Validation of a population coronary disease predictive system: the CASSANDRA model

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ABSTRACT

Background The use of validated multivariate cardiovascular predictive models in a population setting is of interest for public health policy makers. We aimed to validate the estimations of the CASSANDRA model (coronary heart disease (CHD) incidence and CHD risk distribution), considering the population changes in age, sex and CHD risk factors prevalence in a 10-year period.

Methods We compared the projected CHD incidence estimated with CASSANDRA with that observed in the Girona Heart Registry (REGICOR) for 1995–2004 and 2000–2009 in the population of Girona (Spain) aged 35–74 years. We used official age and sex distributions for this population. Baseline cardiovascular risk factors prevalence and the distribution of cardiovascular risk were obtained from three cross-sectional studies performed in 1995, 2000 and 2005. To validate the future distribution of cardiovascular risk, we tested the yearly CHD risk variance over the study period.

Results No significant differences between the estimated and observed annual CHD incidence per 100 000 men were found in 1995–2004 (CASSANDRA=457.8 and REGICOR=420.3, incidence rate ratio (IRR) (95% CI)=0.92 (0.89 to 0.96)) and in 2000–2009 (441.4 and 409.6, respectively, IRR=0.93 (0.90 to 0.96)). However, overpredictions of 18% and 22%, respectively, were observed in women (198.8 and 160.4, IRR=0.82 (0.77 to 0.86), and 197.1 and 152.8, IRR=0.78 (0.74 to 0.83), respectively). No significant differences were found in the CHD risk variance in the three different cross-sectional studies.

Conclusions The CASSANDRA model produces valid estimates, particularly in men, of the future burden of disease and in the distribution of cardiovascular risk in individuals aged 35–74 years.

Although disease modelling is not a novel issue,5 the use of validated multivariate predictive models with high accuracy and established ability to discriminate risk may be of particular interest for health promotion planners and public health policy makers.9–10

To test the hypothesis that a predictive model may help to substantiate health planning, we designed the CASSANDRA project. A model was fitted to provide estimations of the number of coronary heart disease (CHD) events (ie, angina, fatal and non-fatal myocardial infarction (MI)), and the CHD incidence rates within the next 10 years, and to describe the cardiovascular risk distribution in the population free of cardiovascular disease in the same period of time. The CASSANDRA model performs all predictions considering the expected demographic evolution (ie, changes in age and sex distribution) of the population and user-proposed changes in the prevalence of cardiovascular risk factors that will occur in the next 10 years beginning at a known baseline prevalence.

The aims of this study are: (1) to validate the estimations of the CASSANDRA model regarding the projection of CHD events (angina pectoris, MI and CHD death), the annual CHD incidence rate and the cardiovascular risk distribution, considering population changes in age and sex and in the prevalence of one or more cardiovascular risk factors in a 10-year period; and (2) to apply the CASSANDRA model to the Spanish population to ascertain the number of CHD events, the annual CHD incidence rate and the cardiovascular risk distribution according to different health interventions and considering the expected 10-year population changes in age and sex over the 2013–2022 period.

INTRODUCTION

The primary prevention of cardiovascular diseases is a paramount priority of the public health agenda because it is the main cause of death in the developed world and is increasing alarmingly in developing countries.1 The strategies for the primary prevention of cardiovascular diseases aim at reducing cumulative lifetime morbidity by postponing their clinical onset.2 Most cardiovascular disease cases are related to lifestyle and other modifiable factors, whose improvement leads to a reduction in the incidence of this disease.3

Several authors have highlighted the potential usefulness of cardiovascular risk functions for ascertaining the future incidence of cardiovascular diseases at population scale, considering the future changes in the population age distribution and in the prevalence of cardiovascular risk factors.4–7

