



Cost-Effectiveness of Bempedoic Acid in High Cardiovascular Risk Patients with Statin Intolerance: An Analysis of the CLEAR Outcomes Trial

Stephen J. Nicholls¹ · Kausik K. Ray² · A. Michael Lincoff³ · Evelyn Sarnes⁴ · Kristin K. Gillard⁴ · LeAnne Bloedon⁴ · Kristen Migliaccio-Walle⁵ · David Elsea⁵ · Steven E. Nissen³

Accepted: 14 July 2025 / Published online: 20 August 2025
© The Author(s) 2025

Abstract

Background In the CLEAR Outcomes study, 13,970 high cardiovascular risk patients with hypercholesterolemia and statin intolerance were randomized to treatment with bempedoic acid or standard of care (placebo). Bempedoic acid reduced the risk of major adverse cardiovascular events by 13%. However, the cost-effectiveness of bempedoic acid in this patient population is unknown.

Methods Markov modeling estimated cost-effectiveness of bempedoic acid versus standard of care alone to reduce cardiovascular risk from a US third-party payer perspective. Baseline risk was estimated by applying individual patient characteristics from the trial to established risk equations. Treatment benefit was extrapolated over a lifetime horizon using hazard ratios for individual major adverse cardiovascular event (MACE) components from CLEAR Outcomes. Scenario analyses included on-treatment analysis, alternate bempedoic acid costs, and modeling effects of the fixed-dose combination with ezetimibe on low-density lipoprotein cholesterol (LDL-C) reduction and predicted MACE.

Results Bempedoic acid was estimated to reduce lifetime MACE (1.58 versus 1.95 per patient) versus standard of care. At list price, bempedoic acid was associated with increased costs (+ \$22,600) and improved quality-adjusted life-years (QALYs, + 0.14), resulting in an incremental cost-effectiveness ratio (ICER) of \$166,830 per QALY. The on-treatment analysis resulted in an ICER of \$70,279 per QALY. Reduction in bempedoic acid price by 25% resulted in lower incremental total costs and an ICER of \$99,993 per QALY. Modeling the effects of the fixed-dose combination resulted in an ICER of \$40,317 per QALY.

Conclusions Use of bempedoic acid offers improved lifetime cardiovascular (CV) risk reduction over standard of care in patients with or at high risk for CV disease (CVD) at common cost-effectiveness thresholds (\$150,000 per QALY).

Trial Registration ClinicalTrials.gov identifier: NCT02993406 (CLEAR Outcomes study).

1 Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the USA and worldwide. By 2035, an estimated 45% of the US population is expected to have

CVD, incurring \$749 billion in medical costs [1, 2]. The sequelae of CVD can be devastating to patients, resulting in premature death or disability, as well as impose a significant economic burden to patients and the healthcare system [3, 4]. For example, data from the National Inpatient Sample has shown an average cost of acute myocardial infarction (MI) hospitalization ranging from \$21,898 to \$71,788, and stroke hospitalization from \$21,844 to \$29,027 [4]. The cost burden for these events extends beyond the hospitalization, with increased healthcare utilization continuing 2–3 years after the acute event [5]. As such, interventions that reduce the risk of cardiovascular morbidity may provide substantial economic value at a population- and health-system level.

The causal role of low-density lipoprotein cholesterol (LDL-C) in atherosclerotic cardiovascular disease (ASCVD) has been well established by preclinical, observational, and genetic studies [6]. The importance of LDL-C in

Kristin K. Gillard, David Elsea: At time of study.

✉ Stephen J. Nicholls
stephen.nicholls@monash.edu

¹ Victorian Heart Institute, Monash University, 631 Blackburn Road, Clayton, VIC 3168, Australia

² Imperial College London, London, UK

³ Cleveland Clinic, Cleveland, OH, USA

⁴ Esperion Therapeutics, Ann Arbor, MI, USA

⁵ Curta Inc., Seattle, WA, USA

Key Points

While statins are the cornerstone for lowering LDL-C, non-statin therapies may provide an effective lipid-lowering alternative in patients who are unable to tolerate or unwilling to take statin therapy.

Clinicians, policy makers, and payers should understand the clinical benefits and economic value of non-statin oral agents, such as bempedoic acid, to lower LDL-C and cardiovascular risk in primary and secondary prevention patients.

Our findings suggest that the use of bempedoic acid at prices resembling those paid by payers provides good economic value, with incremental cost-effectiveness ratios well below the threshold commonly used in the USA of < \$150,000 per QALY.

cardiovascular risk is further supported by consistent observations from randomized clinical trials, demonstrating that lowering LDL-C levels with statins [7] and other interventions [8–10] results in less cardiovascular events. The findings of these studies have influenced treatment guidelines, which have placed LDL-C lowering with statins, as monotherapy and in combination with other agents, as a cornerstone approach to reducing cardiovascular risk [11]. However, most high cardiovascular risk patients are not treated with recommended high-intensity statins, and as such, fail to reach guideline directed LDL-C levels [12, 13].

Partial or complete statin intolerance is a major contributing factor to suboptimal lipid management, preventing some patients from reaching recommended cholesterol levels. Symptoms of intolerance to statins are experienced by 10–30% of patients [14]. Patients who are either unwilling or unable to take guideline-directed statin therapy often remain at high LDL-C levels and at an elevated risk of experiencing major adverse cardiovascular events (MACE) [14, 15]. Accordingly, there is a need for effective lipid-lowering therapies that can be used to lower cardiovascular risk in patients who cannot tolerate statins.

The ATP citrate lyase inhibitor, bempedoic acid, has been demonstrated to lower LDL-C levels. The Cholesterol Lowering via Bempedoic Acid, an ACL-Inhibiting Regimen (CLEAR) Outcomes trial evaluated the impact of bempedoic acid, compared with placebo, on MACE in high cardiovascular risk patients who were unable or unwilling to take recommended doses of statins. Treatment with bempedoic acid reduced levels of LDL-C by 21.1% and high sensitivity C-reactive protein by 22.2% at 6 months, and was associated with a 13% risk reduction in time to first occurrence of the MACE-4 primary endpoint (composite

endpoint of cardiovascular death, nonfatal MI, nonfatal stroke, and coronary revascularization) [16]. Bempedoic acid also significantly reduced the risk for the key secondary composite endpoint MACE-3 (composite of cardiovascular death, nonfatal MI, nonfatal stroke) by 15%, and the individual components of the composite endpoint: nonfatal MI and coronary revascularization procedures. The CLEAR Outcomes efficacy endpoints were measured as “time to first event.” However, patients at high CV risk may experience multiple clinical events, resulting in a cumulative burden for both patients and the healthcare system. In a prespecified exploratory analysis of the intention-to-treat population, bempedoic acid was associated with a 20% risk reduction in the total incidence of MACE-4 (hazard ratio [HR] 0.80; 95% confidence interval [CI]: 0.72, 0.89) [17].

