Chapter Number

Innovating Medical Knowledge: Understanding Evidence-Based Medicine as a Socio-Medical Phenomenon

Maya J. Goldenberg
University of Guelph, Canada

1. Introduction

Because few would object to evidence-based medicine's (EBM) principal task of basing medical decisionmaking on the most judicious and up-to-date evidence, the debate over this prolific movement may seem puzzling. Who, one may ask, could be against evidence (Carr-Hill, 2006)? Yet this question belies the sophistication of the evidence-based movement. This chapter presents the evidence-based approach as a socio-medical phenomenon and seeks to explain and negotiate the points of disagreement between supporters and detractors. This is done by casting EBM as more than the simple application of research findings to clinical care and improved health outcomes, but rather an umbrella term that harnesses a specific set of pedagogical objectives (some rather radical) under a name that makes it difficult to argue against.

EBM is most popularly defined as the "conscientious and judicious use of current best evidence in the healthcare of individuals and populations" (Sackett et al., 1996b). EBM's influential doctrine first appeared in the *Journal of the American Medical Association* as a brief polemic authored by the Evidence Based Medicine Working Group:

> *A new paradigm for medical practice is emerging. Evidence based medicine de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision-making and stresses the examination of evidence from clinical research. EBM requires new skills of the physician, including efficient literature searching and the application of the formal rules of evidence (Evidence Based Medicine Working Group [EBMWG], 1992).*

EBM rose quickly into prominence in medicine, with virtually every area of healthcare now subscribing to the evidence based mantra. This is a considerable feat for a discipline that is described in the EBM manifesto as largely reliant on conventions and habits of thought and practice.

Yet amidst the hubris, there is a sort of obviousness to EBM that has prompted critics to charge EBM with offering "nothing new" (Benitez-Bribiesca, 1999):

> *"Evidence based medicine," one chemist said to me, "What other kind of medicine could there possibly be?" and a consultant physician said gruffly: "We have always practiced evidence based medicine" (Hope, 1995).*[1]

The EBM pioneers equivocated on the movement's innovation and conservatism. It was described as both a "new paradigm" (EBMWG, 1992) and a historically-supported approach "whose philosophical origins extend back to mid-19th century Paris and earlier" (Sackett et al., 1996b). Yet it will be demonstrated in this chapter that although EBM is not best understood as a new "paradigm" or a radical departure from biomedicine, it offers methodological innovation that has shifted how we pursue, collect, and evaluate medical knowledge.

Beginning with a historical account of the origins of EBM, a focus on three key methodological innovations employed by EBM will be used to advance the argument that EBM's original contribution to medicine, or what separates EBM from other approaches, is the priority it gives to certain forms of evidence, specifically evidence from randomized controlled trials. EBM offers a shift in the sort of evidence that is most highly valued for diagnosis, therapy, and prognosis questions, as heavy emphasis is placed on experimental controls and quantified measures, thus diminishing the previous status of clinical experience and observational studies significantly. This commitment represents not only methodological change, but also a novel regard of the reliability of various forms of medical knowledge. EBM offers a new answer to medicine's fundamental normative question: how ought we to practice medicine?

2. The origins of evidence-based medicine

The origins of the evidence-based medicine movement are traceable back to a series of lectures given by epidemiologist Archie Cochrane in the early 1970s, where he argued that many popularly used medical practices were of unknown or questionable safety and efficacy (Ashcroft, 2004). In these lectures, which were later compiled in *Effectiveness and Efficiency: Random Reflections on Health Services* (Cochrane, 1972), he detailed the injury, waste, and failure to improve care that ensued from widespread acceptance and use of unestablished medical interventions. He maintained that treatments should be evaluated using unbiased methods like the randomized controlled trial, and that health care professionals should regularly update their knowledge base (Ashcroft, 2004). Aschcroft has noted the strong ethical imperative behind Cochrane's recommendations, as they were rooted in concern to do no harm, to do one's best for one's patients, and to do so justly by eliminating waste (Ashcroft, 2004).

Cochrane's programmatic outline was revitalized in 1990 by a group of professors of clinical epidemiology, medical informatics, and biostatistics at McMaster University in Canada, who called themselves the "Evidence Based Medicine Working Group". They introduced the phrase "Evidence Based Medicine" in a ubiquitous 1992 manifesto as a "new paradigm" in medical education and practice (EBMWG, 1992). In the document, the ethical promise was made that the virtuous clinician "whose practice is based on an understanding of the

[1] Hope is a supporter of EBM who maintains that one sign of a movement being important is when its detractors indignantly maintain that it is nothing new.

underlying evidence will provide superior patient care" (EBMWG, 1992). While the ethical imperative to improve patient care remained central, the promise to decrease medical uncertainty by systematic evaluation of the efficacy of current practices was particularly appealing to health care administrators and policy analysts facing a crisis situation with respect to escalating healthcare costs and spending. Added to the gamut of methodologies for data collection and analysis first recommended by Cochrane was the use of emerging information technologies to synthesize the large quantities of published studies, proliferate information, and increase accessibility. The combined picture of EBM as ethically driven to improve patient care, fiscally responsible, and technologically up-to-date likely drove the rapid integration of the movement into medicine, where just over twenty years since the Evidence Based Medicine Working Group formed, EBM is now common parlance within health care. Academic centres and journals dedicated to EBM's advancement have been established with much fanfare, and the evidence-based movement has stretched beyond the health sciences to business management (Kovner et al., 2000; Kovner & Rundall, 2006), public health (McGuire, 2005), speech pathology (Reilly et al., 2004), occupational therapy (Von Zweck, 1999) social work (Cournoyer, 2004; Howard et al., 2003; Grinnell & Unrau, 2010), education (Council for Exceptional Children, 2011; Horner et al., 2005; Slavin, 2002), and other social science disciplines. It is even generating attention as a promising new approach to bioethics ("evidence-based ethics") (Roberts, 2000; Strech, 2008; the rare criticism is found in Goldenberg, 2005). The term "evidence-based everything" has been used to describe the enthusiasm for this movement (Mykhalovskiy & Weir, 2004).

3. What's new about EBM?

Despite the fanfare, it is not immediately obvious that EBM offers something new to medical practice. In response to EBM's demand that medical decisions ought to be based on stringent empirical evidence, critics ask, hasn't modern medicine *always* been evidence-based? Quite surely, by being founded on natural science, biomedicine has always been grounded in the empirical sciences, which bases its claims on observational evidence.

The critics are correct to think that EBM's empirical commitments are not new to medicine's ideal practices (regardless of whether or not they are actually practiced). However, proponents have denied the charge that EBM is "old hat" (Sackett et al., 1996b), and have even been grandiose in their descriptions of EBM as being a "new paradigm" promising to "revolutionize" medicine (EBMWG, 1992). This description suggests the evidence based approach to offer something radically different from previous approaches, and so it is worth investigating this alleged paradigm change.