METHODS

Rationale of the CASSANDRA model

The CASSANDRA model is a predictive risk algorithm based on the Framingham-REGICOR cardiovascular risk function validated for the Spanish population, that estimates the excess risk in cardiovascular disease-free individuals aged 35–74 years according to their prevalence of cardiovascular risk factors compared to the average of the population to which they belong.11,12 Risk functions are designed to estimate risk in a population that shares certain risk factor characteristics, sex and age, and therefore, involve a high degree of uncertainty when applied at the individual level.13–15 The CASSANDRA model aims to predict future CHD events (angina pectoris, MI and CHD death) at a population scale according to different conditions (modifications in demographic population
characteristics, and in the prevalence of cardiovascular risk factors). A priori, given the excellent calibration of the instruments, this population approach may decrease the degree of uncertainty observed for these tools when used at an individual scale.\textsuperscript{11,12}

The data required to apply the CASSANDRA model to a reference population are the 10-year expected changes in demographic distribution (ie, sex and age) and in the prevalence of cardiovascular risk factors (ie, total and high-density lipoprotein (HDL) cholesterol, systolic and diastolic blood pressure, diabetes and smoking).

Validation of the CASSANDRA model
To estimate the outcomes of the CASSANDRA model, the changes in the sex and age distribution of the population in the reference area were taken from the official statistics of Catalonia.\textsuperscript{14} Changes in the prevalence of cardiovascular risk factors were estimated from the three REGICOR (Registre Gironí del Cor, or Girona Heart Registry) population-based cross-sectional studies performed in the province of Girona in 1995, 2000 and 2005,\textsuperscript{15} and from the follow-up assessments of these three independent cohorts conducted in 2010.\textsuperscript{16} The reference population was approximately 600,000 inhabitants. From all three population-based cross-sectional studies, we selected participants aged 35–74 years stratified by 10-year age and sex groups. The selected participants were contacted by a letter informing them of the aims of the study and the tests to be performed. Participants were requested to fast for at least 10 h before their appointment at the health examination site.\textsuperscript{15} All participants were duly informed and signed their consent to participate in the studies. The three cross-sectional studies and the follow-up assessment were performed by a team of trained nurses and interviewers who used the same standard questionnaires and measurement methods. For the purpose of this analysis, we selected participants aged 35–74 years with no previous symptomatic cardiovascular disease.

The CASSANDRA estimates of the number of CHD cases in a 10-year period were compared to the observed number of CHD cases, and the corresponding estimated CHD cumulative incidence to the annual CHD incidence rate obtained from REGICOR, which collected data in the reference area between 1990 and 2009.\textsuperscript{17,18} To record and classify MI cases, the REGICOR registry followed the MONICA (Monitoring of trends and determinants in cardiovascular diseases) algorithm, which takes into account the type of symptoms, electrocardiographic findings, enzymes and, for fatal cases only detected through the registry of deaths, CHD history and the autopsy results, if available.\textsuperscript{19} Define fatal or non-fatal MI cases and possible fatal MI cases in individuals with no previous history of CHD were considered for estimating the number of cases and the MI incidence rate in the two periods considered (ie, 1995–2004 and 2000–2009). As in the adaptation of the Framingham-REGICOR risk function, we further assumed that the angina and silent MI incidence rates described in the Framingham study (ie, 40% in men and 91% in women) applied to our setting. Therefore, the CHD hard event rate obtained from the REGICOR registry was multiplied by 1.40 and 1.91 in men and women, respectively.\textsuperscript{20}

To determine the validity of the future cardiovascular risk distribution predicted by CASSANDRA, we tested whether the linear combination of the eight cardiovascular risk factors necessary to estimate CHD risk (ie, age, sex, total and HDL cholesterol, systolic and diastolic blood pressure, diabetes and smoking) followed a normal distribution in the population, and whether its variance differed between the REGICOR cross-sectional studies conducted in 1995, 2000 and 2005.\textsuperscript{15,20}

All participants included in the studies used in the present analysis were duly informed and signed their consent to participate. The studies were approved by the local ethics committee and have conformed to the principles embodied in the Declaration of Helsinki.