To date, no study has evaluated the cost-effectiveness of bempedoic acid in high cardiovascular risk patients who are unable or unwilling to take statins, similar to the CLEAR Outcomes trial population. Although the Institute for Clinical and Economic Review evaluated the cost-effectiveness of bempedoic acid in combination with ezetimibe in March 2021, their analysis was conducted in patients with established ASCVD on maximally tolerated statin therapy [18]. While the model included a subgroup of statin-intolerant patients with ASCVD, the analysis was conducted prior to the completion of CLEAR Outcomes, and risk reduction was predicted on the basis of LDL-C reduction. In a recently published microsimulation model of statin-intolerant patients in Australia and the UK, Morton et al. found that bempedoic acid and ezetimibe, alone or in combination, were cost-effective for long-term primary prevention of CVD disease [19]. However, the health systems, payment/reimbursement, and drug costs in the USA are substantively different, all of which may impact cost-effectiveness. As such, the aim of the current analysis was to determine the cost-effectiveness of bempedoic acid, over a lifetime horizon, compared with placebo (standard of care alone) for high cardiovascular risk patients with statin intolerance from a US payer perspective.

2 Methods

2.1 CLEAR Outcomes Study Design

The CLEAR Outcomes study design and results have been previously reported [16, 20]. Briefly, eligible patients included those 18–85 years of age and with a baseline LDL-C level at least 100 mg/dL with either clinically manifested ASCVD or at high risk of a cardiovascular event. Patients were required to have reported being unable or unwilling to take recommended doses of statins, owing to symptoms of intolerance that improved or went away when the statin was discontinued. Patients were permitted to be

treated with very low doses of statins, defined as below the lowest approved dose. Stable, background lipid-lowering therapies were permitted, including ezetimibe and proprotein convertase subtilisin-kexin type 9 inhibitors. The trial randomized 13,970 patients to treatment with bempedoic acid 180 mg or matching placebo daily, and patients were followed for a median of 3.4 years. The primary efficacy endpoint of the study was the composite endpoint MACE-4; key secondary endpoints included MACE-3, and the individual components of the primary endpoint. The present analysis followed the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guideline [21] (Supplementary Table 4).

2.2 Cost-Effectiveness Analysis: Patient Population and Model Structure

A de novo cohort Markov model with 4-week cycle lengths was developed in Microsoft® Excel, considering the US third-party payer perspective and assuming a lifetime horizon [18]. A cohort of adult patients who were either at high risk for CVD (primary prevention) or who had a history of CVD (secondary prevention) and who were unable or unwilling to take statin therapy entered the model. Patients could then transition between mutually exclusive health states that matched those observed in CLEAR Outcomes: nonfatal MI, nonfatal stroke, coronary revascularization, cardiovascular death, or non-cardiovascular death (Supplementary Fig. 1). In line with the cardiovascular risk profile of CLEAR Outcomes (where enrollment was capped at 30% primary prevention patients), the distribution of patients entering the simulation were 30% primary prevention and 70% secondary prevention. Primary prevention patients became secondary prevention patients if they experienced a nonfatal MACE during a cycle. Multiple events could occur over the lifetime time horizon.

The baseline risk of MACE was calculated using established risk equations and the actual baseline characteristics of individual patients in CLEAR Outcomes and then aggregated, accounting for increase in risk over time as patients age. This was accomplished by increasing the age parameter in each risk equation without changing any other parameters. In the primary prevention population, the Reynolds Risk Score was used to estimate MACE-4 risk [22, 23]. Since there is no established risk equation for MACE-4 in secondary prevention, MACE-3 risk was calculated using SMART2 [24, 25] then inflated by the proportion of coronary revascularizations observed in the CLEAR Outcomes MACE-4 endpoint (43.3%). The risk of 10-year MACE by age is presented in Supplementary Table 1. In the model, the 10-year probabilities were converted to per-cycle probabilities and applied to all cycles where a patient is that age. For example, using

the Reynolds Risk Score, a primary prevention patient between 69.5 and 70.5 years old would have a 10-year MACE risk of 27.3%. When aggregated, the baseline 10-year risk was 21.6% and 36.5% for primary prevention and secondary prevention patients, respectively. In the analysis, primary and secondary prevention patients were handled similarly to the conduct of the CLEAR Outcomes trial, wherein each had a different level of baseline cardiovascular risk and a different distribution of type of MACE event that occurred, but the primary efficacy analysis was conducted on all 13,970 patients randomized [16].

The model simulated subsequent cardiovascular events, including cardiovascular and non-cardiovascular-related deaths as a function of baseline cardiovascular risk and the risk reduction observed for bempedoic acid and standard of care. Non-cardiovascular-related deaths were applied, based on age and sex norms from the US population [26], excluding cardiovascular deaths to avoid double counting. This follows similar methodology used in previous published models [18, 27, 28]. MACE-4 was used in the base case to align with the primary efficacy endpoint of CLEAR Outcomes [16]. When a MACE occurred, the type of event was determined by the distribution of MACE types observed in CLEAR Outcomes. For primary prevention, this distribution was calculated from the number of patients who had a first event of each type. The cardiovascular mortality rate by age was based on the National Center for Health Statistics [29] and the CDC WONDER database [30].

2.3 Intervention Effects

The impact of treatment with bempedoic acid comes from a reduction in the risk of MACE. Hazard ratios (HR) were based on the individual components of the MACE-4 endpoint in CLEAR Outcomes: nonfatal MI, nonfatal stroke, coronary revascularization, and cardiovascular death (Table 1). Although the primary endpoint of CLEAR Outcomes was the time to first MACE-4 event, patients with or at high CV risk may often experience multiple events over a lifetime. As such, the base case used total event HRs in order to best estimate the totality of the impact of treatment for these patients, similar to previously published models [28, 31].

In CLEAR Outcomes, cardiovascular mortality reduction was not observed within the follow-up period. In the base case, risk reduction for cardiovascular mortality was set at 0%, consistent with the approach used in previous cost-effectiveness modeling [27]. The treatment discontinuation rate observed during the trial was applied during the modeled trial period (32.5% by 3.46 years); thereafter, a fixed value of 3.2% per year was assumed (based on the proportion of patients who discontinued treatment due to serious adverse events in CLEAR Outcomes), also consistent with the approach used in previous cost-effectiveness modeling [32].

2.4 Utilities and Costs

Over the model time horizon, patients incurred short- and long-term (3 year) treatment costs, as well as reductions in quality of life when they experienced a MACE. Health-related quality of life (HRQoL), measured by the EQ-5D, was calculated by applying acute and long-term decreases in quality of life after a nonfatal MI or nonfatal stroke to the baseline utility of patients with CVD [33, 34]. Baseline utility and disutility values were taken from previously published sources (Table 1). A coronary revascularization was assumed to have no impact on HRQoL, similar to other published models [31, 32, 35]. If a patient experienced multiple events, only the most severe permanent HRQoL decrement applied. Utility values did not differ between primary and secondary prevention populations. A utility value of 0 was assigned to death status.

