1. Introduction

In health sciences, the main focus is on health care using both preventive and curative actions, which are constantly evolving and being updated. In this context, research that contributes with evidence to the decision-making of health professionals is required to adequately understand health problems, as well as implement health interventions.

The fundamental aim of research in the health field is to enrich knowledge about the pathophysiological and epidemiological mechanisms of diseases and health problems and propose strategies for their prevention and treatment through different approaches and methodologies, including basic or preclinical research, clinical research, and epidemiological research in public health (Figure 1).

The basic or preclinical research seeks a better knowledge of the molecular, biochemical, and cellular mechanisms involved in the etiopathogenesis of diseases, forming the basis on which future studies are constructed [1]. Clinical research studies the prevention, diagnosis, and treatment of diseases along with the knowledge of their natural history that can be categorized by the period of data collection (prospective, retrospective, and transversal) as well as by its design (observational or experimental), each with its own strengths and weaknesses [2]. Finally, epidemiological research in public health and health services studies the frequency, distribution, and the health needs of the population, their risk factors, and their impact on public health [3].

In general, biomedical research consists of two main categories: in an experimental approach, the researcher deliberately exposes the subjects to a specific treatment or intervention and observes the results. These results can be compared with those obtained by a different treatment. However, in daily clinical practice, experimental studies are difficult to
carry out and often impose enormous logistical and budgetary challenges that are not easy to face. Therefore, health professionals can usually only observe situations and phenomena which are already segregated in groups. Therefore, researchers cannot assign an exposure or treatment, but only observe the results. This observational approach constitutes the typical environment of most clinical studies. In this context, observational studies can be classified according to the presence of a comparison group. When a comparison group is provided, the study is defined as analytical, otherwise it is considered a description. In cohort studies, the design is similar to that of clinical trials, considered the most appropriate for causal inference, with the difference that exposure occurs naturally and is determined by preferences, clinical decisions or other conditions.

As previously shown, cohorts, as well as other observational studies, have several advantages over randomized and controlled trials, including a lower cost, greater opportunity, and a wider range of patients. However, concerns about the inherent bias in these studies have limited their use when comparing treatments. Therefore, observational studies are mainly used to identify risk factors and prognostic indicators, and in situations where randomized controlled trials would be impossible or unethical [1]. Benson et al. [1] suggested that observational studies usually provide valid information and could be used to explore the available databases. Only with a greater willingness to analyze these databases would it be possible
to achieve a realistic understanding of how observational studies can best be used. It should be noted that although clinical trials are considered the gold standard of clinical studies and are at the top of the traditional pyramid of scientific evidence, there may be limitations, for example, external validity that favors designs such as cohort studies [2]. Therefore, regardless of the type of research performed or evaluated in the clinical context, there must be appropriate tools to discriminate the best available evidence for health decision making [3].

2. General aspects of cohort studies

Cohort studies are similar to experimental studies since they are compared, exposed, and unexposed. The difference is that the researcher does not decide who is exposed, that is, does not assign the subject to one group or another; the patients go to one group to another for reasons of routine or daily clinical practice.

The word cohort means a group or group of people and has traditionally been associated with the military concept of the infantry corps of ancient Rome [4]. Consequently, the term cohort in clinical research is used to designate a group of subjects that have a characteristic, or a set of characteristics, in common (factor of study or exposure), and are followed over time [4–6]. In general, in these types of studies, a group of individuals is recruited, none of which manifests the study event at the time of recruitment, but all of which are at risk of suffering or presenting the event [5–8]. This type of study can adopt a prospective, retrospective or ambidirectional modality [4, 8–11] (Figure 2).

Prospective studies are planned in advance and carried out in a future period of time. The researchers pose a question and form a hypothesis about what might cause a disease and then observe a group of people over a period of time that can take several years. They collect data that may be relevant to the outcome or disease under study and, in this way, aim to detect any change in health related to the possible risk factors that they have identified.

Retrospective cohort studies examine the existing data and attempt to identify risk factors for particular conditions. For example, existing medical records are used to look back in time to identify exposed and unexposed subjects and the subsequent development (or not) of the study outcome. The study maintains the sequence from the exposure to the result, although the data collection occurred after the fact. In this case, interpretations are limited because researchers cannot go back and collect missing data.

As the name implies, in ambidirectional studies, data collection goes in both directions. This approach can be useful for exposures that have both short- and long-term results. The researcher can look back through the records that have already been collected and begin to track the subjects in the future for the onset of the outcome, or disease.

Cohorts can also be classified as closed (fixed) or open (dynamic) cohorts [5, 6, 8]. Closed or fixed cohorts (Figure 3) are study designs that do not consider the inclusion of a population under study beyond the recruitment period set by the researchers. That is, the participants are recruited in the same period of time and do not allow the entry of new individuals during the follow-up. All members have follow-up periods that begin at the same time.
In contrast, in an open or dynamic cohort, individuals can enter the cohort at different times during the study period. The study allows the entry and exit of new study subjects during the follow-up phase, so the number of members may vary over time. Participants can enter or leave the cohort when they meet eligibility criteria and are often defined by geographic units and population groups (Figure 4).
Some limitations should be considered when designing or analyzing a cohort study. For example, they are less suitable for studying rare diseases or diseases with a very long latency. In general, they are inadequate for identifying the causes of a sudden disease outbreak. Like any observational researches, it offers clues about the causes of the disease, rather than definitive evidence of the links between risk factors and health. Participants can leave the cohort, perhaps move away, lose contact or die from a cause that is not being studied. This can produce a bias in the results.