Risk factor prevalence reduction and predicted future CHD events in Spain
To achieve a 2022 prediction of Spain’s number of CHD events, annual CHD incidence rate, and cardiovascular risk distribution according to the recommended groups (ie, <5%, ≥5% and <10%, ≥10% and <15%, and ≥15%),\textsuperscript{12} we applied the CASSANDRA model using demographic projections and the cardiovascular risk factor distribution data. We assessed two different scenarios: (1) expected modification in the population distribution of sex and age over the 10-year period (ie, 2013–2022), and (2) scenario 1+ target modification in cardiovascular risk factor prevalence in the same period.

The demographic information was taken from the projected changes in the distribution of population sex and age described in Spain’s official statistics.\textsuperscript{21} The reference prevalence of cardiovascular risk factors in 2013 was taken from the DARIOS Study, a pooled analysis of 11 population-based cross-sectional studies conducted in the first decade of the 21st century.\textsuperscript{22} This study included individuals aged 35–74 years with no previous cardiovascular disease and the prevalence was assumed to hold for the year 2013. To perform a realistic estimation, the risk reduction targets were the best risk factor distribution observed in the component studies of DARIOS.\textsuperscript{22} We defined risk reduction targets only for cardiovascular risk factors, with effective interventions supported by high-grade scientific evidence (ie, total cholesterol, systolic and diastolic blood pressure, diabetes and smoking).\textsuperscript{23}

Statistical analysis
The prevalence of cardiovascular risk factors in the REGICOR cross-sectional studies, the number of individuals aged 35–74 years in the reference area, and the mean age were stratified by sex. Continuous variables were summarised as mean and SD, and categorical variables as proportions. The CASSANDRA model assumes a linear change in the prevalence of cardiovascular risk factors over the 10-year period assessed.

To estimate the annual incidence of CHD events, the CASSANDRA generated 10 different estimates for the 10-year period, divided each estimate by 10, and then calculated the average of these values to obtain an annual rate. Using the population of the reference area for each year studied, the model calculated the number of CHD cases per year using its averaged annual rate.

To estimate the CIs for the annual incidence, a bootstrap method was applied when the model generated the 10 different estimates. To describe the cardiovascular risk distribution at the end of the 10 years, the CASSANDRA model used the age and sex distribution in the population, and the prevalence of cardiovascular risk factors in the last year of the period considered.

To validate the estimates of the CASSANDRA model, we first compared the model’s projected annual CHD incidence rates (angina pectoris, MI and CHD death) with those observed in 1995–2004 and 2000–2009 in the REGICOR population-based registry, calculating the incidence rate ratios and 95% CI. Second, to validate the future distribution of the cardiovascular risk we compared the distribution with normality plots and the
variance of the linear combination of cardiovascular risk factors in the three REGICOR cross-sectional studies.

All the statistical analyses were performed with the R Statistical Package (R Foundation for Statistical Computing, Vienna, Austria; V2.15.0).

RESULTS

From 1995 to 2010, we observed an increasing trend in the number of individuals aged 35–74 in the reference population. In both sexes, there was a decrease in systolic blood pressure and the prevalence of diabetes, and an improvement in the lipid profile (ie, total cholesterol decreased and HDL cholesterol increased slightly). The percentage of smokers decreased in men but increased in women (table 1).

The CASSANDRA model estimated 5715 CHD events in men and 2465 in women, being the annual CHD incidence rate 457.8 and 197.1, respectively. The CASSANDRA model produced a normal distribution of population risk overestimated the annual incidence rate for women (table 2). No signiﬁcant differences were observed in the variance of risk estimates between the studies conducted in 1995 and 2000 (p value=0.454 and p value=0.218, in men and women, respectively), 1995 and 2005 (p value=0.914 and p value=0.234) and 2000 and 2005 (p value=0.240 and p value=0.795).

