Appendix Table 1. Mean (SD) and Number (%) of Studies Reporting Each Item in Quality of Health Economic Studies Instrument (N=76)

	Item	Point	Mean (SD)	N (%)
1	Was the study objective presented in a clear, specific, and measurable manner?	7	6.9 (0.8)	75 (98.7)
2	Were the perspective of the analysis and reasons for its selection stated?	4	1.9 (0.9)	66 (86.8)[a]
3	Were variable estimates used in the analysis from the best available source?	8	8.0 (0.0)	76 (100.0)
4	If estimates came from a subgroup analysis, were the groups pre-specified at the beginning of the study?	1	1.0 (0.0)	NA
5	Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9	5.2 (3.0)	51 (67.1)[b]
6	Was incremental analysis performed between alternatives for resources and costs?	6	5.0 (2.3)	62 (81.6)[c]
7	Was the methodology for data abstraction stated?	5	4.9 (0.6)	75 (98.7)
8	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted and justification given for the discount rate?	7	6.3 (1.6)	74 (97.4)[d]
9	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8	6.5 (2.6)	69 (86.8)[e]
10	Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term was justification given for the measures/scales used?	6	5.3 (2.0)	68 (89.5)
11	Were the health outcomes measures/scales valid and reliable? If previously tested valid and eligible measures were not available, was justification given for the measures/scales used?	7	6.5 (1.7)	71 (93.4)
12	Were the economic model, study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8	6.2 (3.4)	59 (77.5)
13	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7	6.3 (1.6)	74 (97.4)
14	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6	1.5 (2.6)	19 (25.0)
15	Were the conclusions/recommendations of the study justified and based on the study results?	8	8.0 (0.0)	76 (100.0)
16	Was there a statement disclosing the source of funding for the study?	3	2.5 (1.1)	64 (84.2)
	Overall	100	82.5 (13.8)	76 (100.0)

[a]Seven studies stated reasons for their selection (points=4), but 59 studies did not clarify reasons for their selection (partial points=2).
[b]Twenty-three studies handled both random events and assumptions (point=9), but 41 studies only handled assumptions (partial point=4.5).
[c]Forty-three studies provided the ICER values, while 19 studies did not need to report since the intervention was dominant.
[d]Sixty-two studies took an appropriate time horizon and discounted when needed (point=7), but 12 studies did either part (partial point=3.5).
[e]Fifty-five studies measured all appropriate costs and reported unit costs (point=8), but 14 studied did either part (partial point=4).

Appendix Table 2. Summary of Cost Effectiveness Analyses Comparing Intervention Antihypertensive Medicines With No Treatment

Reference	Study setting	Study design	Intervention and outcome		Cost effectiveness evidence		
Author (Year)	**A. Country** **B. Disease** **C. Funding**	**A. Study type** **B. Perspective** **C. Study method** **D. Time horizon** **E. Discount rate** **F. Sensitivity analysis**	**A. Treatment type** **B. Intervention vs comparator** **C. Outcome**	**Original results by authors (Year of cost estimates)**	**Adjustment to 2016 U.S. dollars**	**ICER threshold by authors**	**Conclusions by authors**
Stevanovic (2014)[1]	A. Netherlands B. HTN C. Industry	A. CEA B. Health care C. Model-based (Markov) D. 10 years; Lifetime E. 4%; 1.5% (outcome) F. Probabilistic	A. MONO or COMBO B. HCTZ (+losartan) vs No TX C. LY	[ICER/LY (lifetime)] ▪ €3,074-€4,656 (2013)	[ICER/LY (lifetime)] ▪ $4,178-$6,328	€20,000/LY	HCTZ (+losartan) is more CE than no treatment.
Glasziou (2010)[2]	A. Australia B. HTN + DM C. Non-profit	A. CEA and CUA B. Payer C. Trial-based (ADVANCE) D. 4.17 years (mean) E. 3, 5, 10% F. Deterministic	A. COMBO B. Perindopril + indapamide vs No TX (placebo) C. QALY; LY	[ICER/QALY] ▪ $10,600 [ICER/LY] ▪ $11,842 (2007)	[ICER/QALY] ▪ $12,403 [ICER/LY] ▪ $13,856	NR	Perindopril + indapamide is more CE than no treatment.
Wilson (2010)[3]	A. United Kingdom B. HTN + Stroke C. Non-profit	A. CUA B. Hospital C. Trial-based (CHHIPS) D. 14 days; 3 months E. NA F. Probabilistic	A. MONO B. Labetalol or lisinopril vs No TX (placebo) C. QALY	[ICER/QALY (3 months)] ▪ Dominant [Decreasing cost] ▪ £5,511 [Increasing QALY] ▪ 0.044 (2006)	[ICER/QALY (3 months)] ▪ Dominant [Decreasing cost] ▪ $9,557	£20,000–£30,000 /QALY	Labetalol or lisinopril is more CE than no treatment.
Szucs (2010)[4]	A. Switzerland B. HTN C. NR	A. CEA B. Payer C. Trial-based (HYVET) D. 2 years	A. MONO B. Perindopril + indapamide vs No TX (placebo) C. LY	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ CHF 37,162 [Increasing QALY]	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ $28,342	NA	Perindopril + indapamide is more CE

		E. 5% F. Deterministic		▪ 0.0457 (2007)			than no treatment.
Taylor (2009)[5]	A. United Kingdom B. HTN + MI C. Industry	A. CEA and CUA B. Health care C. Trial-based (VALIANT) and Model-based (Markov) D. 10 years E. 3.5% F. Deterministic and Probabilistic	A. MONO B. Valsartan vs No TX (placebo) C. QALY; LY	[ICER/QALY] ▪ £5,338 [ICER/LY] ▪ £4,672 (2008)	[ICER/QALY] ▪ $8,677 [ICER/LY] ▪ $7,594	£30,000 /QALY	Valsartan is more CE than no treatment.
Tavakoli (2009)[6]	A. United Kingdom B. HTN + Stroke C. Industry + non-profit	A. CUA B. Health care C. Trial-based (PROGRESS) and Model-based (Markov; MCMS) D. 4, 20 years E. 3.5% F. Deterministic	A. MONO or COMBO B. Perindopril (+ indapamide) vs No TX (placebo) C. QALY	[ICER/QALY (20 years)] ▪ £10,133 (2005)	[ICER/QALY (20 years)] ▪ $17,851	£25,000 /QALY	Perindopril (+ indapamide) is more CE than no treatment.
Zethraeus (2008)[7]	A. Sweden B. HTN (+ DM) C. Non-profit	A. CUA B. Societal C. Trial-based (WHI RCT) D. 5 years E. 3% F. Deterministic	A. MONO B. HCTZ vs No TX C. QALY	[ICER/QALY] ▪ $12,000–16,000 ▪ + DM: $4,000–$11,000 (2005)	[ICER/QALY] ▪$14,959–$19,945 ▪ + DM: $4,986–$13,712	$44,000 /QALY kr 330,000 /QALY	HCTZ is more CE than no treatment.
Grover (2008)[8]	A. Canada B. HTN C. Industry	A. CEA B. Health care C. Trial-based (AIRE; HOPE; MICRO-HOPE) and Model-based (Markov) D. 15 month; 4.5 years; Lifetime E. 3% F. NC	A. MONO B. Ramipril vs No TX (placebo) C. LY	[ICER/LY (lifetime)] ▪ C$5,000–C$8,500 (2002)	[ICER/LY (lifetime)] ▪ $5,603–$8,968	NR	Ramipril is more CE than no treatment.

