Archibald Cochrane: evidence, effectiveness and decision-making in health

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Abstract

Currently, Evidence-Based Medicine plays a fundamental role while making medical decisions, considering that through the methods of science it attempts to justify the variety of alternatives that may be offered to patients. In order to understand the historical evolution of this way of practicing medicine, it is necessary to review the contribution of one of the main participants in this cultural movement: Archibald Leman Cochrane, who helped to define the theoretical framework that has allowed the integration of science into the practice of medicine. Since he insisted on the need of integrating scientific evidence into the clinical experience, his role became a fundamental and decisive element in the development of a new discipline: Evidence-Based Medicine.

Key words: Cochrane Collaboration. Evidence-based Medicine. Clinical trials. Clinical effectiveness.

Archibald Cochrane: evidencia, efectividad y toma de decisiones en salud

Resumen

Actualmente, la Medicina Basada en Evidencia tiene un papel fundamental en la toma de decisiones médicas, ya que intenta, a través de los métodos de la ciencia, justificar las diferentes alternativas que se le pueden ofrecer a un paciente. Para entender la evolución histórica de esta forma de practicar la medicina, es necesario revisar la contribución de uno de los principales participantes en este movimiento cultural: Archibald Leman Cochrane, quien ayudó a definir el marco teórico que ha permitido incorporar la ciencia a la práctica de la medicina. Su papel, al insistir en la necesidad de integrar la evidencia científica y conjuntarla con la experiencia clínica, constituyó un elemento fundamental y decisivo en el desarrollo de una nueva disciplina, la Medicina Basada en Evidencia.

Palabras clave: Colaboración Cochrane. Medicina Basada en Evidencia. Ensayos clínicos. Efectividad clínica.

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Introduction

The Cochrane Collaboration is an international organization whose main purpose is to help make rational decisions in the daily clinical practice. Wide availability of relevant and rigorously obtained scientific information is required to achieve this purpose. However, given the exponential growth of scientific health information, the need to synthesize the existent medical literature, as well as facilitate its rapid access to practice medicine effectively and efficiently has emerged.

Traditionally, the practice of medicine has had the experience of the medical personnel in each one of the specialized areas of healthcare as its main fundament. Experience, however, has a limited scope, since the number of patients a physician has access to along the course of his/her life cannot be compared to the collective experience. Given human variability, both in health and in disease, the possibilities that can be collected by experience are practically infinite. For this reason, the methods of the clinical sciences that are based on the collection of healthy or diseased persons with common characteristics have allowed the incorporation of this information into individualized clinical decision making. Evidence-based medicine derives from the efforts of the medical community, to practice a type of medicine that is mainly based on scientific methods.

The Cochrane Collaboration is internationally recognized as one of the first efforts of Evidence-Based Medicine. This organization takes its name from one of the pioneers of the scientific practice of medicine, Archie Cochrane, who stated that evidence should be the norm in the daily practice of every health professional, anywhere in the world.

His early years

Archibald (Archie) Leman Cochrane was born on January 12, 1909, in Galashiels, Scotland, a city with abundant fabric factories^{1,2}. He was the first son of Walter Francis Cochrane and Emma Mabel Purdom, who were dedicated to the production of “tweed” (characteristic fabric in Scotland), which is why the family did not face any economic problems^{3,4}. He had three brothers, Helen Mabel Cochrane, Archibald’s only sister, two years older; Robert Purdom Cochrane, who was born in 1910, and Walter Lees Cochrane who was born in 1913, being the youngest in the family⁵.

From an early age, Archie faced important losses in his life; his father died in 1917 in the battle of Gaza (Israel), in which he held the position of captain of the

battalion of the King of Scotland, a tragedy that happened when Archibald had only eight years. The loss of his father was followed by that of his two brothers; Walter, who died when he was barely two-years-old due to pulmonary tuberculosis, and Robert, his other brother, who died in a motorcycle accident at the age of 21^{2,4,5}.

From a very young age, Archie demonstrated a great academic potential, which is why, in 1922 a scholarship at the Uppingham school in Rutland, England was granted to him^{4,5}. By demonstrating his great intellectual gifts, in 1927 he was granted another scholarship, this time, for a bachelor’s degree in Natural Sciences at King’s College, Cambridge University, where he graduated three years later with honors^{1,6}.

Shortly after graduating, he participated in research activities due to his interest in science, especially those related to tissue culture, first in Cambridge and then in Toronto for a year, which was enough time to realize that research at the laboratory did not satisfy entirely. It was then, in 1931, when he decided to start his studies in medicine^{3-5,7}.

