National Institute for Health and Care Excellence

Final

Hypertension in adults: diagnosis and management

[A] Evidence review for diagnosis

NICE guideline NG136

Diagnostic evidence review underpinning recommendations 1.2.1 to 1.2.5 and 1.2.8 in the guideline

August 2019

Final

This evidence review was developed by the National Guideline Centre

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1 Diagnostic clinical effectiveness

1.1 Review question: In adults with suspected primary hypertension, what is the best method of measuring blood pressure (home, ambulatory or clinic measurement) to establish the diagnosis and prevent cardiovascular events?

1.2 Introduction

The diagnosis of hypertension is based on an individual's blood pressure being above a pre-defined threshold. There are 3 main methods of blood pressure measurement that are used clinically: home blood pressure, ambulatory blood pressure and clinic blood pressure. While all 3 of these methods can provide a diagnosis of hypertension and inform the decision to start treatment, it is unknown whether cardiovascular outcomes differ based on the method of measurement used for diagnosis. For example, is a diagnosis of hypertension made using clinic blood pressure better at preventing cardiovascular events than a diagnosis made using home blood pressure? This chapter looks at the evidence for the different methods that can be used to diagnose hypertension and compares their effect on preventing cardiovascular events.

1.3 PICO table

For full details, see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	Adults (over 18 years) with suspected primary hypertension* *People previously diagnosed with hypertension who are not on antihypertensive treatment (minimum washout 4 weeks) will also be included
Intervention(s)	Different methods of measuring blood pressure followed by appropriate treatment** based on the blood pressure measurement (test plus treatment): • Home measurement (HBPM) without telemonitoring • HBPM with telemonitoring • Ambulatory measurement (ABPM) • Clinic or office measurement (CBPM) • Pharmacy measurement Stratify results by: • Upper arm cuff • Wrist cuff • Non cuff **Note that studies will be included when the treatment strategy is the same in all arms
Comparison(s)	• Each other
Outcomes	**Assess at ≥ 12 months** **Critical** • All-cause mortality

	• Health-related quality of life • Stroke (ischaemic or haemorrhagic) • Myocardial infarction (MI) **Important** • Heart failure needing hospitalisation • Vascular procedures (including both coronary and carotid artery procedures) • Angina needing hospitalisation • Intolerance to device
Study design	Randomised control trials (RCT) and systematic reviews (SR)

1.4 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual.[128] Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy.

1.5 Clinical evidence

1.5.1 Included studies

No relevant clinical studies investigating the clinical effectiveness of different diagnostic methods were identified.

See also the study selection flow chart in appendix C.

1.5.2 Excluded studies

See the excluded studies list in appendix I.

1.5.3 Summary of clinical studies included in the evidence review

No relevant clinical studies were identified.

1.5.4 Quality assessment of clinical studies included in the evidence review

No relevant clinical studies were identified.

1.6 Economic evidence

1.6.1 Included studies

No relevant health economic studies were identified.

1.6.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix F.

1.6.3 Resource costs

Unit costs of diagnostic measurement methods are presented in section 2.6.5

1.7 Evidence statements

1.7.1 Clinical evidence statements

No relevant published evidence was identified.

1.7.2 Health economic evidence statements

No relevant economic evaluations were identified.

2 Diagnostic accuracy

2.1 Review question: In people with suspected hypertension, which test is most accurate in identifying whether hypertension is present, as indicated by the reference standard, ambulatory blood pressure measurement?

2.2 Introduction

Hypertension is one of the most important treatable causes of premature morbidity and mortality in the UK. It is a predominantly asymptomatic condition until the features of vascular and renal damage emerge after many years of high blood pressure. These consequences of hypertension are preventable through appropriate treatment, but this is only possible with an accurate diagnosis.

The accuracy of the test used to diagnose hypertension is important. A test that incorrectly diagnoses hypertension may result in an individual receiving inappropriate treatment, and a test that misses a diagnosis of hypertension may delay appropriate treatment to lower cardiovascular risk.

Currently, ambulatory blood pressure monitoring is accepted as the best test to diagnose hypertension as it has been shown to predict cardiovascular events more accurately than other available tests. However, increasingly, researchers have investigated whether other methods (such as home blood pressure monitoring with or without telemonitoring) may be as good. This chapter looks at the evidence for the different tests that can be used to diagnose hypertension and compares them against the reference standard of ambulatory blood pressure measurement.

2.3 PICO table

For full details, see the review protocol in appendix A.

Table 2: PICO characteristics of review question

Population	Population: Adults (over 18 years) with suspected primary hypertension
Target condition	Hypertension
Index test(s)	• HBPM without telemonitoring • HBPM with telemonitoring • Clinic or office measurement • Pharmacy measurement Stratify interventions by: • Cuff upper arm measurement • Cuff wrist measurement • Non cuff
Reference standard	Ambulatory blood pressure measurement (daytime or 24 hour)
Statistical measures	**Critical** • Sensitivity • Specificity • Raw data to calculate 2x2 tables to calculate sensitivity and specificity

	Important • Area under the curve • Likelihood ratios • Predictive values
Study design	Cross-sectional studies, diagnostic accuracy observational cohort studies, SRs of observational cohort

2.4 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual.[128] Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy.

2.5 Clinical evidence

2.5.1 Included studies

Thirteen studies were included in the review and these are summarised in Table 3 below. [39, 56, 57, 103, 120, 134, 139, 143, 162, 170, 178, 179, 192] Evidence from these studies is summarised in the clinical evidence summary below (Table 4).

Data from 2 studies could not be included in the analysis, as only the sensitivity and specificity values were reported, without 2x2 table values, variation data or prevalence rates.[170, 56]

See also the study selection flow chart in appendix C, sensitivity and specificity forest plots and receiver operating characteristics (ROC) curves in appendix E and study evidence tables in appendix D.

2.5.2 Excluded studies

See the excluded studies list in appendix I. Table 24 outlines the full excluded studies list, and Table 23 provides additional detail of studies that were included in the previous guideline iteration (CG127) but excluded from this update.

2.5.3 Summary of clinical studies included in the evidence review

Table 3: Summary of studies included in the evidence review

Study	Population	Index test	Reference standard	Comments
den Hond 2003[39]	People with a diastolic office blood pressure of more than 95 mmHg (n=257)	HBPM (without telemonitoring) Threshold >135/85 mmHg.	24-hour ABPM. Threshold >135/85 mmHg.	Unclear if participants were already diagnosed with hypertension
Gerc 2000[56]	Consecutive people referred to a hypertension clinic	Clinic blood pressure measurement (CBPM)	Daytime ABPM. Threshold >140/90mmHg	People under the age of 18 also included; proportion not specified

Study	Population	Index test	Reference standard	Comments
	(n=1,466)	Threshold 140/90 mmHg		
Gill 2017[57]	Hypertensive people recruited from primary care (n=340)	CBPM Threshold 140/90 mmHg) HBPM (without telemonitoring) Threshold 135/85 mmHg	Daytime ABPM Threshold 135/85 mmHg	Unclear if participants were taking antihypertensive medication
Mansoor 2004[103]	People being referred to a health centre from a physician office with an office blood pressure (BP) of >140/09 mmHg (n=48)	HBPM (with telemonitoring). Threshold systolic blood pressure ≥ 135 mmHg.	Daytime ABPM. Threshold >135 mmHg systolic blood pressure or >85 diastolic blood pressure daytime readings	Unclear if participants were already diagnosed with hypertension
Mutlu 2016[120]	Adults that were eligible for ABPM; baseline blood pressure unclear (n=160)	HBPM (without telemonitoring) Threshold ≥130-135/85 mmHg)	24-hour ABPM Threshold ≥125-130/80 mmHg	Diagnosis prior to study is unclear
Nunan 2015[134]	Systolic blood pressure between 130–179 mmHg (n=247)	HBPM (with telemonitoring) Threshold ≥135/85 mmHg	Daytime ABPM Threshold 135/85 mmHg	Participants already diagnosed with hypertension or receiving antihypertensive treatment were excluded
Ozdemir 2000[139]	Eligible renal transplant donors in an outpatient department (n=126)	CBPM. Threshold ≥140/90 mmHg	24-hour ABPM Thresholds ≥140/90 mmHg daytime and ≥120/80 mmHg night time	Population not 'suspected hypertension'; mix of hypertensive and normotensive
Park 2017[143]	Clinic blood pressure above 140/90 mmHg (n=319)	HBPM. 3 different diagnostic thresholds used (1) ≥systolic blood pressure 135 mmHg and or diastolic blood pressure ≥85 mmHg (2) systolic blood pressure ≥130 mmHg and or diastolic blood	24-hour ABPM. Threshold 24-hour average of over ≥130 mmHg systolic blood pressure or ≥80 mmHg diastolic blood pressure	Population not 'suspected hypertension'

Study	Population	Index test	Reference standard	Comments
		pressure ≥85 mmHg (3) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg		
Shimbo 2009[162]	Normotensive or Stage 1 hypertensive (140–159 mmHg/90–99 mmHg) (n=229)	HBPM (with telemonitoring) Threshold 135/85 mmHg or higher	Daytime ABPM. Threshold 135/85 mmHg or higher	Unclear if participants were diagnosed prior to the study or on antihypertensive medication Participants with a normotensive office blood pressure measurement were excluded (after to being included in the study initially, n=145)
Stergiou 2000[170]	Diastolic clinic blood pressure of 90–115 mmHg, diagnosis of hypertension was questionable. (n=142)	HBPM (without telemonitoring). Threshold ≥140/90 mm Hg	ABPM Threshold 135/85 mmHg or higher	2-week washout period given to participants. CBPM were also taken but not compared to the reference standard therefore results not extracted for this arm.
Uen 2002[178]	Participants were either normotensive systolic blood pressure <140 mmHg, or hypertensive. (n=46)	(1) HBPM (wrist device; with and without position sensor. Threshold systolic BP ≥135 mmHg or diastolic BP ≥85 mmHg (2) CBPM. Threshold systolic ≥140 mmHg or diastolic ≥90 mmHg measurements.	24-hour ABPM. Threshold systolic BP ≥130 mmHg or diastolic BP ≥80 mmHg for the 24-hour BP measurement; systolic BP ≥135 mmHg or diastolic BP ≥85 mmHg for the daytime values of the 24-hour BP measurement	Diagnosis and antihypertensive treatment unclear.
Ungar 2004[179]	People being referred to an outpatient clinic for suspected or established hypertension (n=388)	CBPM Threshold ≥140/90 mmHg	Daytime ABPM. Threshold ≥135/85 mmHg	Participants were a subgroup of the original study not taking antihypertensive medication
Zhuo 2009[192]	Systolic BP above or equal to 130 mmHg and below 160	HBPM. Threshold ≥138/85 mmHg	ABPM. Threshold in those with a clinic systolic BP <140 mmHg was	Not 'suspected hypertension' population

Study	Population	Index test	Reference standard	Comments
	mmHg (diastolic blood pressure 80–100 mmHg) (n=126)		based on a 24-hour ambulatory threshold of ≥130/80 mmHg. Threshold for diagnosis in those with a clinic systolic BP of >140 mmHg based on daytime measurement of ≥135/85 mmHg	

See appendix D for full evidence tables.

2.5.4 Quality assessment of clinical studies included in the evidence review

Table 4: Clinical evidence summary: diagnostic test accuracy for blood pressure monitors (HBPM, CBPM)

Index Test (Threshold)	Number of studies	n	Quality	Specificity % (95% CI)	Sensitivity % (95% CI)
Home blood pressure measurement (without telemonitoring)					
HBPM (≥135/85 mmHg)[f]	4	963	VERY LOW[a,c,d] due to very serious risk of bias, serious indirectness, serious imprecision	Pooled[e] 84 (53-96)	Pooled[e] 90 (68-98)
HBPM (≥135/85 mmHg)	1	340	LOW[a,c] due to serious risk of bias, serious indirectness	62.4 (54.8-69.5)[g]	84 (77.4-89.2)[g]
HBPM (≥130/85 mmHg)	1	203	VERY LOW[a,c] due to very serious risk of bias, serious indirectness	81 (74- 85)	71 (56-83)
HBPM (≥130/80 mmHg)	1	203	VERY LOW[a,c] due to very serious risk of bias, serious indirectness	90 (85-94)	63 (48-76)
HBPM with wrist cuff (≥135/85 mmHg)	1	47	MODERATE[a] due to serious risk of bias	70 (45- 84)	100 (82-100)
HBPM with wrist cuff and position sensor (≥135/85 mmHg)	1	43	MODERATE[a] due to serious risk of bias	76 (47-87)	100 (83-100)
Home blood pressure measurement (with telemonitoring)					
HBPM (2 studies ≥135/85 mmHg; 1 study ≥135 mmHg)	3	539	VERY LOW[a,b,c,d] due to serious risk of bias, very serious imprecision, serious	Pooled[e,h] 63 (20-93)	Pooled[e,h] 80 (25-98)

Index Test (Threshold)	Number of studies	n	Quality	Specificity % (95% CI)	Sensitivity % (95% CI)
			inconsistency, serious indirectness		
Clinic blood pressure measurement					
CBPM (≥140/90 mmHg)	3	1,250	VERY LOW[a,b,c,d] due to serious risk of bias, very serious imprecision, serious inconsistency, serious indirectness	Pooled[e,i] 76 (20-98)	Pooled[e,i] 81 (47-95)
CBPM (≥140/90 mmHg; using second and third readings over 3 days)	1	340	LOW[a,b] due to serious risk of bias, serious indirectness	89.3 (83.8-93.4)	41.4 (33.7-49.4)
CBPM (≥140/90 mmHg; using second – sixth readings over 3 days)	1	340	LOW[a,b] due to serious risk of bias, serious indirectness	78.7 (71.9-84.4)	61.1 (53.1-68.7)
CBPM (≥140/90 mmHg; using first reading on day 1 only)	1	340	LOW[a,b] due to serious risk of bias, serious indirectness	59 (51.4-66.3)	44.4 (36.6-52.4)

The assessment of the evidence quality was conducted with emphasis on specificity as the committee identified this as the primary measure in guiding decision-making.

(a) Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias and downgraded by 2 increments if the majority of studies were rated at very high risk of bias.

(b) Inconsistency was assessed by inspection of the sensitivity and specificity plots and summary area under the curve (AUC) plots. Particular attention was placed on the sensitivity or specificity threshold(s) the committee set as an acceptable level to recommend a test. The evidence was downgraded if subgroup analyses did not explain the heterogeneity. The evidence was downgraded by:

- *1 increment if the individual study values varied across f2 areas: where AUC values of individual studies are both above and below 50%*
- *2 increments if the individual study values varied across 3 areas, where AUC values of individual studies are above and below 50%.*

(c) Indirectness was assessed using the QUADAS-2 checklist items referring to applicability. The evidence was downgraded by 1 increment if the majority of studies were seriously indirect and downgraded by 2 increments if the majority of studies are very seriously indirect.

(d) Imprecision was assessed based on inspection of the confidence region of sensitivity or specificity in the diagnostic meta-analysis or, where diagnostic meta-analysis has not been conducted, assessed according to the range of confidence intervals in the individual studies. Particular emphasis was placed on specificity as the primary outcome. The evidence was downgraded by 1 increment when the range of the confidence interval around the point estimate was 20–40%, and downgraded by 2 increments when there was a range of >40%.

(e) Pooled sensitivity or specificity from diagnostic meta-analysis

(f) One study used a threshold of ≥130-135/85 mmHg
(g) Data from 1 study could not be combined in the analysis, as only the sensitivity and specificity values and not the 2x2 table values or prevalence were reported.
(h) Data from 1 study was based on a protocol using HBPM from days 2–7 only.
(i) Diagnostic meta-analysis model did not converge due to limited data. Pooled results represented used the results from the model as the statistics indicated this was the best fit available

2.6 Economic evidence

2.6.1 Included studies

One health economic study was identified with the relevant comparison and has been included in this review. [96] This is summarised in the health economic evidence profile below (Table 5) and the health economic evidence table in appendix G.

The study included is the model constructed in the previous version of the guideline (2011).

2.6.2 Excluded studies

Three economic studies relating to this review question were identified but were excluded due to a combination of limited applicability and methodological limitations and the availability of more applicable evidence. [91, 54, 145] These are listed in appendix I with reasons for exclusion given.

One of these studies was included in this question in the previous version of the guideline but has been excluded because it is a US study in which case the costs are not applicable to the UK.

See also the health economic study selection flow chart in appendix F.

2.6.3 Summary of studies included in the economic evidence review

Table 5: Health economic evidence profile: ABPM versus HBPM versus CBPM

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Lovibond 2011 (CG127 original analysis)[96]	Directly applicable [(a)]	Potentially serious limitations [(b)]	Markov model with 3-month cycles comparing clinic, home, and ambulatory measurement for confirming a diagnosis of hypertension in a screening population with a BP greater than 140/90. The model includes cardiovascular event health states and estimates lifetime costs and QALYs.	ABPM associated with lower costs for all age and sex subgroups.	ABPM associated with higher incremental effect in all subgroups except 40-year-old males and 40- and 50-year-old females.	ABPM most cost effective in all subgroups.	Probabilistic analysis undertaken using 1,000 Monte Carlo simulations. Most parameters were subjected to sensitivity analysis.

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial; BP: blood pressure

(a) Relevant interventions, UK NHS perspective, CUA.

(b) The data used for the accuracy of the comparisons did not use the data identified from the clinical review (which was based on 1 systematic review) but used a sensitivity analysis from the systematic review. It is uncertain as to how conclusions might change using different data.

2.6.4 Health economic model

Methods

The previous guideline (CG127) [127] economic analysis (see Table 5) undertook a cost–utility analysis to look at different blood pressure monitoring methods for confirming a diagnosis of hypertension. Methods compared were ambulatory blood pressure monitoring, clinic blood pressure monitoring, and home blood pressure monitoring. The data used for the accuracy of the comparisons was based on a sensitivity analysis from the single systematic review that informed the CG127 clinical review, because this sensitivity analysis excluded studies that had a low mean pressure and this was thought to be most approporiate for the population being modelled.

A previous sensitivity analysis of the CG127 model had shown that if HBPM were as accurate as ABPM, then HBPM would be a dominant intervention if cheaper and just as effective. The clinical review identified new diagnostic accuracy data for CBPM and HBPM. A diagnostic meta-analysis was undertaken in WinBUGS software for the CBPM and HBPM data separately. This identified that the specificity of HBPM increased compared to the previous model inputs by almost 20%, with the sensitivity also increasing slightly. The specificity of clinic measurement also increased but sensitivity decreased slightly (see Table 6). A higher specificity would mean fewer false positives and therefore fewer people who would be having unnecessary treatment. The committee was interested in the comparison of HBPM and ABPM and whether this improvement in the accuracy of HBPM would change the model results. As a result, a new analysis was added to the CG127 model as a minor update, in which the only input that was changed was the inclusion of the new accuracy data. All other inputs remain the same, and data on the methods of the previous model can be found in appendix J of the previous guideline. In the WinBUGS software, 60,000 paired estimates that form the joint posterior distribution for sensitivity and specificity were generated and extracted from the WinBUGS output of the diagnostic meta-analysis. In the PSA we sampled at random a pair of sensitivity and specificity, thus preserving the inverse correlation. 5000 simulations were run in the probabilistic analysis. The new accuracy data and their distribution based on the WinBUGS output can bee seen in Table 6.

Table 6: New diagnostic accuracy data

Input		Data	Sources	Probability distribution
Sensitivity	**CBPM**	78%	Diagnostic meta-analysis	(95% CI: 46, 95)
	HBPM	88%		(95% CI: 67, 98)
	ABPM	100%	Gold standard	Fixed
Specificity	**CBPM**	72%	Diagnostic meta-analysis	(95% CI: 20, 98)
	HBPM	81%		(95% CI: 52, 96)
	ABPM	100%	Gold standard	Fixed

Results

In this new analysis using more up to date diagnostic accuracy data, confirming a diagnosis of hypertension with ABPM following an initial raised screening blood pressure remained the most cost-effective option in all age or sex subgroups.

Probabilistic results are summarised in Table 7 and shown graphically in

Table 20: New diagnostic accuracy data analysis - deterministic results

Subgroup	Incremental QALYs vs CBPM		Incremental costs vs CBPM		Optimal strategy
	HBPM	ABPM	HBPM	ABPM	
Male, 40 years	0.004	0.003	-£49	-£159	ABPM
Male, 50 years	0.011	0.016	-£34	-£102	ABPM
Male, 60 years	0.018	0.029	-£28	-£72	ABPM
Male, 70 years	0.020	0.034	-£23	-£53	ABPM
Male, 75 years	0.018	0.031	-£13	-£29	ABPM
Female, 40 years	0.000	-0.003	-£67	-£218	ABPM
Female, 50 years	0.005	0.005	-£37	-£117	ABPM
Female, 60 years	0.009	0.014	-£34	-£97	ABPM
Female, 70 years	0.013	0.022	-£21	-£51	ABPM
Female, 75 years	0.009	0.015	-£11	-£29	ABPM

Figure 11 in appendix H at the end of this chapter.

