Cost-Effectiveness of Rivaroxaban and Acetylsalicylic Acid Combination Therapy in Stable Cardiovascular Disease: A Global Perspective

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Poster Board Number: 1037
Acceptance code: EE88

BACKGROUND: THE COMPASS TRIAL

- **Patients:** 27,395 participants with stable atherosclerotic vascular disease
- **Interventions:** Low-dose rivaroxaban (2.5 mg BID) + acetylsalicylic acid (ASA) (100 mg OD) and rivaroxaban (5 mg BID)
- **Comparators:** ASA (100 mg OD) + rivaroxaban matched placebo BID
- **Outcomes:**
  - **Low-dose rivaroxaban + ASA:** lower risk of primary and secondary efficacy outcomes compared to ASA alone.
  - **Rivaroxaban alone:** did not significantly reduce the risk of primary composite outcomes compared to ASA alone.
- **Time of Intervention:** March 2013 - May 2016
- **Follow up:** 23 months (max. duration: 47 months)
- **Study design:** double-blind, randomized trial
- **Effectiveness:** Reduced mortality in the rivaroxaban + ASA group compared to ASA alone
- **Safety:** 20% lower risk with rivaroxaban + ASA compared to ASA alone → Significant benefit of combination therapy

AIMS AND METHODS

- To provide an overview of published evidence on the cost-effectiveness of rivaroxaban (2.5mg twice daily) plus ASA versus ASA alone (100mg once daily) in stable cardiovascular disease, on a global scale.

- Search Strategy:
  - PubMed: rivaroxaban AND aspirin AND cost-effectiveness
  - Initial Results: 39 identified manuscripts
  - Prespecified Inclusion Criteria Applied: Based on COMPASS population, intervention and comparator characteristics
- Results: 9 manuscripts included in our review
- Data extraction was conducted manually

RESULTS

- The included cost-effectiveness analyses (CEAs) from national healthcare payers: Italy, Netherlands, France, Germany, United Kingdom, Australia, USA, Canada, & China all show consistent results with the COMPASS trial
- The combined regimen (low-dose rivaroxaban + ASA) compared to ASA alone is more cost-effective in the prevention of recurrent cardiovascular events
- In patients with both coronary artery disease and peripheral artery disease
- Only CEA from Taiwan diverged in its conclusion, suggesting that a combined regimen may not be as cost-effective in preventing recurrent cardiovascular events

CONCLUSION

- Low-dose rivaroxaban plus ASA in patients with stable CVD is **cost-effective.**
- Must weigh **CV benefits vs bleeding risks** when considering antithrombotic therapy for prevention of secondary cardiovascular events in patients with stable atherosclerotic vascular disease.
- These pharmacoeconomic findings offer valuable insights for managing this patient population, impacting policy and laying the basis and directions for **updated clinical strategies/guidelines.**