3.1 Is EBM a new paradigm?

To illustrate the unique workings of EBM, the new paradigm of medicine, the Evidence Based Medicine Working Group presented the following clinical scenario:

> *A junior medical resident working in a teaching hospital admits a 43-year old previously well man who experiences a witnessed grand mal seizure. He had never had a seizure before and had not had any recent head trauma…Findings on physical examination are normal. The patient is given a loading dose of phenytoin intravenously and the drug is continued orally. A computed tomographic head scan is completely normal, and an electroencephalogram shows only non-*

> *specific findings. The patient is very concerned about his risk of seizure recurrence. How might the resident proceed (EBMWG, 1992)?*

The Working Group explain that the resident practicing "*the way of the past*" (pre-EBM) would consult the senior resident, who, supported in his view by the attending physician, informs her that the risk of seizure recurrence is high, although its precise risk factor is unknown to him. He instructs the resident to relay this information and the related precautions to the patient. The resident does as she is told and the patient, still fearful, is discharged (EBMWG, 1992). In "*the way of the future*", however, the EBM-trained resident asks herself whether she knows the prognosis of a first seizure and, realizing that she does not, proceeds to the library and conducts a literature search on the *Grateful Med* (now *PubMed*) search engine. Her search on the medical subject headings "epilepsy", "prognosis", and "recurrence" retrieves twenty-five titles, of which one is deemed by the resident to be directly relevant. Exercising the critical appraisal skills that she learned in medical school, she reviews the paper, deems the study and its conclusions to be valid, and returns to her patient after only thirty minutes. She conveys the risk of recurrence over time post-incident, and recommends follow-up with his family physician. The patient leaves "with a clear idea of his likely prognosis" (EBMWG, 1992).

In their comparative analysis of EBM and its biomedical predecessor, Sehon and Stanley argue that the EBM programmatic literature's likening of its approach to a Kuhnian paradigm shift is a gross exaggeration (Sehon & Stanley, 2003). The authors contend that EBM is not a new paradigm because Kuhn described such a large-scale scientific revolution as involving dramatic changes of worldview and even a different world in which scientists must operate (Kuhn, 1996). A Kuhnian paradigm is an "entire constellation of beliefs, values, techniques, and so on shared by the members of a given community" (Kuhn, 1996). The new paradigm will be *incommensurable*, to some extent, with the previous paradigm, a condition that is not met with the evidence based approach in comparison to biomedicine's "basic science approach", which involves "studying the physiological mechanisms of the body and the biochemical properties of drugs" (Sehon & Stanley, 2003).

When EBM is suggested to be a new paradigm, this fosters the impression that an entire set of beliefs, values, and techniques are being discarded, "and that the whole world of medical research and clinical practice is completely different than it was in the days before EBM" (Sehon & Stanley, 2003). This impression is certainly false. Furthermore, the language of paradigms suggests that health care practitioners must make a "stark choice" between EBM and "traditional" biomedicine, where one can "accept the new regime and completely reject the old, or defensively hold onto the old and dismiss EBM entirely" (Sehon & Stanley, 2003). Aside from not being a productive atmosphere in which to hold a critical debate about EBM, this polarization exaggerates the merits, demerits, and differences between EBM and its biomedical "predecessor".

Numerous commentators have characterized the EBM debate as dredging up the hoary "art versus science" dispute regarding the nature of modern clinical medicine. The critics worry that EBM overemphasizes the latter at the expense of the former. Sullivan and MacNaughton, for example, comment that

> *the doctor does not deal with illnesses alone but with people who are ill, and for each individual the illness is unique in terms of his or her experience of it and in its presentation to the doctor (Sullivan & MacNaughton, 1996).*

Understanding the unique circumstances of the individual case is thought to involve a form of practical knowledge or judgment quite different from the *technical* knowledge offered by EBM. The "grey zones" of practice (Naylor, 1995), that is, areas where the evidence from randomized trials about risk-benefit ratios of competing clinical options is incomplete, inconclusive, or contradictory and so clinical judgment must be relied on,[2] are repeatedly argued to be missing from EBM's formulaic knowledge base (Tanenbaum, 1993). Indeed, EBM struggles to account for the interpretive dimensions of clinical care, as evidence-based decisionmaking is largely an effort to standardize and rationalize the application of evidence to clinical care. It is no wonder that critics fail to be persuaded by EBM's conciliatory efforts, such as making the first principle of EBM "*evidence is never enough*" in the authoritative *Users' Guides to the Medical Literature* textbook (Guyatt & Rennie, 2002). It is also worth asking: if evidence is not the fundamental base of medicine, are we still practicing evidence *based* medicine?

In light of these grey zones, EBM is charged with creating and sustaining the idea that *evidence* and *practice* are opposing concepts (Pope 2003; Wood et al., 1998). Other dualisms reinforced in the EBM literature include technical vs. experiential/intuitive knowledge, empirical vs. theoretical knowledge, evidence based vs. patient-centred care, and, of course, EBM vs. its biomedical predecessor, which is inappropriately referred to as "traditional medicine".[3] Adherence to these artificial bifurcations seems to misdirect the EBM debate, as they promote undue polarization between EBM and its biomedical alternatives. For instance, the references to pre-EBM as "traditional medicine" in some of the early EBM programmatic literature (EBMWG, 1992; Sackett et al, 1996b) is an obvious misnomer, as the term typically refers to folk and alternative healing practices. The selection of this inappropriate term was presumably deliberate, as it permitted the EBM originators to emphasize what they alleged to be the widespread tendency of clinical medicine to operate without sufficient evidentiary support to establish the efficacy of their practices. Pre-EBM biomedicine was therefore "traditional" insofar as it is unscientific or at least insufficiently scientific. Some support for this claim has been found in the phenomenon of small area variations of healthcare practice among different geographical regions (Parchman, 1995). However invoking "traditional medicine" is polemical (and distracting) in its misrepresentation of biomedicine, as it cannot account for biomedicine's modern scientific framework, its significant technological advances and achievements, and, of course, EBM's ties to the biomedical tradition.

Despite not invoking revolution (or comparable large-scale upheaval) in medical practice, it will now be demonstrated that EBM brings something new to medicine. The critics who deny this claim likely do so because they misunderstand EBM to be asking for no more than rigorous empirical research in medicine. But the term "evidence based" amounts to much more. While the evidence based approach certainly does call for rigorous empirical research in medicine, this call is accompanied by novel accounts of what counts as valid evidence

[2] Among the procedures cited by Naylor to be in the "grey zone" are: carotid endarterectomy, upper gastrointestinal (GI) endoscopy, hysterectomy, and percutaneous transluminal coronary angioplasty. Randomized controlled trials have been done in these areas, but the results have not produced unequivocal conclusions.

[3] Accompanying these imposed bifurcations are, of course, efforts at integration, such as "evidence-based patient centred care" (Borgmeyer, 2005), and "evidence-based patient choice" (Hope, 1996; Edwards & Elwyn, 2001; Parker, 2001). The literature also includes an effort to overcome (or possibly deny) the evidence/judgment divide (Downie et al., 2000).

and what qualifies as the most rigorous methods of empirical research. Rather than a revolution or paradigm change, EBM represents an important *shift* in biomedical thinking and practice that is a significant alternative to its biomedical predecessor. Specifically, EBM offers a shift in the sort of evidence that is most highly valued for diagnostics, prognostics, and therapeutics, in its emphasis on experimental controls and quantitative research, which undermines previous regard of clinical experience and observational studies significantly (Sehon & Stanley, 2003). At minimum, this shift is signified by a change from a medical model grounded in basic science to a novel statistically-based medicine (Henry, 2006). EBM's hierarchy of evidence is at the service of outcomes research, which uses a cluster of statistical and epidemiological methods for analyzing the therapeutic effectiveness of clinical interventions (Gifford, 1996). This commitment to highly controlled data and methods of statistical analysis that were previously used only for population-based research (such as public health) represents not only methodological change, but also a novel regard of the reliability of various forms of medical knowledge.

