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Abstract

The practice of medicine is the latter-day solution to that intensely human and social predicament we call illness. Medical discourse, however, increasingly tends towards guidelines, protocols, cost considerations and other institutionally-derived issues. This dissertation examines a single concept, therapeutic equivalence, and utilizes it as a metaphor for this focal shift, arguing that this reduced perspective not only ignores the considerable socio-cultural context in which illness takes place, but adversely affects the paradigms and practice of medicine – as well as research, policy and clinical care.

Therapeutic equivalence is the basis for a health (pharmaceutical) policy usually called reference-based pricing, used in many jurisdictions and institutions around the world (such as New Zealand’s Pharmac, the BC Reference Drug Program and the majority of American HMO’s), in which pharmacoeconomic analyses determine the most cost-effective drug(s) within a certain class of drugs in order to restrict general access. Using the well-studied BC reference drug program (RDP) as its primary example, this work examines the regulatory and evidentiary framework of the term “equivalence”, analyzes the medical research on therapeutic equivalence and delves into the deeper socio-cultural and epistemological questions the term raises to demonstrate how institutional and statistical interpretations of pathology now dominate medical discourse. The many uncertainties, ambiguities and variations inherent to physiology, pharmacodynamics and
pharmacokinetics are thus ignored; risk is minimized and subjective states and individual narratives of illness, largely disregarded.

Moving from drug classifications/definitions and the conceptual underpinnings of medical research to the increased convergence of corporate and research interests, this work examines the limitations of ontological disease classifications which assume knowledge is static and questions the current emphasis on biomarkers and numeric results (e.g., blood pressure or cholesterol readings). This work argues that such classification systems are limiting and frame illness in reductionist ways – and have ethical, iatrogenic, medical, social and personal consequences. Broader and more nuanced communications, with greater patient input, are called for.

Keywords: equivalence, therapeutic equivalence, reference based pricing, reference drug program, health economics, ethics of pharmaceutical policy, health policy criticism, epistemology of health, sociology of pharmaceutical policy, patient involvement, participatory action research and empowering patients
This book is dedicated to the memory of my father,

Mark Baxter, M.S., Pharm.D. (1919-1986),

a thinker ahead of his time.
Acknowledgements

No-one works or learns in a vacuum and this project could not have come to fruition without the generosity, time, encouragement and help of many people, both inside the academy and out.

First off I would like to express my gratitude to Simon Fraser University for their support and for their openness to interdisciplinary research with all its academic fluidity and (often) problematic aspects. In particular I would like to thank the Dean of Graduate Studies, Jon Driver, and his associate, Vivian Blaker.

My supervisor, Pat Howard of the Department of Communications and the other members of my committee, health economist John Fountain, business (ethics) professor Mark Wexler and family physician and pharmacologist Morley Sutter are all superb thinkers and I was privileged to have them as mentors and guides. When they took on this project they really didn’t know me well and I appreciate their leap of faith. I would also like to thank Robert Woollard, Gary McCarron and Catherine Murray who agreed to participate in my defense. Morris Barer of the Canadian Institutes of Health Research has also been supportive of my work and I am grateful. Perhaps paradoxically, I would also like to thank Steve Morgan at UBC who compelled me to solidify my position and realize what I was against as well as what I was for. But most of all I would like to express my gratitude to the many patients and clinicians who, over the years, shared their problems, insights and wisdom with me throughout my medical writing career and made
me aware of their centrality to medicine. Within that group, my own family doctor, Larry Collins, stands out, as do Elaine Drysdale and John Whelan.

Last but not least, I thank the two most medically literate people I know: my mother, Pamela Baxter, RN and my husband, Robert Hewko, MD, without whom I'd not have had the fortitude to embark on this project. Their faith in me (as well as their good-natured nagging) kept me focused and on track. I also thank my friend, philosopher Robert Smith, whose staggering depth and breadth of knowledge has always been a source of inspiration; my friends Maryse de la Giroday and Nancy Petersen who not only edited and commented but were a constant source of strength; Diane Quinlan and Susan Mackey-Jamieson who listened and encouraged and Renee Fountain and Dooley Goumeniouk who always had what seemed like an inordinate amount of faith in my intellect.

Thank you.
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Acronyms

AMA American Medical Association
BMA British Medical Association
BMJ British Medical Journal
CIHI Canadian Institute of Health Information
CIHR Canadian Institute of Health Research
CMA Canadian Medical Association
CMAJ Canadian Medical Association Journal
CPG Clinical practice guidelines
EBM Evidence based medicine
FDA Food and Drug Administration (U.S.)
GMO Genetically modified (or transgenic) organism
HMO Health Maintenance Organization (U.S.)
HRT Hormone Replacement Therapy
(usually refers to estrogen given at menopause)
HRQOL Health-related quality-of-life (measure)
JAMA Journal of the American Medical Association
MCID minimal clinically important difference
(a term used in epidemiology)
NEJM New England Journal of Medicine
NIH National Institutes of Health (U.S.)
OECD Organization for Economic Co-operation and Development
PTE proportion of treatment effect (a term used in epidemiology)
RCT randomized clinical trial
TI Therapeutics Initiative (a group at UBC who parses drug evidence)
WHO World Health Organization
UBC University of British Columbia
Prologue

The overarching theme ... is authority – the authority of medicine. This authority is not the same as that of your physician. Rather, the authority of which I speak belongs to the institution of medicine, the organizational structure to which your physician must conform. To paraphrase Robespierre, institutions are born to die; it is the people who are born to live. The twentieth century has witnessed the birth of two institutions of medicine: the first elevated medicine to be the arbiter of normalcy; the second superimposed the trappings of enterprise and created the “health care delivery system.” (Hadler, 2004, 201)

Much like the practice of medicine itself, any attempt to analyze even one small sub-group of health policy within a broader context (social, cultural, linguistic, economic, historic) can easily become complicated. To do so within an interdisciplinary framework only exacerbates this complexity, for, no matter how much more nuanced this conceptual framework might be, crossing disciplines invariably contains “demanding challenges with respect to dialogue and collaboration across traditional cultural boundaries” (Malterud, 2001b). The term “interdisciplinary”, nevertheless, is all the rage at the moment in health and health policy. Regrettably, the general tendency has not been any genuine attempt to meet the challenges to which Malterud refers but largely cosmetic, with the bulk of such work consisting of explanatory and numeric descriptions of existing

1 Also known as multidisciplinary, trans-disciplinary or cross-disciplinary.
circumstances, derived primarily from statistical and quantitative analyses of population health and usage data, e.g., numbers of visits to doctors or hospitals, dollars spent on various and sundry services, treatments or medications. The focus is often on cost-benefit analysis, with an eye towards setting health care priorities in ways that provide “a population with more benefit per dollar than another intervention” (Ubel, DeKay, Baron, & Asch, 1996); technology (whether administrative, organizational, diagnostic, medical or informational) and/or systems. People, whether patients or clinicians, are not particularly central if referred to at all.

Extrapolating values, ethical problems and complex social phenomena from such analyses is virtually impossible given the limitations of the data since there is rarely, if ever, any attempt made to include the heterogeneity of patient values, physiology, narratives or social circumstances – much less any ethical, sociologic, anthropologic, political, cultural or other contextual elements. While the statistical and numeric literacy involved in this type of work is often impressive, such analyses are not only oblivious to the socio-cultural and historical influences on how disease (and health) are defined but display a rather cavalier disregard for the subtleties of patient care and a disturbing lack of understanding of what it means to be ill.3

This dissertation uses the concept of therapeutic equivalence, used as a basis for reference-based pricing (a policy intended to reduce certain types of drug use), as its

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2 Beyond the equally quantitative quality-of-life measures or “quallies” occasionally mentioned.
entry point for an analysis, examination and discussion of many of the fundamental assumptions, ambiguities and historical accidents inherent to the practice of Canadian medicine. The interdisciplinary focus of this dissertation is such that it cannot be said to “fit” – neatly or otherwise – into any existing research lexicon since no such lexicon exists. However, insofar as this work can be considered a kind of hybrid exploratory research, the objective is to describe a rationale (and discourse) for patient-centred social science and/or participatory action research into medical practice and health care systems; one which incorporates social and cultural factors, involves an understanding of the importance of communication and understands how people acquire and use medical information – expanding the types of information they find “credible to their situation” (Mechanic, 2002, 459).

**Therapeutic Equivalence and Reference Pricing**

Therapeutic equivalence is the basis for a type of drug restriction, usually referred to as reference-based pricing, now used in British Columbia, New Zealand and by some 80% of American Health Maintenance Organizations or HMO’s (Horn, Sharkey, & Phillips-Harris, 1998). Often considered an alternative “that fits well with the goal of creating an evidence based [drug] list”, various groups implement this policy differently. In BC, for instance, patients can take the non-reference drug(s) but must pay the price difference, while in Australia a more centralized and restrictive approach is taken towards

³ For example, as I researched this work I came across many “data-mining” expeditions describing drug spending, physician billing patterns and so on. None even attempted to make an educated guess as to context or even hinted that there might be personal, social, economic or cultural trends at work.
“which drugs should be listed on the public pharmaceutical benefits scheme” (Ellner, 2003, 1398). Whatever the degree of restriction, the basis for the practice is an analysis of the evidence of equivalence as compared to measurable outcomes or, in other words, pharmacoeconomics.

At present, the “gold standard” of medical evidence is considered to be the randomized clinical trial or RCT. This entails randomly separating a group identified to have a pathology of some kind into two groups, with the experimental group given the therapeutic in question and the control group administered the placebo. To reduce bias, the trial is often blinded so that neither experimenter nor subject knows who is being given what. Then, *ceteris paribus*, all else being equal, any difference in result (detected through tests of statistical probability) may be attributed to properties of the experimental compound or other intervention. This deceptively simple process, by allowing for the “objective” testing of treatments, has, in recent years, attained “near-paradigmatic status” in medical and health policy lore. Yet, as medical historian Marcia Meldrum points out in *Departures from the Design, The Randomized Clinical Trial in Historical Context, 1946-1970*:

> The RCT takes an essentially social problem – how do we treat disease – with complex epistemological aspects – what is disease? what is effective treatment? how do we know? – and structures it as a mathematical problem of probabilities to deal with the multiple unknown variables and the issue of subjectivity. (Meldrum, 1994, 8)

However much the RCT has to offer for regulatory purposes and in broad-brushed policy discussions, the process inevitably invokes ethical dilemmas – for, no matter how
technically proficient or statistically elegant the result(s), no group conclusion can provide sufficient or appropriate information for individual clinical care. In theory, the clinical judgement and experience of the clinician fill that gap, but, as the quote at the start of this Prologue explains, the authority of medicine no longer resides in individuals.

