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Evidence-Based Orthodontics – Its Evolution and Clinical Application

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Introduction

Health-care information escalated towards the end of the twentieth century. This created a serious challenge for clinicians trying to make informed decisions for their patients concerning the relative effectiveness of alternative treatment interventions. The lack of systematic reviews from prospective well-designed clinical trials led to delays in incorporating and testing new information while fostering the continuation of less-effective, less-efficient, and even harmful interventions; the proponents believing clinical experience, as the gold standard, for supporting and recommending treatment procedures and interventions.

Medicine pioneered an evidence-based approach to clinical practice in the eighteenth century at a time when navigation was important for overseas trading in Britain. Long voyages to Australia and the Far East were undertaken with sailors deprived of fresh fruit and vegetables, resulting in scurvy and other medical problems. James Lind MD, surgeon to the British Navy, wrote a *Treatise of the Scurvy* which was ignored for many years but considered the first controlled clinical trial to be translated into clinical practice by equipping long-distance trade ships with lemons and limes to avoid the ship's crew succumbing to scurvy.

In 1971, the British epidemiologist, Archie Cochrane (Figure 1.1), in his influential monograph entitled *Effectiveness and Efficiency* (Cochrane 1971) introduced this "new" concept in clinical medicine that all treatment interventions must be proven to be effective. This was supported by an early example in which data were combined from multiple clinical trials investigating premature births and infant mortality. By 1974, all controlled trials in perinatal medicine had been systematically identified and entered into a clinical trials register. By 1987, the year before Archie Cochrane died, 600 systematic reviews on health-care topics had been conducted. How one man, whose ideas were initially unacceptable to the medical community, had such a profound impact on medicine is recounted in the autobiographical monograph *One Man's Medicine* (Cochrane and Blythe 1989). His revolutionary observations and convictions were fashioned by his experiences of growing up in Britain during the tumultuous years surrounding the two World Wars, and the death of his father in the First World War. The loss of his father had a profound effect on the young Archie Cochrane, with the responsibilities expected from the eldest son to take over as head of the family to care for his mother and siblings.

Archie Cochrane and the development of evidence-based medicine

The early years

Archie Cochrane was born in a small town in Scotland in 1909 to a privileged and wealthy family. His successful grandfather and great-grandfather pioneered the textile industry and benefited from the textile manufacture of the popular Scottish tweeds. As a young boy with an elder sister, two younger brothers, and devoted

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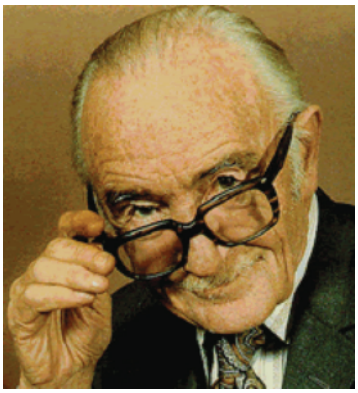

Figure 1.1 Professor Archibald Leman Cochrane CBE, FRCP, FFCM (1909–1988). The Cochrane Collaboration is named in honor of Archie Cochrane, a British medical researcher who contributed greatly to the development of epidemiology as a science. *Source:* courtesy of the Cochrane Collaboration.

parents, he lived an affluent but disciplined life in a large house with multiple servants. His youthful world was disrupted in 1914 when the First World War was declared. His father joined a Scottish regiment and was killed in 1917 while attempting to rescue a wounded brother officer. Archie Cochrane was 8 years old and now carried the responsibilities of being the eldest son with three siblings and a grieving mother. The desolation accompanying the loss of his father was followed by the death of his younger brother to tuberculosis during the severe wartime restrictions.