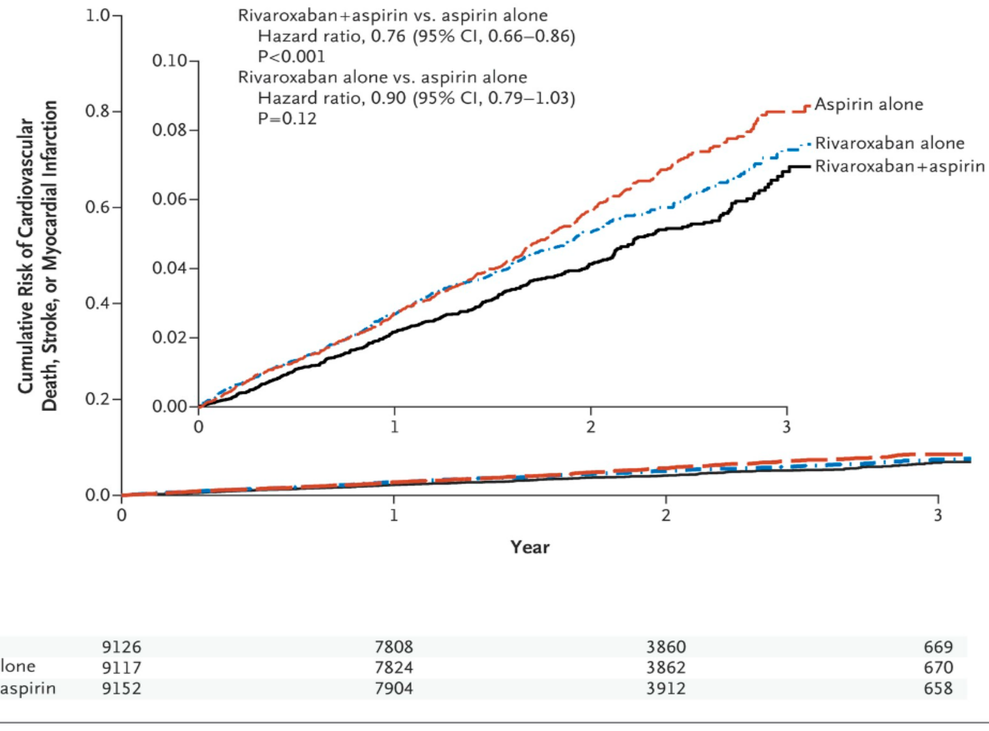

Figure 1. Cumulative incidence of the primary efficacy outcome among participants receiving rivaroxaban plus ASA, rivaroxaban alone, or ASA alone.

Table 1. An overview of published evidence on the cost-effectiveness of rivaroxaban (2.5mg twice daily) plus ASA versus ASA alone (100mg once daily) in stable cardiovascular disease, on a global scale.