Western Medicine as a Microcosm of Society, Culture and Politics

The large, multi-centre pre-marketing trials undertaken for drug approval at present create ambiguities of a magnitude never before seen in medicine. Often funded by drug companies, these studies are ambiguous and contradictory and sifting through the information is a Byzantine task. When methodology is key, messy human problems have to be assigned a tertiary role (if considered at all) and determining whether differences between large groups of people is due to chance or not is a tricky business. Often, the only people really qualified to sift through the mounds of data are statisticians and health economists. Rarely are either patients or doctors up to the task. This work, however slightly, attempts to redress that imbalance and to incorporate within that matrix some broader questions of health and disease – primarily using literature from the medical arena but also sociology, health economics, ethics and statistics – to question the questions themselves.

Medicine may have become more sophisticated, and medical and health information may have expanded exponentially in recent years, but, fundamentally,
questions of disease and health today are analogous to those which faced Herodotus or Galen thousands of years ago:

The practice of medicine is fundamentally a social and personal act. The great Prussian pathologist and politician Rudolf Virchow once wrote that the “progress of medicine should be as the progress of humanity”. Virchow, a consummate scientist, recognized that clinical medicine is in essence humane, representing the best qualities of mankind: kindness, empathy, sympathy, and mercy. But if the literature of medicine is devoid of human sentiment, how can it truly reflect our methods and aspirations. Medicine has long been recognized as an art and a science. It is time to restore art to medical writing. (Reese, 1999, 586)

This “progress of humanity”, coupled with our current fascination and reverence for numeric reasoning (Vandenbroucke, 1998a), forms the subtext and framework for this dissertation, which argues that the same overarching themes affecting trends in global politics and economics have also transformed medicine – with potentially disastrous results.

Whether we turn our gaze to politics in the Middle East or towards the profound societal changes arising from what we call “globalization”, our planet – at least for power brokers and elites – has shrunk, the spotlight expanded to shine not on the individual or even the community but the region, the nation, the continent, the planet. Ably assisted by new technologies, the movement of money, goods and services has been transformed from a hand-written ledger and oral communication to instant electronic transmission, twenty-four hours a day, seven days a week. The vision is based in economics and is of a “self-regulating, self-equilibrating system”, intended to increase the common good (Evans, 2001, 6), run by experts and a nexus of complex regulations, negotiations and
agreements. Navigating one’s way through such an elaborate web of interconnected threads requires heft and might, which is no doubt why larger corporations and institutions dominate the landscape. Such a power-elite driven, top-down process, however, may work well for cars or refrigerators or tech support but it is not, I would argue, a model that applies to medicine and health care. Unfortunately, it seems to have become the only paradigm in town.

Illness, like life itself, takes place within a diverse, complicated, conflicted, often-confusing and multifaceted environment and even the smallest aspect “contains multitudes”, as Emerson once said about the individual. Little about it is simple. We are all subject to illness and disability, with its chaotic blend of personal, physiological, social and other elements and rarely is anyone fortunate enough to live a perfectly healthy life then (presumably) drop dead from the exhaustion of it. Western health care, however, increasingly driven by American corporate and institutionalized models, tends to make a mockery of this complexity. Whether it is a drug company exhorting us to take our pills; disease groups reminding us to have our colons or cholesterol tested; magazine articles reminding us of the grand possibilities of genetic research; TV shows dramatizing the miracles of modern medicine; professional groups extolling the value of their particular specialty or government encouraging us to engage in healthy habits, the onus has fallen on the hapless individual to sift through these mixed messages and comply – much as we

Ironically, perhaps the most compelling image of this “open” worldview, in recent years, has been the closed doors and chain link fences surrounding trade negotiations, where nameless experts decide the fate of millions of people – some of whom are outside the fence, trying to be heard.
must do when far-away trade agreements or corporate head offices shut down industries, raise electricity rates or tinker with our food.

Health discourse has consequently become sparse and minimalist, as though individuals and their personal, social, cultural, political and economic circumstances were somehow incidental to the picture. In recent months, for example, as fears have mounted about a flu pandemic (the world appears to have become too globalized for a mere epidemic), the millions who died in the 1918 flu epidemic are often referred to. The flu is spoken of in terms of an invading army which, once unleashed, rages through the population leaving the dead in its wake. Rarely, if ever, does anyone consider that the year might have been significant, marking, as it did, the end of World War I, one of the most devastating conflicts in western history. Surely, the mental, physical, emotional, financial and immunologic state of the people who succumbed to the flu virus had an impact on their susceptibility (Rothman, 2002) and at least deserves mention.

This inability to appreciate the centrality of personal circumstance to states of health persists in media and other reports, whether it is cardiac risk factors or mammography and breast cancer. The focus remains fixed on the organ, the tumour, the disease. The person’s environment, personal, economic and social milieu – everything from the air we breathe to how happy we are in our jobs or how much money we have – seems irrelevant. In a somewhat dissimilar vein but also to the point, medical errors are often phrased in parallel terms to aviation and airplane disasters (Sexton, Thomas, & Helmreich, 2000), as though the human body were merely a sophisticated machine that could be understood by taking it apart or patients were there solely to be acted “upon”.
Making Policy

One must reasonably concede, however, that pragmatic generalizations are necessary at times, in medicine as in anything else. The public demands that governments take some responsibility for macro-management of drugs and health systems, and policymakers and others involved in medical decision-making would be stymied, their work ground to a halt, if they studied and attempted to incorporate every individual idiosyncrasy before making a move. For example, if we tried to ensure that a new drug or technology was safe for every single person all the time, no innovation would ever be approved. What this work contends, however, is that in recent years these trends towards standardization and institutionalized information-gathering and dissemination (including corporate influences), along with an enthusiasm for unfettered quantification, guidelines and protocols, have become excessively powerful, resulting in over-simplification, a surfeit of rules and a stultifying amount of reductionist thinking, not to mention an over-reliance on third-party expertise and data.5

Data is not knowledge. It has no inherent meaning and says nothing about what impact something has, neither does it inform with respect to values, ethics or any social, human, personal or communitarian agenda. Data merely reflects those aspects of the external world measured. Whether it is the correlation between cholesterol and coronary artery disease or the increase in drug spending over the last decade, numeric information

5 It has also led to circumstances in which we blithely ignore diseases like malaria and TB from which millions in the developing world die and obsess about (for instance) the lack of MRI’s on our doorstep. Yet MRI’s have been shown to have little or no benefits for most of the minor ailments, such as back or knee pain, for which we primarily want more of them (Jarvik et al., 2003).
tells us only that something happens – not how or why. Current social, political and economic trends, however, propel us down a road driven by business and monetary concerns in which nature, up to and including human nature, is reduced to the vocabulary of resources and consumption.

**A Question of Values**

Whether these systems, from globalization to guidelines, will serve or subvert the public “good” is neither the subject of this work nor a question any one researcher or any one work can answer. What this work examines is how fundamental questions of health and illness have been affected by such utilitarian and economics-based ideas from the vantage point of reference-based pricing and therapeutic equivalence.Parsed primarily through the medical literature, the discussion works its way outwards, deductively, from the issues raised by equivalence and restrictive formularies to larger questions that such policies imply but sidestep: What underlying concepts of health (versus illness) do such policies assume? What do they suggest in terms of how we define “disease”? What values do they reflect? What impact do they have outside their narrow “official” function? Are they based on well-reasoned assumptions or do they reduce the drama of human illness in ways that might, under examination, be considered unacceptable? How have prevailing belief systems, from scientific “progress” to what we mean by medical “evidence” permeated the development of such policies? How “factual” is the evidentiary basis for this information and how do we know that what we call facts today will stand
the test of time? How and why have these policies developed and, most important, what do they imply for patients?

These questions have no neat, quantifiable answers and the closest medical analogy would perhaps be the old-fashioned internist attempting to discover why a patient whose test results are negative still feels ill. Helping that patient requires finesse, experience and a delicate blend of art and science, creativity, intuition and a thorough understanding of that particular patient. Success is not guaranteed and no solution is likely to be a panacea.

The Evolution of a Medical Writer

Despite the general acceptance of (and lip service paid to) the complexity of physiology and medical treatment, our corresponding social and cultural template for illness and medical care is simple, simplistic even: Normal healthy functioning goes awry for some reason; whereupon medical advice is sought. Through a series of “investigations”, scans, blood tests and the like, experts zero in on the problem, diagnose it and devise a treatment plan. Once engaged, the process fulfils its promise, life returns to normal, homeostasis is restored. Unfortunately, this parable, like most, bears little relation to reality and is as inaccurate as other parables we hold dear, from fairy tales to television commercials (ask anyone who’s lost a wallet in a foreign country about the truth of the Parable of the Lost Travellers Cheques). What it reflects is the social narrative we have constructed around medicine and health care and – as the many sufferers of chronic illness can attest – is less about the reality of medicine than our faith
in progress, technology and science; our trust in the power of expertise and our belief in those snippets of medical news that assure us daily that advances in biology, genetics, pharmaceutical science and informatics are expanding our knowledge by leaps and bounds. On occasion, when there is blame to be apportioned, it is (depending on one’s perspective) the fault of the pharmaceutical companies, or socialized medicine, or doctors, or the current government, or private care.

Over nearly fifteen years of medical writing I have dealt with questions of medicine, disease, illness and therapy; attended medical conferences; interviewed clinicians, patients, policy-makers and administrators; covered changes in health policy and hospital closures and tried to explain research and technology to doctors and to the general public. I have written on a host of conditions from delirium to diabetes and learned the language of medicine, becoming conversant with the terms and conventions. Over time I have also become painfully aware of the shortcomings of media coverage of medicine and the limitations of the current medical discourse, both from a communications and a medical perspective. Meanwhile, social and political realities affected my work as they did everyone else’s. As newspapers, TV stations and magazines merged and large media outlets bought out what had formerly been independent publications, editorial focus shifted to the general, the statistical, the latest research. In the early nineties, for instance, I wrote detailed pieces for doctors outlining pain and thoughtful articles on how to communicate bad news to patients. By 1999 those same magazines were only interested in conferences and my covering the “latest” research in
cardiac care or residency requirements. The whole tone and tenor had changed, even though patients and their problems had not.