Ekman (2008)[9] *(additionally reported in Appendix E)*	A. Sweden B. HTN C. Industry	A. CUA B. Health care C. Model-based (Markov) D. Lifetime E. 3% F. Deterministic	A. COMBO: +HCTZ B. Irbesartan or Losartan or Valsartan vs No TX (placebo) C. QALY	[ICER/QALY] ▪ Irbesartan: €4,351–€7,704 ▪ Losartan: dominant ▪ Valsartan: dominant (2007)	[ICER/QALY] ▪ Irbesartan: $6,199–$10,976 ▪ Losartan: dominant ▪ Valsartan: dominant	€50,000–€60,000 /QALY	Irbesartan, losartan, and valsartan are more CE than no treatment.
Hogan (2002)[10]	A. U.S. B. HTN + Renal disease C. Industry	A. CUA B. Third party payer C. Trial-based (AIPRI) and Model-based (Markov) D. 7 years E. 3% F. Deterministic	A. MONO B. Benazepril vs No TX (placebo) C. QALY	[ICER/QALY] ▪ Dominant [Cost/QALY] ▪ Benazepril: $17,783 ▪ Placebo: $20,767 (1999)	[ICER/QALY] ▪ Dominant [Cost/QALY] ▪ Benazepril: $17,777 ▪ Placebo: $31,330	NA	Benazepril is more CE than no treatment.
Malik (2001)[11]	A. United Kingdom B. HTN C. Non-profit	A. CEA B. Third party payer C. Trial-based (HOPE) D. 5 years; Lifetime E. 6% F. Deterministic	A. MONO B. Ramipril vs No TX (placebo) C. LY	[ICER/LY (lifetime)] ▪ £100–£5,300 (1998)	[ICER/LY (lifetime)] ▪ $214–$11,352	£25,000 /LY	Ramipril is more CE than no treatment.
Backhouse (2000)[12]	A. United Kingdom B. HTN C. NR	A. CEA B. Health care C. Trial-based (HOPE) D. 5 years E. 6% F. Deterministic	A. MONO B. Ramipril vs No TX (placebo) C. LY	[ICER/LY] ▪ £5,544 (1999)	[ICER/LY (lifetime)] ▪ $11,524	NR	Ramipril is more CE than no treatment.
Cook (1998)[13]	A. U.S. B. HTN + LVD C. NR	A. CEA B. NR C. Trial-based (SOLVD) D. Lifetime E. 5% F. Deterministic	A. MONO B. Enalapril vs No TX (placebo) C. LY	[ICER/LY] ▪ $1,820 (1996)	[ICER/LY] ▪ $2,923	NR	Enalapril is more CE than no treatment.
Kiberd (1998)[14]	A. U.S. B. HTN + DM C. NR	A. CUA B. Payer + patient	A. MONO B. Captopril vs No TX C. QALY	[ICER/ QALY] ▪NR [Cost]	[ICER/ QALY] ▪ NR [Cost]	NA	Captopril is more CE

	C. Model-based (Markov) D. 60 years E. 5% F. NC	▪ $29,180–$29,350 [QALY] ▪ 19.15–19.34 (1995)	▪ $47,960–$48,239	than no treatment.

Appendix Table 3. Summary of Cost Effectiveness Analyses Comparing Intervention Antihypertensive Medicines With Conventional Therapy

Reference	Study setting	Study design	Intervention and outcome	Cost-effectiveness evidence			
Author (Year)	**A. Country** **B. Disease** **C. Funding**	**A. Study type** **B. Perspective** **C. Study method** **D. Time horizon** **E. Discount rate** **F. Sensitivity analysis**	**A. Treatment type** **B. Intervention vs comparator** **C. Outcome**	**Original results by authors (Year of cost estimates)**	**Adjustment to 2015 U.S. dollars**	**ICER threshold by authors**	**Conclusions by authors**
Ker (2008)[15]	A. South Africa B. HTN + HL C. Industry	A. CEA B. NR C. Model-based (Simulation) D. 10 years E. NR F. NC	A. COMBO B. Amlodipine + CVTX vs CVTX C. Percent risk reduction	[ICER/Percent risk reduction] ▪ R 20.60 (2006)	[ICER/Risk reduction] ▪ $7	NR	Adding amlodipine is more CE than CVTX.
Palmer (2008)[16]	A. U.S. B. HTN + DM C. Industry	A. CUA B. Third party payer C. Model-based (Markov; MCMS) D. 25 years E. 3% F. Probabilistic	A. COMBO B. Irbesartan + CVTX vs CVTX C. QALY	[ICER/QALY] ▪ $20,011 (2000)	[ICER/QALY] ▪ $29,331	$50,000 /QALY	Adding NP screening + irbesartan is more CE than CVTX.
Annemans (2008)[17] *(additionally reported in Appendix D)*	A. China, Malaysia, Thailand, South Korea, Taiwan B. HTN + DM + Renal disease C. Industry + Non profit	A. CEA B. Third party payer C. Trial-based (IRMA-2; IDNT) and Model-based (Markov; MCMC) D. 25 years E. 3% F. Deterministic and Probabilistic	A. COMBO B. Irbesartan + CVTX vs CVTX C. ESRD incidence, Dialysis days, ESRD free years, Life expectancy	[ICER/Each outcome] ▪ Dominant [Decreasing cost] ▪ $6,189–$21,148 [ESRD incidence] ▪ Irbesartan: 9%–14% ▪ No irbesartan: 22%–31% [Decreasing dialysis days] ▪ 62% [Increasing ESRD free] ▪ 9.6–11.2 years [Increasing life expectancy] ▪ 4%–6% (2004)	[ICER/Each outcome] ▪ Dominant [Decreasing cost] ▪ $7,954–$27,180	NA	Adding irbesartan is more CE than CVTX.
Palmer (2007)[18]	A. United Kingdom	A. CEA B. Health care	A. MONO or COMBO B. Irbesartan + CVTX vs CVTX C. LY; ESRD incidence	[ICER/LY] ▪ Dominant [Decreasing cost]	[ICER/LY] ▪ Dominant [Decreasing cost]	NA	Adding irbesartan is

	B. HTN + DM + renal disease C. Industry	C Trial-based (IRMA-2; IDNT) and Model-based (Markov; MCMC) D. 25 years E. 3.5% F. Probabilistic		▪ £1,491–£1,801 (2002 GBP) [Increasing LY] ▪ 0.03–1.41 years [Decreasing ESRD incidence] ▪ 3.68%–12.42%	▪ $2,978–$3,579		more CE than CVTX.
Palmer (2007)[19]	A. Hungary B. HTN + DM + renal disease C. Industry	A. CEA B. Perspective C Trial-based (IRMA-2; IDNT) and Model-based (Markov; MCMC) D. 25 years E. 5% F. Probabilistic	A. MONO or COMBO B. Irbesartan vs CVTX C. LY; ESRD incidence	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ HUF 519,993 [Increasing LY] ▪ 0.98 years [Decreasing ESRD incidence] ▪ 8% (2002)	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ $6,064	NA	Irbesartan is more CE than CVTX.
Palmer (2006)[20]	A. France B. HTN + DM + renal disease C. Industry	A. CEA and CUA B. Perspective C. Trial-based (IRMA-2; IDNT) and Model-based (Markov; MCMC) D. 25 years E. 3% F. Probabilistic	A. MONO or COMBO B. Irbesartan + CVTX vs CVTX C. QALY; ESRD incidence	[ICER/QALY] ▪ Dominant [Decreasing cost] ▪ €6,619–€22,314 (2002 EUR) [Increasing QALY] ▪ 0.06–1.03 [Decreasing ESRD incidence] ▪ 3.9-14.0%	[ICER/QALY] ▪ Dominant [Decreasing cost] ▪ $10,702–$36,077	NA	Adding irbesartan is more CE than CVTX.
Vora (2005)[21]	A. United Kingdom B. HTN C. Industry	A. CEA B. Health care C Trial-based (RENAAL) D. Lifetime E. 3.5% F. Deterministic	A. MONO B. Losartan vs CVTX C. LY	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ £6,622 [Increasing LY] ▪ 0.44 years (2004)	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ $12,371	NA	Losartan is more CE than CVTX.
Lundkvist (2005)[22]	A. Sweden B. HTN C. NR	A. CEA and CUA B. Societal C. Trial-based (SCOPE) and Model-based (Markov) D. Lifetime E. 3% F. Deterministic	A. MONO B. Candesartan vs CVTX C. QALY; Stroke prevention	[ICER/QALY] ▪ €13,000 [ICER/stroke prevention] ▪ €26,000 (2001)	[ICER/QALY] ▪ $21,444 [ICER/stroke prevention] ▪ $42,887	€66,000 /QALY	Candesartan is more CE than CVTX.

