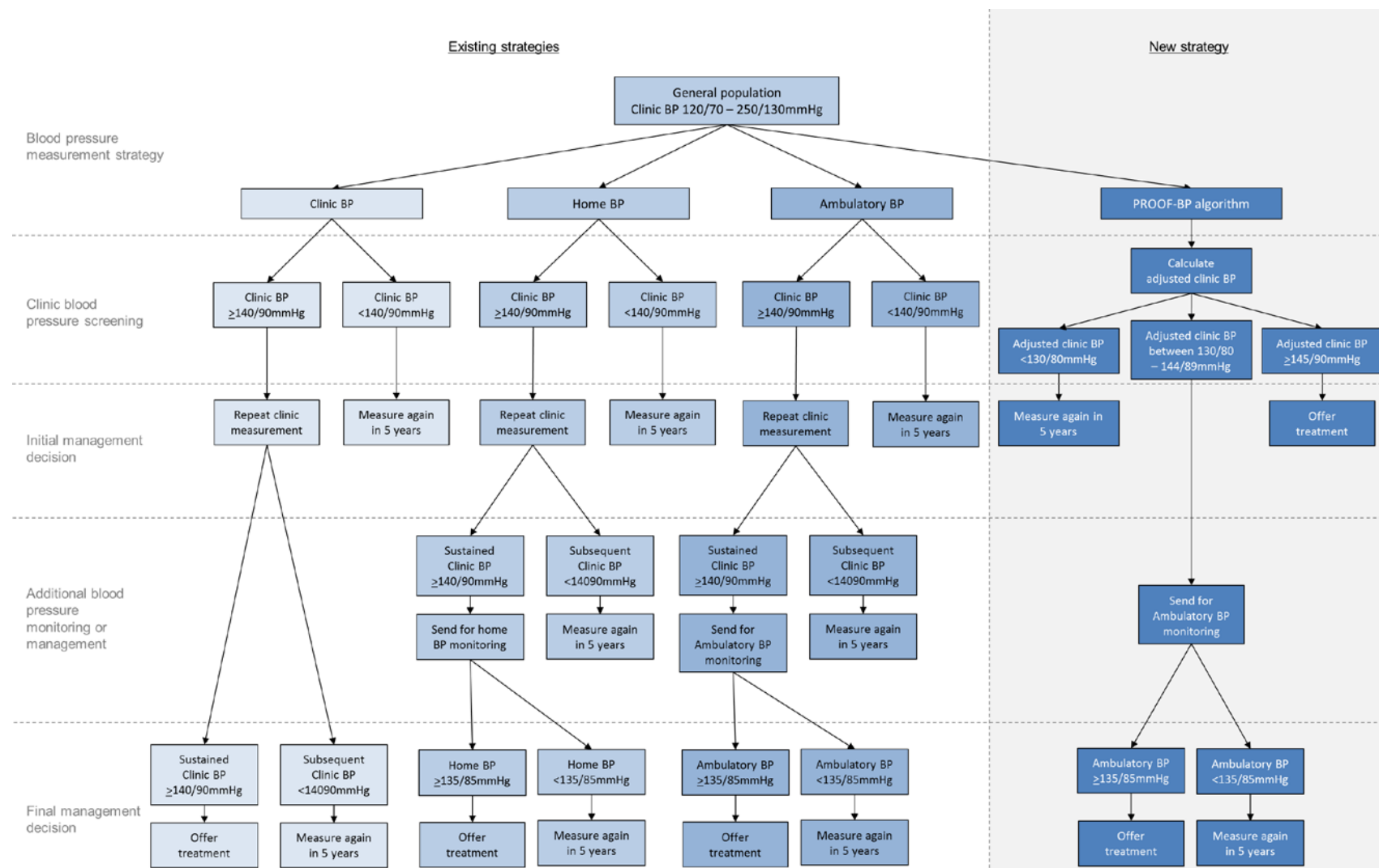
Results are per patient. CI=Confidence Interval. CBPM= Clinic Blood Pressure Monitoring. HBPM= Home Blood Pressure monitoring. ABPM= Ambulatory Blood Pressure Monitoring. PROOF-BP=Predicting out-of-office blood pressure. CE= cost-effective at £20,000 threshold. QALYs= quality-adjusted life years. ICER= Incremental Cost Effectiveness Ratio. Strategies are ordered by ascending costs.

Table 5. Sensitivity Analysis Scenarios

Strategy	QALYs	Costs	ICER	Strategy	QALYs	Costs	ICER
Basecase				Risk reduction based on half doses for masked hypertensives			
ABPM	12.694	£3225		ABPM	12.664	£3,306	
PROOF-BP	12.742	£3247	£447	PROOF-BP	12.704	£3,349	£1,073
HBPM	12.686	£3303	Dominated	HBPM	12.658	£3,381	Dominated
CBPM	12.684	£3325	Dominated	CBPM	12.656	£3,402	Dominated
1% utility decrement on treatment				Higher prevalence of masked hypertension (125%)			
ABPM	12.640	£3225		ABPM	12.680	£3,282	
PROOF-BP	12.662	£3247	£961	PROOF-BP	12.739	£3,286	£80
HBPM	12.619	£3303	Dominated	HBPM	12.672	£3,359	Dominated
CBPM	12.613	£3325	Dominated	CBPM	12.670	£3,382	Dominated
2% utility decrement on treatment				Lower prevalence of masked hypertension (75%)			
ABPM	12.586	£3225	Dominant	ABPM	12.708	£3,169	
PROOF-BP	12.582	£3247	Dominated	PROOF-BP	12.746	£3,207	£1,009
HBPM	12.553	£3303	Dominated	HBPM	12.700	£3,246	Dominated
CBPM	12.542	£3325	Dominated	CBPM	12.699	£3,268	Dominated
Higher hypertension treatment costs				Antihypertensive treatment benefits assumed for all people			
ABPM	12.694	£4,309		PROOF-BP	12.798	£3,111	Dominant
HBPM	12.686	£4,567	Dominated	ABPM	12.714	£3,175	Dominated
CBPM	12.684	£4,636	Dominated	HBPM	12.727	£3,201	Dominated
PROOF-BP	12.742	£4,669	£7,497	CBPM	12.731	£3,210	Dominated
Risk reduction based on half doses				Antihypertensive intensive treatment assumed			
ABPM	12.664	£3306		PROOF-BP	12.817	£3,123	Dominant
PROOF-BP	12.704	£3348	£1,066	ABPM	12.753	£3,127	Dominated
HBPM	12.658	£3381	Dominated	HBPM	12.742	£3,208	Dominated
CBPM	12.656	£3402	Dominated	CBPM	12.740	£3,231	Dominated
ABPM strategy considers individuals with a screening clinic BP of 130/80mmHg							
ABPM	12.741	£3230					
PROOF-BP	12.742	£3247	£10,860				
HBPM	12.686	£3303	Dominated				
CBPM	12.684	£3325	Dominated				

Results are per patient. CBPM= Clinic Blood Pressure Monitoring. HBPM= Home Blood Pressure monitoring. ABPM= Ambulatory Blood Pressure Monitoring. PROOF-BP=Predicting out-of-office blood pressure. QALYs= quality-adjusted life years. ICER= Incremental Cost Effectiveness Ratio. Strategies are ordered by ascending costs.

Figure 1. Diagnostic strategies examined



BP=blood pressure; PROOF-BP=Predicting out-of-office blood pressure

Figure 2. Markov state transition diagram