Breakdowns of clinical events and costs and a summary of the number of people initially misdiagnosed and how misdiagnosis changes over time, can also be found in appendix H at the end of this chapter. Deterministic results are also presented in appendix H.

In all subgroups, both ABPM and HBPM were cost saving compared to CBPM, but ABPM was associated with lower costs than both CBPM and HBPM. In all except 1 subgroup (females aged 40), ABPM was associated with higher QALYs than CBPM and HBPM. ABPM was therefore dominant (both cheaper and more effective) in all except 1 subgroup. However, ABPM was still the most cost effective option in 40-year-old females because the additional benefit of HBPM did not justify the additional cost (as can be seen from the ICER on the top left cost effectiveness plane in

Table 20: New diagnostic accuracy data analysis - deterministic results

Subgroup	Incremental QALYs vs CBPM		Incremental costs vs CBPM		Optimal strategy
	HBPM	ABPM	HBPM	ABPM	
Male, 40 years	0.004	0.003	-£49	-£159	ABPM
Male, 50 years	0.011	0.016	-£34	-£102	ABPM
Male, 60 years	0.018	0.029	-£28	-£72	ABPM
Male, 70 years	0.020	0.034	-£23	-£53	ABPM
Male, 75 years	0.018	0.031	-£13	-£29	ABPM
Female, 40 years	0.000	-0.003	-£67	-£218	ABPM
Female, 50 years	0.005	0.005	-£37	-£117	ABPM
Female, 60 years	0.009	0.014	-£34	-£97	ABPM
Female, 70 years	0.013	0.022	-£21	-£51	ABPM
Female, 75 years	0.009	0.015	-£11	-£29	ABPM

Figure 11 in Appendix H: at the end of this chapter) as the cost-effectiveness ratio for HBPM compared to ABPM was above the £20,000 threshold.

Table 7: New diagnostic accuracy data analysis - probabilistic results

Subgroup	Incremental QALYs versus CBPM		Incremental costs versus CBPM		Most CE strategy	Probability CE
	HBPM	ABPM	HBPM	ABPM		
Male, 40 years	0.007 (CI: -0.013, 0.053)	0.007 (CI: -0.009, 0.047)	-£35 (CI: -£259, £190)	-£130 (CI: -£312, £29)	ABPM	88%
Male, 50 years	0.015 (CI: -0.018, 0.081)	0.021 (CI: -0.003, 0.080)	-£26 (CI: -£179, £121)	-£85 (CI: -£219, £14)	ABPM	92%
Male, 60 years	0.021 (CI: -0.027, 0.102)	0.034 (CI: 0.004, 0.111)	-£24 (CI: -£142, £86)	-£62 (CI: -£165, £7)	ABPM	96%
Male, 70 years	0.022 (CI: -0.024, 0.096)	0.037 (CI: 0.009, 0.106)	-£20 (CI: -£116, £72)	-£47 (CI: -£136, £6)	ABPM	97%
Male, 75 years	0.019 (CI: -0.021, 0.077)	0.033 (CI: 0.009, 0.084)	-£10 (CI: -£83, £52)	-£23 (CI: -£87, £16)	ABPM	98%
Female, 40 years	0.002 (CI: -0.008, 0.023)	0.000 (CI: -0.008, 0.017)	-£50 (CI: -£350, £256)	-£186 (CI: -£406, £31)	ABPM	91%
Female, 50 years	0.007 (CI: -0.011, 0.043)	0.009 (CI: -0.006, 0.042)	-£27 (CI: -£216, £149)	-£96 (CI: -£253, £30)	ABPM	91%
Female, 60 years	0.011 (CI: -0.014, 0.061)	0.017 (CI: -0.001, 0.064)	-£27 (CI: -£176, £119)	-£81 (CI: -£210, £12)	ABPM	95%
Female, 70 years	0.013 (CI: -0.015, 0.058)	0.023 (CI: 0.006, 0.065)	-£16 (CI: -£109, £71)	-£42 (CI: -£130, £14)	ABPM	97%
Female, 75 years	0.009 (CI: -0.011, 0.041)	0.016 (CI: 0.004, 0.044)	-£7 (CI: -£97, £71)	-£21 (CI: -£106, £36)	ABPM	97%

CE=cost effective at a £20,000 threshold; CI=95% confidence interval; QALYs=quality-adjusted life years.

In the previous model, for some of the younger male and female groups, the incremental QALYs of both HBPM and ABPM versus CBPM were negative, which meant that home and ambulatory measurement provided fewer QALYs than clinic, but they were also cheaper. ABPM was still the most cost effective method of diagnosis because the additional benefit of the other comparators did not justify their cost. These lower QALYs of HBPM and ABPM, could be explained because misdiagnosing people with a measurement method that had a lower specificity (CBPM) led to an unexpected advantage of some people getting treatment, and therefore cardiovascular risk reduction, sooner, before they became hypertensive and potentially untreated in the period before they next have a BP check-up. This effect worked to counteract some of the benefits of accurately diagnosing people with hypertension with more accurate methods, such as ABPM. The effect was more prominent in younger people because they have a lower prevalence of hypertension and therefore specificity plays a greater role in the results than sensitivity (see previous model write-up in appendix J of the previous guideline for more detail). However, in this new analysis, as the specificity of CBPM has increased, this anomalous effect is less prominent, and ABPM is dominant in more

subgroups than it was previously, predominantly because the new accuracy data is showing higher specificities for CBPM and HBPM.

The initial misdiagnoses per 1,000 people with suspected hypertension are shown in Table 23 in appendix H. As the specificity of CBPM and HBPM has increased, then the number of false positives has fallen compared to the base-case analysis of the previous model. The sensitivity of CBPM has fallen in the new data used, which leads to a slight increase in the number of false negatives (those who are normotensive but have been labelled as being hypertensive and will be subjected to treatment).

The number of false positives for ABPM has also decreased, and this is likely to be because those who fail ABPM are diagnosed with CBPM. As the specificity of CBPM has improved, this has led to fewer false positives.

Overall, the update to the previous model has shown that ABPM is dominant in more subgroups than it was previously and is still the most cost effective option in all subgroups evaluated.

2.6.5 Resource costs

Unit costs in relation to the different measurement methods are presented below. These are costs that were used in the base case analysis of Lovibond 2011[96] based on unit costs and assumptions regarding resource use. Other costs and resource use was tested in extensive sensitivity analysis.

Table 8: Resource use for diagnosis confirmation by CBPM, HBPM and ABPM

Cost element	Associated resource use	Cost per diagnosis
Diagnosis confirmation based on CBPM [(b)]	Consultation 1 (CBPM) [(a)] • Practice nurse appointment Consultation 2 (CPBM +/- treatment consultation) [(a)] • GP appointment	£38.00
Diagnosis confirmation based on HBPM	Consultation 1 (train patient in HBPM) • Practice nurse appointment 7 days HBPM • HBPM monitor use Consultation 2 (review results +/- treatment consultation) • GP appointment	£39.13
Diagnosis confirmation based on ABPM	Consultation 1 (fit ABPM monitor) • Practice nurse appointment 24 hours ABPM • ABPM monitor use Download data • Practice nurse appointment Consultation 2 (review results +/- treatment consultation) • GP appointment (review results +/- treatment consultation)	£53.40

(a) It is recommend that following an initial high BP reading CBPM is done at least twice more at monthly intervals to confirm diagnosis.

(b) The cost of the CBPM monitor is not included, as GPs will still require clinic monitors even if HBPM or ABPM at diagnosis in instigated and so this cost will not vary dependant on the diagnosis strategy.

The costs were not updated in the model, because although the committee considered that the cost of ABPM was likely to have reduced, the average cost of ABPM devices from the NHS supply chain remained roughly similar. Additionally, other cost inputs such as the cost of staff are likely to have increased over time, and as APBM required fewer staff resources, this was also unlikely to change the results of the model because this would only lead to favouring ABPM even more by making the comparator strategies more costly, resulting in a smaller cost difference between ABPM and the other measurement methods.

2.7 Evidence statements

2.7.1 Clinical evidence statements

The evidence included 13 studies that evaluated 3 diagnostic tests. Of these, the committee noted that HBPM without telemonitoring demonstrated the best sensitivity and specificity for identifying primary hypertension. The evidence was of moderate to very low quality. Evidence was identified for the following diagnostic tests:

- Home blood pressure measurement without telemonitoring:
  - Very low quality evidence from 4 studies (n=963) showed that HBPM without telemonitoring has a specificity of 84% and a sensitivity of 90% at a diagnostic threshold of ≥135/85 mmHg. which met the pre-specified threshold of 80% specificity set by the committee for possible recommendation.
  - Low quality evidence from 1 study (n=340) showed that HBPM without telemonitoring had a specificity of 62.4% and a sensitivity of 84%, which did not meet the pre-specified threshold of 80% specificity set by the committee for possible recommendation. This study could not be combined in the meta-analysis, as only the sensitivity and specificity values and not the 2x2 table values or prevalence were reported.
  - Very low quality evidence from 1 study (n=203) showed that HBPM without telemonitoring has a specificity of 81% and a sensitivity of 71% at a diagnostic threshold of ≥130/85 mmHg, which met the pre-specified threshold of 80% specificity set by the committee for possible recommendation.
  - Very low quality evidence from 1 study (n=203) showed that HBPM without telemonitoring has a specificity of 90% and a sensitivity of 63% at a diagnostic threshold of ≥130/80 mmHg, which met the pre-specified threshold of 80% specificity set by the committee for possible recommendation.
  - Moderate quality evidence from 1 study (n=47) showed that HBPM without telemonitoring (with a wrist cuff) has a specificity of 70% and a sensitivity of 100% at a diagnostic threshold of ≥135/85 mmHg, which did not meet the pre-specified threshold of 80% specificity set by the committee for possible recommendation.
  - Moderate quality evidence from 1 study (n=43) showed that HBPM without telemonitoring (with a wrist cuff and position sensor) has a specificity of 76% and a sensitivity of 100% at a diagnostic threshold of ≥135/85 mmHg, which did not meet the pre-specified threshold of 80% specificity set by the committee for possible recommendation.
- Home blood pressure measurement with telemonitoring:
  - Very low quality evidence from 3 studies (n=539) showed that HBPM with telemonitoring has a specificity of 63% and a sensitivity of 80% at a diagnostic threshold of ≥135/85 mmHg, which did not meet the pre-specified threshold of 80% specificity set by the committee for possible recommendation.
- Clinic blood pressure measurement:

- Very low quality evidence from 3 studies (n=1,250) showed that CBPM has a specificity of 76% and a sensitivity of 81% at a diagnostic threshold of ≥140/90 mmHg, which did not meet the pre-specified threshold of 80% specificity set by the committee for possible recommendation.
- Low quality evidence from 1 study (n=340) showed that CBPM has a specificity of 89.3% and a sensitivity of 41.4% at a diagnostic threshold of ≥140/90 mmHg (using second and third readings over 3 days), which met the pre-specified threshold of 80% specificity set by the committee for possible recommendation.
- Low quality evidence from 1 study (n=340) showed that CBPM has a specificity of 78.7% and a sensitivity of 61.1%, at a diagnostic threshold of ≥140/90 mmHg (using second to sixth readings over 3 days), which did not meet the pre-specified threshold of 80% specificity set by the committee for possible recommendation.
- Low quality evidence from 1 study (n=340) showed that CBPM has a specificity of 59% and a sensitivity of 44.4% at a diagnostic threshold of ≥140/90 mmHg (using first reading from day 1 only), which did not meet the pre-specified threshold of 80% specificity set by the committee for possible recommendation.

2.7.2 Health economic evidence statements

- One cost–utility analysis found that ABPM was either dominant (cheaper and more effective) or cost effective (at £20,000 per QALY gained) compared to HBPM and CBPM for establishing the diagnosis of hypertension in subgroups split by sex and age (ranging from 40 to 75).
- One original cost utility analysis found that ABPM was either dominant (cheaper and more effective) or cost effective (at £20,000 per QALY gained) compared to HBPM and CBPM for establishing the diagnosis of hypertension in subgroups split by sex and age (ranging from 40 to 75).

2.8 The committee's discussion of the evidence

2.8.1 Interpreting the evidence

2.8.1.1 The diagnostic measures that matter most

The committee agreed that sensitivity and specificity were both critical outcomes for this review. Specificity was considered critical because inappropriate antihypertensive treatment may cause harm, and it has long-term cost implications to the NHS. Higher specificity results in fewer people being inappropriately diagnosed as hypertensive, thereby avoiding unnecessary hypertensive treatment. The implications of unnecessary treatment are twofold. Firstly, it places the person at a risk of medication-related side effects for a potential reduction in cardiovascular risk that is not supported by current evidence. Secondly, once a person has commenced antihypertensive therapy, the person tends to continue taking this therapy for the rest of their life unless side effects or other medical issues require cessation. Life-long antihypertensive therapy has significant cost implications due to the requirement for ongoing prescription of medication and regular monitoring of blood pressure.

Sensitivity was also considered critical as a delay in the diagnosis and subsequent delay in initiation of antihypertensive treatment would result in people with hypertension remaining at a higher risk of developing irreversible cardiovascular disease. A high sensitivity results in fewer people who are hypertensive being inappropriately identified as normotensive. The implications of a missed diagnosis are that the person does not receive timely antihypertensive therapy and so remains at an elevated risk of cardiovascular events. Although sensitivity was considered as critical, it was given less weight than specificity when conducting this review. The rationale for this decision was based on the likelihood that there will be multiple other opportunities to diagnose hypertension correctly if missed at the first

visit. For example, the guideline carries forward the 2011 recommendation that blood pressure should be checked at least every 5 years in adults and more frequently if their blood pressure is close to the diagnostic threshold. Prioritising specificity was also considered important in order to avoid the inappropriate initiation of antihypertensive treatment. A minimum threshold of 80% for both specificity and sensitivity was agreed for recommending a test.

The committee chose the reference standard of ABPM for this review because ambulatory blood pressure is accepted as having the best evidence among commonly used blood pressure measurement techniques for correlation to target organ damage and prognosis. The committee was aware of evidence to support this notion, such as a recent registry study investigating the relationship between ABPM and mortality.[13] As such, it is widely used to arbitrate on both the diagnosis and management of hypertension. However, the limitations of this are that there are no RCTs investigating the diagnostic clinical effectiveness of ambulatory blood pressure measurement or any other kind of measurement. The correlation found between ABPM and target organ damage and prognosis is based on observational data. Identified by the previous guideline iteration (CG127). ABPM does correlate well with invasive blood pressure measurement techniques, which are thought to be the 'true' gold standard but are rarely used due to costs and harm to people with hypertension. Another benefit of ABPM is that it can identify white-coat and masked-effect hypertension, thus improving its accuracy of identifying primary hypertension.

2.8.1.2 The quality of the evidence

No diagnostic RCTs were identified that matched the protocol for this evidence review. Thirteen diagnostic accuracy studies were included. Of these, 6 evaluated the diagnostic accuracy of HBPM without telemonitoring, 4 evaluated HBPM with telemonitoring and 5 evaluated clinic blood pressure measurements. Meta-analysis was performed where possible but could not be carried out for all of the index tests due to the lack of adequate data reporting, and the differences between the index tests between studies.

The quality of the diagnostic accuracy evidence was assessed per index test and ranged from moderate to very low quality. Most of the evidence was assessed to be at serious or very serious risk of bias often due to a lack of blinding (although it was noted it is impossible to blind to either home, clinic or ambulatory blood pressure monitoring) and poor reporting of index test analysis. Some of the studies also had high attrition rates, which were related to a high number of participants excluded from analyses for not having enough valid blood pressure measurements. Furthermore, heterogeneity in the meta-analyses resulted in inconsistency with serious or very serious imprecision; this was particularly true for the clinic blood pressure meta-analysis. Although the reason for this was unclear and subgroup analyses did not explain this heterogeneity, the committee agreed that this could be due to the limited amount of evidence and disparities in the included populations.

Despite the limitations, the committee agreed that the evidence should be considered more relevant to current practice than that included in the previous guideline, particularly due to the publication cut-off date of the year 2000 applied in the updated systematic review; the committee agreed that devices issued prior to this date were no longer relevant to the diagnosis of hypertension. In clinical practice, mercury-based sphygmanometers have now been replaced by electronic sphygmanometers due to control of substances hazardous to health regulations and reduction in observer bias.

2.8.1.3 Discussion of the evidence

The evidence for the use of blood pressure measurement for the diagnosis of hypertension was heterogeneous. Most of the included studies were small, enrolled different populations and had different protocols for obtaining measurements; for example, they used a different number of measurements each day or measured blood pressure for a different number of

days. Consequently, the guideline committee agreed that it was difficult to interpret the evidence in a meaningful way.

The evidence did not show different diagnostic thresholds to be more accurate than the currently recommended thresholds for any of the methods of blood pressure measurement. The committee agreed not to change these thresholds and to retain those recommended in the previous guideline. These remain in line with most international norms.

The committee agreed that accuracy data for HBPM without telemonitoring was not considerably different to those reported in the previous guideline. In CG127, specificity and sensitivity values were 62% and 86% respectively. This update found the values to be increased at 84% and 90%, however, the new confidence intervals, are similar to CG127, and demonstrate serious imprecision in the diagnostic estimates. Specificity improved somewhat, but the committee could not be sure that this was the true effect due to serious imprecision within the evidence for this outcome. The committee also noted that the differences between HBPM with and without telemonitoring were interesting because telemonitoring had lower sensitivity and specificity values. In theory, it agreed that telemonitoring should aid the accuracy of results. The evidence review was not consistent with this belief and found no benefits to the addition of telemonitoring; as a result, the committee agreed not to include telemonitoring in any recommendations for diagnosis of hypertension.

For clinic blood pressure measurement, the committee noted that the values were similar to the previous guideline. The committee put particular emphasis on the large confidence intervals for both specificity and sensitivity within the meta-analysis, and they considered that the true accuracy of clinic-based blood pressure monitoring was highly variable and remained uncertain. It noted that specificity, which is the prioritised outcome, was also lower than HBPM without telemonitoring. The committee also took into consideration that the specificity and sensitivity values did not reach the minimum threshold of 80% the committee set for recommending a test. Other important influences were white-coat hypertension and masked-effect hypertension, which could have serious implications for measurement in the clinic. Taking all of these concerns into account, the committee agreed that CBPM should not be used as an alternative to ABPM on its own to diagnose hypertension. Considering the results of both HBPM and CBPM, the committee agreed that HBPM was still the best alternative where ABPM could not be tolerated. As the clinical evidence for HBPM was consistent with the previous guideline as well as the cost-effectiveness evidence, the committee decided to carry forward the recommendations of CG127 for HBPM.

The committee discussed repeated blood pressure measurements when there was a difference in blood pressure between arms. The committee noted that clinical practice could vary greatly although it was agreed that a difference in arms could be an indication of vascular disease. They agreed that a cut-off of 15 mmHg would be more suitable than the previous 20 mmHg and would be in line with recent evidence to suggest that a smaller difference between arms is associated with cardiovascular events, possibly due to the indication of vascular damage.[176]

The committee assessed the small amount of evidence available from 1 study evaluating HBPM with a wrist cuff. They agreed that results were similar to arm-cuff measurement although there wasn’t enough evidence to make a fully informed conclusion about this method. The committee was concerned regarding whether wrist cuffs are generally used properly, as best practice is for these to be held at the level of the heart. They noted that this was the reason that previous guidelines had not recommended them for general use. The committee agreed that wrist cuffs are currently essential for people with a larger arm circumference. There is currently no better alternative or evidence to suggest these devices are inaccurate when properly used. The committee discussed the use of extra-large cuffs and agreed that there is variation in availability of these within clinical practice. Taking the lack of evidence into account as a whole, the committee agreed that there was not enough

evidence to make a recommendation on wrist-cuff use. The evidence also did not warrant the use of a position sensor with wrist cuff measurement because this could be too costly with an unknown clinical benefit.

In terms of the number of measurements taken, the committee agreed that the evidence was in line with previous recommendations; although this evidence was only low quality from a small number of studies, so firm conclusions could not be drawn. In particular, the evidence related to clinic blood pressure measurements was difficult to interpret; the results were not compared to current practice and therefore any differences in accuracy were not measureable. The alternative protocols found in the review were to measure across 3 days, and using the second to sixth measurement of each day or the second and third measurement of each day. It was unclear how this would compare to current practice.

2.8.2 Cost effectiveness and resource use

One economic evaluation was included in the updated evidence review. This is the model from the previous hypertension guideline comparing ABPM (the reference standard) with HBPM and CBPM.

