ORIGINAL RESEARCH ARTICLE

Cost Effectiveness of Ambulatory Blood Pressure Monitoring Compared with Home or Clinic Blood Pressure Monitoring for Diagnosing Hypertension in Australia

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Abstract

Objectives The aim of this study was to evaluate the cost effectiveness of ambulatory blood pressure monitoring (ABPM) compared with home blood pressure monitoring (HBPM) and clinic blood pressure monitoring (CBPM) in diagnosing hypertension in Australia.

Methods A cohort-based Markov model was built from the Payer's perspective (Australian government) comparing lifetime costs and effectiveness of ABPM, HBPM and CBPM in people aged ≥ 35 years with suspected hypertension who have a CBPM between ≥ 140/90 mmHg and ≤ 180/110 mmHg using a sphygmomanometer and have not yet commenced anti-hypertensive treatment. The main outcome measures were incremental cost-effectiveness ratio (ICER) assessing cost per quality-adjusted life-year (QALY) and life-years (LYs) gained by ABPM versus HBPM and CBPM. Cost was measured in Australian dollars (A$).

Results Over a lifetime model, ABPM had lower total costs (A$8,491) compared with HBPM (A$9,648) and CBPM (A$10,206) per person. ABPM was associated with a small but significant improvement in the quality and quantity of life for people with suspected hypertension with 12.872 QALYs and 17.449 LYs compared with 12.857 QALYs and 17.433 LYs with HBPM, and 12.850 QALYs and 17.425 LYs with CBPM. In the base-case analysis, ABPM dominated HBPM and CBPM. In scenario analyses, at 100% specificity of HBPM, ABPM no longer remained cost effective at a A$50,000/QALY threshold. However, in probabilistic sensitivity analysis, over 10,000 iterations, ABPM remained dominant.

Conclusion ABPM was the dominant strategy for confirming the diagnosis of hypertension among Australian adults aged ≥ 35 years old with suspected hypertension. The findings of this study are important for reimbursement decision makers to support policy change and for clinicians to make practice changes consistent with ABPM recommendations in primary care.

1 Introduction

The National Health Survey, published by the Australian Bureau of Statistics, reports that one in three (34%) adults had high blood pressure in 2017–2018 [1]. Hypertension is a major risk factor for chronic conditions such as stroke, coronary heart disease, heart failure and chronic kidney disease [1]. In 2015, 5.8% of the total disease burden and

Key Points for Decision Makers
Lifetime analyses of cost and quality and quantity of life estimates (QALYs and LYs) indicated ABPM was the most cost-effective strategy for confirming the diagnosis of hypertension among adults aged ≥ 35 years old with suspected hypertension in Australia.
The results support practice change in primary care for diagnosing hypertension.

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38% of cardiovascular disease burden were attributed to high blood pressure. It was ranked in Australia's top five risk factors causing the most burden [2].

High blood pressure is defined by the National Heart Foundation of Australia guidelines as a clinic blood pressure monitoring (CBPM) results of ≥ 140/90 mmHg [3]. However, patients with suspected 'white-coat' hypertension with a reading of between ≥ 140/90 mmHg and ≤ 180/110 mmHg are known to give misleading results on CBPM. 'White-coat' hypertension relates to an elevated blood pressure reading above the normal range when measured with CBPM in the clinic but which is normal when measured using a portable device (ambulatory blood pressure monitoring [ABPM] or home blood pressure monitoring [HBPM]) [4]. ABPM is a portable monitor connected to a standard cuff on the upper arm and measures blood pressure at intervals of 20–30 minutes over a period of ≥ 24 hours, while HBPM involves a patient self-measuring blood pressure around the same time in the morning and evening at home for over 1 week using a validated and automated device [4].

In Australia, the current guidelines for diagnosing hypertension recommend ABPM and/or HBPM if CBPM is ≥ 140/90 mmHg [3]. Blood pressure measurements with ABPM and HBPM have a stronger association with cardiovascular outcomes than CBPM [3]. Furthermore, the guidelines from the United Kingdom (UK) and Canada recommend ABPM for patients with a CBPM of ≥ 140/90 mmHg for diagnosing hypertension in the case of suspected hypertension [5, 6]. ABPM and HBPM have better diagnostic accuracy than CBPM but may have higher costs to implement due to the cost of equipment or the clinician consultation service. Hence, cost-effectiveness analyses are essential before recommendations on device usage can be made in the Australian setting [7].

Internationally, studies have suggested that ABPM is more cost effective than HBPM or CBPM for adults with initially suspected hypertension [8, 9]. However, data are sparse for the long-term impact on costs and the impact of these diagnostic strategies in the Australian primary care setting to guide reimbursement decisions. A local economic evaluation is essential as the results of international studies do not apply directly to the Australian context for decision makers. This study aimed to model the long-term costs and health benefits of ABPM, HBPM and CBPM among adults suspected of hypertension from an Australian health system perspective.

2 Methods

The cost-effectiveness study was undertaken and reported according to best practice guidelines, using the Consolidated Health Economic Evaluation Reporting Standards

(CHEERS) checklist (electronic supplementary material [ESM]) [10].

2.1 Literature Search

A literature search was performed on October 17, 2019, using OVID MEDLINE, EMBASE, NHS Economic Evaluation Database and the Health Technology Assessment (HTA) agency websites for studies published from January 1, 2012, to October 17, 2019. The National Institute for Health and Care Excellence (NICE) clinical guideline on Hypertension in Adults: Diagnosis and Management undertook a systematic review up to 2011 and an economic analysis to study the diagnostic accuracy and cost effectiveness of blood pressure monitoring methods for confirming hypertension [5]. The economic analysis as part of the guideline was published in 2011 [8]. The NICE systematic review was used as the foundation review; therefore, the timeframe for a review starting in 2012 was considered appropriate. A total of 486 citations were retrieved, and one relevant cost-utility analysis of ABPM versus CBPM and versus HBPM in the United States (US) population was found relevant [9]. On searching HTA agency websites, one Canadian HTA report was found relevant [11].