Ref	First Author	Year	Country	Perspective	Study Type	Time Horizon	Model Type	Population	Intervention/Comparator	Economic Outcome
1	Ferrara	2021	Italy	National health care payer perspective	CEA	Lifetime horizon	Markov model	Stable CVD (CAD and PAD)	• Rivaroxaban (2.5mg twice daily) plus ASA (100mg once daily) • ASA alone (100mg once daily)	• Low-dose rivaroxaban in combination with ASA was more cost-effective than treatment with ASA alone • Base Case: QALY: Not reported** • ICER of USD$7937.30 per QALY gained • 2 Year Time Horizon: ICER of USD$13,609.23 per QALY • 5 Year Time Horizon: ICER of USD$7822.49 per QALY • WTP threshold of USD$11,000 **In the base case analysis rivaroxaban plus ASA therapy delivered an average of 0.43 additional QALYs over 13 years for 1000 patients over ASA therapy
2	Zomer	2019	Australia	National health care payer perspective	CEA	Lifetime horizon	Markov model	PAD and Carotid Artery Disease	• Rivaroxaban (2.5mg twice daily) plus ASA (100mg once daily) • ASA alone (100mg once daily)	• Rivaroxaban in combination with ASA cost effective to Australian public healthcare system • Cost per YoLS gained $27.037 • QALY was 6.3 and 6.0 for patients in the rivaroxaban plus ASA and ASA alone group, respectively • ICER of AUD$26,769 per QALY gained • WTP threshold of AUD$50,000
3	Ademi	2018	Australia	National health care payer perspective	CEA	20-year time horizon	Markov model	CVD (Stable atherosclerotic vascular disease)	• Rivaroxaban (2.5mg twice daily) plus ASA (100mg once daily) • ASA alone (100mg once daily)	• Rivaroxaban and ASA more cost-effective • Rivaroxaban plus ASA (total cost $67,631; 7.38 QALYs) compared with ASA alone (total cost $55,475; 6.996 QALYs) • ICER of AUD $31,436 per QALY gained • Rivaroxaban plus ASA and ASA alone lived for 9.53 years and 9.01 years lived • ICER of AUD $23,560 per YoLS • WTP threshold of AUD$50,000/QALY
4	Feng	2022	China	National health care payer perspective	CEA	2-year time horizon and 5-year time horizon	Markov model	Stable CVD (CAD and PAD)	• Rivaroxaban (2.5mg twice daily) plus ASA (100mg once daily) • ASA alone (100mg once daily)	• Rivaroxaban in combination with ASA more effective than ASA alone • QALYs 9.62 and 9.27 for patients in the two groups, respectively • ICER of €16,522 per QALY gained Similar trends for the PAD and CAD subgroups, with respective ICERs of €8003 and €18,599, respectively • WTP threshold of €40,000 per QALY gained
5	Lamy	2022	Canada France Germany	National health care payer perspective	CEA	Lifetime horizon	Markov model	Stable CVD (CAD and PAD)	• Rivaroxaban (2.5mg twice daily) plus ASA (100mg once daily) • ASA alone (100mg once daily)	• Rivaroxaban 2.5 mg twice daily plus ASA highly cost-effective (high value) in Canada, France and Germany • Rivaroxaban plus ASA was associated with 1.17 QALYs gained for all 3 countries. **QALYs 16.02 ASA alone and 17.19 (extracted from Lamy 2023) • Canada: An ICER of $3946/QALY • France: An ICER of USD$9962/QALY • Germany: An ICER of USD$10,264/QALY • WTP threshold of USD$25,000
6	Lamy	2023	USA	National health care payer perspective	CEA	Lifetime horizon	Markov model	Stable CVD (CAD and PAD)	• Rivaroxaban (2.5mg twice daily) plus ASA (100mg once daily) • ASA alone (100mg once daily)	• Rivaroxaban 2.5 mg BID plus ASA more cost-effective (high value) in USA • QALYs 16.02 ASA alone and 17.19 • Incremental QALY 1.17 • An ICER of USD$23,295 per QALY gained • WTP threshold of USD$50,000 per QALY
7	Cowie	2019	UK	National health care payer perspective	CEA	Lifetime horizon up to 100 years	Markov model	Stable CVD (CAD and PAD)	• Rivaroxaban (2.5mg twice daily) plus ASA (100mg once daily) • ASA alone (100mg once daily)	• Rivaroxaban 2.5mg twice daily in combination with ASA considered cost-effective compared to ASA alone • QALYs for Rivaroxaban plus ASA 9.7 and ASA alone 9.3 • An ICER of £16,360 per QALY gained £14,380 per LY saved • WTP threshold of £30,000 per QALY
8	Lee	2020	Taiwan	National health care payer perspective	CEA	30-year time horizon	Markov model	Stable CVD (CAD and PAD)	• Rivaroxaban (2.5mg twice daily) plus ASA (100mg once daily) • ASA alone (100mg once daily)	• From Taiwan national payer's perspective less likely cost-effective due to drug price, treatment fees of CVDs and WTP threshold • Low-dose rivaroxaban plus ASA more QALYs 16.47 versus ASA alone QALYs 15.93 • An ICER USD$38,591 per QALYs gained • WTP thresholds of USD$20,000 and USD$60,000
9	Petersohn	2020	Netherlands	National health care payer perspective	CEA	Lifetime horizon	Markov model	Stable CVD (CAD and PAD)	• Rivaroxaban (2.5mg twice daily) plus ASA (100mg once daily) • ASA alone (100mg once daily)	• Rivaroxaban combined with ASA is more cost-effective versus ASA alone • QALYs ASA alone 7.773 and rivaroxaban + ASA 8.089 in CAD • QALYs ASA alone 7.489 and Rivaroxaban + ASA 7.878 in PAD • An ICER of €32,109 per QALY gained in CAD and €26,381 in PAD patients • WTP threshold of €50,000/QALY

ASA, Acetylsalicylic Acid; CAD, Coronary Artery Disease; CEA, Cost-Effectiveness Analysis; CVD, Cardiovascular Disease; ICER, Incremental Cost-Effectiveness Ratio; PAD, Peripheral Artery Disease; QALY, Quality-Adjusted Life Year; WTP, Willingness to Pay; YoLS, Years of Life Saved.

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