
Article:
Franklin, M., Fotheringham, J., Taylor, R.S. et al. (2026) A systematic literature review of health economic modelling approaches used to evaluate treatment resistant and uncontrolled hypertension: a critical appraisal and considerations for the design of future model analyses. PharmacoEconomics. ISSN: 1170-7690

https://doi.org/10.1007/s40273-026-01625-0

PharmacoEconomics
https://doi.org/10.1007/s40273-026-01625-0

SYSTEMATIC REVIEW

A Systematic Literature Review of Health Economic Modelling Approaches Used to Evaluate Treatment Resistant and Uncontrolled Hypertension: A Critical Appraisal and Considerations for the Design of Future Model Analyses

Matthew Franklin[1] · James Fotheringham[1] · Rod S. Taylor[2] · Philip A. Powell[1] · Lise Retat[3] · Jieling Chen[4] · Juan Jose Garcia Sanchez[3] · Amy Gamble[5] · Patrice Carter[5]

Received: 28 November 2025 / Accepted: 10 May 2026

Abstract

Background and Aims Uncontrolled hypertension (ucHTN) and treatment-resistant hypertension (trHTN) are associated with a substantial increase in the risk of cardiorenal events and mortality compared with well-controlled hypertension. Treatment strategies that can optimise blood pressure management are urgently needed to improve health outcomes in ucHTN and trHTN populations; health economic models play a key role in assessing the economic value of new and existing treatments and supporting resource allocation. This systematic literature review critically assesses the construct and quality of existing health economic modelling used in the evaluation of management approaches for ucHTN and trHTN, to inform the design and development of future health economic models.

Materials and Methods This review was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist. Searches were conducted on Medline, Embase, EconLit, the Cost-effectiveness Analysis and the International HTA database. Searches were run from inception to May 2024 and re-run in February 2026. Although no date limits were placed on the electronic searches, a limit of 2005 and onwards was applied during study selection. Economic model studies were included if they assessed pharmacological or renal denervation (RDN) interventions for treatment of either ucHTN or trHTN in adult populations. Study eligibility, data extraction and quality assessment using the Drummond checklist were conducted independently by two reviewers.

Results After deduplication, a total of 2754 records were identified. Of these, 2556 did not meet the eligibility criteria after title and abstract screening; 198 full texts were reassessed for eligibility. A total of 21 modelling studies were included: 16 economic evaluations (14 cost-utility analyses, 1 cost-effectiveness analysis and 1 cost-minimization analysis), 4 burden-of-illness studies and 1 budget impact analysis. The majority of studies focused on people with ucHTN and employed a healthcare system perspective. Economic evaluations were based on treatment effects on systolic blood pressure estimated from clinical trials. Several models predicted long-term cardiorenal events and mortality on the basis of published, validated risk equations; however, these risk equations were not developed in populations with ucHTN or trHTN. Although models were generally assessed to be of good quality, models incorporated health-related quality of life and cost data from controlled hypertensive or non-hypertensive populations, rather than those with ucHTN and trHTN.

Conclusions A range of economic models were identified and considered structurally relevant. These models demonstrated that treatment related improvements in blood pressure were cost-effective and robust in scenario analysis. However, important model limitations include their lack of use of population-specific health-related quality-of-life data and risk equations which may result in underestimation of treatment cost effectiveness. To reduce uncertainty and support improved economic modelling that can accurately contextualize emerging therapies for ucHTN and trHTN, future economic model analyses in ucHTN and trHTN need appropriate population health and cost data for these underserved populations.

Extended author information available on the last page of the article

Published online: 01 June 2026

Key Points for Decision Makers

Included models generally demonstrated improvements to blood pressure were cost-effective, with these findings being robust across scenarios.

The reliance on clinical inputs from non-hypertensive and general hypertension populations likely underestimates risk of cardiovascular events for ucHTN and trHTN, which adds uncertainty to the cost-effectiveness estimates of interventions.

The existing evidence base used to populate current economic models is not ideal; future research should focus on the generation of data in the ucHTN and trHTN populations.

Despite the potential economic burden of ucHTN and trHTN, no models were identified that evaluated emerging pharmacotherapies.

1 Introduction

Hypertension (HTN) is the leading modifiable risk factor for cardiovascular disease (CVD), associated with an increased risk of adverse events including coronary heart disease (CHD), heart failure (HF), chronic kidney disease (CKD), stroke, myocardial infarction (MI), and death [1, 2]. It is estimated that over 1.4 billion adults worldwide have HTN, with only one in four having their HTN adequately controlled [3]. However, 'uncontrolled HTN' (ucHTN) is typically not well defined, and may encompass patients with HTN on one or more therapies whose blood pressure (BP) remain above target [4, 5]. A sub-group of people with ucHTN have treatment-resistant hypertension (trHTN), commonly defined as BP that remains above guideline-specified targets despite the use of three or more antihypertensive agents at optimal doses [6]. Current prevalence estimates of trHTN range from 10% in the HTN population, to 30% in those with CKD [4]. Importantly, the risk of cardiovascular, renal and all-cause mortality outcomes is increased in people with trHTN compared with people with controlled HTN (cHTN) [7, 8].

Commonly used antihypertensive agents include angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), diuretics and long-acting calcium channel blockers (CCBs) [6], many of which predate the widespread use of health technology assessment (HTA) processes. Despite the high prevalence of HTN and lack of adequate control observed by many people, few novel treatments have emerged in the past decade. However, there are several drug candidates for the treatment of ucHTN and trHTN in development which will require economic assessment as part of their HTA submission. Economic models are an integral part of HTA processes, as they allow decision-makers to contextualise and evaluate the health benefits and cost differences of emerging therapies/strategies against those in existence. Comprehensive economic models that capture the chronic, systemic nature of HTN are required, and a review of existing models is timely. To understand and interpret model outcomes, it is crucial to explore the underlying model assumptions, constructs and input parameters. The objective of the current study was to conduct a systematic literature review (SLR) to critically evaluate and summarise published health economic modelling approaches, including modelling-based economic evaluations, conducted in ucHTN or trHTN populations. This could include cost-effectiveness analysis (CEA), cost-utility analysis (CUA), cost-minimisation analysis (CMA), budget impact analysis (BIA) and burden-of-illness (BOI) analyses. The aim was to compile a compendium of evidence that may be used to inform future model design in the ucHTN or trHTN populations.

2 Methods

2.1 Study Identification

Prior to initiation of the SLR, a protocol was developed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidance [9, 10] and registered on PROSPERO (CRD42024531565) [11, 12]. The protocol included search strategies exclusively developed for each database; searches were conducted on Medline, and Embase via the OVID platform (from database inception to 1 May 2024), on the Cost-effectiveness Analysis (CEA2) database (https://cear.tuftsmedicalcenter.org/), on EconLit and on the International HTA (INAHTA) database (https://database.inahta.org/). Searches were re-run in February 2026 to ensure up-to-date evidence was sourced. Searches were developed to capture economic models, and cost and utility data; however, this publication focuses on health economic models only. All search strategies underwent a quality assessment for accuracy in spelling, syntax and line combinations using an adapted version of the PRESS checklist [13]. Additionally, supplementary searches of conference proceedings (published between 2022 and 2024), bibliographies of SLRs (published between 2019 and 2024) and relevant HTA bodies were manually screened. Finally, we employed backwards and forwards citation searching of all included articles using the CitationChaser

application (https://estech.shinyapps.io/citationchaser/). The search strategy for Medline and full details of the supplementary searches can be found in the supplementary material (Supplementary Tables S1 and S2).

2.2 Study Selection

Following the Populations, Interventions, Comparisons, Outcomes and Study type (PICOS) framework, all potentially relevant publications were assessed for relevancy against predefined criteria. To be considered eligible for inclusion, publications were required to report economic models developed for either trHTN (defined as receiving three or more antihypertensive drugs, including one diuretic, with BP over target) or ucHTN (defined as receiving one or more antihypertensive with BP over target) populations, aged ≥ 18 years. The selected populations were informed by, and follow HTA submission requirements, ensuring the populations align with both treatment guidelines which intensify treatment on the basis of the number of treatments that an individual receives, and with clinical trials which define populations on the basis of the lines of therapies described in the treatment guidelines. Only pharmacological or renal denervation (RDN) interventions were considered relevant; data pertaining to RDN was only included if it was published since 2019 to reflect that the technology and approach underlying RDN has developed in more recent years. No geographical restrictions were applied; however, publications reported in non-English language were excluded. No date limits were placed on the electronic searches; however, a date limit of 2005 and onwards was applied during study selection to ensure only the most up-to-date and relevant literature was included. The eligibility criteria were applied initially to the titles and abstracts of the identified records, and then to the full-text publications deemed potentially relevant. Assessment of eligibility was conducted independently by two reviewers at both stages, with disagreements resolved by an arbiter. The reasons for exclusion at full-text stage were documented according to the PICOS criteria. Full eligibility criteria and the list of studies excluded at full-text screening are available in the supplementary material (Supplementary Tables S3 and S4).

2.3 Data Synthesis and Quality Assessment

A data extraction grid was developed and piloted to ensure all studies were extracted consistently. Data relevant for extraction included: publication details (e.g., author, study design, location, etc.); population characteristics (e.g., population size, age, sex, comorbidities, etc.); model structure (e.g., type of model, discount rates, time horizon, etc.,); model inputs (e.g., costs, healthcare resource utilisation [HCRU], clinical inputs, probabilities, utility values); and model outcomes (e.g., incremental cost-effectiveness ratios [ICERs] and quality adjusted life years [QALYs]). Data extraction was conducted by a single reviewer; all extraction points were quality checked by a second reviewer against the original source publication. A quality assessment was conducted on each full-text study using the Drummond tool, a tool for critically appraising the methodological quality and transparency of health economic evaluations [14]. All quality assessments were performed independently by two reviewers, with disagreements adjudicated by an arbiter.

For synthesis, post-hoc categorisation of the models into three types of economic analysis was carried out: economic evaluation (CEA, CUA or CMA), BOI, or BIA. Our results are presented according to these categories. An overview of the categories is provided in Table 1.

3 Results

3.1 Study Selection

An overview of the study selection process is provided in Fig. 1. A total of 2754 records were identified after 1599 duplicate records were removed. Of these, 2556 did not meet the eligibility criteria when assessed at the title and abstract screening stage. Full texts of the remaining 198 records were screened for eligibility: 21 studies were eligible for inclusion. Reasons for exclusion are detailed in Fig. 1 and Supplementary Table S4. No additional studies were identified via supplementary searching.

Table 2 provides an overview of the 21 included studies. There were 16 economic evaluations, (14 CUAs [15–28], 1 CEA [29] and 1 CMA) [30], 4 BOIs [31–34] and 1 BIA [35]. Of the 14 CUAs, 12 evaluated RDN: of these, 7 evaluations comparing radio frequency (RF) RDN plus standard of care (SoC) to SoC alone in different healthcare settings were based on the same model [15, 19–24], while 3 evaluations were based on another model which compared ultrasound RDN (uRDN) plus SoC to SoC alone in different settings [17, 26, 27]. One CUA evaluated plasma-renin-activity (PRA) guided treatment [16], and one evaluated treatment optimisation [18]. The CEA model (Fontil et al. [29]) evaluated system-wide improvements in HTN care, and the CMA (Belsey et al. [30]) evaluated HTN treatment switching. Three of the four BOI analyses evaluated the broad economic burden of HTN, including ucHTN, across several outcomes [31, 32, 34]; Roseleur et al. [33] evaluated the economic cost of ucHTN in Australian general practice, and estimated cost-savings from reducing acute hospitalisation by improving BP control. The BIA, Ogden et al. [35], compared costs of triple-agent single-pill with two- and three-pill loose combinations.

Table 1 Types of health economic models identified in this review

Type of health economic model	Definition	Purpose(s)
Economic evaluation	• Compares the costs and outcomes of two or more care interventions to infer comparative value-for-money [97] • Types of economic evaluations include: [97] o Cost-effectiveness analysis (CEA): outcomes are based on natural health units (e.g., life years saved) o Cost-utility analysis (CUA): outcomes are based on preference-based/utility-weighted health units, which are often referred to as representing health-related quality of life, typically over a given time horizon (e.g., quality adjusted life years [QALYs]) o Cost-minimisation analysis (CMA): outcomes are assumed to be equivalent and therefore, the main focus is on costs o Cost-benefit analysis (CBA): outcomes are monetised	• To inform reimbursement decisions by HTA bodies such as NICE [80] • To inform resource allocation [97]
Burden-of-illness	• Examines the broad impact of a specific illness on a population (e.g., morbidity and mortality), which may include an assessment of economic costs, and may or may not be directly compared to an alternative illness or living without the illness to suggest the comparative burden-of-illness [98]	• To understand the broad burden of disease to inform prioritisation of care/spending to prevent/treat a given illness [98]
Budget impact analysis	• Estimates the financial consequences of adoption and diffusion of a new healthcare intervention within a specific healthcare setting or system given inevitable resource constraints [99]	• To understand the cost of introducing care interventions into a given setting/system to understand potential affordability within a given budget [82] • To compliment CEA in aiding reimbursement decisions [82]

CBA cost-benefit analysis, *CEA* cost-effectiveness analysis, *CMA* cost-minimisation analysis, *CUA* cost-utility analysis, *HTA* health technology assessment, *NICE* National Institute for Health and Care Excellence