The US model had the same structure as the UK model, however it also included people who were not suspected of hypertension at initial clinic BP reading [9]. The Canadian model did not have HBPM as the comparator, and the structure did not represent all the cardiovascular health states [11]. Therefore, the UK model was appropriate in the Australian setting.

2.2 Model Overview

A cost-effectiveness analysis was undertaken comparing ABPM with (i) repeat CBPM using a validated and regularly maintained non-mercury sphygmomanometer taken during a consultation with a medical practitioner and (ii) multiple HBPM measurements (over a 7-day period) taken using a validated and automated device by patients in their home. The target population consisted of a hypothetical cohort of adults aged ≥ 35 years with suspected hypertension, with a clinic blood pressure measurement between ≥ 140/90 mmHg (Grade 1, mild hypertension) and ≤ 180/110 mmHg (Grade 2, moderate hypertension) using a sphygmomanometer, who had not commenced anti-hypertensive therapy. Adults with Grade 3 severe hypertension and blood pressure of ≥ 180/110 mmHg were excluded.

A standard cohort-based Markov model was developed comparing lifetime costs, life-years (LYs) and quality-adjusted life-years (QALYs) associated with different blood pressure monitoring approaches in the proposed population

[12, 13]. The model was constructed in TreeAge Pro software (version 2021).

Figure 1 illustrates the main health states in the model and the possible transitions at regular intervals. Similar to the UK model, it was assumed in the Australian setting that it would take 3 months to confirm the diagnosis of hypertension with CBPM. Hence 3-monthly transitions (cycle length) were chosen [8]. The proposed population entering the model were adults with suspected hypertension (starting age 35 years), that is, they may be truly hypertensive or truly normotensive based on the first CBPM. The starting age of 35 years was chosen in the model as the proportion of people with hypertension increases with age, especially from the age of 35 years [8, 14].

Upon entering the model, an individual received a blood pressure measurement using ABPM, HBPM or repeat CBPM. The individual then transitioned to a diagnosed health state (true positive, true negative, false positive, false negative for hypertension), non-fatal coronary heart diseases (i.e., stable angina, unstable angina, myocardial infarction), stroke, transient-ischaemic attack health states, or death based on the underlying model probabilities.

The model was run in repeated 3-monthly cycles for the individual's lifetime, a total of 192 cycles (equivalent to 48 years), to calculate lifetime costs and QALYs. All the health states were attributed a specific cost and quality-of-life weight. Hence, the time spent in each health state was used to calculate the total costs and QALYs of ABPM,

HBPM and CBPM. The model took the perspective of the Australian health care payer, with future costs and QALYs discounted at the standard rate of 5%, and does not include any indirect costs (e.g., productivity losses due to unemployment) [15]. The authors set a willingness-to-pay threshold of A$50,000 per QALY or LY to assess the incremental cost-effectiveness ratio (ICER). Although there is no single threshold per QALY in Australia, Lowe and Dyson (2013) suggested that previous decisions by the Pharmaceutical Benefits Advisory Committee (PBAC) indicate that the willingness to pay is around A$50,000 per QALY gained [16]. Furthermore, we conducted a sensitivity analysis in line with a recent paper recommending an empirical threshold of A$28,003 per QALY in Australia [17]. All the model inputs are listed in Table 1.

2.3 Model Mechanism and Assumptions

The transition probability to a true-positive, true-negative, false-positive or false-negative health state depended on the sensitivity and specificity of the blood pressure measurement test and the prevalence of hypertension (i.e., Grade 1 and Grade 2 hypertension at 35 years). The diagnostic accuracy of ABPM, HBPM and CBPM was based on a meta-analysis conducted which used ABPM as the reference standard (100% sensitive; 100% specific) [18]. We assumed ABPM may not always work correctly, therefore, in the base case, a 5% failure rate was considered, requiring repeat testing [8,

Fig. 1 State-transition Markov model with all the health states. Individuals suspected of hypertension based on the initial CBPM reading undergo further test with either ABPM, HBPM or repeat CBPM. Based on the test results, their progression to different health states begins. Model structure adapted from Lovibond et al. with permission. Copyright © 2011, Elsevier Ltd. *ABPM* ambulatory blood pressure monitoring, *CBPM* clinic blood pressure monitoring, *CHD* coronary heart disease, *HBPM* home-based blood pressure monitoring, *MI* myocardial infarction, *SA* stable angina, *TIA* transient ischaemic attack, *UA* unstable angina
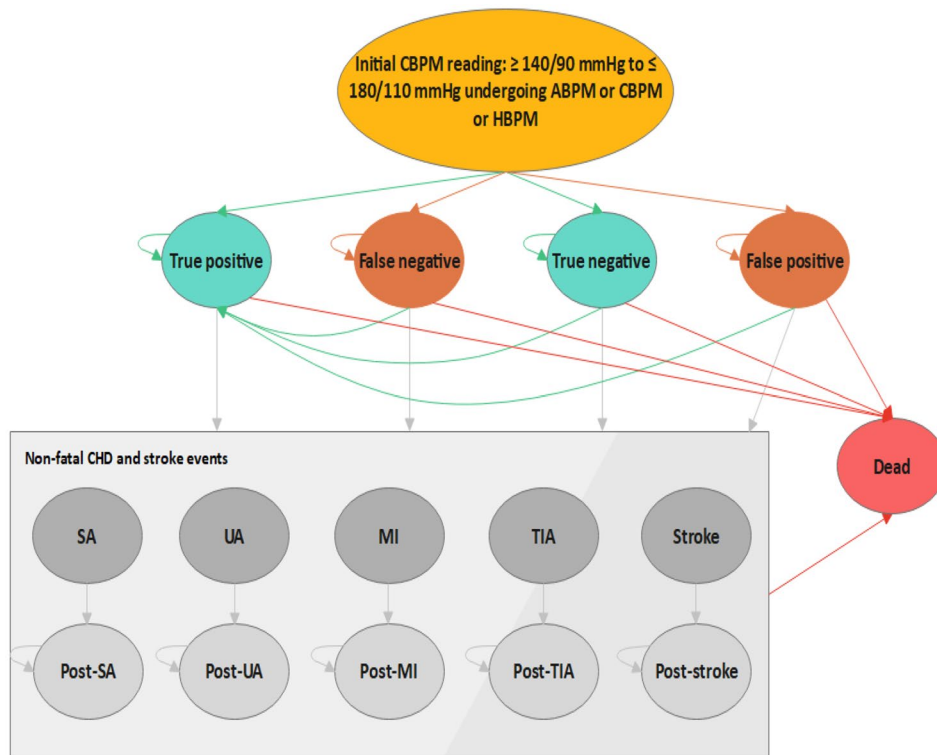
Table 1 Model inputs for base-case analysis