Direct medical costs associated with MACE were sourced from US claims data (IMS LifeLink PharMetrics Plus) [5]. Each type of MACE incurred an immediate cost of management (1–4 weeks) as well as costs over the following 3 years; costs differed between primary and secondary prevention patients (Supplementary Table 2). Secondary prevention

patients also incurred an annual cost of \$8329 to reflect the increased monitoring and management of established CVD [36]. Cardiovascular deaths had a one-time cost incurred at the time of death of \$23,527 [31]; non-cardiovascular deaths were assumed to incur no incremental costs. Drug costs for bempedoic acid were based on the 2024 RedBook wholesale acquisition cost of \$408 for 30 tablets (\$13.60 per dose) [37]. Costs for other background lipid-lowering therapies were not included, as baseline usage of background statins and ezetimibe was equal between the intervention and control arms in CLEAR Outcomes [16]. All costs were inflated to 2024 US dollars using the consumer price index for medical care [38].

2.5 Base-Case Cost-Effectiveness Analysis

The model base case simulated quality-adjusted life-years (QALYs), MACE (individual and composite), and total costs for bempedoic acid and standard of care over a lifetime time horizon in the intention-to-treat cohort. The incremental cost per QALY and the incremental cost to avoid a MACE for bempedoic acid versus standard of care were calculated as the incremental cost-effectiveness ratio (ICER) expressed as:

Table 1 Key clinical inputs

Input	Value (95% CI)	Source
ITT hazard ratios (base case) ^a		
Nonfatal MI	0.69 (0.58, 0.83)	[17]
Nonfatal stroke	0.80 (0.63, 1.03)	[17]
Coronary revascularization	0.78 (0.68, 0.89)	[17]
CV death	1.0 ^b	Assumption
On-treatment hazard ratios ^c		
Nonfatal MI	0.69 (0.57, 0.84)	Unpublished data from CLEAR Outcomes database
Nonfatal stroke	0.69 (0.52, 0.92)	Unpublished data from CLEAR Outcomes database
Coronary revascularization	0.74 (0.63, 0.86)	Unpublished data from CLEAR Outcomes database
CV death	0.91 (0.74, 1.12)	[52]
Health state utility values		
Baseline utility	0.854 (0.844, 0.864)	[33, 34]
Acute (4-week) decrement		
Nonfatal MI	− 0.191 (− 0.192, − 0.190)	[43]
Nonfatal stroke	− 0.256 (− 0.257, − 0.256)	[43]
Coronary revascularization	0.000	Assumption
Long-term decrement		
Nonfatal MI	− 0.150 (− 0.150, − 0.1496)	[43]
Nonfatal stroke	− 0.204 (− 0.204, − 0.204)	[43]
Coronary revascularization	0.000	Assumption

CI, confidence interval; CV, cardiovascular; MACE, major adverse cardiac event; MI, myocardial infarction

^aTotal events, ITT

^bHR for CV death assumed = 1.0. 95% CI (0.88, 1.24) from trial used for one-way sensitivity analysis

^cTotal events, on-treatment analysis

$(BA^{Cost} - SOC^{Cost}) / (BA^{QALYs} - SOC^{QALYs})$, where BA is bempedoic acid and SOC is standard of care

Ranges for cost-effectiveness were set at \$50,000 to \$200,000 per QALY, based on commonly used thresholds [39, 40]. In the base case, the model considered MACE-4, including nonfatal MIs, nonfatal strokes, coronary revascularizations, and CV deaths. All costs and QALYs were discounted at an annual rate of 3% [41].

2.6 Sensitivity and Scenario Analyses

One-way and probabilistic sensitivity analyses were conducted to test the influence of individual parameters, as well as overall uncertainty in model results. In the one-way sensitivity analysis, each parameter was varied by $\pm 10\%$ or by a clinically relevant range (e.g., the 95% confidence interval [CI]). Probabilistic sensitivity analyses were performed by simultaneously varying all model parameters over 2500 simulations to generate a cost-effectiveness acceptability curve. Threshold analyses were conducted across a range of ICERs (\$50,000 to \$200,000 per QALY).

Several scenario analyses were conducted. In one scenario, total event HRs from the on-treatment analysis, a prespecified analysis of CLEAR Outcomes, which removed patients after they stopped adhering to scheduled treatment (and incurring its cost), were used to best reflect real-world effectiveness of therapy over the long-term (Table 1), given that a therapy can only be effective if it is taken. Additional scenarios included: (1) varying the cost of bempedoic acid to reflect a more realistic average US payer price; (2) using the MACE-3 endpoint instead of MACE-4; (3) applying the HRs for the occurrence of the first event rather than total events; (4) applying an age adjustment to the baseline utility value instead of a fixed value; and (5) an exploratory analysis of the cost-effectiveness of the fixed-dose combination of bempedoic acid and ezetimibe in the same patient population.

2.7 Model Validation

Internal validity was established through a robust quality control check by an independent team member not involved in the model development to minimize the likelihood of programming errors. External validation was conducted against previously published models for other lipid-lowering therapies, including bempedoic acid, as well as against actual trial results. To evaluate consistency with the key trial, the model compared modeled MACE with MACE observed during the follow-up period in CLEAR Outcomes.

3 Results

3.1 Base-Case Cost-effectiveness

Demographic and clinical characteristics of the population have been previously described [16] (Supplementary Fig. 2). In the base case analysis using the risk reduction in MACE-4 total events from CLEAR Outcomes, mean lifetime costs were estimated to be \$142,670 per patient treated with standard of care and \$165,940 per patient treated with bempedoic acid, for an incremental cost of \$23,270. Treatment with bempedoic acid resulted in a reduction in lifetime MACE compared with standard of care (1.58 versus 1.95 composite MACE-4 per patient; difference of -0.37). In total, the standard of care group experienced 365.6 more events for every 1000 patients compared with the bempedoic acid group (+ 147.1 nonfatal MIs, + 42.8 strokes, + 179.6 coronary revascularizations, and 3.8 fewer cardiovascular deaths). Fewer MACE-4 led to additional QALYs: the incremental number of QALYs gained with bempedoic acid were 0.14 per patient (10.25 versus 10.11), as summarized in Table 2. Compared with standard of care alone, treatment with bempedoic acid resulted in an ICER of \$166,830 per QALY gained and \$63,649 per MACE-4 avoided.

3.2 Sensitivity Analyses

In a one-way sensitivity analysis, the model was most sensitive to the HR for cardiovascular death, as the upper end of the 95% CI exceeds 1.0, which is most likely attributable to the uncertainty in rare events over the trial period. (Supplementary Fig. 3) The cost-effectiveness acceptability curve shows that the likelihood of bempedoic acid being cost-effective increases from 0.2% at \$50,000 per QALY, to 25.4% at \$100,000, 45.2% at \$150,000, 54.7% at \$200,000, and 60.8% at \$250,000 (Fig. 1). A plot of the incremental costs and incremental QALYs for each of the 2500 probabilistic sensitivity analysis iterations can be found in Supplementary Fig. 4.