People still struggled with arthritis and cancer and heart disease, still juggled medications they had trouble understanding the need for. Doctors and nurses, meanwhile, had to wade through ever-expanding mountains of information ranging from clinical guidelines and drug company data to directives from one agency or another. Often they encountered conflicting information on how to best (and most cost-effectively) treat their patients and sometimes that information contradicted their own clinical experience. Definitions of normalcy changed suddenly and for no apparent reason: “ideal” blood pressure went from 140/80 to 120/80, overnight it seemed, with no-one having any real clue as to why. New drugs and technologies proliferated, often for conditions that previously were under the radar, from osteoporosis to colon cancer. Patients were exhorted to be proactive, to have tests and scans. Whether these were genuinely beneficial did not seem to enter the discussion.

The Question of Drugs

Drugs have become the fastest-growing segment of health care expenditures in many Western societies. According to the Canadian Institutes of Health Information (CIHI), prescription drug costs reached $18 billion in Canada in 2004 (CMAJ, Editorial, 2005). Are these costs justified? Certainly the preponderance of drug advertising would suggest that pharmaceutical companies are just as sales-oriented as any other business and that factors other than therapeutic appropriateness can drive drug sales. Conversely,
many medications, from the AIDS "cocktail" to the immune suppressants that make solid organ transplants possible, extend lives and improve quality of life for many people.

Higher drug use has led to many jurisdictions and organizations instigating various ways of restricting drugs. In BC, as in many other jurisdictions, one such method was reference-based pricing. In 1997, I attended a press conference at which the Minister of Health announced that an additional category of drugs, ACE-inhibitors, which lower blood pressure by affecting a chemical in the heart and blood vessels called angiotensin, had been added to the reference pricing repertoire. Flanked by well-dressed experts, the Minister spoke in glowing terms of how much money this would save and how BC was a pioneer in reducing drug company influence. In many ways her words made sense. As a medical writer I was often on the receiving end of pharmaceutical company information and knew many of the PR people. I was neither naïve nor trusting: I understood how clever and subtle the tactics were and understood that many so-called "patient advocacy" groups were funded primarily by drug companies. Reference pricing certainly made sense from the Ministry's perspective. The announcement nevertheless made me uneasy. It seemed to me that what was at stake was power, not patient care, particularly since patients only figured as cardboard cutouts, exhibiting certain signs for which drugs were recommended.

This work grew out of that disquiet.

The blend of disciplines used in this dissertation does not conform to any standard academic vocabulary, for, to paraphrase Roland Barthes, genuinely interdisciplinary work
does not simply pick a theme and tuck on extra subjects but constitutes its own object (personal communication, Robert Smith, November 2005). The language, therefore, is deliberately uncomplicated and as jargon-free as possible, the intent being to create a narrative that is less structured and perhaps more "literary" than is usual; although in some ways it is "deceptively accessible" (personal communication, Maryse de la Giroday, September 2005). The bottom line, if one may semi-ironically refer to it this way, has to do with the individuals often consigned to the sidelines of health and policy discourse, patients, and the extent to which policy decisions can be considered ethical, equitable or right:

Over the past decade and more, the economic, political, and social contexts of Western health care delivery have undergone rapid and often devastating changes. In Canada and other Western countries, this has led to an era in which there is a widely held assumption that actions to save money in health care and other social services are inherently justifiable. Efficiency considerations have come to trump considerations of quality of care in the implementation of a great deal of health policy . . . . A corporate ethos has infused health care policy processes with resultant power inequities that have generated a number of (presumably unintended) negative consequences. (Rodney & Street, 2004, 209)

This dissertation begins with an overview and introduction of the main themes, such as equivalence, evidence-based medicine, randomized clinical trials and patient involvement, themes which will be developed throughout the work. The term equivalence is explained, along with its connection to medicine and its bureaucratic and statistical overtones are discussed. The next following chapters analyze the research on therapeutic equivalence and reference-based pricing using the well-studied British Columbia reference drug program (RDP) as the primary example. As a rule, proponents point to the
power, money and marketing abilities of drug companies and consider reference pricing an appropriate counterbalance, while critics decry the bureaucratic layer that the policy inserts within the clinical encounter and point to the dampening effects on future drug research and development. Only rarely is patient input sought and that, where it exists, is confusing and inconsistent, probably because people’s lives are not static. As the BC (Seaton) Commission report on health care reform over a decade ago wisely noted, people’s opinions differ depending on whether or not they themselves have experience of illness. Those who are sick, or know someone who is, have very different ideas as to what constitutes good health care compared to people who are healthy. The latter favour health promotion; the former more acute and chronic illness care (Seaton, 1991, B-4). In any event, the questions asked in polls and focus groups are often slanted in favour of what we want to hear, and true qualitative research is difficult, expensive and time-consuming – and is often considered less valid than quantitative “scientific” research.

Unfortunately, the so-called scientific tradition of evidence, used as the mainstay for guidelines and directives, is not particularly scientific either, merely grand and statistical. As Jane Jacobs writes in Dark Age Ahead:

The combination of the appearance of professional respect for scientific rigor coupled with professional contempt for scientifically rigorous behavior is toxic, a poison that infects ... activities in North America .... It cripples foreign aid programs, pedagogy, and illegal-drug policies, and it promotes dubious and harmful medical treatment fads, nutrition and other lifestyle advice, and agricultural recommendations. (Jacobs, 2004, 99)

Jacobs targets biology and medical treatment for particular criticism and she is correct in pointing out that in many areas, from genetics and cancer to the workings of the immune
system, we have moved away from questions on how organisms work in their entirety, interactively and in concert with their environment, in favour of research on details. Yet to criticize evidence-based, guideline-driven models of health care, or to speak out in favour of a more holistic model (and call for greater patient involvement), is to subject oneself to the charge of being unscientific. But as Kuhn wrote:

Normal science, the activity in which most scientists inevitably spend almost of their time, is predicated on the assumption that the scientific community knows what the world is like. Much of the success of the enterprise derives from the community’s willingness to defend that assumption, if necessary at considerable cost. Normal science, for example, often suppresses fundamental novelties because they are necessarily subversive of its basic commitments. (Kuhn, 1970, 5)

This final chapters of this analysis raise currently unfashionable questions of ethics and values and cover broad questions such as:

- What is health and how do we differentiate between normal physiology and pathology?
- How do experts and expert groups gloss over the many uncertainties and ambiguities of medicine in creating guidelines, rules and policies?
- What troubling and fundamental problems are obscured by statistical modeling of complex medical questions?
- To what extent are health policy guidelines reductive?
- How did evidence-based medicine develop and how well does the use of biomarkers and surrogate end points in randomized clinical trials stand up to scrutiny?
- What values permeate our discussions of equivalence and how ethical are economic ideas of efficiency?
- How “healthy” are health initiatives recommending “proactive” health measures, screening programs or aggressive preventive care?
- How do narratives of illness conflict?
Medical care has significance far beyond federal or provincial boundaries, politics, budget considerations or policy for people who are ill (and their families and friends). It goes to the very heart of who we are and ought, at the very least, to be discussed in broader terms. This would require an enormous shift in focus on the part of governments, medical schools, funding bodies, health professionals and patients, but, in the end, it is, I would submit, the only rational long-term solution to our present dilemmas in health care.
I. Equivalence: Introduction and Overview

*Can words have force in and of themselves? Of course not. They acquire force only through their influence on human actors. Through their influence on scientists, administrators, and funding agencies, they provide powerful rationales and incentives for mobilizing resources, for identifying particular research agendas, for focusing our scientific energies and attention in particular directions.* (Keller, 1995, 21)

The term “equivalence” and its resultant notion of parity and “sameness” entered the regulatory and technical lexicon roughly three decades ago (Piaggio & Pinol, 2001, 3572). Since then the term has steadily proliferated, garnering only the occasional criticism or comment. Transgenic crops, for instance, are said to be “substantially equivalent” to conventionally grown varieties, while the synthesized, genetically-modified insulin now available to diabetics is considered equivalent to the former, biologically-derived kind, made from animal pancreases. By the same token, drugs are said to be equivalent or “bio-equivalent” when the end point of their proposed action(s) is the same.

6 The manufacturer admits that for some patients “early warning symptoms for hypoglycemia were less pronounced than they were with animal-source insulin” (CPS, 2000, 758). Some 20% of insulin-dependent diabetics find the genetically-modified insulin’s side effects intolerable (private communication, Colleen Fuller, August 2001).
Equivalence itself is a fairly bland term, but the technologies and modifications it represents are not. These involve sophisticated genetic, biomolecular, pharmacologic, biomedical or chemical processes, intricacies which the term obscures by grounding the concept in the familiar context of the past and implying a simplicity and transparency that physiologic and biologic interactions simply do not have. The term equivalence, therefore, transcends mere description and affects not only how we rationalize, mobilize, regulate or fund activities and decisions around these practices but the extent to which we, as a society, accept or reject them. Only relevant from a technical and regulatory standpoint when a substitution is possible, the term equivalence is, at a basic level, a triumph of sound-bite simplicity, a reference to a quasi-formal process that has assessed the “essence” of the technology in question, compared it to an old method or substance and pronounced them similar enough to be considered the same. Underlying the term is a meta-message of science and authority, of expert evaluations and proof that ought not be questioned – no matter that the term lacks rigour and is ambiguous in the extreme since it neither sets boundaries nor defines what that essential quality being compared consists of.

The “substantial equivalence” of genetically modified plants, for example, was first described in a 1993 Organisation for Economic Co-Operation and Development (OECD) report where the safety of transgenic crops was assumed because of equivalence – or as it was later described in a Royal Society of Canada report, if it looks like a duck and quacks like a duck, then, for all practical purposes, it must be a duck. The report concluded that “substantial equivalence is not a scientific basis for the application of a safety standard”, but is rather “a decision procedure” (RSC, 2001, 179). Other observers
have suggested that equivalence and interchangeability are not genuine scientific
concepts as such but bureaucratic constructs (Furniss & Zammit-Lucia, 1997) which
inadequately reflect the complexities of nature.