Input	Data	Distribution	Sources
Starting age	35 years	Fixed	[14]
Prevalence of hypertension in individuals aged 35 years	15%	Fixed	[14]
Cycle length	3 months	Fixed	[5, 8, 9]
Discount rate	5%	Fixed	[15]
Willingness-to-pay threshold	A$50,000	Fixed	[16]
Diagnosis inputs			
Sensitivity	CBPM = 78% (95% CI 46–95) HBPM = 88% (95% CI 67–98) ABPM = 100%	Beta: bounded between 0 and 1. Derived from mean and its standard error. SE was calculated using: [(upper − lower)/1.96²] Alpha and beta values were calculated as follows: alpha = mean² × [(1 − mean)/SE²] − mean, beta = alpha × [(1 − mean)/mean]	[18]
Specificity	CBPM = 72% (95% CI 20–98) HBPM = 81% (95% CI 52–96) ABPM = 100%	Beta: Bounded between 0 and 1. Derived from mean and its standard error. SE was calculated using: [(upper − lower)/1.96²] Alpha and beta values were calculated as follows: alpha = mean² × [(1 − mean)/SE²]−mean, beta = alpha × [(1 − mean)/mean]	
Failure rate	ABPM = 5% HBPM = 0%	Fixed	[5, 8, 9]
Rates			
Probability of CHD event if truly normotensive (age-dependent)	2.44–11.83%	Fixed	[5, 14]
Probability of CHD event if truly hypertensive (age-dependent)	3.88–16.36%	Fixed	
Probability of stroke event if truly normotensive (age-dependent)	0.40–4.27%	Fixed	
Probability of stroke event if truly hypertensive (age-dependent)	0.87–9.86%	Fixed	
Distribution of CHD events (age-dependent)	SA: 41–57% UA: 12–17% MI: 21–32% CHD death: 8–17%	Fixed	[5, 14]
Distribution of stroke events (age-dependent)	TIA: 15–32% Stroke: 55–69% Stroke death: 13–16%	Fixed	
Relative risk of CHD events on treatment—true positives (age-dependent)	0.64–0.71	Fixed	[5, 14]
Relative risk of stroke events on treatment—true positives (age-dependent)	0.54–0.71	Fixed	

Table 1 (continued)

Input	Data	Distribution	Sources
SMR post-SA	1.95 (95% CI 1.65–2.31)	Lognormal: the natural log of the standard error was calculated by: SE = [ln (upper 95% CI) – ln (lower 95% CI)]/(1.96*2)	[5, 22–25]
SMR post-UA	2.19 (95% CI 2.05–2.33)	The natural log of mean was calculated as: mean = ln (mean) – SE²/2	
SMR post-MI	2.68 (95% CI 2.48–2.91)		
SMR post-TIA	1.4 (95% CI 1.1–1.8)		
SMR post-stroke	2.72 (95% CI 2.59–2.85)		
All-cause mortality	0.001 (35 years) to 0.324 (100 years)	Fixed	[21]
Risk of hypertension and method of diagnosis over time			
Probability of hypertension (true negatives and false positives)	25–43%	Fixed	[14]
Probability of retesting if false negative	10%	Fixed	Assumed
Utilities			
Normotensive (age-dependent)	0.70–0.78 (95% CI 0.69–0.80)	Beta: bounded between 0 and 1. Derived from mean of a domain or total quality of life score and its standard error. SE was calculated using: [(upper – lower)/1.96²]	[26]
Hypertensive (age-dependent)	0.70–0.77 (95% CI 0.69–0.80)	Alpha and beta values were calculated as follows: alpha = mean² × [(1 – mean)/SE²] – mean, beta = alpha × [(1 – mean)/mean]	[5, 8, 9, 26–31]. The quality-of-life multipliers obtained from the UK NICE HTA were multiplied by the Australian population norm. For hypertension, the quality-of-life multiplier obtained from Beyhagi et al. was multiplied by the Australian population norm. SE reported for quality-of-life multipliers (in row below) were used for the Beta distribution
SA (age-dependent)	0.57–0.63 (95% CI 0.56–0.65)		
UA (age-dependent)	0.54–0.60 (95% CI 0.53–0.62)		
MI (age-dependent)	0.53–0.59 (95% CI 0.52–0.61)		
TIA (age-dependent)	0.70–0.78 (0.69–0.80)		
Stroke (age-dependent)	0.44–0.49 (0.43–0.50)		
Quality of life multipliers			
Hypertensive	0.994 (SE 0.05)	Fixed	[9, 28]. SE was assumed to be 5% of the mean value.
SA	0.808 (SE 0.038)		[5, 8, 9, 26, 29–31]
UA	0.770 (SE 0.038)		
MI	0.760 (0.018)		
TIA	1 (SE 0.025)		
Stroke	0.628 (SE 0.040)		
Death	0		
† *Costs (AUD)*			N/A

Table 1 (continued)