Considering only the demographic changes expected in the Spanish population (see online supplementary table S1), the number of future CHD events and the annual CHD incidence rate for the period 2013–2022, were 627 197 and 523.4/100 000 men and women, respectively, and 290 166 and 232.3/100 000 women (table 3 and ﬁgure 2). Additionally, 25.3% of men and 7.8% of women with no history of cardiovascular disease will be at high cardiovascular risk (≥10%). However, an improvement in the cardiovascular risk proﬁle (mean cardiovascular risk 4.5% and 2.2% in men and women, respectively, in scenario 2) (see online supplementary table S1) would decrease the number of CHD cases (581 591 in men and 277 168 in women), the annual CHD incidence rate (485.5 and 222.0/100 000 men and women, respectively) and the percentage of individuals at high risk (20.2% and 6.4% of men and women respectively) (table 3 and ﬁgure 2).

DISCUSSION

The CASSANDRA model, based on the Framingham-REGICOR risk function, aims to give a comprehensive picture of CHD for the next 10 years in a certain population. Fitted with the demographic and epidemiologic changes that occurred in Girona Province between 1995 and 2010, the model produced valid estimations, particularly in men, of the number of individuals who would develop a CHD event, the annual CHD incidence rate, and the future distribution of cardiovascular risk in individuals with no history of cardiovascular disease. Therefore, the CASSANDRA model could prove to be a useful tool for research purposes.

Table 1 Prevalence of cardiovascular risk factors in men in the REGICOR cross-sectional studies conducted in 1995, 2000 and 2005 and in the cohort follow-up conducted in 2010