Archie Cochrane was educated in the traditional upper-class prerogative of "building character" by sending young boys to preparatory boarding school, followed by a prestigious and expensive "public" school, before entering University. Archie Cochrane excelled in athletics and mathematics, and his aptitude for literature resulted in his successful admittance to King's College, Cambridge. A rugby football accident curtailed the time he devoted to acting, riding, tennis, and golf but made him focus on his studies. He graduated with a double first-class honors degree. His grandfather's death, while he was at Cambridge, resulted in his becoming independently wealthy early in his adult life, which he believed contributed to his later success. However, this was also the time of another family tragedy when his remaining younger brother died in a motorcycle accident. Archie was now the eldest and only son of his family, and he undertook responsibility for his widowed mother and elder sister.

The influences in developing an evidence-based approach

Archie Cochrane was a man of the turbulent 1930s who witnessed the events leading to the Second World War. His emotional and intellectual independence and conviction of moral values caused him to often reject political solutions. When he was a medical student at University College Hospital, in London, the Spanish civil war broke out, and Archie Cochrane risked his life and career by volunteering to join the Spanish Medical Aid Unit following Franco's invasion. A year later he returned to England to complete his medical training while believing fascism a menace to Western civilization.

His experience of seeing the consequences of war prepared him for joining the British Army during the Second World War and serving overseas. His fluency and aptitude for languages, including German, French, and Spanish, resulted in his joining a commando regiment that included 70 Spanish refugees from the civil war who had enlisted in the British Army. The regiment was deployed to Crete where Archie was captured by the invading Germans. He spent the next 4 years as a prisoner of war (POW), serving as the medical officer to a camp of 20 000 POWs from diverse cultures and countries, whom he cared for with compassion and fortitude (Doll 1997).

This ordeal resulted in his abiding beliefs in patient care and that medical interventions should be available for all individuals whatever their circumstance. As the medical officer in the POW camp he shared the same diet and conditions as his fellow prisoners. His courage and endurance as a compassionate medical officer resulted in his first clinical trial. He was emaciated and jaundiced himself, with pitting edema above the knees, but he set up a trial with yeast he had acquired from the German prison guards. He describes this as "my first, worst, and most successful clinical trial" (Cochrane 1984).

Having survived the Second World War, he subsequently spent time in the United States before returning to England with a mission and commitment to change the imperfect British medical system. His firm belief in finding evidence for the effectiveness of medical interventions resulted in the development of randomized clinical trials (RCTs) and systematic reviews of the scientific literature. This initiated a new era in

medicine – one that would ultimately influence dentistry. A new evidence-based approach to patient care was destined to revolutionize clinical practice, and the methodology had its roots in his experiences as a POW medical officer with limited medical supplies, never knowing what might or might not work. This uncertainty proved to be fertile ground for Archie to test his theories, as it allowed him to ethically randomize patients to alternative treatments. This randomization usually resulted in well-matched groups that received different interventions, thus allowing the investigation to determine the most effective treatment.

Figure 1.2 The Cochrane Collaboration logo. The outer blue semicircles represent the Cochrane Collaboration and the inner circle the globe to represent international collaborations. The forest plot of clinical trials represents the effectiveness of administering corticosteroids to pregnant women delivering prematurely; the diamond to the left of the "no effect" line indicates the meta-analysis favored the intervention.

The Cochrane legacy

The Cochrane Collaboration was established a year after Archie Cochrane's death and is recognized in the twenty-first century as an international organization that prepares, maintains, and promotes accessible systematic reviews of the effectiveness of health-care interventions from which well-informed decisions emerge (Antes and Oxman 2001).

The familiar logo of the Cochrane Collaboration (Figure 1.2) exemplifies and recognizes the impact of Archie Cochrane's life. The circle, representing the global and international collaboration, encircles the forest plot, which depicts the results of a quantitative meta-analysis. This forest plot represents one of the earliest systematic reviews and meta-analyses of the literature on the therapeutic intervention of corticosteroids in women who were to deliver their babies prematurely. By a statistical combination of data from the clinical trials, the highest evidence, and ultimately the gold standard for clinical practice in caring for pregnant women delivering prematurely, was established. The benefits of the effectiveness of administering perinatal corticosteroids were undeniably correlated with the outcome of perinatal and neonatal survival with a consequent reduction in mortality and morbidity.