Palmer (2004)[23]	A. U.S. B. HTN + DM + renal disease C. Industry	A. CEA B. Third party payer C. Trial-based (IRMA-2; IDNT) and Model-based (Markov; MCMC) D. 25% E. 3% F. Probabilistic	A. MONO or COMBO B. Irbesartan (+ CVTX) vs Placebo (+ CVTX) C. LY	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ $3,252–$11,922 [Increasing LY] ▪ 0.07–1.55 years (2000)	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ $4,767–$17,475	NA	Irbesartan is more CE than CVTX.
Szucs (2004)[24]	A. Switzerland B. HTN + DM + renal disease C. Industry	A. CEA B. Health care C. Trial-based (RENAAL) D. 3.5 years E. NC F. Deterministic	A. MONO or COMBO B. Losartan (+ CVTX) vs Placebo (+ CVTX) C. ESRD days	[ICER/ESRD days] ▪ Dominant [Decreasing cost] ▪ CHF 4,084 [Decreasing ESRD days] ▪ 33.6 days (2001)	[ICER/ESRD days)] ▪ Dominant [Decreasing cost] ▪ $3,278	NA	Losartan is more CE than no treatment.
Palmer (2004)[25] *(additionally reported in Appendix D)*	A. United Kingdom B. HTN + DM + renal disease C. Industry	A. CEA B. Healthcare payer C. Trial-based (IDNT) and Model-based (Markov) D. 10 years E. 6%; 1.5% (outcome) F. Deterministic	A. MONO or COMBO B. Irbesartan + CVTX vs CVTX C. LY	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ £2,919 [Increasing LY] ▪ 0.21 years (2003)	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ $5,574	NA	Adding irbesartan is more CE than CVTX.
Coyle (2004)[26] *(additionally reported in Appendix D)*	A. Canada B. HTN + DM + renal disease C. Industry	A. CEA B. Third party payer C. Trial-based (IDNT) and Model-based (Markov; MCMS) D. 25 years E. 5% F. Deterministic and Probabilistic	A. MONO or COMBO B. Irbesartan + CVTX vs CVTX; Amlodipine + CVTX vs CVTX C. LY	[ICER/LY] ▪ Irbesartan: dominant ▪ Amlodipine: C$ 86,000 (2001)	[ICER/LY] ▪ Irbesartan: dominant ▪ Amlodipine: $99,805	C$ 30,000–50,000	Adding irbesartan is more CE than CVTX.
Palmer (2003)[27] *(additionally reported in Appendix D)*	A. Belgium, France B. HTN + DM + renal disease C. Industry	A. CEA B. Healthcare payer C. Trial-based (IDNT) and Model-based (Markov) D. 25 years E. 3% F. Deterministic	A. MONO or COMBO B. Irbesartan + CVTX vs CVTX C. LY	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ Belgium: €11,885; France: €16,345 [Increasing LY] ▪ Belgium: 0.91 years; France: 0.90 years (2002)	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ Belgium: $19,216; France: $26,426	NA	Adding irbesartan is more CE than CVTX.

Rodby (2003)[28] *(additionally reported in Appendix D)*	A. U.S. B. HTN + DM + renal disease C. Industry	A. CEA B. Healthcare payer C. Trial-based (IDNT) and Model-based (Markov) D. 3, 10, 25 years E. 3% F. Deterministic	A. MONO or COMBO (+CVTX) B. Placebo vs Irbesartan C. LY	[ICER/LY (25 years)] ▪ Dominated [Increasing cost] ▪ £15,607 [Decreasing LY] ▪ 0.740 years (2003)	[ICER/LY (25 years)] ▪ Dominated [Increasing cost] ▪ $29,801	NR	Adding irbesartan is more CE than CVTX.
Schädlich (2001)[29]	A. German B. HTN + renal disease C. Industry	A. CEA B. Health care C. Trial-based (REIN) and Model-based (Decision tree) D. 1, 2, 3 years E. 5% F. Probabilistic	A. COMBO B. Ramipril + CVTX vs Placebo + CVTX C. Dialysis avoided	[ICER/dialysis avoided (3 years)] ▪ Dominant (DM - 81,930) (1999)	[ICER/dialysis avoided (3 years)] ▪ dominant ($–129,565)	NA	Adding ramipril is more CE than CVTX.
Garattini (1997)[30]	A. Italy B. HTN + DM + renal disease C. Non-profit	A. CEA B. Healthcare payer C. Model-based (Decision tree) D. 10 years E. 5% F. Deterministic	A. COMBO B. Captopril + CVTX vs Placebo + CVTX C. Dialysis avoided	[ICER/dialysis avoided] ▪ Dominant [Cost] ▪ Captopril: £21,910,625 ▪ Placebo: £30,352,590 (1993) [Increasing dialysis avoided] ▪ 2.4 months	[ICER/dialysis avoided] ▪ Dominant [Cost] ▪ Captopril: $24,612 ▪ Placebo: $34,094	NA	Adding captopril is more CE than CVTX.

Appendix Table 4. Summary of Cost Effectiveness Analyses Comparing Antihypertensive Medicines Between Different Medicine Classes

Reference	Study setting	Study design	Intervention and outcome	Cost effectiveness evidence			
Author (Year)	**A. Country B. Disease C. Funding**	**A. Type B. Perspective C. Method D. Time horizon E. Discount rate F. Sensitivity analysis**	**A. Treatment type B. Intervention vs comparator C. Outcome**	**Original results by authors (Year of cost estimates)**	**Adjustment to 2015 U.S. dollars**	**ICER threshold by authors**	**Conclusions by authors**
Chan (2016)[31]	A. Taiwan B. HTN C. Industry	A. CUA B. Third party payer C. Model-based (Markov) D. 5 years E. 3% F. Deterministic	A. MONO B. Amlodipine vs Valsartan C. QALY	[ICER/QALY] ▪ Dominant [Decreasing cost] ▪ NT$2,251/year (2011 NTD) [Increasing QALY] ▪ 0.0058/5 years	[ICER/QALY] ▪ Dominant [Decreasing cost] ▪ $81/year	NA	Amlodipine is more CE than valsartan.
Chowdhury (2015)[32]	A. Australia B. HTN + DM C. Industry + non profit	A. CUA B. Health care C. Trial-based (ANBP2) D. 5 years E. 5% F. Deterministic and Probabilistic	A. MONO B. Enalapril vs HCTZ C. QALY	[ICER/QALY] ▪ A$27,698 (2012)	[ICER/QALY] ▪ $19,357	A$50,000 /QALY	Enalapril is more CE than HCTZ.
Wu (2013)[33]	A. China B. HTN C. Industry	A. CUA B. Third party payer C. Model-based (Markov) D. 5 years E. 3% F. Deterministic	A. MONO B. Amlodipine vs Valsartan C. QALY	[ICER/QALY] ▪ Dominant [Decreasing cost] ▪ ¥2,033 [Increasing QALY] ▪ 0.01278 (2012)	[ICER/QALY] ▪ Dominant [Decreasing cost] ▪ $599	NA	Amlodipine is more CE than valsartan.
Sangle (2013)[34]	A. India B. HTN C. NR	A. CEA B. NR C. Trial-based D. 8 weeks E. NA F. NC	A. MONO B. Amlodipine vs Atenolol C. BP reduction	[ICER/BP reduction] ▪ NR [Cost/BP reduction] ▪ Amlodipine: ₹3.43 ▪ Atenolol: ₹5.05 (2012)	[ICER/BP reduction] ▪ NR [Cost/BP reduction] ▪ Amlodipine: $0.223 ▪ Atenolol: $0.328	NA	Amlodipine is more CE than atenolol.
Ekwunife (2013)[35]	A. Nigeria B. HTN	A. CUA B. Third party payer	A. MONO	[NMB] ▪ HCTZ: $101,927	[NMB] ▪ HCTZ: $110,267	NA	HCTZ is more CE

