Archibald Cochrane (1909–1988): the father of evidence-based medicine

Antonio Stavrou, Dimitrios Challoumas and Georgios Dimitrakakis

School of Medicine, Cardiff University, Cochrane Medical Education Centre, Cardiff, UK
Department of Cardiothoracic Surgery, University Hospital of Wales, Cardiff, UK

Abstract

Professor Archibald Cochrane (1909–1988) is considered to be the originator of the idea of evidence-based medicine in our era. With his landmark book ‘Effectiveness and Efficiency: Random Reflections on Health services’ he managed to inspire and positively influence the medical society with respect to the proper assessment of reliable evidence for the provision of the best medical care. His vision combined with his scientific achievements can be considered as the foundation of the Cochrane Collaboration; named after him in recognition of and gratitude for his pioneering work. We present the highlights of his adventurous and vibrant personal and academic life in an attempt to honour his contribution to shaping modern medical research.

Keywords: Archibald Cochrane • Evidence-based medicine • Cochrane collaboration

BACKGROUND

Evidence-based medicine (EBM) can be defined as the formal practice of making decisions regarding the best treatment of patients based on the systematic and detailed approach of current best research evidence. EBM is of paramount importance in the provision of the best health care policy [1–3].

Professor Archibald Cochrane was a pioneer in this area and can be considered the father of EBM in our era. His passionate call to require collection and analysis of systematic reviews led to the creation of The Cochrane Collaboration 5 years after his death [4].

We present details of the life of this unprecedented personality, his inspirations and his pivotal role in epidemiology, public health and medicine in general.

EARLY LIFE

Archibald (Archie) Leman Cochrane was born in 1909 in Galashiels, Scotland, a town south of Edinburgh. He was the first son of a wealthy family, as his parents, Walter Francis and Emma Mabel Cochrane, were successful tweed makers. However, from very early on in his life, he was forced to cope with family tragedies. Firstly his father, a captain of the King’s Own Scottish Borderers regiment, died in the battle of Gaza (Israel), when Archibald was only 8 years old. To make things worse, his father’s loss was followed by the loss of his two brothers; his youngest brother Walter died at the age of two due to tuberculosis pneumonia, while the other one, Robert, died after a motorcycle accident at the age of 21 [4–6].

Archibald Cochrane had a charismatic personality and his potential for further development was recognized at a young age, when he was offered a scholarship for Uppingham School in Rutland (England). Here he excelled. This was the first sign of his forthcoming remarkable academic achievements [4–7].

Further to his academic strengths in school, Cochrane was also enthusiastic about athletic activities. He became a member of his school rugby team and, thereafter, engaging in sports and keeping fit were activities he valued throughout his active life [7].

In 1927, he was offered a second scholarship for the Natural Sciences course at King’s College in Cambridge. He was awarded a First Class Honours degree upon graduation in 1930, having successfully completed Parts I and II of his course trips [5–6].

Being eager to further his knowledge and a keen admirer of science, he continued his studies in multiple areas over the following years.

Soon after graduating, he participated in research activities in Cambridge and Toronto for a year. This is when he realized that despite his adoration for academia, laboratory research would not give him a lifetime satisfaction—a self realization that subsequently proved to be tremendously beneficial to the medical community [5–6].

As a result, Cochrane decided to begin his medical studies in 1931. These were completed only after attending medical schools in Vienna, Leiden and London [4–7].

He managed to publish his first article, entitled ‘Elie Metchinikoff’, as a medical student in Vienna in 1933, expanding his theory of an ‘instinct de la mort’ [7].

His medical school years were rather difficult, as he had to interrupt his studies twice and did not graduate until 1938. The first time was between 1933 and 1934 when he decided to tackle...
a sexual problem that was troubling and distressing him. In order to do this he enlisted the help of the prestigious psychoanalyst Theodor Reik, one of the most successful students of Sigmund Freud. Reik, as a member of the Jewish community, was forced to leave Berlin after the existing aggressive discriminative policies against this ethnic group in force at the time. Cochrane followed him to Vienna and The Hague in order to continue his psychoanalysis. He took advantage of this period to study psychoanalysis and become fluent in German, which later proved to be invaluable to his survival during the Second World War [7].