Three economic evaluations were identified but excluded due to a combination of limited applicability and methodological limitations. One of these studies was included in the previous guideline; however, it was excluded here because it is a US study. Another study was a comparative costing study comparing the addition of HBPM versus no HBPM in a population tested positive for hypertension on CBPM and was assessed as partially applicable with very serious limitations. The final study was a comparative costing study comparing the addition of ABPM versus no ABPM in a population positive for hypertension on CBPM; it was also assessed as partially applicable with very serious limitations. There is more applicable evidence available from the original model undertaken in the previous guideline.

The CG127 model was developed because it was identified as a high priority area for modelling. Although ABPM is the most effective, it is also the most expensive method of diagnosing hypertension, which leads to a cost benefit trade-off.

The cost-effectiveness analysis compared CBPM, HBPM or ABPM for confirming a diagnosis in people with suspected hypertension. As well as initial diagnosis costs, the analysis took into account downstream costs including hypertension treatment, check-ups and development of cardiovascular disease. Health benefits were quantified in terms of QALYs. Full details of the analysis are available in appendix J of CG127.

Contrary to what might have been expected and mindful of the higher costs of ABPM devices, the CG127 cost-effectiveness analysis found ABPM to be the most cost-effective option for the diagnosis of hypertension across a range of age groups in both men and women. In most groups, ABPM was actually found to improve health (increased QALYs, due to reduced cardiovascular events) and reduce costs, suggesting that use of ABPM for the diagnosis of hypertension has the potential to be cost saving for the NHS. The committee noted that this conclusion was robust to a wide range of sensitivity analyses including those varying the cost of ABPM, the failure rate for ABPM, the level of cardiovascular disease (CVD) risk and the prevalence of true hypertension in the population. Unsurprisingly, the conclusion was sensitive to assumptions regarding the accuracy of diagnosis with each method; for example, when the other methods (CBPM or HBPM) were assumed to be as accurate as ABPM – which the effectiveness analysis suggested that they are not. The conclusion was also sensitive to the assumption that people who were not hypertensive but were treated did not receive benefits from treatment, which they might have received. On the other hand, the analysis did not model the impact of unnecessarily treating people who are not hypertensive and the costs, inconvenience, adverse effects of treatment and impact disease labelling may have on individual people incorrectly diagnosed as hypertensive.

These are likely to favour ABPM; in fact, a sensitivity analysis assuming a decrease in QALYs from adverse effects from treatment supported this.

The committee thought about how the inputs in the CG127 analysis may have changed that might lead to the model conclusion changing. A previous sensitivity analysis of the CG127 model had shown that if HBPM was as accurate as ABPM, then HBPM would be a dominant intervention if cheaper and just as effective. Therefore, if the update guideline clinical review showed that HBPM was closer in accuracy to ABPM, then this might impact the results. In terms of costs, the committee felt that the cost of ABPM equipment was likely to have decreased because there was a large demand for the ABPM monitors after the publication of the last guideline, and manufacturers reduced their prices in response to this. In fact, the cost of ABPM monitors have slightly reduced. In which case, this would only favour ABPM even more. Other inputs such as cost of staff or treating cardiovascular events are also likely to have increased over time. However, as APBM required fewer staff resources and led to fewer events, this was also unlikely to change the results of the model because this would only lead to favouring ABPM even more by making the comparator strategies more costly.

The update guideline clinical review identified that the specificity of HBPM increased by over 20% and the specificity of clinic measurement also increased. As the committee was interested in the comparison of HBPM and ABPM and whether this improvement in HBPM would change the model results, a new analysis was added to the CG127 model as a minor update, which included the new clinical review accuracy data. All other inputs were exactly the same as the CG127 model. For further information on the new analysis, see appendix 1: Treatment initiation model write-up.

This new analysis identified that ABPM was still the most cost-effective strategy for all age and sex subgroups. The incremental costs have fallen for ABPM versus the other strategies because the specificity of the other strategies have increased, meaning that there are fewer false positives accruing unnecessary treatment costs, so ABPM is still cost saving but not to such a higher extent. ABPM is also now dominant for more of the age and sex groups. This means that using the old accuracy data created an effect in the lower prevalence groups (the younger age groups) whereby having a test with a low specificity was appearing as a good thing because misdiagnosing people before they become hypertensive means that they derive treatment benefit. This outweighed the benefit of a more accurate test because there were only a few people to identify correctly in a subgroup with a lower prevalence of hypertension. Whereas with the new review data with higher specificities for CBPM and HBPM, this effect is not so prominent. ABPM now has higher QALYs than the other strategies in all subgroups expect 1 (the male 40 year group) and lower costs in all subgroups (that is, dominant). In the male aged 40 group, the ICER was over £50,000 for HBPM versus ABPM, making HBPM not cost effective according to the NICE threshold.

Based on these results, the committee carried forward the CG127 recommendations about diagnosis.

It was acknowledged that implementing this strategy would still be a challenge. The uptake of ABPM since the last guideline has not been 100% in practice. Therefore, there is still likely to be some resource impact from carrying forward the previous recommendation on ABPM. Presently, some but not all primary care practices have access to ABPM devices; others do not. Some practices access ABPM through referral to secondary care. However, most practices have access to devices to increase their use, as this guideline recommendation requires. A 2017 survey in one part of the country showed that around 1 in 10 practices still do not have access to ABPM. [110] When being implemented in areas that don't currently have access, staff would need to be trained in the use and the interpretation of data generated by the ABPM reports.

The existing recommendations on use of appropriate cuff size (see the section on measuring blood pressure) and recognition that automated measurements may be unreliable or impossible in people with significant pulse irregularity (for example, atrial fibrillation; see the

section on measuring blood pressure) still apply, and therefore the previous guideline recommendation was carried forward. Some people will not tolerate ABPM, and in others, the procedure will fail. The CG127 model anticipated a failure rate of 5% ranging to a more extreme failure rate of 10% in sensitivity analyses, and ABPM remained the most cost-effective option for the diagnosis of hypertension. In those unable to tolerate or unwilling to undergo ABPM, the committee also carried forward the recommendation on HBPM as an alternative means of confirming the diagnosis of hypertension with emphasis that ABPM is the preferred method. For those with significant pulse irregularity, ABPM and HBPM are likely to be unreliable methods for blood pressure measurement and a series of CBPM readings via manual auscultation (see the section on measuring blood pressure) remains the only suitable option.

2.8.3 Other factors the committee took into account

The committee discussed the acceptability of the different diagnostic methods in different populations. Specific references were made to patient preference, the failure rates of ABPM (the index test) and the difficulty some people may have in performing HBPM. The committee noted that although the failure rate for ABPM may be higher in certain subgroups, the resulting delay in confirming or excluding hypertension would be unlikely to lead to harm, and the failure of 1 method does not prevent an alternative method to be used subsequently. The committee decided that the superior diagnostic accuracy and economic advantages of ABPM outweighed these issues.

The committee were aware of some evidence that people of South Asian origin tend to tolerate ABPM less well than other populations. It was agreed that the recommendation to offer HBPM for those in who could not tolerate ABPM or in whom it was unsuitable, would apply for this group.

Although there was no evidence for diagnostic RCTs informing this research question, the committee did not agree that this was an area that warranted a research recommendation as there was sufficient evidence available from the diagnostic test accuracy and cost effectiveness evidence.

The diagnostic methods considered in this review are used commonly throughout primary and secondary care, so no additional training requirements were anticipated if the review recommended an alternative to existing pathways.

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Appendices

Appendix A: Review protocols

Table 9: Review protocol: diagnostic effectiveness

Field	Content
Review question	In adults with suspected primary hypertension, what is the best method of measuring blood pressure (home, ambulatory or clinic measurement) to establish the diagnosis and prevent cardiovascular events?
Type of review question	Diagnostic RCT review A review of health economic evidence related to the same review question was conducted in parallel with this review. For details, see the health economic review protocol for this NICE guideline.
Objective of the review	To investigate the impact of different tests used to diagnose hypertension on patient outcomes.
Eligibility criteria – population / disease / condition / issue / domain	Population: Adults (over 18 years) with suspected primary hypertension* *also including people previously diagnosed with hypertension not on antihypertensive treatment (minimum washout 4 weeks)
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	Different methods of measuring blood pressure followed by appropriate treatment* based on the blood pressure measurement (test plus treatment): • HBPM without telemonitoring • HBPM with telemonitoring • ABPM • CBPM • Pharmacy measurement Stratify results by: • Upper arm cuff • Wrist cuff • Non cuff *To note that studies will be included when the treatment strategy is the same in all arms
Eligibility criteria – comparator(s) / control or reference (gold) standard	Each other
Outcomes and prioritisation	**Assess at ≥ 12 months (latest endpoint)** **Critical** • All-cause mortality • Health-related quality of life • Stroke (ischaemic or haemorrhagic) • Myocardial infarction **Important** • Heart failure needing hospitalisation • Vascular procedures (including both coronary and carotid artery procedures) • Angina needing hospitalisation

	• Side effect 1: intolerance to device • [Combined cardiovascular disease outcomes in the absence of MI and stroke data] • [Coronary heart disease outcome in the absence of MI data]
Eligibility criteria – study design	RCTs and SRs
Other inclusion exclusion criteria	Minimum follow up time: 1 year Exclusions: • Studies including participants with type 1 diabetes or chronic kidney disease (A3 or above [heavy proteinuria]). For the Type 2 diabetes strata: studies including participants with chronic kidney disease (A2 or above [heavy proteinuria]) • Indirect populations with secondary causes of hypertension such as tumours or structural vascular defects (Conn's adenoma, phaeochromocytoma, renovascular hypertension) • Pregnant women • Crossover trials • Children (< 18 years) • Studies where more than 5% of the population have atrial fibrillation
Proposed sensitivity / subgroup analysis, or meta-regression	Subgroups for analysis of heterogeneity: • Age (75 as a cut off)* • Presence or absence of type 2 Diabetes • Family origin (African and Caribbean, White, South Asian) • ABPM daytime versus 24 hour (12 hour versus 24 hour) • Number of measurements taken (under 3 versus over 3) *To note that we will also extract evidence in those >80 years old if this evidence is reported separately.
Selection process – duplicate screening / selection / analysis	A senior research fellow will undertake quality assurance prior to completion.
Data management (software)	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). GRADEpro will be used to assess the quality of evidence for each outcome. Endnote will be used for bibliography, citations, sifting and reference management.
Information sources – databases and dates	Medline, Embase, the Cochrane Library **Date cut off: 2000** Language: Restrict to English only
Identify if an update	Yes, 2011
Author contacts	https://www.nice.org.uk/guidance/cg127
Highlight if amendment to previous protocol	For details, please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for 1 database	For details, please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details, please see evidence tables in appendix D (clinical evidence tables) or H (health economic evidence tables).

Methods for assessing bias at outcome / study level	Standard study checklists were used to appraise individual studies critically. For details, please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details, please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details, please see the separate Methods report for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details, please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details, please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details, please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Anthony Wierzbicki in line with section 3 of Developing NICE guidelines: the manual. Staff from the NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details, please see Developing NICE guidelines: the manual.
Sources of funding / support	The NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	The NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds the NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

Table 10: Review protocol: Diagnostic accuracy

Field	Content
Review question	In adults with suspected primary hypertension, what is the best method of measuring blood pressure (home, ambulatory or clinic measurement) to establish the diagnosis and prevent cardiovascular events?
Type of review question	Diagnostic accuracy review A review of health economic evidence related to the same review question was conducted in parallel with this review. For details, see the health economic review protocol for this NICE guideline.
Objective of the review	To evaluate the accuracy of different diagnostic test strategies for diagnosing hypertension compared to the reference standard of ambulatory blood pressure measurement.

Eligibility criteria – population / disease / condition / issue / domain	Population: Adults (over 18 years) with suspected primary hypertension* *Note that studies will be included if participants have already diagnosed with hypertension but not on antihypertensive medication (minimum washout 4 weeks).
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	• HBPM without telemonitoring • HBPM with telemonitoring • Clinic or office measurement (CBPM) • Pharmacy measurement Stratify interventions by: • Cuff upper arm measurement • Cuff wrist measurement • Non cuff
Eligibility criteria – comparator(s) / control or reference (gold) standard	Ambulatory blood pressure measurement (daytime or 24 hour)
Outcomes and prioritisation	Diagnostic accuracy outcomes **Critical** • Sensitivity • Specificity • Raw data to calculate 2x2 tables to calculate sensitivity and specificity **Important** • Area under the curve • Likelihood ratios • Predictive values
Eligibility criteria – study design	Cross-sectional studies, diagnostic accuracy observational cohort studies, SRs of observational cohort
Other inclusion exclusion criteria	Exclusions: • Studies that do not report sensitivity and specificity data, and there is insufficient data for these to be derived • Studies including participants with type 1 diabetes or chronic kidney disease (A3 or above [heavy proteinuria]). For the Type 2 diabetes strata: studies including participants with chronic kidney disease (A2 or above [heavy proteinuria]) • Indirect populations with secondary causes of hypertension such as tumours or structural vascular defects (Conn's adenoma, phaeochromocytoma, renovascular hypertension) • Pregnant women • Children (< 18 years) • Studies with a population of inpatients • Studies where more than 5% of the population have atrial fibrillation
Proposed sensitivity / subgroup analysis, or meta-regression	Subgroup analysis for heterogeneity: • Age (above and below 75 years)* • Presence or absence of type 2 diabetes • Family origin (African and Caribbean, White, South Asian) • ABPM daytime versus 24 hour (12 hour versus 24 hour) • Number of measurements taken (under 3 versus over 3)

	*Note that evidence in those >80 years old will also be separated in the subgroup analysis if this evidence is reported separately
Selection process – duplicate screening / selection / analysis	A senior research fellow will undertake quality assurance prior to completion.
Data management (software)	Sensitivity and specificity plots will be presented using Cochrane Review Manager (RevMan5). Diagnostic meta-analysis will be undertaken where appropriate (3 or more studies presenting data for the same test at the threshold) using WinBUGS package. Endnote will be used for bibliography, citations, sifting and reference management.
Information sources – databases and dates	Medline, Embase, the Cochrane Library Date cut off: 2000 (to exclude papers published before 2000) Language: Restrict to English only Key paper: http://www.bmj.com/content/342/bmj.d3621
Identify if an update	Yes, 2011
Author contacts	https://www.nice.org.uk/guidance/cg127
Highlight if amendment to previous protocol	For details, please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for 1 database	For details, please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details, please see evidence tables in Appendix D (clinical evidence tables) or G (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to appraise individual studies critically. For details, please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details, please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details, please see the separate Methods report for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details, please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details, please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details, please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Anthony Wierzbicki in line with section 3 of Developing NICE guidelines: the manual. Staff from the NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence

	review in collaboration with the committee. For details, please see Developing NICE guidelines: the manual.
Sources of funding / support	The NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	The NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds the NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Registered: CRD42018089451

Table 11: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below. No date cut-off from the previous guideline was used.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, abstract-only studies and studies from non-OECD countries or the US will also be excluded. Studies published after 2002 that were included in the previous guideline(s) will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014). **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations', then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations', then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both, then there is discretion over whether it should be included. **Where there is discretion**

	The health economist will make a decision based on the relative applicability and quality of the available evidence for that question in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to exclude selectively the remaining studies. All studies excluded based on applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the US will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2002 or later (including any such studies included in the previous guideline[s]) but that depend on unit costs and resource data entirely or predominantly before 2002 will be rated as 'Not applicable'. • Studies published before 2002 (including any such studies included in the previous guideline[s]) will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review, the more useful the analysis will be for decision-making in the guideline. • Generally, economic evaluations based on excludes from the clinical review will be excluded.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well

described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 12: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946–02 October 2018	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
Embase (OVID)	1974–02 October 2018	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies Prognostic studies Qualitative studies
The Cochrane Library (Wiley)	Cochrane Reviews to Issue 8 of 12, August 2018 CENTRAL to Issue 7 of 12, July 2018 DARE and NHSEED to Issue 2 of 4, April 2015 HTA to Issue 4 of 4, October 2016	None

Table 13: Medline (Ovid) search terms

1.	exp Hypertension/
2.	hypertens*.ti,ab.
3.	(elevat* adj2 blood adj pressur*).ti,ab.
4.	(high adj blood adj pressur*).ti,ab.
5.	(increase* adj2 blood pressur*).ti,ab.
6.	((systolic or diastolic or arterial) adj2 pressur*).ti,ab.
7.	or/1-6
8.	exp pregnancy/
9.	exp Hypertension, Pregnancy-Induced/ not exp Hypertension/
10.	(pre eclampsia or pre-eclampsia or preeclampsia).ti,ab.
11.	exp Hypertension, Portal/ not exp Hypertension/
12.	exp Hypertension, Pulmonary/ not exp Hypertension/
13.	exp Intracranial Hypertension/ not exp Hypertension/
14.	exp Ocular Hypertension/ not exp Hypertension/
15.	exp Diabetes Mellitus, Type 1/ not exp Diabetes Mellitus, Type 2/
16.	or/8-15
17.	7 not 16
18.	letter/
19.	editorial/
20.	news/
21.	exp historical article/
22.	Anecdotes as Topic/
23.	comment/

24.	case report/
25.	(letter or comment*).ti.
26.	or/18-25
27.	randomized controlled trial/ or random*.ti,ab.
28.	26 not 27
29.	animals/ not humans/
30.	exp Animals, Laboratory/
31.	exp Animal Experimentation/
32.	exp Models, Animal/
33.	exp Rodentia/
34.	(rat or rats or mouse or mice).ti.
35.	or/28-34
36.	17 not 35
37.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
38.	36 not 37
39.	limit 38 to English language
40.	exp Blood Pressure Determination/
41.	Blood Pressure Monitoring, Ambulatory/
42.	((ambulatory or home or self or office or clinic or surgery or pharmac* or telemonitor* or daytime or 12 hour or 24 hour or continuous) adj3 (blood pressure* or BP)).ti,ab.
43.	(ABPM or HBPM).ti,ab.
44.	Blood Pressure Monitors/
45.	exp Sphygmomanometers/
46.	((blood pressure or BP) adj3 (monitor* or meter* or device*)).ti,ab.
47.	((arm* or wrist* or cuff or non cuff or automatic or electronic or digital or wireless or remote) adj3 (monitor* or meter* or measur*)).ti,ab.
48.	sphygmomanometer*.ti,ab.
49.	or/40-47
50.	39 and 49
51.	randomized controlled trial.pt.
52.	controlled clinical trial.pt.
53.	randomi#ed.ti,ab.
54.	placebo.ab.
55.	randomly.ti,ab.
56.	Clinical Trials as topic.sh.
57.	trial.ti.
58.	or/51-57
59.	Meta-Analysis/
60.	exp Meta-Analysis as Topic/
61.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
62.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
63.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
64.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
65.	(search* adj4 literature).ab.

66.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
67.	cochrane.jw.
68.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
69.	or/59-68
70.	Epidemiologic studies/
71.	Observational study/
72.	exp Cohort studies/
73.	(cohort adj (study or studies or analys* or data)).ti,ab.
74.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
75.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
76.	Controlled Before-After Studies/
77.	Historically Controlled Study/
78.	Interrupted Time Series Analysis/
79.	(before adj2 after adj2 (study or studies or data)).ti,ab.
80.	or/70-79
81.	exp case control study/
82.	case control*.ti,ab.
83.	or/81-82
84.	80 or 83
85.	Cross-sectional studies/
86.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
87.	or/85-86
88.	80 or 87
89.	80 or 83 or 87
90.	exp "sensitivity and specificity"/
91.	(sensitivity or specificity).ti,ab.
92.	((pre test or pretest or post test) adj probability).ti,ab.
93.	(predictive value* or PPV or NPV).ti,ab.
94.	likelihood ratio*.ti,ab.
95.	likelihood function/
96.	((area under adj4 curve) or AUC).ti,ab.
97.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
98.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
99.	gold standard.ab.
100.	or/90-99
101.	comparative study.pt.
102.	50 and (58 or 69 or 89 or 100) or (50 and 101)

Table 14: Embase (Ovid) search terms

1.	exp Hypertension/
2.	hypertens*.ti,ab.
3.	(elevat* adj2 blood adj pressur*).ti,ab.
4.	(high adj blood adj pressur*).ti,ab.
5.	(increase* adj2 blood pressur*).ti,ab.