	C. None	C. Model-based (Markov; MCMS) D. 30 years E. 3% F. Probabilistic	B. HCTZ vs Propranolol vs Lisinopril vs Nifedipine C. QALY	▪ Propranolol: $94,094 ▪ Lisinopril: $98,619 ▪ Nifedipine: $101,790 (2010)	▪ Propranolol: $101,793 ▪ Lisinopril: $106,766 ▪ Nifedipine: $110,119		than propranolol, lisinopril, and nifedipine. Nifedipine is more CE than propranolol, and lisinopril.
Schwander (2009)[36]	A. Belgium, Germany, Norway, Spain, Sweden, United Kingdom B. HTN C. Industry	A. CUA B. Healthcare payer C. Model-based (Markov; MCMS) and Trial-based (MOSES) D. Lifetime E. Belgium: 3.5%; Germany: 5%; Norway: 4%; Spain: 3.5%; Sweden: 3%; United Kingdom: 3.5% F. Probabilistic	A. MONO B. Eprosartan vs Enalapril or Nitrendipine C. QALY	[ICER/QALY] ▪ vs enalapril Belgium: €17,863; Germany: €24,036; Norway: €13,834; Spain: €7,918; Sweden: €11,691; United Kingdom: €16,364 ▪ vs nitrendipine Belgium: dominant; Germany: €9,136; Norway: €1,695; Spain: dominant; Sweden: €907; United Kingdom: €6,008 (2007)	[ICER/QALY] ▪ vs enalapril Belgium: $25,449; Germany: $34,244; Norway: $19,709; Spain: $11,281; Sweden: $16,656; United Kingdom: $23,314 ▪ vs nitrendipine Belgium: dominant; Germany: $13,016; Norway: $2,415; Spain: dominant; Sweden: $1,292; United Kingdom: $8,560	€30,000 /QALY	Eprosartan is more CE than enalapril, and nitrendipine.
Heidenreich (2008)[37]	A. U.S. B. HTN C. Industry	A. CEA and CUA B. Payer C. Trial-based (ALLHAT) D. 6 years; Lifetime E. 3% F. Deterministic	A. MONO B. Lisinopril or Amlodipine vs CTD C. QALY; LY	[ICER/QALY (lifetime)] ▪ lisinopril: NR ▪ amlodipine: $41,700 [ICER/LY (lifetime)] ▪ lisinopril: dominated ▪ amlodipine: $48,400 (2004)	[ICER/QALY (lifetime)] ▪ lisinopril: NR ▪ amlodipine: $53,594 [ICER/LY (lifetime)] ▪ lisinopril: dominated ▪ amlodipine:$62,205	$50,000 /QALY	Amlodipine is more CE than CTD and lisinopril. CTD is more CE than lisinopril.
Annemans (2008)[17]	A. China, Malaysia, Thailand,	A. CEA B. Third party payer C. Trial-based (IRMA-2; IDNT) and	A. COMBO: CVTX B. Irbesartan vs Amlodipine	[ICER/Each outcome] ▪ Dominant [Decreasing cost] ▪ $8,200–$29,723	[ICER/Each outcome] ▪ Dominant [Decreasing cost] ▪ $10,539–$38,201	NA	Irbesartan is more CE than amlodipine.

(additionally reported in Appendix C)	South Korea, Taiwan B. HTN + DM + Renal disease C. Industry + non profit	Model-based (Markov; MCMC) D. 25 years E. 3% F. Deterministic and Probabilistic	C. ESRD incidence; Dialysis days; ESRD free years; Life expectancy	[ESRD incidence] ▪ irbesartan: 9%–14% ▪ amlodipine: 24%–30% [Decreasing dialysis days] ▪ 63% [Increasing ESRD free] ▪ 9.5–11.1 years [Increasing life expectancy] ▪ 4%–6% (2004)			
Boersma (2007)[38]	A. Netherlands B. HTN + LVH C. Industry	A. CEA B. Health care C. Trial-based (LIFE) D. 5.5 years; Lifetime E. 4% F. Deterministic	A. MONO or COMBO B. Losartan (+HCTZ) vs Atenolol (+HCTZ) C. LY	[ICER/LY] ▪ $790, $1,003 (2006)	[ICER/LY] ▪ $955, $1,212	$25,000 /LY	Losartan is more CE than atenolol.
Littlewood (2007)[39]	A. Netherlands B. HTN + Renal disease C. Industry	A. CEA B. Health care C. Model-based (Markov) D. 3 years E. 4%; 1.5% (outcome) F. Deterministic and Probabilistic	A. COMBO B. Moxonidine + PT vs Nitrendipine + PT C. LY	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ €27,615 (2004) [Increasing LY] ▪ 0.044 years	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ $41,451	NA	Adjunctive moxonidine is more CE than adjunctive nitrendipine.
Wessels (2007)[40]	A. South Africa B. HTN + Stroke C. NR	A. CEA and CUA B. Third party payer C. Trial-based (MOSES) and Model-based (Markov; MCMC) D. Lifetime E. 5% F. Probabilistic	A. MONO B. Eprosartan vs Amlodipine or Perindopril C. QALY; LY	[ICER/QALY] ▪ vs amlodipine: dominant (R –53,132) ▪ vs perindopril: dominant (R –72,888) [ICER/LY] ▪ vs amlodipine: dominant (R –67,611) ▪ vs perindopril: dominant (R –92,751) (2006)	[ICER/QALY] ▪ vs amlodipine: dominant ($–17,829) ▪ vs perindopril: dominant ($–24,459) [ICER/LY] ▪ vs amlodipine: dominant ($–22,688) ▪ vs perindopril: dominant ($–31,124)	R 95,000	Eprosartan is more CE than amlodipine and perindopril.

Anis (2006)[41]	A. Canada B. HTN + LVH C. Industry	A. CUA B. Societal C. Trial-based (LIFE) and Model-based (Markov) D. Lifetime E. 3% F. Deterministic and Probabilistic	A. MONO or COMBO B. Losartan (+HCTZ) vs Atenolol (+HCTZ) C. LY	[ICER/QALY] ▪ C$1,337 (2002)	[ICER/QALY] ▪ $1,498	C$20,000 for PSA	Losartan is more CE than atenolol.
McInnes (2006)[42]	A. United Kingdom B. HTN + LVH C. None	A. CUA B. Health care C. Trial-based (LIFE) and Model-based (Markov) D. Lifetime E. 3.5% F. Probabilistic	A. MONO or COMBO B. Losartan (+HCTZ) vs Atenolol (+HCTZ) C. QALY; LY	[ICER/QALY] ▪ £2,130 [ICER/LY] ▪ £1,643 (2003)	[ICER/QALY] ▪ $4,067 [ICER/LY] ▪ $3,138	£30,000 /QALY £30,000 /LY	Losartan is more CE than atenolol.
Stafilas (2005)[43]	A. Greece B. HTN C. NR	A. CMA B. Health care C. Trial-based D. 5 years E. 5% F. Deterministic	A. MONO B. CTD vs Propranolol vs Amlodipine vs Enalapril vs Losartan C. Death	[ICER/Death] ▪ NR [Cost/Death] ▪ CTD: €60,231 ▪ Propranolol: €70,370 ▪ Amlodipine: €105,597 ▪ Enalapril: €75,301 ▪ Losartan: €158,659 (2004)	[ICER/Death] ▪ NR [Cost/Death] ▪ CTD: $90,408 ▪ Propranolol: $105,628 ▪ Amlodipine: $158,504 ▪ Enalapril: $107,281 ▪ Losartan: $226,040	NA	CTD is more CE than propranolol, amlodipine, enalapril, and losartan.
Jönsson (2005)[44]	A. Sweden B. HTN + LVH C. Industry	A. CEA and CUA B. Health care; Societal C. Trial-based (LIFE) and Model-based (Bootstrap) D. Lifetime E. 3% F. Deterministic	A. MONO or COMBO B. Losartan (+HCTZ) vs Atenolol (+HCTZ) C. QALY; LY	[ICER/QALY] ▪ Health care: €4,188 ▪ Societal: €11,710 [ICER/LY] ▪ Health care: €3,141 ▪ Societal: €8,783 (2003)	[ICER/QALY] ▪ Health care: $6,486 ▪ Societal: $18,137 [ICER/ LY] ▪ Health care: $4,865 ▪ Societal: $13,603	€50,000 /QALY	Losartan is more CE than atenolol.
Szucs (2004)[45]	A. Swiss B. HTN + LVH C. Industry	A. CEA B. Health care C. Trial-based (LIFE) D. 4.8 years	A. MONO or COMBO B. Losartan (+HCTZ) vs Atenolol (+HCTZ) C. LY	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ CHF 31	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ $24	NA	Losartan is more CE than atenolol.