3.3 Scenario Analyses

The cost-effectiveness of treatment benefit scenarios that have potential implications for clinical practice were further investigated, as illustrated in Table 3. While the primary analysis included the intention-to-treat cohort, an on-treatment analysis permitted the opportunity to evaluate patients who continued to take the study drug, as originally intended

Table 2 Cost-effectiveness results in the base case analysis

	Bempedoic Acid	Standard of care	Difference	ICER
Base case (per patient)				
Lifetime costs	\$165,940	\$142,670	\$23,270	–
QALYs	10.25	10.11	0.14	\$166,830 per QALY gained
ASCVD QALYs	7.39	6.74	0.64	
Acute MACE decrements	– 0.07	– 0.10	0.03	
Post MACE QALYs	2.94	3.47	– 0.53	
MACE	1.58	1.95	– 0.37	\$63,649 per MACE avoided
MACE per 1000 patients				
Total MACE	1584.9	1950.5	– 365.6	–
Nonfatal MI	320.3	467.4	– 147.1	–
Nonfatal stroke	171.3	214.1	– 42.8	–
Coronary revascularization	605.3	784.8	– 179.6	–
CV death	488.0	484.2	3.8	–

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; ICER, incremental cost-effectiveness ratio; MACE, major adverse cardiovascular event; MI, myocardial infarction; QALY, quality-adjusted life-year

at the time of randomization. This demonstrated an ICER of \$70,279 per QALY and \$57,124 per MACE avoided.

The base-case ICER of \$166,830 per QALY reflects the list price of bempedoic acid; however, if the cost of bempedoic acid was discounted by 25% from the list price (\$306 per month), aligning more closely with actual payer costs, the ICER would be \$99,993 per QALY. If a net price of bempedoic acid were used, accounting for all discounts and rebates taken in 2022 (\$226 per month using the SSR Health's net pricing data) [42], the ICER would be reduced even further to \$47,572 per QALY and \$18,150 per MACE avoided compared with standard of care. The relationship between the cost-effectiveness and monthly drug acquisition cost of bempedoic acid is shown in Fig. 2.

When the efficacy endpoint employed was MACE-3 rather than MACE-4, higher incremental costs were observed owing to the removal of coronary revascularization. Compared with standard of care, treatment with bempedoic acid resulted in greater lifetime costs (incremental cost + \$27,666 per patient), but also more QALYs (incremental + 0.14 per patient), resulting in an ICER of \$204,450 per QALY gained and \$148,397 per MACE-3 avoided.

A scenario analysis was conducted using the HR for first occurrence of MACE-4, rather than total number of events, to align with the primary endpoint of CLEAR Outcomes. This resulted in fewer MACE-4 avoided and QALYs gained with bempedoic acid, and an ICER of \$205,891 per

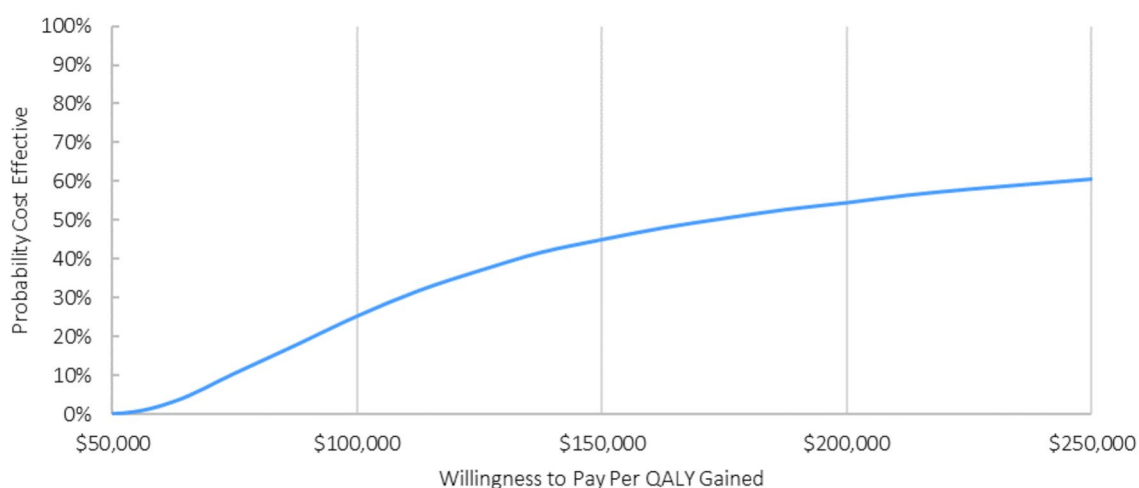


Fig. 1 Cost-effectiveness acceptability curve: probability that bempedoic acid will be cost-effective according to the willingness-to-pay per QALY gained. QALY, quality-adjusted life-year

Table 3 Cost-effectiveness of bempedoic acid in additional modeling scenarios

	Bempedoic acid	Standard of care	Difference	ICER
Base case (per patient)				
Lifetime costs	\$165,940	\$142,670	\$23,270	–
QALYs	10.25	10.11	0.14	\$166,830/QALY gained
MACE	1.58	1.95	– 0.37	\$63,649/MACE avoided
On-treatment analysis				
Lifetime costs	\$166,595	\$142,670	\$23,925	–
QALYs	10.46	10.11	0.34	\$70,279/QALY gained
MACE	1.53	1.95	– 0.42	\$57,124/MACE avoided
25% Reduction in bempedoic acid price (\$306/month)				
Lifetime costs	\$156,618	\$142,670	\$13,947	–
QALYs	10.25	10.11	0.14	\$99,993/QALY gained
MACE	1.58	1.95	– 0.37	\$38,150/MACE avoided
Net bempedoic acid price (\$226/month) ^a				
Lifetime costs	\$149,306	\$142,670	\$6636	–
QALYs	10.25	10.11	0.14	\$47,572/QALY gained
MACE	1.58	1.95	– 0.37	\$18,150/MACE avoided
MACE-3 endpoint (without coronary revascularization)				
Lifetime costs	\$144,698	\$117,032	\$27,666	–
QALYs	10.04	9.90	0.14	\$204,450/QALY gained
MACE	1.05	1.24	– 0.19	\$148,397/MACE avoided
First event versus total events				
Lifetime costs	\$167,780	\$142,670	\$25,110	–
QALYs	10.24	10.11	0.12	\$205,891/QALY gained
MACE	1.63	1.95	– 0.32	\$78,780/MACE avoided
Reduction in utility per additional year of age				
Lifetime costs	\$165,940	\$142,670	\$23,270	–
QALYs	9.96	9.84	0.12	\$191,788/QALY gained
MACE	1.58	1.95	– 0.37	\$63,649/MACE avoided

ICER, incremental cost-effectiveness ratio; MACE, major adverse cardiovascular event; QALY, quality-adjusted life-year

^aBased on data from SSR Health (2022) which estimates drug prices net of all discounts, rebates, concessions to wholesalers and distributors, and costs of patient assistance programs

QALY gained and \$78,780 per MACE avoided. Similarly, using a reduction in utility of – 0.002 per additional year of age (based on the annualized change in EQ-5D scores by age strata reported from nationally representative surveys [43, 44]) resulted in an ICER of \$191,788 per QALY and \$63,649 per MACE avoided. When these additional scenario analyses were conducted in the on-treatment cohort, the results demonstrated more favorable ICER per QALY gained and MACE avoided (Supplementary Table 3; Supplementary Figs. 5 and 6).