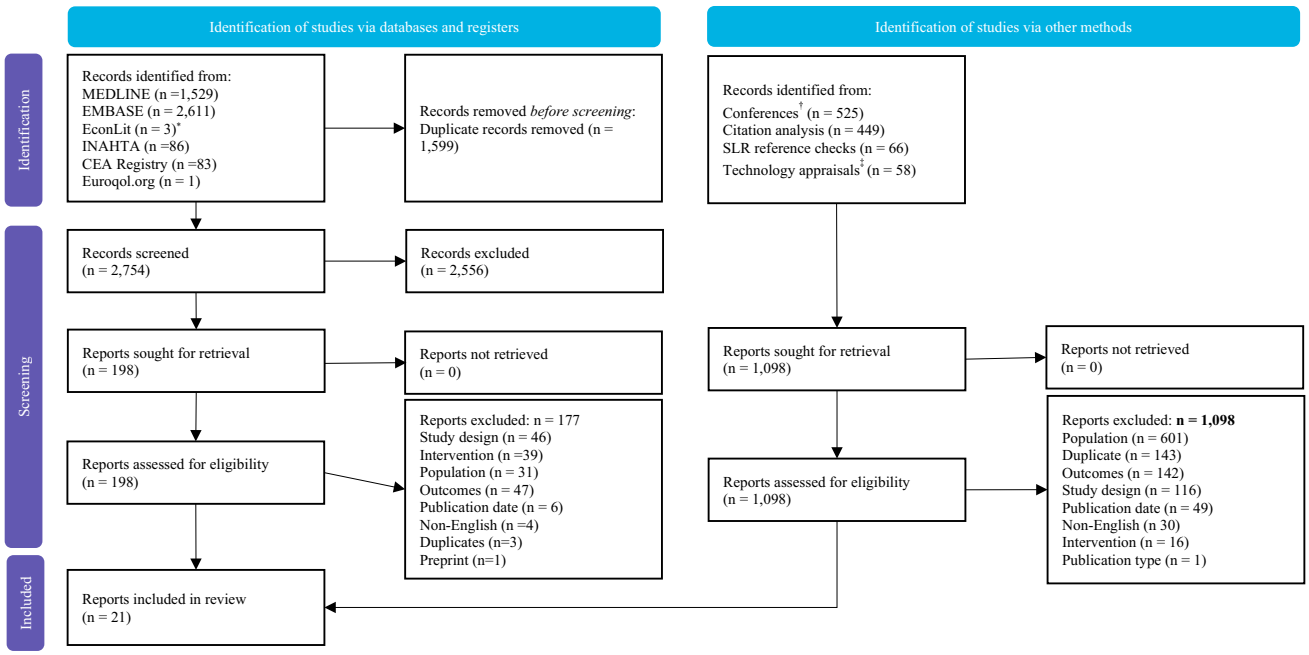

Fig. 1 PRISMA flow diagram. *CEA Registry* Cost-Effectiveness Analysis Registry, *INAHTA* International Network of Agencies for Health Technology Assessment, *SLR* systematic literature review. *In the initial search EconLit was searched via Ovid; however, in the update search, we used EBSCO. †The following conferences were searched: ACC 2024, ACNAP 2022, ASN 2022-23, ERA 2024, ESC 2022, ESH 2024, ESO 2024, ISC 2023-24, ISN 2024, ISPOR US 2024. ‡Technology appraisals were identified from the following organisations: CADTH, ICER, NICE and PBAC

3.2 Population Characteristics

The identified studies were conducted in the UK ($n = 4$) [15, 17, 18, 30], USA ($n = 5$) [16, 23, 26, 29, 35], Japan ($n = 3$) [24, 25, 31], Australia ($n = 2$) [32, 33], The Netherlands ($n = 2$) [20, 27], Belgium ($n = 1$) [27], Canada ($n = 1$) [19], China ($n = 1$) [25], Ethiopia ($n = 1$) [34], France ($n = 1$) [27], Sweden ($n = 1$) [22], Taiwan ($n = 1$) [21], Thailand ($n = 1$) [25] and Uzbekistan ($n = 1$) [28].

The characteristics of modelled populations were inconsistently reported across studies, with some studies only reporting characteristics for an overall, mixed population of general HTN, ucHTN, and no HTN, rather than providing characteristics for those with ucHTN or trHTN (Supplementary Table S5).

To be included in this SLR, studies were required to include either ucHTN or trHTN populations. Across the identified studies, ucHTN was frequently defined as systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, [17, 31–33]; however, this was not universal. Several studies defined ucHTN as those receiving one to three medications, but did not provide a BP threshold, [15, 19, 20, 23]. Kario et al. [24] and Huang et al. [21] did not explicitly state a definition of ucHTN; however, SoC was defined as a treatment regimen consisting of one, two or three antihypertensive medication classes. Lian et al. [25] also did not provide a definition, but included individuals receiving at least two antihypertensive medications for a minimum of 8 weeks. Ogden et al. [35] included patients described as uncontrolled on dual therapy without defining a BP threshold. Wu et al. [18] defined ucHTN as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg in those under 80 years old but SBP ≥ 150 mmHg or DBP ≥ 90 mmHg for those 80 years or older. Smith et al. [16] compared patients with cHTN or ucHTN with no BP definition provided, Besley et al. [30] did not define ucHTN, and Fontil et al. [29] only used SBP ≥ 140 mmHg to define ucHTN. Sharp et al. [15], Daemen et al. [20], McFarlane et al. [19], Kahan et al. [22] and Kandzari et al. [23] stated that their definitions of ucHTN incorporates those with trHTN [15, 19, 20, 23]. Xursandov et al. [28] and the three studies by Taylor et al. [17, 26, 27] included people with trHTN, defined as BP of ≥ 140/90 mmHg despite treatment with at least three antihypertensive medications, including a diuretic.

3.3 Decision Problem and Model Approach

An overview of the model approach is provided in Table 2. The aims, interventions and decision problems of the identified models are summarised, along with the model assumptions, limitations and extrapolation methods, in the supplementary material (Supplementary Table S6).

Table 2 An overview of included studies[a]

Author, year/sponsor	Analysis type	Population, definition of ucHTN/trHTN	Model aim	Model type	Model perspective	Health states included in the model	Time horizon, cycle length	Model outputs
Economic evaluations								
Belsey, 2008 [30] Merck Sharpe & Dohme Ltd	CMA	ucHTN Defined as BP ≥ 140/90 mmHg	To assess the 5-year cost consequences of treatment based on losartan, candesartan, valsartan or irbesartan, to determine the best value for money option	Cohort-level Markov model using Monte Carlo microsimulations	UK healthcare perspective	• Starting dose of ARB • Higher dose of ARB or starting dose of ARB plus thiazide • Higher dose of ARB plus thiazide • Higher dose of ARB plus thiazide plus amlodipine	NR	Total cost (discounted/undiscounted) per patient (GBP, year not reported) Losartan: £506/£536 Candesartan: £610/£662 Valsartan: £809/£869 Irbesartan: £696/£754
Daemen 2025 [20] Medtronic Plc	CUA	ucHTN Defined as prescribed 1–3 antihypertensive medications	To evaluate the cost-effectiveness of RF RDN as compared with SoC in the Dutch healthcare setting	Cohort level decision-analytic, state transition Markov model Approach built on Sharp's 2024 model [15]	Dutch healthcare payer perspective	• HTN alone • ESRD • AP/other CHD • MI • Post-MI • Stroke • Post-stroke • HF • Death	• The 10-year and lifetime horizon • Cycle length not stated	Base case, lifetime ICER= €6784 per QALY gained (Euro 2024)
Fontil 2015 [29] UCSF[b] and Lincy foundation	CEA	ucHTN Defined as SBP ≥ 140 mmHg	To compare the potential effects of system-wide isolated improvements in medication adherence, visit frequency and higher physician prescription rate on achieving BP control	Patient-level Markov, microsimulation model	USA healthcare perspective	• Office visit/no office visit • BP measurement; controlled or uncontrolled BP • Treatment intensification/no treatment intensification • Medication effect • Adherent/non-adherent to medication	• Outcomes at 52 weeks • Weekly cycle	A combination of interventions results in 18.3% of ucHTN patients achieving SBP control at 52 weeks

Table 2 (continued)

Author, year/sponsor	Analysis type	Population, definition of ucHTN/trHTN	Model aim	Model type	Model perspective	Health states included in the model	Time horizon, cycle length	Model outputs
Huang 2025 [21] Medtronic Inc	CUA	ucHTN No definition provided; however, SoC was defined as a treatment regimen consisting of one, two or three antihypertensive medication classes	To project costs and effects of RDN with SoC compared with SoC alone.	Cohort level decision-analytic, state transition Markov model Approach built on Sharp's 2024 model [15]. Also referenced Kandzari et al. [23]	Taiwanese societal perspective	• HTN alone • ESRD • AP/other CHD • MI • Post-MI • Stroke • Post-stroke • HF • Death	• Lifetime horizon • 10-year horizon • 1-month cycle length	Base case lifetime ICER = 850,932 TWD per QALY (TWD 2024)
Kahan 2025 [22] Medtronic Inc	CUA	ucHTN & trHTN No definitions provided	To evaluate the cost-effectiveness of RF RDN plus SoC compared to SoC alone in Sweden	Cohort level decision-analytic, state transition Markov model Approach built on Sharp's 2024 model [15]	Swedish healthcare payer perspective	• HTN alone • ESRD • AP/other CHD • MI • Post-MI • Stroke • Post-stroke • HF • Death	• Lifetime horizon • 10-year horizon • 1-month cycle with half-cycle correction	Base case lifetime ICER = SEK 139,280 per QALY gained (SEK 2024).
Kandzari 2024 [23] Medtronic Inc	CUA	ucHTN Defined as uncontrolled HTN despite prescription of 1–3 antihypertensive medications.	To evaluate the health-economic value of RF RDN in the US healthcare system	Cohort level decision-analytic, state transition Markov model Approach built on Sharp's 2024 model [15]	USA, Medicare payer perspective	• HTN alone • ESRD • AP/other CHD • MI • Post-MI • Stroke • Post-stroke • HF • Death	• Lifetime horizon • 1-month cycle length	Base case lifetime ICER = $32,732 per QALY (USD, year not reported)
Kario 2024 [24] Medtronic Inc	CUA	ucHTN No definition provided; however, SoC was defined as a treatment regimen consisting of one, two or three antihypertensive medication classes	To assess the cost-effectiveness of RF RDN plus SoC as compared to SoC alone in the Japanese public health insurance system	Cohort level decision-analytic, state transition Markov model Approach built on Sharp's 2024 model [15]	Japanese public healthcare payer perspective	• HTN alone • ESRD • AP/other CHD • MI • Post-MI • Stroke • Post-stroke • HF • Death	• Lifetime horizon • 10-year • 1-month cycle length	Base case lifetime ICER = ¥2,565,236 per QALY (JPY 2022)

Table 2 (continued)

Author, year/sponsor	Analysis type	Population, definition of ucHTN/trHTN	Model aim	Model type	Model perspective	Health states included in the model	Time horizon, cycle length	Model outputs
Lian 2025 [25] Shanghai Golden Leaf MedTech	CUA	ucHTN Defined as receiving at least two antihypertensive medications for a minimum of 8 weeks	To evaluate cost-effectiveness of RDN technology in Asian populations across countries with varying levels of economic development	Cohort-level Markov decision-analytic model	Western Pacific region health care payer perspectives, including mainland China, Japan and Thailand	• HTN without events • Post-coronary CHD • Post-stroke • Post-CHD and stroke • ESRD • Death	• 30-year horizon • 1-year cycle length with half-cycle correction	Base case scenario ICER for Japan = $3451, Thailand = $ 13,932, China = $19,049 per QALY. (USD 2023)
McFarlane 2025 [19] Medtronic Inc	CUA	ucHTN Defined as receiving 1–3 antihypertensive medications	To evaluate cost-effectiveness of RF RDN for ucHTN in a Canadian setting	Cohort level decision-analytic, state transition Markov model Approach built on Sharp's 2024 model [15]	Canadian (publicly funded) healthcare payer perspective	• HTN alone • ESRD • AP/other CHD • MI • Post-MI • Stroke • Post-stroke • HF • Death	• Lifetime horizon • 10-year horizon • 1-month cycle length and a half-cycle correction	Base case lifetime ICER = $11,809 per QALY (Canadian $ 2023)
Sharp, 2024 [15] Medtronic Inc	CUA	ucHTN, and trHTN Defined as receiving 1–3 antihypertensive medications	To determine cost-effectiveness of RF RDN for ucHTN patients	Cohort level decision–analytic, state-transition Markov model	UK healthcare payer perspective	• HTN alone • MI • Post-MI • AP/other CHD • Stroke • Post-stoke • HF • ESRD • Death	• Lifetime horizon • 10-year horizon • 1-month cycle length with half-cycle correction	Base case lifetime ICER = £13,482 per QALY (GBP 2022)
Smith, 2013 [16]	CUA	ucHTN No definition provided	To determine the cost effectiveness of a PRA-guided treatment strategy compared with standard care in a ucHTN population.	Patient-level Markov state transition model	USA healthcare perspective	• Uncomplicated ucHTN • Acute MI • Post-MI • CHF • Stroke • Post-stroke • ESRD • Death	• 30- year horizon • 1-year cycle length	Base case ICER = $14,497 per QALY for male patients and $40,449 per QALY for female patients (USD 2012)

Table 2 (continued)

Author, year/sponsor	Analysis type	Population, definition of ucHTN/trHTN	Model aim	Model type	Model perspective	Health states included in the model	Time horizon, cycle length	Model outputs
Taylor, 2024 [17] Recor Medical	CUA	trHTN BP ≥ 140/90 mmHg despite treatment with at ≥ 3 antihypertensive medications, including a diuretic	To assess the cost effectiveness of the addition of the Paradise uRDN System to SoC compared with SoC alone in patients with trHTN	Patient-level, state transition Markov model	UK healthcare perspective	• HTN • ESRD • AP/CHD • MI • Post-MI • HF • Stroke • Post-stroke • Recurrent stroke • Post-recurrent stroke • Death	• Lifetime horizon • 1-month cycle and half-cycle correction	Base case lifetime ICER = £5600 per QALY (GBP 2021/2)
Taylor 2025(a) [26] Recor Medical	CUA	trHTN BP ≥ 140/90 mmHg despite treatment with at ≥ 3 antihypertensive medications, including a diuretic	To determine the effect of treatment with uRDN plus SoC as compared with SoC alone in the USA	Patient-level, state transition Markov model. Approach based on the Taylor 2024 model [17]	USA healthcare system perspective	• HTN • ESRD • AP/CHD • MI • Post-MI • HF • Stroke • Post-stroke • Recurrent stroke • Post-recurrent stroke • Death	• Lifetime horizon • 1-month cycle and half-cycle correction	Base case lifetime ICER = $12,900 per QALY (USD 2022)
Taylor 2025(b) [27] Recor Medical	CUA	trHTN Defined as BP ≥ 140/90 mmHg despite treatment with at ≥ 3 antihypertensive medications, including a diuretic, a renin-angiotensin-system blocker and a calcium channel blocker at maximally tolerated dose	To estimate cost-effectiveness of uRDN plus SoC as compared with SoC alone in Belgium, France and the Netherlands	Patient-level, state-transition Markov model. Approach based on the Taylor 2024 model [17]	Belgian, French and Dutch healthcare system perspective	• HTN • ESRD • AP/CHD • MI • Post-MI • HF • Stroke • Post-stroke • Recurrent stroke • Post-recurrent stroke • Death	• Lifetime horizon • 1-month cycle and half-cycle correction	Base case lifetime ICER for Belgium = € 4426; France = € 6261 Netherlands = € 1654 per QALY (Euro 2023)