Unfortunately, the psychoanalytic therapy turned out to be ineffective. Cochrane attributed his sexual dysfunction to porphyria, a condition he was diagnosed with later on in his life which he never managed to overcome [4]. It has also been suggested that his problem was actually due to tuberculosis, which he suffered from in childhood. Whatever the true cause, the ineffectiveness of psychoanalysis was an early stimulus that prompted Cochrane to develop an interest in treatments proven to be effective by evidence [8].

In 1934, he returned to England to continue his medical training in the University College Hospital (UCH) in London [4–7]. Cochrane was a multifaceted personality with political interests; his experiences in Europe drove him to become a member of the Socialist Medical Association. In 1936, the association decided to send doctors, nurses and medical students to the Spanish Civil War. Cochrane decided to interrupt his studies, for the second time, between 1935 and 1937, to travel to Spain as a volunteer, where he served in the democratic army as an assistant in an ambulance unit and in the triage in the hospital [6–7].

He returned to the UK in 1937 and finally graduated from UCH in 1938 [5–7].

CONTRIBUTION TO MEDICINE

Soon after qualifying, Cochrane worked as a house officer (resident) in the West London Hospital and then as a research assistant in the UCH until the commencement of the Second World War [7].

During this period, he was recruited to the Royal Army Medical Corps as a captain. He participated in a military action in Crete, Greece (in 1941), where he was captured by the Germans. He spent the rest of the war years (1941–1945) as a prisoner of war, with the speciality of medical officer in Salonika (Greece), Hildburghausen, Elsterhorst and Wittenberg an der Elbe (Germany). Thanks to his fluency in German, he was appointed to the position of chief medical officer in the concentration camps during his captivity [5, 7].

It was during this period that Cochrane performed his first trial as described in his paper in 1984, with the rather cynical title: ‘Sickness in Salonika: My first, worst and most successful clinical trial’ [9]. What led him to conduct the trial was the high incidence of ankle oedema of unknown origin among the prisoners, many of whom, including Cochrane himself, developed oedema even up to above the knee.

He hypothesized that the underlying cause was vitamin deficiency resulting in ‘wet beriberi’, as the prisoners were provided with scanty nutrition of 400–500 calories per day. He expressed his concerns to the Germans who firmly refused to help in any way. In order to test his hypothesis, he bought yeast and vitamin C supplements from the black market in the camp and randomly selected a sample of 20 prisoners, which he divided into two groups of 10. The subjects in the first group received daily portions of yeast, while those in the other one were given vitamin C supplements. Prisoners in both groups limited their water intake and measured the frequency of urination. After 4 days, Cochrane confidently observed that the prisoners in the yeast-eating group had improved; the ankle oedema had subsided and the subjects felt better. There was no considerable change in the health of prisoners from the other group. He carefully wrote down the results of this primitive clinical trial and presented them to the Germans, who then agreed to provide the camp prisoners with yeast, a ‘generous’ gesture as yeast was scarce at those times. Indeed, the incidence of pitting oedema among the prisoners dropped dramatically [9].

Cochrane thought of this trial to be of poor quality and that an element of luck was a great contributor to its success; However, considering the adverse conditions and the limited recourse available, its positive findings and the resulting beneficial outcome were impressive. This was his first ever clinical trial and it can be considered both randomized and controlled, at least to a certain extent. Notably, according to Cochrane, randomized controlled trials (RCTs) were almost unknown to the medical community at the time [7, 9].

After the end of the war, Cochrane continued his studies in preventive medicine at the London School of Hygiene and Tropical Medicine, where he attended a public health course. His statistics Professor, Austin Bradford Hill (1897–1991), was the first scientist to prove a correlation between cigarette smoking and lung cancer and his teaching on RCTs and epidemiology mesmerized Cochrane, who acknowledged Hill’s influence on him for the rest of his life [4–7].

As a result of his academic achievements and his genuine interest in public health, Cochrane won a Rockefeller Scholarship in 1947, which led him to the Henry Phipps Clinic in Philadelphia, PA, USA. There, he developed an interest in the use of X-rays and their reliability in the diagnosis and prognosis of pulmonary tuberculosis and he became enthusiastic about the study of observer error, a passion he sustained throughout his life [4–7].