Input	Data	Distribution	Sources
Cost of CBPM	$114.60	Gamma. SD was assumed to be 20% of the point estimate. Alpha and lambda values were calculated as follows: alpha = $((mean)^2)/((mean*SD)^2)$, Lambda = $(mean)/((mean*SD)^2)$	(MBS item 23, frequency of 3 tests) [36]
Cost of HBPM	$76.40		(MBS item 23, frequency of 2 tests) [36]
Cost of ABPM	$108.90		Proposed price for ABPM. Now item 11607 [36]
Cost of hypertension treatment per cycle	$158.50		[35]
Initial cost of SA per cycle	$506.30		[5, 37]. Taken from the UK NICE 2019 guideline and converted to AUD 2020
Post-SA cost per cycle	$152.22		[5, 37]. Taken from the UK NICE 2019 guideline and converted to AUD 2020
Initial cost of UA per cycle	$15,973.11		[32]
Post-UA cost per cycle	$152.22		Assumed to be 60% of the post-MI cost. A similar assumption was made in the UK NICE 2019 guideline
Initial cost of MI per cycle	$24,119		[33]
Post-MI cost per cycle	$428.23		[5, 37]. Taken from the UK NICE 2019 guideline and converted to AUD 2020
Initial cost of TIA per cycle	$24,162.02		[34]
Post-TIA cost per cycle	$327.31		[5, 37]. Taken from the UK NICE 2019 guideline and converted to AUD 2020
Initial cost of stroke per cycle	$28,367.09		[34]
Post-stroke cost per cycle	$2890.02		[5, 37]. Taken from the UK NICE 2019 guideline and converted to AUD 2020

The table provides information on the base-case inputs used in the model along with the sources of those inputs

ABPM ambulatory blood pressure management, *ABS* Australian Bureau of Statistics, *AUD* Australian dollars, *CBPM* clinic blood pressure management, *CHD* coronary health disease, *GP* General Practitioner, *HBPM* home blood pressure management, HTA Health Technology Assessment, *MBS* Medicare Benefit Schedule, *MI* myocardial infarction, *NICE* National Institute for Health and Care Excellence, *SA* stable angina, *SD* standard deviation, *SE* standard error, *SF-6D* short-form six dimensions, *SMR* standardised mortality ratio, *TIA* transient ischaemic attack, *UA* unstable angina, *UK* United Kingdom

†All the cost values were varied by ± 20% in probabilistic sensitivity analysis

9]. It was assumed that HBPM would provide a successful diagnosis, and no failure rate was accounted for with HBPM [8, 9]. After diagnosis, an individual continued to remain in either a true-positive, true-negative, false-positive, or false-negative health state if they didn't have a non-fatal coronary heart disease, stroke, transient ischaemic attack, or death.

For normotensive individuals (true negative and false positive), the transition probability to the hypertension health state depended on the age-specific probability of becoming hypertensive over subsequent cycles. Moreover, these individuals were assumed to receive only an accurate diagnosis (i.e., true positive) if they became hypertensive irrespective of the test used. This was a conservative assumption as these individuals may have received an incorrect diagnosis, especially if the test used was CBPM or HBPM.

For individuals diagnosed as false-negative, there was a lack of evidence on their next screening period for hypertension and the probability of receiving a correct diagnosis. Hence, in the model, 10% of individuals diagnosed as false-negative with HBPM and CBPM were assumed to undergo another test at each cycle (3-monthly) and received a confirmed true-positive diagnosis, transitioning to the hypertension health state. The remaining individuals continued to be false-negative until they transitioned to the hypertension health state in the subsequent cycles. The individuals continuing in the false-negative health state had a higher risk of cardiovascular disease because their true status of hypertension was not detected. The assumption of 10% of false-negative individuals receiving a correct diagnosis at each cycle was deemed appropriate as these individuals were expected to receive an accurate diagnosis at some point in their lifetime; this also avoided the complexity of re-introducing subsequent false-positive and false-negative test results. This was a conservative assumption (against ABPM) as HBPM and CBPM, if used again for screening, would have inferior diagnostic accuracy compared with ABPM.

The risk of non-fatal coronary heart diseases, stroke and the transient ischaemic attack were dependent on the age group of the individual and their diagnosed state (i.e., hypertensive or normotensive). It was assumed that anti-hypertensive treatment would affect the transition to these health states. To this end, age-specific relative risk reductions related to anti-hypertensive medications were taken from the literature and applied to the transition probabilities to the relevant health states [5, 8, 9, 19, 20].

It was assumed that all individuals diagnosed as true positive and false positive would commence anti-hypertensive medications and remain adherent to these medications for the time horizon. However, in the real world, it is likely that individuals may have moderate medication adherence, and their risk of cardiovascular events may be higher. It was also assumed that false-positive individuals taking anti-hypertensive medications would receive no health benefits, and their future risk of hypertension and cardiovascular disease events would be similar to that of the general population.

2.4 Death

The probability of death due to other causes was estimated using 2018–2020 Australian life tables [21]. Deaths related to coronary heart disease, stroke and transient ischaemic attack were calculated using the standardised mortality ratios obtained from best evidence sources [5, 8, 9, 22–25].

2.5 Quality of Life

Following best-practice methods, the quality of life or QALY weights for each health state reported in UK and US studies were multiplied by the age-specific Australian general population short-form six domains (SF-6D) index (0 = death and 1 = full health) to produce Australian utility values required to calculate QALYs [8, 9, 26–31]. The methodology of deriving utility weights used in these studies is described elsewhere [26, 28–31]. The quality-of-life weight for the health states in the model based on the estimates derived from the economic analysis performed in other studies with reference to the primary source is summarised in Table 1.

2.6 Costs

Healthcare use associated with modelled health states was obtained from studies published in Australia and internationally (NICE HTA) [32–36]. The costs related to healthcare resources were estimated from the Australian Government—subsidised, the Medicare Benefits Schedule (MBS, 2020), published economic evaluations and costing studies [32–37]. International studies' costs were converted to 2020 Australian dollars (A$) and adjusted for purchasing power parity [38]. The studies reporting costs in Australian dollars were inflated to the 2019–2020 reference year using the appropriate health price index [39].