Table 2 (continued)

Author, year/sponsor	Analysis type	Population, definition of ucHTN/trHTN	Model aim	Model type	Model perspective	Health states included in the model	Time horizon, cycle length	Model outputs
Wu, 2021 [18] Barts Charity REAL-Health Cardiovascular disease	CUA	ucHTN Defined as BP ≥ 140/90 mmHg in those < 80 years Defined as BP ≥ 150/90 mmHg in those ≥ 80 years	To quantify the health and economic impacts of optimizing antihypertensive treatment	Cohort-level Markov model;	UK primary healthcare perspective	• Vascular and non-vascular death • Non-fatal major vascular event§ • Other vascular event¶	• Lifetime horizon • 10-year horizon • 5-year horizon	Lifetime gains: QALYs gained: 16,698 LYs gained: 22,228 Hospital cost savings (GBP): £41,069,942
Xursandov 2025 [28] No sponsor stated	CUA	trHTN Defined as receiving at least three doses of antihypertensive medications, including a diuretic	To identify the cost-effectiveness of RDN in low resource settings	Cohort level analytical Markov model	Uzbekistan payer perspective	NR	• 10-year horizon	Base case 10-year ICER = $4150 per QALY (USD, year not reported)
Burden of illness studies								
Asakura, 2021 [31] No sponsor stated	BOI	ucHTN Defined as BP ≥ 140/90 mmHg	To estimate the disease, productivity, and economic burden of HTN	Life table modelling/Japanese labour productivity	Japanese healthcare perspective	• Working age population	NR	PALYs lost: • ucHTN: 388,927 Value of PALYs lost (USD billion, 2017): • ucHTN = $30.8 billion LYs lost: • ucHTN = 236,321
Hird, 2019 [32] No sponsor stated	BOI	ucHTN Defined as BP ≥ 140/90 mmHg	To estimate excess mortality, years of life lost, and PALYs lost among Australians of working age (20–69 years)	Life tables models	Australian healthcare perspective	• Working age population	NR	PALYs lost: • ucHTN = 101,378 Value of PALYs lost (AUD billion, 2017): • ucHTN $21.8 LYs lost • ucHTN = 109,282

Table 2 (continued)

Author, year/sponsor	Analysis type	Population, definition of ucHTN/trHTN	Model aim	Model type	Model perspective	Health states included in the model	Time horizon, cycle length	Model outputs
Roseleur, 2023 [33] CUAL and its Member Institutions	BOI	ucHTN Defined as BP ≥ 140/90 mmHg following prescription for antihypertensive mediation	To estimate costs of ucHTN for those attending general practice and to estimate cost saved for acute hospitalization	Cohort-based cost saving model	Australian general practice	• Geneal population aged 45–74 years • Those who visit GP • Those who visit GP and have no CVD history and HTN • Estimated number of expected CVD events with ucHTN • Estimated number of CVD events with various HTN control	• 5- year risk of CVD	Total CVD costs (AUD billion, 2019–2020): • ucHTN: $1813 • SBP control to 139 mmHg: $1634 • SBP control to 129 mmHg: $1424 Expected reduction in CVD costs (AUD billion, 2019–2020): • SBP control to 139 mmHg: −$179 • SBP control to 129 mmHg: −£389
Sorato, 2022 [34] No sponsor stated	BOI	ucHTN BP ≥ 140/90 mmHg	To determine the societal economic burden of HTN at selected hospitals in Southern Ethiopia	Prevalence-based cost of illness study	Sub-Saharan Africa (Ethiopian) societal perspective	• HTN diagnosis • Active treatment • Palliative care • Death	• working age population (15–64 years of age)	LYs lost • ucHTN: 440.55
Budget impact models								
Ogden, 2014 [35] Daiichi Sankyo, Inc. .	BIA	ucHTN Defined as receiving dual therapy	To estimate the managed care budget impact of greater use of triple-agent SPC versus comparable 2- and 3-pill LDC regimens for ucHTN patients on dual therapy	Budget impact model	USA healthcare perspective	• Triple drug regimen • Pill burden (1, 2 or 3) • Adherence (low, moderate, high) • persistence • CV outcomes, related medical care costs • HTN drug costs • Total costs	• 1 year	Total cost for increased SPC = $51,034,883 as compared with $50,627,280 on 1, 2 or 3 pill regimens (USD 2012)

ACEi angiotensin converting enzyme inhibitor, *AHA* American Heart Association, *ARB* angiotensin receptor blocker, *AUD* Australian dollars, BIA budget impact analysis, *BOI* burden-of-illness, *BP* blood pressure, *CCB* calcium channel blocker, *CEA* cost-effectiveness analysis, *cHTN* controlled hypertension, *CMA* cost-minimisation analysis, *COI* cost of illness, *CUA* cost-utility analysis, *CVD* cardiovascular disease, *DBP*, diastolic blood pressure, *GBP* Great British pound, *GP* general practitioner, *HTN* hypertension, ICER incremental cost-effectiveness ratio, *JPY* Japanese yen, *LDC* loose-dose combination, *LY* life year, *mmHg* millimetre of mercury, *NA* not applicable, *NR* not reported, *PALY* productivity-adjusted life year, *PRA* plasma renin activity, *QALY* quality-adjusted life year, *RDN* renal denervation, *SBP* systolic blood pressure, *SEK* Swedish krona, *SoC* standard of care, *SPC* single-pill combination, *trHTN* treatment-resistant hypertension, *TWD* Taiwanese new dollar, *ucHTN* uncontrolled hypertension, *USD* US dollars

[a]Additional details on model structure, including model assumptions and limitations can be found in supplementary material, Supplementary Table S6

[b]Center for Vulnerable Populations at San Francisco General Hospital and UCSF Primary Care Research fellowship

Five studies used a patient-level microsimulation approach (Smith et al. [16], Fontil et al. [29], and studies from Taylor et al. [17, 26, 27]), whilst other studies modelled at the cohort-level. The majority of publications assessed an emerging technology (RDN) against standard of care (SoC); other models had varied purposes but focused mainly on policy evaluations, reflecting the limited innovation of pharmacological therapies within the HTN landscape over the last 20 years.

3.3.1 Economic Evaluations

The three CUAs by Taylor et al. [17, 26, 27] estimated the long-term cost-effectiveness of endovascular uRDN in people with trHTN. Whilst the studies by Sharp et al. [15], Daemen et al. [20], Huang et al. [21], Kahan et al. [22], Kandzari et al. [23], Kairo et al. [24], McFarlane et al. [19], Lian et al. [25] and Xursandov et al. [28] all aimed to estimate the cost-effectiveness of radiofrequency (RF) RDN in people with ucHTN, including those with trHTN. The other two CUAs investigated changes in care practices; Smith et al. [16] sought to determine the cost-effectiveness of using PRA-guided therapy as compared with SoC. Wu et al. [18] aimed to quantify the health and economic impact of treatment optimisation by comparing 'optimally treated' individuals (defined as patients receiving first-line treatment recommended by the National Institute for Health and Care Excellence [NICE], with the addition of a further two classes of antihypertensive treatments) with those who were receiving suboptimal treatment or who were untreated.

The CEA by Fontil et al. [29] aimed to determine the benefit to BP control (as determined by the percentage of patients with SBP < 140 mmHg) at the end of 1 year if system-wide improvements in medication adherence, visit frequency and higher physician prescription rates were incorporated into care. The CMA by Belsey et al. [30] aimed to determine the 'cost-minimisation' (described as 'cost-consequence' and measured as the average expenditure of treatment regimens per patient over 5 years) of different pharmacological switching strategies, which included maintaining current ARB treatment, and adding a thiazide or providing a higher dose ARB as the individual maintained DBP above 90 mmHg; they considered only treatment costs, and did not consider clinical events.

The identified CMA, CUA and CEA models were mostly cohort-level state-transition models with a healthcare payer perspective [15, 18–25, 28, 30]. The CUAs by Smith et al. [16] and by Taylor et al. [17, 26, 27]. and the CEA by Fontil et al. [29] all used a patient-level microsimulation approach.

Discount rates ranged from 1.5% [18, 19] to 5% [25]. Time horizon and cycle length varied; most of the CUA studies modelled over a lifetime horizon [15, 17–24, 26, 27], and cycle length ranged from 1 week [29] to 1 year [16, 25]. Methods of model validation were reported by most studies [15, 17, 19–25, 29]. In general, this included validation of absolute risk projections against real world values, including validation using the QRISK algorithm [15, 17, 36] and VALUE trials [37, 38].

In terms of health states and events, three CUA studies utilised similar health states: all included at least HTN, end-stage renal disease (ESRD), stroke, MI, HF, and death [15–25]. In all cases, HTN was represented as a single state, i.e., there was no ability for people to move between ucHTN and cHTN states; SBP was modelled as a continuous variable. In general, individuals commenced in their initial HTN state (e.g., 'uncomplicated HTN,' 'HTN alone') and progressed to the various CVD or renal health events over time; death was an absorbing state which individuals could transition to from all other states [15–17, 19–27]. Xursandov et al. [28] did not provide any information on health states included in their model. In the CUA by Wu et al. [18], three optimisation scenarios were modelled to project non-fatal vascular events. Belsey et al. [30] reported five different decision tree nodes in their CMA, all in relation to different treatment options. All patients entered the model on a starting dose of ARB; if DBP remained above 90 mmHg after treatment effects were applied, the individual would progress to the next treatment step [30].

3.3.2 Burden-of-Illness Studies

Three BOI studies were developed from a societal perspective and utilised a life table modelling approach [31, 32, 34], a survival model which estimates probability of mortality in a cohort of individuals over a set time period (in these examples, based on HTN status) [39]. In these studies, working-age cohorts (defined differently by each model based on the country) with HTN were followed in a model simulation over their working lifetime. The same cohorts were then re-simulated, but assumed to be free of HTN [31, 32, 34]. Sorato et al. [34] conducted a BOI analysis (which they referred to as a cost of illness [COI] study) to determine the economic burden of HTN in Ethiopian public hospitals from a societal perspective between 2010 and 2020. Both Asakura et al. [31] and Hird et al. [32] compared 'treated' to 'untreated' individuals, with the aim of understanding the productivity burden of HTN in working-age people, including those with ucHTN; individuals were treated with antihypertensives, but therapies were not clearly defined. The model used by Roseleur et al. [33] was described by its original development team [40] as a burden of disease (i.e., BOI) model, and we have aligned with this classification. The study aimed to estimate the health and acute hospitalisation costs saved over a 5-year time horizon by controlling SBP to either 129 or 139 mmHg among people with HTN attending general practices in Australia.

3.3.3 Budget-Impact Analyses

Ogden et al. [35] conducted a BIA to assess the impact over 1 year of greater use of a triple-agent single pill combination versus a 2–3 pill regimen of ARB, amlodipine and hydrochlorothiazide for people with ucHTN on dual therapy, taking into account drug costs and clinical events-related costs.

3.4 Model Inputs

3.4.1 Economic Evaluations

3.4.1.1 Clinical Treatment Effects All economic evaluations included a reduction in BP as a result of various treatments (generally provided as a mean reduction in SBP). The publications by Taylor et al. [17, 26, 27] used published efficacy and safety data from the RADIANCE-HTN TRIO trial [41]. The evaluations from Sharp et al. [15], Daemen et al. [20], Huang et al. [21], Kahan et al. [22], Kandzari et al. [23], Kario et al. [24] and McFarlane et al. [19] all used published data from the SPYRAL HTN-ON MED trail [42]. Lian et al. [25] used published data from the Netrod-HTN trial [43] and Smith et al. [16] utilised data from an RCT evaluating a PRA-guided treatment algorithm for people with treated but ucHTN [44]. Xursandov et al. used data from an RCT comparing RDN to pharmacotherapy optimization, the study outcomes were provided in the same publication as the results of the economic evaluation [28].

The three publications by Taylor et al. [17, 26, 27] reported the relative risk (RR) of CHD (RR:0.78; 95% confidence interval (CI): 0.72–0.88), stroke (RR: 0.63; 95% CI 0.56–0.71) and HF (RR: 0.54; 95% CI 0.45–0.64) per 10 mmHg SBP, based on a published SLR and meta-analysis [45], Several of the other CUAs reference the same meta-analysis [45] to inform event rates, but did not provide further details [15, 19–24]. Wu et al. [18] reported the risk of either cardiovascular (CV) events or death as a result of a reduction in BP, which were from a different published SLR [46] and included risk ratios for vascular death per 4.5 mmHg reduction in SBP (RR: 0.85; 95% CI 0.76–0.95), and risk of all vascular events or death per 5 mmHg reduction in SBP (RR: 0.83; 95% CI 0.79–0.87). Lian et al. [25] applied a fixed ratio for incidence of CHD event-free patients [47] and used data from the Netrod-HTN trial [43]. Belsey et al. [30] did not provide a reference for where their clinical data inputs for their CMA were derived from, and Xursandov et al. [28] provided event-rate data in the same publication as the model [28].