The Cochrane Collaboration

The Cochrane Collaboration (Cochrane Collaboration 2017) has influenced and driven the science and methodology of systematic reviews and has been compared to the revolutionary Human Genome Project in its potential implications for contemporary health care (Naylor 1995). Nevertheless, changing the standard of care in clinical practice does not move quickly, and information gained from research experience has a long gestation period and time lag before it becomes incorporated into clinical practice.

Historically, medical and dental regimens have remained unchanged even when well-designed clinical trials have provided counterevidence. Treatment decisions based on clinical experience and beliefs are difficult to change, and it has been shown to take an average of 17 years for the findings from clinical trials to be implemented into clinical practice. For example, there were clinical trials in 1960 of thrombolytic therapy and the administration of streptokinase. By 1975, 40 RCTs had been conducted, and by 1985 there were 50 000 patients enrolled, with evidence that thrombolytic therapy was effective. When a systematic review and meta-analysis conclusively showed the effectiveness of thrombolytic agents, it was finally accepted as a standard of care in 1990. If the contemporary methodological approach to evidence-based practice had been established 30 years previously, many lives could have been saved. Unfortunately, even in the twenty-first century, when evidence is convincing, clinicians may still find it difficult to relinquish their beliefs based on their clinical experience.

The influence of an evidenced-based approach

The establishment of the evidence-based approach resulted in rapid changes in the health-care system and in the education of students and residents in the health-care professions. A paradigm shift had occurred from the paternalistic choice of a treatment intervention by doctors for their trusting patients to a partnership in which the doctor and patient make choices together to determine the "best" treatment. It was therefore incumbent on the health-care provider to have knowledge of the best available evidence pertaining to the risks, costs, benefits, burden of care, and probability of success for alternative treatment interventions. The caveat was that if evidence exists to support the effectiveness and efficiency of treatment interventions, an integration of the best research evidence with clinical expertise and patient values and preferences should occur (Sackett *et al*. 1991, 2000). Although the new movement of Evidence Based Medicine and Clinical Trialists was flourishing in Britain with the leadership of the Cochrane Collaboration, other influences were playing their part on the other side of the Atlantic. Alvan Feinstein MD, Professor of Medicine and Epidemiology at Yale, promoted "clinical care as science," and advanced knowledge with clinimetrics. The term clinimetrics, as its name suggests, embraced science, technology, and clinical care with reproducible consistency as the basic science underlying clinical decision making. During his formative years, in 1963 David Sackett read a paper by Alvan Feinstein on Boolean algebra and taxonomy and wrote Feinstein a fan letter, following which Alvan Feinstein became a mentor to Sackett (Smith 2015). Clinicians and academics interested in evidence-based medicine consider Cochrane, Feinstein, and Sackett as the "fathers" of a new and currently flourishing movement of evidence-based medicine. Dentistry has embraced an evidence-based approach and has ridden on the coattails of medicine in teaching and practicing an evidence-based approach, and conducting systematic reviews and meta-analysis of treatment interventions with well-defined, reliable, and valid outcomes.

The impact of David Sackett and clinical epidemiology resonated with the orthodontic attendees when Bob Moyers invited David Sackett to participate in the Moyers Symposium on three occasions over a 30-year period, starting in 1985. By 2015, when Sackett attended his third Moyers Symposium, he cited his comments from 1985 when he excoriated orthodontics, suggesting the trials in orthodontics was lagging behind "such treatment modalities as acupuncture, hypnosis, homeopathy and orthomolecular therapy and on a par with scientology, dianetics and podiatry" (Sackett 1995). There were no RCTs in orthodontics prior to 1967 and there was a rate of one trial every 2 years during the next decade. By 1994, when Sackett next participated in the Moyers Symposium, orthodontic trials had increased 18-fold, and by 2005 had risen to 129 per year (Sackett 1995, 2014). David Sackett's unique perspective and encouragement in the world of orthodontics had a major influence on the now classic orthodontic Class II RTCs funded by National Institutes of Health/ National Institute of Dental and Craniofacial Research. So who was the late David Sackett and what influenced his interest in an evidence-based approach in medicine (Figure 1.3)?