6.	((systolic or diastolic or arterial) adj2 pressur*).ti,ab.
7.	or/1-6
8.	exp pregnancy/
9.	exp Maternal Hypertension/
10.	(pre eclampsia or pre-eclampsia or preeclampsia).ti,ab.
11.	exp Hypertension, Portal/ not exp Hypertension/
12.	exp Hypertension, Pulmonary/ not exp Hypertension/
13.	exp Intracranial Hypertension/
14.	exp Ocular Hypertension/ not exp Hypertension/
15.	exp Diabetes Mellitus, Type 1/ not exp Diabetes Mellitus, Type 2/
16.	or/8-15
17.	7 not 16
18.	letter.pt. or letter/
19.	note.pt.
20.	editorial.pt.
21.	case report/ or case study/
22.	(letter or comment*).ti.
23.	or/18-22
24.	randomized controlled trial/ or random*.ti,ab.
25.	23 not 24
26.	animal/ not human/
27.	nonhuman/
28.	exp Animal Experiment/
29.	exp Experimental Animal/
30.	animal model/
31.	exp Rodent/
32.	(rat or rats or mouse or mice).ti.
33.	or/25-32
34.	17 not 33
35.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
36.	34 not 35
37.	limit 36 to English language
38.	blood pressure measurement/
39.	*blood pressure monitoring/
40.	((ambulatory or home or self or office or clinic or surgery or pharmac* or telemonitor* or daytime or 12 hour or 24 hour or continuous) adj3 (blood pressure* or BP)).ti,ab.
41.	(ABPM or HBPM).ti,ab.
42.	exp blood pressure monitor/
43.	exp blood pressure meter/
44.	exp Sphygmomanometer/
45.	((blood pressure or BP) adj3 (monitor* or meter* or device*)).ti,ab.
46.	((blood pressure or BP) adj measur*).ti,ab.
47.	((arm* or wrist* or cuff or non cuff or automatic or electronic or digital or wireless or remote) adj3 (monitor* or meter* or measur*)).ti,ab.
48.	sphygmomanometer*.ti,ab.
49.	or/38-47
50.	37 and 49
51.	random*.ti,ab.

52.	factorial*.ti,ab.
53.	(crossover* or cross over*).ti,ab.
54.	((doubl* or singl*) adj blind*).ti,ab.
55.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
56.	crossover procedure/
57.	single blind procedure/
58.	randomized controlled trial/
59.	double blind procedure/
60.	or/51-59
61.	systematic review/
62.	meta-analysis/
63.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
64.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
65.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
66.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
67.	(search* adj4 literature).ab.
68.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
69.	cochrane.jw.
70.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
71.	or/61-70
72.	Clinical study/
73.	Observational study/
74.	family study/
75.	longitudinal study/
76.	retrospective study/
77.	prospective study/
78.	cohort analysis/
79.	follow-up/
80.	cohort*.ti,ab.
81.	79 and 80
82.	(cohort adj (study or studies or analys* or data)).ti,ab.
83.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
84.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
85.	(before adj2 after adj2 (study or studies or data)).ti,ab.
86.	or/72-78,81-85
87.	exp case control study/
88.	case control*.ti,ab.
89.	or/87-88
90.	86 or 89
91.	cross-sectional study/
92.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
93.	or/91-92
94.	86 or 93

95.	86 or 89 or 93
96.	exp "sensitivity and specificity"/
97.	(sensitivity or specificity).ti,ab.
98.	((pre test or pretest or post test) adj probability).ti,ab.
99.	(predictive value* or PPV or NPV).ti,ab.
100.	likelihood ratio*.ti,ab.
101.	((area under adj4 curve) or AUC).ti,ab.
102.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
103.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
104.	diagnostic accuracy/
105.	diagnostic test accuracy study/
106.	gold standard.ab.
107.	or/96-106
108.	comparative study.pt.
109.	50 and (60 or 71 or 95 or 107) or (50 and 108)

Table 15: Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Hypertension] explode all trees
#2.	hypertens*:ti,ab
#3.	(elevat* near/2 blood next pressur*):ti,ab
#4.	(high near/1 blood near/1 pressur*):ti,ab
#5.	(increase* near/2 blood pressur*):ti,ab
#6.	((systolic or diastolic or arterial) near/2 pressur*):ti,ab
#7.	(or #1 or #6)
#8.	MeSH descriptor: [Blood Pressure Determination] explode all trees
#9.	MeSH descriptor: [Blood Pressure Monitoring, Ambulatory] explode all trees
#10.	((ambulatory or home or self or office or clinic or surgery or pharmac* or telemonitor* or daytime or 12 hour or 24 hour or continuous) near/3 (blood pressure* or BP)):ti,ab
#11.	(ABPM or HBPM):ti,ab
#12.	MeSH descriptor: [Blood Pressure Monitors] this term only
#13.	MeSH descriptor: [Sphygmomanometers] explode all trees
#14.	((blood pressure or BP) near/3 (monitor* or meter* or device*)):ti,ab
#15.	((arm* or wrist* or cuff or non cuff or automatic or electronic or digital or wireless or remote) near/3 (monitor* or meter* or measur*)):ti,ab
#16.	sphygmomanometer*:ti,ab
#17.	(or #8-#16)
#18.	#7 and #17

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to hypertension in adults population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 16: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014–28 August 2018	Exclusions Health economics studies
Embase	2014–28 August 2018	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception–28 August 2018 NHSEED - Inception to March 2015	None

Table 17: Medline (Ovid) search terms

1.	exp Hypertension/
2.	hypertens*.ti,ab.
3.	(elevat* adj2 blood adj pressur*).ti,ab.
4.	(high adj blood adj pressur*).ti,ab.
5.	(increase* adj2 blood pressur*).ti,ab.
6.	((systolic or diastolic or arterial) adj2 pressur*).ti,ab.
7.	or/1-6
8.	letter/
9.	editorial/
10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/8-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice).ti.
25.	or/18-24
26.	7 not 25
27.	limit 26 to English language
28.	Economics/
29.	Value of life/
30.	exp "Costs and Cost Analysis"/
31.	exp Economics, Hospital/
32.	exp Economics, Medical/
33.	Economics, Nursing/
34.	Economics, Pharmaceutical/
35.	exp "Fees and Charges"/

36.	exp Budgets/
37.	budget*.ti,ab.
38.	cost*.ti.
39.	(economic* or pharmaco?economic*).ti.
40.	(price* or pricing*).ti,ab.
41.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
42.	(financ* or fee or fees).ti,ab.
43.	(value adj2 (money or monetary)).ti,ab.
44.	or/28-43
45.	27 and 44

Table 18: Embase (Ovid) search terms

1.	exp Hypertension/
2.	hypertens*.ti,ab.
3.	(elevat* adj2 blood adj pressur*).ti,ab.
4.	(high adj blood adj pressur*).ti,ab.
5.	(increase* adj2 blood pressur*).ti,ab.
6.	((systolic or diastolic or arterial) adj2 pressur*).ti,ab.
7.	or/1-6
8.	letter.pt. or letter/
9.	note.pt.
10.	editorial.pt.
11.	case report/ or case study/
12.	(letter or comment*).ti.
13.	or/8-12
14.	randomized controlled trial/ or random*.ti,ab.
15.	13 not 14
16.	animal/ not human/
17.	nonhuman/
18.	exp Animal Experiment/
19.	exp Experimental Animal/
20.	animal model/
21.	exp Rodent/
22.	(rat or rats or mouse or mice).ti.
23.	or/15-22
24.	7 not 23
25.	limit 24 to English language
26.	health economics/
27.	exp economic evaluation/
28.	exp health care cost/
29.	exp fee/
30.	budget/
31.	funding/

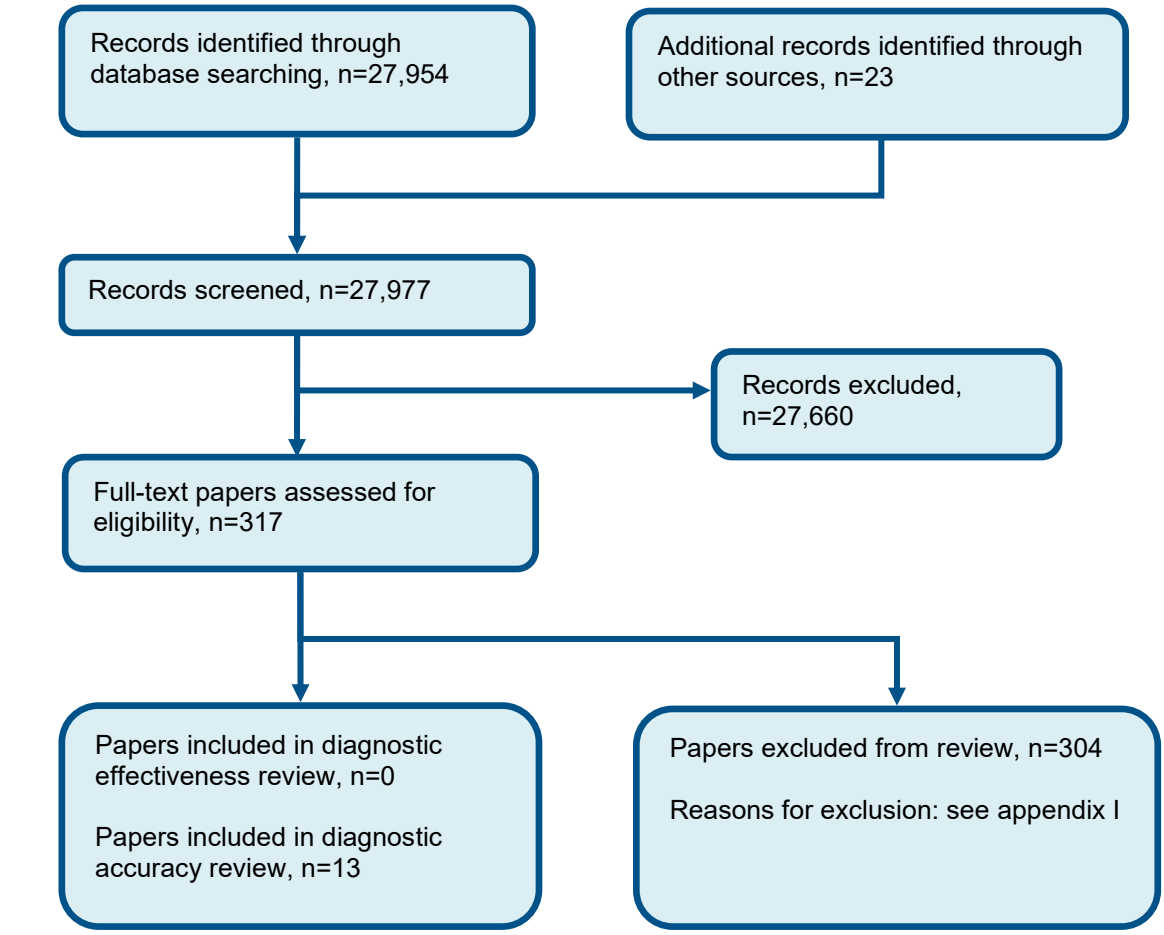
32.	budget*.ti,ab.
33.	cost*.ti.
34.	(economic* or pharmaco?economic*).ti.
35.	(price* or pricing*).ti,ab.
36.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
37.	(financ* or fee or fees).ti,ab.
38.	(value adj2 (money or monetary)).ti,ab.
39.	or/26-38
40.	25 and 39

Table 19: NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Hypertension EXPLODE ALL TREES IN NHSEED,HTA
#2.	(Hypertens*) IN NHSEED, HTA
#3.	(elevat* adj2 blood adj pressur*) IN NHSEED, HTA
#4.	(high adj blood adj pressur*) IN NHSEED, HTA
#5.	(increase* adj2 blood pressur*) IN NHSEED, HTA
#6.	((systolic or diastolic or arterial) adj2 pressur*) IN NHSEED, HTA
#7.	#1 OR #2 OR #3 OR #4 OR #5 OR #6

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of diagnostic accuracy



Appendix D: Clinical evidence tables

Reference	**den Hond[39]**
Study type	Cross-sectional
Study methodology	Data source: Treatment of Hypertension According to Home or Office Blood Pressure (THOP) study Recruitment: Untreated hypertensive patients (primary care)
Number of patients	n=475 screened but 218 excluded as on antihypertensive drugs n=247 (n=257 but 10 excluded from analysis as not hypertensive on the last visits conventional blood pressure reading) Used baseline data from Treatment of Hypertension According to Home or Office Blood Pressure (THOP) study
Patient characteristics	Age, mean (SD): 50.4 (11.0) Sex (male to female ratio): 46/54% Family origin: Unknown Setting: Not reported but further details in THOP study protocol Country: Belgium Inclusion criteria: Blood pressure measurements at baseline whose sitting diastolic blood pressure was 95 mmHg or higher on conventional measurement by a doctor with a standard mercury sphygmomanometer (mean of 2 office visits during a 1-month run-in period). At each visit, 3 blood pressure readings were obtained after the person had rested for 5 minutes in the sitting position. Exclusion criteria: people taking antihypertensive drugs
Target condition(s)	Hypertension
Index test(s) and reference standard	Index test – Home blood pressure measurement Used Omron HEM-705CP digital blood pressure monitors. Measures brachial artery pressure. Doctor of study nurse instructed the participants how to use the recorders and provided written guidelines for their operation at home. The participants recorded their blood pressure in the morning (between 06.00 and 10.00 hours) and in the evening (18.00-22.00 hours) during the week immediately preceding their second clinic visit. Each measurement session consisted of 3 readings after 5 minutes of rest in the sitting position. Diagnostic threshold: 135/85 mmHg

Reference	**den Hond[39]**			
	Reference standard – 24 hour ambulatory blood pressure measurement Measured between the 2 office visits with oscillometric Space-Labs 90207 monitors. Readings at 15-minute intervals from 08.00-22.00 and at 30 minute intervals for the remainder of the day. Daytime and nighttime ambulatory blood pressures were calculated as the time-weighted means of the readings obtained from 10.00 to 20.00 hours and from 00.00 to 06.00 hours respectively. Diagnostic threshold: 135/85 mmHg Time between measurement of index test and reference standard: Same size cuffs used for all blood pressure readings. If arm circumference exceeds 31 cm, larger cuffs were used.			
2×2 table		Reference standard +	Reference standard −	Total
	Index test +	202	6	208
	Index test −	26	13	39
	Total	228	19	247
Statistical measures	Index text – self measurement at home Sensitivity 89% (84-92) Specificity 68% (43-87) PPV 0.97 NPV 0.33 PLR 2.81 (1.45-5.45) NLR 0.17 (0.10-0.27) AUC Not reported			
Source of funding	THOP trial financially supported by AstraZeneca NV/SA (Brussels, Belgium), AstraZeneca (Brussels, Belgium) and Pfizer corporation donated the study medications.			
Limitations	Risk of bias: Serious Indirectness: Serious; unclear population – inclusion criteria based on diastolic measurement only			
Comments	Purpose of study to diagnose white- coat hypertension.			

Reference	**Gerc 2000[56]**
Study type	Retrospective
Study methodology	Data source: Division of hypertension and vascular medicine of the university hospital in Lausanne – database of all ambulatory blood pressure recordings performed over the period 1985-1991 Recruitment: Consecutive patients referred to the hypertension clinic for the performance of ABPM who had been examined by their GP and classified as having an elevated blood pressure as measured in the physician's office using a mercury sphygmomanometer. They were referred to the hypertension clinic ether for confirmation of the diagnosis of hypertension (untreated patients) or to evaluate the

<table>
<tr><td>Reference</td><td colspan="5">Gerc 2000[56]</td></tr>
<tr><td></td><td colspan="5">effectiveness of the prescribed antihypertensive therapy (treated patients). Before ABPM a form was filled in form each patient that included office blood pressure.</td></tr>
<tr><td>Number of patients</td><td colspan="5">n=2,385 (n=1,466 not treated patients)
2,555 records of which 2,385 reported nurse and ambulatory blood pressure measures</td></tr>
<tr><td>Patient characteristics</td><td colspan="5">Age, mean (SD): 46.9 ± 14.9 (n=2373); age range 13-85 years

Sex (male to female ratio): 58.4/41.6%

Family origin: Not reported

Setting: hypertension clinic

Country: Switzerland

Inclusion criteria: Records from the database that reported nurse and ambulatory systolic and diastolic blood pressure values. Quality of the ambulatory recording – more than 10 values from the 12-hour daytime reading.
Exclusion criteria: None specified</td></tr>
<tr><td>Target condition(s)</td><td colspan="5">Hypertension</td></tr>
<tr><td>Index test(s) and reference standard</td><td colspan="5"><u>Index test – Clinic blood pressure measurement</u>
Nurse-measured BP was obtained 3 times in a sitting position using a Y-tube connecting the sphygmomanometer and the recorder. Korotkoff phases I and V were used to identify the systolic and diastolic blood pressure values respectively. Mean value reported.

<u>Reference standard – Daytime ambulatory blood pressure measurement</u>
Three automatic measurements were taken simultaneously with auscultatory readings, using a Y-tube connecting the mercury column and the blood pressure recorder. The 3 values obtained by the nurse were compared with the machine reading said and had to be within 5 mmHg for the recording to be considered valid and proceed with the 12 hour daytime ABPM. If repeatedly greater than 5 mmHg, even after reposition of the arm cuff, they were not included in the study.
Ambulatory blood pressure was recorded every 20 minutes during the 12 hour daytime period (at least 10 per 12 hours). ABPM was always performed on working days. Participants were asked to carry out their routine activities but to avoid unusual physical exercise.
Diagnostic threshold 140/90 mmHg but also reported statistical measures with threshold of 135/85, which was used.
83% of recordings were made with the Remler M2000 apparatus and 17.1% with the SPS and Profilomat 1 devices.
Time between measurement of index test and reference standard: Index test was taken before setting up ambulatory measurement.</td></tr>
<tr><td>2×2 table</td><td></td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td><td rowspan="3">Note: figures given for untreated patients that had WCH as 520 and 971 with newly diagnosed hypertension confirmed. The total 1,491 does</td></tr>
<tr><td>Index test +</td><td>Not reported</td><td>520</td><td>Not reported</td></tr>
<tr><td>Index test −</td><td>Not reported</td><td>Not reported</td><td>Not reported</td></tr>
</table>

Reference	**Gerc 2000[56]**				
	Total	Not reported	Not reported	1,466	not match the figure 1,466 given as number of untreated patients.
Statistical measures	Index text - Clinic blood pressure by nurse Sensitivity 86.9 Specificity 58.7 PPV 89.1 NPV 53.3 PLR Not reported NLR Not reported AUC Not reported				
Source of funding	Not reported				
Limitations	Risk of bias: Serious patient selection Indirectness: Serious. Population includes < 18 years				
Comments	Reported outcomes for people with and without treatment and at different thresholds.				

Reference	**Gill 2017[57]**
Study type	Cross-sectional
Study methodology	Recruitment: From practices that are members of the Central England Primary Care Research Network (PCRN-CE).
Number of patients	n=551 (only 340 of which included in this review)
Patient characteristics	Age, mean (SD): 59.5(9.4) years Sex (male to female ratio): 277:274 Family origin: 246 White British, 158 African or Caribbean, and 147 South Asian Setting: Practices within PCRN-CE Country: UK Inclusion criteria: (1) between 40 and 74 years (2) belonging to 1 of the 4 family origin groups under investigation (white British, white Irish, South Asian, African-Caribbean). Exclusion criteria: (1) People who are unable to consent to participation (2) participants that didn't have at least 1 blood pressure recorded in their electronic medical records within the last 5 years.

<table>
<tr><td>Reference</td><td colspan="4">Gill 2017[57]</td></tr>
<tr><td>Target condition(s)</td><td colspan="4">Hypertension</td></tr>
<tr><td>Index test(s) and reference standard</td><td colspan="4">Index test: Home blood pressure measurement (with telemonitoring). Threshold >135/85 mmHg. Participants were fitted with a device on either the first or the second visit. The third and final visit took place 10 days after the first to allow adequate time for measurements. Home measurements were taken twice each morning and evening for 1 week, the first days readings discarded and the mean of the remaining readings calculated. A minimum of 12 readings were considered valid if there were 4 or more days readings using the average except the first day's readings.

Index test: Clinic blood pressure measurement. Six sets of CBP measurements were taken by the research nurse at 3 clinic visits (BpTru Medical Devices BPM- 100). On the first occasion BP was measured simultaneously on both arms and thereafter it was measured on the non-dominant arm unless the difference in systolic pressure was >20 mmHg between both arms, in which case it was measured in the arm with the higher reading. Mean of the second and third readings over 3 days used. Threshold >140/90 mmHg.

Index test: Clinic blood pressure measurement. Six sets of CBP measurements were taken by the research nurse at 3 clinic visits (BpTru Medical Devices BPM- 100). On the first occasion, BP was measured simultaneously on both arms and thereafter it was measured on the non-dominant arm unless the difference in systolic pressure was >20 mmHg between both arms, in which case it was measured in the arm with the higher reading. Mean of the second to sixth readings over 3 days used. Threshold >140/90 mmHg.