		E. 5% F. Deterministic		[Increasing LY] ▪ 0.0498 years (2003)			
Smith (2004)[46]	A. U.S. B. HTN + DM + Renal disease C. Industry	A. CUA B. Third party payer C. Trial-based (MARVAL) and Model-based (Markov) D. 8 years E. 3% F. Deterministic	A. MONO B. Valsartan vs Amlodipine C. QALY	[ICER/ QALY] ▪ Dominant ($–58,400) (2001)	[ICER/ QALY] ▪ Dominant ($–82,692)	NA	Valsartan is more CE than amlodipine.
Palmer (2004)[25] *(additionally reported in Appendix C)*	A. United Kingdom B. HTN + DM + Renal disease C. Industry	A. CEA B. Healthcare payer C. Trial-based (IDNT) and Model-based (Markov) D. 10 years E. 6%; 1.5% (outcome) F. Deterministic	A. MONO or COMBO B. Irbesartan (+CVTX) vs Amlodipine (+CVTX) C. LY	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ £5,125 [Increasing LY] ▪ 0.07 years (2003)	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ $9,786	NA	Irbesartan is more CE than amlodipine.
Coyle (2004)[26] *(additionally reported in Appendix C)*	A. Canada B. HTN + DM + Renal disease C. Industry	A. CEA B. Third party payer C. Trial-based (IDNT) and Model-based (Markov; MCMS) D. 25 years E. 5% F. Deterministic and Probabilistic	A. MONO or COMBO B. Irbesartan (+CVTX) vs Amlodipine (+CVTX) C. LY	[ICER/LY] ▪ Dominant [Cost] ▪ irbesartan: C$89,304 ▪ amlodipine: C$109,280 [LY] ▪ irbesartan: 6.80 ▪ amlodipine: 6.46 (2001)	[ICER/LY] ▪ Dominant [Cost] ▪ irbesartan: $103,539 ▪ amlodipine: $126,822	C$30,000–50,000	Irbesartan is more CE than amlodipine.
Palmer (2003)[27] *(additionally reported in Appendix C)*	A. Belgium, France B. HTN + DM + Renal disease C. Industry	A. CEA B. Healthcare payer C. Trial-based (IDNT) and Model-based (Markov) D. 25 years E. 3% F. Deterministic	A. MONO or COMBO B. Irbesartan (+CVTX) vs Amlodipine (+CVTX) C. LY	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ Belgium: €21,163; France: €27,044 [Increasing LY] ▪ Belgium: 0.71 years; France: 0.69 years (2002)	[ICER/LY] ▪ Dominant [Decreasing cost] ▪ Belgium: $34,216; France: $43,725	NA	Irbesartan is more CE than amlodipine.

Rodby (2003)[28] *(additionally reported in Appendix C)*	A. U.S. B. HTN + DM + Renal disease C. Industry	A. CEA B. Healthcare payer C. Trial-based (IDNT) and Model-based (Markov) D. 3, 10, 25 years E. 3% F. Deterministic	A. MONO or COMBO B. Amlodipine (+CVTX) vs Irbesartan (+CVTX) C. LY	[ICER/LY (25 years)] ▪ Dominated [Increasing cost] ▪ £26,290 [Decreasing LY] ▪ 0.624 years (2003)	[ICER/LY (25 years)] ▪ Dominated [Increasing cost] ▪ $50,200	NR	Irbesartan is more CE than amlodipine.
Baio (2003)[47]	A. Italy B. HTN C. Industry	A. CEA B. Health care C. Model-based (MCMC) D. 1 year E. NA F. NC	A. MONO or COMBO B. Losartan vs Indapamide or Fosinopril or Atenolol or Amlodipine C. Medication persistence	[ICER/persistence] ▪ NR [Cost] ▪ Losartan: €176 ▪ Indapamide: €46 ▪ Fosinopril: €87 ▪ Atenolol: €44 ▪ Amlodipine: €120 [Medication persistence] ▪ Losartan: 18.4 ▪ Indapamide: 13.7 ▪ Fosinopril: 8.4 ▪ Atenolol: 15.3 ▪ Amlodipine: 12.8 (1997)	[ICER/persistence] ▪ NR [Cost] ▪ Losartan: $316 ▪ Indapamide: $82 ▪ Fosinopril: $156 ▪ Atenolol: $79 ▪ Amlodipine: $215	NA	Losartan is more CE than fosinopril and amlodipine.
Nordmann (2003)[48]	A. Canada B. HTN C. Non-profit	A. CEA and CUA B. Third party payer C. Model-based (Markov) D. Lifetime E. 5% F. Deterministic	A. MONO B. Enalapril vs HCTZ or Atenolol C. QALY; LY	[ICER/QALY] ▪ $700,000 [ICER/LY] ▪ $525,000 (1999)	[ICER/QALY] ▪ $1,056,065 [ICER/LY] ▪ $792,049	$100,000	HCTZ or atenolol is more CE than enalapril.
Gray (2001)[49]	A. United Kingdom B. HTN + DM C. Industry + Non-profit	A. CEA B. Health care C. Trial-based (UKPDS) D. 8.4 years (median) E. 3%; 6% F. Deterministic	A. MONO B. Atenolol vs Captopril C. LY	[ICER/LY] ▪ NR [Decreasing cost] ▪ £945–£1,039 [Increasing LY] ▪ 0.2–0.3 years (1997)	[ICER/LY] ▪ NR [Decreasing cost] ▪ $2,099–$2,308	NA	Atenolol is more CE than captopril.
Doyle (2001)[50]	A. U.S. B. HTN	A. CEA B. NR	A. MONO or COMBO	[Cost/Treatment success] ▪ NR	[Cost/Treatment success] ▪ NR	NA	Amlodipine is more CE

	C. Industry	C. Trial-based D. 50 weeks E. NA F. Deterministic	B. Amlodipine (+ HCTZ) vs Enalapril (+ HCTZ) C. Treatment success	[Cost/Treatment success] ▪ amlodipine: £609 ▪ enalapril: £772 (1997)	[Cost/Treatment success] ▪ amlodipine: $1,353 ▪ enalapril: $1,715		than enalapril.
Plans-Rubió (1998)[51]	A. Spain B. HTN C. NR	A. CEA B. Societal C. Model-based D. NR E. 5% F. Deterministic	A. MONO B. HCTZ vs Propranolol vs Nifedipine vs Prazosin vs Captopril C. LY	[ICER/LY] ▪ NR [Cost/ LY] ▪ HCTZ: $6,351–$28,539 ▪ Propranolol: $6,500–$30,316 ▪ Nifedipine: $7,252–$39,610 ▪ Prazosin: $8,562–$52,499 ▪ Captopril: $28,858–$126,990 (1996)	[ICER/LY] ▪ NR [Cost/ LY] ▪ HCTZ: $10,200–$45,837 ▪ Propranolol: $10,440–$48,691 ▪ Nifedipine: $11,647–$63,618 ▪ Prazosin: $13,751–$84,319 ▪ Captopril: $46,349–$203,959	NA	HCTZ, propranolol, and nifedipine are more CE than prazosin and captopril.
Johannesson (1993)[52]	A. Sweden B. HTN C. Industry + Non-profit	A. CEA B. NR C. Trial-based (MAPHY) D. 5 years E. 5% F. Deterministic	A. MONO B. Metoprolol vs HCTZ C. LY	[ICER/LY] ▪ $2,400 (1991)	[ICER/LY] ▪ $4,748	NR	Metoprolol is more CE than HCTZ.
Edelson (1990)[53]	A. U.S. B. HTN C. Non-profit	A. CEA B. NR C. Model-based (Simulation) D. 20 years E. 5% F. Deterministic	A. MONO B. HCTZ vs Propranolol vs Nifedipine vs Prazosin vs Captopril C. LY	[ICER/LY] ▪ NR [Cost/ LY] ▪ propranolol: $10,900 ▪ HCTZ: $16,400 ▪ nifedipine: $31,600 ▪ prazosin: $61,900 ▪ captopril: $72,100 (1987)	[ICER/LY] ▪ NR [Cost/ LY] ▪ propranolol: $29,303 ▪ HCTZ: $44,088 ▪ nifedipine: $84,951 ▪ prazosin: $166,407 ▪ captopril: $193,828	NA	Propranolol, is more CE than HCTZ, nifedipine, prazosin, and captopril.