Figure 1.3 David Lawrence Sackett, OC, MD, MMSc, FRSC, FRCP (Canada, England, and Scotland). *Source:* Per Kjeldsen with permission of Dr. James McNamara.

The influence of David Sackett and medical clinical trials

David L. Sackett (1934–2015) was born in Chicago, the third son of "a bibliophile mother and artist-designer father" (Smith 2015). His childhood was not without adversity as he was bedridden for months with polio, from which he recovered as a 12 year old. He became a voracious reader and as he recovered from polio he became an accomplished runner. He started his medical training at the University of Illinois in 1956 and in 1962 was drafted into the US Public Health

service as a result of the Cuban missile crisis. He also had a Master of Science degree from the Harvard School of Public Health. He was diverted from a career in bench science by his love for clinical medicine, and was influenced by Walter Holland, Professor of Clinical Epidemiology at St Thomas's Hospital Medical School in London, to have an enduring interest and career in clinical epidemiology. He was only 32 years old when he was recruited to the new Canadian Medical School at McMasters University, in Hamilton, Canada. This was a difficult decision as Sackett did not want to leave the United States. Nevertheless, the opportunity to develop a different way to educate medical students by finding evidence from systematic reviews rather than conventional teaching "in my clinical experience" was irresistible. This proved a new and exciting challenge, embraced by a new generation of medical students who flourished in the innovative educational methods, although these were not popular with the senior experienced clinicians. Sackett was not a man with a big ego and once considered an expert it was time to move on and let new talent emerge. This trait was exemplified by his decision, when he was 49 years old, to repeat his Medical Residency. He considered clinical practice had changed so much that he was no longer a "good enough doctor anymore". It took courage to return to medical school but he believed he would become a better doctor if he adopted contemporary methods and became updated. Sackett believed that evidence-based medicine went beyond critical appraisal by combining evidence from research with clinical skills and the values and preferences of patients (Sackett 2015). In 1994, Sackett became a clinician at the John Radcliffe Hospital in Oxford where he was the Director of the Center of Evidence-based Medicine. Five years later, in 1999, he gave his last lecture on evidence-based medicine in Krakow and retired from clinical practice. He returned to Canada to live with his wife and family in a wood cabin beside a lake and set up the Trout Research and Education Center (Smith 2015).

The application of evidence-based dentistry to orthodontics

One method of achieving an evidence-based approach in dentistry and its advanced specialty programs is to carry out a systematic review of all RCTs from which a quantitative analysis of the available data can be statistically included into a meta-analysis. This approach was developed in medicine, with the benefit of patients and doctors making informed decisions on the most effective treatment intervention. The basis of a systematic review is that it provides a method of identifying all the available literature on a topic and synthesizing it into an easily accessible knowledge base. The clinician practicing in the twenty-first century has the computer literacy to access electronic data bases to make informative choices and decisions. As this approach became accepted in dentistry, leaders in the field developed a Cochrane Oral Health Group.