An exploratory scenario analysis was investigated examining the potential cost-effectiveness of the fixed-dose combination of bempedoic acid and ezetimibe in the CLEAR Outcomes patient population. As this was not the research question addressed in the CLEAR Outcomes study, an estimated composite MACE-4 risk reduction was calculated for the fixed-dose combination in the model. The fixed-dose

combination product is priced equivalent to that of bempedoic acid monotherapy (\$408 monthly). A previous clinical trial that evaluated the impact of the fixed-dose combination of bempedoic acid and ezetimibe in patients with high cardiovascular risk and hypercholesterolemia, treated with maximally tolerated statins, demonstrated that the combination produced LDL-C lowering by 38% compared with placebo [45]. This relative reduction was applied to the CLEAR Outcomes baseline LDL-C (3.59 mmol/L), to derive an absolute reduction of 1.37 mmol/L. Subsequently, the Cholesterol Treatment Trialists' Collaboration calculation of overall risk reduction in major vascular events, defined as any major coronary event (coronary death or nonfatal MI), coronary revascularization, or stroke (22% per 1 mmol/L) [7] was applied to the absolute LDL-C reduction, with the resulting HR of 0.71 applied for composite MACE-4. The composite MACE-4 was used, as the HRs for each individual

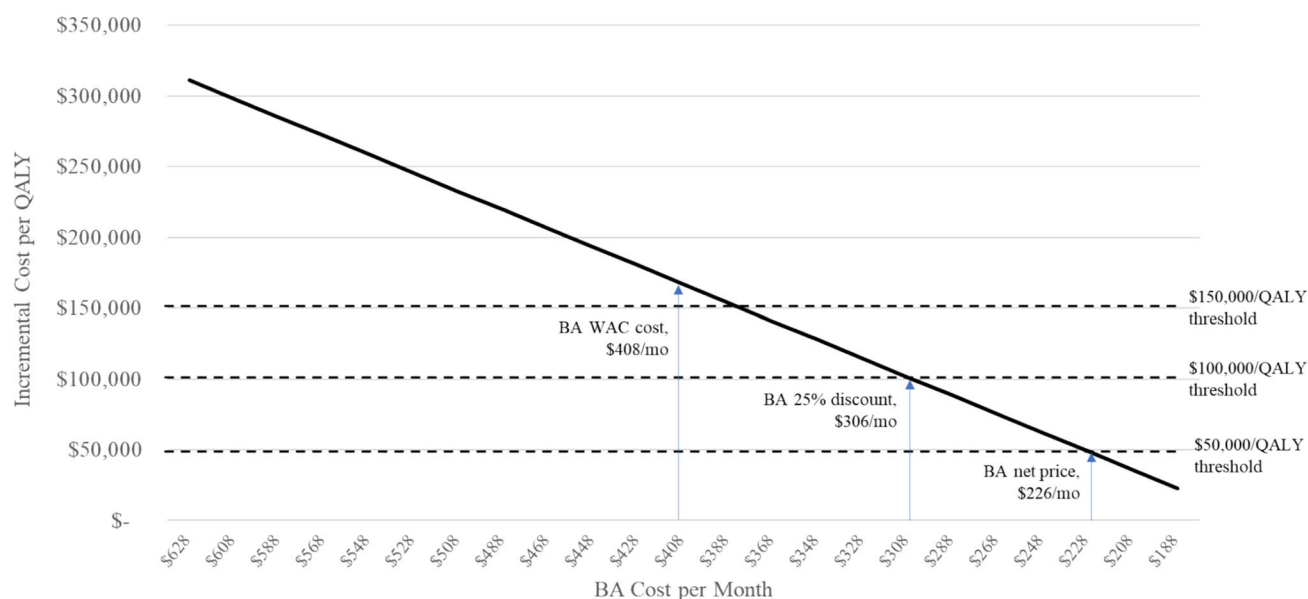


Fig. 2 Relationship between bempedoic acid cost and ICER at different willingness-to-pay thresholds. BA, bempedoic acid; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; WAC, wholesale acquisition cost

component was not available. The ICER for the fixed-dose combination was \$40,317 per QALY gained and \$70,452 per MACE-4 avoided. These findings represent an optimistic scenario, as the use of the overall composite HR instead of the individual component HRs assumed that the effect of treatment on cardiovascular death was equivalent to the overall MACE-4 reduction. The ICER progressively increased when the HR for cardiovascular death was increased from 0.71 to 0.80 (\$48,896), 0.90 (\$68,411), and 1.00 (\$135,768), while holding the HR for all other components equivalent at 0.71 (Table 4).

4 Discussion

The current analysis examined the cost-effectiveness of bempedoic acid used in the management of high cardiovascular risk patients with high levels of LDL-C and statin intolerance. The CLEAR Outcomes study demonstrated that administration of bempedoic acid resulted in a 13% reduction in the primary composite endpoint of cardiovascular death, nonfatal MI, nonfatal stroke, and coronary revascularization, as well as a 15% reduction in the combination of cardiovascular death, nonfatal MI, and nonfatal stroke. This cost-effectiveness analysis estimated that, at its list price, bempedoic acid had an ICER of \$166,830 per QALY in the intention-to-treat cohort. Although this ICER exceeds the threshold generally established by the Institute for Clinical and Economic Review for cost-effectiveness and the American College of Cardiology/American Heart

Association for intermediate versus low value ($> \$150,000$ per QALY) [39, 40], when the list price was discounted to reflect actual payer pricing, the ICERs fell well below this threshold. The ICER was \$99,993 per QALY using the discounted WAC (-25%) and \$47,572 per QALY using the net SSR price. As drug rebates and other discounts are routinely offered to commercial and government health insurers, and can range from 18 to 37% or greater [46, 47], it is likely that the true economic value of bempedoic acid lies somewhere between. We also modeled cost-effectiveness using the combination of bempedoic acid and ezetimibe and demonstrated that more effective LDL-C lowering should result in greater lowering of cardiovascular death, MI, stroke, and coronary revascularization (-29%), with an incremental cost per QALY gained ranging from \$40,317 to \$135,768. These data suggest the use of bempedoic acid at either a cost encountered in clinical practice or in a commonly used fixed-dose combination should result in favorable health economic outcomes.

