

Original article

## Usefulness of a Cardiovascular Polypill in the Treatment of Secondary Prevention Patients in Spain: A Cost-effectiveness Study

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ABSTRACT

**Introduction and objectives:** To estimate the health benefits and cost-effectiveness of a polypill intervention (aspirin 100 mg, atorvastatin 20 mg, ramipril 10 mg) compared with multiple monotherapy for secondary prevention of cardiovascular events in adults with a history of myocardial infarction from the perspective of the Spanish National Health System.

**Methods:** An adapted version of a recently published Markov model developed and validated in Microsoft Excel was used to compare the cost-effectiveness of the polypill with that of its combined monocomponents over a 10-year time horizon. The population included in the model had a mean age of 64.7 years; most were male and had a history of myocardial infarction. The input parameters were obtained from a systematic literature review examining efficacy, adherence, utilities, and costs. The results of the model are expressed in events avoided, incremental costs, incremental life years, incremental quality-adjusted life years, and the incremental cost-effectiveness ratio.

**Results:** Over a 10-year period, use of the cardiovascular polypill instead of its monocomponents simultaneously would avoid 46 nonfatal and 11 fatal cardiovascular events per 1000 patients treated. The polypill would also be a more effective and cheaper strategy. Probabilistic analysis of the base case found a 90.9% probability that the polypill would be a cost-effective strategy compared with multiple monotherapy at a willingness-to-pay of 30 000 euros per quality-adjusted life year.

**Conclusions:** The polypill would be a cost-effective strategy for the Spanish National Health System with potential clinical benefits.

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## Utilidad de un policomprimido cardiovascular en el tratamiento de pacientes en prevención secundaria en España: un estudio de coste-efectividad

RESUMEN

**Introducción y objetivos:** Estimar los beneficios en salud y el coste-efectividad de una intervención con un policomprimido (ácido acetilsalicílico 100 mg, atorvastatina 20 mg y ramipril 10 mg) para la prevención secundaria de eventos cardiovasculares desde la perspectiva del Sistema Nacional de Salud español en comparación con la monoterapia múltiple.

**Métodos:** Se utilizó una versión adaptada de un modelo de Markov publicado recientemente y desarrollado y validado en Microsoft Excel para evaluar el coste-efectividad del policomprimido frente a sus monocomponentes combinados en un horizonte temporal de 10 años. La población incluida en el modelo tenía antecedentes de infarto de miocardio y una media de edad de 64,7 años, y la mayoría eran varones. Los parámetros de entrada se obtuvieron de una revisión sistemática de la literatura que informara sobre eficacia, adherencia, utilidades y costes. Los resultados del modelo se expresan en eventos evitados, costes incrementales, años de vida incrementales, años de vida ajustados por calidad incrementales y la razón de coste-efectividad incremental.

Palabras clave:

Prevención secundaria cardiovascular

Policomprimido

Adherencia

Coste-efectividad

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**Resultados:** En 10 años, la utilización de un policomprimido cardiovascular en lugar de sus monocomponentes evitaría 46 eventos cardiovasculares no fatales y 11 fatales por cada 1.000 pacientes tratados. Además, el policomprimido es una estrategia más efectiva y más barata. En el análisis probabilístico del caso base, se observa un 90,9% de probabilidad de que el policomprimido sea una estrategia coste-efectiva para una disposición a pagar 30.000 euros por año de vida ajustado por calidad comparada con la monoterapia múltiple.

**Conclusiones:** Se demuestra que el policomprimido es una estrategia coste-efectiva para el Sistema Nacional de Salud español con potencial beneficio clínico.

