BUDGET IMPACT ANALYSIS OF ROUTINE TESTING FOR GENETICALLY BASED CARDIOPATHIES ASSOCIATED WITH HIGH RISK OF SUDDEN DEATH IN SPAIN: PRELIMINARY RESULTS.

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BACKGROUND

- Heritable cardiac diseases are primarily caused by mutations of genes that encode for ion channels or their regulators[1].
- A positive genetic test allows to confirm the diagnosis or to identify silent carriers within families. In certain conditions, the identification of a mutation has a further impact on risk stratification and treatment[2].
- Routine management of families with cardiomyopathies and channelopathies at risk of sudden cardiac death (SCD) includes periodic lifetime clinical screening of family members.
- Limitations in availability and costs have meant genetic testing not to be considered in routine practice for many families.

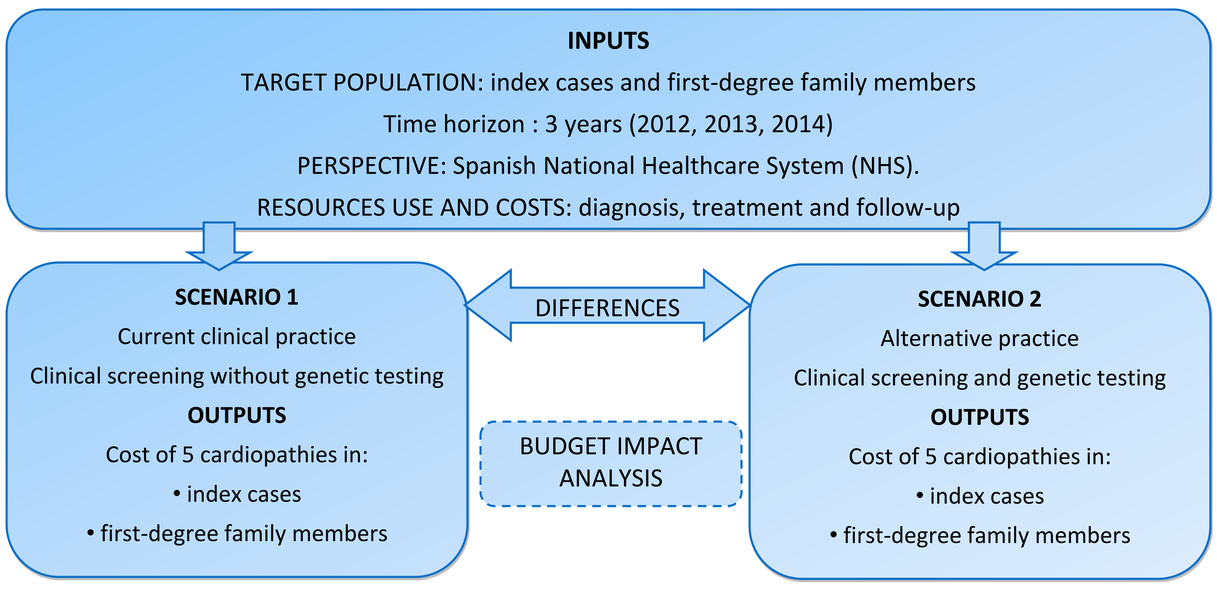
OBJECTIVES

- The objective is to estimate the economic impact of introducing the genetic test for diagnosing the five cardiopathies associated to SCD linked to the currently best known genes in Spain:
  1. **Hypertrophic Cardiomyopathy** (HCM)
  2. **Arrhythmogenic Right Ventricular Cardiomyopathy** (ARVC)
  3. **Long-QT Syndrome** (LQTS)
  4. **Catecholaminergic Polymorphic Ventricular Tachycardia** (CPVT)
  5. **Brugada Syndrome** (BrS)

METHODS

- A 3-year budget impact analysis was carried out based on international sources of epidemiological and healthcare resource utilization data; local costs; market share estimates, and expert opinion.
- Two scenarios were compared: **SCENARIO 1:** current clinical practice (clinical screening alone, without genetic testing) vs. **SCENARIO 2:** alternative clinical practice (clinical screening with genetic testing).
- The perspective adopted was that of the **Spanish National Healthcare System** (NHS). Only direct costs associated to diagnosis, treatment and follow-up of patients were taken into account. All costs referred to €,2012.