3. The contribution of cohort studies as evidence in health research

Compared with randomized controlled trials (RCTs), observational studies are likely to be faster, less expensive, and include patients that are more representative of routine clinical practice. Also, they avoid the ethical problems caused by the commitment of the therapeutic options. However, validity can be questioned by the inherent limitations of the design [12].

Analyzing the differences between the results of observational studies—such as cohort studies—and clinical trials suggests that there is little evidence of significant differences when estimating the effects between observational studies and RCTs, regardless of the study design, the heterogeneity or the inclusion of studies with pharmacological interventions. Consequently, when exploring the reasons for the lack of consistency between results from the RCTs and observational studies, other factors must be taken into account apart from the study design per se [13].

However, even with the mentioned limitations, cohort studies have delivered important findings that contribute to the understanding of multiple diseases and their risk factors (Table 1), for example, the Framingham Heart Study and the Nurses’ Health Study, among others.
<table>
<thead>
<tr>
<th>Name of cohort study</th>
<th>Type of cohort study</th>
<th>Year</th>
<th>Participants</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framingham heart study [14–16]</td>
<td>Prospective</td>
<td>1948</td>
<td>5209 men and women in ages of 30–62 years residents of the eastern Massachusetts town of Framingham</td>
<td>To examine the relationship between several factors and cardiovascular disease</td>
</tr>
<tr>
<td>British doctors’ cohort study [17]</td>
<td>Prospective</td>
<td>1951</td>
<td>34,439 British male doctors</td>
<td>To assess the risk associated to smoking habits (lung cancer)</td>
</tr>
<tr>
<td>Whitehall study I [18–20]</td>
<td>Prospective</td>
<td>1967</td>
<td>19,019 male civil service (government) employees from London, United Kingdom aged 40–69 years</td>
<td>To examine the role of social determinants in health; association of socioeconomic, behavioral, and metabolic characteristics with the risk of prostate cancer mortality; To assess life expectancy in relation to cardiovascular risk factors recorded in middle age</td>
</tr>
<tr>
<td>Nurses’ health study [21, 22]</td>
<td>Prospective</td>
<td>1976</td>
<td>121,701 female registered nurses</td>
<td>The primary goal of the study was to evaluate the long-term consequences of oral contraceptive (OC) use, particularly its potential association with breast cancer risk</td>
</tr>
<tr>
<td>Whitehall study II [23–25]</td>
<td>Prospective</td>
<td>1986</td>
<td>10,308 (6895 men and 3413 women) civil servant aged 35–55 years</td>
<td>Role of social determinants of disease and mortality; to evaluate effect on health and disease of the work environment, the moderating effect on these relationships of social supports, and, the interaction between psychosocial factors in the etiology of chronic disease</td>
</tr>
<tr>
<td>European prospective investigation into cancer and nutrition (EPIC study) [26, 27]</td>
<td>Prospective</td>
<td>1992</td>
<td>521,457 adults, recruited by 23 centers in 10 European countries</td>
<td>To examine the relationship between diet and cancer</td>
</tr>
<tr>
<td>The Korea nurses’ health study (KNHS) [28, 29]</td>
<td>Prospective</td>
<td>2013</td>
<td>20,213 female registered nurses aged 20–45 years from Republic of Korea</td>
<td>To evaluate the effects of occupational, environmental, and lifestyle risk factors on the health</td>
</tr>
<tr>
<td>The Dutch famine birth cohort study [30]</td>
<td>Retrospective</td>
<td>1944/1946</td>
<td>1116 Dutch female children born I Amsterdam during the “Hunger Winter”</td>
<td>To examine short- and long-term effects of a limited period of extreme nutritional deprivation</td>
</tr>
<tr>
<td>Seveso women’s health study [31, 32]</td>
<td>Retrospective</td>
<td>1976</td>
<td>Women who were newborn to 40 years of age on July 10, 1976 residing around Seveso, Italy at the time of an industrial accident on July 10, 1976</td>
<td>To study the relationship of dioxin (TCDD) on reproductive health</td>
</tr>
</tbody>
</table>

Table 1. Examples of cohort studies.
4. Conclusion

Cohort studies are classified as the most robust form of medical research after experiments such as randomized controlled trials and may be the only alternative for evaluating causal relationships when it is impossible to perform experimental studies. Therefore, cohorts should be considered for studying various health problems both in hospitals and in the ambulatory context.

Conflicts of interest

The author has no conflict of interests to declare.

Author details

René Mauricio Barría

Address all correspondence to: rbarria@uach.cl

Director of the Institute of Nursing and the Evidence-Based Health Office, Faculty of Medicine, Universidad Austral de Chile, Valdivia, Chile

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