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N=666</td>
<td>N=1216</td>
<td>N=2592</td>
<td>N=2678</td>
<td>N=756</td>
<td>N=1295</td>
<td>N=2988</td>
<td>N=3163</td>
</tr>
<tr>
<td>Total Cholesterol, %</td>
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<tr>
<td>&lt;0.1 mmol/L</td>
<td>5.2</td>
<td>5.1</td>
<td>7.9</td>
<td>9.8</td>
<td>4.5</td>
<td>5.0</td>
<td>8.4</td>
<td>7.6</td>
</tr>
<tr>
<td>≥0.1 and &lt;5.1 mmol/L</td>
<td>21.5</td>
<td>24.3</td>
<td>33.5</td>
<td>35.3</td>
<td>22.4</td>
<td>21.8</td>
<td>32.8</td>
<td>30.8</td>
</tr>
<tr>
<td>≥5.2 and &lt;6.1 mmol/L</td>
<td>36.1</td>
<td>39.2</td>
<td>38.5</td>
<td>38.4</td>
<td>34.7</td>
<td>36.1</td>
<td>36.2</td>
<td>40.2</td>
</tr>
<tr>
<td>≥6.2 and &lt;7.1 mmol/L</td>
<td>27.3</td>
<td>23.4</td>
<td>15.3</td>
<td>14.4</td>
<td>24.6</td>
<td>26.2</td>
<td>17.0</td>
<td>17.7</td>
</tr>
<tr>
<td>≥7.2 mmol/L</td>
<td>9.9</td>
<td>10.9</td>
<td>4.9</td>
<td>2.1</td>
<td>13.8</td>
<td>10.8</td>
<td>5.6</td>
<td>3.8</td>
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<tr>
<td>HDL Cholesterol, %</td>
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<td></td>
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<tr>
<td>&lt;0.9 mmol/L</td>
<td>14.4</td>
<td>12.9</td>
<td>11.9</td>
<td>5.9</td>
<td>3.5</td>
<td>4.3</td>
<td>2.8</td>
<td>1.2</td>
</tr>
<tr>
<td>≥0.9 and &lt;1.17 mmol/L</td>
<td>34.6</td>
<td>37.0</td>
<td>33.5</td>
<td>32.8</td>
<td>17.6</td>
<td>18.3</td>
<td>15.6</td>
<td>12.4</td>
</tr>
<tr>
<td>≥1.17 and &lt;1.30 mmol/L</td>
<td>14.5</td>
<td>18.4</td>
<td>17.8</td>
<td>21.7</td>
<td>14.4</td>
<td>15.3</td>
<td>13.5</td>
<td>14.2</td>
</tr>
<tr>
<td>≥1.30 and &lt;1.55 mmol/L</td>
<td>22.1</td>
<td>20.5</td>
<td>23.2</td>
<td>27.5</td>
<td>29.1</td>
<td>27.6</td>
<td>29.5</td>
<td>34.3</td>
</tr>
<tr>
<td>≥1.55 mmol/L</td>
<td>14.4</td>
<td>11.2</td>
<td>13.7</td>
<td>12.1</td>
<td>35.4</td>
<td>34.6</td>
<td>38.6</td>
<td>37.8</td>
</tr>
<tr>
<td>Blood Pressure, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>&lt;120/80 mm Hg</td>
<td>19.8</td>
<td>12.5</td>
<td>25.4</td>
<td>21.5</td>
<td>29.1</td>
<td>31.1</td>
<td>45.4</td>
<td>43.3</td>
</tr>
<tr>
<td>≥120–129/80–84 mm Hg</td>
<td>37.3</td>
<td>37.7</td>
<td>35.8</td>
<td>36.8</td>
<td>32.0</td>
<td>30.6</td>
<td>28.0</td>
<td>29.3</td>
</tr>
<tr>
<td>≥130–139/85–89 mm Hg</td>
<td>21.7</td>
<td>25.9</td>
<td>19.1</td>
<td>23.0</td>
<td>20.3</td>
<td>18.7</td>
<td>14.8</td>
<td>15.5</td>
</tr>
<tr>
<td>≥140–159/90–99 mm Hg</td>
<td>18.1</td>
<td>19.8</td>
<td>14.4</td>
<td>15.8</td>
<td>15.9</td>
<td>13.1</td>
<td>10.0</td>
<td>10.1</td>
</tr>
<tr>
<td>≥160/100 mm Hg</td>
<td>3.2</td>
<td>4.1</td>
<td>2.3</td>
<td>3.0</td>
<td>2.8</td>
<td>4.5</td>
<td>1.9</td>
<td>1.9</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>17.3</td>
<td>16.4</td>
<td>16.7</td>
<td>16.8</td>
<td>13.6</td>
<td>12.5</td>
<td>10.6</td>
<td>9.0</td>
</tr>
<tr>
<td>Smoker, %</td>
<td>32.2</td>
<td>31.8</td>
<td>31.4</td>
<td>24.4</td>
<td>12.2</td>
<td>16.0</td>
<td>17.3</td>
<td>16.1</td>
</tr>
</tbody>
</table>

HDL, High-density Lipoprotein.
population-based cardiovascular disease prevention, health planning, cost-effectiveness and cost-utility analyses. In fact, the application of the CASSANDRA method to the most recent Spanish epidemiologic data showed an increasing trend in the number of CHD events that will occur between 2013 and 2022, and in the annual CHD incidence rate, mainly explained by the progressive ageing of the population. However, the improvement in the cardiovascular risk profile might attenuate this natural trend.

The CASSANDRA model provides three important pieces of information on CHD evolution: the projection of new CHD events and cardiovascular risk distribution in individuals with no history of cardiovascular disease at the end of the 10-year period and the population-wide benefit that could be achieved if risk factor prevalence targets were reached by specific or combined health interventions.

### Projection of new CHD cases

The most common models used for projecting new cases of a particular disease examine the past incidence of a disease and then extrapolate observed trends into the future, often incorporating the projected changes in the population’s age structure. However, the main advantage of using predictive risk algorithms, such as the CASSANDRA model, is the ability to directly incorporate baseline exposure characteristics in addition to age and sex and also the evolution of these risk factors along the 10-year reference period. Previous models did use the Framingham risk function to estimate the future number of cardiovascular events according to particular interventions (eg, dietary salt reductions, obesity prevention, or lipid-lowering strategies), or to ascertain hospital admission rates generated by cardiovascular events. The novelty of the CASSANDRA model is the multifactorial view of CHD, allowing simultaneous assessment of the benefit of different interventions in terms of the incidence rate, which includes prehospital CHD deaths.