2.7 Modelling Uncertainty

A thorough and systematic approach was used to identify key drivers of the model. Deterministic one-way sensitivity analyses accounting for parameter uncertainty of key variables was conducted. Each variable was deviated by a constant proportion of ±10% to mitigate any issues relating to upper bound or lower bound values (such as proportions

deviating above 100% or below 0%). We conducted a probabilistic sensitivity analysis using a second-order Monte-Carlo simulation with appropriate distribution for the parameters, which generated uncertainty in the deterministic analysis (Gamma distribution for costs, Beta distribution for utilities and diagnostic accuracy and lognormal distribution for standardised mortality ratio of the cardiovascular events). Precision estimates reported were used to propagate uncertainty. The uncertainty was propagated for cost variables by changing the base-case value by a fixed proportion of $\pm$ 20% as the precision estimates were unavailable. The input values in the model were randomly propagated across 10,000 simulations.

The impact of utility values was further explored using alternative values that may be appropriate in this patient population [40]. Furthermore, the effect of the starting age in the model, the model's time horizon, the discount rate, failure rate of ABPM and the cost of HBPM and CBPM monitoring were also tested. Lastly, the assumption of 10% of false-negative patients receiving a confirmed true-positive diagnosis (on repeat testing) at each cycle was varied over the range of 0% to 20%.

3 Results

3.1 Base Case

Over a lifetime time horizon, the total direct costs associated with ABPM were A\$8,491, and the costs associated with HBPM and CBPM were A\$9,648 and A\$10,206 per person, respectively. In terms of QALYs and LYs gained, ABPM showed superior effectiveness of 12.872 QALYs and 17.449 LYs gained compared with 12.857 QALYs and 17.433 LYs gained with HBPM; and 12.850 QALYs and 17.426 LYs gained with CBPM (Table 2).

ABPM was dominant with lower costs and higher effectiveness (higher quality and quantity of life measured in QALYs and LYs) compared with HBPM and CBPM in confirming the diagnosis of hypertension among adults aged $\geq$ 35 years old with suspected hypertension (Table 2). The cost effectiveness and incremental cost-effectiveness planes of ABPM versus HBPM and CBPM with base-case assumptions are shown in Figs. 2 and 3, respectively.

3.2 Sensitivity Analysis

Tables 3 and 4 show the results of deterministic one-way sensitivity analyses of the key variables. ABPM remained dominant with lower costs and higher QALY gains when any model parameter was changed by $\pm$ 10%. Furthermore, as shown in Table 5, in most of the scenarios tested, ABPM remained a cost-effective strategy. The exceptions to this were when the specificity of ABPM was assumed to be
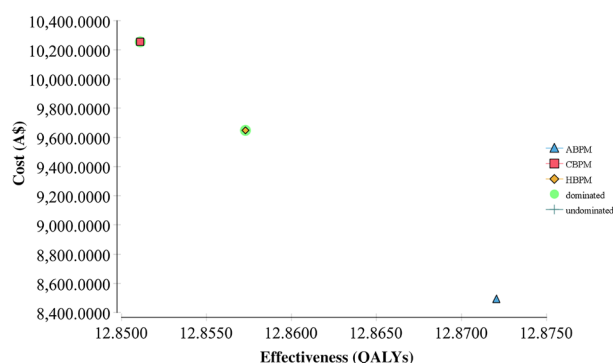

Fig. 2 Cost-effectiveness plane. ABPM has the lowest costs and highest effectiveness and is the dominant strategy compared with HBPM and CBPM. *ABPM* ambulatory blood pressure monitoring, *AU* Australian dollars, *CBPM* clinic blood pressure monitoring, *HBPM* home blood pressure monitoring, *QALYs* quality-adjusted life-years

Table 2 Base-case incremental costs and effectiveness of ABPM vs HBPM and ABPM vs CBPM in QALYs and LYs

	Cost (AUD)	Incremental cost (AUD)	Effectiveness	Incremental effectiveness	ICER
QALYs					
ABPM	\$8,491		12.872	0.0148 vs HBPM	Dominant (lower costs, higher QALYs)
HBPM	\$9,648	\$1,157	12.857	0.022 vs CBPM	Dominated (higher costs, lower QALYs)
CBPM	\$10,206	\$1,714	12.850		Dominated (higher costs, lower QALYs)
LYs					
ABPM	\$8,491		17.449	0.0159 vs HBPM	Dominant (lower costs, higher QALYs
HBPM	\$9,648	\$1,157	17.433	0.0231 vs CBPM	Dominated (higher costs, lower QALYs)
CBPM	\$10,206	\$1,714	17.426		Dominated (higher costs, lower QALYs)

The table provides incremental cost-effectiveness ratios for ABPM vs HBPM and CBPM. ABPM is cost effective with lower costs and higher QALYs/LYs and was a dominant strategy compared with HBPM and CBPM

ABPM ambulatory blood pressure monitoring, *AUD* Australian dollars, *CBPM* clinical blood pressure monitoring, *HBPM* home blood pressure monitoring, *ICER* incremental cost-effectiveness ratio, *LYs* life-years, *QALYs* quality-adjusted life-years

