

Modelling Cardiovascular Event Reduction and Cost Savings With a CV Polypill (ASA + Atorvastatin + Ramipril) Versus Standard of Care in Post-Myocardial Infarction Patients in Spain

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1. INTRODUCTION AND OBJECTIVE

Atherosclerotic cardiovascular (ASCVD) disease remains the leading cause of morbidity and mortality globally¹. Several studies have shown a recurrence rate close to 50% for any CVD event or for subsequent revascularisation in the year after a myocardial infarction (MI) and up to 75% of patients have a recurrent event within 3 years². In Spain, cardiovascular disease is the second most common cause of death, accounting for 26.5% of all fatalities³.

Clinical practice guidelines recommend the use of antiplatelet drugs, statins, and ACE inhibitors for preventing recurrent MACE in patients with established ASCVD or multiple risk factors⁴.

The Phase III Secondary Prevention of Cardiovascular Disease in the Elderly (SECURE) randomized controlled trial (NCT02596126) compared a CV polypill (ASA + atorvastatin + ramipril) versus the individual components administered separately, i.e. standard of care (SoC), in reducing MACE after a MI. The trial showed a 24% reduction in the relative risk of the primary endpoint (MI, ischemic stroke [IS], urgent revascularization, and CV death), over 4 years. Additionally, a key secondary outcome, comprising cardiovascular death, non-fatal MI, and stroke, saw a relative risk reduction of 30% ($p=0.005$). Moreover, the secondary outcome of cardiovascular death alone was reduced by 33%⁵.

Based on the SECURE results, the ESC included the CV-polypill in their acute coronary syndrome (ACS) guideline to improve outcome and adherence after ACS (IIaB)⁶. Furthermore, the CV-polypill is recommended for secondary prevention in hypertensive patients by the European Society of Hypertension (IIA)⁷ and was recently added to the 2023 Essential Medicines List published by the World Health Organisation for secondary CV prevention⁸.

Objective: This analysis aimed to estimate, through modelling, the potential MACE reduction and economic savings of adopting the CV polypill in Spain, compared to the SoC, considering the annual MI incidence, over a 4-year time horizon.

2. METHODS

The probability of experiencing MI, IS and CV death was estimated from the SECURE study and applied to the simulated patient cohorts, consisting of the annually incident patients, over a 4-year time horizon, in line with the follow-up length of the SECURE study. A new incident cohort of 36,539 patients who recently experienced a non-fatal MI in Spain was simulated each year. The number of patients at risk was adjusted over time according to the overall survival observed in the SECURE trial.

Estimation of the annual non-fatal MI incidence in Spain

The annual non-fatal MI incidence in Spain was estimated at 36,539, combining data from the RECALCAR 2023 Registry (50,002 MI cases in 2021)⁹ and the National Institute of Statistics (13,463 MI deaths in 2021)³.

Estimation of the probability of MACE from the SECURE trial

Individual patient level data from 2,466 patients who were enrolled in the SECURE trial was used to derive Kaplan-Meier data for time to reinfarction, time to stroke and time to cardiovascular death, to inform input parameters to inform the comparative efficacy of the CV-polypill versus SoC. A complete case analysis (N=2,305) was conducted.

The number of simulated patients at risk over time were accounted for overall survival in SECURE, as the Kaplan-Meiers for time to event treated death as a censoring event (therefore, Kaplan-Meier represent the probability of an event, conditional on being alive).

The number of events is estimated at each time point ($t = \text{days}$), according to the probability of suffering an event and the estimated number of patients at risk at each specific time.

Estimation of the hospitalization costs

A one-time in-hospital tariff cost was applied to patients who experienced reinfarction, stroke or CV death, to account for the costs associated with either event. The applied hospitalization costs are presented in table 1. CV death cost was €11,871, calculated from fatal MI (€12,026) and IS (€7,473) events, with the SECURE study proportions (MI: 96.6%, IS: 3.4%).

Table 1. Unit costs of cardiovascular events¹⁰

Cardiovascular event	Code	Cost (in 2021 €)
Non-fatal reinfarction	APR-DRG-190	€6,288
Fatal reinfarction	APR-DRG-190	€12,026
Non-fatal stroke	APR-DRG-047	€5,204
Fatal stroke	APR-DRG-047	€7,473
CV death	NA. Calculated from SECURE study proportions (fatal MI: 96.6%, fatal IS: 3.4%)	€11,871

Abbreviations: APR-DRG, All Patient Refined Diagnosis-Related Group.

3. RESULTS

The adoption of the CV polypill could result in the avoidance of 3,062 MI, 1,557 IS, and 5,086 CV deaths in Spain over a 4-year period. The savings in direct hospitalization costs were estimated to be € 87,730,986. Figure 1 represents visually the 4 modelled cohorts and its MACE avoided and respective savings.

Figure 1. Visual representation of the 4 modelled cohorts with the respective MACE avoided and respective savings