4. The novel contents of EBM

The unique content offered to medicine by EBM remains difficult for many to grasp. Hardly anyone can disagree with the goal of getting clinicians to make "conscientious, explicit, and judicious use of current best evidence" for decisions in patient care. Any expressions of doubt about EBM activities are usually greeted with vigorous accusations of disregarding "today's harsh realities", or ignoring "what happens in clinical medicine" (Sackett et al., 1996a). Furthermore, critics are frequently denounced for erroneous beliefs that EBM only uses evidence from randomized controlled trials, that it involves "merely the mindless application of the results of megatrials", and that "other forms of evidence are heavily discounted" (Rosenberg & Donald, 1995). Feinstein and Horwitz have wisely suggested that much of the confusion surrounding what EBM actually stands for lies in the distinction between the contents of EBM itself and its application in clinical practice. It is only when this distinction is blurred that many clinicians claim EBM to offer "nothing new" (Feinstein & Horwitz, 1997). Many practitioners have seen little novelty in EBM because they regularly assemble evidence, develop clinical judgment, read medical literature, attend medical meetings, and have discussions with one another. These activities seem entirely compatible with the statement that the practice of EBM consists of "integrating individual clinical expertise with the best available external clinical evidence from systematic research" (Sackett et al., 1996b). The activities surrounding the practice of EBM also seems fairly standard, as the data informing evidence-based practice "is not restricted to randomized trials and meta-analyses" (Sackett et al., 1996b). It contains "clinically relevant research, often from the basic sciences of medicine" and it includes studies of diagnostic tests, prognostic markers, and "the efficacy and safety of the therapeutic, rehabilitative and preventive regimes" (Sackett et al., 1996b). With this description of what is done when EBM is *practiced* and with the overt acknowledgement by the EBM originators that EBM is rooted in the medical thought of mid-nineteenth century France, specifically "the call for external evidence expressed in Paris 150 years ago by Louis, Bichat and Magendie" (Sackett et al., 1997), clinicians can easily conclude that EBM is not particularly novel, and may wonder why it has stirred so much fuss and controversy (Feinstein & Horwitz, 1997).

The novelty lies, however, in the organization and privileging of information. While a wide range of evidentiary sources are permitted in evidence-based practice, the evidence collected for EBM itself is confined almost exclusively to RCTs and meta-analyses of those

trials. The RCT is consistently ranked at the top of the hierarchy of evidence, thus confirming the former's privileged position (Feinstein & Horwitz, 1997). For instance, Sackett et al. maintain that for questions of therapy,

> *we should try to avoid the nonexperimental approaches, since they routinely lead to false-positive conclusions about efficacy…The randomized trial, and especially the systematic review of several randomized trials…has become the "gold standard" (Sackett et al, 1996b, as cited in Feinstein & Horwitz, 1997).*

The analysis in the next three sections will further examine the novel contents of EBM captured in its methodological privileging of (1) the hierarchy of evidence, (2) the randomized controlled trial, and (3) outcomes measures.

4.1 The hierarchy of evidence

The hierarchy of evidence captures EBM's basic methodological and epistemic commitments in a fairly straightforward ranking of methods. EBM proponents strongly hold that the trustworthiness or validity of evidence is a function of the design of the study from which the evidence is obtained (Sackett, 1989, 1997; Sackett et al., 1991; Solomon & McLeod, with the Canadian Task Force on the Periodic Health Examination, 1994), and so the desire to use only the "best evidence from clinical research" in the management of individual patients (Sackett et al, 1996b, 1997) has resulted in intricate classificatory schemes for ranking the value of different types of studies. Among the numerous published formulations, there is a consistent placement of randomized controlled trials or the systematic review of these trials at the top, retrospective studies well down the list, and clinical anecdotes are seen as providing little if any evidence for the value of intervention (see Fig. 1).

A Hierarchy of Strength of Evidence for Treatment Decisions

- N of 1 randomized controlled trial
- Systematic reviews of randomized controlled trials
- Single randomized trial
- Systematic review of observational studies addressing patient-important outcomes
- Single observational study addressing patient-important outcomes
- Physiologic studies (studies addressing blood pressure, cardiac output, exercise capacity, bone density, and so forth)
- Unsystematic clinical observations

Fig. 1. *Users' Guide to Medical Literature* hierarchy of evidence (Rennie & Guyatt, 2002)

While EBM has evolved over time, most notably in its self-regard from a (polemical) "new paradigm" to a more tempered technique for clinicians to manage vast quantities of research information (for example, Haynes, 2002), the core belief that evidence belongs in fixed hierarchical order with the systematic review of randomized controlled trials always on top remains unshaken (Upshur et al., 2001). In the evaluation of treatment effects, for example, a large, well-designed, randomized trial is considered more reliable than those findings from non-randomized prospective or retrospective studies (Sackett, 1997). Similar schemes have been developed for the ranking of evidence in other clinical categories such as prognosis, aetiology, and diagnosis (Centre for Evidence-Based Medicine, 2006; Sackett et al., 1997). At

the bottom of each of these clinical scales is evidence obtained from case reports and personal experience.

The logic behind the ranking of evidence is simple: randomization is the best method for distinguishing between the effects of active treatment from the effects of known and unknown potentially biasing influences (Peto & Baigent, 1988). It follows that we should make every effort to identify and catalogue these studies. And this is exactly what is happening. EBM proponents initially endorsed the teaching of critical analysis skills in medical schools so that physicians could properly assess the quality of a study (EBMWG, 1992). The hierarchy of evidence is one of the tools used in this task. It was quickly realized, however, that more advanced informatics were needed in order for clinicians to manage the massive amount of research data available. The Cochrane Collaboration has undertaken the monumental task of identifying and evaluating well over a million randomized controlled trials (U.S. Cochrane Center, 2002). Systematic reviews and meta-analyses of randomized trials in specific areas of medicine are now widely available on EBM databases and in EBM journals.

The privileging of "hard" evidence—the quantified data generated by randomized controlled trials—over knowledge generated from clinical experience (EBMWG, 1992) and qualitative measures (Gray, 1997) speaks to an epistemic distrust of subjective or personal experience, which cannot guard against biasing influences. Methodologies like blinding, randomization, placebo-control, the use of large subject populations, and replication of results serve to abstract from values to reveal empirical facts. Of the types of trials available, clinical trials offer the strongest and clearest support for any claim that a treatment is effective because they allow scientists to control extraneous variables and test one factor at a time (Schick & Vaughn, 2002). The hierarchy of evidence is, by the founders' own admission, based on levels of certainty, where the quantified and the scientific forms of evidence are placed on top because they are understood to be most resistant to sceptical refutation (Sackett et al., 1991).