Appendix Table 5. Summary of Cost Effectiveness Analyses Comparing Antihypertensive Medicines Within Same Medicine Class

Reference	Study setting	Study design	Intervention and outcome	Cost effectiveness evidence			
Author (Year)	**A. Country** **B. Disease** **C. Funding**	**A. Type** **B. Perspective** **C. Method** **D. Time horizon** **E. Discount rate** **F. Sensitivity analysis**	**A. Treatment type** **B. Intervention vs comparator** **C. Outcome**	**Original results by authors (Year of monetary unit)**	**Adjustment to 2015 U.S. dollars**	**ICER threshold**	**Conclusions by authors**
Patel (2014)[54]	A. India B. HTN C. NR	A. CEA B. NR C. Trial-based D. NR E. NA F. NC	A. MONO B. Nebivolol vs Metoprolol C. BP reduction (1 mmHg)	[Cost/BP reduction] ▪ Nebivolol: ₹33.6–₹64.0 ▪ Metoprolol: ₹52.7–₹66.5 (2013)	[Cost/BP reduction] ▪ Nebivolol: $2.1–$4.0 ▪ Metoprolol: $3.3–$4.2	NR	Nebivolol is more CE than metoprolol.
Kourlaba (2013)[55]	A. Greece B. HTN C. Industry	A. CEA and CUA B. Third party payer C. Model-based (Markov) D. 10 years E. 3.5% F. Probabilistic	A. COMBO B. Telmisartan + HCTZ vs. Losartan + HCTZ or Valsartan + HCTZ C. QALY; LY	[ICER/QALY] ▪ vs losartan: €3,002–€10,856 ▪ vs valsartan: €4,806–€25,847 [ICER/LY] ▪ vs losartan: €1,765–€7,061 ▪ vs valsartan: €7,656–€20,123 (2012)	[ICER/QALY] ▪vs losartan: $4,029–$14,569 ▪vs valsartan: $6,450–$34,687 [ICER/LY] ▪vs losartan: $2,369–$9,476 ▪vs valsartan: $10,275–$27,006	$50,000 €62,000	Telmisartan is more CE than losartan and valsartan.
Baker (2012)[56]	A. U.S. B. HTN C. Industry	A. CEA and CUA B. Third party payer C. Model-based (Markov) D. 20 years E. 3% F. Deterministic	A. MONO B. Valsartan vs Losartan C. QALY; LY; CVD avoided	[ICER/QALY] ▪ $30,170–$32,313 [ICER/LY] ▪ $25,460–$27,268 [ICER/CVD avoided] ▪ $53,646–$57,457 (2012)	[ICER/QALY] ▪ $31,341–$33,567 [ICER/LY] ▪ $26,448–$28,326 [ICER/CVD avoided] ▪ $55,727–$59,686	$100,000	Valsartan is more CE than losartan.
Granström (2012)[57]	A. Sweden B. HTN C. Industry	A. Type B. Health care C. Model-based (Markov) D. 4 years	A. MONO B. Candesartan vs Losartan C. QALY; LY	[ICER/QALY and LY] ▪ Dominant [Decreasing cost] ▪ kr 4,259–kr 4,692	[ICER/QALY and LY] ▪ Dominant [Decreasing cost] ▪ $510–$562	NA	Candesartan is more CE than losartan.

		E. 3% F. Deterministic and Probabilistic		[Increasing QALY] ▪ 0.053–0.057 [Increasing LY] ▪ 0.050–0.054 (2011)			
Belsey (2011)[58]	A. United Kingodm B. HTN C. Industry	A. CBA B. Health care C. Method (MCMS) D. 12x28 days E. NA F. NC	A. MONO or COMBO B. Olmesartan (+ HCTZ + amlodipine) vs Candesartan (+ BFTZ + amlodipine) C. Monetary value	[Cost/target BP] ▪ Olmesartan: £171 ▪ Candesartan: £190 (2010)	[Cost/target BP] ▪ Olmesartan: $264 ▪ Candesartan: $293	NA	Olmesartan is more CE than candesartan.
Grosso (2011)[59]	A. United Kingdom B. HTN + HF C. Industry	A. CUA B. Health care C. Model-based (Markov) D. 10 years E. 3.5% F. Deterministic	A. MONO B. Candesartan vs Losartan C. QALY	[ICER/QALY] ▪ £41,469–£85,244 (2009)	[ICER/QALY] ▪ $64,908–$133,426	£30,000 /QALY	Losartan is more CE than candesartan.
Maniadakis (2011)[60]	A. Greece B. HTN C. Industry	A. CUA B. Payer C. Model-based (Markov) D. Lifetime E. 3% F. Deterministic	A. COMBO B. Irbesartan + HCTZ vs Losartan + HCTZ or Valsartan + HCTZ C. QALY	[ICER/QALY] ▪ Dominant [Cost] ▪ Irbesartan: €12,945, €15,146 ▪ Losartan: €13,424, €15,696 ▪ Valsartan: €13,379, €15,613 [QALY] ▪ Irbesartan: 14.29, 12.67 ▪ Losartan: 14.27, 12.63 ▪ Valsartan: 14.27, 12.64 (2008)	[ICER/QALY] ▪ Dominant [Cost] ▪ Irbesartan: $18,361, $21,430 ▪ Losartan: $18,994, $22,209 ▪ Valsartan: $18,930, $22,091	NA	Irbesartan is more CE than losartan and valsartan.
Boersma (2010)[61]	A. The Netherlands B. HTN C. Industry	A. CEA B. Health care C. Trial-based D. 1, 5 years	A. MONO B. Olmesartan vs Losartan or Valsartan or Irbesartan C. CVD avoided	[ICER/QALY] ▪ Dominant [Cost/QALY]	[ICER/QALY] ▪ Dominant [Cost/QALY]	NA	Olmesartan is more CE than losartan, valsartan, and irbesartan.

		E. 4%; 1.5% (outcome) F. NC		▪ Olmesartan: €39,100 ▪ Losartan: €77,100 ▪ Valsartan: €70,770 ▪ Irbesartan: €50,900 (2006)	▪ Olmesartan: $57,151 ▪ Losartan: $112,693 ▪ Valsartan: $103,441 ▪ Irbesartan: $74,398		
Ekman (2008)[9] *(additionally reported in Appendix B)*	A. Sweden B. HTN C. Industry	A. CUA B. Health care C. Model-based (Markov) D. Lifetime E. 3% F. Deterministic	A. COMBO: +HCTZ B. Irbesartan vs Losartan or Valsartan C. QALY	[ICER/QALY] ▪ Dominant [Cost] ▪ Irbesartan: €12,378, €16,329 ▪ Losartan: €13,160, €16,590 ▪ Valsartan: €13,081, €15,497 [QALY] ▪ Irbesartan: 14.228, 13.204 ▪ Losartan: 14.226, 13.195 ▪ Valsartan: 14.225, 13.197 (2007)	[ICER/QALY] ▪ Dominant [Cost] ▪ Irbesartan: $17,635, $23,264 ▪ Losartan: $18,749, $23,636 ▪ Valsartan: $18,636, $22,078	€50,000–€60,000	Irbesartan is more CE than losartan and valsartan.
Saito (2008)[62]	A. Japan B. HTN C. NR	A. CEA B. Insurer C. Trial-based (ADVANCE-Combi) D. 16 weeks E. NA F. Deterministic and Probabilistic	A. COMBO B. Nifedipine + valsartan vs Amlodipine + valsartan C. BP reduction (target)	[ICER/target BP] ▪ Dominant [Cost] ▪ Nifedipine: ¥31,615 ▪ Amlodipine: ¥35,599 [Target BP achievement] ▪ Nifedipine: 61.2% ▪ Amlodipine: 34.6% (2004)	[ICER/target BP] ▪ Dominant [Cost] ▪ Nifedipine: $303 ▪ Amlodipine: $341	NA	Nifedipine is more CE than amlodipine

Simons (2003)[63]	A. U.S. B. HTN C. Industry	A. CBA B. Managed care C. Trial-based D. 1, 3, 5 years E. NC F. NC	A. MONO B. Olmesartan vs Losartan or Valsartan or Irbesartan C. Monetary value	[Incremental benefit (5 years)] ▪ vs losartan: $14–$151 ▪ vs valsartan: $17–$162 ▪ vs irbesartan: $5–$54 (1999)	[Incremental benefit (5 years)] ▪ vs losartan: $21–$228 ▪ vs valsartan: $26–$244 ▪ vs irbesartan: $8–$81	NA	Olmesartan is more CS than losartan, valsartan, and irbesartan.
Anderson (2000)[64]	A. South Africa B. HTN C. Industry	A. CEA B. Third party payer C. Trial-based D. 1 month E. NA F. Deterministic	A. MONO B. Candesartan vs Losartan or Valsartan or Irbesartan C. BP reduction (1 mmHg)	[ICER/BP reduction] ▪ NR [Cost/BP reduction] ▪ Candesartan: R22.3 ▪ Losartan: R26.5 ▪ Valsartan: R32.9 ▪ Irbesartan: R29.6 (2000)	[ICER/BP reduction] ▪ NR [Cost/BP reduction] ▪ Candesartan: $12 ▪ Losartan: $14 ▪ Valsartan: $18 ▪ Irbesartan: $16	NA	Candesartan is more CE than losartan, valsartan, and irbesartan.
Milne (1997)[65]	A. New Zealand B. HTN C. Industry	A. CEA B. Societal (partial) C. Trial-based D. 5 years E. 5% F. Deterministic	A. MONO B. Celiprolol vs Atenolol C. LY	[ICER/LY] ▪ NR [Cost/LY] ▪ Celiprolol: NZ$5,707–NZ$105,298 ▪ Atenolol: NZ$8,657–NZ$134,339 (1997)	[ICER/LY] ▪ NR [Cost/LY] ▪ Celiprolol: $6,206–$114,513 ▪ Atenolol: $9,415–$146,096	NR	Celiprolol is more CE than atenolol.

