

Prospective Population-Based Study: The Strengths of Historical Cohort Studies



Rodolfo Pizarro

Rodolfo Pizarro,¹ Walter Masson²

¹ Head of Cardiology, Hospital Italiano Master in Clinical Effectiveness.

² Head of Cardiovascular Prevention. Hospital Italiano.

Ciudad Autónoma de Buenos Aires, Argentina.

Cohort studies are characterized by being observational, longitudinal and analytical. In all of them, an exposure or “exposure factor” must be considered, a predetermined follow-up period (which must be complete for each individual that makes up the cohort, from the moment of enrollment to the end of the period considered) and the outcome of a result, (which will largely depend on the follow-up of the cohort).¹ The predetermined period of time should be sufficient for all study subjects to have the option of developing the event of interest or not. Likewise, eventual losses to the follow-up should not exceed 20%, as this could invalidate the results.

In short words, we could say that cohort studies must have an exposure, a follow-up period and an outcome.

Cohort studies can be prospective (the exposure oc-

curred or not, but the event has not yet occurred) or retrospective (the exposure and the event have already occurred). The retrospective design could be especially useful when the latency time is very long. The limitation of this type of cohort is that we must ensure that the data to be collected are recorded (exposures and potential confounders). In the case of prospective cohort studies, recording the data “forward” is more likely to be more effective.

The objectives of the cohort studies include: knowing the aspects of the natural history or the clinical course of a disease or an event of interest, determining incidence rates and risks, identifying protective or risk factors for the development of a disease event. interest, study the survival, etc. The advantages and disadvantages of cohort studies can be seen in table 1.

Table 1. *Advantages and Disadvantages of Cohort Studies*

Advantages	Disadvantages
You can investigate multiple outcomes that may be associated with multiple exposures.	Susceptible to losses during the follow up.
It allows to study the change in the exposure and the result over time.	It does not eliminate the risk of unmeasured or no recorded confounders.
Useful for examining rare exposures.	Susceptible to information bias and recall bias (retrospective cohort).
Useful to measure the incidence of the result.	Inefficient to evaluate rare events.
You can infer causality.	Costly in time and resources (higher in prospective cohorts).

Population-Based Cohort Studies (Framingham Study)

They are studies of large cohorts based on a defined part of the population or in its entirety, constituting a valuable resource to obtain scientific evidence oriented to the prevention and treatment of the main diseases of the population.

The first iconic study in cardiovascular disease was the Framingham study of cardiovascular risk that began in 1948 and included to 5209 men and women between 30 and 62 years of age from the city of Framingham (near Boston, of 60,000 inhabitants) who did not suffer from symptoms cardiovascular or cerebrovascular.² The study continued to recruit the descendants of the first subjects included between the years 1971 and 1975 (known as the Framingham Offspring Study).

The contribution of this large epidemiological study was relevant. Thanks to the monitoring of the population over a long period of time, it was possible to determine, (among other things), that age was a risk factor for the occurrence of the vascular events. In addition, it was found that coronary disease, and (in particular acute myocardial infarction), was twice as frequent in men compared to women and that it appeared earlier in the male sex. Likewise, the association between certain cardiovascular risk factors was established (in that historical context it was not yet established) such as arterial hypertension, smoking, diabetes or high cholesterol and the increased risk of presenting a cardiovascular event.

Thanks to the follow-up of the natural history of atherosclerotic disease new normality criteria were formulated and active behaviors aimed at cardiovascular prevention were established.

Finally, model building is common in the context of cohort studies. Researchers may need to build explanatory models or predictive models. In the explanatory model, the interest is focused on identifying variables that have a clinically possible and statistically significant association with the clinical outcome or event. Instead in the predictive modeling, the goal is to predict the probability or risk of presenting the outcome of interest in the future (prognosis).

From this large epidemiological study, functions or scores were developed to predict cardiovascular risk (predictive models). These functions allow in a practical and simple way the multifactorial estimation of risk, considering the impact of several risk factors together.

Risk scores are very useful tools in clinical practice, since they allow "classifying" people into different risk

groups and thus, to prioritize interventions with useful drugs in cardiovascular prevention in those subjects with a risk higher cardiovascular.

The first and classic cardiovascular risk score emerged from the Framingham cohort uses a scoring method to calculate coronary risk (acute myocardial infarction and death of coronary origin) at 10 years based on the following variables: age (35-74 years), sex, HDL-C, total cholesterol, systolic blood pressure, smoking (yes / no) and blood pressure medication (yes / no). Subsequently, and based on the data from the original cohort, other risk functions were created with the objective of predicting other vascular events (or a combination of them). Even some elaborated scores estimate risk with a longer time horizon (30 years).³ This was possible because the follow-up of the original cohort could be long, and the loss of information during follow-up (data collection over time) was not relevant. However, risk scores have limitations related to calibration and discrimination ability.⁴ This is so because the characteristics of the cohort (type of population, historical moment) from which the risk score arises are not necessarily the same as those observed in other populations where the score is to be applied. Ideally, if we want to use in our population risk scores arising from other cohorts, we must first validate it. Validity is the degree to which an instrument measures what it really intends or wants to measure. For this, it is usually compared with a reference standard (*gold standard*). In the case of risk functions, the *gold standard* will be the true proportion of cardiovascular events that occurred during a period of time. The validation analyzes to what extent the prediction of the risk score corresponds to reality. In this validation process, calibration (compares what is predicted by the risk function with what is actually observed) and discrimination (ability of risk functions to distinguish patients who will or will not have a cardiovascular event). In this sense, some countries have adapted the original Framingham functions, after validating them in their population.⁵

Many other prospective cohorts in various countries have been used to design risk scores. Thus, as an example, we have the PROCAM score (Germany), the QRISK (United Kingdom), or the SCORE project (Europe).⁶⁻⁸

In conclusion, cohort studies constitute one of the types of observational studies in which a group of people

who share or not share some characteristic (exposure) is followed over time, recording the results (events) in one or more time points. Like all types of studies, it has advantages and disadvantages. The generation of the explanatory and predictive models from these types of studies have great scientific value the iconic Framingham study is one such example of it.

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