Fig. 3 Incremental cost-effectiveness plane. ABPM lies in quadrant D, that is, less costly, and more effective than HBPM and CBPM. *ABPM* ambulatory blood pressure monitoring, *AU* Australian dollars, *CBPM* clinic blood pressure monitoring, *HBPM* home blood pressure monitoring, *QALYs* quality-adjusted life-years
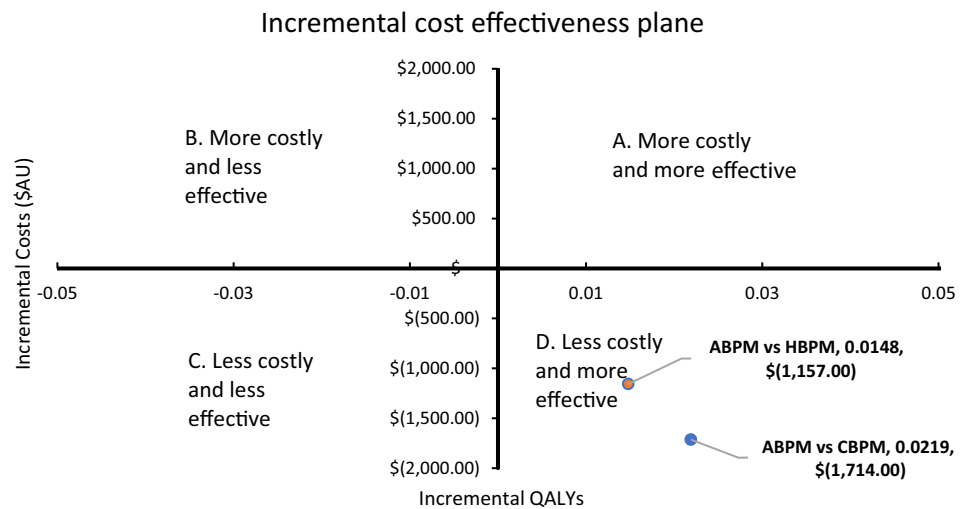

Table 3 Sensitivity analysis: varying key drivers of the economic model—ABPM vs HBPM

	Incremental cost (AUD)	Incremental benefit (QALYs)	ICER (cost/QALY)	Incremental cost (AUD)	Incremental benefit (QALYs)	ICER (cost/QALY) ABPM
	− 10%			+ 10%		
Changing utility values for normotension and hypertension health state	− $1,157	0.008	Dominant	− $1,157	0.017	Dominant
Cost of ABPM	− $1,160	0.015	Dominant	− $1,153	0.015	Dominant
Prevalence of hypertension age 35–45 y	− $1,180	0.015	Dominant	− $1,133	0.015	Dominant
Sensitivity of HBPM	− $1,137	0.015	Dominant	− $1,176	0.014	Dominant
Specificity of HBPM	− $1,666	0.021	Dominant	− $1,714	0.009	Dominant
Sensitivity of ABPM	− $1,179	0.014	Dominant	− $1,157	0.015	Dominant
Specificity of ABPM	− $527	0.007	Dominant	− $1,157	0.015	Dominant

The table provides information on deterministic sensitivity analysis of the key parameters in the model and its impact on the ICER of ABPM versus HBPM. The values of each parameter were changed by a fixed ± 10% from its base-case value. ABPM was found to be a dominant strategy compared with HBPM on changing values of most of the parameters

ABPM ambulatory blood pressure monitoring, *AUD* Australian dollars, *CBPM* clinical blood pressure monitoring, *HBPM* home blood pressure monitoring, *ICER* incremental cost-effectiveness ratio, *QALYs* quality-adjusted life-years

80%. At this specificity, ABPM was dominant over CBPM, however, it was dominated by HBPM, and the most optimal strategy would be to use HBPM. Furthermore, on increasing the specificity of HBPM and CBPM to 100%, the ICER for ABPM was A$72,052 and A$48,013 per QALY, respectively. At a willingness to pay threshold of A$50,000 per QALY, ABPM no longer remained cost effective when the specificity of HBPM was similar to ABPM.

In probabilistic analysis, on changing parameters across 10,000 simulations, ABPM still had higher QALY gains than HBPM and CBPM. The total mean cost per patient with ABPM was A$8,966 (95% CI A$7,087–A$11,093) and QALYs of 13.087 (95% CI 12.946–13.226). The total mean costs per person were

A$10,138 (95% CI A$7,667–A$13,328) and A$10,721 (95% CI A$7,767–A$15,271) with QALYs of 13.071 (95% CI 12.935–13.205) and 13.063 (95% CI 12.922–13.200) with HBPM and CBPM, respectively. At a willingness-to-pay threshold of A$28,003 and A$50,000, ABPM was an optimal strategy in 99% iterations, respectively (Fig. 4).

4 Discussion

This study assessed the cost effectiveness of ABPM, HBPM and CBPM over a lifetime model for individuals with initial raised blood pressure measured in the clinic from an Australian healthcare system's perspective. Our study findings show

Table 4 Sensitivity analysis: varying key drivers of the economic model—ABPM vs CBPM

	Incremental cost (AUD)	Incremental benefit (QALYs)	ICER (cost/QALY)	Incremental cost (AUD)	Incremental benefit (QALYs)	ICER (cost/QALY)
	− 10%			+ 10%		
Changing utility values for normotension and hypertension health state	− $1,714	0.011	Dominant	− $1,714	0.025	Dominant
Cost of ABPM	− $1,718	0.022	Dominant	− $1,711	0.022	Dominant
Specificity of CBPM	− $2,168	0.027	Dominant	− $1,261	0.017	Dominant
Sensitivity of CBPM	− $1,697	0.022	Dominant	− $1,731	0.022	Dominant
Prevalence of hypertension age 35–45 y	− $1,732	0.022	Dominant	− $1,678	0.022	Dominant
Sensitivity of ABPM	− $1,736	0.022	Dominant	− $1,714	0.022	Dominant
Specificity of ABPM	− $1,085	0.015	Dominant	− $1,714	0.022	Dominant

The table provides information on deterministic sensitivity analysis of the key parameters in the model and its impact on the ICER of ABPM versus CBPM. The values of each parameter were changed by a fixed ± 10% from its base-case value. ABPM was found to be a dominant strategy compared with CBPM on changing values of most of the parameters

ABPM ambulatory blood pressure monitoring, *AUD* Australian dollars, *CBPM* clinical blood pressure monitoring, *HBPM* home blood pressure monitoring, *ICER* incremental cost-effectiveness ratio, *QALYs* quality-adjusted life-years

that ABPM is the dominant strategy with lower costs and higher QALY gains than HBPM and CBPM. The conclusion is consistent and robust across a wide range of deterministic one-way sensitivity analyses and probabilistic sensitivity analyses of the key variables suggesting ABPM to be both cost-saving and generating more QALYs (0.002–0.03 QALYs) and LYs compared with HBPM and CBPM.