Appendix Table 6. Summary of Cost Effectiveness Analyses Comparing Different Combination Therapies

Reference	Study setting	Study design	Intervention and outcome	Cost effectiveness evidence			
Author (Year)	**A. Country** **B. Disease** **C. Funding**	**A. Type** **B. Perspective** **C. Method** **D. Time horizon** **E. Discount rate** **F. Sensitivity analysis**	**A. Treatment type** **B. Intervention vs comparator** **C. Outcome**	**Original results by authors (Year of monetary unit)**	**Adjustment to 2015 U.S. dollars**	**ICER threshold by authors**	**Conclusions by authors**
Tsuji (2012)[66]	A. Brazil B. HTN C. Industry	A. CEA B. NR C. Trial-based D. NR E. NR F. NC	A. COMBO B. Grade 1 and 2 HTN: Atenolol + HCTZ (+ enalapril) vs Amlodipine + losartan (+ HCTZ); Grade 3 HTN: (+ clodine) Atenolol + enalapril + HCTZ vs Amlodipine + enalapril + HCTZ C. BP reduction (1 mm Hg)	[ICER/BP reduction] ▪ Grade 1 and 2 HTN: SBP: $1,150; DBP: dominant ▪ Grade 3 HTN: SBP: $27; DBP: $76 (2007)	[ICER/BP reduction] ▪ Grade 1 and 2 HTN: SBP: $1,346; DBP: dominant ▪ Grade 3 HTN: SBP: $32; DBP: $89	NR	Atenolol + HCTZ (+enalapril) is more CE than amlodipine + losartan (+HCTZ).
Lindgren (2009)[67]	A. United Kingdom, Sweden B. HTN C. Industry	A. CEA and CUA B. Health care, Societal C. Trial-based (ASCOT-LLA) and Model-based (Markov) D. Lifetime E. United Kingdom: 3.5%; Sweden: 3% F. Deterministic and Probabilistic	A. MONO or COMBO B. Amlodipine (+ perindopril) vs Atenolol (+ bendroflumethiazide) C. QALY; LY	[ICER/QALY] ▪ United Kingdom: €9,548; Sweden: €3,965 [ICER/LY] ▪ United Kingdom: €21,875; Sweden: €16,868 (2007)	[ICER/QALY] ▪ United Kingdom: $13,599; Sweden: $5,649 [ICER/LY] ▪ United Kingdom: $31,165; Sweden: $24,032	United Kingdom: £20,000 /QALY (€29,000) Sweden: kr 100,000 /QALY (€11,000)	Amlodipine-based TX is more CE than atenolol-based TX.
Lindgren (2008)[68]	A. United Kingdom, Sweden B. HTN C. Industry	A. CEA and CUA B. NR C. Trial-based (ASCOT-BPLA) and Model-based (Markov) D. Lifetime E. United Kingdom: 3.5%; Sweden: 3%	A. MONO or COMBO B. Amlodipine (+ perindopril) vs Atenolol (+ bendroflumethiazide) C. QALY; LY	[ICER/QALY] ▪ United Kingdom: €21,876; Sweden: €16,868 [ICER/LY] ▪ United Kingdom: €17,857; Sweden: €14,022 (2006)	[ICER/QALY] ▪ United Kingdom: $31,975; Sweden: $24,655 [ICER/LY] ▪ United Kingdom: $26,101; Sweden: $20,495	United Kingdom: £20,000 /QALY (€29,000) Sweden: kr 500,000 /QALY (€55,000)	Amlodipine-based TX is more CE than atenolol-based TX.

		F. Deterministic and Probabilistic					
Saito (2008)[69]	A. Japan B. HTN (+ DM) C. Industry	A. CUA B. Payer C. Model-based (Markov; MCMS) D. Lifetime E. 3% F. Deterministic	A. MONO or COMBO B. AZEL + olmesartan vs AZEL or Olmesartan C. QALY	[ICER/QALY] ▪ Dominant [Cost: with DM] ▪ AZEL+olmesartan: ¥9.86 million ▪ AZEL: ¥11.01 million ▪ Olmesartan: ¥6.21 million [QALY: with DM] ▪ AZEL+ olmesartan:15.00 ▪ AZEL: 14.25 ▪ Olmesartan: 14.69 (2006)	[ICER/QALY] ▪ Dominant [Cost: with DM] ▪ AZEL+olmesartan: $95,577 ▪ AZEL: $106,724 ▪ Olmesartan: $69,196	¥5 million /QALY ($50,000)	AZEL + olmesartan is more CE than AZEL or olmesartan.
Saito (2007)[70]	A. Japan B. HTN + Renal disease C. NR	A. Type B. NR C. Trial-based D. 5 months E. NA F. NC	A. MONO or COMBO B. ARB (+ benidipine) vs Benidipine (+ ARB) C. BP reduction (1 mm Hg) (ARB: losartan or candesartan or valsartan)	[ICER/BP reduction] ▪ NR [Monthly cost /BP reduction] ▪ ARB-based: ¥439 ▪ Benidipine-based: ¥235 (2004)	[ICER/BP reduction] ▪ NR [Monthly cost /BP reduction] ▪ ARB-based: $4 ▪ Benidipine-based:$2	NA	Benidipine-based TX is more CE than ARB-based TX.
Robberstad (2007)[71]	A. Tanzania B. HTN C. Non-profit	A. CEA B. Health care C. Model-based (Markov) D. Lifetime E. 3% F. Deterministic	A. COMBO B. (vs no TX) 1. ASA+HCTZ 2. ASA +atenolol 3. HCTZ+atenolol 4. ASA +HCTZ+atenolol 5. ASA +HCTZ+lovastatin 6. HCTZ+atenolol+losartan 7. ASA+atenolol+lovastatin 8. ASA+HCTZ+atenolol+lovastatin 9.ASA+HCTZ+atenolol+nifedipine +lovastatin+folic acid C. DALY	[ICER/DALY] 1. $143 2. dominated 3. dominated 4. $317 5. dominated 6. dominated 7. dominated 8. $999 9. $1,476 (2005)	[ICER/DALY] 1. $178 2. dominated 3. dominated 4. $395 5. dominated 6. dominated 7. dominated 8. $1,245 9. $1,840	NR	Using HCTZ is more CE than other combination TX.
Saito (2005)[72]	A. Japan B. HTN (+ DM)	A. CEA B. General practice	A. MONO or COMBO	[ICER/LY] ▪ NR [Cost: male with DM]	[ICER/LY] ▪ NR [Cost: male with DM]	NA	Olmesartan (+ AZEL) is more CE than