Index test: Clinic blood pressure measurement. Six sets of CBP measurements were taken by the research nurse at 3 clinic visits (BpTru Medical Devices BPM- 100). On the first occasion BP was measured simultaneously on both arms and thereafter it was measured on the non-dominant arm unless the difference in systolic pressure was >20 mmHg between both arms, in which case it was measured in the arm with the higher reading. First reading from the first day used. Threshold >140/90 mmHg.

Reference standard: Daytime ambulatory blood pressure measurement. Threshold >135 mmHg systolic blood pressure/85 diastolic blood pressure. Participants were fitted with an ambulatory monitor (Spacelabs 90217-1Q) on either the first or the second visit. The third and final visit took place 10 days after the first to allow adequate time for measurements. Readings were recorded at half-hourly intervals during the day (07.00 to 23.00) and hourly overnight and the mean daytime BP calculated. ABPM readings were considered to be valid if there were 14 or more daytime (07.00 to 23.00readings for a person.

Time between measurement of index test and reference standard: consecutive visits</td></tr>
<tr><td>2×2 table</td><td colspan="4"><table>
<tr><td>HBPM</td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td>Index test +</td><td>Not reported</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Index test −</td><td>Not reported</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Total</td><td>Not reported</td><td>Not reported</td><td>Not reported</td></tr>
</table></td></tr>
<tr><td>Statistical measures</td><td colspan="4">Index text HBPM (hypertension population)
Sensitivity 84% (77.4 to 89.2%)</td></tr>
</table>

Reference	Gill 2017[57]
	Specificity 62.4% (54.8-69.5%) PPV Not reported NPV Not reported PLR Not reported NLR Not reported AUC Not reported Index text CBPM (2nd and 3rd readings over 3 days; hypertension population) Sensitivity 41.4% (33.7-49.4) Specificity 89.3% (83.8-93.4%) PPV Not reported NPV Not reported PLR Not reported NLR Not reported AUC Not reported Index text CBPM (2nd-6th reading over 3 days; hypertension population) Sensitivity 61.1% (53.1-68.7%) Specificity 78.7% (71.9-84.4%) PPV Not reported NPV Not reported PLR Not reported NLR Not reported AUC Not reported Index text CBPM (day 1 reading 1; hypertension population) Sensitivity 44.4% (36.6-52.4%) Specificity 59% (51.4-66.3%) PPV Not reported NPV Not reported PLR Not reported NLR Not reported AUC Not reported
Source of funding	None specified
Limitations	For all index tests:

Reference	**Gill 2017[57]**
	Risk of bias: Serious. Blinding not stated; number of participants enrolled in the study not stated (only number analysed) Indirectness: Serious; unclear if participants already diagnosed with hypertension were taking medication

Reference	**Mansoor 2004[103]**
Study methodology	Data source: Not reported Recruitment: Referrals to a health centre from a physician office
Number of patients	n=48
Patient characteristics	Age, mean (SD): 49(14) years Sex (male to female ratio): 22:26 Family origin: Not specified Setting: Outpatient clinic Country: USA Inclusion criteria: (1) Office BP of >140/09 mmHg on at least 2 occasions (2) free of antihypertensive drugs for at least 4 weeks Exclusion criteria: (1) known or suspected secondary hypertension (2) night shift workers
Target condition(s)	Hypertension
Index test(s) and reference standard	Index test: Home blood pressure measurement (with telemonitoring). Threshold systolic blood pressure >135 mmHg. Performed using a Welch Allyn trans-telephonic BP device that transmitted data over analogue telephone lines. People were taught by nurses on how to measure BP and check the devices' accuracy. A large cuff was used for mid-arm circumference >34cm. People were asked to make 3 readings between 07.00 and 22.00, 3 readings in the evening 07.00 to 22.00 for 7 days. The device was set to allow readings at 1-minute intervals and participants were instructed to sit quietly for 5 minutes beforehand. Reference standard: daytime ambulatory blood pressure measurement. Threshold >135 mmHg systolic blood pressure or >85 diastolic blood pressure daytime readings. Welch-Allyn QuieetrTrak device. All participants were studied on a typical workday. At least 75% of readings had to be valid for a participant to be included and with no more than a 3-hour gap without a reading per hour. Participant diaries were used to check sleep times to calculate nighttime averages. Time between measurement of index test and reference standard: not specified
2×2 table	HBPM | Reference standard + | Reference standard − | Total

Reference	**Mansoor 2004[103]**			
	Index test +	14	2	16
	Index test −	20	12	32
	Total	34	14	48
Statistical measures	Index text HBPM Sensitivity 41% Specificity 86% PPV 0.85 NPV 0.35 PLR 2.5 NLR 0.76 AUC Not reported			
Source of funding	None specified			
Limitations	Risk of bias: Serious. Blinding not stated, unclear how long the reference test measures were taken for, Indirectness: Serious. 24-hour ABPM diagnostic threshold stated as a range.			

Reference	**Mutlu 2016[120]**
Study type	Cross-sectional
Study methodology	Recruitment: From clinic; eligible candidates for 24 hour ambulatory blood pressure measurement
Number of patients	n=160
Patient characteristics	Age, mean (SD): 44.44 (15.32) years Sex (male to female ratio): 87:73 Family origin: Turkish Setting: Clinic of tertiary care hospital Country: Turkey Inclusion criteria: (1) candidate for ABPM Exclusion criteria: None specified
Target condition(s)	Hypertension; results given as masked hypertension and white-coat hypertension

Reference	**Mutlu 2016[120]**
Index test(s) and reference standard	Index test: Home blood pressure measurement. People were instructed on how to measure blood pressure and were informed to visit the pharmacy to have their blood pressure checked (1 day of measurement). Diagnostic threshold 130-135/85 mmHg Reference standard: 24-hour ambulatory blood pressure measurement (diagnostic threshold 125-130/80 mmHg; no further details). Time between measurement of index test and reference standard: recorded simultaneously
2×2 table	HBPM / Reference standard + / Reference standard − / Total Index test + / 96 / 2 / 98 Index test − / 2 / 60 / 62 Total / 98 / 62 / 160
Statistical measures	Index text HBPM Sensitivity 98% Specificity 96.8% PPV 0.98 NPV 0.97 PLR 30.63 NLR 0.02 AUC OR 1482.25
Source of funding	Not specified
Limitations	Risk of bias: Very serious. Blinding not stated, unclear how long each index and reference test measures were taken for Indirectness: Serious. 24-hour ABPM diagnostic threshold stated as a range.
Comments	Clinic BP also measured but reference standard for some was HBPM

Reference	**Nunan 2015[134]**
Study type	Cross-sectional (prospective)
Study methodology	Data source: Not specified Recruitment: General practitioners from 4 participating clinics opportunistically identified potential participants
Number of patients	n=247
Patient characteristics	Age, mean (SD): 56.4(9.7) Sex (male to female ratio): 56:47

<table>
<tr><td>Reference</td><td colspan="4">Nunan 2015[134]</td></tr>
<tr><td></td><td colspan="4">Family origin: 90.4% White, 1.6% Asian, 1.6% Black, 0.5% Chinese, 2.1% other

Setting: Outpatient clinic

Country: UK

Inclusion criteria: (1) 40 to 85 years (2) systolic blood pressure between 130–179mmHg (3) not previously diagnosed with hypertension, atrial fibrillation, autonomic failure or dementia
Exclusion criteria: (1) received antihypertensive treatment prior to the study; participants were also excluded if their physician decided they needed treatment during the timeframe of the study (30 days).</td></tr>
<tr><td>Target condition(s)</td><td colspan="4">Hypertension</td></tr>
<tr><td>Index test(s) and reference standard</td><td colspan="4"><u>Index tests</u>
Home blood pressure measurement with telemonitoring:
• 2-7 day measurement
• 1-5 day measurement
• 2-5 day measurement
• 1-5 day measurement
Threshold 135/85 mmHg. A 5-minute seated test was used to identify which arm should be used for HBPM. The non-dominant arm was used unless a difference of at least 10 mmHg systolic blood pressure was observed between arms, in which case the arm giving the highest reading was used for all subsequent readings. Participants were asked to perform 6 sequential measurements separated by a 1-minute rest using the same device. Following this, participants self-monitored their blood pressure daily for 28 days by performing 2 readings in the morning and 2 readings in the evening (with a 1-3 minute gap between the first and second readings and following a 5 minute seated rest). The automated sphygmomanometer was paired to a mobile phone via Bluetooth, which was used to transmit blood pressure readings securely to a dedicated web database. Email alerts were automatically generated for critically high or low blood pressure values.

<u>Reference standard</u>
Daytime hour ambulatory measurement: undertaken after index tests, using the clinically validated Microlife WatchBP03 monitor. Readings were obtained half-hourly between 07.00 and 23.00 and hourly between 23.00 and 07.00. Threshold 135/85 mmHg.</td></tr>
<tr><td>2×2 table</td><td>2-7 day</td><td>Reference standard +</td><td>Reference standard −</td><td>Total</td></tr>
<tr><td></td><td>Index test +</td><td>102</td><td>46</td><td>148</td></tr>
<tr><td></td><td>Index test −</td><td>7</td><td>48</td><td>55</td></tr>
<tr><td></td><td>Total</td><td>109</td><td>94</td><td>203</td></tr>
</table>

Reference	**Nunan 2015[134]**				
	1-7 day	Reference standard +	Reference standard −	Total	
	Index test +	101	47	148	
	Index test −	8	47	55	
	Total	109	94	203	
	2-5 day	Reference standard +	Reference standard −	Total	
	Index test +	102	44	148	
	Index test −	7	50	55	
	Total	109	94	203	
	1-5 day	Reference standard +	Reference standard −	Total	
	Index test +	101	44	148	
	Index test −	8	50	55	
	Total	109	94	203	
Statistical measures	Index text: 2-7 day home blood pressure measurement with self-monitoring (pre-defined index test) Sensitivity 93.6% Specificity 51.1% PPV 68.9% NPV 87.3% PLR Not reported NLR Not reported AUC 0.72 (0.67 to 0.78) 150/203 correctly classified (73.9%) Index text: 1-7 day home blood pressure measurement with self-monitoring (pre-defined index test) Sensitivity 92.7% Specificity 50% PPV 68.2% NPV 85.5% PLR Not reported NLR Not reported AUC 0.71 (0.66 to 0.77) 148 correctly classified (72.9%)				

Reference	**Nunan 2015[134]**
	Index text: 2-5 day home blood pressure measurement with self-monitoring (post hoc) Sensitivity 93.6% Specificity 53.2% PPV 69.9% NPV 87.7% PLR Not reported NLR Not reported AUC 0.73 (0.69 to 0.79) Correctly classified 152 (74.9%) Index text: 1-5 day home blood pressure measurement with self-monitoring (post hoc) Sensitivity 92.7% Specificity 53.2% PPV 69.7% NPV 87.7% PLR Not reported NLR Not reported AUC 0.73 (0.67 to 0.79) Correctly classified 152/203 74.9%
Source of funding	National Institute for Health Research
Limitations	Risk of bias: Serious. Not all participants included in analysis (17.8% excluded) Indirectness: None. Participants included in the study if they had a CBPM of 130-179 mmHg and didn't have a previous diagnosis of hypertension or had received treatment for hypertension.

Reference	**Ozdemir 2000[139]**
Study type	Cross-sectional
Study methodology	Data source: Not specified Recruitment: potential living-related renal transplant donors
Number of patients	n=126

Reference	**Ozdemir 2000[139]**
Patient characteristics	Age, mean (SD): 45(12.4) years Sex (male to female ratio): 65:61 Family origin: Not specified Setting: transplantation outpatient department Country: Turkey Inclusion criteria: (1) blood pressures normal or borderline to mildly elevated (140/09 mmHg-159/104 mmHg) Exclusion criteria: Non specified
Target condition(s)	Hypertension
Index test(s) and reference standard	Index test: Clinic blood pressure measurement. Measurements taken during clinical visits prior to the start of ABPM. Three consecutive measurements were taken and the mean of the 3 was recorded. Reference standard. 24-hour ambulatory blood pressure measurement. Fully automatic Accutracker II was used. Measurements taken every 20 minutes through the day (06.00 to 23.00) and every 45 minutes at night (23.00 to 06.00). Participants were educated in how to care for the monitor and improve the measurements taken. If more than 10% of measurements were unsuccessful, participants were re-evaluated with ABPM. Time between measurement of index test and reference standard: Immediate
2×2 table	

	Reference standard +	Reference standard −	Total
Index test +	24	13	37
Index test −	6	83	89
Total	30	96	126

Statistical measures	Index text: OBPM Sensitivity 80% Specificity 86% PPV Not reported NPV Not reported PLR Not reported NLR Not reported AUC Not reported

Reference	Ozdemir 2000[139]
Source of funding	Not specified
Limitations	Risk of bias: Serious. Unclear if reference standard results were interpreted without knowledge of the results of the index test. Indirectness: Serious. Ambulatory thresholds for diagnosis 140/90 mmHg daytime and 120/80 mmHg night-time

Reference	Park 2017[143]
Study type	Cross sectional
Study methodology	Data source: Not specified Recruitment: From outpatient clinic
Number of patients	n=319
Patient characteristics	Age, mean (SD): 51.8 (9.7) years Sex (male to female ratio): Not reported Family origin: Korean Setting: Clinical trial centres Country: Korea Inclusion criteria: (1) Blood pressure above 140/90 as confirmed by clinic measurement Exclusion criteria: (1) Secondary hypertension (2) hypertensive emergency or urgency (3) heart failure or other clinically significant cardiac abnormalities or conditions (4) pregnancy (5) night labour or shift work (6) history of abusing drugs or alcohol within 6 months (7) current participant in other studies (8) taking drugs known to affect blood pressure.
Target condition(s)	Hypertension
Index test(s) and reference standard	Index test: Home blood pressure measurement. 3 different diagnostic thresholds used (1) ≥systolic blood pressure 135 mmHg and or diastolic blood pressure ≥85 mmHg (2) systolic blood pressure ≥130 mmHg and or diastolic blood pressure ≥85 mmHg (3) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg. Measurements were taken for 7 consecutive days and ended on the morning of the eighth day.

Reference	Park 2017[143]			
	Reference standard: 24-hour ambulatory blood pressure measurement. Diagnostic threshold 24-hour average of over ≥130 mmHg systolic blood pressure and or ≥80 mmHg diastolic blood pressure. Readings started on the eighth day for 1 day. Measurements taken on the non-dominant arm using an automated oscillometric device (Mobil-O-Graph) with a measurement interval of 30 minutes. A valid measurement defined as valid readings for more than 70% of attempts with at least 14 daytime and 7 nighttime readings. Time between measurement of index test and reference standard: consecutive day			
2×2 table	135/8 5mmHg	Reference standard +	Reference standard −	Total
	Index test +	158	11	169
	Index test −	47	40	87
	Total	205	51	256
	135/80 mmHg	Reference standard +	Reference standard −	Total
	Index test +	166	15	181
	Index test −	39	36	75
	Total	205	51	256
	130/80 mmHg	Reference standard +	Reference standard −	Total
	Index test +	185	19	204
	Index test −	20	32	52
	Total	205	51	256
Statistical measures	Index text HBPM 135/85 mmHg Sensitivity 77.1% Specificity 78.4% PPV 93.5 NPV 45.9 PLR Not reported NLR Not reported AUC Not reported Index text HBPM 135/80 mmHg Sensitivity 81%			

Reference	Park 2017[143]
	Specificity 70.6% PPV 91.7 NPV 48 PLR Not reported NLR Not reported AUC Not reported Index text HBPM 130/80 mmHg Sensitivity 90.2 Specificity 62.8 PPV 90.7 NPV 61.5 PLR Not reported NLR Not reported AUC Not reported
Source of funding	Industry: Dong-A ST Co Ltd
Limitations	Threshold 135/85 mmHg Risk of bias: Very serious. 20% not included in the analysis (mainly due to withdrawal of consent and exclusion from the analysis due it invalid ABPM measurements. Blinding not specified Indirectness: None Threshold 135/80 mmHg Risk of bias: Very serious. 20% not included in the analysis (mainly due to withdrawal of consent and exclusion from the analysis due it invalid ABPM measurements. Blinding not specified Indirectness: Serious. Threshold does not match that of the protocol Threshold 130/80 mmHg Risk of bias: Very serious. 20% not included in the analysis (mainly due to withdrawal of consent and exclusion from the analysis due it invalid ABPM measurements. Blinding not specified Indirectness: Serious. Threshold does not match that of the protocol

Reference	**Shimbo 2009[162]**
Study type	Cross-sectional
Study methodology	Data source: Not-specified Recruitment: from the Hypertension Centre at Mount Sinai Medical Centre NYC
Number of patients	n=229
Patient characteristics	Age, mean (SD): 52.6 (14.6) years Sex (male to female ratio): 105:124 Family origin: 69.9% White, 19.2% Black, 6.1% Asian, Indian or Pacific Islander, 4.7% Other. Setting: Hypertension clinic Country: USA Inclusion criteria: (1) normotensive or Stage 1 hypertension (140–159 mmHg /90–99 mmHg), according to Joint National Committee (JNC VI) criteria, (2) aged 18 to 80 years, (3) willing to come off antihypertensive medication (if treated) for 2 weeks prior to the first study visit, and to remain off for the duration of the study, and (4) had no history of overt cardiovascular disease. Exclusion criteria: Non specified
Target condition(s)	Hypertension
Index test(s) and reference standard	Index test: Home blood pressure measurement. 135/85 mmHg or higher for hypertension threshold. Performed over a 10-week period using an automatic HBP monitor (Omron HEM-747 IC). The monitor had a modem that provided a telephone link to a server located at the measurement centre. This provided a time and date stamp for each reading, and could store 125 readings in memory (these could not be edited by the participant). Participants were instructed to take 3 HBP measurements on 4 days a week in the morning and evening, plus additional measurements mid-day on 2 days a week, for a total of 36 measurements per week. The analysis used the first 12 values (in line with the minimum required as per AHA systematic review). Reference standard: Daytime ambulatory blood pressure measurement. 135/85 mmHg or higher for hypertension threshold. At the first visit, ambulatory measurement was initiated over a period of 36 hours. For 75% of these recordings, ABPM took BP readings every 30 minutes and for the remaining recordings measurements were taken at 15-minute intervals (between 06.00 and 22.00). Only the first 24 hours of measurements were included in the analysis. SpaceLabs Model 90207. ABPM was then repeated at week 4 and week 8 (but not used in analyses).