The assumption of the superior diagnostic accuracy of ABPM (100% sensitivity and 100% specificity) was the key driver as it resulted in zero misdiagnoses. In comparison, the inferior diagnostic accuracy of HBPM and CBPM led to the misdiagnosis of truly hypertensive individuals (false-negative), who thereby did not receive any benefit from the treatment as they were not prescribed anti-hypertension medications, putting them at increased risk of non-fatal cardiac events and death. Overall, it resulted in higher costs and lower QALYs with HBPM and CBPM. Furthermore, individuals who were truly normotensive but diagnosed as hypertensive (false-positive) with HBPM and CBPM received an unnecessary prescription of anti-hypertension medications, adding more costs. We understand the assumption of the perfect diagnostic accuracy of ABPM may be flawed; therefore, similar to the previous models, a 5% failure rate was allowed with ABPM to address any device failure requiring retesting and tested this assumption in the sensitivity analysis [8, 9]. Furthermore, a lower diagnostic accuracy was permitted in the sensitivity analysis. Reducing the diagnostic accuracy of the ABPM by 10% still resulted in cost savings and QALY gains, and it remained a dominant strategy. However, the conclusions in the model were sensitive to the variations in the specificity of the diagnostic tests, with HBPM becoming an optimal strategy at a specificity of 100% and when the specificity of ABPM was assumed to

be 80%. Although the variation in the diagnostic accuracy is essential to capture, the NICE 2019 hypertension guideline agreed that ABPM remains the gold standard for the accurate measurement of blood pressure in primary care and retains it as the preferred method of diagnosing hypertension [18]. Therefore, using ABPM as the model's reference standard with 100% sensitivity and specificity was appropriate.

Unlike the previous economic models, we assumed that 10% of individuals diagnosed by CBPM and HBPM as false-negative would receive an accurate diagnosis (i.e., hypertensive) upon repeat testing within the same cycle. This was a conservative assumption (against ABPM) as these individuals may remain falsely diagnosed in the model for several years, thereby increasing the risk of cardiovascular disease events, subsequent healthcare costs and lowering their QALYs. However, this assumption was deemed appropriate to make the model simple and avoid the complexity of screening these individuals again. We conducted a series of sensitivity analyses to test this assumption, and ABPM remained a cost-effective strategy.

The cost-effectiveness model presented in this study is helpful for clinicians and policymakers to understand the incremental costs and benefits and whether any changes in parameters might apply to their patients and practices and further ABPM recommendations in their clinics. Similar to the results from our study, previous studies in the UK and US also suggested ABPM be the most cost-effective strategy for individuals suspected of hypertension and recommended using it before commencing anti-hypertension medications [8, 9]. In our study, we found modest gains in QALYs and LYs per individual undergoing ABPM versus HBPM and CBPM. However, these gains will likely become significant when the prevalent population suspected of hypertension is

Table 5 Scenario analysis of the model parameters

Description	Incremental cost (AUD)	Incremental benefit (QALYs)	ICER (cost/QALY)
ABPM vs HBPM			
Base case	− $1,157	0.0148	Dominant
Starting age: 45 years	− $1,053	0.009	Dominant
Starting age: 55 years	− $939	0.007	Dominant
Starting age: 65 years	− $812	0.008	Dominant
Starting age: 75 years	− $644	0.002	Dominant
Time horizon: 10 years	− $673	0.011	Dominant
Time horizon: 20 years	− $966	0.014	Dominant
Time horizon: 25 years	− $1,040	0.014	Dominant
Time horizon: 65 years	− $1,162	0.015	Dominant
Discount rate: 0%	− $2,295	0.023	Dominant
Discount rate: 3.5%	− $1,375	0.017	Dominant
Cost of CBPM—2 consultations ($38.20*2)	− $1,156	0.015	Dominant
Cost of HBPM—1 consultation ($38.20)	− $1,143	0.015	Dominant
Utility values—EQ-5D value sets by McCaffery et al. [40]	− $1,157	0.017	Dominant
Retest rate for false negative—0%	− $1,060	0.021	Dominant
Retest rate for false negative—20%	− $1,167	0.015	Dominant
Failure rate of ABPM—0%	− $1,158	0.015	Dominant
Failure rate of ABPM—10%	− $1,155	0.015	Dominant
Failure rate of ABPM—20%	− $1,151	0.015	Dominant
Specificity of ABPM—80%	$102	0.0002	Dominated
Sensitivity of ABPM—80%	− $1,200	0.014	Dominant
Specificity of HBPM—100%	$39	− 0.0005	ICER $72,052/QALY
Sensitivity of HBPM—100%	− $1,183	0.014	Dominant
ABPM vs CBPM			
Base case	− $1,714	0.022	Dominant
Starting age: 45 years	− $1,564	0.014	Dominant
Starting age: 55 years	− $1,397	0.011	Dominant
Starting age: 65 years	− $1,214	0.013	Dominant
Starting age: 75 years	− $964	0.004	Dominant
Time horizon: 10 years	− $996	0.017	Dominant
Time horizon: 20 years	− $1,433	0.021	Dominant
Time horizon: 25 years	− $1,542	0.021	Dominant
Time horizon: 65 years	− $1,723	0.022	Dominant
Discount rate: 0%	− $3,397	0.035	Dominant
Discount rate: 3.5%	− $2,038	0.025	Dominant
Cost of CBPM—2 consultations ($38.20*2)	− $1,700	0.022	Dominant
Cost of HBPM—1 consultation ($38.20)	− $1,714	0.022	Dominant
Utility values—EQ-5D value sets by McCaffery et al. [40]	− $1,714	0.026	Dominant
Retest rate for false negative—0%	− $1,535	0.034	Dominant
Retest rate for false negative—20%	− $1,733	0.021	Dominant
Failure rate of ABPM—0%	− $1,716	0.022	Dominant
Failure rate of ABPM—10%	− $1,713	0.022	Dominant
Failure rate of ABPM—20%	− $1,709	0.022	Dominant
Specificity of ABPM—80%	− $558	0.007	Dominant
Sensitivity of ABPM—80%	− $1,758	0.021	Dominant
Specificity of CBPM—100%	$50	− 0.001	ICER $48,013/QALY
Sensitivity of CBPM—100%	− $1,763	0.02	Dominant