The cost-effectiveness of bempedoic acid in our analysis is higher than that reported by the Institute for Clinical and Economic Review in their 2021 assessment, although the patient populations and methodologies are different, limiting comparisons. The model by Lin et al. evaluated bempedoic acid plus ezetimibe in a subgroup of statin-intolerant adults with established ASCVD, and demonstrated an ICER of \$92,000 per QALY gained compared with ezetimibe plus maximum tolerated statin therapy [18]. At the time, the Outcomes trial was not yet completed, and cardiovascular risk reduction, including cardiovascular death, was predicted

Table 4 Modeled cost-effectiveness of the bempedoic acid and ezetimibe fixed-dose combination

	Lifetime cost	QALY	MACE/1000 patients
Standard of care	\$142,670	10.11	1950.5
Overall MACE HR 0.71 (CV death HR 0.71)			
BA + EZE	\$172,603	10.86	1525.6
Difference versus standard of care	\$29,933	0.74	– 424.9
ICER	–	\$40,317 per QALY gained	\$70,452 per MACE avoided
CV death HR 0.80			
BA + EZE	\$169,680	10.61	1524.1
Difference versus standard of care	\$27,010	0.50	– 426.4
ICER	–	\$48,896 per QALY gained	\$63,349 per MACE avoided
CV death HR 0.90			
BA + EZE	\$166,559	10.46	1522.1
Difference versus standard of care	\$23,889	0.35	– 428.4
ICER	–	\$68,411 per QALY gained	\$55,763 per MACE avoided
CV death HR 1.0			
BA + EZE	\$163,563	10.27	1519.7
Difference versus standard of care	\$20,893	0.15	– 430.8
ICER	–	\$135,768 per QALY gained	\$48,504 per MACE avoided

BA, bempedoic acid; CV, cardiovascular; EZE, ezetimibe; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; LY, life-year; MACE, major adverse cardiovascular event; QALY, quality-adjusted life-year

using the Cholesterol Treatment Trialists' calculation from an LDL-C reduction of 24.6% (subgroup analysis of two statin-intolerant clinical trials). The CLEAR Outcomes study, on which our model was based, evaluated both primary and secondary prevention patients who were unable to tolerate statin therapy, and had low ezetimibe use (11.5%) [16]. In the trial, while bempedoic acid was associated with a 13% risk reduction in time to first occurrence of MACE-4, there was no significant reduction in the single component of cardiovascular death, a finding that limited its cost-effectiveness in the modeling, and likely accounted for some of the differences in results.

The base-case analysis was performed in the intention-to-treat cohort, following the primary endpoint of the clinical trial. Additional analyses were performed using the on-treatment cohort, as a high rate of discontinuation was observed in both the placebo (31.7%) and bempedoic acid (29.1%) groups [16]. The on-treatment analysis removed patients after they discontinued, given that therapy needs to be taken in order to derive clinical benefit, and resulted in an ICER of \$70,279 per QALY. The high discontinuation rates observed during the trial may have been caused by a combination of the statin-intolerant population and the challenge of conducting a clinical trial during the coronavirus disease 2019 (COVID-19) pandemic. Patients with statin-related muscle symptoms are more likely to discontinue lipid-lowering therapy [48]; real-world studies have shown that statin-intolerant patients have impaired quality of life, are less likely to reach LDL-C goals, and more likely

to experience costly CV events than statin-tolerant patients [48, 49]. These factors support the use of the on-treatment analysis scenario to examine potential cost-effectiveness.

In addition to having an impact on discontinuation rates, a sensitivity analysis of CLEAR Outcomes data suggests that the global COVID-19 pandemic may have had an impact on the cardiovascular death component [50]. Among all cardiovascular deaths, 24.7% were in the undetermined category. Compared with the pre-pandemic period, rates of all cause death, non-cardiovascular death, and cardiovascular death of unknown causes increased during the pandemic period, while rates of cardiovascular death with a known reason remained stable. The sensitivity analysis excluded undetermined deaths during the pandemic period from the cardiovascular death endpoint and yielded a hazard ratio of 0.94 (95% CI 0.76–1.16) for cardiovascular death, compared with 1.04 (95% CI 0.88–1.24), respectively, in the original analysis [50]. It is of interest that in our base case, we assumed no cardiovascular mortality reduction (HR of 1.0). If we were to instead use the HR observed after the COVID-19 pandemic sensitivity analysis [50], the resulting ICER would have been \$98,177 per QALY gained (using list price), which is closer to that found by Lin et al. [18].

In order to evaluate the effects of uncertainty, we conducted external validation of the model for the simulated event rate versus actual event rate observed in CLEAR Outcomes as part of the model development. As expected, total events as modeled are greater than first events as observed in CLEAR Outcomes. The model does overestimate the

absolute number of events, but the relative number of events between bempedoic acid and standard of care is as expected, which is what drives the model results (i.e., the relative effect). After the mean follow-up in CLEAR Outcomes (3.46 years), the model simulated a total MACE-4 event rate of 22.4% in the standard of care arm and 17.2% in the bempedoic acid arm. At this point in CLEAR Outcomes, there were 1471 total MACE-4 events (in 6978 patients; 21.1%) and 1190 events (in 6992 patients; 17.0%) in the standard of care and bempedoic acid arms, respectively.

4.1 Limitations

Several caveats should be considered with regard to the current analysis. The findings were modeled from a clinical trial conducted in patients who were either unable or unwilling to take guideline-mandated doses of statin therapy. While use of statins below the lowest daily approved dose was permitted in the study, this was only evident in 22% of patients. Therefore, the cost-effectiveness of bempedoic acid in primary and secondary patients treated with intensive statin therapy remains unknown.

It is noteworthy that bempedoic acid produced a greater proportional reduction in cardiovascular events in those patients without clinically manifest ASCVD at baseline [51]. In fact, the primary prevention subgroup analysis suggested a significant reduction in cardiovascular death in the bempedoic acid group. Whether this would result in more favorable cost-effectiveness remains uncertain, although the absolute clinical event rate and absolute risk reduction with bempedoic acid would likely be lower in this setting. Future modeling efforts may be undertaken to examine this. It is also possible that there are specific subgroups, in which bempedoic acid produces more favorable reductions in absolute risk, which should theoretically result in improved cost-effectiveness. This requires additional investigation.

Finally, economic modeling entails a variety of assumptions regarding disease states, treatment patterns, and costs. This cost-effectiveness analysis represents a simplified approach to a more complex integration of all these factors to estimate the cost-effectiveness of bempedoic acid in the specified population, and therefore, may not be generalizable to all situations. The rate of clinical events and treatment benefit from the CLEAR Outcomes trial were extrapolated beyond the period of follow-up, and the model assumed that the treatment benefit would remain constant over the lifetime horizon. If the clinical benefits differed, the cost-effectiveness findings could be over or underestimated.

5 Conclusions

Bempedoic acid provides a novel therapeutic option for management of hyperlipidemia in high cardiovascular risk patients. At its list price, bempedoic acid has a 45% likelihood of being cost-effective for primary and secondary prevention in patients who cannot take recommended statin therapy at a willingness-to-pay threshold of \$150,000. At prices reflective of actual payer costs, the ICER for bempedoic acid falls well below generally accepted cost-effectiveness thresholds. These data continue to support increasing use of bempedoic acid in the management of patients at high risk of cardiovascular events.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s40256-025-00753-w>.