Since his student days, Cochrane had been concerned about the lack of scientific evidence substantiating medical interventions. The longer he practised medicine, his concerns grew and were intensified by various experiences he had. In his attempt to cure the camp patients suffering from tuberculosis, some of whom were his friends, he had worries about actually doing more harm than good. The concepts of effectiveness and efficiency in the clinical practice were becoming very important to him and made him sceptical about every treatment, even those that were well established and widely accepted. He firmly believed that no medical intervention should be performed unless there is evidence validating its effectiveness and he believed that a more thoughtful, systematic and scientifically based approach to the clinical practice of medicine should govern clinical decisions [10, 11].

This inspiring notion is further demonstrated in another one of his actions. Both he and his sister Helen, to whom he was very close as the only remaining sibling, were diagnosed with porphyria. Taking into account its heritable nature, he was worried that other members of his large, scattered family might have also been carriers of the disorder, and therefore he requested faecal and urinary samples from all 153 of them to find out which ones were unwittingly at risk from the condition [5].

Cochrane never ceased to challenge the existing medical diagnostic and investigational strategies in order to improve the provision of health care at any point during his lifetime. Ultimately, the ground-breaking concepts he formulated, namely the necessity of
RCTs to determine the appropriate treatment and the introduction of cost-effectiveness, had an enormous positive impact not only on his personal practice, but also on clinical medicine as a whole [7, 11].

Although EBM evolves and continuously adapts in modern times, the core principles upon which it operates are based on Cochrane’s innovative ideas.

Although Cochrane was not the first to use the term effectiveness, the concepts he devised improved the way medical research has been performed and led to the renaissance of clinical medicine [4, 5, 7, 11].

In 1948, Cochrane joined the Medical Research Council’s Pneumoconiosis Unit at Llandough Hospital in Cardiff (Wales, UK), which was affiliated with the Welsh National School of Medicine, where he was under the supervision of Director Charles Fletcher [6].

During this time, Cochrane studied the effects of dust in coal miners from the ‘Welsh valleys’ area using comparative studies. Driven by his urge to prove a possible correlation between the different X-ray findings of pneumoconiosis and progressive massive fibrosis, he initiated the Rhondda Fach Scheme that involved conducting high-quality clinical trials that revolutionized the design of epidemiological studies ever since. He persisted to ensure a high response rate, adherence to patients’ follow-up, and reproducibility of his results. He completed the 20- and 30-year follow-up of the population and published the results in 1974 and 1986, respectively [4, 7, 12–14].

His constant dedication and ceaseless efforts did not remain unfruitful—the high quality of his work and sophistication of the design of his studies were soon recognized. In 1960, the Welsh National School of Medicine offered him the ‘David Davies Chair of Tuberculosis and Diseases of the Chest’ and later in the year he was awarded a professorship of tuberculosis [4].

In the same year, he was granted the position of the honorary director of a new epidemiology unit, which was founded in Cardiff (UK), by the Medical Research Council (MRC), an opportunity that Cochrane embraced, relinquishing the pneumoconiosis research. After retiring from the professorship chair in 1969, he was appointed as the unit’s Director and it was not long before the new unit gained worldwide reputation for the innovative approach to epidemiological studies and the credibility of their results. The aetiology of numerous conditions was studied while the Vale of Glamorgan in Wales became the most accurately epidemiologically mapped area in the UK [4–7].

Over a period of 9 years, Cochrane coordinated several RCTs with great success. These included, but were not limited to, his ground-breaking studies in collaboration with Peter Elwood, which managed to prove the effectiveness of aspirin in reducing cardiovascular disease, and his investigations aiming to deduce whether recovering in hospital or at home is best for patients with uncomplicated myocardial infarction [7, 15].