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### Abbreviations

ACEI: angiotensin-converting enzyme inhibitors  
NNT: number of patients needed to treat  
QALY: quality-adjusted life year

## INTRODUCTION

The recent deterioration in population health and increased prevalence of chronic disease is a worldwide problem with multifactorial and complex causes. Population aging, together with increases in poor nutritional habits, obesity, and hypertension, contribute more and more to the epidemiological development of cardiovascular diseases.<sup>1</sup> Accordingly, the population receiving long-term drug therapies and the number of polymedicated patients have significantly increased, exposing the alarmingly low drug adherence rate in both primary and secondary prevention. The situation is so critical that patient adherence to long-term treatments is one of the public health priorities of the European Union.<sup>2</sup> Despite the proven efficacy of the drugs used in secondary prevention, the estimated adherence is only 57%.<sup>3</sup> This poor therapeutic adherence has an economic and health impact and is associated with the abysmal achievement of therapeutic targets and increased admissions and mortality rates. Both relative and absolute risk estimates show that a considerable proportion of cardiovascular events (about 9% in Europe) can be attributed to poor therapeutic adherence.<sup>4</sup> Ho et al.<sup>5</sup> found that lack of adherence to cardioprotective drugs was common: 22% for angiotensin-converting enzyme inhibitors (ACEI), 26% for statins, and 29% for beta-blockers. Part of the cost burden of cardiovascular disease springs from a lack of therapeutic effectiveness due to poor adherence. Indeed, the direct and indirect costs of poor adherence in the United States range from 100 000 to 289 000 million dollars per year.<sup>6,7</sup> This is one of the factors driving industry, insurance companies, and regulatory and government bodies to identify ways to successfully and cost-effectively promote adherence.

The cost-effectiveness of the polypill has been studied in multiple socioeconomic settings.<sup>8</sup> More recently, the results were published of a Markov model created using clinical trial data to analyze the role of a cardiovascular polypill in secondary prevention in the United Kingdom.<sup>9</sup> This model compared the use of a polypill (composed of aspirin 100 mg, atorvastatin 20 mg, and ramipril 10 mg) with monotherapy. The model estimated that each 10% increase in adherence could prevent 6.7% of additional

fatal and nonfatal cardiovascular events. Based on these and other results, the use of a cardiovascular polypill in secondary prevention could be a strategy with a low cost-effectiveness ratio for preventing cardiovascular events.

In the present article, we compared the cost-effectiveness ratio of a secondary prevention therapeutic strategy involving a polypill containing aspirin 100 mg, atorvastatin 20 mg, and ramipril 10 mg with that of multiple monotherapy in the Spanish taxpayer-funded health system.

## METHODS

### Design of the Model

An adapted version was used of a recently published Markov model<sup>9</sup> developed in Microsoft Excel for the United Kingdom with a 3-month cycle length to evaluate cardiovascular outcomes, costs, and benefits and estimate the incremental cost-effectiveness ratio per life year and quality-adjusted life year (QALY) gained from a polypill over a 10-year time horizon. The analysis was performed from the perspective of the Spanish taxpayer-funded health system and included noncardiac mortality data from the Spanish population and costs for Spain. The population included in the model comprised patients older than 40 years who had experienced a myocardial infarction more than 1 year before and who should thus be receiving antiplatelet therapy, preferably with aspirin, a statin, and an ACEI. The population chosen was based on a study by Zeymer et al.<sup>10</sup> The population had a mean age of 64.7 years and 72% were men with a previous diagnosis of myocardial infarction. These patients are susceptible to 1 of the following 5 cardiovascular events: acute coronary syndrome, nonfatal stroke, congestive heart failure requiring hospitalization, unplanned revascularization procedures, or death from cardiovascular causes. These patients may also die of noncardiac causes. Patients who have had a nonfatal cardiovascular event remain in the acute phase (health states 3a 4a, 5a, 6a) for 1 cycle of the model; subsequently, they progress to postacute coronary syndrome (health state 7), postcongestive heart failure (health state 8), or poststroke (health state 9). A diagram of the model is shown in Figure 1. The model does not actually reflect all possible options, as that would require the transition probabilities of each state, data currently unavailable in the literature.

Patients could have any of the distinct clinical events according to various key equations reflecting the final probability of a patient experiencing 1 of the 5 cardiovascular events according to patient adherence to the medication. The rates were determined based on adherence to aspirin, statin, and ACEI, as well as the relative risk reduction with each of the 3 medications in specific types of cardiovascular events for

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