The central goal behind the EBM movement is quality of care, and this goal serves as the grounds for encouraging medical practice that utilizes the latest and best evidence. Evidence-based practices, including the ranking of evidence, are thought to enhance effective and efficient clinical decision-making. But, critics argue, "effectiveness" need not be limited to clinical- or cost-effectiveness. It could also refer to patient-based outcomes indicating satisfaction with the treatment provided. The hierarchy prioritizes evidence of clinical effectiveness and necessarily excludes subjective perceptions (Malterud, 1995, 2001; Rogers 2002). Yet patient narratives and the interpretive features of clinical practice are thought by many to be crucial features of quality healthcare (Greenhalgh & Hurwitz, 1998; Greenhalgh, 1999; Malterud 2001; Silva et al., 2011).

4.2 Randomized controlled trials: The "gold standard" of medical research

The methodological debates that make up the bulk of the EBM literature revolve around the general question whether or not the refined focus on clinical evidence (as prioritized in the EBM hierarchy of knowledge), or the search for secure knowledge in general, improves our ability to decipher best practices and therefore prescribe the most effective treatments. Alternatively, the methods may leave out too many important features of clinical care that are not readily measurable through evidence-based approaches. This leads to the important

further question of whether the randomized controlled trial rightfully deserves the title of "gold standard".

Regarded as a maverick among his peers, Cochrane strongly promoted the controversial view that randomized controlled trials offer the best test for the effects of medical interventions and could thereby correct ineffectiveness and even harms perpetrated by contemporary medical practice (this was another heretical claim) (Pope, 2003). With time, this view came to be accepted and randomized trials became "a yardstick by which other sources of information were judged and ranked within a hierarchy of evidence" (Pope, 2003). The introduction of randomized trials to medical research has been credited by Iain Chalmers, one of the original founders of the Cochrane Collaboration who was knighted in 2000 for his activism in cumulating evidence in medical research, and others for revolutionizing therapeutic development and increasing the life expectancy of patients from three to seven years over the past half century (Chalmers, 1998). When substantial uncertainty exists about treatment effects, it is widely thought to be not only scientifically correct to answer it in a study with the smallest amount of built-in bias, but also most ethical to expose patients to alternative treatment options based on chance only and not upon the biased opinion of a physician (Edwards et al., 1998; Frazier & Mosteller, 1995; Freedman, 1997; Lilford & Jackson, 1995).

Many EBM critics point to the "experiential nature" of medical practice for being not only inextricable from but also inappropriately maligned by the evidence based approach (Tanenbaum 1993; Williams & Garner, 2002). However, supporters of EBM insist that experiential knowledge is worth minimizing because experience allows for the repetition of mistakes. EBM proponents point to the data available suggesting human fallibility and bias in drawing conclusions based on uncontrolled experience (Dawson & Arkes, 1987; MacCoun, 1998). Others argue that investigators with relationships or experience with a subject form expectations with respect to treatment outcomes that make them less able to produce objective reviews of scientific evidence than non-experts trained in critical appraisal of evidence (Oxman & Guyatt, 1993). A logical deductive framework for interpretation of evidence is therefore argued to be needed if we are to avoid practicing medicine based on uncontrolled experience, which may do more harm than good (Sackett, 1989). The nature of research is meant to reduce uncertainty, even if it cannot be completely eliminated. Yet what randomized controlled trials gain in experimental certainty (internal validity), they lose in applicability to the clinical context (external validity) (Cartwright, 2007). The EBM hierarchy indicates a strong presumption in favour of internal validity in experimental design.

The randomized controlled trial design is better geared for certain kinds of intervention questions than others. These trials are ideal for the direct comparison between simple treatments such as two single drugs, and so the pronounced "hegemony of the double-blind randomized controlled trial" (Charlton, 1991) can both undermine research into the use of complex interventions and result in a failure to meet the complex needs of individual patients. Regarding the former, the critics worry that because randomized controlled trial design is increasingly favoured, and because the expectation to provide "best evidence" of effectiveness before implementing interventions is growing, complex interventions are by default less likely to be supported over time (DeVries & Lemmens, 2006). As a result, behavioural, psychosocial, community based, and multiple-component interventions lose out in favour of individual patient-based treatments (Dieppe, 1998; Tallon et al., 2000) and resultant public health policy-setting increasingly focuses on individuals rather than on

groups (Davey-Smith et al., 2001). Speaking more abstractly, numerous philosophers of science deny that there is any universal method in science, randomized trial or otherwise (Cartwright, 2007; Urbach, 1993; Worrall, 2002).

In the arena of individual patient care, critics argue that because EBM guidelines are derived from controlled trials of simplified clinical situations using criteria that often exclude other complicating serious conditions, the evidence may not be applicable to complex clinical situations. The "gold standard" of clinical research is widely thought to have a problem of generalizability of its results to individual patient care (Britton et al., 1998; Culpepper & Gilbert, 1999; Feinstein & Horwitz, 1997). Even Cochrane recognized that while the RCT can measure effectiveness, its results may not be directly replicable in clinical practice (Cochrane, 1972), and so Dingwall et al. seem correct in their suggestion that Cochrane's ideas have been used somewhat selectively in EBM (Dingwall et al., 1988, as cited in Pope, 2003). The problem of generalizability begins with the narrow eligibility criteria for randomized trials, which limit conclusions about a treatment's effectiveness to patients who fulfill those criteria (Feinstein & Horwitz, 1997). To demonstrate optimal efficacy, randomized controlled trials often use relatively homogenous subject populations (Djulbegovic et al., 2000). Patients excluded from such trials can differ substantially from study patients in a variety of ways that could influence treatment outcomes (i.e. disease severity, comorbid conditions, gender, race) (Britton et al., 1998; Tanenbaum, 1995). Furthermore, the time periods covered in clinical trials and the measures used to assess outcomes frequently differ from those used to assess the success of a therapy in actual practice. In an effort to be efficient, clinical trials typically use the shortest time possible for determining valid results, employing surrogate endpoints rather than clinically relevant outcomes. Surrogate endpoints are physiological or biochemical markers that can be ascertained quickly and taken to be predictive of clinically meaningful endpoints—such as how a patient feels, functions, or survives—that take much longer to observe. They are "surrogate" insofar as they are outcome measures that are not of direct practical importance but are believed to reflect outcomes that are clinically relevant. For example, cholesterol studies frequently use cholesterol reduction as a surrogate for reduced mortality. Direct demonstration of mortality reduction requires lengthy trials using large subject populations, while cholesterol reduction is known to be strongly associated with mortality benefits, and can be measured easily in smaller numbers of patients. Similarly, blood pressure is not directly important to patients but it is often used as an outcome in clinical trials because it is a risk factor for stroke and heart attacks (Bandolier, n.d.).