The Cochrane Oral Health Group/ Collaboration

The Cochrane Collaboration is made up of over 50 review groups, of which the Cochrane Oral Health Group (COHG) is one (Shaw 2011). Originally, the COHG was established in 1994 in the United States by Alexia Antczak Bouckoms, based at Harvard University in Boston Massachusetts. In 1996, the editorial base of the COHG (COHG 2017) was relocated to the School of Dentistry, University of Manchester, in England, with Professors Bill Shaw and Helen Worthington as the coordinating editors (Shaw 2011). The COHG is part of the Cochrane Collaboration based in Oxford, England and the University of Dundee in Scotland, directed by Professor Jan Clarkson, and comprises an international network of researchers involved in producing and disseminating systematic reviews of controlled RCTs in the field of oral health. Searching for trials to include in a systematic reviews is a complex process; in order to avoid bias in the results of the review, it is important to include as many relevant trials as possible (see Chapter 3 of this text). The search process relies on initially defining the question, and this has been described in detail in Chapter 2. Finding the best available evidence from sources of published and unpublished studies requires a standardized systematic approach to avoid the

different types of recognized bias (Eggar *et al*. 2001). The quality of data retrieved from a careful, systematic, and standardized review of the scientific literature may be quantitative and/or qualitative in nature (Glasziou *et al*. 2001). Therefore, discrete steps to find the relevant studies are required in searching computer databases to retrieve a body of literature that then requires careful selection and appraisal.

Evidence-based dentistry in education: Commission on Dental Accreditation guidelines

Dentistry did not adopt this revolutionary concept in guiding clinical practice and the education of dental students and residents in the advanced specialty programs until the mid-1990s. To a certain extent, it was forced on the profession by several events that occurred in 1995 owing to the publication of *Dental Practice Parameters for Oral Health* (McNeil *et al*. 1995). The American Dental Association practice parameters stressed the need to develop and implement aids to assist in clinical decision making, which stated the need for:

- condition-based parameters, not procedure-based;
- integrated oral health care in an interdisciplinary approach;
- parameters to aid clinical decision making;
- process of care to be emphasized as well as the outcome;
- balancing patient needs with scientific soundness.

In the same year, the Institute of Medicine report (Field 1995) was published on the future of dental education. This had 22 recommendations, which among others emphasized the need to implement:

- evidence-based care;
- patient-centered treatment;
- elimination of unnecessary/ineffective treatment interventions;
- scientific evidence, outcome research, and formal consensus processes in clinical practice guidelines;
- research to evaluate outcomes of alternative treatments.

With the need to make major changes in the practice and education of oral health-care professionals, at the end of the twentieth century the Pew Trust also identified the critical challenges necessary for health-care professions (Pew Health Professions Commission 1995).

Making rational decisions in orthodontic practice

In orthodontics, clinical experience suggests that some conditions are best treated early for biological, social, or practical reasons, whereas others should be deferred. So how do we reconcile these conflicting issues? When anterior crossbites exist in the early mixed dentition due to a Class I crowded dentition or with a mild developing Class III skeletal pattern, should we wait until the permanent successors have erupted in the late mixed dentition or correct earlier to avoid perpetuating the malocclusion with possible labial gingival recession on the mandibular incisor from the traumatic incisor relationship (Vig *et al*. 2007)? When using a protraction face mask in an attempt to move the nasomaxillary complex forward, our knowledge of craniofacial growth and development indicates early intervention when the circum-maxillary suture system should be responsive. Correcting the anterior crossbite early supports the concept of effective and efficient early treatment intervention. However, with further growth the Class III skeletal pattern may result in the anterior crossbite being re-established. Problems exist when using an evidence-based approach to clinical decision making in orthodontics, as the scientific literature in our specialty has relatively few prospective RCTs, and this study design is considered to provide the highest level of evidence.