3.4.1.2 Clinical Prediction Models Clinical prediction models, or 'risk equations,' were utilised by 13 of the 14 economic evaluations to predict the risk of CV events; Xursandov et al. [28] did not mention the use of risk equations for their model. Most models utilised the Framingham Heart study to predict the risk of CHD [48], stroke [49], and HF [50] alongside the Prospective Cardiovascular Munster (PROCAM) risk equation to predict the risk of MI [51]. Additionally, the Framingham Heart study was used by Smith et al. [16] to predict the risk of HF [52], stroke [53] and acute MI [54]. Lian et al. based their model on the China-PAR project to predict the risk of CHD [55] and stroke [56]. The QRISK-3 risk equation was utilised by Wu et al. [18] to predict the risk of CVD [36]. None of the risk equations utilised by the models were derived specifically in ucHTN or trHTN populations and instead were developed in general populations with/without HTN. References to the risk equations used by each study can be found in the supplementary material (Supplementary Table S7). How models considered recurrent events was not discussed in any of the studies.

3.4.1.3 Independent Transition Probabilities In addition to the data from published risk equations, the economic evaluations also utilised data from clinical trials. All of the CUAs except Xursandov et al. [28] reported transition event probabilities of moving from a CV or renal event to another event, or death [15–24, 26, 27]. Most referenced the same studies for their values for transition from stroke to mortality [57], and from MI to HF [50]. Lian et al. [25] categorised events into AMI, HF and sudden cardiac death on the basis of a fixed proportion derived from prior studies [47, 58]. Wu et al. [18] reported the annual risks of individuals moving between health states, such as major vascular events, other vascular events, vascular and non-vascular death. These transition inputs were quantified through the probability of non-vascular death, hazard ratios for CV risk in those without previous CVD and CVD mortality and morbidity rates [18]. The CEA by Fontil et al. [29] reported the probabilities for treatment intensification and treatment persistence.

3.4.1.4 Utility Inputs for Cost-utility analyses The CUA by Wu et al. [18] did not report utility values used per state: QoL was estimated on the basis of patient characteristics by a linear regression model using EQ-5D-3L questionnaire data. Xursandov et al. [28] made no reference to utility values or QoL in their publication. All other CUAs reported utilities linked to several health states. The methods used by the source publications to elicit utility values were mainly based on indirect methods, such as EuroQol's EQ-5D. However, it was not always clear which specific version of the EQ-5D was used nor the exact publication the source utility value was derived. Only Lian et al. [25] reported the use of country-specific preference-based value sets.

In the models evaluating cost-effectiveness of uRDN in the UK, Belgium, France and The Netherlands, Taylor et al. [17, 27], used the same source utility values in both

Table 3 Utility inputs utilised by the cost-utility analysis studies

Health state [Utility range]	Utility aspect	Daemen 2025[20]	Huang 2025[21]	Kahan 2025[22]	Kandzari 2024[23]	Kario 2025[24]	Lian 2025[25]	McFarlane 2025[19]	Sharp 2024[15]	Smith 2013[16]	Taylor 2024[17]/ 2025(b)[27]
Angina (stable) [Range; 0.71 to 0.96]	**Utility value**	**0.80**	**0.83**	**0.76**	**0.84**	**0.83**	**-**	**0.71**	**0.81**	**-**	**0.96**
	Measure	EQ-5D	EQ-5D-5L	EQ-5D	Unclear	EQ-5D-5L	-	Unclear	Unclear	-	EQ-5D
	Value set	N/R	N/R	N/R	N/R	N/R	-	N/R	N/R	-	N/R
	Population	CVD	General	CAD	General	General	-	General	CVD risk	-	Chest pain
	Ref	100	101	102	103	101	-	103,104	63	-	105
Angina (unstable) [Range; 0.71 to 0.91]	**Utility value**	**0.80**	**-**	**0.76**	**0.74**	**-**	**-**	**0.71**	**0.77**	**-**	**0.91**
	Measure	EQ-5D	-	EQ-5D	Unclear	-	-	Unclear	Unclear	-	Unclear
	Value set	N/R	-	N/R	N/R	-	-	N/R	N/R	-	N/R
	Sample	CVD	-	CAD	T2DM	-	-	Geneal	CVD risk	-	CVD risk
	Ref	100	-	102	62	-	-	103,104	63	-	63
Angina + ESRD [0.84]	**Utility value**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**0.84**
	Measure	-	-	-	-	-	-	-	-	-	Unclear
	Value set	-	-	-	-	-	-	-	-	-	NR
	Population	-	-	-	-	-	-	-	-	-	Unclear
	Ref	-	-	-	-	-	-	-	-	-	63,105,106
ESRD [Range; 0.61 to 0.92]	**Utility value**	**0.65**	**0.78**	**0.71**	**0.63**	**0.78**	**0.61**	**0.71**	**0.72**	**0.63**	**0.92**
	Measure	EQ-5D-3L	Unclear	EQ-5D	N/R	Unclear	N/R	Unclear	Unclear	N/R	Unclear
	Value set	N/R	N/R	N/R	N/R	N/R	Chinese EQ-5D-5L value set	N/R	N/R	N/R	N/R
	Population	ICU	CKD + dialysis¶	CKD + dialysis	CKD + dialysis	CKD + dialysis¶	CKD + dialysis	Geneal	CKD	CKD + dialysis	CKD
	Ref	107	Unclear	108,109	110	Unclear	111	103,104	106	110	106
HF [Range; 0.64 to 0.88]	**Utility value**	**0.67**	**0.85**	**0.71**	**0.71**	**0.76**	**-**	**0.64**	**0.68**	**0.71**	**0.88**
	Measure	EQ-5D-3L	NR	EQ-5D-3L	Unclear	Unclear	-	Unclear	EQ-5D	Unclear	EQ-5D
	Value set	N/R	NR	N/R	N/R	N/R/	-	N/R	N/R	N/R	N/R
	Population	CHF	NR	HF	HF	HF¶	-	General	HF	HF	HF
	Ref	112	113	114	115,116	Unclear	-	103,104	117	115,116	117
HF + ESRD [0.80]	**Utility value**	-	-	-	-	-	-	-	-	-	**0.80**
	Measure	-	-	-	-	-	-	-	-	-	Unclear
	Value set	-	-	-	-	-	-	-	-	-	NR
	Population	-	-	-	-	-	-	-	-	-	Unclear
	Ref	-	-	-	-	-	-	-	-	-	106,117
HTN* [Range; 0.94 to 1.00]	**Utility value**	**1.0**	**0.98**	**1.0**	**0.96**	**0.98**	**0.94**	**0.96**	**1.0**	**0.96**	**1.0**
	Measure	Assumed	Assumed	Assumed	Assumed	Assumed	EQ-5D-5L	Unclear	Assumed	Unclear	Assumed
	Value set	-	-	-	-	-	Chinese EQ-5D-5L value set	N/R	-	N/R	-
	Population	-	-	-	-	-	HTN	General	-	General	-
	Ref	N/A	N/A	N/A	N/A	N/A	118	103	N/A	103	N/A
HTN + ESRD [0.92]	**Utility value**	-	-	-	-	-	-	-	-	-	**0.92**
	Measure	-	-	-		-	-	-	-	-	Unclear
	Value set	-	-	-		-	-	-	-	-	N/R
	Population	-	-	-		-	-	-	-	-	CKD
	Ref	-	-			-	-	-	-	-	106
MI (≤6 months) [Range; 0.63 to 0.90]	**Utility value**	**0.63‡**	**0.83‡**	**0.84•**	**0.76**	**0.83‡**	**-**	**0.73**	**0.76**	**0.76**	**0.90**
	Measure	EQ-5D-3L	EQ-5D-5L	EQ-5D-3L	Unclear	EQ-5D-5L	-	Unclear	Unclear	Unclear	Unclear
	Value set	N/R	N/R	N/R	N/R	N/R	-	N/R	N/R	N/R	N/R
	Population	General (older people)	General	Post MI	Unclear	General	-	General	CVD risk	Unclear	Unclear
	Ref	119	101	120	61,62	101	-	103,104	63	61,62	63,105
MI (>6 months) [Range; 0.73 to 0.88]	**Utility value**	**-**	**-**	**-**	**0.88**	**-**	**-**	**0.73**	**0.88**	**0.88**	**-**
	Measure	-	-	-	N/R	-		Unclear	N/R	N/R	-
	Value set	-	-	-	N/R	-		N/R	N/R	N/R	-
	Population	-	-	-	Unclear	-		General	trHTN	Unclear	-
	Ref	-	-	-	64,65	-		103,104	66	64,65	-
Stroke [Range; 0.54 to 0.85]	**Utility value**	**0.73**	**0.54**	**0.68**	**0.63**	**0.58**	**0.79**	**0.69**	**0.63**	**0.63**	**0.85**
	Measure	EQ-5D-3L	EQ-5D-3L	EQ-5D-3L	Unclear	EQ-5D-5L	NR	Unclear	Unclear	Unclear	Unclear
	Value set	N/R	N/R	N/R	N/R	N/R	Chinese EQ-5D-5L value set	N/R	N/R	N/R	N/R
	Population	Stoke	Stroke	Stroke	HTN/HF/ Stroke	General	HTN	General	CVD risk	HTN/HF/ Stroke	CVD risk /stroke
	Ref	121	122	123	64,67	101	58	103,104	63	64,67	63,124
Stroke + ESRD [0.78]	**Utility value**	-	-	-	-	-	-	-	-	-	**0.78**
	Measure	-	-	-	-	-	-	-	-	-	Unclear
	Value set	-	-	-	-	-	-	-	-	-	NR
	Population	-	-	-	-	-	-	-	-	-	T2DM
	Ref	-	-	-	-	-	-	-	-	-	62

Table 3 key					
Utility value	Value provided as model input				
Measure Tool cited in the source publication	EQ-5D-5L	EQ-5D-3L	EQ-5D [non-specified version]	Unclear [Unclear across source publications which tool has been used to derive the provided utility input for the model]	Not reported [The source publication does not clearly cite which tool has been used]
Value set	Value set cited in the model publication				
Population	Population included in the source publication which the utility is derived from.				
Ref	The reference of the publication cited by the model				

‡Where no reference is provided, this is a stated cohort assumption
‡Timeframe for MI not provided in the model publication
¶The publication cites multiple publications for the utility value; however, it is unclear which publication is relevant to the value cited.
Abbreviations: CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; ESRD, end-stage renal disease; HF, heart failure; HTN, hypertension; ICU, intensive care unit; N/A, not applicable; N/R, not reported,

publications (Table 3). However, in the publication evaluating the model in a USA setting, Taylor et al. [26] did not report utility values; they stated age-related decrements were derived for specific health states from multiple published sources [59, 60]. Sharp et al. [15] and Taylor et al. [17, 27] based some of their utility inputs on the same source publications. However, the utility inputs used in the Taylor et al. [17, 27] model were observably higher than the inputs utilised in the Sharp et al. [15] model. This difference could be attributed to Taylor et al. [17, 27] reporting age-adjusted utility values, whereas Sharp et al. [15] presented the utility values as originally reported in the source papers, before any adjustment. Kahan et al. [22], Kandzari et al. [16], Lian et al. [25] and McFarlane et al. [19] all reported that utility values were adjusted for age, whereas Daemen et al. [20], Huang et al. [21] and Kario et al. [24] made no reference to age adjustment. Smith et al. [16], Sharp et al. [15] and Kandzari et al. [23] reported the same utility values for MI (0.76) [61–63], post-MI (0.88) [64–66] and stroke (0.63) [63, 64, 67], despite using different sources. The utility values incorporated into the models are provided in Table 3.

3.4.1.5 Cost Inputs Cost inputs included in the models were mostly associated with health states and their management costs. The publication by Taylor et al. [17] which evaluated the cost-effectiveness of RDN in a UK setting provided more granular costs relating to inpatient and outpatient care as well as diagnostic and monitoring costs. Xursandov et al. [28] did not provide any cost inputs for their model. Across the majority of studies, costs were identified from a range of different sources, including databases [15–17, 19–27], and published observational studies [15–17, 19–23, 25–27] which were relevant to the geographic locations that the model was evaluating. Other cost inputs were derived from economic models [16, 17, 19, 20, 22, 23, 25–27], SLRs [16, 23, 26] and treatment guidelines [15]. With the exception of Xursandov et al. [28], all studies reported input costs for RDN therapy, although they were informed by different sources and were provided in the relevant currency for their respective settings. The cost of different classes of antihypertensive treatments were used as inputs in several models; however, these varied [17, 18, 27, 30]. Wu et al. included hospitalisation costs [18]. Only the CUA by Taylor et al. [17] and the CEA by Fontil et al. [29] explicitly included 'per unit' HCRU-associated cost inputs (for example, costs associated with GP consultations or outpatient visits); all inputs reported by Taylor et al. [17] were associated with ESRD.

3.4.2 Burden-of-Illness Studies

3.4.2.1 Clinical Treatment Effects Sorato et al. [34] incorporated clinical inputs, including the risk of all-cause mortality amongst those with treated, ucHTN and untreated HTN from a cohort study examining the association between HTN control-status and the risk of mortality in the USA [68], despite the model being based in Ethiopia. Asakura et al. [31] and Hird et al. [32] took an analogous approach to modelling excess mortality, despite their respective settings (Japan and Australia). Roseleur et al. [33] incorporated clinical inputs including the risk of CV events taken from an Australian national primary healthcare database [69], plus the 5-year risk of CVD events per 10 mmHg reduction in SBP (RR: 0.8; 95% CI 0.77–0.83) derived from an SLR and meta-analysis of RCTs evaluating BP-lowering treatment to assess the extent of the effect of BP-lowering on CVD [70]. All trials evaluating BP-lowering treatments, including trials assessing the use of antihypertensives for indications other than HTN, were eligible for inclusion in the meta-analysis [70]; therefore, the clinical treatment effect inputs used in the Roseleur et al. [33] model were not from specific populations with ucHTN or trHTN.

3.4.2.2 Clinical Prediction Models Sorato et al. [34] included data from risk equations, referencing both the Framingham Heart study risk equation to predict CV risk [71] and an additional risk equation predicting CV death, MI and stroke in a general population with/without HTN (Supplementary Table S7) [72]. Roseleur et al. [33] incorporated data from the Framingham Heart study [71] to predict CV risk. Asakura et al. [31] and Hird et al. [32] did not utilise risk equations.