Yet the requirement that surrogate endpoints reliably predict the overall effect of the clinical outcome frequently fails in practice (Fleming & DeMets, 1996). The disease process can affect the clinical outcome through several causal pathways that are not mediated by the surrogate. Therefore the effect of the intervention on these pathways will be different from the effect on the surrogate (Fleming & DeMets, 1996). It is more likely, however, that "the intervention affects the clinical outcome by unintended, unanticipated, and unrecognized mechanisms of action that operate independently of the disease process" (Fleming & DeMets, 1996). Fleming and DeMets argue that surrogate endpoints frequently mislead regarding the actual effects that treatments have on health outcomes. For instance, although lipid levels are widely seen to be important predictors of cardiovascular-related mortality, there is debate over the relationship between lipid lowering and reduction in overall mortality. The Coronary Drug Project in the 1970's showed clofibrate and niacin to decrease cholesterol levels, however neither agent reduced total mortality (Fleming & DeMets, 1996).

Taken together, the numerous controls utilized to guard against bias and promote efficiency in medical research limits the relevancy of, and may even distort, the "best evidence from clinical research" in the management of individual patients. While there are differences of opinion regarding the challenges posed in making clinical evidence applicable, EBM fails to engage significantly with this problem. EBM's penchant for methodological rigour may be at odds with the ad hoc nature of clinical practice. Tanenbaum has suggested that the precision of "best evidence" is fundamentally irreconcilable with its clinical relevance, given the particularity of patients and the significant improvisational dimensions of clinical practice (Tanenbaum, 1995). Shaughnessy et al. refer to this improvisational feature as "clinical jazz" (Shaughnessy et al., 1998). The debate over randomized controlled trials highlight that the problem of evidence in EBM does not only concern what knowledge is missing from the evidence based decisionmaking framework, but also the nature of the knowledge that *does* enter into consideration.

4.3 Outcomes measures: Clinical effectiveness and the quality movement in medicine

EBM was introduced to healthcare in the wake of what has been famously described as the "third revolution" in health care (Relman, 1988),[4] a turn toward assessment and accountability in light of escalating health care costs creating a "crisis" situation in health care spending throughout the industrialized world. Patients and payers widely subscribed to a "waste theory" that described physicians wasting healthcare money on poorly performing diagnostics and treatments (Tanenbaum, 1994a). Furthermore, the documentation of notable geographical variations in practice that could not be explained by local organizational and financial arrangements caused alarm (Clancy & Eisenberg, 1988). Health care advocates wanted the consistent practice of only the best health care interventions. The "best" was determined by the "end results" or "outcomes" of medical practice. The urgency with which the public demanded that physicians pay attention to medical outcomes led to what soon became known as the "outcomes movement" in health policy (Epstein, 1990). Evaluating clinical effectiveness was seen as a fiscally responsible means of only financing the most promising therapies and research. EBM facilitated the clinical data that outcomes research requires in order to evaluate best practices.

Outcomes research refers to all activity directed towards the assessment of outcomes, analysis of effectiveness, and quality assurance (Epstein, 1990). It uses statistical analysis of clinical data to determine associations between particular therapeutic interventions and particular results (Tanenbaum, 1994a). Unlike laboratory research which measures definable clinical events like lipid lowering or blood pressure, outcomes research can employ patient-derived endpoints, the outcomes that patients care about (Clancy & Eisenberg, 1988). Common themes in outcomes research are: safety, effectiveness, equity, efficiency, timeliness, and patient centeredness (Institute of Medicine, 2001). The benefits of outcomes research to healthcare include better informed patients and providers, the development of clinical guidelines that reflect those assessments, and wiser purchasing of health care technologies (Agency for Health Care Research and Quality, n.d.). This move towards

[4] Relman later lamented that this "third revolution" was never realized due to lack of government initiative by any of the US governmental administrations elected since the 1988 writing of his editorial (Relman, 2009).

accountability is supposed to serve as a rational basis for decision making and, by extension, make medical care more efficient.

The outcomes movement argues for the primacy of probabilistic knowledge derived from statistical studies for medical practice and the vigorous adoption of this position within health care indicates a radical shift in medical rationality (Tanenbaum, 1994a). Polychronis et al., for example, regard the ascendancy of EBM as the triumph of statistics over clinical common sense based on deterministic reasoning (Polychronis et al., 1996). Clinical epidemiology, the application of epidemiologic and biometric methods to direct patient care (Sackett, 1969), is now held by some to be a basic medical science (Sackett et al., 1991). EBM distinguishes itself from pre-evidence based biomedicine by its orientation toward outcomes research, while biomedicine is more dependent on bench science. Biomedical research employs laboratory science that aims to understand the causal relationship between an intervention and a desired effect, whereby therapeutic efficacy can then be inferred. EBM seeks to generate probabilistic knowledge regarding what is likely to work for whatever reason (Tanenbaum, 1994a). John Wennberg, director of the Centre for Evaluative Clinical Science at Dartmouth Medical School, regards biomedical science to be at the service of evaluative science in treatment decisionmaking. He argues that biomedicine generates new technologies, while evaluative science provides the crucial data linking treatments to outcomes (Wennberg, 1992).

The consistent placement of the randomized controlled trial at the top of the EBM hierarchy of evidence is better understood in light of the biomedical versus evidence-based distinction, as this research method serves the objectives of outcomes research by appearing to bracket out a whole range of scientifically and epistemologically difficult questions about why treatments do or not work (Ashcroft, 2002). For instance, rather than determining the properties that enable or hinder an intervention's success, randomized controlled trials establish efficacy by comparing the outcomes of the experimental arm with those found in a similar subject population receiving a comparator intervention. Eliminating bench science's focus on determining *why* a treatment works or not through appeal to deeper biological theory has certain advantages for healthcare decision-making (Ashcroft 2002; Gifford 1996).[5] Definitive biological explanation has not always led to safe or beneficial treatment of actual patients. The randomized trial "acts as a practical filter permitting the calibration of scientific good ideas against clinical reality (however that is constructed)" (Ashcroft, 2002). By comparing two or more competing courses of treatment (including placebo), the RCT "offers a technique for dispute resolution within medicine: where there is discord, let a trial be" (Ashcroft, 2002).

Because EBM and outcomes research are closely allied, the concerns regarding the latter are similar to those launched against the former. The task of outcomes research, to solve the problems of quality and cost that beset the healthcare system and to do so by scientific rather than political means, raises the concern about the tenability of value-free measures. Furthermore, Tanenbaum's account of the "epistemological politics" of the US outcomes movement (Tanenbaum, 1994a) brings into question whether this research can ever be so benign that it merely informs decision makers and helps them make better decisions (Sage, 1994). The championing of probabilistic knowledge to improve clinical practice is argued to replace subjective professional judgment with micromanagement by insurance companies and government (Tanenbaum 1993, 1995).

[5] Of course there are several ways in which "does it work?" can be construed (Ashcroft et al., 1997).

While Tanenbaum is accused of pandering to the fears of physicians and other professionals who perceive outcomes research to be a threat to autonomous practice (Cangialose, 1994), her criticisms are not against outcomes research *per se*, as she recognizes the usefulness of statistical analysis in evaluating medical care. Her target is rather the outcomes *movement*, the "organized effort of one research community and its champions to gain special privilege for statistical evidence, to consider it the only true evidence of medical effectiveness, and to predicate an accountable health care system on physicians' adherence to norms of practice derived from outcomes studies" (Tanenbaum, 1994b). Similar to EBM, the critics find utility in outcomes research for improving patient care, but they question its near-hegemonic status in influential health policy and administrative circles.