Reference	**Shimbo 2009[162]**			
	Time between measurement of index test and reference standard: Not specified			
2×2 table	Home	Reference standard +	Reference standard −	Total
	Index test +	64	5	75
	Index test −	11	4	9
	Total	75	9	84
Statistical measures	Index text HBPM Sensitivity 85% Specificity 44% PPV 93% NPV 27% PLR 1.54 NLR 0.33 AUC 0.863			
Source of funding	Not specified			
Limitations	Risk of bias: Very serious risk of bias, blinding unclear. 145 participants did not receive reference standard because their CBPM was normotensive, unclear why not all of the ambulatory measurements were used in assessment. Indirectness: None			

Reference	**Stergiou 2000[170]**
Study type	Nonrandomised trial
Study methodology	Data source: Not specified Recruitment: Outpatient hypertension clinic
Number of patients	n=142 recruited, 9 lost to follow-up.
Patient characteristics	Age, mean (SD): 48.4 (10.2) Sex (male to female ratio): 73:60 Family origin: not specified Setting: outpatient hypertension clinic

Reference	**Stergiou 2000[170]**
	Country: Greece Inclusion criteria: Untreated individuals with average diastolic clinic blood pressure of 90-115 mmHg and treated individuals (given a washout period of 2 weeks) whose diagnosis of hypertension was questionable. Exclusion criteria: Electrocardiographic left ventricular hypertrophy, nephropathy, diabetes mellitus, known cardiovascular disease, clinic blood pressure greater than 200/115 mmHg, secondary hypertension and unwillingness to participate in the study.
Target condition(s)	Hypertension
Index test(s) and reference standard	Index test Home blood pressure measurement; 3 workdays per week for 2 weeks, duplicate morning and evening measurements taken after 5 minutes of sitting with 1 minutes between recordings. Reference standard Ambulatory blood pressure measurement; every 20 minutes for 24 hours Time between measurement of index test and reference standard: ambulatory blood pressure measurements were taken before and after the home measurement period.
Statistical measures	Index text- Home blood pressure measurement Sensitivity 90% Specificity 69% PPV 90% NPV 69%
Source of funding	Not specified
Limitations	Risk of bias: Serious – there was no mention of blinding the investigators to the index test when carrying out the reference standard test, not all participants included were followed up (9 lost to follow-up). Indirectness: None
Comments	White coat hypertension was recorded as an outcome: Sensitivity 61%, specificity 79%, PPV 48%, NPV 86%

Reference	**Uen 2002[178]**
Study type	RCT (crossover)
Study methodology	Data source: Not specified Recruitment: Not specified

Reference	Uen 2002[178]
Number of patients	n=46
Patient characteristics	Age, mean (SD): 51(14.3) years Sex (male to female ratio): 24:19 Family origin: Not specified Setting: Not specified Country: Germany Inclusion criteria: (1) aged over 18 years Exclusion criteria: (1) previous experience with wrist BP measurement devices (2) wrist circumference of less than 13.5 cm and more than 19.5 cm (3) history of cardiac abnormalities (4) wrist injuries (5) participation in other trials (6) participants that were pregnant or lactating. Participants were either normotensive systolic blood pressure <140mmHg, or hypertensive.
Target condition(s)	Hypertension
Index test(s) and reference standard	Index test Home blood pressure measurement (wrist device with position sensor). Study duration 16 days, 8 days using each home BP device. Performed with the BP 2000 (Braun GmbH). Measurements taken twice in the morning and twice in the evening. Only stored data were used. Index test Home blood pressure measurement (wrist device without position sensor) Index test Clinic blood pressure measurement. Performed sitting at 2-minute intervals with an auscultatory BP measurement device. Two office measurements per arm were performed at study entry. Reference standard 24-hour ambulatory blood pressure measurement. Recorded on days 8 and 9. Device A&D TM-2530. Measurements were taken during working days and BP was measured at 15 minute intervals from 07.00 to 22.00 (daytime readings, and at 20-minute intervals at night (nighttime readings). Subjects were classified as hypertensive if the following criteria were fulfilled: • systolic BP ≥130 mmHg or diastolic BP ≥80 mmHg for the 24-hour BP measurement • systolic BP ≥135 mmHg or diastolic BP ≥85 mmHg for the daytime values of the 24-hour BP measurement

Reference	**Uen 2002[178]**				
	• systolic BP ≥135 mmHg or diastolic BP ≥85 mmHg for self-BP measurement • systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg for office measurements. Time between measurement of index test and reference standard: Measured simultaneously				
2×2 table	HBPM with position sensor	Reference standard +	Reference standard −	Total	
	Index test +	16	0	16	
	Index test −	7	20	27	
	Total	23	20	43	
	HBPM without sensor	Reference standard +	Reference standard −	Total	
	Index test +	16	0	16	
	Index test −	8	19	27	
	Total	24	19	43	
	Clinic	Reference standard +	Reference standard −	Total	
	Index test +	14	2	16	
	Index test −	7	20	27	
	Total	21	22	43	
Statistical measures	Index text HBPM with position sensor Sensitivity 70% Specificity 100% PPV 100% NPV 74% PLR Not reported NLR 0.3 AUC Not reported Index text HBPM without position sensor Sensitivity 67% Specificity 100% PPV 100% NPV 70% PLR Not reported NLR 0.33 AUC Not reported				

Reference	**Uen 2002[178]**
	Index text Clinic BPM Sensitivity 67% Specificity 91% PPV 88% NPV 74% PLR 7.33 NLR 0.37 AUC Not reported
Source of funding	Braun GmbH Germany
Limitations	For all index tests (HBPM with and without position sensor, CBPM) Risk of bias: Serious. Blinding not specified Indirectness: None

Reference	**Ungar 2004[179]**
Study type	Cross-sectional
Study methodology	Data source: Recruitment: Referred to outpatient centre for evaluation of hypertension (suspected or established)
Number of patients	n=388
Patient characteristics	Age, mean (SD): 60(15) years Sex (male to female ratio): 165:173 Family origin: Not specified Setting: Outpatient clinic Country: Italy Inclusion criteria: (1) suspected or established hypertension Exclusion criteria: (1) participants excluded from subgroup analysis if they were taking antihypertensive treatment

Reference	**Ungar 2004[179]**
Target condition(s)	Hypertension
Index test(s) and reference standard	Index test: Clinic blood pressure measurement Threshold above or equal to140/90 mmHg. Cuff used; a larger than standard cuff was used if arm circumference exceeded 32 cm. Two measurements were taken 24 hours apart after at least 10 minutes of sitting. A third measurement was taken if the first 2 differed by more than 5 mmHg. Reference standard: Daytime ambulatory blood pressure measurement. Threshold above or equal to 135/85 mmHg. SpaceLabs 90207 oscillometric device used with cuff placed on the non-dominant arm. Three separate cuff sizes were used based on arm circumference. Device recorded BP every 15 minutes during the daytime and every 20 minutes during nighttime, carried out on a working day. Subjects were asked to keep their arm in a relaxed and stable position during measurements and were encouraged to record their activities. Time between measurement of index test and reference standard: Taken in between the 2 office measurements
2×2 table	

	Reference standard +	Reference standard −	Total
Index test +	254	66	320
Index test −	33	35	68
Total	287	101	388

Statistical measures	Index text OBPM Sensitivity 89% Specificity 35% PPV 79% NPV 51% PLR 1.35 NLR 0.33 AUC OR 4.08
Source of funding	Supported by the Hy-Oldest project
Limitations	Risk of bias: Serious. Blinding not stated Indirectness: None

Reference	**Zhuo 2009[192]**
Study type	Cross-sectional

Reference	**Zhuo 2009[192]**
Study methodology	Data source: Recruitment: From Shijing-Shan community in Beijing
Number of patients	n=126
Patient characteristics	Age, mean (SD): 54.4 (8.6) years Sex (male to female ratio): 70:52 Family origin: Chinese Setting: General practitioners Country: China Inclusion criteria: (1) over 30 years old (2) systolic blood pressure above or equal to 130 mmHg and below 160 mmHg (diastolic blood pressure 80-100 mmHg) Exclusion criteria: (1) serious cardiovascular events or conditions, anxiety, secondary hypertension (2) people who were in other studies (3) lack of mental or physical capacity to monitor BP at home
Target condition(s)	Hypertension: study defines as masked hypertension and white coat hypertension in (1) a prehypertensive population as defined by clinic measurement and (2) a hypertensive population as defined by clinic measurement. These results were pooled.
Index test(s) and reference standard	Index test: Home blood pressure measurement. Diagnostic threshold ≥138/85 mmHg. Automatic KP-66, Albert Hengrong Beijing Ltd, device used. Participants were taught how to use devices and self-measurements were taken at 1-minute intervals after 10 minutes of rest in a quiet room. The second and third measurements at each measurement were averaged. These were taken between 06.00 and 08.00 and 18.00 to 20.00. Reference standard 24-hour ambulatory blood pressure measurement. Diagnostic threshold in the prehypertensive population (according to clinic measurement) was based on a 24-hour ambulatory threshold of ≥130/80 mmHg. Threshold for diagnosis in the hypertensive (according to clinic measurement) population based on daytime measurement of ≥135/85 mmHg. Oscillomertic DynaPulse 5000 device. Measurements taken in non-dominant arm. Immediately after visit 1, ambulatory blood pressure was recorded over a 24-hour period throughout the person's normal daily activities (but they had to stay still with the forearm extended during each measurement). The device was set to obtain BP readings at 30-minute intervals during the period of 07.00 to 22.00 and 1-hour intervals during the period of 22.00 to 07.00. If less than 80% of readings were available, participants were not included in the analysis, and a maximum of 2 hours was allowed to be unaccounted for in the 24-hour period. Time between measurement of index test and reference standard: 1 day

2×2 table		Reference standard +	Reference standard −	Total

Reference	**Zhuo 2009[192]**				
	Index test +	63	8	71	
	Index test −	9	22	31	
	Total	72	30	102	
Statistical measures	Index text HBPM Sensitivity 88% Specificity 73% PPV 89 NPV 71 PLR 3.28 NLR 0.19 AUC 19.25				
Source of funding	None specified				
Limitations	Risk of bias: Very serious. Blinding not stated and different ambulatory thresholds used in participants Indirectness: None				

Appendix E: Coupled sensitivity and specificity forest plots and sROC curves

E.1 Coupled sensitivity and specificity forest plots

Figure 2: Home blood pressure measurement without telemonitoring (threshold ≥135/85 mmHg)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Den Hond 2003	202	6	26	13	0.89 [0.84, 0.92]	0.68 [0.43, 0.87]
Mutlu 2016	96	2	2	60	0.98 [0.93, 1.00]	0.97 [0.89, 1.00]
Park 2017	158	11	47	40	0.77 [0.71, 0.83]	0.78 [0.65, 0.89]
Zhuo 2009	63	8	9	22	0.88 [0.78, 0.94]	0.73 [0.54, 0.88]

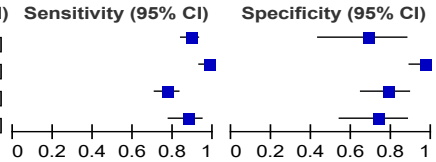


Figure 3: Home blood pressure measurement without telemonitoring (threshold ≥130/85 mmHg)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Park 2017	156	15	39	36	0.80 [0.74, 0.85]	0.71 [0.56, 0.83]

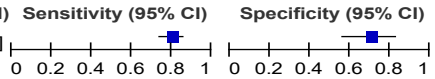


Figure 4: Home blood pressure measurement without telemonitoring (threshold ≥130/80 mmHg)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Park 2017	185	19	20	32	0.90 [0.85, 0.94]	0.63 [0.48, 0.76]

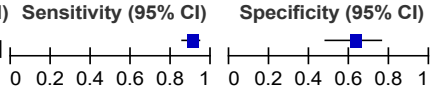


Figure 5: Home blood pressure measurement with wrist cuff (threshold ≥135/85 mmHg)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Uen 2002	16	0	8	19	0.67 [0.45, 0.84]	1.00 [0.82, 1.00]

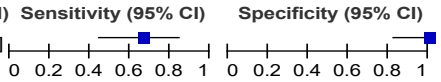


Figure 6: Home blood pressure measurement with wrist cuff and position sensor (threshold ≥135/85 mmHg)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Uen 2002	16	0	7	20	0.70 [0.47, 0.87]	1.00 [0.83, 1.00]

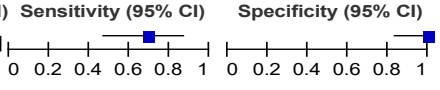


Figure 7: Home blood pressure measurement with telemonitoring (threshold ≥135/85 mmHg)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mansoor 2004	14	2	20	12	0.41 [0.25, 0.59]	0.86 [0.57, 0.98]
Nunan 2015	102	46	7	48	0.94 [0.87, 0.97]	0.51 [0.41, 0.62]
Shimbo 2009	64	5	11	4	0.85 [0.75, 0.92]	0.44 [0.14, 0.79]

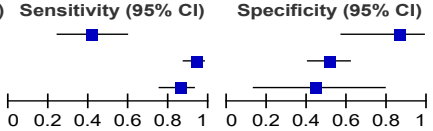
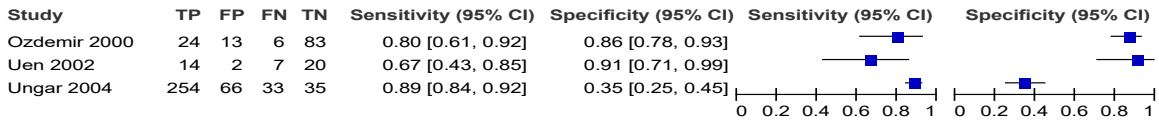
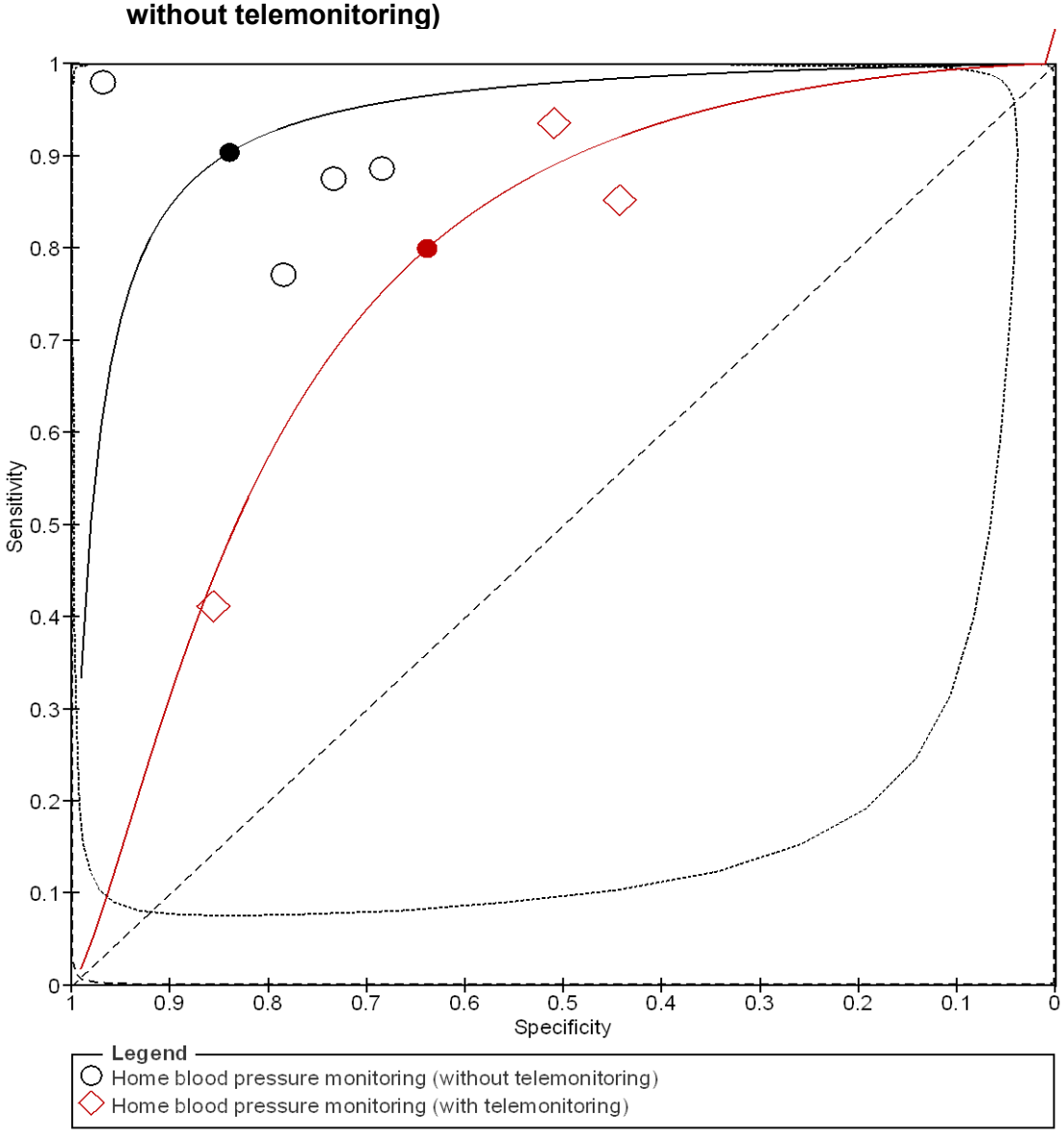


Figure 8: Clinic blood pressure measurement (≥140/90 mmHg)



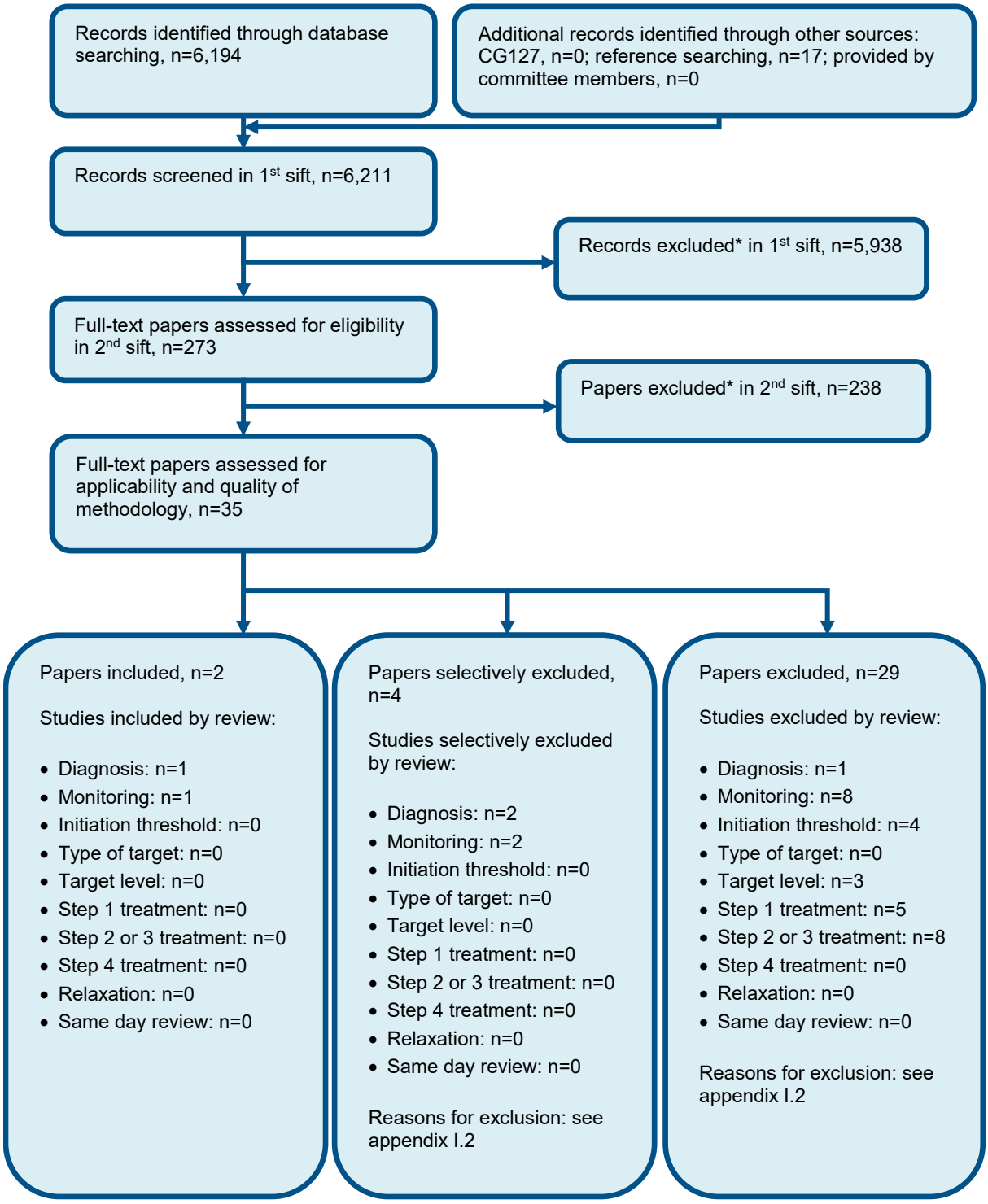
E.2 ROC curves

Figure 9: sROC curve for home blood pressure monitoring meta-analysis (with and without telemonitoring)



Appendix F: Health economic evidence selection

Figure 10: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix G: Health economic evidence tables

Study	Lovibond 2011[96]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Probabilistic decision analytic model **Approach to analysis:** Markov model with 3-month cycles comparing clinic, home, and ambulatory measurement for confirming a diagnosis of hypertension in a screening population with a BP greater than 140/90. The model includes cardiovascular event health states and estimates lifetime costs and QALYs. **Perspective:** UK NHS **Time horizon/Follow-up:** lifetime	**Population:** People with suspected hypertension – those with a screening clinic blood pressure measurement equal or above 140/90. **Cohort settings:** The analysis was run separately for 10 age- and sex-stratified groups: • male and female • age 40, 50, 60, 70, and 75 **Intervention 1:** Clinic blood pressure measurement (CBPM). Diagnosis involves 2 visits 1 month apart. **Intervention 2:**	**Total costs (mean per person):** **Male, 40 years:** Incremental (3−1): -£235 (95% CI: -£322, -£117; p=NR) Incremental (2−1): -£48 (95% CI: -£128, £17; p=NR) **Male, 50 years:** Incremental (3−1): -£156 (95% CI: -£233, -£62; p=NR) Incremental (2−1): -£34 (95% CI: -£89, £11; p=NR) **Male, 60 years:** Incremental (3−1): -£112 (95% CI: -£178, -£43; p=NR) Incremental (2−1): -£26 (95% CI: -£70, £7; p=NR) **Male, 70 years:**	**QALYs (mean per person):** **Male, 40 years:** Incremental (3−1): -0.004 (95% CI: -0.009, 0.005; p=NR) Incremental (2−1): -0.001 (95% CI: -0.006, 0.004; p=NR) **Male, 50 years:** Incremental (3−1): 0.006 (95% CI: -0.003, 0.017; p=NR) Incremental (2−1): 0.001 (95% CI: -0.009, 0.009; p=NR) **Male, 60 years:** Incremental (3−1): 0.017 (95% CI: 0.006, 0.029; p=NR) Incremental (2−1): 0.003	ABPM was the most cost-effective strategy for every subgroup at a threshold of £20,000 (pa). **Analysis of uncertainty:** Probabilistic sensitivity analysis was conducted using 1,000 Monte Carlo simulations. This resulted in the most optimal strategy being ABPM. Deterministic sensitivity analysis was conducted for males aged 60 years. When diagnostic costs, failure rates, time until diagnosis, CV risk, check-up frequency, quality of life, cost of hypertension treatment and cost of cardiovascular events were varied individually, the optimal strategy did not change. When sensitivity and specificity was changed to ABPM=HBPM and when HBPM sensitivity was set to 100%, the most optimal strategy changed to HBPM. When risk reduction was applied to all treated people, the most optimal strategy changed to CBPM.