3.4.2.3 Independent Transition Probabilities Asakura et al. [31] and Hird et al [32]. both reported the probability of all-cause mortality by age and sex in patients with ucHTN and in patients with untreated HTN. In each study the probability inputs were taken from national life tables published in the corresponding model country and for the corresponding HTN state (cHTN versus ucHTN) [73, 74].

3.4.2.4 Cost Inputs Sorato et al. incorporated hospitalisation cost inputs, including the cost of antihypertensive treatments, diagnostics and monitoring and outpatient care [34]. Most cost inputs were based on hospital price lists or were identified from published SLRs. Roseleur et al. reported the cost of hospitalisation associated with various CV events [33]. Most cost inputs were identified from databases or published literature, including modelling papers [75], SLRs [76] and observational studies [77]. Input costs were not provided by Asakura et al. [31] and Hird et al. [32].

3.4.3 Budget Impact Analyses

3.4.3.1 Clinical Treatment Effects Ogden et al. [35] did not incorporate clinical treatment effects and instead modelled

different treatment adherence levels on the basis of medication possession ratios from published estimates.

3.4.3.2 Clinical Prediction Models Ogden et al. [35] did not utilise risk equations, nor report independent transition probabilities. The model considered adherence in terms of a patient's medication possession ratio, assuming that lower daily pill burden is associated with higher patient persistence with therapy. Estimates were drawn from several publications relating to treatment adherence. Risk of CV-related events and healthcare costs were modelled on the basis of these estimated levels of adherence.

3.4.3.3 Cost Inputs Ogden et al. [35] reported the cost of antihypertensive treatments and outpatient care, and reported healthcare resource utilisation inputs, which included the number of CV-related hospitalisations and emergency room admissions per year [35], identified in an observational study [78].

3.5 Model Outputs

Outputs across all identified models are summarised in Table 2 and in the supplementary materials. Details on sensitivity analysis and scenario analysis conducted can also be found in the supplementary materials (Supplementary Tables S8, S9 and S10).

3.5.1 Economic Evaluations

Incremental cost-effectiveness ratios (ICERs), defined as cost per QALY, were reported by 13 of the 14 CUA studies [15–17, 19–28]; only Wu et al. [18] did not report an ICER value (Table 4). Based on the reported ICER values and the cost-effectiveness threshold in each location (including Europe, North America and Asian settings), RDN was assessed as cost-effective compared with SoC in people with ucHTN [15, 19, 21–25] and trHTN [17, 20, 26–28]. For example, the two studies evaluating RDN in a UK healthcare setting, reported that RDN was considered cost-effective based on the UK cost-effectiveness threshold at time of publication of £20,000 per QALY [15, 17]. Additionally, across all studies, RDN had over 90% probability of being cost-effective on the basis of the probabilistic sensitivity analysis. Despite studies conducting sensitivity analysis and determining key drivers, these were not reported with consistency. Generally, when scenario analyses were reported, the most common scenario examined how proposed differences in SBP reduction would impact the ICER. Xursandov et al. [28] and Lian et al. [25] were the only publications to report the ICERs corresponding to the author-stated key model drivers. (Table 4).

PRA-guided treatment for people with ucHTN as compared with SoC in the USA demonstrated that the ICER remained below the accepted approval threshold in the USA in all scenarios [16]. Wu et al. [18] reported the QALYs gained by optimising antihypertensive therapy in patients with HTN (Table 4). The study also reported the life years gained, hospital care costs savings, non-fatal major vascular and other vascular events avoided and vascular deaths avoided (Supplementary Table S8) [18]. The CEA by Fontil et al. [29] reported the proportion of people achieving BP control after improving medication adherence, visit frequency and higher physician prescription rates. Belsey et al's CMA reported the median cost per patient of various ARB treatments in people with ucHTN (Supplementary Table S8) [30].

3.5.2 Burden-of-Illness Studies

Hird et al. [32] and Asakura et al. [31] reported the productivity-adjusted life years (PALYs) and the value of PALYs. In both studies, the value of productivity loss owing to HTN was greater in the untreated populations compared with patients with treated, ucHTN [31, 32]. The main outputs reported by Sorato et al. [34] were the cost of lost productivity due to premature mortality and HTN morbidity in an overall HTN population, rather than by ucHTN or trHTN status. However, the model predicted the years of life lost in these populations to formulate the overall cost of lost productivity; the paper did not report a sensitivity analysis [34]. The analysis by Roseleur et al. [33] reported the expected reduction in CVD costs over 5 years by controlling SBP in 8.7 million Australian patients to either 139 mmHg or 129 mmHg (AUD $179 million and $389 million, respectively).

3.5.3 Budget Impact Analyses

The BIA by Ogden et al. [35] reported that a 15% increase in a single triple-therapy pill in patients with ucHTN on dual therapy would result in two fewer CV events, slightly lower all-cause medical costs and higher pharmacy costs, with a net-neutral economic impact from a healthcare plan perspective over 1 year.

3.6 Author-Reported Model Limitations

All the included studies reported limitations and assumptions (Supplementary Table S6). Generally, limitations included issues with generalisability, variations in BP targets, lack of input data and limitations in treatment effects. In terms of generalisability, several studies flagged that their model projections or adjustments and model input data were based on populations that were not specific to the model population [15,

Table 4. Economic evaluations reporting ICER values

Author, year	Country (currency, year)	HTN status	Intervention	ICER (cost/QALY)	Incremental cost	Incremental QALY	Discount rate	Cost-effectiveness threshold (source)	Probability, cost effective at threshold	Author-reported key drivers	Deterministic sensitivity analysis[a]
Daemen 2025 [20]	Netherlands (EUR, 2024)	trHTN	RF RDN	6784	4137	0.61	N/R	20,000 EUR (Dutch health economic guidelines [125])	99%	• Adjustment factor for stroke from SBP reduction • Costs for RF RDN therapy	• ICER = 2473 at 9.9 mmHg SBP reduction from baseline • ICER = 3247 at 8.7 mmHg SBP reduction versus control at 24 months
Huang 2025 [21]	Taiwan (TWD, 2024)	ucHTN	RDN	850,932	216,381	0.25	3%	1,000,000 TWD 3,000,000 TWD (World Health Organization; 1–3 times GDP per capita [126])	77.4% 100%	• Adjustment factor for stroke from SBP reduction • Costs for RF RDN therapy • Adjustment factor for HF from SBP reduction	• At 0% discount rate, ICER = 390,359 • At 5% discount rate ICER = 1, 331,269
Kahan 2025 [22]	Sweden (SEK, 2024)	ucHTN	RDN	139,280	63,136	0.45	3%	500,000 SEK (reimbursement for pharmaceuticals in Sweden [127])	100%	• Adjustment factor for CHD from SBP reduction • Costs for RF RND therapy • Adjustment factor for HF from SBP reduction	In one-way sensitivity analysis the ICER ranged from 100,428 to 192,195 SEK per QALY

Table 4. (continued)

Author, year	Country (currency, year)	HTN status	Intervention	ICER (cost/QALY)	Incremental cost	Incremental QALY	Discount rate	Cost-effectiveness threshold (source)	Probability, cost effective at threshold	Author-reported key drivers	Deterministic sensitivity analysis[a]
Kandzari 2024 [23]	US (USD, N/R)	ucHTN	RF RDN	32,732	11,275	0.34	3%	50,000 USD 150,000 USD (American College of Cardiology guidance [128])	100% 100%	• RF RDN therapy costs • Adjustment factors for baseline stroke and CHD risk	• ICER ranged from $33,040 to $70,846 per QALY for patients aged 45–80 years. • ICER ranged from $31,884 to $41,524 per QALY for baseline SBP of 140–174mmHg ICER ranged from $28,779–$36,725 for 20% lower baseline mortality to 20% higher baseline mortality
Kario 2024 [24]	Japan (JPY, 2022)	ucHTN	RF RDN	2,565,236	923,723	0.36	2%	5,000,000 JPY (Central Social Insurance Medical Council [129] and C2H [130])	98%	• Costs for RDN therapy • Adjustment factor for risk of HF, CHD • SBP reduction in therapy arm	ICER exceeded 5, 000 000 JPY if RDN therapy exceeded 2, 376,741 JPY or the SBP reduction was less than 2.8mmHg

Table 4. (continued)

Author, year	Country (currency, year)	HTN status	Intervention	ICER (cost/QALY)	Incremental cost	Incremental QALY	Discount rate	Cost-effectiveness threshold (source)	Probability, cost effective at threshold	Author-reported key drivers	Deterministic sensitivity analysis[a]
Lian 2025 [25]	China, Japan, Thailand (USD, 2023)	ucHTN	RDN	China: 19,049 Japan: 15,821 Thailand: 18,525	China: 7091 Japan: 5889 Thailand: 6896	0.37	5%	China: 1.52 GDP per capita Japan: 0.1 GDP per capita Thailand: 1.90 GDP per capita (World Health Organization [126])	Japan: 98%, Thailand: 66% China: 91%	• Discount rate	At 3% discount rate, • ICER = 19,586 in China • ICER = 41,542 in Japan • ICER = 12,287 in Thailand
McFarlane 2024 [19]	Canada (CAD, 2023)	ucHTN	RDN	11,809	6031	0.51	1.5%	22,000 CAD (CADTH guidance [131])	100%	• Adjustment factor for stroke risk • Costs for RDN therapy • Adjustment factor for CHD risk	• ICER = 8497 at 6.6mmHg • ICER = 12, 034 at 4.8mmHg • ICER = 10,138 at 5.7mmHg • ICER = 6097 at 9% discount rate • ICER = 19,521 at 3% discount rate • ICER = 33, 406 at 5% discount rate
Sharp, 2024 [15]	UK (GBP, 2022)	ucHTN	RDN	13,482	4763	0.35	3.5%	20,000 GBP 30,000 GBP (NICE 2022 [132])	92.7% 100%	• Adjustment factor for stroke and CHD from SBP • Costs for RDN therapy	ICER = 7865 with 9.9 mmHg SBP reduction from baseline

Table 4. (continued)

Author, year	Country (currency, year)	HTN status	Intervention	ICER (cost/QALY)	Incremental cost	Incremental QALY	Discount rate	Cost-effectiveness threshold (source)	Probability, cost effective at threshold	Author-reported key drivers	Deterministic sensitivity analysis[a]
Smith, 2013 [16]	US (USD, 2012)	ucHTN (male)	PRA-guided treatment	14,497	1571	0.11	3%	100,000 USD (no reference)	No	• Treatment effect • Cost of the PRA	• ICER = 1110 with 20mmHg SBP reduction • ICER = 43,078 with 5mmHg SBP reduction
		ucHTN (female)	PRA-guided treatment	40,449	2232	0.06					
Taylor , 2024 [17]	UK (GBP, 2021/2022)	trHTN	RDN	5600	3523	0.63	3.5%	20,000 GBP 30,000 GBP (NICE 2022 [132])	No – state that over 1000 iterations there is >99% probability that uRDN is cost-effective	• Relative risk of stroke per 10mmHg SBP reduction	ICER = 6087 with SBP reduction of 5 mmHg
Taylor 2025(a) [26]	US (USD 2022)	trHTN	RDN	12,900	7600	0.59	3%	15,000 USD 50,000 USD (No reference)	73.2% 100%	• Maintenance cost of stroke • Maintenance cost of HF	Despite uncertainty around parameters uRDN remained cost effect (i.e., under the $50,000 CE threshold)
Taylor 2025(b) [27]	Belgium, France, Netherlands (EUR, 2023)	trHTN, Belgium	RDN	4426	4291	0.97	3%	40,000 EUR [133]	99%	• Risk of stroke per 10mmHg SBP reduction (for all three countries) • Risk of HF per 10mmHg SBP reduction (for Belgium and France) • Stroke mortality (for the Netherlands)	N/R
		trHTN, France	RDN	6261	5897	0.90	2.5% up to 10 years, 1.5%	50,000 EUR [134]	99%		
		trHTN, The Netherlands	RDN	1654	1594	1.00	3%	20,000 EUR [125]	99%		

Table 4. (continued)

Author, year	Country (currency, year)	HTN status	Intervention	ICER (cost/QALY)	Incremental cost	Incremental QALY	Discount rate	Cost-effectiveness threshold (source)	Probability, cost effective at threshold	Author-reported key drivers	Deterministic sensitivity analysis[a]
Wu, 2021 [18]	UK (GBP 2019)	ucHTN	HTN treatment optimisation	N/R	N/R	N/R	1.5%	N/R	N/R	• Optimization of antihypertensive and statin treatment • Age	N/R
Xursandov 2025 [28]	Uzbekistan (USD, NR)	trHTN	RDN	4150	1700	0.40	N/R	5000 USD 7000 USD (1x GDP per capita) 10,000 USD (no reference)	78% 85% 92%	• Discount rate • Cost of RDN procedure	Discount Rate: 0% ICER = 2800 6% ICER = 5900 Cost of RDN: −20% ICER = 2100 +20% ICER = 6200

CAD Canadian dollar, *CHD* coronary heart disease, *CE* cost-effectiveness, *EUR* Euro, *HF* heart failure, *GDP* gross domestic product, *GBP* Great British Pound, *HTN* hypertension, *ICER* incremental cost-effectiveness ratio, *JPY* Japanese Yen, *mmHg* millimetre of mercury, *NICE* National Institute for Health and Care Excellence, *N/R* not reported, *PRA* plasma renin activity, *QALY* quality-adjusted life year, *RDN* renal denervation, *RF* radiofrequency, *SBP* systolic blood pressure, *SEK* Swedish krona, *trHTN* treatment resistant hypertension, *TWD* Taiwan dollar, *ucHTN* uncontrolled hypertension, *uRDN* ultrasound renal denervation, *UK* United Kingdom, *USD* United States dollar

[a]Where provided we extract the ICER aligned to the key drivers, alternatively we provide those noted by the author in the main body of the publication

16, 18, 19, 21, 22, 24, 25]. For example, Smith et al. [16], Sharp et al. [15] and McFarlane et al. [19] raised concerns that their model projections were primarily derived from the Framingham cohort, and therefore may not be applicable to all patients with ucHTN and trHTN or represent the country-specific population. Similarly, Lian et al. [25] noted that they utilised risk equations based on a Chinese population, yet they also evaluated the model in Japanese and Taiwanese settings. A frequently reported limitation was that the model represented a simplification of clinical reality; for example, some sequelae of HTN, such as peripheral vascular disease were not captured. [19, 21, 24, 25] Several models raised limitations surrounding treatment effects [15–17, 29, 30]. This included a lack of consideration for differences in BP-lowering effects between different drug classes and between drugs within the same class [29, 30]. The majority of studies flagged that the assumption of long-term treatment effects with no treatment waning may be considered a limitation [15–17, 19, 21, 22, 24, 25], yet authors investigating RDN highlighted that this assumption is supported by evidence that RDN demonstrates a stable, long-term treatment effect.