Declarations

Disclosures Dr. Nicholls has received research support from AstraZeneca, Amgen, Anthera, CSL Behring, Cerenis, Eli Lilly, Esperion, Resverlogix, Novartis, InfraReDx, and Sanofi-Regeneron; and is a consultant for Amgen, Akcea, AstraZeneca, Boehringer Ingelheim, CSL Behring, Eli Lilly, Esperion, Kowa, Merck, Takeda, Pfizer, Sanofi-Regeneron, Novo Nordisk, CSL Sequiris, and Vaxxinity. Dr. Ray has received grants to his institution from Amgen, Daiichi Sankyo, Regeneron, and Sanofi; and received consulting fees from Daiichi, Esperion, Amgen, Novartis, Sanofi, Eli Lilly, Silence Therapeutics, Kowa, Bayer, Abbott, AstraZeneca, Cargene, New Amsterdam, Scribe, Vaxxinity, CRISPR, Beren, Novo Nordisk, and Boehringer Ingelheim. Dr. Lincoff has received Esperion research funding; receiving grants from Eli Lilly, AbbVie, CSL, AstraZeneca, and Novartis; and received personal fees from Novo Nordisk, Glaxo, Akebia, Endologix, Fibrogen, Provention, and Becton Dickinson. Dr. Nissen has received grants to perform clinical trials from AbbVie, AstraZeneca, Amgen, Bristol Myers Squibb, Eli Lilly, Esperion Therapeutics Inc, Medtronic, MyoKardia, New Amsterdam Pharmaceuticals, Novartis, and Silence Therapeutics.

Funding Open Access funding enabled and organized by CAUL and its Member Institutions. This study was funded by Esperion Therapeutics, Inc.

Conflict of interest Dr. Sarnes and Ms. Bloedon are employees of Esperion Therapeutics; Dr. Gillard was an employee at the time of this research. Ms. Migliaccio-Walle is an employee of Curta, Inc. and Dr. Elsea was an employee of Curta, Inc. at the time of this research, which received funding to conduct this study. Dr. Nicholls and Dr. Lincoff are Editorial Board members of the *American Journal of Cardiovascular Drugs*. Dr. Nicholls and Dr. Lincoff were not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions.

Authors' contributions All authors had full access to the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis. All authors conceptualized and designed the study. E.S., L.B., and K.K.G. were responsible for project funding and administration. K.M.W. and D.E. conducted the analyses, and S.J.N., K.K.R., E.S., A.M.L., and S.E.N. drafted the manuscript. All

authors critically reviewed the manuscript for intellectual content and approved the final version of the manuscript.

Data availability statement The data will not be shared.

Code availability statement Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

References

- Martin SS, et al. 2024 Heart disease and stroke statistics: a report of US and global data from the American Heart Association. *Circulation*. 2024;149(8):e347–913. <https://doi.org/10.1161/CIR.0000000000001209>.
- American Heart Association/American Stroke Association. Cardiovascular disease: a costly burden for America—projections through 2035. 2017. <https://www.heart.org/-/media/Files/About-Us/Policy-Research/Fact-Sheets/Public-Health-Advocacy-and-Research/CVD-A-Costly-Burden-for-America-Projections-Through-2035.pdf>. Accessed 15 Jan 2025.
- Tsao CW, et al. Heart disease and stroke statistics—2023 update: a report from the American Heart Association. *Circulation*. 2023;147(8):e93–621. <https://doi.org/10.1161/CIR.0000000000001123>.
- Tajew GS, et al. Cost of cardiovascular disease event and cardiovascular disease treatment-related complication hospitalizations in the United States. *Circ Cardiovasc Qual Outcomes*. 2024;17(3):e009999. <https://doi.org/10.1161/CIRCOUTCOMES.123.009999>.
- Fox KM, et al. Clinical and economic burden associated with cardiovascular events among patients with hyperlipidemia: a retrospective cohort study. *BMC Cardiovasc Disord*. 2016. <https://doi.org/10.1186/s12872-016-0190-x>.
- Ference BA, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J*. 2017;38(32):2459–72. <https://doi.org/10.1093/eurheartj/ehx144>.
- Baigent C, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376(9753):1670–81. [https://doi.org/10.1016/s0140-6736\(10\)61350-5](https://doi.org/10.1016/s0140-6736(10)61350-5).
- Cannon CP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med*. 2015;372(25):2387–97. <https://doi.org/10.1056/NEJMoa1410489>.
- Sabatine MS, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med*. 2017. <https://doi.org/10.1056/NEJMoa1615664>.
- Schwartz GG, et al. Alirocumab and cardiovascular outcomes after acute coronary syndrome. *N Engl J Med*. 2018;379(22):2097–107. <https://doi.org/10.1056/NEJMoa1801174>.
- Mach F, et al. 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2020;41(1):111–88. <https://doi.org/10.1093/eurheartj/ehz455>.
- Ray KK, et al. EU-wide cross-sectional observational study of lipid-modifying therapy use in secondary and primary care: the DA VINCI study. *Eur J Prev Cardiol*. 2021;28(11):1279–89. <https://doi.org/10.1093/eurjpc/zwaa047>.
- Navar AM, et al. Gaps in guideline-based lipid-lowering therapy for secondary prevention in the United States: a retrospective cohort study of 322 153 patients. *Circ Cardiovasc Qual Outcomes*. 2023;16(8):533–43. <https://doi.org/10.1161/CIRCOUTCOMES.122.009787>.
- Bytyci I, et al. Prevalence of statin intolerance: a meta-analysis. *Eur Heart J*. 2022;43(34):3213–23. <https://doi.org/10.1093/eurheartj/ehac015>.
- Serban MC, et al. Statin intolerance and risk of coronary heart events and all-cause mortality following myocardial infarction. *J Am Coll Cardiol*. 2017;69(11):1386–95. <https://doi.org/10.1016/j.jacc.2016.12.036>.
- Nissen SE, et al. Bempedoic acid and cardiovascular outcomes in statin-intolerant patients. *N Engl J Med*. 2023;388(15):1353–64. <https://doi.org/10.1056/NEJMoa2215024>.
- Nicholls SJ, et al. Impact of bempedoic acid on total cardiovascular events: a prespecified analysis of the CLEAR outcomes randomized clinical trial. *JAMA Cardiol*. 2024;9(3):245–53. <https://doi.org/10.1001/jamacardio.2023.5155>.
- Lin GA, Kazi DS, Jih J, Agboola F, Chapman R, Pearson SD. Inclisiran and bempedoic acid for patients with heterozygous familial hypercholesterolemia and for secondary prevention of atherosclerosis: effectiveness and value; evidence report. Institute for Clinical and Economic Review. 2021. <https://icer.org/assessment/high-cholesterol-2021/#timeline>.
- Morton JI, et al. Rethinking cardiovascular prevention: cost-effective cholesterol lowering for statin-intolerant patients in Australia and the UK. *Eur J Prev Cardiol*. 2025. <https://doi.org/10.1093/eurjpc/zwaf114>.
- Nicholls S, et al. Rationale and design of the CLEAR-outcomes trial: evaluating the effect of bempedoic acid on cardiovascular events in patients with statin intolerance. *Am Heart J*. 2021;235:104–12. <https://doi.org/10.1016/j.ahj.2020.10.060>.
- Husereau D, et al. Consolidated health economic evaluation reporting standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. *BMC Med*. 2022;20(1):23. <https://doi.org/10.1186/s12916-021-02204-0>.
- Ridker PM, et al. Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds risk score. *JAMA*. 2007;297(6):611–9. <https://doi.org/10.1001/jama.297.6.611>.
- Ridker PM, et al. C-reactive protein and parental history improve global cardiovascular risk prediction: the Reynolds risk score for men. *Circulation*. 2008;118(22):2243–51.
- Hageman SHJ, et al. Estimation of recurrent atherosclerotic cardiovascular event risk in patients with established cardiovascular disease: the updated SMART2 algorithm. *Eur Heart J*. 2022;43(18):1715–27. <https://doi.org/10.1093/eurheartj/ehac056>.
- Pennells L, et al. Equalization of four cardiovascular risk algorithms after systematic recalibration: individual-participant meta-analysis of 86 prospective studies. *Eur Heart J*. 2019;40(7):621–31. <https://doi.org/10.1093/eurheartj/ehy653>.