So how are clinical judgments made when they cannot be based solely on evidence at the highest level but rather rely on lesser-quality studies and/or clinical experience? One of the most common early orthodontic treatment interventions is the correction of posterior crossbites in the mixed dentition, which may be considered a well-accepted clinical practice. But what evidence exists in the scientific literature? A systematic review published by Harrison and Ashby (2001), *Orthodontic treatment for posterior crossbites*, resides in the Cochrane database of systematic reviews. This is a very comprehensive review of randomized and controlled clinical trials in the scientific literature that reported data on the outcomes of crossbite correction. An extensive number of publications on this topic exist, but until a systematic approach was made to review the literature and identify the quality of studies that should be included, stronger inferences could not be made. The result of the search strategy to identify studies of orthodontic treatment for posterior crossbites, limited by a priori inclusion criteria, resulted in only seven RCTs and five controlled clinical trials. Cochrane reviews have the advantage of being regularly updated as new information becomes available. The updated abstract included studies since 2001, and for this update 113 abstracts were assessed for potential inclusion. Of these, 38 papers were obtained and assessed for eligibility. An additional five reports for three RCTs and one controlled clinical trial (CCT), together with another report to a previously included CCT, satisfied the inclusion criteria.

It becomes clear when trying to quantify the evidence using systematic reviews and meta-analyses that a definition of evidence-based clinical practice requires the careful and considered use of statistics and may be defined as "the enhancement of a clinician's traditional skills in diagnosis, treatment, prevention and the related areas through the systematic framing of relevant and answerable questions and the use of mathematical estimates of probability and risk" (Donald and Greenhalgh 2001). The advantage of a systematic review is that it will limit bias by a methodological approach to strict inclusion criteria of articles, and the conclusions are more reliable and accurate (Greenhalgh 2001). This is covered in Chapter 2 of this text.

Even when evidence is available, clinicians may still be unable to relinquish their beliefs based on their clinical experience. In orthodontic clinical practice, treatment decisions are made based on early intervention for Class II patients being beneficial, even when evidentiary data does not appear to support the effectiveness, efficiency, and benefits of this approach. (O'Brien and Sandler 2011).

Orthodontics, while the oldest specialty in dentistry, recognizes that strong scientific evidence is an important goal for the future of the profession. However, patients are waiting to be treated even though we cannot provide good estimates for the outcomes of alternative treatments at the time of the consultation. In the face of this uncertainty, it becomes even more important for patients to have their preferences considered during the treatment planning stage (Vig and O'Brien 2017).

Advances are often first brought to our attention by anecdotal case reports and observation, as was the discovery of penicillin. Although low on the strength of evidence, these initial reports still have value, as do case series, retrospective studies, and clinical experience. Although there is a paucity of clinical trials in orthodontics from which systematic reviews may be conducted, the methodology is still relatively new. In medicine there was also considerable opposition to Archie Cochrane's insistence that clinical trials needed to be done to establish evidence for the effectiveness of clinical interventions. The lack of RCTs in orthodontics does not mean we should accept the present state of orthodontics as a science but rather that we should demand more rigor in designing clinical trials to determine what works, what doesn't work, and what is just inspired rhetoric with little scientific support or substance. If the very expensive RCT cannot answer the question/hypothesis we would like to test, then perhaps well-designed cohort studies should be a starting place.

The American Dental Association website

The initiative by the American Dental Association (ADA 2017) to develop a website for both clinicians and the public to access current information has provided a rich resource to search for the best information we have concerning alternative treatment interventions. By identifying authors who are publishing in a field of interest, it is possible to easily contact, communicate, and collaborate with researchers all over the world.

Research cannot be set up overnight, but undertaking a systematic review on a chosen topic will allow areas of strength and weakness to be identified. This will reveal further fertile research opportunities and stimulate the development of hypothesis-driven research.

The future of an evidence-based approach in orthodontics

Attacks on an evidence-based approach and severe criticism of clinical epidemiology and the evaluative clinical sciences was in response to the impact and change in clinical practice standards. Doctors were urged to defend clinical reasoning based on the clinician's experience and their understanding of pathology and physiological mechanisms. If we cannot accept applying the highest level of evidence, we will be doomed to muddle along with our best guess. A choice needs to be made based on the alternative outcomes of a clinical intervention combined with the patient's preferences and the clinician's expertise. In the interest of providing the best available care to our patients, the current best evidence must be incorporated into the treatment recommendations that each clinician makes.

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