3.7 Author-Reported Model Assumptions

Several studies made assumptions relating to treatment effects, including that treatment effects would be maintained either over a long-term period [16] or over a lifetime [15, 19–24, 26]. Several studies made assumptions on the cost of RDN treatment as pricing had not yet been established in the geographic locations of interest [24, 25, 27]. Belsey et al. [30] assumed that all patients were being treated with ARBs as a first-line therapy and that the BP lowering effects were consistent across the drug class. Two studies made assumptions relating to adherence [29, 35]. Fontil et al. [29] acknowledged that adherence and persistence to medication would be imperfect but assumed that this would be captured in the average treatment effect and would not need to be modelled separately. Ogden et al. [35] assumed that lower daily pill burden was associated with higher persistence with medication. Other assumptions made per study are summarised in the supplementary material (Supplementary Table S6).

3.8 Risk of Bias Assessment

Most studies were considered to have low risk of reporting bias (Supplementary Table S11); areas of uncertainty were mainly related to the data collection domain, and the analysis and interpretation domain. This consisted of unclear or lack of reporting on the methods used to estimate inputs and the justification of the choice of model, the key input parameters, and decisions around discounting rates. Additionally, the risk of bias assessment concluded that there was unclear reporting across most studies on whether generalisability issues were addressed.

4 Discussion

4.1 Principal Findings

The SLR identified multiple studies that demonstrated improvements in BP control were cost-effective in populations with ucHTN or trHTN, and where tested, findings were robust across scenarios [15–28]. In addition, studies concluded that ucHTN places a significant economic burden on society. However, most studies did not incorporate input parameters specific to the ucHTN/trHTN populations in their models; therefore, the true burden may be underestimated, as people with ucHTN or trHTN have greater underlying risk of CV events. Despite the detrimental outcomes associated with ucHTN and trHTN, few novel treatments have been evaluated for their economic value, with only RDN therapy being compared with SoC. Importantly multiple studies utilised the same models to evaluate cost-effectiveness of RF RDN [15, 19–24] and uRDN [17, 26, 27], in different geographical settings. The other models identified in this review assessed benefits associated with switching between existing treatments or optimising current care practices, demonstrating a lack of new emerging pharmacological therapies available to alleviate burden associated with ucHTN and trHTN.

4.2 Discussion of the Evidence

The SLR identified a variety of model types, consisting mainly of economic evaluations, including 14 CUAs [15–28], a CEA [29], and a CMA [30]. CUAs utilising the QALY are typically the preferred method of economic evaluation to inform reimbursement decisions by HTA bodies, although where these are not possible, generalised CEAs (i.e., not using preference-based effectiveness metrics such as the QALY) can be accepted [80]. CMAs are not typically utilised owing to their outdated approach and the unlikeliness of two healthcare interventions providing the exact same benefit: although the benefit point estimates may be the same for any care interventions being compared, the distribution around these estimates are unlikely to be the same. Thus, a key CMA assumption that benefits are equivalent between care interventions being compared is typically violated [81]. This SLR only identified one CMA; despite limitations regarding this study, it met our pre-defined eligibility criteria and was therefore included and critiqued [30].

The review only identified one BIA [35], although these are increasingly used to complement CEA in aiding reimbursement decisions by investigating the affordability of

interventions within a specific setting or system [82]. The SLR also identified four BOI models [31–34], which are less commonly used in reimbursement decisions; however, they can be used to provide researchers and decision-makers with relevant information regarding the cost components associated with illness and clinical burden, whilst describing healthcare spending and indirect costs of disease [83]. They can also be a source of model inputs for health economic evaluations.

Overall, the economic evaluations took similar approaches, using published risk equations to estimate baseline risk of CV events, and using data from clinical trials and estimated relative risk reduction from published meta-analyses. The majority incorporated clinical inputs associated with risk of stroke, HF, MI, ESRD and death. Importantly, none of the risk equations or transition probabilities cited within the modelling studies were developed in populations with ucHTN and/or trHTN, or incorporated ucHTN or trHTN as a risk factor [36, 48, 49, 51–54, 71, 72, 84]. The application of risk equations based on non-hypertensive and cHTN populations likely underestimates the true risk of CV events, as it is generally accepted that the risk of cardiovascular, renal and all-cause mortality outcomes are increased in people with trHTN compared with those with cHTN [7, 8]. Several studies acknowledged this limitation, reporting they were obliged to use data from populations different to those being modelled, owing to a lack of population-specific inputs. Therefore, future research should focus on evidence generation in the ucHTN and trHTN populations.

Several of the included studies acknowledged that their models were limited by the over-simplification of HTN, noting omission of some sequelae, such as peripheral vascular disease [19, 21, 24, 25]. However, additional consequences such CKD, HTN-mediated organ damage or cognitive decline were not considered [85–87]. Future models should take a more comprehensive approach to reflect the systemic impact of HTN as well as the potential benefits that treatment may bring to the overall health of individuals. In addition, all models identified modelled SBP on the basis of office-based BP measurement. Accurate outcomes prediction is paramount to economic modelling. However, in terms of long-term outcomes such as CV events, home- and ambulatory-BP monitoring have been shown to offer improved predictive power compared with office-based measurement [88]. Similarly, ambulatory BP is more informative about risk of all-cause death and CV death than office-based BP [89]. The reliance of modelling to-date on office-based BP therefore introduces uncertainty, and future models would benefit from including alternative BP metrics.

The CUA models evaluating interventions in ucHTN used similar utility values for health states; however, the utility inputs ranged considerably across the models. Two models included different values despite using the same source publications [15, 17]. The difference was attributed to the trHTN model presenting age-adjusted values [17], rather than the values reported in the original source publication [15]. It is notable that the use of country-specific preference-based value sets was only reported by Lian et al. [25]; however, this information may be reported in the original source publications rather than in the modelling paper itself. In the wider literature, it has been shown that utilities for health states can vary between different country-specific value sets, highlighting the importance of using country-specific value sets when selecting utility values for modelling, which should be considered in future models [90]. Most models attempted to incorporate data from appropriate geographic populations; only McFarlane et al. [19] acknowledged that not all HRQoL data were from Canadian-specific populations in their limitations. Additionally, the methods used to elicit utility values varied; however, most models utilising indirect methods such as the EQ-5D to measure health-related quality of life (NICE's preferred method) [81]. Frequently, several citations were provided for one utility value, making it difficult to determine the true source; however, the source publications were generally in appropriate populations for the given health state of interest, although not in ucHTN or trHTN groups. Improved transparency on where values are derived and which country-specific value set has been used would aid model critique and interpretation.

Three BOI studies assessed the effects of HTN with different treatment and control status on productivity [31, 32, 34]. Despite heterogeneity in location and types of outcomes reported, all three studies using a life table-modelling approach concluded that ucHTN places a significant economic burden on society and that measures to control BP are needed. The main outputs reported by two of these models were related to the number and value of PALYs lost or saved as a metric of productivity [31, 32]. The other study (Sorato et al.) [34] used sex-specific life-expectancy in Ethiopia multiplied by sex-specific employment rate based on monthly average income as a metric of productivity. The PALY is a metric similar to the QALY; however, PALYs adjust for impairment in productivity rather than health-related quality of life [91, 92]. Although the use of PALYs has been suggested for the purposes of economic evaluation, the identified studies only used PALYs to estimate the burden-of-illness (i.e., no comparison of care interventions to reduce this productivity loss at a given cost in the given condition) and thus are categorised as BOI studies rather than economic evaluations. Of note, the study by Sorato et al. [34] referred to itself as a COI study despite using disability-adjusted life years and having a focus on productivity (i.e., a broader burden focus than costs alone); thus, we classed the study as a BOI rather than COI analysis.

The cost of intervention was reported as a key driver in the majority of models which evaluated RDN [15, 19–24, 28]. The cost of PRA-guided treatment evaluated by Smith et al. [16] was also reported as a key cost driver. However, despite authors frequently stating that the ICER estimates remained within the approval thresholds, they did not consistently report the ICER corresponding to changes in treatment cost. We recommend that sensitivity analyses around the key drivers should be conducted and reported transparently.

The models all suggest that RDN and PRA-guided therapy are cost-effective interventions. Importantly, the cost-effectiveness of RDN was evaluated across a range of geographic locations and remained below the cost-effectiveness threshold in all locations. Moreover, all models demonstrated that the interventions evaluated had over a 90% probability of being cost-effective at the given approval thresholds. The suggestion is that the outputs from these models are potentially robust and resilient to uncertainty in the input parameters.

Finally, definitions of ucHTN and trHTN varied between studies. Though most studies reported a target BP threshold of 140/90 mmHg, the definitions of ucHTN did not indicate whether they required patients to have been previously treated. This inconsistency impacts upon model comparison and interpretation; a clear and precise definition would improve generalizability. The definition of trHTN was more consistent across studies: a BP measurement of $\geq$ 140/90 mmHg and at least three or more antihypertensive therapies, including a diuretic, which aligns with published global HTN practice guidelines [93].

4.3 Strengths and Limitations

Although our review followed robust SLR methodology, yielding a comprehensive overview of published evidence, some limitations should be considered. The PICOS criteria excluded non-English language publications, introducing potential evidence-source bias (e.g., the results may not be transportable to countries that report their evidence in a non-English language). However, previous research has shown that restricting searches to the English language has little impact on the results and conclusions of SLRs [94, 95]. To mitigate the risk of potential evidence-source bias, no restrictions were applied to study location and the review identified and included data from a range of countries. Although there is extensive literature exploring the benefit of improved BP management in more general HTN populations, our study focused on populations with ucHTN or trHTN and employed restrictive search criteria. Accordingly, several HTN studies and their associated models were not captured in our searches (e.g., Zhang et al. [79]) or were excluded. We also acknowledge that lifestyle modifications or non-pharmacological changes in disease management (e.g., team-based care), which were not included in this review, can contribute to improvements in BP. Additionally, owing to differences in definitions and reporting of ucHTN, we cannot exclude the possibility that some potentially relevant studies were not identified.

Our data extraction was conducted by a single reviewer, and quality-checked against the source publication for accuracy; however, this should not be considered dual extraction. Furthermore, to obtain their model inputs, many of the economic models utilised grey literature such as databases and registries. Despite our comprehensive search strategies and supplementary searches, such sources would not have been identified in our review.

We did not exclude any study based on the outcomes of their quality assessment, yet there were several domains flagged as potential sources of bias, mainly surrounding the lack of justifications for model approaches and input parameters used. This is worth noting when reviewing the identified models to determine the best approach for future modelling activities.

To facilitate review and comparison, we grouped studies into high-level categories; inconsistent use of nomenclature across the identified studies introduced additional challenges to our review. For example, although presented and described as a COI analysis, we included Sorato et al. [34] within BOI because this description more accurately reflects the models' functionality. Additionally, all identified models share a common limitation: the overall applicability of model outputs to the ucHTN and trHTN populations is uncertain, due to inputs not being derived from these populations. There is a need for risk prediction models and clinical inputs that are relevant to people with ucHTN and trHTN. We would recommend retrospective analysis of available clinical data to determine the true impact of ucHTN and trHTN. We also recommend the collection of utility data specific to these underserved populations. In a current SLR of published risk equations for ucHTN and trHTN, we identified a paucity of evidence [96] and would suggest population-specific risk equations should be developed; alternatively, commonly used risk prediction tools could be validated in the ucHTN and trHTN populations. Moreover, future models should provide clearer justifications for decisions regarding model inputs, for example to limit the introduction of selection bias (i.e., the model not representing the target population of interest).

5 Conclusions

Hypertension, especially when treatment-resistant, presents substantial burden to the healthcare system and to society in general. This could potentially be ameliorated by the use of

effective and cost-effective novel treatments. Economic evaluation requires appropriate modelling; our review identified a range of economic models designed to evaluate the benefit to be realised through treating HTN. However, few models evaluated emerging therapies other than RDN, reflecting the limited innovation in pharmacotherapy for HTN in the past two decades.

Most models employed similar structures to capture changes in BP and relate those to long-term clinical impacts. Our findings demonstrate that the majority of economic models were generally considered structurally relevant; however, they utilised model input parameters not specific to the ucHTN or trHTN populations, thus introducing uncertainty as to their applicability, and likely underestimating true cost to society and the individual.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40273-026-01625-0.

Acknowledgements The search strategy was developed by Shelley Dekock, Principal Information Scientist at Health Economics and Outcomes Research Ltd. Dr Jacoby Paterson, Senior Research Consultant (self-employed) supported screening and data extraction, and medical writing and professional editorial assistance was provided by Geraint Roberts, Senior Medical Writer at Health Economics and Outcomes Research Ltd.

Funding Sponsorship for this study was funded by AstraZeneca. The funder provided support with the design, review and medical writing of the study.

Declarations

Conflict of interest MF, RST and PP declare no conflicts of interest. JF received consultancy funding to support the design and conduct of the systematic review, paid to his employer, and is Chair of NICE Technology Appraisal Committee C. JJGS, LR, JC and PGDF are employees and shareholders of AstraZeneca. AG and PC are, or were employees of HEOR Ltd, who are paid consultants to AstraZeneca in connection with the development of this manuscript.