The CASSANDRA model predicted that CHD incidence will increase in Spain for 2013–2022, mainly due to population ageing. This trend could be softened by controlling the prevalence of cardiovascular risk factors. The low incidence rate observed in women from Girona was the most likely reason why the estimated CHD incidence was lower than that observed for Spain. We consider the overestimation observed in women to be an acceptable conservative approach for health planning and policy making. Additionally, the 2013–2022 projections for

### Table 2 Comparison of the number of coronary heart disease cases and annual incidence rate observed in the REGICOR population-based registry and estimated by the Cassandra model

<table>
<thead>
<tr>
<th></th>
<th>REGICOR registry</th>
<th>CASSANDRA model</th>
<th>REGICOR registry</th>
<th>CASSANDRA model</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Period 1995–2004</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of CHD cases</td>
<td>5274</td>
<td>5715</td>
<td>2009</td>
<td>2465</td>
</tr>
<tr>
<td>Annual incidence rate/100 000</td>
<td>420.3</td>
<td>457.8</td>
<td>160.4</td>
<td>198.8</td>
</tr>
<tr>
<td>Incidence Rate Ratio (95% CI)</td>
<td>0.92 (0.89 to 0.96)</td>
<td>0.82 (0.77 to 0.86)</td>
<td></td>
<td></td>
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<tr>
<td>Period 2000–2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of CHD cases</td>
<td>6061</td>
<td>6511</td>
<td>2200</td>
<td>2817</td>
</tr>
<tr>
<td>Annual incidence rate/100 000</td>
<td>409.6</td>
<td>441.4</td>
<td>153.9</td>
<td>197.1</td>
</tr>
<tr>
<td>Incidence Rate Ratio (95% CI)</td>
<td>0.93 (0.90 to 0.96)</td>
<td>0.78 (0.74 to 0.83)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Women</strong></td>
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<tr>
<td>Period 1995–2004</td>
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<td>Number of CHD cases</td>
<td>2009</td>
<td>2465</td>
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<td>Annual incidence rate/100 000</td>
<td>160.4</td>
<td>198.8</td>
<td>160.4</td>
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<tr>
<td>Incidence Rate Ratio (95% CI)</td>
<td>0.82 (0.77 to 0.86)</td>
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</table>

CHD, coronary heart disease.

![Figure 1](image1.png)  
**Figure 1** Annual CHD incidence rate (left) and annual number CHD of cases (right) estimated by CASSANDRA and observed in the REGICOR registry between 1995 and 2010, by sex. CHD, coronary heart disease.
all of Spain were more robust due to the higher number of events included in the model for this purpose.

Description of cardiovascular risk distribution
The population health term ‘risk diffusion’ has been described as an equivalent to the clinical term ‘risk stratification’. Risk diffusion is crucial when estimating the potential for population-wide changes in risk factor levels and deciding the best population strategy for the primary prevention of cardiovascular disease. Therefore, anticipating the population distribution of cardiovascular risk with a 10-year perspective might help to design accurate prevention strategies for cardiovascular diseases that would have an impact on the population burden of disease.

Contribution of cardiovascular risk factors to population risk
The contribution of specific risk factors to CHD mortality and to the distribution of population risk has been explored in many countries using a historical focus in most of them. However, it should be noted that fatal MI cases represented less than 40% of all MI cases, and cases of angina pectoris were not considered. Additionally, the prospective approach, as in the CASSANDRA model, is likely to yield more uncertainty than a retrospective approach. However, the community-based information provided will be of greater preventive and planning value, and allows the calculation of future efficacy and effectiveness of preventive programmes.