5. Conclusion

While this analysis dampens some of the hubris surrounding the evidence-based movement, it highlights the significant methodological innovation that EBM has brought to medicine. The evidence based approach is marked by the flourishing relationship that the evaluative sciences and informatics, once solely the domain of business and managerial studies, now have with medicine. Eliciting EBM's place within the "quality movement" (Bodenheimer, 1999) captures a shift in medical rationality and knowledge away from previous incarnations of biomedicine by way of EBM's insistent epistemological privileging of standardized information over judgment, quantified measurement over experience, and epidemiology over bench science.

6. References

Agency for Health Care Research and Quality (n.d). Outcomes Research Fact Sheet. In: *U.S. Department for Health & Human Services*, October 2011, Available from: http://www.ahrq.gov/clinic/outfact.htm

Ashcroft, R. E. (2002). What is clinical effectiveness? *Studies in the History and Philosophy of Science Part C: Biological and Biomedical Sciences*, Vol. 33, No. 2, (July 2002), pp. 219-233, 0039-3681

Ashcroft, R. E. (2004). Current epistemological problems in evidence-based medicine. *Journal of Medical Ethics* 30, 2, (April 2004), pp. 131-135, 0306-6800

Ashcroft, R. E., Chawick, D. W., Clark, S. R., Edwards, R. H., Frith, L. & Hutton, J. L. (1997). Implications of socio-cultural contexts for the ethics of clinical trials." *Health Technology Assessment*, Vol. 1, No. 9, (July 1997), pp. 1-65, 1366-5278

Bandolier. (n.d.). Surrogate Endpoints. In: *Bandolier Glossary of Terms*, October 2011, Available from: http://www.medicine.ox.ac.uk/bandolier/booth/glossary/surrog.html

Benitez-Bribiesca, L. (1999). Evidence-based medicine: A new paradigm? *Archives of Medical Research*, 30, 2, (March-April 1999), pp. 77-79, 0188-4409

Bodenheimer, T. (1999). The movement for improved quality of health care. *New England Journal of Medicine* 340, 6, (February 1999), pp. 488-492, 0028-4793

Borgmeyer, C. (2005). Guideline showcases AAFP's commitment to evidence-based, patient-centered care. *Annals of Family Medicine*, Vol. 3, No. 4, (July-August 2005), pp. 378-380, 1544-1709

Britton, A., McKee, M., Black, N., McPherson, K., Sanderson, C. & Bain, C. (1998). Choosing between randomized and non-randomized studies: A systematic review. *Health Technology Assessment*, Vol. 2, No. 13, (May 1998), pp. 1-124, 1366-5278

Cangialose, C. B. (1994). Outcomes research [letter]. *New England Journal of Medicine*, Vol. 330, No. 6, (February 1994), p. 435, 0028-4793

Carr-Hill, R. (1995). Welcome? To the brave new world of evidence-based medicine. *Social Science & Medicine*, 41, 11, (December 1995), pp. 1467-1468, 02779536

Cartwright, N. (2007). Are RCTs the gold standard? *Biosocieties,* Vol. 2, No. 1, (March 2007), pp. 11-20, 1745-8552

Centre for Evidence-Based Medicine. (2006). Levels of evidence and grades of recommendation. In: *Centre for Evidence-Based Medicine,* October 2011, Available from: http://www.cebm.net/levels_of_evidence.asp

Chalmers, I. (1998). Unbiased, relevant, and reliable assessments in health care. *British Medical Journal*, Vol. 317, No. 7167, (October 1998), pp. 1167-1168, 0959-8138

Charlton, B. (1991). Medical practice and the double-blind, randomized controlled trial. *British Journal of General Practice* ,Vol. 41, No. 350, pp. 335-336, 0960-1643

Clancy, C. M. & Eisenberg, J. M. (1988). Outcomes research: Measuring the end results of health care. *Science*, Vol. 282, No. 5387, (October 1988), pp. 245-246, 0036-8075

Cochrane, A. L. (1972). *Effectiveness and Efficiency. Random Reflections on Health Services*, Nuffield Provincial Hospitals Trust, 0900574178, London

Council for Exceptional Children. (2011). Evidence-based practice—Wanted, needed, and hard to get. In: *Council for Exceptional Children*, October 2011, Available from: http://www.cec.sped.org/AM/Template.cfm?Section=Home&CONTENTID=6515&TEMPLATE=/CM/Co ntentDisplay.cfm&CAT=none

Cournoyer, B. R. (2004). *The Evidence-Based Social Work Skills Book*, Pearson, 0205358624, Boston

Culpepper, L. & Gilbert, T. T. (1999). Evidence and ethics. *Lancet*, Vol. 353, No. 9155, (March 1999), pp. 829-831, 0140- 6736

Davey-Smith, G., Ebrahim, S., & Frankel, S. (2001). How policy informs the evidence. *British Medical Journal*, Vol. 322, No. 7286, (January 2001), pp. 184-185, 0959-8138

Dawson, N. V. & Arkes, H. R. (1987). Systematic errors in medical decision making: Judgment limitations. *Journal of General Internal Medicine*, Vol. 2, No. 3, (May-June 1987), pp. 183-187, 1525-1497

De Vries, T. & Lemmens, T. (2006). The social and cultural shaping of medical evidence: Case studies from pharmaceutical research and obstetric science. *Social Science and Medicine*, Vol. 62, No. 11, (June 2006), pp. 2694-2706, 02779536

Dieppe, P. (1998). Evidence-based medicine or medicine-based evidence? *Annals of Rheumatological Disease*, Vol. 57, No. 7, (July 1998), pp. 385-386, 0003-4967

Djulbegovic, B., Morris, L., Lyman, G. H. (2000). Evidentiary challenges to evidence-based medicine. *Journal of Evaluation in Clinical Practice*, Vol. 6, No. 2, (May 2000), pp. 99-109, 1365-2753

Downie, R. S., Nacnaughton, J., & Randall, F. (2000). *Clinical Judgment: Evidence in Practice*. Oxford University Press, 0192632167, London

Edwards, A. & Elwyn, G., eds. (2001). *Evidence-Based Patient Choice: Inevitable or Impossible?* Oxford University Press, 0-19-263194-2, Oxford

Edwards, S. J. L., Lilford, R. J., Braunholtz, D. A., Jackson, J. C., Hewison, J. & Thornton, J. (1988). Ethical issues in the design and conduct of randomized controlled trials. *Health Technology Assessment*, Vol. 2, No. 15, (December 1988), pp. 1-132, 1366-5278

Epstein, A. M. (1990). The outcomes movement—will it get us where we want to go? *New England Journal of Medicine*, Vol. 323, No. 4, (July 1990), pp. 266-270, 0028-4793

Evidence-Based Medicine Working Group (EBMWG). (1992). Evidence-based medicine: A new approach to teaching the practice of medicine. *Journal of the American Medical Association*, Vol. 268, No. 17, (November 1992), pp. 2420-2425, 0098-7484