Cochrane, the physician

Once he started his studies in medicine, they had to be interrupted on two occasions due to various complications¹. Firstly, in 1933, due to a problem that troubled him (anejaculation), for which he decided to seek help, which was denied by British physicians. This situation took him to the Kaiser Wilhelm Institute in Berlin, where Theodor Reik, a brilliant student of Sigmund Freud, helped him. Once psychoanalytic therapy was started in Berlin, discriminatory policies towards Jews burst and forced Reik to flee to Vienna, and later to Holland, where Cochrane followed him to continue his treatment. During this time, Cochrane studied and inquired about psychoanalysis, and at the same time, he acquired great fluency in the German language, an achievement that would later become of great help^{2,5-7}.

Archie undertook some complementary studies in medicine in Vienna and Leiden, during that time and as a medical student he published his first article entitled “Elie Metchnikoff and his theory of an ‘instinct de la mort’,” in the 1934 International Journal of Psychoanalysis; by then, he was 25 years. That year he returned to England to continue studying medicine at the University College Hospital (UCH) in London³⁻⁵. Cochrane did not see any evident results with its psychoanalytic therapy, so he considered it a failure. Whichever the cause was, the ineffectiveness of psychoanalysis

was a stimulus that made him develop a great interest in effective treatments^{4,6,7}.

In 1935, as a medical student, he marched through the streets of London holding a sign that stated: "Every *effective* treatment must be free." His slogan contrasted with that of the members of the syndicate, along with those who marched and whose banners read: "Every treatment must be free." According to him, nobody noticed the difference^{8,9}.

Cochrane was a person with political interests, which led him to become a member of the Socialist Medical Association. In 1936, he decided to interrupt his studies on a second occasion, to serve as a volunteer in the Spanish Civil War, along with other colleagues of the Association. In 1937, his mother Emma died in Edinburgh, Scotland; Archibald returned to England to continue his studies in medicine in August 1937, and he finally graduated March 14, 1938^{2,4,5,7}.

Cochrane and the Second World War

After graduating, Cochrane worked at West London Hospital as a resident and then as a research assistant at the UCH, until the beginning of the second World War, when he was recruited by the Royal Army Medical Corps. In 1941, he was captured by the Germans at Crete and held prisoner the rest of the war in concentration camps in Salonika (Greece) and Hildburghausen and Wittenberg (Germany)^{1,3-5}.

Despite the difficulties of being a prisoner, he conducted his first clinical trial, a quasi-experiment, that he entitled: "Sickness in Salonika: My first, worst and most successful clinical trial"¹⁰. The observation from which Cochrane parted to conduct his trial was the high incidence of ankle edema amongst prisoners, which he suffered, and had an unknown origin. Archie raised the hypothesis that the cause of the edema was vitamin B1 (thiamine) deficiency, consequently causing "wet Beriberi," for which he expressed his concern to the Germans, which refused to provide any assistance. To prove his hypothesis, he purchased yeast and vitamin C supplements at the black market; he selected a sample of 20 prisoners, which he divided into groups of ten. The first groups received daily portions of yeast, while the other group was given vitamin C supplements. After four days, Cochrane observed that the group that had been fed yeast improved, the edema decreased, and the prisoners felt better, while the other group showed no detectable changes in their health status. Cochrane described the results and presented them to the Germans, which

agreed to give yeast to the prisoners; a generous act, since yeast was scarce during war^{1-4,6}.

The proximity of this study to a real experiment is remarkable; Cochrane would later indicate that his study was not considered to be "randomized" since allocation of the prisoners had been made in alternation and not by truly randomized allocation^{10,11}. It is curious how, even though Archie was pursuing a wrong hypothesis, the treatment worked, despite the sample being too small and the time of administration of the yeast and evaluation of the results very shortly. The explanation could be that the small number of proteins present in the yeast was sufficient to elevate serum proteins and, this way, the fluid balance that led to the edema was corrected; nevertheless, the true cause could never be corroborated. Later, Archie reflected on "the surprising thing that a little science and a bit of luck had achieved"^{3,10}.

The first recognized randomized clinical trial in history is the one related to streptomycin and tuberculosis, in which Bradford Hill participated in 1947¹². The study that Cochrane conducted in such difficult conditions in 1941, even though it was not completely randomized, deserves an ample recognition by the methods and circumstances in which it was conducted⁴.