In terms of the substantial equivalence of genetically modified organisms, many
biologists, geneticists, farmers and plant-breeders have rejected the simplistic assumption
that organic life is a mechanistic or linear process of playing out the instructions
contained within the genome, and scientists such as British biochemist Mae-Wan Ho and
Harvard geneticist Richard Lewontin have criticized the term and the model it assumes:

Risk assessment on the principle of equivalence is the stuff of farce. It is a
case of ‘don’t need – don’t look – don’t see.’ Biotech companies are in
effect given carte blanche to do as they please, while regulators are
serving to defuse and allay legitimate public fears and opposition. (Ho,
2000, 149)

The problem of telling a coherent causal story ... based on knowledge of
the DNA sequence ... is that we do not know even in principle all of the
functions of the different nucleotides in a gene, or how the specific context
in which a nucleotide appears may affect the way in which the cell
machinery interprets the DNA; nor do we have any but the most
rudimentary understanding of how a whole functioning organism is put
together from its protein bits and pieces. (Lewontin, 1991, 69)

In other words, simply knowing or defining an end function or product cannot give us
any idea of the complexities of the developmental processes or provide any idea of how
the end result arrived where it did.

The mere act of using a term such as equivalence to describe reality involves what
biologist and philosopher of science Evelyn Fox Keller (1995) refers to as the
"performative character of language" and has more than a glancing impact on how we perceive the world:

Some of the force of descriptive statements, then, derives from the role of metaphor in constituting similarity and difference, in defining the "family resemblances" that form the bases on which we categorize natural phenomena .... Needless to say, not all metaphors are equally useful or, for that matter, equally captivating. The effectiveness of a metaphor, like that of a speech-act, depends on shared social conventions and, perhaps especially, on the authority conventionally granted to those who use it. (xi-xii)

That authority is key, but so is the environment in which the statement exists. Keller goes on to describe how terminology, metaphors and other descriptive language evolve as social, scientific and laboratory means or resources change. For example, forty years ago in vitro fertilization was adequately described in ways that evoked the Sleeping Beauty myth ("penetration, vanquishing, or awakening of the egg by the sperm"). At the time, both image and metaphor matched the available technology and the prevailing sexual stereotypes. Today, the language describing fertilization is "cast in the language of equal opportunity", as, thanks to shifts in social context as well as changes in scientific and laboratory techniques, the egg is no longer considered a passive recipient in the fertilization process (Keller, 1995, xii). Similarly, the term equivalence only emerged as a viable term once biotechnology and pharmaceutical science had become sophisticated

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7 Keller distinguishes between "speech acts" (citing J.L. Austin's 1962 book, How To Do Things With Words, from a series of 1955 lectures at Harvard) — or words which directly affect reality like bets, marriage pronouncements and declarations of war — and what she calls "performative" words which are not mere descriptions but "a way of grounding the social dependency of truth in material reality" (x).
enough to allow for the manipulation and finessing of genes and other molecular minutiae.

This dissertation examines a lesser-known and currently less controversial aspect of equivalence, “therapeutic equivalence”, also called “therapeutic substitution” and “bioequivalence”, a medical – or more accurately pharmacologic – description of drugs within a class considered interchangeable for regulatory and/or institutional (hospital, government, insurance) purposes. As with transgenic crops, this use of the term only evolved as multiple new drugs became available (often for conditions for which therapies already existed) and as practical matters such as cost necessitated its use.

**Therapeutic Equivalence**

Lists of approved medicines, also called formularies, “are nearly ubiquitous in the United States and internationally” (Ellner, 2003, 1397). Typically, and depending on the institution, these lists are compiled by groups of experts that often include physicians, pharmacists, pharmacoэкономists and so on, with cost containment their primary rationale (1398). Designating a restrictive formulary or a list of “approved” drugs means that, within a loosely-defined sub-genre of drugs, only certain, pre-determined ones will routinely be provided within an institution or geographic region.⁸ As Ellner explains:

> Formulary systems vary in the number of drugs and medical conditions they cover and the extent to which they restrict access to unlisted

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⁸ These drugs are usually (though not always) grouped on the basis of function, e.g., histamine (H2) blockers that reduce stomach acid or non-steroidal anti-inflammatory drugs such as ibuprofen or naproxn to reduce the pain and swelling of osteoarthritis.
medicines. With open formularies, patients are reimbursed for drugs whether or not they are listed. Other formularies may be accompanied by programmes that offer patients price incentives to choose listed drugs or that reimburse patients for only the drugs on the list. (1397)

The latter types of restrictive formularies are often referred to as reference-based pricing in which only the referenced, or approved, drug will be subsidized. In the United States, companies called “pharmacy benefits managers” often act as intermediaries between patients, employers, insurance companies, public health insurance programmes, pharmaceutical manufacturers and pharmacies (1398).

Substitutions can be made covertly, without the doctor or patient necessarily being aware of it. For example, the physician could write a prescription for ramipril (an antihypertensive or blood-pressure lowering drug in a class of drugs known as ACE inhibitors), but at the pharmacy the patient would be dispensed moexipril, a different ACE (Antman & Ferguson, 2003, 2606). Usually, if the patient (via the doctor) could convincing prove that the ramipril was essential, depending on the specifics of the plan, an exception might be made – provided some kind of special authority form were provided. Often this would only be possible if the dispensed drug had had onerous side effects or did not have the desired clinical or therapeutic outcome. Alternatively, the patient could opt to pay for the drug out-of-pocket. Metaphorically, the position of the insurance plan is that we will pay to get you from point A to point B, but only on the bus. If you want a taxi (or a tram or a bicycle) you have to prove why you need one, and, if we find your explanation compelling, we will pay for it. Otherwise, you pay for it yourself.
Pharmacy benefit managers have appeared on the scene as fiscal intermediaries [and] we have had the experience of attempting to explain our medical reasoning over the phone to an individual who is not medically trained, is ill-equipped to understand the subtleties of clinical medicine, and simply states, “The patient will be faced with a larger copay if the switch is not made.” Among the most disturbing of such encounters are those in which a request is made for therapeutic substitution to a drug from the same class that has never been evaluated. (2606)

The underlying rationale, therefore, is value for money or cost-effectiveness; while the basis for the medical soundness of the decision is the available medical evidence, extrapolated primarily from studies that demonstrate the lack of superiority between treatments, or, when these studies are lacking, from an assumption or analysis of biologic plausibility.

Such pharmacoeconomic analyses can be contradictory depending on the perspective, their accuracy difficult to pinpoint. In medicine, as in life, absolutes are few and far between and one’s vantage point often determines one’s slant of light and how and what one sees. A series of articles on health economics in The Lancet succinctly describes this problem, explaining how the position from which an analysis is undertaken “greatly affects the costs and benefits considered, and the value placed on … negative

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9 Generic drugs may also be substituted for brand names at the pharmacy, but as these are loosely defined as the same chemical entity, merely of a different and cheaper brand, equivalence would not seem to present the same problem. Nevertheless, the term “generic” has many definitions and the awkward phrase “interchangeable multisource pharmaceutical product” has been suggested as an alternative (Welage, Kirking, Ascione, & Gaither, 2001).
and positive consequences" (Mansley & McKenna, 2001, 1169) (my emphasis). Unsurprisingly, patients and policy experts or health managers may have widely divergent views as to what constitutes a benefit. The authors identify nine different viewpoints which, consciously or unconsciously, influence decision-making ranging from the individual patient to doctors, insurers, managers and administrators, the healthcare system generally and society as a whole. For example, a physician might consider risk/benefit for a single patient without necessarily considering what it might cost the system-at-large; whereas for a hospital administrator the overall budget for that particular institution would be a major criterion. In addition, not all treatments or interventions are well-studied, and often there is more evidence published on older drugs simply because they have been around longer. The authors warn that a real concern in economic evaluations “from a societal perspective is that they generally have very little knowledge of patient preferences and values” (1172). The pharmacoeconomic model, which considers “allocative efficiency” based on institutional definitions of health can be narrow and limited “with respect to ‘welfare’ from a societal perspective” (Oliver, Healey, & Donaldson, 2002, 1772).

The evidence itself, as will become clear throughout this work, can also be problematic and contradictory and merely grouping drug evidence according to class does not adequately reflect patient diversity or the uncertainties of clinical care. There is, moreover, a tendency at present to give great weight to certain types of evidence, in particular the randomized clinical trial or RCT, often called the “gold standard” of evidence:
The "evidence" is evidence-based medicine, which defines therapeutic efficacy and safety for specific pharmacological interventions. The "weight" or power of evidence in support of treatment is maximum when determined by large, placebo-controlled, randomized trials ..., less definite when based on smaller randomized trials and/or clinical registries ..., and least reliable when dependent on expert panel consensus .... Pharmacotherapeutic agents have traditionally been grouped into classes on the basis of a demonstrated affinity for a single biological target. However, individual members of a therapeutic class may be widely disparate in pharmacokinetic and pharmacodynamic response, side effect profile, and propensity for drug-drug interactions. (Kereiakes & Willerson, 2003, 2611)

There are further questions as to whether or not the evidence from one drug within a class can be safely extrapolated onto others or if studies establishing equivalence reflect clinical truths to begin with.

Many studies of clinical or therapeutic equivalence make claims for difference or equivalence not through any "thoughtful examination of the data but by tests of statistical significance that are often misapplied or accompanied by inadequate sample sizes", which, in turn, can lead to false claims, inconsistent policy decisions and, ultimately, harm to patients (Greene, Concato, & Feinstein, 2000, 715). In addition, since thresholds are decided in advance as to what size clinical effect is to be considered effective in a certain situation, these thresholds, also called "limits of equivalence" between which "an effect is designated as being too small to be important" are derived statistically and are often "not straightforward" (Alderson, 2004, 477). How large a difference is to be considered important? Who decides and on what basis? How different should the thresholds be for different groups of patients and different outcomes? These are complicated questions that ideally require "considering results of a particular study in the
context of all available research” (477), which is difficult, and mirror the concerns Ho expresses in relation to genetically modified organisms in her book, *Genetic Engineering: Dream or Nightmare?*

Claims for substantial equivalence can, and often are, made early on in the deliberative and regulatory process, resulting in often perfunctory risk assessment – since the decision, for all intents and purposes, has already been made to accept the product in question. (Ho, 2000, 149)

This regulatory ambiguity – do we accept or reject a certain drug when evidence is lacking or incomplete – is reminiscent of the circular arguments used in the early days of drug regulation, writes historian Meldrum, when the newly-formed US Federal Drug Agency (FDA) required “substantial evidence” for patent licensing and drug approval, evidence which was typically defined as “adequate and well-controlled investigations by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved”. In other words, the evidence is whatever the experts say it is, and the experts are those who are qualified to assess the evidence (Meldrum, 1994, 18). So, even in the absence of meaningful evidence, those same experts who have convened to make the regulations are themselves the arbiters of the information for the assessment process.