Feinstein, A. R. & Horwitz, R. I. (1997). Problems in the 'evidence' of 'evidence-based medicine'. *American Journal of Medicine*, Vol. 103, No. 6, (December 1995), pp. 529-535, 0002-9343

Fleming, T.R. & DeMets, D.L. (1996). Surrogate end points in clinical trials: Are we being misled? *Annals of Internal Medicine*, Vol. 125, No. 7, (October 1996), pp. 605-613, 0003-4819

Frazier, H. S. & Mosteller, F. (1995). *Medicine Worth Paying For: Assessing Medical Innovations*, Harvard University Press, 0-674-56362-X, Cambridge

Freedman, B. (1987). Equipoise and the ethics of clinical research. *New England Journal of Medicine*, Vol. 317, No. 3, (July 1987), pp. 141-145, 0028-4793

Gifford, F. (1996). Outcomes research: Upstream issues for downstream users. *Hastings Center Report*, Vol. 26, No. 2, (March-April 1996), pp. 38-44, 0093-0334

Goldenberg, M. J. (2005). Evidence based ethics? On evidence-based practice and the empirical turn from normative bioethics. *BMC Medical Ethics*, Vol. 6:11, (November 2005), 1472-6939

Gray, J. A. M. (1997). *Evidence-Based Healthcare: How to Make Health Policy and Management Decisions*. Churchill Livingstone, 978-0443057212, London

Greenhalgh, T. (1999). Narrative based medicine: Narrative based medicine in an evidence based world. *British Medical Journal*, Vol. 318, No. 7179, (January 1999), pp. 323-325, 0959-8138

Greenhalgh, T. & Hurwitz, B., eds. (1998). *Narrative Based Medicine: Dialogue and Discourse in Clinical Practice*, BMJ Publishing Group, 978-0727912237, London

Grinnell, R. M. & Unrau, Y., A. (2010). *Social Work Research and Evaluation: Foundations of Evidence-Based Practice* (9th), Oxford, 978-0-19-973476-4, New York

Guyatt, G. & Rennie, D. (2002). *Users' Guides to the Medical Literature: A Manual for Evidence-Based Practice* (2nd), American Medical Association, 1-57947-174-9, Chicago

Haynes, R. B. (2002). What kind of evidence is it that evidence-based medicine advocates want health care providers and consumers to pay attention to? *BMC Health Services Research*, Vol. 2:3, (March 2006), 1472-6963

Henry, S. G. (2006). Recognizing tacit knowledge in medical epistemology. *Theoretical Medicine and Bioethics*, Vol. 27, No. 3, (May 2006), pp. 187-213, 1386-7415

Hope, T. (1995). Evidence based medicine and ethics. *Journal of Medical Ethics*, Vol. 21, No. 5, (October 1995), pp. 259-260, 0306-6800

Hope, T. (1996). *Evidence Based Patient Choice*, King's Fund Publishing, 9781857171297, London

Horner, R. H., Carr, E. G., Halle, J., McGee, G., Odom, S., & Wolery, M. (2005). The use of single-subject research to identify evidence-based practice in special education. *Exceptional Children*, Vol. 71, No. 2, pp. 165-179, 0014-4029

Howard, M. O., McMillen, C. J. & Pollio, D. E. (2003). Teaching evidence-based practice: Toward a new paradigm for social work education. *Research on Social Work Practice*, Vol. 13, No. 2, (March 2003), pp. 234-259, 1552-7581

Institute of Medicine. (2001). *Crossing the Quality Chasm: A New Health System for the 21st Century*. National Academy Press, 0-309-07280-8, Washington

Kovner, A. R., Elton, J., & Billings, J. (2000). Evidence-based management. *Frontiers of Health Services Management*, Vol. 16, No. 4, (Summer 2000), pp. 3-26, 0748-8157

Kovner, A. R. & Rundall, T. G. (2006). Evidence-based management reconsidered. *Frontiers of Health Services Management*, Vol. 22, No. 3, (Spring 2006), pp. 3-21, 0748-8157

Kuhn, T. (1996). *The Structure of Scientific Revolutions* (3rd), University of Chicago Press, 0226458083, Chicago

Lilford, R. J. & Jackson, J. (1995). Equipoise and the ethics of randomization. *Journal of the Royal Society of Medicine*, Vol. 88, No. 10, (October 1995), pp. 552-559, 0141-0768

MacCoun, R. J. 1998. Biases in the interpretation and use of research results. *Annual Review of Psychology*, Vol. 49, (February 1998), pp. 259-287, 0066-4308

Malterud, K. (1995). The legitimacy of clinical knowledge: Toward a medical epistemology embracing the art of medicine. *Theoretical Medicine*, Vol. 16, No 2, (June 1995), pp. 183-198, 1573-1200

Malterud, K. (2001). The art and science of clinical knowledge: Evidence beyond measures and numbers." *Lancet*, Vol. 358, No. 9279, (April 2001), pp. 397-400, 0140-6736

McGuire, W. L. (2005). Beyond EBM: New directions for evidence-based public health. *Perspectives in Biology and Medicine*, Vol. 48, No. 4, (Autumn 2005), pp. 557-569, 1529-8795

Mykhalovskiy, E. & Weir, L. (2004). The problem of evidence-based medicine: Directions for social medicine. *Social Science & Medicine*, Vol. 59, No. 5, (September 2004), pp. 1059-1069, 02779536

Naylor, C. D. (1995). Grey zones of clinical practice: Some limits to evidence-based medicine. *Lancet*, Vol. 345, No. 8953, (April 1995), pp. 840-842, 0140-6736

Oxman, A. D. & Guyatt, G. H. (1993). The science of reviewing research. *Annals of the New York Academy of Science*, Vol. 703, (December 1993), pp. 125-133, 0077-8923

Parchman, M. L. (1995). Small area variation analysis: A tool for primary care research. *Family Medicine*, Vol. 272, No. 4, (April 1995), pp. 272-276, 0742-3225

Parker, M. (2001). The ethics of evidence-based patient choice. *Health Expectations*, Vol. 4, No. 2, (June 2001), pp. 87-91, 1369-7625

Peto, R. & Baigent, C. (1988). Trials: The next 50 years. *British Medical Journal*, Vol. 317, No. 7167 (October 1988), pp. 1170-1171, 0959-8138

Polychronis, A., Miles, A., & Dentley, D. (1996). Evidence-based medicine: Reference? Dogma? Neologism? New orthodoxy? *Journal of Evaluation in Clinical Practice*, Vol. 2, No. 1, (February 1996), pp. 1-3, 1365-2753

Pope, C. (2003). Resisting evidence: The study of evidence-based medicine as a contemporary social movement. *Health: An Interdisciplinary Journal for the Social Study of Health, Illness, and Medicine*, Vol. 7, No. 3, (July 2003), pp. 267-282, 1363-4593

Reilly S., Douglas, J. & Oates, J. (2004). *Evidence Based Practice in Speech Pathology*, Wiley, 978-1-86156-320-0, San Francisco

Relman, A. (1988). Assessment and accountability: The third revolution in medical care. *New England Journal of Medicine*, Vol. 319, No. 18, (November 1988), pp. 1220-1222, 0028-4793