While he was held in the concentration camp he wrote various poems, all of them gathered in a book entitled: Poems from Prison. These describe his feelings regarding the terrible conditions in which he and the other prisoners lived in the camps^{1,5,13}. In 1945, once the war was over and having been released, his services as a physician during the conflict were recognized, bestowing upon him the Order of the British Empire by the King George VI^{1,5}.

Cochrane, epidemiology, and research

Once the war was over, Archie decided to specialize in Preventive Medicine at the School of Hygiene and Tropical Medicine in London, where he took the course of Public Health. In this place, is where he meets Austin Bradford Hill, which would be his statistics professor and the first to show the association existing between the tobacco consumption and lung cancer. Under Hill's tutelage, Cochrane delves into the methodology of randomized clinical trials and Epidemiology, without it being possible to imagine the enormous influence that both characters would have in medicine years later^{2-5,7}.

As a distinction to his academic achievements and his growing interest in Public Health, he received the Rockefeller Scholarship in 1947. This way, Cochrane

arrives at the Henry Phipps Institute in Philadelphia, U.S.A., where a great interest for the use of the X-rays for the diagnosis and prognosis of pulmonary tuberculosis would arise. This interest would later become a true passion for the study of intra- and interobserver error in the interpretation of radiographs^{2-5,7}. Cochrane always questioned the existing medical strategies for diagnosis and research and, although he was not the first to use the term effectiveness, the concepts that he came up with improved the conceptual frame of medical research, leading to the rebirth of clinical medicine⁴.

Under the direction of Charles Fletcher, in the year 1948, he joined the Pneumoconiosis Research Unit, of the Medical Research Council at the Llandough Hospital, in Cardiff, a circumstance that allowed him to investigate on the effects of dust in the coal miners at the Welsh valley area.

Excited to demonstrate the relationship between pneumoconiosis and progressive pulmonary massive fibrosis, he started the Fach Rhondda Plan, which incorporated conducting a clinical trial, therefore, giving a complete turn to the design of epidemiological studies of those times. Finally, after a follow-up of 20 and 30 years, the study was concluded, with published results in 1974 and 1986, respectively^{2,3,5,14}.

Due to his efforts, dedication, high quality, and innovation in his studies, the Welsh National School of Medicine (now the Cardiff University School of Medicine) offered him the position of president of "David Davies tuberculosis and Chest Diseases"²⁻⁵ in 1960. A year later, the position of Honorary Director of the new Epidemiology Unit at Cardiff. This unit has been gaining a great reputation worldwide due to the innovative way of conducting studies and the credibility of their results^{2,3,5,7}.

In 1963, his sister Helen was admitted to a psychiatric hospital with the diagnosis of dementia; however, Archie, with some skepticism, asked to explore other explanatory alternatives to her symptoms. Cochrane asked one of his friends, who was a psychiatrist, to examine his sister. After an exhaustive investigation, porphyria was diagnosed^{5,15} (a group of metabolic disorders of the biosynthesis pathway of the heme group, characterized by acute neurosensory symptoms, skin lesions or both)¹⁶. Knowing the hereditary character of this disease, Cochrane has himself examined, and the same disorder was diagnosed, which was documented to come from his maternal grandfather². Not happy with having studied himself, Archibald sent stool and urine samples of 153 members of his family^{4,5,15}. Later, Archie attributed to this cause an episode diagnosed as polio which he suffered in 1952, as well as his sexual

dysfunction, which, however, has not been ruled out that it was caused by tuberculosis which he contracted during childhood^{4,15}. In 1968, the honorary title of Commander of the British Empire was granted to him, for his services at the Welsh National School of Medicine⁴.

Cochrane and effectiveness

Since he was a student, Archie manifested his concern with the lack of evidence in which medical interventions are supported. These concerns were reinforced by the diverse experiences he had throughout his practice as a physician. One of these fundamental experiences happened when caring for tuberculosis patients at various camps, some of them were even his friends. In his attempt to cure them, the question arose as to whether there was enough evidence about whether the treatment did more good than harm⁵. He soon became a skeptic of all treatments, even those who were widely accepted. Cochrane had the firm idea that no medical intervention should be done unless there was enough evidence to validate its effectiveness. It was then that concepts such as effectiveness and efficiency in clinical practice would become important to him^{5,7}.