Ethics approval This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data availability The data sets generated during and/or analysed during the current review are available from the corresponding author on reasonable request.

Author contributions All authors contributed to the development of the study protocol. AG and PC conducted the screening, data extraction and synthesis of the SLR. All authors contributed to the interpretation of data, preparation and review of the manuscript, and gave approval of the final manuscript for publication.

References

1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020;16(4):223–37.
2. Zhou B, Carrillo-Larco RM, Danaei G, et al. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. The Lancet. 2021;398(10304):957–80.
3. World Health Organisation. Hypertension. 2025. https://www.who.int/news-room/fact-sheets/detail/hypertension. Accessed 09/10/2025.
4. Bourque G, Hiremath S. Rethinking resistant hypertension. J Clin Med. 2022;11(5):1455. https://doi.org/10.3390/jcm11051455.
5. Rose AJ, Berlowitz DR, Orner MB, Kressin NR. Understanding uncontrolled hypertension: is it the patient or the provider? J Clin Hypertens. 2007;9(12):937–43.
6. Carey RM, Calhoun DA, Bakris GL, et al. Resistant hypertension: detection, evaluation, and management: a scientific statement from the American Heart Association. Hypertension. 2018;72(5):e53–90.
7. Daugherty SL, Powers JD, Magid DJ, et al. Incidence and prognosis of resistant hypertension in hypertensive patients. Circulation. 2012;125(13):1635–42.
8. Sim JJ, Bhandari SK, Shi J, et al. Comparative risk of renal, cardiovascular, and mortality outcomes in controlled, uncontrolled resistant, and nonresistant hypertension. Kidney Int. 2015;88(3):622–32.
9. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev. 2021;10(1):1–11.
10. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015;350:g7647.
11. Carter P, Garcia Sanchez J, Retat L, Coto E, Ouwens M, Solorzano J, Agiro A, Linganathan K, Gait C, Gomes de Freitas P, Song B, Fotheringham J, Franklin M, Powell P, Carlton J, Hill H, Taylor R, Chen J. Economic models and health utility data for treatment resistant and uncontrolled hypertension [CRD42024531565]. 2024. https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=5315652024.
12. National Institute for Health Research. PROSPERO: International prospective register of systematic reviews 2022 [Internet]. https://www.crd.york.ac.uk/PROSPERO/. Accessed 17 Jan 2024.
13. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. J Clin Epidemiol. 2016;75:40–6.
14. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. BMJ (Clin Res Ed). 1996;313(7052):275–83.
15. Sharp ASP, Cao KN, Esler MD, et al. Cost-effectiveness of catheter-based radiofrequency renal denervation for the treatment of uncontrolled hypertension: an analysis for the UK based on

recent clinical evidence. Eur Heart J Qual Care Clin Outcomes. 2024;09:09.
16. Smith SM, Campbell JD. Cost-effectiveness of renin-guided treatment of hypertension. Am J Hypertens. 2013;26(11):1303–10.
17. Taylor RS, Bentley A, Metcalfe K, et al. Cost effectiveness of endovascular ultrasound renal denervation in patients with resistant hypertension. Pharmacoeconom Open. 2024;30:30.
18. Wu R, Rison SCG, Raisi-Estabragh Z, et al. Gaps in antihypertensive and statin treatments and benefits of optimisation: a modelling study in a 1 million ethnically diverse urban population in UK. BMJ Open. 2021;11(12):e052884.
19. McFarlane PA, Madan M, Ryschon AM, et al. Cost-effectiveness analysis of radiofrequency renal denervation for uncontrolled hypertension in Canada. J Med Econ. 2025;28(1):70–80.
20. Daemen J, Saville KA, Ryschon AM, et al. Cost-effectiveness of radiofrequency renal denervation for uncontrolled and resistant hypertension in The Netherlands. Blood Press. 2025;34(1):2573034.
21. Huang H-C, Cao KN, Ryschon AM, Phay K-W, Wang T-D, Pietzsch JB. Cost-effectiveness of radiofrequency renal denervation in Taiwan based on clinical evidence and regional event rates. J Clin Hypertens Greenwich. 2025;27(6):e70090.
22. Kahan T, Johansen ML, Ryschon AM, et al. Cost-effectiveness analysis of radiofrequency renal denervation for uncontrolled hypertension in Sweden. Blood Press. 2025;34(1):2487583.
23. Kandzari DE, Cao KN, Ryschon AM, Sharp ASP, Pietzsch JB. Catheter-based radiofrequency renal denervation in the United States: a cost-effectiveness analysis based on contemporary evidence. J Soc Cardiovasc Angiogr Interv. 2024;3(10):102234.
24. Kario K, Cao KN, Tanaka Y, Ryschon AM, Pietzsch JB. Cost-effectiveness of radiofrequency renal denervation for uncontrolled hypertension in Japan. J Clin Hypertens Greenwich. 2024;26(12):1502–12.
25. Lian D, Suo Y, Gai R, et al. Renal denervation for hypertension: cross-country cost-effectiveness insights from mainland China, Japan, and Thailand. Health Econ Rev. 2025;15(1):69.
26. Taylor RS, Murphy K, Kirson N, et al. Cost-utility analysis of endovascular ultrasound renal denervation to treat resistant hypertension in the United States. J Soc Cardiovasc Angiogr Interv. 2025;4(6):103601.
27. Taylor RS, Metcalfe K, Cremer A, et al. Cost-effectiveness of ultrasound renal denervation for resistant hypertension in Belgium, France and The Netherlands. Pharmacoeconomics. 2025;9(4):585–95.
28. Xursandov I, Raximberganov JR, Rakhmatova M, Jalolova M, Oripov F, Boyjanov N, et al. Cost-effectiveness of renal denervation vs. pharmacotherapy for treatment-resistant hypertension in low-resource settings. Revista Latinoamericana de Hipertensión. 2025;20(9):644.
29. Fontil V, Bibbins-Domingo K, Kazi DS, et al. Simulating strategies for improving control of hypertension among patients with usual source of care in the United States: the blood pressure control model. J Gen Intern Med. 2015;30(8):1147–55.
30. Belsey JD. Switch strategies in the management of hypertension: a cost minimisation analysis of angiotensin receptor blocker based regimen. Curr Med Res Opin. 2008;24(2):581–9.
31. Asakura E, Ademi Z, Liew D, Zomer E. Productivity burden of hypertension in Japan. Hypertens Res. 2021;44(11):1524–33.
32. Hird TR, Zomer E, Owen AJ, Magliano DJ, Liew D, Ademi Z. Productivity burden of hypertension in Australia. Hypertension. 2019;73(4):777–84.
33. Roseleur J, Gonzalez-Chica DA, Harvey G, Stocks NP, Karnon J. The cost of uncontrolled blood pressure in Australian general practice: a modelling study using electronic health records (MedicineInsight). Pharmacoeconomics. 2023;41(5):573–87.
34. Sorato MM, Davari M, Kebriaeezadeh A, Sarrafzadegan N, Shibru T. Societal economic burden of hypertension at selected hospitals in southern Ethiopia: a patient-level analysis. BMJ Open. 2022;12(4):e056627.
35. Ogden K, Kaila S, Neil N. Single-pill versus loose-dose combination triple therapy for hypertension: formulary impact. Am J Pharm Benefits. 2014;6(3):e79–86.
36. Hippisley-Cox J, Coupland C, Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. BMJ. 2017;357:j2099.
37. Julius S, Weber MA, Kjeldsen SE, et al. The Valsartan Antihypertensive Long-Term Use Evaluation (VALUE) trial. Hypertension. 2006;48(3):385–91.
38. Julius S, Kjeldsen SE, Weber M, et al. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial. The Lancet. 2004;363(9426):2022–31.
39. Turkson AJ. A closer look at the Kaplan–Meier and life table models in survival analysis. OALib. 2021.
40. Lloyd A, Schmieder C, Marchant N. Financial and health costs of uncontrolled blood pressure in the United Kingdom. Pharmacoeconomics. 2003;21(Suppl 1):33–41.
41. Azizi M, Sanghvi K, Saxena M, et al. Ultrasound renal denervation for hypertension resistant to a triple medication pill (RADIANCE-HTN TRIO): a randomised, multicentre, single-blind, sham-controlled trial. Lancet. 2021;397(10293):2476–86.
42. Kandzari DE, Townsend RR, Kario K, et al. Safety and efficacy of renal denervation in patients taking antihypertensive medications. J Am Coll Cardiol. 2023;82(19):1809–23.
43. Li Y, Gao F, Ren C, et al. The Netrod™ six-electrode radiofrequency renal denervation system for uncontrolled hypertension: a sham-controlled trial. Eur Heart J. 2024;45(44):4761–4.
44. Egan BM, Basile JN, Rehman SU, et al. Plasma Renin test-guided drug treatment algorithm for correcting patients with treated but uncontrolled hypertension: a randomized controlled trial. Am J Hypertens. 2009;22(7):792–801.
45. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension. 1. Overview, meta-analyses, and meta-regression analyses of randomized trials. J Hypertens. 2014;32(12):2285–95.
46. Collaboration BPLTT. Blood pressure lowering and major cardiovascular events in people with and without chronic kidney disease: meta-analysis of randomised controlled trials. BMJ Br Med J. 2013;347:f5680.
47. Han C, Liu F, Yang X, et al. Ideal cardiovascular health and incidence of atherosclerotic cardiovascular disease among Chinese adults: the China-PAR project. Sci China Life Sci. 2018;61(5):504–14.
48. D'Agostino RB, Russell MW, Huse DM, et al. Primary and subsequent coronary risk appraisal: new results from the Framingham study. Am Heart J. 2000;139(2 Pt 1):272–81.
49. Wolf PA, D'Agostino RB, Belanger AJ, Kannel WB. Probability of stroke: a risk profile from the Framingham study. Stroke. 1991;22(3):312–8.
50. Velagaleti RS, Pencina MJ, Murabito JM, et al. Long-term trends in the incidence of heart failure after myocardial infarction. Circulation. 2008;118(20):2057–62.
51. Voss R, Cullen P, Schulte H, Assmann G. Prediction of risk of coronary events in middle-aged men in the Prospective Cardiovascular Münster Study (PROCAM) using neural networks. Int J Epidemiol. 2002;31(6):1253–62 (**discussion 62–64**).
52. Kannel WB, D'Agostino RB, Silbershatz H, Belanger AJ, Wilson PW, Levy D. Profile for estimating risk of heart failure. Arch Intern Med. 1999;159(11):1197–204.