26. Arias E, Xu JQ. United States life tables, 2019. National Vital Statistics Reports; vol. 70, issue 19. Hyattsville, MD: National Center for Health Statistics; 2022.
27. Fonarow GC, et al. Cost-effectiveness of evolocumab therapy for reducing cardiovascular events in patients with atherosclerotic cardiovascular disease. *JAMA Cardiol.* 2017;2(10):1069. <https://doi.org/10.1001/jamacardio.2017.2762>.
28. Weintraub WS, et al. Cost-effectiveness of icosapent ethyl for high-risk patients with hypertriglyceridemia despite statin treatment. *JAMA Netw Open.* 2022;5(2): e2148172. <https://doi.org/10.1001/jamanetworkopen.2021.48172>.
29. Miniño AM, Klein RJ. Health mortality from major cardiovascular diseases: United States, 2007. New York: Health E-Stats National Center for Health Statistics; 2010.
30. Centers for Disease Control and Prevention and National Vital Statistics System. Mortality 2018-2020 on CDC WONDER Online Database, released in 2021. 2021 May 28, 2022. <https://www.cdc.gov/nchs/nvss/deaths.htm>. Accessed 15 Jan 2025.
31. Bhatt DL, et al. Cost-effectiveness of alirocumab in patients with acute coronary syndromes: the ODYSSEY OUTCOMES trial. *J Am Coll Cardiol.* 2020;75(18):2297–308. <https://doi.org/10.1016/j.jacc.2020.03.029>.
32. Ollendorf D, et al. Additive therapies for cardiovascular disease: effectiveness and value. Boston: Institute for Clinical and Economic Review; 2019.
33. Stevanović J, et al. Multivariate meta-analysis of preference-based quality of life values in coronary heart disease. *PLoS ONE.* 2016;11(3): e0152030. <https://doi.org/10.1371/journal.pone.0152030>.
34. Cohen DJ, et al. Quality of life after PCI with drug-eluting stents or coronary-artery bypass surgery. *N Engl J Med.* 2011;364(11):1016–26. <https://doi.org/10.1056/NEJMoa1001508>.
35. Kazi DS, et al. Cost-effectiveness of genotype-guided and dual antiplatelet therapies in acute coronary syndrome. *Ann Intern Med.* 2014;160(4):221–32. <https://doi.org/10.7326/m13-1999>.
36. Valero-Elizondo J, et al. Favorable cardiovascular risk profile is associated with lower healthcare costs and resource utilization: the 2012 medical expenditure panel survey. *Circ Cardiovasc Qual Outcomes.* 2016;9(2):143–53. <https://doi.org/10.1161/circoutcomes.115.002616>.
37. Micromedex (2022). Red Book. Retrieved January 1, 2025, from Micromedex. <https://www.micromedexsolutions.com/home/dispatch>. Accessed 15 Jan 2025.
38. U.S. Bureau of Labor Statistics. Consumer Price Index for All Urban Consumers: Medical care in U.S. city average, all urban consumers, not seasonally adjusted. 2024. <https://www.bls.gov>. Accessed 15 Jan 2025.
39. Anderson JL, et al. ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2014;63(21):2304–22. <https://doi.org/10.1016/j.jacc.2014.03.016>.
40. ICER. Perspectives on cost-effectiveness threshold ranges. 2019. https://icer.org/wp-content/uploads/2023/08/ICER_2019_Perspectives-on-Cost-Effectiveness-Threshold-Ranges.pdf. Accessed 15 Jan 2025.
41. https://icer.org/wp-content/uploads/2023/10/ICER_2023_VAF_For-Publication_101723.pdf. 2023 [cited 2024 May 9]. https://icer.org/wp-content/uploads/2023/10/ICER_2023_VAF_For-Publication_101723.pdf. Accessed 15 Jan 2025.
42. Pearson SD, et al. Assessment of barriers to fair access. Boston: Institute for Clinical and Economic Review; 2023.
43. Sullivan PW, Ghushchyan V. Preference-based EQ-5D index scores for chronic conditions in the United States. *Med Decis Mak.* 2006;26(4):410–20. <https://doi.org/10.1177/0272989X06290495>.
44. Jiang R, Janssen MFB, Pickard AS. US population norms for the EQ-5D-5L and comparison of norms from face-to-face and online samples. *Qual Life Res.* 2021;30(3):803–16. <https://doi.org/10.1007/s11136-020-02650-y>.
45. Ballantyne CM, et al. Bempedoic acid plus ezetimibe fixed-dose combination in patients with hypercholesterolemia and high CVD risk treated with maximally tolerated statin therapy. *Eur J Prev Cardiol.* 2020;27(6):593–603. <https://doi.org/10.1177/2047487319864671>.
46. Plummer E, et al. Trends of prescription drug manufacturer rebates in commercial health insurance plans, 2015–2019. *JAMA Health Forum.* 2022;3(5): e220888. <https://doi.org/10.1001/jamahealthforum.2022.0888>.
47. Feldman WB, et al. Estimating rebates and other discounts received by Medicare part D. *JAMA Health Forum.* 2021;2(6): e210626. <https://doi.org/10.1001/jamahealthforum.2021.0626>.
48. Laufs U, et al. Characteristics and outcomes of patients with and without statin-associated muscle symptoms treated with bempedoic acid in the CLEAR outcomes trial. *J Clin Lipidol.* 2025;19(2):337–47. <https://doi.org/10.1016/j.jacl.2024.12.014>.
49. Sturzebecher PE, et al. Quality of life in patients with statin intolerance: a multicentre prospective registry study. *Lancet Reg Health Eur.* 2024;43: 100981. <https://doi.org/10.1016/j.lanepe.2024.100981>.
50. Singh A, et al. Impact of the COVID-19 pandemic on conduct and results of CLEAR outcomes trial. *Clin Cardiol.* 2024;47(8): e24328. <https://doi.org/10.1002/clc.24328>.
51. Nissen SE, et al. Bempedoic acid for primary prevention of cardiovascular events in statin-intolerant patients. *JAMA.* 2023;330(2):131–40. <https://doi.org/10.1001/jama.2023.9696>.
52. Lincoff AM, et al. Comparative cardiovascular benefits of bempedoic acid and statin drugs. *J Am Coll Cardiol.* 2024;84(2):152–62. <https://doi.org/10.1016/j.jacc.2024.04.048>.