Population-predictive algorithms for health planning
Several characteristics make the CASSANDRA model a useful and methodologically robust algorithm for population health planning purposes following the requirements published by other authors. The estimations could be performed using population data routinely collected in primary care settings or health surveys (ie, sex, age, total and HDL cholesterol, systolic and diastolic blood pressure, diabetes and smoking). Additionally, this tool is available online for the scientific community. It provides estimations by sex and allows the identification of high-risk groups based on the software’s estimates of the future distribution of cardiovascular risk in the population. Finally, the CASSANDRA model could be adapted to different populations. The three requirements are: (1) the availability of a cardiovascular risk function adapted and validated, if possible, for the reference population; (2) a recent estimation of the prevalence of cardiovascular risk factors, to be used as the reference point for defining the different scenarios; (3) the projected 10-year changes in the distribution of population sex and age. Validation of this new adapted model is then based on the comparison of the observed CHD incidence (eg, estimated from a MI registry or high-quality administrative databases) and the incidence estimated by the adapted CASSANDRA model. This process will be sensitive to the changes in the prevalence of cardiovascular risk factors in the same population between at least two time points in 10 years.

Characteristics and limitations of the study
The development of robust risk algorithms and their validation with high-quality population-based studies improves their practical application. The final aim is the integration of risk evaluation and disease prevention into routine functioning of healthcare systems. The CASSANDRA model allows the estimation of the potential benefits of single or combined health interventions, together with the changes in age and sex distribution in the population, an approach that matches the multifactorial aetiology of cardiovascular disease. Finally, the model could be adapted to validated cardiovascular risk functions, which could further include lifestyle changes (physical activity and diet) that affect the 10-year incidence of MI.

This model has several limitations. First, the health benefit derived from interventions is analysed for the population as a whole; thus, the CASSANDRA model does not identify
individuals who will get the maximum benefit from the interventions. Second, many current policies related to cardiovascular prevention are based on an individual risk factor epidemiology, and do not consider that many individual attitudes are shaped by the community’s attitude toward health problems. Multivariate risk tools have been described as the most discriminating risk approach available, and as well suited to examine social inequalities, even though the estimates do not include specific variables for identifying vulnerable groups. Finally, higher volumes of data might produce more reliable predictions with the CASSANDRA model. For instance, the model’s estimates for women were less precise, but this could be due to the low number of CHD cases observed in our female population.

In conclusion, the CASSANDRA model produces valid estimates, particularly for men, of the number of CHD events over 10 years, and of the annual CHD incidence rate, given baseline data on cardiovascular risk factor prevalence and a targeted prevalence at the end of the study period in a population with known 10-year shifts in sex and age. Additionally, the model provides the future distribution of cardiovascular risk (<5%, 5.9–9%, 10–14.9% and 15% or greater) in individuals aged 35–74 years with no history of cardiovascular disease. Applying the CASSANDRA model to official Spanish data showed that the number of CHD events and the CHD incidence rate will increase between 2013 and 2022 merely due to the progressive ageing of the population. However, this trend was attenuated by improvement of the population’s cardiovascular risk profile (ie, decrease in total cholesterol, systolic and diastolic blood pressure). The benefit of these interventions could also decrease the percentage of individuals at high cardiovascular risk.

Figure 2  Estimations performed by the CASSANDRA model for the annual CHD incidence rate (left) and annual number of CHD cases (right) in Spain in the period 2013–2022, by sex, and considering two different scenarios: no change in risk factor prevalence, and achieving the best risk profile observed in 11 Spanish population-based cross-sectional studies; both scenarios take into account expected demographic changes in sex and age. CHD, coronary heart disease.
Cardiovascular risk functions are useful tools for ascertaining the future incidence of cardiovascular diseases at population scale, considering the future changes in the population age distribution and in the prevalence of cardiovascular risk factors.

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