53. D'Agostino RB, Wolf PA, Belanger AJ, Kannel WB. Stroke risk profile: adjustment for antihypertensive medication. The Framingham study. Stroke. 1994;25(1):40–3.
54. Anderson KM, Odell PM, Wilson PW, Kannel WB. Cardiovascular disease risk profiles. Am Heart J. 1991;121(1 Pt 2):293–8.
55. Yang X, Li J, Hu D, et al. Predicting the 10-year risks of atherosclerotic cardiovascular disease in Chinese population: the China-PAR Project (Prediction for ASCVD Risk in China). Circulation. 2016;134(19):1430–40.
56. Xing X, Yang X, Liu F, et al. Predicting 10-year and lifetime stroke risk in Chinese population. Stroke. 2019;50(9):2371–8.
57. Saposnik G, Hill MD, O'Donnell M, Fang J, Hachinski V, Kapral MK. Variables associated with 7-day, 30-day, and 1-year fatality after ischemic stroke. Stroke. 2008;39(8):2318–24.
58. Dong X, He X, Wu J. Cost effectiveness of the first-in-class ARNI (Sacubitril/Valsartan) for the treatment of essential hypertension in a Chinese setting. Pharmacoeconomics. 2022;40(12):1187–205.
59. Geisler BP, Egan BM, Cohen JT, et al. Cost-effectiveness and clinical effectiveness of catheter-based renal denervation for resistant hypertension. J Am Coll Cardiol. 2012;60(14):1271–7.
60. Ara R, Brazier JE. Populating an economic model with health state utility values: moving toward better practice. Value Health. 2010;13(5):509–18.
61. Aasa M, Henriksson M, Dellborg M, et al. Cost and health outcome of primary percutaneous coronary intervention versus thrombolysis in acute ST-segment elevation myocardial infarction-Results of the Swedish Early Decision reperfusion study (SWEDES) trial. Am Heart J. 2010;160(2):322–8.
62. Glasziou P, Alexander J, Beller E, Clarke P, the ACG. Which health-related quality of life score? A comparison of alternative utility measures in patients with Type 2 diabetes in the ADVANCE trial. Health Qual Life Outcomes. 2007;5(1):21.
63. Ward S, Lloyd Jones M, Pandor A, et al. A systematic review and economic evaluation of statins for the prevention of coronary events. Health Technol Assess. 2007;11(14):178.
64. Grosso AM, Bodalia PN, Macallister RJ, Hingorani AD, Moon JC, Scott MA. Comparative clinical- and cost-effectiveness of candesartan and losartan in the management of hypertension and heart failure: a systematic review, meta- and cost-utility analysis. Int J Clin Pract. 2011;65(3):253–63.
65. Pignone M, Earnshaw S, Pletcher MJ, Tice JA. Aspirin for the primary prevention of cardiovascular disease in women: a cost-utility analysis. Arch Intern Med. 2007;167(3):290–5.
66. Henry TL, De Brouwer BFE, Van Keep MML, Blankestijn PJ, Bots ML, Koffijberg H. Cost-effectiveness of renal denervation therapy for the treatment of resistant hypertension in The Netherlands. J Med Econ. 2015;18(1):76–87.
67. Darlington A-SE, Dippel DWJ, Ribbers GM, van Balen R, Passchier J, Busschbach JJV. Coping strategies as determinants of quality of life in stroke patients: a longitudinal study. Cerebrovasc Dis. 2007;23(5–6):401–7.
68. Zhou D, Xi B, Zhao M, Wang L, Veeranki SP. Uncontrolled hypertension increases risk of all-cause and cardiovascular disease mortality in US adults: the NHANES III Linked Mortality study. Sci Rep. 2018;8(1):9418.
69. Busingye D, Gianacas C, Pollack A, et al. Data resource profile: MedicineInsight, an Australian national primary health care database. Int J Epidemiol. 2019;48(6):1741-h.
70. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. The Lancet. 2016;387(10022):957–67.
71. D'Agostino RB Sr, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart study. Circulation. 2008;117(6):743–53.
72. WHO. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. Lancet Glob Health. 2019;7(10):e1332–45.
73. Statistics Bureau of Japan MoIAaC. The Statistical Yearbook 2020. Chapter 2 population and households. Table 2-22 Life table. 2020. https://www.stat.go.jp/english/data/nenkan/69nenkan/1431-02.html. Accessed 08/05/2025.
74. Australian Institute of Health and Welfare. General Record of Incidence of Mortality (GRIM) books. 09/04/2025 2018. https://www.aihw.gov.au/reports/life-expectancy-deaths/grim-books/contents/grim-excel-workbooks. Accessed 08/05/2025.
75. Goldstein BA, Bhavsar NA, Phelan M, Pencina MJ. Controlling for informed presence bias due to the number of health encounters in an electronic health record. Am J Epidemiol. 2016;184(11):847–55.
76. National Heart Foundation of Australia. Economic cost of acute coronary syndrome in Australia: the cost to governments. 2018.
77. Smith SL, Norman R, Moxon JV, Velu R, Quigley F, Golledge J. Outcomes and costs of open and endovascular revascularisation for chronic limb ischaemia in an Australian cohort. Heart Lung Circ. 2021;30(10):1552–61.
78. Pittman DG, Tao Z, Chen W, Stettin GD. Antihypertensive medication adherence and subsequent healthcare utilization and costs. Am J Manag Care. 2010;16(8):568–76.
79. Zhang F, Bryant KB, Moran AE, et al. Effectiveness of hypertension management strategies in SPRINT-eligible US adults: a simulation study. J Am Heart Assoc. 2024;13(2):e032370.
80. NICE. The guidelines manual: NICE process and methods. 2012. https://www.nice.org.uk/process/pmg6/chapter/assessing-cost-effectiveness. Accessed 02/07/2025.
81. NICE. Developing NICE guidelines: the manual. 29/05/2024 2014. https://www.nice.org.uk/process/pmg20/chapter/incorporating-economic-evaluation. Accessed 02/07/2025.
82. Mauskopf JA, Sullivan SD, Annemans L, et al. Principles of good practice for budget impact analysis: report of the ISPOR task force on good research practices—budget impact analysis. Value Health. 2007;10(5):336–47.
83. Schnitzler L, Roberts TE, Jackson LJ, Paulus ATG, Evers SMAA. A consensus-based checklist for the critical appraisal of cost-of-illness (COI) studies. Int J Technol Assess Health Care. 2023;39(1):e34.
84. Khan SS, Ning H, Shah SJ, et al. 10-Year risk equations for incident heart failure in the general population. J Am Coll Cardiol. 2019;73(19):2388–97.
85. Ku E, Lee BJ, Wei J, Weir MR. Hypertension in CKD: core curriculum 2019. Am J Kidney Dis. 2019;74(1):120–31.
86. Vasan RS, Song RJ, Xanthakis V, et al. Hypertension-mediated organ damage: prevalence, correlates, and prognosis in the community. Hypertension. 2022;79(3):505–15.
87. Pacholko A, Iadecola C. Hypertension, neurodegeneration, and cognitive decline. Hypertension. 2024;81(5):991–1007.
88. Kollias A, Kyriakoulis KG, Komnianou A, Stathopoulou P, Stergiou GS. Prognostic value of home versus ambulatory blood pressure monitoring: a systematic review and meta-analysis of outcome studies. J Hypertens. 2024;42(3):385–92.
89. Staplin N, de la Sierra A, Ruilope LM, et al. Relationship between clinic and ambulatory blood pressure and mortality: an observational cohort study in 59 124 patients. The Lancet. 2023;401(10393):2041–50.
90. Gerlinger C, Bamber L, Leverkus F, et al. Comparing the EQ-5D-5L utility index based on value sets of different countries: impact on the interpretation of clinical study results. BMC Res Notes. 2019;12(1):18.
91. Ademi Z, Ackerman IN, Zomer E, Liew D. Productivity-adjusted life-years: a new metric for quantifying disease burden. Pharmacoeconomics. 2021;39(3):271–3.

92. Hansen KS, Moreno-Ternero JD, Østerdal LP. Quality- and productivity-adjusted life years: from QALYs to PALYs and beyond. J Health Econ. 2024;95:102885.
93. Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension Global Hypertension practice guidelines. Hypertension. 2020;75(6):1334–57.
94. Dobrescu AI, Nussbaumer-Streit B, Klerings I, et al. Restricting evidence syntheses of interventions to English-language publications is a viable methodological shortcut for most medical topics: a systematic review. J Clin Epidemiol. 2021;137:209–17.
95. Nussbaumer-Streit B, Klerings I, Dobrescu AI, et al. Excluding non-English publications from evidence-syntheses did not change conclusions: a meta-epidemiological study. J Clin Epidemiol. 2020;118:42–54.
96. Carter PMG, Garcia Sanchez JJ, Jackson D, Norris T, Ouwens M, Jarbrink K, Coto E, Papas M, Solozano J, Eryd SA, Hill H, Franklin M, Fotheringham J. Risk equations for adverse clinical events in people with treatment resistant or uncontrolled hypertension. Under development. 2024.
97. Turner HC, Archer RA, Downey LE, et al. An introduction to the main types of economic evaluations used for informing priority setting and resource allocation in healthcare: key features, uses, and limitations. Front Public Health. 2021;9-2021.
98. Jo C. Cost-of-illness studies: concepts, scopes, and methods. Clin Mol Hepatol. 2014;20(4):327–37.
99. Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. Value Health. 2014;17(1):5–14.
100. Dyer MTD, Goldsmith KA, Sharples LS, Buxton MJ. A review of health utilities using the EQ-5D in studies of cardiovascular disease. Health Qual Life Outcomes. 2010;8(1):13.
101. Shiroiwa T, Noto S, Fukuda T. Japanese population norms of EQ-5D-5L and Health Utilities Index Mark 3: disutility catalog by disease and symptom in community settings. Value Health. 2021;24(8):1193–202.
102. Kiessling A, Henriksson P. Time trends of chest pain symptoms and health related quality of life in coronary artery disease. Health Qual Life Outcomes. 2007;5(1):13.
103. Sullivan PW, Ghushchyan V. Mapping the EQ-5D index from the SF-12: US general population preferences in a nationally representative sample. Med Decis Mak. 2006;26(4):401–9.
104. Marra C, Johnston K, Santschi V, Tsuyuki RT. Cost-effectiveness of pharmacist care for managing hypertension in Canada. Can Pharm J Ott. 2017;150(3):184–97.
105. Goodacre S, Nicholl J, Dixon S, et al. Randomised controlled trial and economic evaluation of a chest pain observation unit compared with routine care. BMJ. 2004;328(7434):254.
106. Gorodetskaya I, Zenios S, McCulloch CE, et al. Health-related quality of life and estimates of utility in chronic kidney disease. Kidney Int. 2005;68(6):2801–8.
107. Soliman IW, de Lange DW, Peelen LM, et al. Single-center large-cohort study into quality of life in Dutch intensive care unit subgroups, 1 year after admission, using EuroQoL EQ-6D-3L. J Crit Care. 2015;30(1):181–6.
108. Sennfält K, Magnusson M, Carlsson P. Comparison of hemodialysis and peritoneal dialysis—a cost-utility analysis. Perit Dial Int. 2002;22(1):39–47.
109. Wijkström J, Caldinelli A, Bruchfeld A, et al. Results of the first nationwide cohort study of outcomes in dialysis and kidney transplant patients before and after vaccination for COVID-19. Nephrol Dial Transplant. 2023;38(11):2607–16.
110. Lee CP, Chertow GM, Zenios SA. An empiric estimate of the value of life: updating the renal dialysis cost-effectiveness standard. Value Health. 2009;12(1):80–7.
111. Yang F, Liao M, Wang P, Liu Y. Cost-effectiveness analysis of renal replacement therapy strategies in Guangzhou city, southern China. BMJ Open. 2021;11(2):e039653.
112. Albuquerque de Almeida F, Al MJ, Koymans R, Riistama J, Pauws S, Severens JL. Impact of hospitalisation on health-related quality of life in patients with chronic heart failure. Health Quality Life Outcomes. 2020;18(1): 262.
113. Wang S-T, Lin T-Y, Chen TH-H, Chen SL-S, Fann JC-Y. Cost-effectiveness analysis of personalized hypertension prevention. J Personal Med. 2023;13(6):1001.
114. Jonsson Å, Orwelius L, Dahlstrom U, Kristenson M. Evaluation of the usefulness of EQ-5D as a patient-reported outcome measure using the Paretian classification of health change among patients with chronic heart failure. J Patient Rep Outcomes. 2020;4(1):50.
115. Chen L, Hay JW. Cost-effectiveness of primary implanted cardioverter defibrillator for sudden death prevention in congestive heart failure. Cardiovasc Drugs Ther. 2004;18(2):161–70.
116. Fryback DG, Dasbach EJ, Klein R, et al. The Beaver Dam Health Outcomes study: initial catalog of health-state quality factors. Med Decis Making. 1993;13(2):89–102.
117. Comin-Colet J, Lainscak M, Dickstein K, et al. The effect of intravenous ferric carboxymaltose on health-related quality of life in patients with chronic heart failure and iron deficiency: a subanalysis of the FAIR-HF study. Eur Heart J. 2012;34(1):30–8.
118. Sang S, Kang N, Liao W, et al. The influencing factors of health-related quality of life among rural hypertensive individuals: a cross-sectional study. Health Qual Life Outcomes. 2021;19(1):244.
119. Mangen MJ-J, Bolkenbaas M, Huijts SM, van Werkhoven CH, Bonten MJM, de Wit GA. Quality of life in community-dwelling Dutch elderly measured by EQ-5D-3L. Health Quality Life Outcomes. 2017;15(1):3.
120. Humphries S, Wallert J, Mars K, Held C, Hofmann R, Olsson EMG. Association between β-blocker dose and quality of life after myocardial infarction: a real-world Swedish register-linked study. Eur Heart J Acute Cardiovasc Care. 2022;11(6):491–500.
121. van Eeden M, van Heugten C, van Mastrigt GAPG, van Mierlo M, Visser-Meily JMA, Evers SMAA. The burden of stroke in the Netherlands: estimating quality of life and costs for 1 year poststroke. BMJ Open. 2015;5(11):e008220.
122. Lu W-S, Huang S-L, Yang J-F, Chen M-H, Hsieh C-L, Chou C-Y. Convergent validity and responsiveness of the EQ-5D utility weights for stroke survivors. J Rehabil Med. 2016;48(4):346–51.
123. Lindgren P, Glader E-L, Jönsson B. Utility loss and indirect costs after stroke in Sweden. Eur J Cardiovasc Prev Rehabil. 2008;15(2):230–3.
124. Tengs TO, Lin TH. A meta-analysis of quality-of-life estimates for stroke. Pharmacoeconomics. 2003;21(3):191–200.
125. Zorginstitutt Nederland. Guideline for economic evaluations in healthcare. 2024. https://english.zorginstituutnederland.nl/documents/2024/01/16/guideline-for-economic-evaluations-in-healthcare.
126. Edejer TT-T, World Health O. Making choices in health: WHO guide to cost-effectiveness analysis. Geneva: World Health Organization; 2003.
127. Svensson M, Nilsson FOL, Arnberg K. Reimbursement decisions for pharmaceuticals in Sweden: the impact of disease severity and cost effectiveness. Pharmacoeconomics. 2015;33(11):1229–36.
128. Anderson JL, Heidenreich PA, Barnett PG, et al. ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures. J Am Coll Cardiol. 2014;63(21):2304–22.
129. Hasegawa M, Komoto S, Shiroiwa T, Fukuda T. Formal implementation of cost-effectiveness evaluations in Japan: a

unique health technology assessment system. Value Health. 2020;23(1):43–51.
130. Center for Outcomes Research and Economic Evaluation for Health NIoPHCH. Guideline for preparing cost-effectiveness evaluation to the Central Social InsuranceMedical Council. 2022. https://c2h.niph.go.jp/tools/guideline/guideline_en.pdf.
131. Guidelines CMa. Guidelines for the Economic Evaluation of Health Technolgogies: Canada. 2017. https://www.cda-amc.ca/sites/default/files/pdf/guidelines_for_the_economic_evaluation_of_health_technologies_canada_4th_ed.pdf.
132. National Institute for Health Research. NICE technology appraisal and highly specialised technologies guidance: the manual. 2022. https://www.nice.org.uk/process/pmg36.
133. Belgian Health Care Knowledge Centre (KCE). Belgian guidelines for economic evaluations and budget impact analyses. https://kce.fgov.be/en/belgian-guidelines-for-economic-evaluations-and-budget-impact-analyses-third-edition.
134. Haute Autorite De Sante (HAS). Choices in methods for economic evaluation. 2020. https://www.has-sante.fr/jcms/r_1499251/en/choices-in-methods-for-economic-evaluation.

Authors and Affiliations

Matthew Franklin[1] · James Fotheringham[1] · Rod S. Taylor[2] · Philip A. Powell[1] · Lise Retat[3] · Jieling Chen[4] · Juan Jose Garcia Sanchez[3] · Amy Gamble[5] · Patrice Carter[5]

✉ Patrice Carter
patrice.carter@heor.co.uk; patricepc154@gmail.com

1 Sheffield Centre for Health and Related Research (SCHARR), Division of Population Health, School of Medicine and Population Health, The University of Sheffield, Sheffield, UK

2 School of Health and Well Being, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, UK

3 AstraZeneca, Avinguda de Roma, 81 Eixample, 08029 Barcelona, Spain

4 AstraZeneca R&D Pharmaceuticals, One Medimmune Way, Gaithersburg, MD 20878, USA

5 Health Economics & Outcomes Research Ltd, Rhymney House, Unit A Copse Walk, Cardiff Gate Business Park, Cardiff CF23 8RB, UK