The table provides information on scenario analysis of important parameters in the model and its impact on the ICER. The values of each parameter were changed by a plausible range from its base-case value. ABPM was found to be a dominant strategy compared with both HBPM and CBPM

ABPM ambulatory blood pressure monitoring, *AUD* Australian dollars, *CBPM* clinical blood pressure monitoring, *EQ-5D* EuroQoL five dimensions, *HBPM* home blood pressure monitoring, *ICER* incremental cost-effectiveness ratio, *QALYs* quality-adjusted life-years
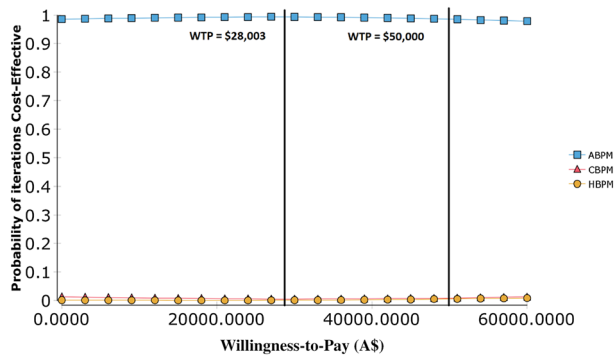
Fig. 4 Cost-effectiveness acceptability curve. The cost-effectiveness acceptability curve shows that ABPM is cost effective in most iterations. *ABPM* ambulatory blood pressure monitoring, *AU* Australian dollars, *CBPM* clinic blood pressure monitoring, *HBPM* home blood pressure monitoring

considered. Furthermore, a significant amount of cost savings is expected at a population level.

The strengths of our study are that we adopted a comprehensive and validated model published in other healthcare settings and included all relevant health states reflecting the patient progression over a lifetime. Furthermore, this is a unique Australian study that modelled longer-term costs and effects of all the diagnostic strategies relevant in the current clinical setting in the population suspected of hypertension who have a CBPM between ≥ 140/90 mmHg and ≤ 180/110 mmHg.

The results of our study should be interpreted in light of a few limitations. First, unlike the study in the US, where the starting age was 21 years, the population in our model was > 35 years of age. We did not model the younger population who might be at risk of white-coat hypertension. However, as per the Australian Bureau of Statistics, the proportion of people with hypertension increases with age, especially from the age of 35 years; hence, the model's starting age was 35 years [14]. Second, unlike the US study, we only included individuals who tested positive with initial CBPM (suspected of hypertension) and did not include those who tested negative. These individuals might have masked hypertension. The individuals with masked hypertension were out of the scope of the current study. In the US study, ABPM remained a cost-effective strategy despite including both white-coat hypertension and masked hypertension populations [9]. Third, we assumed all true-positive patients remained compliant to their anti-hypertension medications treatment regimen throughout the model; however, in the real world, patients may not remain adherent to the treatment. This may lead to uncontrolled blood pressure levels, increasing the risk of cardiovascular disease events. However, to keep the model simple and to reduce further uncertainty without better evidence on adherence rates, all

true-positive patients receiving anti-hypertension treatment were modelled with a lower probability of cardiovascular disease events. Fourth, we assumed all false-positive patients will commence on the anti-hypertension medications but will not receive any benefit, and their risk of cardiovascular disease events will be similar to that of the general population. The blood pressure-lowering drugs may reduce the risk of cardiovascular disease events at a constant proportion irrespective of pre-treatment blood pressure [19]; however, it was not well established, and the UK and the US models used the same assumption. Fifth, similar to the model by Lovibond et al. (2011) [8], once a non-fatal cardiac event (e.g., stroke) occurred, an individual remained in that health state (post-stroke) until death. Our model did not account for repeat non-fatal cardiovascular events. While this approach is typical for pragmatic reasons, any additional healthcare resource utilisation and associated quality of life would not be accounted for in the model. Lastly, there are some applicability issues in our model that used utility weights and costs of health states from other countries. This included using utilities specific to cardiac events and quality-of-life multipliers from international studies, and health state costs (for initial stable angina and post-cardiovascular events) from the UK where costs were transformed to the Australian setting using the currency converter. These substitutes were needed as no Australian-specific data were available for these abovementioned measures.

Future health economic analysis would benefit from including a younger cohort, and individuals who failed to test positive on initial CBPM (masked hypertension). Furthermore, the availability of the Australian data on population-level risk factor prevalence (hypertension, diabetes mellitus, smoking and cholesterol) to estimate the risk of coronary heart disease and cerebrovascular disease (stroke and transient ischaemic attack), and although minor, Australian-specific post-coronary heart disease, stroke and transient ischaemic disease would improve the future analysis.

5 Conclusion

This study suggests that ABPM is the most cost-effective strategy for confirming the diagnosis of hypertension among adults suspected of hypertension, compared with HBPM and CBPM in Australia. The superior diagnostic accuracy of ABPM resulted in identifying truly hypertensive and normotensive individuals, thereby substantially saving costs due to avoidance of unnecessary hypertension treatment and future cardiovascular disease events. The findings of this study are important for reimbursement decision makers to support policy change and clinicians to make practice change consistent with ABPM recommendations in primary care.

Declarations

Disclaimer This manuscript is based on a health technology assessment report commissioned by the Australian Government Department of Health: Diagnosis of hypertension using ambulatory blood pressure monitoring (ABPM) in individuals with clinic blood pressure ≥ 140/90 mmHg and ≤ 180/110 mmHg, MSAC Application 1572, Assessment Report (Commonwealth of Australia, Canberra, ACT). This manuscript was an independent assessment conducted by the authors, and the Australian Department of Health had no role in the study design, analysis and interpretation. All the opinions expressed solely belong to the authors or cited writers alone.

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Conflict of interest None.

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