Treatment effect duration:[(a)] lifetime **Discounting:** Costs: 3.5%; Outcomes: 3.5%	Home blood pressure measurement (HBPM) Involves 1 week of measurement. **Intervention 3:** Ambulatory blood pressure measurement (ABPM) Involves 24-hour measurement.	Incremental (3−1): -£89 (95% CI: -£150, -£30; p=NR) Incremental (2−1): -£23 (95% CI: -£65, £7; p=NR) **Male, 75 years:** Incremental (3−1): -£56 (95% CI: -£105, -£10; p=NR) Incremental (2−1): -£16 (95% CI: -£49, £6; p=NR) **Female, 40 years:** Incremental (3−1): -£323 (95% CI: -£389, -£222; p=NR) Incremental (2−1): -£68 (95% CI: -£167, £25; p=NR) **Female, 50 years:** Incremental (3−1): -£182 (95% CI: -£256, -£79; p=NR) Incremental (2−1): -£40 (95% CI: -£106, £15; p=NR) **Female, 60 years:** Incremental (3−1): -£146 (95% CI: -£220, -£55; p=NR) Incremental (2−1): -£32 (95% CI: -£83, £11; p=NR) **Female, 70 years:** Incremental (3−1): -£82 (95% CI: -£142, -£25; p=NR)	(95% CI: -0.010, 0.015; p=NR) **Male, 70 years:** Incremental (3−1): 0.022 (95% CI: 0.012, 0.035; p=NR) Incremental (2−1): 0.005 (95% CI: -0.009, 0.017; p=NR) **Male, 75 years:** Incremental (3−1): 0.021 (95% CI: 0.012, 0.030; p=NR) Incremental (2−1): 0.004 (95% CI: -0.007, 0.015; p=NR) **Female, 40 years:** Incremental (3−1): -0.006 (95% CI: -0.008, -0.003; p=NR) Incremental (2−1): -0.001 (95% CI: -0.004, 0.001; p=NR) **Female, 50 years:** Incremental (3−1): -0.001 (95% CI: -0.006, 0.007; p=NR) Incremental (2−1): -0.001 (95% CI: -0.006, 0.004; p=NR)	Deterministic sensitivity analysis was also conducted for all subgroups varying the prevalence of true hypertension and the sensitivity and specificity, which resulted in ABPM remaining as the optimal strategy. To explore further the areas where results changed, probabilistic sensitivity analysis was conducted on all male subgroups for various factors. Sensitivity and specificity of ABPM set to HBPM resulted in HBPM being the optimal strategy for all male subgroups. Sensitivity was set to 100% for all interventions and probabilistic analysis resulted in the optimal strategy changing to HBPM for the male 50 years group. When CVD risk reduction applied to all treated people the optimal strategy for all subgroups changed to CBPM. Lastly, the check-up frequency in those diagnosed without hypertension resulted in the optimal strategy changing to HBPM for the male 40 years and 50 years groups only.

		Incremental (2−1): -£20 (95% CI: -£59, £8; p=NR) **Female, 75 years:** Incremental (3−1): -£63 (95% CI: -£121, -£8; p=NR) Incremental (2−1): -£17 (95% CI: -£52, £11; p=NR) **Currency & cost year:** 2009/10 UK pounds **Cost components incorporated:** Cost of interventions (device costs depreciated and staff costs), hypertensive treatment costs and event costs (for example, stroke).	**Female, 60 years:** Incremental (3−1): 0.006 (95% CI: 0.000, 0.015; p=NR) Incremental (2−1): 0.001 (95% CI: -0.006, 0.008; p=NR) **Female, 70 years:** Incremental (3−1): 0.014 (95% CI: 0.008, 0.021; p=NR) Incremental (2−1): 0.003 (95% CI: -0.005, 0.011; p=NR) **Female, 75 years:** Incremental (3−1): 0.010 (95% CI: 0.006, 0.015; p=NR) Incremental (2−1): 0.002 (95% CI: -0.004, 0.007; p=NR)	

Data sources

Health outcomes: People enter the model suspected of having hypertension and can be in 1 of 2 health states: suspected hypertensive (true raised BP) and suspected normotensive (false raised BP). From here, people can move to a diagnosed state (true positive, false positive, true negative, false negative) or a non-fatal event state (Myocardial infarction [MI], stable angina [SA], unstable angina [UA], Stroke, Transient ischaemic attack [TIA]), or death. Repeat events are not explicitly modelled. MI and angina are defined as coronary heart disease (CHD) events, and stroke and TIA are defined as stroke events. In the model, CHD and stroke events are each implemented as an event state and post-event state. The prevalence of true hypertension varies by age (data from HSE 2006 was used based on the prevalence of untreated hypertension by 10 year age bands), but a constant estimate of sensitivity and specificity was used. Diagnostic accuracies of the measurement methods were based on a systematic review by Hodgkinson and colleagues. A sensitivity analysis of the review was used for the accuracy in the model. It excluded studies comparing to normotensive people. ABPM is assumed the reference standard and so sensitivity or specificity is 100%. ABPM was assumed to have a small failure rate but the other methods didn't. Cardiovascular risk for those with and without hypertension was calculated using Framingham risk equations (Framingham CHD risk equation and

Framingham stroke risk equation). Risk factor inputs for each age group, by sex, were taken from the Health Survey for England (HSE) 2006 (proportion that smoke, have diabetes, total and HDL cholesterol, Left ventricular hypertrophy (LVH) was not available and assumed 0%). The midpoint for each range was used. The remaining risk factor of BP for hypertensives and normotensives for each age group, by sex, was calculated using HSE 2006 individual level data. The distribution of CHD and stroke events in the model (as the risk equations give the total CHD or stroke risk) into the specific CHD and stroke health states are from the NICE statins health technology assessment (HTA) model. People who are hypertensive and receiving treatment (true positives) receive a relative risk reduction from the treatment. These are based on a meta-analysis by Law and colleagues (2009) that presented relative risks for CHD events and stroke stratified by pre-treatment systolic blood pressure or diastolic blood pressure and number and dose of drugs. The probability of normotensive people becoming hypertensive in a particular 10-year age band was included. It is assumed that people who are diagnosed as not having hypertension have their blood pressure rechecked every 5 years. It is assumed that all people in the population will be suspected of having hypertension again at this check-up and will be re-diagnosed using the same method as previously – either repeated CBPM, HBPM or ABPM. If ABPM or HBPM failed initially and the person was diagnosed using CBPM, it was assumed that CBPM was used again at re-diagnosis.

Quality-of-life weights: Quality of life weights (utilities) were applied to people in the model based on general population EQ-5D estimates stratified by age and sex. This was obtained by analysing the HSE 2006 dataset. It was assumed that having hypertension did not reduce quality of life in itself and that treatment had no impact on quality life. However, if a person had an event, then utilities were applied associated with the specific CHD or stroke event. The NICE statins HTA model was used as a source of quality of life values following cardiovascular events.

Cost sources: The costs per person of confirming a diagnosis with CBPM, HBPM, and ABPM were £38.00, £39.13 and £53.40 respectively. The cost of the CBPM monitor was not included, as GPs will still require clinic monitors even if HBPM or ABPM at diagnosis in instigated, so this cost will not vary dependant on the diagnosis strategy. HBPM and ABPM device costs per use were estimated taking into account the cost of the devices, estimated typical usage per year, calibration or servicing costs, battery costs and cuff costs. Device costs were based on prices listed in the NHS supply chain catalogue. Uses per year were based on expert opinion. Staff costs were from PSSRU 2010. The annual cost of hypertension treatment was assumed to consist of antihypertensive drug therapy and an annual check-up with a GP. Typical average antihypertensive drug costs were calculated taking into account the percentage of people on 1, 2 or 3 or more drugs by 10-year age band and sex based on the HSE 2006 report. For each age-band, typical drug classes (ACE inhibitor or ARB, CCB and diuretic) were assigned when on 1, 2 or 3 drugs based on the 2011 NICE hypertension guideline recommended treatment algorithm. Costs for each class were based on BNF 60 costs. When people in the model experienced a cardiovascular event, they were assigned an initial cost in the first cycle representing the acute management or diagnosis cost. In subsequent post-event cycles they were assigned an ongoing cost representing the average costs following an event. Cost data was sought from national cost sources and published studies by non-systematic searches. Note that the cost of hypertension management was also applied in all alive people (drug costs and 1 GP visit per year).

Comments

Source of funding: NICE **Limitations:** The accuracy data used does not match the clinical review.

Overall applicability: Directly applicable[(b)] **Overall quality:** Potentially serious limitations[(c)]

Abbreviations: 95% CI: 95% confidence interval; CUA: cost–utility analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years

[(a)] For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

[(b)] Directly applicable / Partially applicable / Not applicable

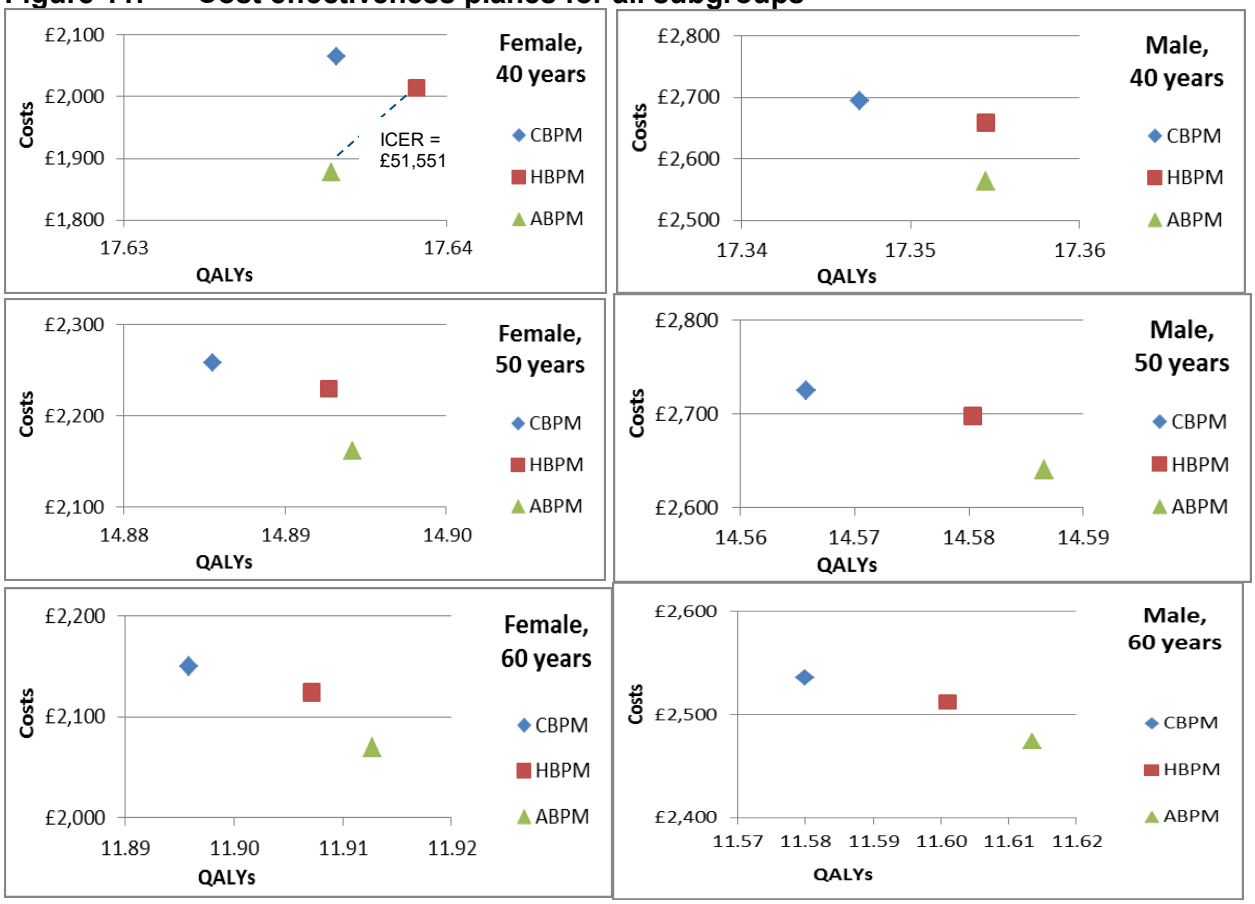
[(c)] Minor limitations / Potentially serious limitations / Very serious limitations

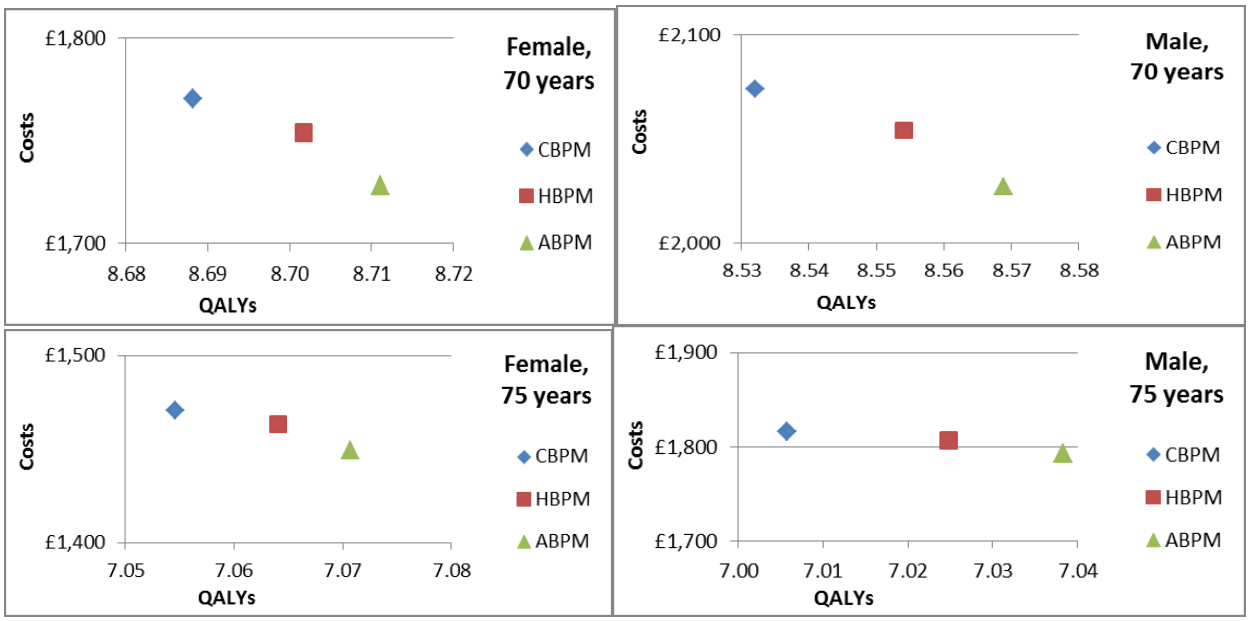
Appendix H: Health economic analysis – additional information on update to diagnostic model

Table 20: New diagnostic accuracy data analysis - deterministic results

Subgroup	Incremental QALYs vs CBPM		Incremental costs vs CBPM		Optimal strategy
	HBPM	ABPM	HBPM	ABPM	
Male, 40 years	0.004	0.003	-£49	-£159	ABPM
Male, 50 years	0.011	0.016	-£34	-£102	ABPM
Male, 60 years	0.018	0.029	-£28	-£72	ABPM
Male, 70 years	0.020	0.034	-£23	-£53	ABPM
Male, 75 years	0.018	0.031	-£13	-£29	ABPM
Female, 40 years	0.000	-0.003	-£67	-£218	ABPM
Female, 50 years	0.005	0.005	-£37	-£117	ABPM
Female, 60 years	0.009	0.014	-£34	-£97	ABPM
Female, 70 years	0.013	0.022	-£21	-£51	ABPM
Female, 75 years	0.009	0.015	-£11	-£29	ABPM

Figure 11: Cost effectiveness planes for all subgroups





ICER=incremental cost-effectiveness ratio; QALYs=quality-adjusted life years. Where a line is shown, this represents the cost-effectiveness frontier and the ICER displayed is for HBPM compared to the lower cost intervention (ABPM) because CBPM is dominated by HBPM. In all other scenarios, ABPM dominates (higher QALYs and lower costs).

Table 21: New diagnostic accuracy data analysis results (probabilistic analysis) – clinical outcome breakdown

	Cardiovascular events per 1,000					Mean per person		
	MI	UA	SA	Stroke	TIA	Life years	QALYs	Disc QALYs
Male, 40 years								
CBPM	125.5	55.4	163.4	69.5	23.4	39.12	31.51	17.35
HBPM	125.2	55.3	163.0	69.4	23.3	39.14	31.53	17.35
ABPM	125.3	55.4	163.3	69.4	23.4	39.14	31.52	17.35
Male, 50 years								
CBPM	114.1	52.2	154.6	71.0	23.2	30.42	23.87	14.57
HBPM	113.6	52.0	154.0	70.7	23.0	30.45	23.90	14.58
ABPM	113.5	52.0	153.8	70.6	23.0	30.46	23.92	14.59
Male, 60 years								
CBPM	100.5	48.2	132.1	69.7	21.3	22.32	17.12	11.58
HBPM	99.9	48.0	131.1	69.2	21.0	22.36	17.16	11.60
ABPM	99.7	47.9	130.5	68.9	20.9	22.39	17.18	11.61
Male, 70 years								
CBPM	82.8	41.1	99.4	62.7	16.7	15.27	11.45	8.53
HBPM	82.0	40.7	98.4	61.9	16.4	15.31	11.49	8.55
ABPM	81.5	40.4	97.8	61.4	16.2	15.34	11.51	8.57
Male, 75 years								
CBPM	71.2	35.8	84.5	59.3	13.8	12.26	9.02	7.01
HBPM	70.3	35.4	83.4	58.5	13.6	12.29	9.05	7.02
ABPM	69.7	35.1	82.7	57.9	13.5	12.31	9.07	7.04
Female, 40 years								
CBPM	46.0	27.0	104.9	66.8	17.4	41.99	32.97	17.64
HBPM	45.9	26.9	104.7	66.6	17.4	41.99	32.97	17.64
ABPM	46.1	27.0	105.1	66.8	17.4	41.98	32.96	17.64
Female, 50 years								
CBPM	45.2	23.7	97.5	68.7	16.6	32.93	25.06	14.89
HBPM	45.1	23.5	96.9	68.3	16.5	32.94	25.08	14.89
ABPM	45.1	23.5	96.9	68.4	16.4	32.94	25.08	14.89
Female, 60 years								
CBPM	41.9	18.0	76.6	65.7	14.2	24.32	18.00	11.90
HBPM	41.7	17.8	75.8	65.1	14.0	24.34	18.02	11.91
ABPM	41.6	17.7	75.4	64.9	14.0	24.35	18.03	11.91
Female, 70 years								
CBPM	33.3	12.0	50.7	58.3	12.0	16.59	11.87	8.69
HBPM	32.8	11.9	50.0	57.3	11.8	16.61	11.89	8.70
ABPM	32.5	11.7	49.5	56.7	11.7	16.63	11.91	8.71
Female, 75 years								
CBPM	27.2	9.1	39.8	51.5	10.9	13.28	9.24	7.05
HBPM	26.8	8.9	39.2	50.6	10.7	13.30	9.25	7.06
ABPM	26.6	8.9	38.8	50.0	10.6	13.31	9.26	7.07

Table 22: NEW diagnostic accuracy data analysis results (probabilistic analysis) – cost breakdown (mean per person)