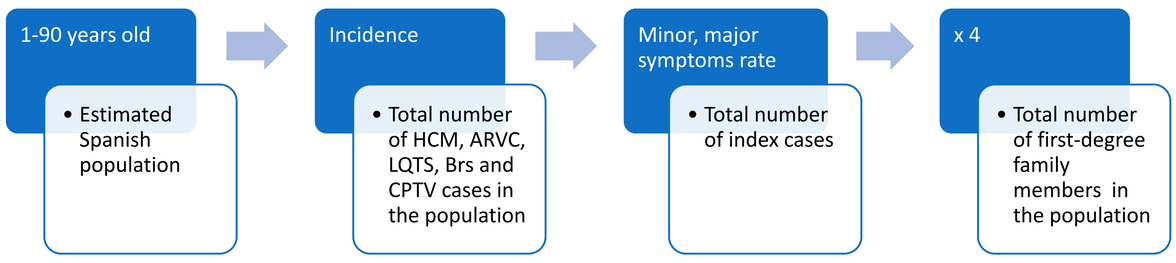
Figure 1: Model scheme



Target population

- The target population at risk of SCD was calculated for the **Spanish population of 1 to 90 years of age**.
- To determine the size of the **index cases** population the annual incidence of the 5 cardiopathies was considered. Based on these figures, it was calculated the number of patients presenting minor or major symptoms, being asymptomatic, or having a SCD. Minor symptoms included palpitations, dizziness, fatigue, chest pain, dyspnea while major symptoms encompassed syncope and an aborted SCD. Data were derived from relevant trials and registries, complemented with experts' opinion in case of unavailable data. To input each year new cases, the number of index cases was yearly updated.
- The number of index cases resulting each year was multiplied by 4 (expert opinion) to determine the number of **first-degree family members** potentially affected by the hereditary cardiopathy.

Figure 2: Calculation of the target population

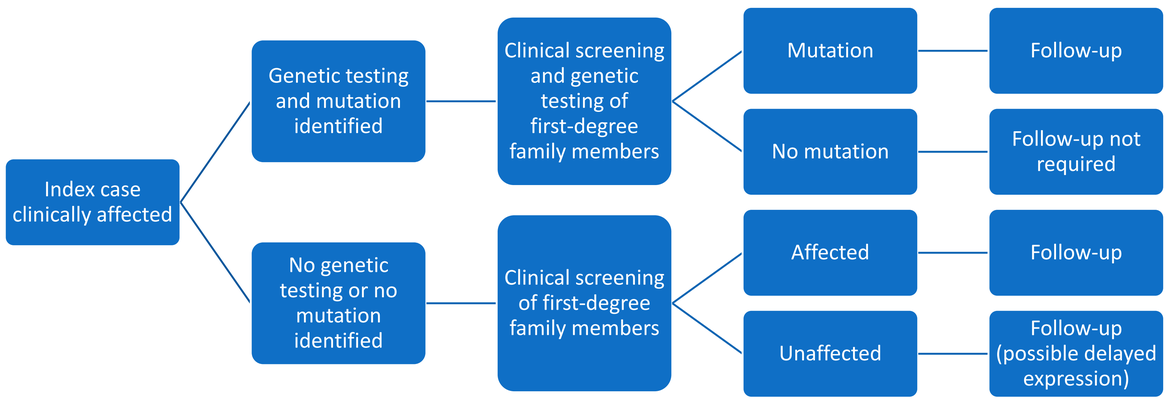


- The **target population** at risk of SCD was estimated on **25,220** patients for the first year**; 26,352** for the second year, and **26,340 fo**r the third year.

Clinical screening strategies

- It was assumed that clinical screening alone has a given probability of identifying patients with each studied cardiopathy (expert opinion), and that genetic testing has a probability of identifying a mutation in index cases (according to relevant trials and registries). The prevalence of mutation in first-degree family members was 50% (autosomal dominant inheritance). Figure 3 illustrate clinical screening strategies in each scenario.

Figure 3: Clinical screening strategies



RESULTS

- **Genetic testing would be conducted in 350, 550 and 700 patients** in 2012, 2013 and 2014, respectively.
- The **economic impact** of introducing the genetic test for all five cardiopathies would imply an additional cost of **€ 315,168, € 540,549, and € 733,578** each subsequent year, respectively, to the National Health System (Table 1).
- The highest costs of managing patients at risk of SCD due to hereditary cardiopathies corresponds to HCM individuals followed by ARVC, LQTS, CPTV and BrS patients in both scenarios.

Table 1: Budget impact results

Scenario 1: no genetic testing	1st year	2nd year	3rd year
HCM	€ 30,523,762	€ 44,649,726	€ 46,459,247
ARVC	€ 24,358,113	€ 30,821,596	€ 32,205,652
LQTS	€ 5,879,464	€ 7,501,147	€ 8,318,479
CPVT	€ 4,470,904	€ 5,241,523	€ 5,584,011
BrS	€ 1,139,310	€ 1,624,662	€ 1,753,645
TOTAL	**€ 66,371,553**	**€ 89,838,654**	**€ 94,321,033**
Scenario 2: genetic testing	**1st year**	**2nd year**	**3rd year**
HCM	€ 30,703,507	€ 44,960,837	€ 46,886,349
ARVC	€ 24,432,255	€ 30,943,247	€ 32,363,199
LQTS	€ 5,913,853	€ 7,564,006	€ 8,406,889
CPVT	€ 4,494,019	€ 5,280,119	€ 5,636,162
BrS	€ 1,143,087	€ 1,630,994	€ 1,762,012
TOTAL	**€ 66,686,721**	**€ 90,379,203**	**€ 95,054,612**
Difference (total)	**€ 315,168**	**€ 540,549**	**€ 733,578**