Noteworthily, the Nuffield Provincial Hospitals Trusts (London, UK) awarded the Rock Carling Fellowship to Cochrane. This is granted on a yearly basis and is a means of evaluating the extent of knowledge of scientists in their field of main interest or expertise and is subsequently published as a monograph [16, 17]. He was, therefore, invited to prepare a lecture regarding the assessment and evaluation of the British National Health System (NHS). As a result of his convincing presentation, Cochrane published his landmark book with the title ‘Effectiveness and Efficiency: Random Reflections on Health Services’ in 1972. The book was enthusiastically accepted by the medical community and was translated into eight languages [4–7].

This book is considered to be Cochrane’s most influential work and within it, he expresses his concerns and criticisms of the lack of scientific evidence guidance that should steer medical practice in the NHS, regarding both the effectiveness of treatments and the appropriate usage of resources (doctors, nurses, equipment, etc.). Firmly believing in the significance of RCTs, he suggested that all types of treatment should be based on them, characteristically stating in the book ‘You should randomise till it hurts’, when asked to what extent he would use this type of research [4, 10]. Importantly, the book triggered debates and controversies on health care systems all over the world. Furthermore, it describes ideas that encapsulated the essence of Cochrane’s philosophy and his vision for the future of medicine and are now considered to be fundamental in the way modern medical research is performed. Although this monograph was originally directed at medical students and non-medical professionals, it was embraced by the medical community as it was well-written and contained clinical examples of a wide spectrum of medical disciplines. His continuous emphasis on the terms of efficiency, effectiveness and equality, as well as the concept of cost-effectiveness, intrigued the medical world to apply treatments to patients according to these principles. This book rendered him highly respected for a whole generation of clinicians and epidemiologists to this day [4–7, 11].

Following the success of Cochrane’s book in raising awareness of the issues of the NHS and its policies, he continued to advocate for the value of RCTs in health care systems.

In 1974, under Cochrane’s influence, the identification of all controlled trials in perinatal medicine began in MRC in Cardiff (UK) and later on, in 1976, Iain Chalmers, a young medical doctor, performed the first systematic review (meta-analysis) of these trials. This was the trigger for the World Health Organization and the UK Department of Health to fund the National Perinatal Epidemiology Unit in Oxford, UK, to develop a register of controlled trials in perinatal medicine in 1978 [18].

In 1979, Cochrane expressed his concerns regarding the absence of a valid and organized summary of all RCTs related to each specialty or subspecialty. The valid collection of all RCTs would facilitate clinicians in reaching accurate conclusions [18, 19].

Results from the collection of trials, concerning perinatal medicine, started to be published in medical journals and books [18]. In the foreword of the book ‘Effective Care in Pregnancy and Childbirth’ by Chalmers et al. [19], Cochrane highlights that the work described ‘represents a real milestone in the history of randomized controlled trials and in the evaluation of care, and I hope that it will be widely copied by other medical specialties’.

The need for maintenance of accurate reviews of all RCTs related to all medical fields separately eventually led to the development of the Cochrane Centre in Oxford (UK) in 1992. Therefore, in 1993 this ‘Cochrane Centre’ was transformed into the Cochrane Collaboration [18].

The Cochrane Collaboration is a non-profitable international organization of more than 28 000 scientists from one hundred countries around the world and so far they have published 5000 systematic reviews in the Cochrane Database of Systematic Reviews [20].

Cochrane’s hard work and dedication were recognized during his lifetime. In 1968, he was awarded the honorary title of Commander of British Empire in the Queen’s Birthday Honours List for his services in the Welsh National School of Medicine. He was also appointed first President of the Faculty of Community Medicine of the Royal College of Physicians in the UK between 1972 and 1975. The University of Rochester, USA, awarded him a Honorary
Doctorate in 1977. In the same year, he became a Honorary Fellow of the International Epidemiological Association [17].

During the last few years of his life, Cochrane suffered from cancer and finally passed away peacefully on 18 June 1988 [4–7].

Cochrane spent an important part of his career in Cardiff and in the Welsh National School of Medicine, which is now known as the Cardiff University School of Medicine. Cardiff University decided to honour Archibald Cochrane for his worldwide, ground-breaking contribution to the medical community. In 2010, the brand new medical school building was named after him, so that ‘students would always be reminded of the principles of academic excellence and equality in healthcare for which he stood’ [17].

Conflict of interest: none declared.

REFERENCES