Relman, A. (2009). Assessment and accountability. *Journal of Health Services Research and Policy*, Vol. 14, No. 4, (October 2009), pp. 249-250, 1355-8196 Roberts, L. W. (2000). Evidence-based ethics and informed consent in mental illness research. *Archives of General Psychiatry*, Vol. 57, No. 6, (June 2000), pp. 540-542, 0003-990x

Rogers, W. (2002). Is there a tension between doctors' duty of care and evidence-based medicine? *Health Care Analysis*, Vol. 10, No. 3, (September 2002), pp. 277-287, 1065-3058

Rosenberg, W. M. C. & Donald, A. (1995). Evidence based medicine: An approach to clinical problem-solving. *British Medical Journal*, Vol. 310, No. 6987, (April 1995), pp. 1122-1126, 0959-8138

Sackett, D. L. (1969). Clinical epidemiology. *American Journal of Epidemiology*, Vol. 89, No. 2, (February 1969), pp. 125- 128, 1476-6256

Sackett, D. L. (1989). Rules of evidence and clinical recommendations on the use of antithrombotic agents. *Chest*, 95, 2 Suppl., (February 1989), 2S-4S, 1931-3543

Sackett, D. L. (1997). A science for the art of consensus. *Journal of the National Cancer Institute*, Vol. 89, No. 14, (July 1997), pp. 1003-1005, 1460-2105

Sackett, D. L., Haynes, R. B., Guyatt, G. H., & Tugwell, P. (1991). *Clinical Epidemiology: A Basic Science for Clinical Medicine*. Little Brown & Co., 0316765996, Boston

Sackett, D. L., Richardson, W. S., Rosenberg W. M. C., Haynes, R. B. (1997). *Evidence-Based Medicine: How to Practice and Teach EBM*. Churchill Livingstone, 0-443-05686-2, New York, Edinburgh, London, Madrid, Melbourne

Sackett, D. L., Rosenberg, W. M. C., Muir Gray, J. A., Haynes R. B. & Richardson W. S. (1996a). Evidence based medicine. Authors' reply. *British Medical Journal*, Vol. 313, No. 7049, (July 1996), pp. 170–171, 0959-8138

Sackett, D. L., Rosenberg, W. M. C., Muir Gray, J. A., Haynes, R. B. & Richardson, W. S. (1996b). Evidence based medicine: What it is and what it isn't. *British Medical Journal*, Vol. 312, No. 7023, (January 1996), pp. 71-72., 0959-8138

Sage, W. M. (1994). Outcomes research [letter]. *New England Journal of Medicine*, Vol. 330, No. 6, (February 1994), pp. 434-435, 0028-4793

Schick, T. & Vaughn, L. (2002). *How to Think about Weird Things: Critical Thinking for a New Age*, McGraw-Hill, 0767400135, New York

Sehon S. R. & Stanley, D. E. (2003). A philosophical analysis of the evidence-based medicine debate. *BMC Health Services Research*, Vol. 3:14, (July 2003), 1472-6963-3-14

Shaughnessy, A. F., Slawson, D. C., Becker, L. (1998). Clinical jazz: Harmonizing clinical experience and evidence based medicine. *Journal of Family Practice*, Vol. 47, No. 6, (December 1998), pp. 425-428, 0094-3509

Silva, S. A. & Charon, R. (2011). The marriage of evidence and narrative: Scientific nurturance within clinical practice. *Journal of Evaluation in Clinical Practice*, Vol. 17, No. 4, (September 2011), pp. 585-593, 1365-2753

Slavin, R. E. (2002). Evidence-based educational policies: Transforming educational practice and research. *Educational Researcher*, Vol. 31, No. 7 (October 2002), pp. 15-21, 1935-102X

Solomon, M. J., McLeod, R. S., with the Canadian Task Force on the Periodic Health Examination. (1994). Periodic health examination, 1994 update: 2. Screening strategies for colorectal cancer. *Canadian Medical Association Journal*, Vol. 150, No. 12, (June 1994), 1961-1970, 0820-3946

Strech, D. (2008). Evidence-based ethics—what it should be and what it shouldn't be. *BMC Medical Ethics*, Vol. 9:16, (October 2008), 1472-6939

Sullivan, F. M. & MacNaughton, R. J. (1996). Evidence in consultations: Interpreted and individualized. *Lancet*, Vol. 348, No. 9032, (October 1996), pp. 941-943, 0140-6736

Tallon, D., Chard, J. A., & Dieppe, P. (2000). Relation between agendas of the research community and the research consumer. *Lancet*, Vol. 355, No. 9220, (June 2000), pp. 2037-2040, 0140-6736

Tanenbaum, S. J. (1993). What physicians know. *New England Journal of Medicine*, Vol. 329, No. 17, (October 1993), pp. 1268-1271, 0028-4793

Tanenbaum, S. J. (1994a). Knowing and acting in medical practice: The epistemological politics of outcomes research. *Journal of Health Politics Policy & Law*, Vol. 19, No. 1, (Spring 1994), pp. 27-44, 0361-6878

Tanenbaum, S. J. (1994b). Outcomes research. Author responds. *New England Journal of Medicine*, Vol. 330, No. 6, (February 1994), p. 435, 0028-4793

Tanenbaum, S. J. (1995). Getting from there to here: evidentiary quandaries of the U.S. outcomes movement. *Journal of Evaluation in Clinical Practice*, Vol. 1, No. 2, 97-103, 1365-2753

Upshur, R. E. G., VanDenKerkof, E. G., Goel, V. (2001). Meaning and measure: An inclusive model of evidence in health care. *Journal of Evaluation in Clinical Practice*, Vol. 7, No. 2, (May 2001), pp. 91-96, 1365-2753

Urbach, P. (1993). The value of randomization and control in clinical trials. *Statistics in Medicine*, Vol. 12, No. 15-16, (August 1993), pp. 1421-31, 0277-6715

U.S. Cochrane Center. (2002). *Training Manual for Handsearchers*. In: *Resources for Handsearchers*, October 2011, Available at: http://us.cochrane.org/resources-handsearchers

von Zweck, C. (1999). The promotion of evidence-based occupational therapy practice in Canada. *Canadian Journal of Occupational Therapy*, Vol. 66, No. 5, December 1999, pp. 208-213, 0008-4174

Wennberg, J. E. (1992). AHCP and the strategy for health care reform. *Health Affairs*, Vol. 11, No. 1, (February 1992), pp. 67-71, 0278-2715

Williams, D. D. R. & Garner, J. (2002). The case against 'the evidence': A different perspective on evidence-based medicine. *British Journal of Psychiatry*, Vol. 180, No. 1, (January 2002), pp. 8-12, 1472-1465

Wood, M., Ferlie, E., & Fitzgerald, L. (1998). Achieving clinical behaviour change: A case of becoming indeterminate. *Social Science and Medicine*, Vol. 47, No. 11, (October 1998), pp. 1729-1758, 02779536

Worrall, J. (2002). What evidence in evidence-based medicine? *Philosophy of Science*, Vol. 69, No. 3, (September 2002), pp. S316-S330, 0031-8248