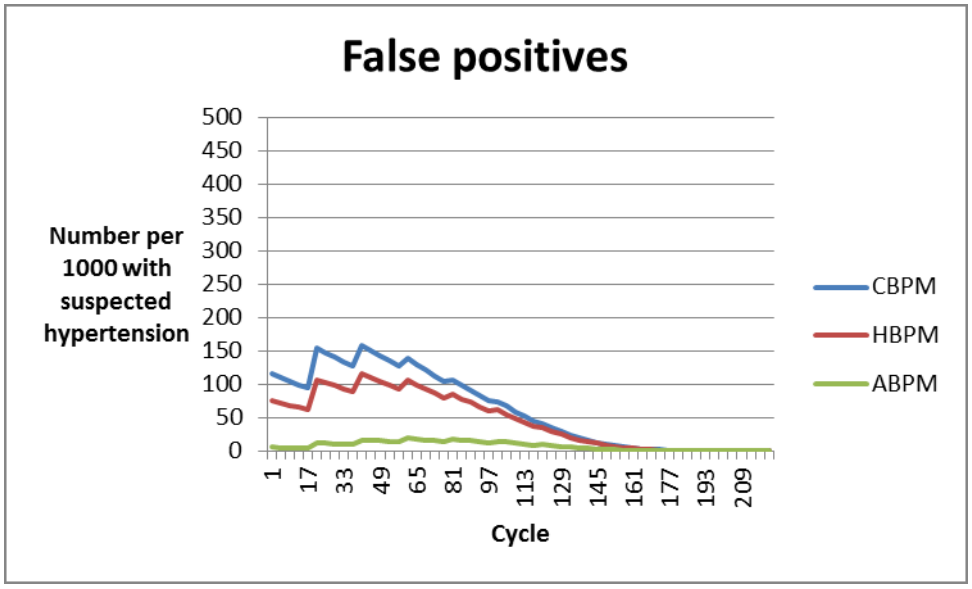
	Diagnosis	Treatment	NT check-ups	MI	UA	SA	Stroke	TIA	Total cost	Disc Cost
Male, 40 years										
CBPM	£92	£1,845	£40	£1,460	£389	£120	£2,191	£59	£6,196	£2,694
HBPM	£104	£1,784	£46	£1,454	£388	£119	£2,180	£58	£6,133	£2,659
ABPM	£190	£1,478	£73	£1,454	£388	£119	£2,181	£58	£5,941	£2,564
Male, 50 years										
CBPM	£76	£1,461	£28	£1,156	£325	£105	£2,021	£54	£5,225	£2,724
HBPM	£83	£1,436	£31	£1,148	£323	£104	£2,002	£53	£5,181	£2,698
ABPM	£139	£1,265	£46	£1,144	£322	£104	£1,996	£53	£5,068	£2,640
Male, 60 years										
CBPM	£66	£1,073	£21	£866	£260	£81	£1,701	£44	£4,111	£2,536
HBPM	£70	£1,066	£22	£859	£258	£80	£1,678	£43	£4,075	£2,512
ABPM	£109	£968	£30	£855	£257	£79	£1,665	£43	£4,006	£2,474
Male, 70 years										
CBPM	£59	£709	£16	£604	£189	£53	£1,234	£29	£2,893	£2,074
HBPM	£62	£713	£16	£597	£186	£52	£1,212	£28	£2,866	£2,054
ABPM	£91	£657	£20	£592	£185	£52	£1,197	£28	£2,823	£2,027
Male, 75 years										
CBPM	£54	£567	£12	£477	£151	£43	£1,044	£22	£2,369	£1,816
HBPM	£55	£582	£12	£470	£149	£42	£1,025	£21	£2,356	£1,806
ABPM	£79	£554	£14	£465	£147	£42	£1,012	£21	£2,333	£1,793
Female, 40 years										
CBPM	£108	£1,914	£51	£512	£230	£83	£2,185	£47	£5,130	£2,064
HBPM	£125	£1,813	£62	£511	£229	£83	£2,176	£47	£5,044	£2,014
ABPM	£240	£1,377	£101	£513	£230	£83	£2,186	£47	£4,775	£1,878
Female, 50 years										
CBPM	£83	£1,581	£33	£472	£180	£72	£2,108	£41	£4,571	£2,257
HBPM	£91	£1,544	£37	£469	£179	£72	£2,089	£40	£4,522	£2,230
ABPM	£157	£1,327	£56	£469	£178	£72	£2,088	£40	£4,387	£2,161
Female, 60 years										
CBPM	£74	£1,147	£26	£391	£114	£50	£1,781	£30	£3,613	£2,151
HBPM	£79	£1,128	£29	£387	£112	£50	£1,755	£29	£3,569	£2,124
ABPM	£129	£982	£40	£386	£111	£50	£1,742	£29	£3,469	£2,069
Female, 70 years										
CBPM	£60	£802	£16	£262	£61	£29	£1,275	£21	£2,526	£1,770
HBPM	£62	£811	£16	£257	£60	£28	£1,247	£21	£2,501	£1,754
ABPM	£90	£758	£20	£254	£59	£28	£1,227	£21	£2,457	£1,728
Female, 75 years										
CBPM	£57	£628	£14	£193	£40	£21	£989	£18	£1,960	£1,471

	Diagnosis	Treatment	NT check-ups	MI	UA	SA	Stroke	TIA	Total cost	Disc Cost
HBPM	£58	£639	£14	£190	£40	£20	£969	£18	£1,947	£1,463
ABPM	£83	£602	£16	£187	£39	£20	£956	£17	£1,921	£1,450

Table 23 : Initial misdiagnosis per 1,000 people with suspected hypertension (deterministic)

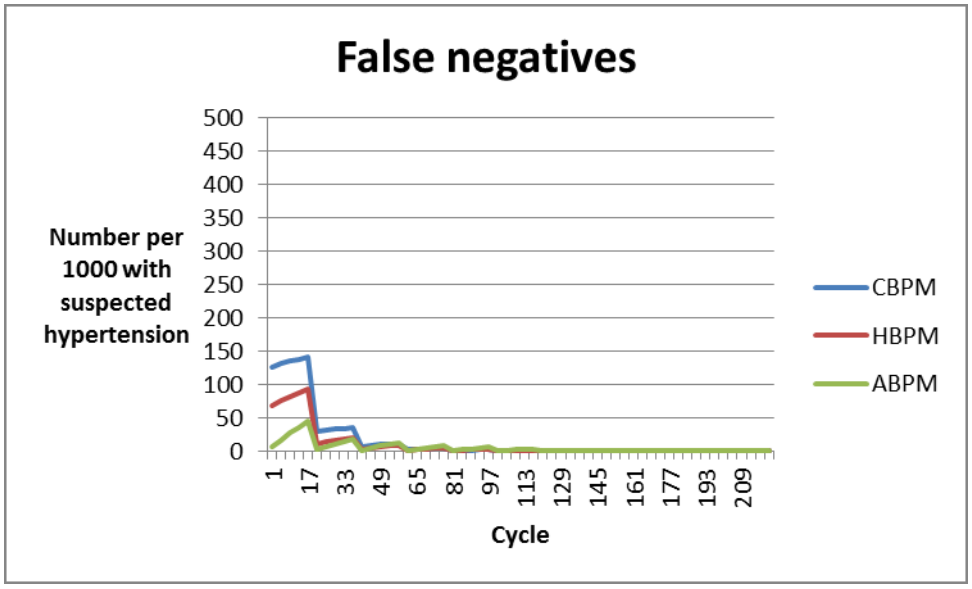
	False positives	False negatives	Total misdiagnosed	False positives	False negatives	Total misdiagnosed
40 years	**Male**			**Female**		
CBPM	190	71	260	236	35	272
HBPM	125	38	163	156	19	175
ABPM	9	4	13	12	2	14
50 years	Male					
CBPM	143	106	249	169	87	255
HBPM	94	58	152	111	47	158
ABPM	7	5	12	8	4	13
60 years	Male					
CBPM	115	126	242	146	103	250
HBPM	76	69	145	96	56	153
ABPM	6	6	12	7	5	12
70 years	Male					
CBPM	104	134	238	90	146	236
HBPM	69	73	142	59	79	138
ABPM	5	7	12	4	7	12
75 years	Male					
CBPM	86	147	233	91	144	235
HBPM	57	80	137	60	78	138
ABPM	4	7	12	5	7	12

Figure 12: Misdiagnosis over time – false positives (deterministic, male, aged 60 years)



The graph shows how the number of people in the model who have a false positive diagnosis changes over time. Overall false positives reduce over time because people develop true hypertension and become true positives. Peaks occur every 5 years when those who were diagnosed as not having hypertension have a blood pressure check-up – a certain proportion of these will have a false positive diagnosis hence the number of false positives increases. This effect diminishes over time as the number of people without a hypertension diagnosis in the model diminishes.

Figure 13: Misdiagnosis over time – false negatives (deterministic, male, aged 60 years)



The graph shows how the number of people in the model who have a false negative diagnosis changes over time. Between blood pressure check-ups (every 5 years) over time, the number of false negatives increases as people who were initially true negatives develop hypertension and so become false negatives. However, at each 5-year check-up a certain proportion of these are correctly identified as true positives when re-diagnosed and the graph sharply dips down.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 24: Studies excluded from the clinical review that were included in the previous guideline (CG127)

Study	Exclusion details
Bjorklund 2004[20]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Bobrie 2004[21]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Bobrie 2001[22]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Dawes 2006[38]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Dolan 2005[43]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Fagard 2008[48]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Fagard 2005[49]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Hansen 2005[69]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Hansen 2007[70]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Hodgkinson 2011[71]	Systematic review, references checked
Ingelsson 2006[74]	No relevant outcomes
Khattar 1999[85]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes, study conducted before the cut-off date of 2000
Kikuya 2007[88]	Incorrect study design; identifying ABPM diagnostic thresholds
Levine 1992[94]	Incorrect study design; behaviour change study investigating adherence, study conducted before the cut-off date of 2000
Mesquita-Bastos 2010[113]	Incorret study design; prognostic study related to monitoring
Niiranen 2010[129]	No relevant outcomes
Ohkubo 1997[137]	No relevant outcomes, incorrect comparison; not diagnostic accuracy, study conducted before the cut-off date of 2000
Palatini 1997[141]	Incorrect comparison; assessment not diagnosis, study conducted before the cut-off date of 2000
Sakuma 1997[155]	Incorrect population; people with a history of stroke, study conducted before the cut-off date of 2000
Schillaci 2000[158]	Incorrect study design; prognostic study predicting cardiovascular events from ABPM
Staessen 1999[165]	Incorrect study design; prognostic study predicting cardiovascular events from ABPM, study conducted before the cut-off date of 2000)
Stergiou 2007[167]	Incorrect study design; prognostic study predicting cardiovascular events from HBPM
Verdecchia 2002[180]	Incorrect study design, no relevant outcomes; prognostic study predicting cardiovascular events, no diagnostic accuracy data

Study	Exclusion details
Verdecchia 1998[181]	Incorrect study design, no relevant outcomes. Study was predicting cardiovascular events based on pulse pressure as measured by ABPM, study conducted before the cut-off date of 2000
Verdecchia 1997[182]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes, study conducted before the cut-off date of 2000

Table 25: Studies excluded from the clinical review

Reference	Reason for exclusion
Abellan-Huerta 2018[1]	Wrong intervention
Agnoletti 2014[2]	Incorrect comparison
Ahmed 2003[3]	No relevant outcomes
Almeida 2013[4]	Incorrect population
Almeida 2014[5]	Incorrect population
Altunkan 2002[7]	Incorrect comparison
Altunkan 2007[6]	No useable outcomes
Anderson 2013[8]	Literature review
Andreadis 2012[9]	No relevant outcomes
Andreadis 2017[10]	Reference standard doesn't match protocol
Appel 1990[11]	This review had a publication cut-off date of 2000
Banegas 2009[12]	Incorrect population
Banegas 2017[14]	Incorrect population, no relevant outcomes
Bassein 1985[15]	This review had a publication cut-off date of 2000
Bassein 1985[16]	This review had a publication cut-off date of 2000
Bayo 2006[17]	Incorrect population; protocol not in English
Beaubien 2002[18]	Incorrect population
Beckett 2005[19]	Incorrect population
Bjorklund 2004[20]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Bobrie 2001[22]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Bobrie 2004[21]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Botomino 2005[23]	Incorrect population
Bottini 1992[24]	This review had a publication cut-off date of 2000
Braam 2005[25]	Systematic review; references checked
Braun 1999[26]	No accuracy outcomes
Brook 2000[27]	Review of studies – no relevant outcomes
Cai 2017[28]	incorrect population (inpatients)
Cappelleri 2017[29]	Incorrect comparison
Cheng 2007[31]	Incorrect study design
Cheng 2013[30]	incorrect comparison
Chrubasik 2007[33]	Incorrect population
Chrubasik-Hausmann 2007[32]	incorrect population, no outcomes of interest
Clark 1991[34]	No useable outcomes
Clement 1998[35]	No accuracy outcomes

Reference	Reason for exclusion
Conway 1988[36]	This review had a publication cut-off date of 2000
Cox 1993[37]	This review had a publication cut-off date of 2000
Dawes 2006[38]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Di Monaco 2016[40]	incorrect population
Dieterle 1998[41]	Incorrect comparison
Divison 2004[42]	Incorrect comparison
Dolan 2005[43]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Durme 2000[44]	Incorrect comparison
Dzien 2000[45]	Incorrect population
Elijovich 1992[46]	Incorrect population
Espinosa 2011[47]	No relevant outcomes
Fagard 2005[49]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Fagard 2008[48]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Fitzgerald 1981[51]	This review had a publication cut-off date of 2000
Fitzgerald 1982[50]	Incorrect population
Floras 1981[52]	No relevant outcomes
Flores 2000[53]	Incorrect population
Gazzola 2017[55]	No relevant outcomes
Gonzalvo 2011[58]	Incorrect comparison
Gorostidi 2013[59]	Incorrect population – chronic kidney disease
Gould 1982[61]	No useable outcomes
Gould 1984[60]	Incorrect comparison, Incorrect population
Gourlay 1993[62]	This review had a publication cut-off date of 2000
Grezzana 2014[63]	incorrect population
Grezzana 2017[64]	Incorrect population
Gums 2015[65]	Incorrect comparison
Gurpreet 2008[66]	Incorrect comparison
Hamilton 2003[67]	Incorrect comparison
Hansen 1991[68]	This review had a publication cut-off date of 2000
Hansen 2005[69]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Hansen 2007[70]	Incorrect study design; not diagnostic accuracy study, prognostic outcomes
Hodgkinson 2011[71]	Systematic review; references checked
Hoegholm 1994[72]	No accuracy outcomes
Imai 1996[73]	This review had a publication cut-off date of 2000
Ingelsson 2006[74]	No relevant outcomes
Irving 2016[75]	SR included non-RCTs, incorrect comparisons
Jegatheswaran 2017[76]	Systematic review references checked, no useable outcomes
Johnson 1999[77]	This review had a publication cut-off date of 2000
Jula 1999[78]	No relevant outcomes
Kang 2015[80]	Incorrect population
Kang 2016[79]	Incorrect comparison

Reference	Reason for exclusion
Kario 2014[81]	Incorrect population
Kay 1998[82]	No useable outcomes
Kengne 2014[83]	Incorrect population
Ker 1998[84]	No useable outcomes
Khattar 1999[85]	Incorrect study design, before cut-off date of 2000
Ki 2013[86]	Incorrect comparison
Kikuya 2002[87]	Incorrect comparison
Kikuya 2007[88]	Incorrect study design
Kim 2018[89]	Incorrect population, wrong intervention
Kjeldsen 1998[90]	No relevant outcomes
Larkin 1998[92]	This review had a publication cut-off date of 2000
Lehmann 1998[93]	This review had a publication cut-off date of 2000
Levine 1992[94]	Incorrect study design, before cut-off date of 2000
Little 2002[95]	Incorrect population; not suspected hypertension
Ma 2009[97]	incorrect comparison
Macdonald 2008[98]	Incorrect comparisons
Maestri 2005[99]	Incorrect population, incorrect comparison
Mallion 2005[100]	incorrect comparison
Mandal 1997[101]	No relevant outcomes
Mann 1992[102]	This review had a publication cut-off date of 2000
Mar 1998[104]	Incorrect comparison
Masding 2001[105]	Incorrect population
Maseko 2011[106]	Incorrect population
Massierer 2016[107]	Incorrect comparison
McCall 1981[108]	Incorrect study design
McGowan 2010[109]	Incorrect population
Mengden 2011[111]	No relevant outcomes
Merrick 1997[112]	This review had a publication cut-off date of 2000
Mesquita-Bastos 2010[113]	Incorret study design
Modesti 1994[114]	This review had a publication cut-off date of 2000
Moller 2003[115]	No relevant outcomes
Møller 2003[116]	Incorrect population
Morgado 2011[117]	incorrect comparison
Mourad 2005[118]	Incorrect comparisons
Mueller 1997[119]	Incorrect population, before cut-off date
Myers 2009[122]	No relevant outcomes
Myers 2012[121]	Incorrect comparison
Nascimento 2011[123]	Not English
Nasothimiou 2012[124]	Incorrect population
Nasothimiou 2012[125]	No relevant outcomes
Nasrolahi 2013[126]	Conference abstract
Niiranen 2006[130]	No relevant outcomes
Noguchi 2013[131]	Incorrect comparison
Nolly 2008[132]	Incorrect comparison
Nong 2012[133]	Short report only

Reference	Reason for exclusion
Ogedegbe 2005[135]	Abstract
Ogedegbe 2008[136]	Incorrect population
Ohkubo 1997[137]	No relevant outcomes, incorrect comparison, before cut-off date of 2000
Owens 1999[138]	This review had a publication cut-off date of 2000
Padwal 2015[140]	Incorrect population
Palatini 1997[141]	Incorrect comparison, before cut-off date of 2000
Pang 2006[142]	No relevant outcomes
Patino 2013[144]	Non English
Pierin 2008[146]	Incorrect population
Rajzer 2007[147]	Not in English
Reino 2015[148]	Incorrect population
Reino-Gonzalez 2017[149]	Systematic review; references checked
Ringrose 2017[151]	Time duration not specified, incorrect study design
Ringrose 2018[150]	No relevant outcomes
Rodrigues 2009[152]	Incorrect population
Rutan 1992[153]	This review had a publication cut-off date of 2000
Sabater 2012[154]	No relevant outcomes
Sakuma 1997[155]	Incorrect population, before cut-off date of 2000
Salazar 2018[156]	Wrong intervention
Santamore 2008[157]	No relevant outcomes
Schillaci 2000[158]	Incorrect study design;
Schwartz 2016[159]	Incorrect population
Scisney 2009[160]	No accuracy outcomes
Selenta 2000[161]	Incorrect population
Song 2001[163]	Not in English
Souza 2011[164]	No relevant outcomes
Staessen 1999[165]	Incorrect study design, before cut-off date of 2000
Stephan 1993[166]	Not in English; This review had a publication cut-off date of 2000
Stergiou 1997[171]	This review had a publication cut-off date of 2000
Stergiou 1998[172]	This review had a publication cut-off date of 2000
Stergiou 2005[169]	Incorrect population
Stergiou 2007[167]	Incorrect study design
Stergiou 2011[168]	Conference Abstract
Thomas 2017[173]	incorrect population, no relevant outcomes
Tian 2015[174]	Incorrect comparison
Tochikubo 2003[175]	Incorrect comparison
Trudel 2009[177]	Incorrect population
Verdecchia 1997[182]	Incorrect study design, study conducted pre-2000
Verdecchia 1998[181]	Incorrect study design, no relevant outcomes, before cut-off date of 2000
Verdecchia 2002[180]	Incorrect study design, no relevant outcomes
Walma 1995[183]	incorrect comparison
Warren 2010[184]	no relevant to extract
Watson 1998[185]	Incorrect comparison
Weber 1986[186]	This review had a publication cut-off date of 2000

Reference	Reason for exclusion
Wing 2018[187]	Wrong comparisons
Wittenberg 1994[188]	No useable outcomes
Yan 2009[189]	Incorrect study design; not a diagnostic accuracy study
Yang 2016[190]	No relevant outcomes; not a diagnostic accuracy study
Zabludowski 1992[191]	This review had a publication cut-off date of 2000
Zillich 2005[193]	Incorrect comparison

I.2 Excluded health economic studies

Table 26: Studies excluded from the health economic review

Reference	Reason for exclusion
Fukunaga 2008[54]	This study is a comparative costing study comparing the addition of HBPM versus no HBPM in a population positive for hypertension on CBPM. This study was assessed as partially applicable with very serious limitations. Also given that a more applicable UK analysis[96] was available, this study was selectively excluded.
Krakoff 2006[91]	This study is a comparative costing study comparing the addition of ABPM versus no ABPM in a population screening positive for hypertension on CBPM. This study was assessed as not applicable because it is a US study and therefore costs would not be applicable to the UK. This was included in the last guideline; however, health economic literature inclusion criteria have since changed, and there was also a more applicable UK analysis available.
Pessanha 2013[145]	This study is a comparative costing study comparing the addition of ABPM versus no ABPM in a population positive for hypertension on CBPM. This study was assessed as partially applicable with very serious limitations. Also given that a more applicable UK analysis[96] was available, this study was selectively excluded.