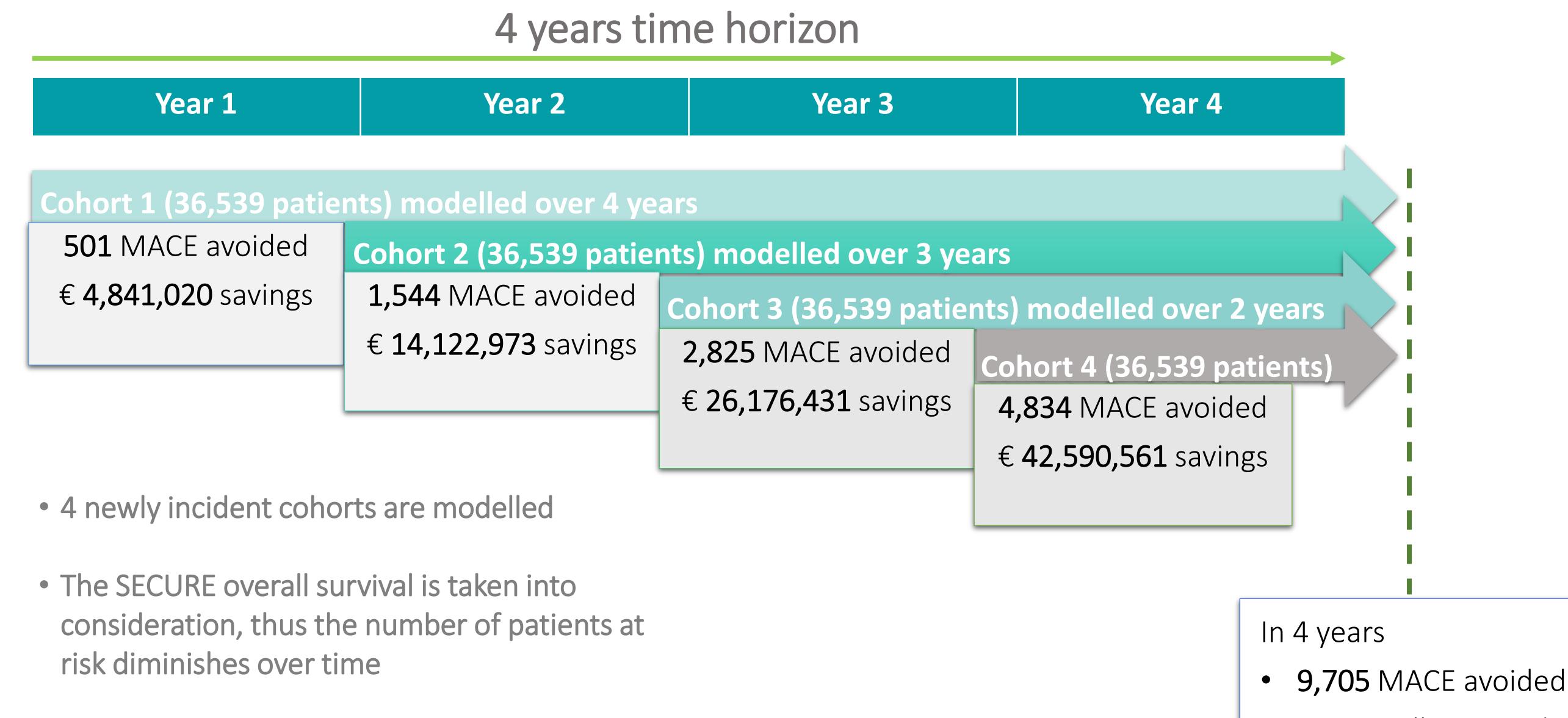


Table 2 presents the MACE avoided and respective cost savings by using the CV polypill instead of SoC, as per the SECURE trial results, over the 4 years modelled time horizon.

Table 2. Difference between CV Polypill and SoC in cumulative MI, stroke, and CV death over 4 years, considering an annual MI incidence of 36,539 patients

Mycardial infarction	Year 1	Year 2	Year 3	Year 4	Total MI avoided
Cohort 1 (36,539 patients)	59	414	408	766	1,647
Cohort 2 (36,539 patients)		59	414	408	882
Cohort 3 (36,539 patients)			59	414	473
Cohort 4 (36,539 patients)				59	59
Total MI avoided	59	473	882	1,647	3,062
Total respective economic savings	€ 372,078	€ 2,975,950	€ 5,543,482	€ 10,359,393	€ 19,250,903
Ischemic stroke	Year 1	Year 2	Year 3	Year 4	Total IS avoided
Cohort 1 (36,539 patients)	117	118	131	472	838
Cohort 2 (36,539 patients)		117	118	131	366
Cohort 3 (36,539 patients)			117	118	235
Cohort 4 (36,539 patients)				117	117
Total MI avoided	117	235	366	838	1,557
Total respective economic savings	€ 608,450	€ 1,225,004	€ 1,904,578	€ 4,363,347	€ 8,101,379
Cardiovascular death	Year 1	Year 2	Year 3	Year 4	Total CVD avoided
Cohort 1 (36,539 patients)	325	511	742	770	2,348
Cohort 2 (36,539 patients)		325	511	742	1,578
Cohort 3 (36,539 patients)			325	511	836
Cohort 4 (36,539 patients)				325	325
Total MI avoided	325	836	1,578	2,348	5,086
Total respective economic savings	€ 3,860,492	€ 9,922,018	€ 18,728,372	€ 27,867,822	€ 60,378,705
Total MACE (MI, IS and CVD)	Year 1	Year 2	Year 3	Year 4	Total MACE avoided
Cohort 1 (36,539 patients)	501	1,043	1,281	2,008	4,834
Cohort 2 (36,539 patients)		501	1,043	1,281	2,825
Cohort 3 (36,539 patients)			501	1,043	1,544
Cohort 4 (36,539 patients)				501	501
Total MACE avoided	501	1,544	2,825	4,834	9,705
Total respective economic savings	€ 4,841,020	€ 14,122,973	€ 26,176,431	€ 42,590,561	€ 87,730,986

Abbreviations: CVD: cardiovascular death; IS: ischemic stroke; MI: myocardial infarction

4. CONCLUSION

Adopting the CV polypill in post-MI patients has the potential to prevent 9,705 MACE in Spain over 4 years, saving €87.7 million for the NHS, making it the preferred therapeutic option at discharge after a MI.

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