A fundamental epistemologic problem, even were one to accept that expert evaluations of equivalence are acceptable and appropriate, is that this reasoning sidesteps the vast social and cultural underpinnings involved in determining what something “is” and therefore what else it can be said to resemble or be equivalent to. What makes an antihypertensive drug what it is? The fact that it lowers blood pressure (measured via a
number, a biomarker and/or surrogate end point)" or what it does to the body during that process, only one measurable effect – the one we understand – being the reduction of a blood pressure measure? What makes a tomato a tomato? Its taste? The fact that it’s red and round and grows on vines? As humourist Dave Barry ruefully points out, tomatoes these days are not bred to be eaten but to survive long truck journeys, which could explain why they taste like croquet balls. Are they in fact the “same” tomatoes that our grandparents ate? Classification systems are neither simple nor obvious and a “range of potential scientific and social responses” can “appropriately [be] brought to bear on biological processes” (Arnowitz, 1998, 58) depending on the standards and values invoked or the rationales used. At present, the primary considerations appears to concern cost and the available evidence, not necessarily medical “appropriateness”.

Oh, My Aching Budget

As was pointed out earlier, the primary rationale for restrictive formularies is cost. As we constantly are told, our (and other countries’) health care is in trouble; the system as it stands is not sustainable (precisely what this means is unclear); drug (and other) costs have soared; the population is ageing. We must therefore concentrate on efficiency, efficacy, value for money. In Canada, this “apocalyptic anticipation” of escalating health costs receives continuous air play as journalists, politicians and others analyze health care and its problems (Kenny, 2002, 31), with solutions ranging from private care and

\[^{10}\text{A biomarker refers to a numeric value derived from a screening or test that is thought to correspond meaningfully to a physiologic state. This will be discussed at length in Chapter Three.}\]
scrapping Medicare altogether to broadening the purview and providing every Canadian with any drugs, screens or therapies considered "medically necessary" (another term nobody defines). The popular story, writes Nuala Kenny, a Nova Scotia paediatrician, ethicist (and nun) in her book, *What Good is Healthcare?*, thus contains powerful assumptions:

That we have the "right" shape of system with its emphasis on acute care interventions; that our drugs and technologies all benefit Canadians; that "more" is always better; that the market is more efficient than government; and that private purchase of health care is either a right or a mechanism which empowers patients. (31)

These are fairly major assumptions that ought to be generating considerable ethical and critical debate; unfortunately that is not the climate of the time. In terms of health care costs however, most reasonable people would agree that when "more" is constantly required, long-term viability depends either on having unlimited resources (which is unlikely) or on some means of equitably restricting what resources there are. Precisely how this might occur is the complicated part – particularly the equitability.

Canada's total (public and private) health spending accounted for 9.7% of GDP in 2001, versus 7.3% in 1975 and 8.4% in 1985 (OECD, 2003). This was considerably less than the United States, the highest spender in the OECD, which devoted 13.9% of GDP to medical expenditures, but more than France (with 9.5% of GDP) and considerably higher than the United Kingdom (7.6%). In Europe, only Germany and Switzerland who spent around 10% of their GDP had higher costs. Throughout the
nineties, medical expenditures increased annually, per capita, by an average of 3.3% throughout the OECD; in Canada, however, the increase in real terms was 1.9%, of which drug expenditures grew the fastest:

The rise in pharmaceutical spending has been one of the factors behind the rise in total health spending in Canada as well as in several other OECD countries. Between 1990 and 2001, the share of health expenditures spent on pharmaceuticals increased from 11.5% of total health spending to 16.2%, one of the steepest increases among OECD countries. In 2001, only the United States, France, and Italy spent more than Canada on pharmaceuticals. (OECD briefing note, 2003)

In 2003, the Canadian Institute of Health Information (CIHI) estimated that in the previous year Canadians spent more than $14 billion on prescription drugs and reported in Drugs Expenditure in Canada, 1985-2002 that the 10% increase in prescription drugs over the previous decade primarily reflected the “entry of new drugs (typically introduced at higher cost) and higher volume of drug use” (CIHI, 2003). Multiple medication use, particularly for seniors, the fastest-growing demographic, has also substantially increased, as have the number of conditions for which drug therapy now exists.

This would be obvious to most people without a report. Throughout the 1990’s there was a noticeable increase in new drugs for hitherto unheard-of conditions (e.g., “erectile dysfunction”), new drugs for old diseases that seem to be on the rise as we become older and fatter (Type 2 diabetes) and new drugs for chronic problems (asthma or hypertension), with little indication that this upward trend will alter or abate in the future. On the contrary, two major factors will affect the future price of drugs: the ongoing

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11 Although one could reasonably argue that a difference of 1.3% from 1985 to 2001 is hardly excessive.
development of “lifestyle drugs” intended for conditions formerly considered outside the realm of medicine such as baldness, obesity or shyness, and the Human Genome Project with all the breathless speculation it has generated with respect to breakthrough drugs and pharmacogenetics (drugs individually tailored to one’s genes). These would continue to raise costs, since one thing we know about new treatments or drugs is that they almost invariably increase costs (Oliver et al., 2002, 1772).

The preponderance of the so-called lifestyle drugs reflects the major attention and advertising efforts that pharmaceutical companies have devoted to both the drugs and to changing consumer attitudes – as demonstrated by the direct-to-consumer advertising on American television stations that exhort viewers to “talk to your doctor” about everything from migraine and high cholesterol to less obviously medical conditions such as obesity and social anxiety. In the latter instance, as Toronto emergency physician and professor Joel Lexchin, a frequent commentator on the Canadian prescription drug scene, warns:

Expanding the definition of what constitutes a treatable medical problem will have a variety of consequences. For example there may be a change in how general practitioners balance the risks and benefits of pharmacotherapy. No drug is without side effects, but the acceptability of those side effects usually increases with the severity of the illness being treated. What degree of side effects would be acceptable in treating someone who feels too shy? … If we redefine treatable medical problems to include normal variants in the population, physicians and patients may become more willing to accept side effects (which might themselves need treatment) that would otherwise be avoided. (Lexchin, 2001, 1449)

Much in the same way as Lexchin describes how increased drug therapy can desensitize us to interaction and side-effect problems (in effect “normalizing” multiple drug use), therapeutic equivalence and reference pricing also normalize drug use by
making fundamental assumptions as to what "constitutes a treatable medical problem". The mere act of defining, regulating and generalizing dysfunction affects general perceptions, whether through definition and standardization or delineation of boundaries and parameters. In other words, when Pharmacare and the Ministry of Health or an HMO give their tacit stamp of approval for certain types of drugs being appropriate for certain conditions – merely differing with pharmaceutical companies in terms of which drugs should be taken – the implication is that drugs are the answer, whether to lower blood pressure, reduce stomach acid or anything else.

Simply knowing the numbers however, or hearing that drug spending has increased exponentially over the last decades, tells us nothing about whether or not these expenditures have value. Are we healthier than we were? Do we generally feel better? Do these therapies benefit us as a society – or have our concepts around health and disease not kept up with pharmaceutical and other technological advances?

**Equivalence as Metaphor**

This dissertation examines therapeutic equivalence both as a basis for formulary management and as a metaphor for fundamental questions on health, illness and health care. The overriding concern is the impact such policies have on patients, often the unrecognized casualties of this regulatory nonchalance. As a professor of mine says, every time a drug is prescribed for a patient it is an experiment (Morley Sutter, private communication, November 2004). The outcome is never certain. When institutions, governments, corporations and statisticians define risk, however, not only are the
singularities and unique qualities of the individual (immunological, physiological, anatomical, genetic, psychosocial) obscured, but the complexities of the pharmacodynamics and pharmacokinetics of the drug are blurred, even devalued. By examining these attitudes and how they touch on therapeutic equivalence in (primarily) the medical literature, this dissertation reviews fundamental questions of disease, disease aetiology (cause) and the narratives constructed around health and illness. The primary focus in this work is the affluent west, where our primary medical concerns are not viral or parasitic (e.g., AIDS, malaria or tuberculosis) with identifiable, if not always direct, “external”, causes (a mosquito borne/injected infectious agent or bacterium), but more “internal” ones such as cardiac disease, cancer or auto-immune disorders such as rheumatoid arthritis or diabetes.

The question at the centre of this work is whether or not individuals, patients, are well-served when regulatory bodies and other institutions (including corporate entities) determine what therapies are “best” and/or most cost-effective, as is done with therapeutic equivalence, or whether the process unacceptably narrows patients’ alternatives, trivializes illness and oversimplifies the medical encounter and its risks. Furthermore, when what is essentially a social problem – how do we treat disease (with multilayered, epistemological foundations inherent in the defining of disease) – and becomes a policy question answered algorithmically and statistically, how is it even

\[12\] Pharmacodynamics is the action that the drug has on the body; pharmacokinetics is the inverse: the effect that the body has on the drug. The latter would include drug interactions and drug clearance metabolism or how quickly the drug is absorbed and processed through one’s system (Kramer, 2003). Drugs also interact with other drugs, food and a myriad other things.
possible not to create ethical and social dilemmas (Meldrum, 1994, 8)? Beliefs rooted in the idea that health is a question of logical problem-solving, which time and research will eventually provide answers to, are, in the end, reductionist and fragmentary and it is impossible to predict what results they may have:

Increasing concerns regarding access to and appropriateness of medicinal drug use have led many governments ... to develop national policies and regulations intended to increase the affordability, supply, safety and rational use of pharmaceuticals. However, little is known about the intended and unintended impacts of these social experiments....