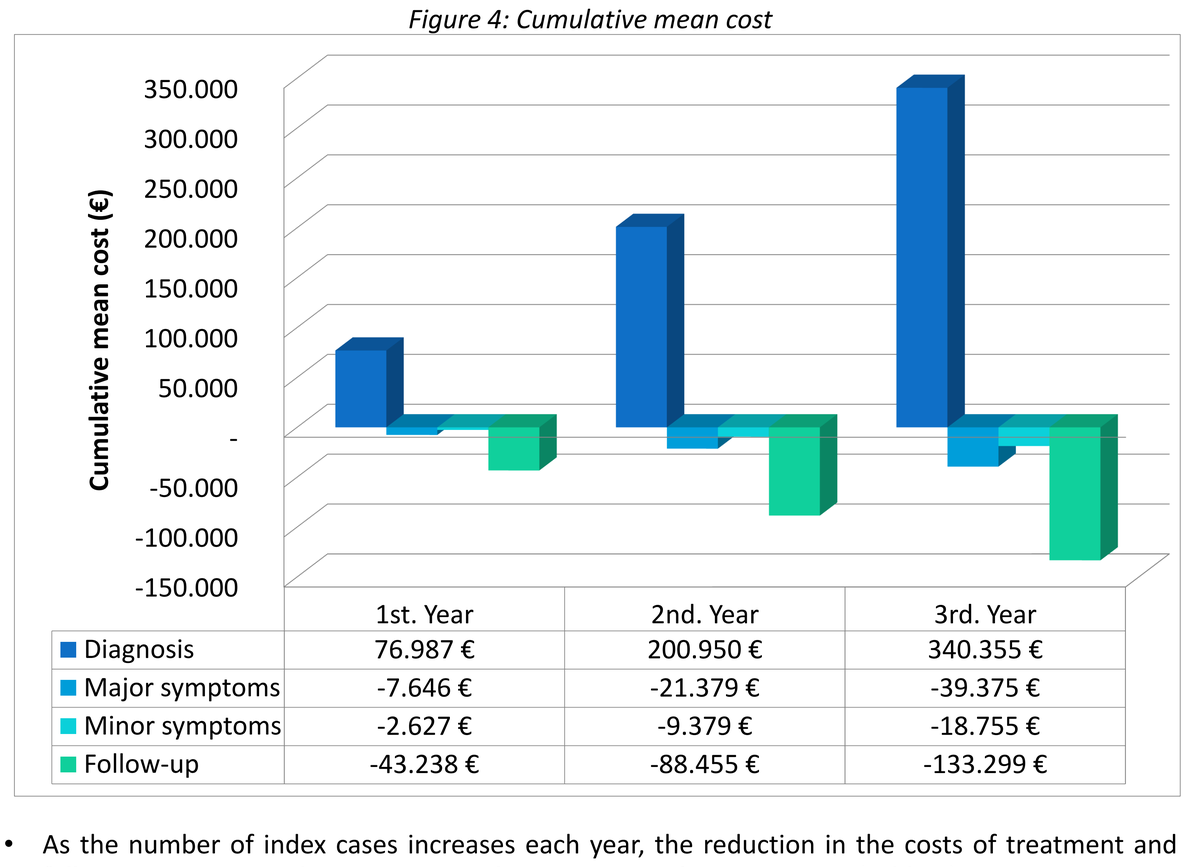
- **Conducting genetic tests in index cases represents the highest costs compared to diagnosing first-degree family members** (Table 2).

Table 2: Proportion of total costs corresponding to index cases and first-degree relatives

Proportion of total cost	1st. Year (%)	2nd. Year (%)	3rd. Year (%)
Index cases	92.55	84.88	79.70
First-degree family members	7.45	15.12	20.30

- Introduction of genetic testing in clinical practice would imply an **increase in diagnosis costs** compared to current practice, and a **decrease in treatment and follow-up costs**.

Figure 4: Cumulative mean cost



- As the number of index cases increases each year, the reduction in the costs of treatment and follow-up progressively compensates the increase on diagnosis costs (Table 3).

Table 3: Differences in cumulative costs (%) according to diagnosis, treatment and follow-up

Difference in cumulative costs (%)	1st. Year	2nd. Year	3rd. Year
Diagnosis	3.20	5.47	7.67
Treatment and follow-up: patients with major symptoms	-0.02	-0.04	-0.07
Treatment and follow-up: patients with minor symptoms	-0.05	-0.08	-0.16
Follow-up	-0.64	-0.83	-0.92
Total	**0.47**	**0.60**	**0.78**

CONCLUSIONS

- **The increases on diagnosis costs of HCM, ARVC, LQTS, BrS and CPVT by genetic testing ithe target population is compensated by a decrease on unnecessary treatment and follow-up costs of first degree relatives in the Spanish NHS. The adequate definition of the group of patients to be followed-up represents the major reduction in costs.**

REFERENCES

1. Lehnart SE, et al. Circulation 2007;116:2325-2345.
2. Priori SG, et al. J Interv Card Electrophysiol 2003;9:93-101.