His worldwide referenced book and most influential work, published in 1972 with the title "Effectiveness and Efficiency: Random Reflections on Health Services," was accepted with enthusiasm by the medical community and translated to eight languages. This book came after Cochrane gave a lecture on the British National Health System in 1971⁵. In his book, he expressed his concerns and critics on the lack of orientation and scientific evidence, related both to the effectiveness of treatments and to the adequate use of resources (physicians, nurses, equipment, among others)^{4,6,7}. The ideas of Cochrane had a clear impact on treatment administration in patients. His proposal was based on the following principles: effectiveness, efficiency, and equality, which generated debate and controversies around the world. Because of the publication of this book, Archie gained profound respect and admiration of an entire generation of physicians and epidemiologists, which has extended to our days^{4,7}.

As a result of all of the above, in 1974, the identification of all controlled clinical trials in perinatal medicine began in Cardiff, United Kingdom and two years later, Iain Chalmers, a young doctor, conducts the first systematic review (meta-analysis). As a consequence of these initiatives, the World Health Organization and the

Department of Health of the United Kingdom decide to finance the National Perinatal Epidemiology Unit in Oxford, United Kingdom, and thus develop a register of controlled clinical trials in perinatal medicine^{3,4}.

Archie was appointed the first president of the School of Community Medicine of the Royal College of Physicians of the United Kingdom during 1972 to 1975^{3,4}. A year later, he expressed his concerns regarding the absence of a valid and organized summary of all the Randomized Clinical Trials by specialty or subspecialty, since this would facilitate physicians arrive at precise conclusions⁴⁻⁷ (Figure 1).

His last years

Cochrane was a gardening enthusiast. On one occasion, his garden won the award of the Royal Horticultural Society. He also had a certain weakness for rugby, tennis, and squash, as well as skiing and collecting modern art and sculptures^{1,11,18}. Archie was never married, but he was always very close to his family and kept a very close relationship with his sister Helen. He spent his last years with his nephew and his wife, Joe, and Maggie, which took care of him in Somerset, England. He finally died of cancer at 79 on June 18, 1988^{1,2}. A year after his death, his autobiography entitled "One Man's Medicine" is published in collaboration with Max Blythe, a close friend, who worked with Archie on this work for three years^{2,3,5}.

Archie bequeathed £300.000 to Green College with the desire that: "...some of this money, should be used for the development of randomized clinical trials...".

The Cochrane Collaboration developed in response to Archie's calling to methodically use scientific information in healthcare. His suggestions were taken by the Research and Development Programme of the National Health Service of the United Kingdom, who granted funds to establish a Cochrane Center with the goals of collaborating with other entities of the country and the rest of the world and conducting systematic reviews of randomized clinical trials in all areas of healthcare.

In October 1992, the Oxford Cochrane Center was inaugurated, in which the desire for an international response for collaboration with the project was expressed. The outline of this idea was presented at a meeting called in March 1993 by the New York Academy of Sciences, headed by Kenneth Warren and Frederick Mosteller denominated, "Doing more good than harm: the evaluation of health care interventions." In October 1993, the Cochrane Collaboration was founded within the framework of what would be the first of the annual

Figure 1. Archie in the garden of his house. California, 1956¹⁷.

Cochrane colloquia, attended by 77 clinical researchers from eleven countries headed by Iain Chalmers^{6,11,19,20}.

Since its beginnings, the organization's mission was to "help people take a well-informed decision regarding healthcare by preparing, developing, updating, and promoting accessible systematic reviews on the effects of health interventions"²¹.

Conclusion

Among the most important ideas that Cochrane defended throughout his life, is that randomized clinical trials are the best evidence available in health decision-making, part of what we know today as Evidence-based Medicine. To him, effective medical intervention is considered valid only if it has been demonstrated through a randomized clinical trial.

The scientific basis should be the rule in the daily practice of every physician anywhere in the world; that was Archie's dream. Finally, this idea managed to inspire and influence medicine regarding the need to carry out, systematically, an appropriate evaluation of the available information with the purpose of providing better medical care. Archibald always tried to contribute

to the development of useful tools to research health in an increasingly valid way; besides that, with a profound democratic desire, he fought so that both society and health professionals could always rely on effective and efficient information. As an extension of his ideas, the Cochrane Collaboration, currently present in 130 countries with around 37,000 collaborators, has turned out to be a vehicle of extraordinary value to decisively promote the practice of medicine with an increasingly more scientific character, thus integrating the accumulated clinical experience with values and preferences of patients and science.

Conflicts of interest

The authors declare no conflicts of interest.

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