(Ratanawijitrasin, Soumerai, & Weerasuriya, 2001)

As the excitement generated by the gene "revolution" and its touting of genetic cure-alls demonstrates, however, most of us, including the bulk of the scientific, political, media and academic community, trust the purity of the current model and continue to hope for that mythical "magic bullet" that will "cure" cancer or some other multidimensional, complex disease.13 It is a satisfying belief and one which, overall, has served us well: that The Truth Is Out There, should we manage to stumble across it on our travels, under the expert tutelage of science and the "experimental apparatus", there simply 'to illustrate the truth of the facts" of which the scientist "is only the good midwife" (Stengers, 1997, 158). Less comfortable is the prospect of the many roads not taken, the promising lines of inquiry dropped for one reason or another, the various influences from political to economic that drive not only the collection of data but their interpretation. As physician Robert Arnowitz writes in Making Sense of Illness, there are
“winners and losers” in choosing among “biologically plausible frameworks” used to understand and define disease (Arnowitz, 1998, 180):

The contemporary cultural and medical landscape is littered with controversial diseases, entities, public policy debates that hinge on definitions of disease and disability, and angst about the reigning biomedical model of disease. While all of these stress points hinge on definitions, classifications, and meanings of ill-health, the underlying historical context for contemporary controversies is frequently ignored. In my view it makes little sense to argue whether such and such disease is legitimate without an understanding of what we generally mean by “legitimate” disease; to argue whether government entitlements should cover disease X, without understanding how and why particular categories of ill health are grouped and named together and granted special status; or even to criticize our health care system ... without some understanding of the historically conditioned values and interests. (2)

Every description or classification of disease – and therapy – makes implicit theoretical and social assumptions, often specific to time and place, and, as readers of history know, the future can be a harsh critic. There was little point in considering angina pectoris anything other than a subjective symptom of chest pain when there was no test or scan to pinpoint it, no underlying hypothesis to define it, no organization like the Heart and Stroke Foundation to publicize it and no drugs to treat it. Once these emerged, however, it became possible to create “objective” boundaries (occluded arteries, plaque disease), create a disease classification and shade in the borders. To what extent these will stand the test of time is simply not clear at this stage.

13 The term “magic bullet” was coined in the late 19th century by Nobel prize winner Paul Ehrlich, one of the early pioneers of microbiology and immunology, and we seem as attracted to the concept as people were a century ago. Stark and hopeful, the concept of a single cause, a single cure, remains appealing.
Yet today, at this gallant start to the 21st century, as it is so often extolled, we seem to feel that our science, our economic and social ideologies, our methodologies and technologies – as well as our definitions of health and disease – have finally hit the mark, with little or no acknowledgement that our explanatory models are driven by our worldview, values, circumstances and methods of inquiry:

Experimental methods, buttressed by ever more complex statistical analyses, have contributed mightily to the generation of effective pharmacological and technological interventions; we should be very grateful. As engineers' close attention to the wiring enables them to detect malfunctioning of a radio's transmitters, and receivers, so the biomedical scientists' focus on neurological, humoral, and chemical pathways enables them to detect malfunctioning of the patient's neurotransmitters and receptors. [We should also] be concerned with the music and messages transmitted and received over the wiring and through the ether. There is a vast difference between the two but neither is good or bad, right or wrong, hard or soft. For effective understanding of health, disease, and suffering both the wiring and the messages deserve investigation. The role of naturalists in medicine has been lost in the wake of biomedicine's growing hegemony. (White, 2000, 1905)

The 20th century was marked by the “rise of quantitative reasoning” and an “ever-increasing role for numeric reasoning in medicine” (Vandenbroucke, 1998a, S12). Yet disease is a not a “constant timeless biological entity” completely devoid of social, cultural, political and economic influences (Arnowitz, 12). Our ongoing conceit, however, is always to consider ourselves at the peak of medical (and economic, scientific, and other) knowledge:

The medical community has always been prone to assume that it knows most of what there is to know. This is a common mistake in science. During the 18th century, physicists decided that their real work was done; the only thing left was to grind out the solutions to the Newtonian equations for complicated problems. Then along came quantum
mechanics. During the mid 1960’s microbiologists concluded that they had already discovered all pathologic bacteria....We should therefore be much more humble in our assumptions about how much we know. (McDonald, 1996, 58)

Humility does not, however, figure strongly in policy decisions which rely on what has become one of the latest buzz words in medicine, “best evidence”, and the statistical analyses on which it rests, even though it would be sensible to at least acknowledge the degree of ambiguity and flux there is in medicine and guard against our tendency towards complacence – or at least not allow our biomedical successes to blind us to the limitations or to the considerable role market forces, politics and other influences play. Our arrogance is particularly oblivious to the impact clean water and air, good sewage systems, mass vaccination and ameliorated social conditions have had. As American physician Nortin Hadler (2004) writes in The Last Well Person: “If anyone is tempted to ascribe the increased longevity in North America to past medical programs ... science tempers any such hubris” (11).

Since Pasteur, Koch, Jenner and others offered us the bacteriological model of disease in the 19th century, medical science has been inspired to believe that “medicine is ‘made’ in the laboratory”; yet medicine, suggests the respected epidemiologist Olli Miettinen in the CMAJ, is, much like farming, both an art and a science – or at least a “scientific art” (Miettinen, 2001a, 442). No matter how much we prefer to think of medical interventions as somehow “pure”, the messy human problems they deal with are not. Even evidence-based medicine (EBM) and its much-touted experimental foundation, the randomized clinical trial or RCT, cannot be said to be value-free or devoid of social
and cultural influence. Yet even a cursory read of medical texts, journals or guidelines demonstrates how awe-inspiringly staunch we tend to be with our prescriptions and proscriptions: Blood pressure and cholesterol counts must be lowered. Women should take hormones at menopause (or maybe not). Men need PSA testing for prostate cancer. Being overweight is a serious health hazard. A strong immune system is good. Are these true? At our current level of knowledge it is impossible to ascertain, but we assume they are, even with our, at best, vague ideas of physiology. Within the immune system, for example, thousands of activities and substances have been identified; yet our knowledge of how the system works in concert is woefully “reductionist and piecemeal” in the words of one immunology text (Unanue, 1995, 3).

Our failure to “distinguish between necessary and sufficient factors in the genesis of ill-health” has also distorted both its theoretical basis and the practice of medicine (White, 2000, 1905). This no doubt explains why the majority of auto-immune disorders such as multiple sclerosis (MS) and diabetes flummox our science as do dangerous diseases like AIDS or cancer, whose basic mechanisms and aetiology remain elusive. At present these are controlled and contained, “managed”, not cured, because we cannot satisfactorily explain how or why they develop (or why they develop in some people and not others). Even risk factors, the idea that certain signs are so directly implicated in an illness that merely controlling them suffices, have only been around for some fifty years, yet both medical and lay literature unthinkingly stress their importance (Arnowitz, 1998,

14 McDonald suggests that our “conceit is an extension of neurologic mechanisms that organize incomplete sensory data into a sensible whole” or is simply “a coping mechanism to give us a sense of control where otherwise we
notably around cardiac disease where blood pressure, cholesterol, diabetes, smoking, and weight control seem to have become more important than the disease itself. What few questions do get posed rarely concern context or examine underlying assumptions, but tend to revolve around possible biases (corporate interests, the merging academic and pharmaceutical company objectives, the need for greater “transparency”), with the subtext being that solutions lie in greater scrutiny and more rules or guidelines on how to comport ourselves. Overall, our focus is on the upper, superficial, echelons of the process and is rarely of the process itself.

**Only the Facts?**

This confidence assumes that medicine has not been shaped and formed by its historical and socio-cultural roots. However, as epidemiologist Jan Vandenbroucke points out in the 1998 lecture to the UK Royal Society of Arts, it is our ideas and theories on physiology and medical method that drive medical and other forms of research, not vice versa. In other words, we do not cast about looking to find “facts” which we can question and theorize about; rather, it is the theories and paradigms we hold which drive the facts we seek and study (Vandenbroucke, 1998b, 2003). By describing, side-by-side, studies on homeopathy and calcium-channel blockers (a blood-pressure lowering medication which has been somewhat controversial in recent years), he demonstrates that the data on both are equally compelling, or not, depending on one’s perspective. Yet the latter is part of mainstream practice and the former is fringe, suggesting that “data” and “facts” are not
the solid truths we have made them out to be but are fluid and open to interpretation. Facts contribute little to the beliefs underlying medical practice, Vandenbroucke argues. On the contrary, we interpret them according to what we believe:

I warned you about this thought experiment. We started out by stating that theories – stars in heaven, molecular immunology – were destroyed by facts [and scientific advances]. Now, we seem to have been led to the contrary: we believe or disbelieve the trial results because we believe or disbelieve the theory. (Vandenbroucke, 1998b, 2002-3)

It is nevertheless important to emphasize that the existing theoretical model has great resonance and to acknowledge that it has had remarkable successes. All of us have gained from medicine’s advances, and, as writer and professor of medicine David Morris writes in *Illness and Culture in the Postmodern Age*, the biomedical model has “continuing power” and deserves respect (Morris, 2000, 14). Morris warns against medical nihilism and this dissertation echoes that stance. This analysis does not seek to deny the existence of real physical illness or suggest in any way that medical practice is a chimera or sham – neither is it a rejection of medical progress. While it is true that medical science as it is practiced in the west has tended to exclude mention of older, “holistic” therapies in favour of perhaps questionable techno-scientific techniques and procedures, the intent here is to broaden the scope of the discourse, not dismiss it, while maintaining an understanding of the backdrop of uncertainty and flux medicine contains.