	C. Industry	C. Model-based (Markov) D. Lifetime E. 3% F. Deterministic	B. Olmesartan (+ AZEL) vs AZEL (+ olmesartan) vs Olmesartan (+ TCMT) vs TCMT (+ olmesartan) C. LY	▪ olmesartan (+ AZEL): ¥17.00 million ▪ AZEL (+ olmesartan): ¥19.52 million ▪ olmesartan (+ TCMT): ¥17.61 million ▪ TCMT (+ olmesartan): ¥19.68 million [LY: male with DM] ▪ olmesartan (+ AZEL): 24.81 ▪ AZEL (+ olmesartan): 24.38 ▪ olmesartan (+ TCMT): 24.71 ▪ TCMT (+ olmesartan): 24.28 (2004)	▪ olmesartan (+ AZEL): $162,796 ▪ AZEL (+ olmesartan): $186,928 ▪ olmesartan (+ TCMT): $168,638 ▪ TCMT (+ olmesartan): $188,461		AZEL(+ olmesartan), olmesartan (+ TCMT), or TCMT (+ olmesartan).
Fujikawa (2005)[73]	A. Japan B. Disease C. Industry	A. CEA B. Third party payer C. Trial-based (NICE-Combi) D. 8 weeks E. NA F. Deterministic	A. MONO or COMBO B. Candesartan (low dose) + nifedipine vs Candesartan C. BP reduction (target)	[ICER/BP reduction] ▪ Dominant [Cost/ BP reduction] ▪ Candesartan + nifedipine: ¥105,063 ▪ candesartan: ¥192,916 (2004)	[ICER/BP reduction] ▪ Dominant [Cost/ BP reduction] ▪ candesartan + nifedipine: $1,006 ▪ candesartan: $1,847	NA	Candesartan (low dose) + nifedipine is more CE than candesartan.
Marshall (2003)[74]	A. United Kingdom B. HTN C. None	A. CEA B. Health service C. Model-based D. 5 yeras E. 6% (cost); 1.5% (outcome) F. Deterministic	A. COMBO B. BNF + atenolol + enalapril vs BNF + atenolol C. Coronary event prevented	[ICER/event prevented] ▪ NR [Cost/event prevented] ▪ With enalapril: £18,300 ▪ Without enalapril: £12,600 (2002)	[ICER/event prevented] ▪ NR [Cost/event prevented] ▪ With enalapril: $36,545 ▪ Without enalapril: $25,162	NA	Adding enalapril is less CE than BNF + atenolol.
Casciano (2001)[75]	A. United Kingdom, Italy B. HTN + DM C. NR	A. CEA B. Government payer C. Trial-based (UKPDS-38) and Model-based (Markov)	A. COMBO B. 1. Captopril + FUR + nifedipine vs. Doxazosin + FUR + nifedipine	[ICER/LY] ▪ United Kingdom 1. £2,224 2. £2,925 3. £3,780 4. £3,751	[ICER/LY] ▪ United Kingdom 1. $4,623 2. $6,080 3. $7,857 4. $7,797	NR	Including doxazosin is more CE than other combination TX.

		D. 10 years E. 3% (cost) F. Deterministic	2. Captopril + FUR + nifedipine vs Captopril +doxazosin + nifedipine 3. Captopril + FUR + nifedipine vs Captopril + FUR + doxazosin 4. Atenolol + FUR + nifedipine vs Doxazisin + FUR + nifedipine 5. Atenolol + FUR + nifedipine vs Atenolol + doxazisin + nifedipine 6. Atenolol + FUR + nifedipine vs Atenolol + FUR + doxazisin C. LY	5. £4,783 6. £3,696 ▪ Italy 1. £1,842,440 2. £9,274,595 3. £7,999,547 4. £7,772,730 5. £8,949,418 6. £7,676,042 (1999)	5. $9,942 6. $7,682 ▪ Italy 1. $1,532 2. $7,710 3. $6,650 4. $6,461 5. $7,439 6. $6,381		
Andersson (1998)[76]	A. Sweden B. HTN C. Industry	A. CEA B. Third party payer C. Trial-based D. 4, 8 weeks E. NA F. NC	A. MONO or COMBO B. Felodipine + metoprolol vs Enarlapril C. BP reduction (target)	[ICER/ BP reduction] ▪ kr 86 (1997)	[ICER/ BP reduction] ▪ $15	NR	Felodipine + metoprolol is more CE than enarlapril.

KEY TERMINOLOGIES

These are the brief definitions of terminologies commonly used for this review.[77]

- Cost-minimization analysis (CMA): "CMA is a type of pharmacoeconomic analysis comparing two alternative therapies only in terms of costs because their outcomes are found to be or expected to be identical."
- Cost-effectiveness analysis (CEA): "CEA is a systematic method of comparing two or more alternative programs by measuring the costs and consequences of each. A distinguishing feature of cost-effectiveness analysis is that the consequences (health outcomes) of all the programs to be compared mist be measured in the same common units – natural units related to the clinical objective of the programs."
- Cost-utility analysis (CUA): "CUA is a methodology of economic analysis that compare two or more alternatives choices in terms of both their costs and their outcomes, where the outcomes are measured in units of utility or preference, often as a QALY."
- Cost-benefit analysis (CBA): "CBA is an analytical technique derived from economic theory that enumerates and compares the net costs of a health care intervention with the benefits that arise as a consequences of applying that intervention."
- Incremental cost-effectiveness ratio (ICER): "If there are just two alternative programs, their difference in costs (incremental costs) is compared to their difference in outcomes (incremental effect) by dividing the former by the later. This ratio is known as the ICER."
- Quality-adjusted life year (QALY): "A QALY is a universal health outcome measure applicable to all individuals and all diseases, thereby enabling comparisons across diseases and across programs. A QALY combines, in a single measure, gains or losses in both quantity of life (mortality) and quality of life (morbidity)."

Note: These were quoted directly from the book, titled "Health care cost, quality, and outcomes: ISPOR book of terms."

ABBREVIATIONS FOR APPENDICES

- Disease: HTN, hypertension; DM, diabetes mellitus; MI, myocardial infarction; myocardial infarction; LVD, left ventricular dysfunction; HL, hyperlipidemia; LVH, left ventricular hypertrophy; HF, heart failure
- **Study type: CEA, cost-effectiveness analysis; CUA: cost-utility analysis; CMA, cost-minimization analysis; CBA, cost-benefit analysis**
- **Study method:** [Trial] ADVANCE, Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation; CHHIPS, Hypertension and Hypotension Immediately Post-Stroke; HYVET, Hypertension in the Very Elderly Trial; VALIANT, Valsartan in Acute Myocardial Infarction; PROGRESS, Perindopril Protection against Recurrent Stroke Study; WHI, Women's Health Initiative; AIRE, Acute Infarction Ramipril Efficacy; HOPE, Heart Outcomes Prevention Evaluation; MICRO-HOPE, Microalbuminuria, Cardiovascular, and Renal Outcomes- Heart Outcomes Prevention Evaluation; AIPRI, ACE Inhibition in Progressive Renal Insufficiency; SOLVD, Studies of Left Ventricular Dysfunction; IRMA, Irbesartan Microalbuminuria Study; IDNT, Irbesartan Diabetic Nephropathy Trial, RENAAL, Reduction in End Points in NIDDM with the Angiotensin II Antagonist Losartan; SCOPE, Study on Cognition and Prognosis in the Elderly; REIN, Ramipril Efficacy In Nephropathy; ANBP-2, Second Australian National Blood Pressure Study; MOSES, Morbidity and Mortality after Stroke - Eprosartan Compared with Nitrendipine for Secondary Preventionl ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; LIFE, Losartan Intervention For Endpoint reduction; MARVEL, Microalbuminuria Reduction

with Valsartan; UKPDS, UK Prospective Diabetes Study; MAPHY, Metoprolol Atherosclerosis Prevention in Hypertensives; ASCOT-LLA, Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm; ASCOT-BPLA, Anglo-Scandinavian Cardiac Outcomes Trial - Blood Pressure Lowering Arm; **NICE-Combi, Nifedipine and Candesartan Combination; [Model] MCMS, Monte Carlo microsimulation; MCMC, Markov chain Monte Carlo;**

- **Treatment type: MONO, monotherapy; COMBO, combination therapy; PT, primary therapy**
- **Intervention and comparator: TX, treatment; CVTX, conventional treatment; HCTZ, hydrochlorothiazide; TCMT, trichlormethiazide;** CTD, chlorthalidone; **AZEL, azelnidipine; BNF, bendrofluazide; FUR, furosemide; ASA, acetylsalicylic acid**
- **Outcome: LY, life year; QALY, quality-adjusted life year; DALY, disability-adjusted life year; ESRD, end-stage renal disease; BP, blood pressure**
- **Cost-effectiveness evidence: ICER, incremental cost-effectiveness ratio; CE, cost-effectiveness**
- Other: NR, not reported; NC, not conducted; NA, not applicable

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