15 This would not surprise philosophers of science and social scientists, but appearing as it does in a medical journal – and in a prestigious one such as *The Lancet* – it is quite extraordinary.
There have been enormous strides made in medicine over the last fifty years and major steps have been taken towards eliminating, or at least controlling, many debilitating conditions and diseases from smallpox to stroke. The accelerating pace of medical change, however, has frequently eroded our awareness of its weaknesses. The distinction between “sick” and “well” has blurred and our social and ethical awareness of medicine lags far behind our technological prowess. In many ways medicine has become a victim of its own success – with the advances in treating acute illness and trauma blinding us to the many limitations and ambiguities there are, particularly in the realm of chronic disease and/or preventive medicine. Furthermore, too much medical discourse lacks nuance and maturity and sidesteps the deep roots North American medicine (in particular) has within the market economy and how complicated it has become to disentangle the commerce of medicine from its practice. It is nevertheless important to try. Medicine cannot be driven by the same paradigms as other aspects of the free market: “more is better” can be applied to many things (vacations, cars, refrigerators) but not medicine. Too much surgery, testing or medication use is in itself dangerous – the word “iatrogenesis” has been coined to describe harm caused by medical intervention, whether damaging scar tissue resulting from a necessary surgery to the side effects of medication.

Any negative sequelae that medical care has which in turn leads to a health problem, illness or dysfunction is iatrogenic and there is growing evidence that the harm of medicine can offset its benefits at various points (Baker et al., 2004). As professor of public health Peter Davis writes in the *CMAJ:*
According to estimates ... nearly 70,000 annual hospital admissions in Canada are associated with an adverse event that was preventable. Most are relatively minor but a good proportion (20.8%) result in death. The impact on an already overtaxed system is not to be underestimated.... The painful paradox is that by lavishing ever more care on our patients we may also be exposing them to a potential hazard. (Davis, 2004, 1688-89)

Davis adds that the more comprehensive, high-tech and elaborate the acute-care environment is, the higher the risk of adverse events – not because teaching hospitals or other high-tech, tertiary care settings are inherently dangerous places but because they are governed by “the unchallenged therapeutic imperative” that continually move patients to a higher level of intervention than they might be able to sustain (1689). This would suggest that a public health service that takes on the grandeur of an open-ended economic model affirming and advocating unfettered progress, total freedom of choice and unlimited options cannot, ultimately, be good for patients, however superb it might sound. It is this idea, to some extent, which has been the motivating factor behind restrictive formularies, although whether yet more institutional, broad-brush directives are the answer remains questionable.

At present, most policy decisions or clinical guidelines, whether on formularies or anything else, are based on data from evidence-based medicine (EBM). Therapeutic equivalence is predicated on the premise that “randomized clinical trials have shown that many drugs within a therapeutic class are equally effective and safe on average” (Bourgault, Elstein, Le Lorier, & Suissa, 1999, 255). But can EBM genuinely demonstrate this or are regulators and policy makers relying on a process that is itself open to question?
Evidence-based Medicine

Epidemiologists and other observers trace the roots of evidence-based medicine to 19th century Paris, “the triumph of numerical observation” and Pierre Charles Alexandre Louis (the founder of Médecine d’Observation). Louis demonstrated that blood-letting did not work for acute pneumonia and his methodological approach is considered the quintessential step for basing medical interventions on science, observation, empiricism and the “facts”. Like most stirring starts, the reality falls somewhat short: Louis did not compare two groups of patients (with or without treatment); he merely compared the time of bloodletting (early versus late in the course of the disease). His work also “contains disturbing arithmetic mistakes”, but he did nevertheless engage in a system of systematic observation vaguely similar to what is now considered medical evidence (Vandenbroucke, 1998, 2001).

The present interest in evidence-based medicine accelerated and gained acceptance as the realization grew that medical possibilities were increasing at an alarming rate and nobody seemed to know which interventions were genuine improvements. Hence, both private and public health insurance organizations, with tacit support from a public that understood the need to become more cost-efficient, decided that the massive costs involved in new technologies, screening and surgical techniques (many benefits of which were a matter of conjecture and convention versus proven practice) required greater scrutiny. Also of concern were the variations (geographic and
otherwise) in medical recommendations and treatments; after all, if there is a "right" and "wrong" way of doing things why is the right one not always done, and why does there seem to be such a range in everything from tonsillectomies to antibiotic use (Eddy, 1996, 2)? Health economists and statisticians were hired to assist in deciding which drugs and treatments were superior and worth paying for. Basing these decisions on the evidence (wherever it existed) gave the practice legitimacy and, as David Eddy, a surgeon, mathematician, and health advisor to Kaiser Permanente, a large American HMO, explains:

One well-designed policy – such as washing hands between deliveries – can improve the quality of care of hundreds of thousands of patients. Conversely ... a poorly-designed [one] can spoil the quality of care for just as many. A shift in a single policy – such as screening women younger than 50 years with mammography – can shift a billion dollars a year .... A statement in 1916 by a single practitioner that "once a cesarian always a cesarian" based on a single patient still dominates that decision. (Eddy, 21)

The less one knows about the effectiveness of a treatment the more important the burden of proof becomes, and in an uncertain field such as medicine the difference between "when in doubt, do it" or "when in doubt, stop" is major. According to Eddy, perhaps 80% to 90% of treatments "have not been adequately evaluated with controlled studies" (241).17

16 Except by the English who tend to hanker back to William Harvey (1578-1657), who demonstrated that blood, not air, flowed through the heart and veins.

17 This figure is from 1978 and comes from the US Congress Office of Technology Assessment. Whether this would still be true is unclear.
Further impetus for EBM came from influential groups such as McMaster University's Evidence-Based Medicine Working Group, headed for many years by the prolific physician and EBM guru David Sackett, leading to a dizzying number of articles on incorporating evidence-based medicine into clinical practice being published in major (English language) peer-reviewed medical journals. These made the phrase – and reverence for the double-blind, placebo-controlled randomized clinical trial – ubiquitous and one of the most overused, albeit persuasive, tools in the cost-cutting arsenal. Most clinicians did not at first take kindly to managers and administrators tinkering with their practices, but, over time, they generally capitulated, particularly since EBM made it easier to find which practices were total wastes of time.\footnote{Unfortunately, as will be discussed later, social, political and commercial considerations can often overpower the evidence.} Policy and consensus meetings were convened and evidence-based guidelines for treating various conditions were drafted (often funded at least partially by drug companies who were well aware of the value of having their drugs be "proven" effective). Today, as even a cursory glance at the Index Medicus or its electronic version, Medline, can confirm, evidence-based medicine has become a force to be reckoned with.

Evidence-based medicine, at its core, is eminently reasonable. The "conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients", EBM seeks experimental proof for various therapies, preferably from randomized clinical trials (Sackett, Rosenberg, Gray, Haynes, & Richardson, 1996, 71). The problem is that medicine does not deal in clean
abstractions or the pure application of logic gleaned from data; it is about individuals and their chaotic blend of problems which culminate in a medical predicament of some kind, out of which confounding elements must be subtly coaxed. Advocates of EBM profess to understand this:

In a widely quoted riposte to critics who accused them of naïve empiricism, Sackett and colleagues claimed that “the practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence … By individual clinical expertise we mean the proficiency and judgment that individual clinicians acquire through clinical experience and clinical practice.” Sackett and colleagues were anxious to acknowledge that there is an art to medicine as well as an objective empirical science but they did not attempt to define or categorise the elusive quality of clinical competence. (Greenhalgh, 1999, 323)

Clinical competence, however, is an “interpretative act” drawing on elusive and complicated patient narratives which must be blended with symptoms, test results, data and knowledge, and it is this sophisticated mix which often stymies EBM. Greenhalgh points out that evidence, guidelines, practice policies and other general rules rest on the “tenuous assumption that diagnostic decision-making follows an identical protocol to scientific enquiry” – in other words, medicine as “a science and the doctor as an impartial investigator who builds differential diagnoses as if they were scientific theories”, excluding competing possibilities in the same way the scientific method discards hypotheses based on experimental evidence and data (323). This assumes an independent and rational medical “truth” that is rarely, if ever, clinically possible. As Vandenbroucke points out in an essay on clinical investigation for *The Lancet*:

Subjectivity is inescapable. By subjectivity, I do not mean mere human capriciousness or even wickedness. Like most medical investigators, I
would strongly oppose the idea that truth is a mere market commodity. However, as at the bedside, scientific explanations in medicine are an integration of numerical (statistical and epidemiological – i.e., probabilistic and empirical) and mechanistic (deterministic and explanatory) reasoning. The one cannot exist without the other. ... At each point in time there is uncertainty. (Vandenbroucke, 1998a, S16)

Assuming that clinical reasoning follows the same lines as pure science also raises ethical questions:

[T]he limited scope and ambiguous nature of available evidence introduces various ethical concerns about the use of the evidence-based framework for decision-making. These concerns arise from the types of decisions to be made, the type of practice within which they are to be made, and the nature of the evidence available and required for decision making. (Culpepper & Gilbert, 1999, 829)

Culpepper and Gilbert add that the dearth of available studies often limits “the relevance of evidence-based medicine” since “activities likely to receive serious research attention” are often short-term ones which result in large unit costs and are therefore more easily measured (829). Paradoxically, using evidence in primary care can increase costs: Culpepper and Gilbert cite a National Institutes of Health conference that recommended routine CT scans for severe headaches; a practice, which, if implemented, could easily cost the United States up to $20 billion annually (830).

Disease classification, furthermore, is ambiguous even beyond the level of the individual patient. Is an occluded artery for which experts recommend cholesterol-lowering treatment a genuine illness or is it an angle on prevention relying on what some ethicists have called “risk factorology”? Is a tumour with cancerous cells found on a mammogram necessarily a diagnosis of cancer and is there any epidemiological evidence
that it will become dangerous? Even with an adequate breakdown of the statistics around the biology of the tumour, it is difficult to predict what a tumour will do in any given individual, and, as American epidemiologist Steven Goodman, interviewed in the July 2002 issue of *Discover*, points out:

> Previously we looked at the world in terms of people who were sick and people who were not. Screening technologies reveal a health state that is neither ... but could go either way. You get it biopsied and it looks cancerous, so you get treated. The problem is that we have no sure way of saying that the disease ever would have progressed into anything life threatening. (Goodman, 2002)

Goodman adds that some people “saved” by early detection have tumours removed that would never have given them any trouble in their lifetime.

> Even something as ostensibly simple as a cold can be ambiguous. Does a person with a virus who does not develop the usual symptoms from their immune response (sneezing, sore throat, malaise) have a cold? Certainly someone who gets that cold from them might think so even if the carrier does not. So what are the ideas, ideologies, heuristics, evidence and/or foundations for the underlying decision-making process and can we rely on their accuracy, whether on a personal or population level? The precise point at which one changes from “well” to “ill” from a personal perspective is complicated and has myriad social, cultural, familial and community aspects (Hardey, 1998, 29), and thoughtful clinicians understand only too well that clinical judgments are usually a far cry from any objective analysis of a set of eminently measurable “facts”. Knowing patients and their circumstances, understanding how one patient differs from another in anything from reporting or tolerating pain to medication use and being able to
interpret the totality of the situation is what allows clinicians to integrate the formal
diagnostic criteria of the suspected disorder (in other words, how the textbook or
guideline explains how a disease typically plays out) to the “case specific features of the
patient’s individual story” within their own accumulated professional expertise
(Greenhalgh, 1999, 323).

From a policy maker’s perspective, however, disease must be considered an
objective or “thing-like” quality (Hardey, 29). This standardization obscures individual
elements and personal and social narratives, transforming awkward ambiguities into
misshapen “facts”, primarily through statistics, which serve as the basis for therapeutic
equivalence. Yet the statistical models used to determine equivalence are themselves a
matter of consensus and convention, for example, whether the assessment of
“bioequivalence or therapeutic equivalence between treatments” is made between one
primary therapeutic result (endpoint) or several (Quan, Bolognese, & Yuan, 1999,
3160). This further complicates the usual problems and uncertainties arising from
medical statistics and exacerbates the difficulties inherent in using group generalizations
in making decisions about individual patients.

**Pharmacoeconomic Analyses**

British Columbia’s reference-based pricing program, now called the Reference
Drug program or RDP, instigated price controls based on therapeutic equivalence in

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*The majority of articles on equivalence appear not in the medical literature per se but in journals such as *Statistics in Medicine*. *
1995. On their web site, Pharmacare assures everyone that the purpose of the program is “to encourage cost-effective first-line prescribing for common medical conditions” and that the drug(s) in the formulary\textsuperscript{20} are “equally efficacious and the most cost effective in that category”. In perhaps too-plain language they go on to say, “Pharmacare obtains independent, expert advice on which prescription drug products within a group of similar medications are equally safe and beneficial, and the most cost-effective”. Patients who are covered (primarily the elderly or those with lower incomes) receive full coverage for the preferred “reference” drug or can pay the difference between that price and that of a more expensive non-referenced one if they prefer – unless their doctors’ reasons for a special exemption are approved and an exception is made.

The framers of this policy are of course absolutely correct in stating that these decisions are not made frivolously and that there is serious, expert input, which in this case is information from the Therapeutics Initiative (TI), a medically mixed group in the Pharmacology Department at the University of British Columbia (consisting primarily of pharmacists, pharmacologists, physicians, epidemiologists and one legal advisor), funded by the BC government.\textsuperscript{21} The TI was originally created to provide physicians with reviews and analyses of the latest research on treatments and has no official position on reference-based pricing. According to their explanatory September 1995 Therapeutics Letter, they are “at arms length from government and other vested interest groups”. Some

\textsuperscript{20} The formulary is more than a list of drugs that a hospital or other institution uses; it involves “complex processes and activities” and value judgements (Scroccaro, 2000).

\textsuperscript{21} The TI received an annual grant of $700,000 from the BC Ministry of Health in 2001, the latest year for which figures are available (Mail et al., 2001).
critics have complained that they nevertheless seem to ignore comments contrary to their position (Fishman, 2001). The Therapeutics Initiative merely responds that cost-benefit analyses emanate from their sister group, the Pharmacoeconomic Initiative of BC, also initiated in 1995, and the TI simply comment on new drugs and therapies and communicate their findings to clinicians and other interested parties.

Nevertheless, whoever makes these decisions, be it the TI or Pharmacare, New Zealand's Pharmac or an American HMO, faces the major obstacle of dealing with "imperfect information" (Weinstein & Stason, 1977, 716). Although it can be argued that this is simply part and parcel of the human condition (after all, when do we ever have perfect knowledge or information?), the methods and quality of reporting "applied to economic evaluations of health care" contain considerable "gaps", which means that "proper allocation of resources on the basis of economic evaluations remains uncertain" (Jefferson, Demicheli, & Vale, 2002, 2809). In addition, as a thorough examination of pharmacoeconomic analyses of submissions on new drugs to the Australian Pharmaceutical Benefits Scheme in The Journal of the American Medical Association (JAMA) suggests, all too often those in the position of instigating policy do not have the capacity or resources to analyze what data or information they do have. The researchers, who reviewed a total of 326 submissions, found that 218 (67%) had "significant" problems and thirty-one had one or more:

Of the 249 problems identified, 154 (62%) related to uncertainty in the estimates of comparative clinical efficacy, and 71 (28.5%) related to

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22 On their web site (www.ti.ubc.ca) the TI currently state that they "act as an expert resource" to Pharmacare.
modeling issues, which included clinical assumptions or cost estimates, used in the construction of economic models. (Hill, Mitchell, & Henry, 2000, p. 2120)

The authors write that while establishing “a formal link between measures of costs and outcomes” of drug therapy is an “appealing” approach in drug policy decisions, this becomes problematic in the “conduct and interpretation” of pharmacoeconomic analyses. While absolving researchers of any malicious intent, Hill et al. found many analyses to be “suboptimal and poorly designed”, making inferences on comparative clinical performance nearly impossible. No amount of statistical manipulation or “complex modeling techniques” could overcome these shortcomings, which where then reflected in policy decisions. The authors strongly urge caution, warning agencies using pharmacoeconomic data to fully appreciate “the intensity of the evaluation process” necessary to ensure that “decisions are based on accurate data” (p. 2121). The implication is, of course, that too few do.

Even agencies using identical data can come to different conclusions, resulting in diverse and divergent policies. This appears to be what has occurred in Canada intra-provincially:

Pharmacoeconomic evaluations are used in several provinces to evaluate new drug products seeking reimbursement eligibility from provincial drug plans, and pharmacoeconomic assessments must accompany all new drug submissions seeking provincial formulary approval in BC and Ontario. … A recent study evaluating the uniformity of coverage for prescription drugs among the Canadian provinces found that the overall level of agreement for funding decisions made in all of the provinces was very low … and below levels of significant concordance. Thus the existing pattern of access to prescription drugs is quite variable across the country …. (Anis, 2000, p. 525)
The appropriateness of the data used may also be questionable. Outcomes measured in terms of years of life saved, for instance, are irrelevant for programs or drugs that improve quality of life without extending it – and the lack of comparability of outcomes across trials makes it difficult to make balanced recommendations (Oliver et al., 2002, 1771). Another confounding factor in pharmacoeconomics is the "variability of the methods" used in conducting and reporting such evaluations (Jefferson & Demicheli, 2002, 2809). The positive bias of most scientific research, furthermore, regardless of funding source, also tends to skew findings: Studies with unfavourable preliminary evidence are less likely to be completed, less likely to be submitted for peer review, and, once submitted, less likely to be published (Friedberg, Saffran, Stinson, Nelson, & Bennett, 1999, 1456). As an editorial in JAMA suggests, no matter how well-intentioned, such analyses cannot help but contain major flaws, ranging from differing standards and benchmarks of comparison to extrapolation difficulties (Rennie & Luft, 2000, p. 2160).

There is also the matter of conflict of interest, a charge which not only has dogged the footsteps of research in general but equivalence in particular. Richard Lewontin writes that "no prominent molecular biologist of my acquaintance is without a stake in the biotechnology business" (Lewontin, 1991, 74), and ethicists have long criticized the enmeshing of corporate, scientific and other interests in medicine, agriculture and so on:

Increasingly, academic biomedicine has become commingled (sic) with corporate interests. Spurred by the burgeoning commercial opportunities of new discoveries such as those in genetics, the growth in academic-industry collaborations has created uneasiness among some observers who suspect that conditions beyond the pure facts of science can influence its outcome. (Krimsky, 1999, 1474)
However obvious it may seem, conflict of interest can be subtle and difficult to pinpoint. Some have even suggested that conflict-of-interest policies could be considered “ethically questionable”, impugning authors “with the implied accusation of wrongdoing without evidence and without recourse” (Krimsky, 1999, 1474).

**Conflict of Interest**

Conflict of interest is a set of conditions under which professional judgement on a primary issue can be unduly influenced by a secondary one. It is not a behaviour, as Richard Smith, the editor of the *British Medical Journal (BMJ)* points out, but a common condition with no inherent meaning: “There is,” he writes, “nothing wrong with having a conflict of interest.” Its mere existence is not an automatic indication of “wickedness” (Smith, 1998). He goes on:

Those who argue against concerns about conflict of interest say that science is science, methods are transparent, data either support the conclusions or do not, and it is neither here nor there whether researchers have, for example, shares in a company that manufactures a drug included in a trial. (291)

Recent evidence suggests otherwise. Many reviews have found authors with industry ties to be considerably more likely to report positive results for the drug or treatment in question. For example, in an examination of studies of blood-pressure lowering drugs (calcium channel blockers), some 96% of positive authors had industry ties compared to 60% of neutral authors and 37% of critical authors (Krimsky, 1999, 1474). An analysis of oncology (cancer) drug studies similarly found that drug company sponsorship of economic analyses of various chemotherapy agents was “associated with
reduced likelihood of reporting unfavorable results” and “contained qualitative
overstatements of quantitative results” (Friedberg et al., 1999, 1455). Another study of
150 cancer drugs that was published in the British Journal of Cancer found that industry-
sponsored studies were nearly twice (1.9) as likely to have “positive qualitative
conclusions about costs than studies sponsored by non-profit organizations” (Dobson,
2003, 1006). On the plus side, industry-sponsored studies were not found to be of poorer
quality than others. Surgical trials were also found to be affected by industry affiliations
(Bhandari et al., 2004, 480). Similarly, in a review of thirty studies based on a Medline
search, a study done by Lexchin noted, “trials sponsored by a pharmaceutical company
were four times more likely to show positive results for that company’s drug”.
Nevertheless, Lexchin’s observation was that drug companies did not deliberately set out
to deceive; rather, it was their decisions on “study design” which tended to “create bias”
(Barclay, 2003).

Drug companies, understandably, fund studies that will demonstrate positive
outcomes for their products (Hirsch, 2004, 481) and, unless one is careful to read the
“competing interests declared” section at the end of the journal article, the industry
affiliations of researchers are not always easily discernable. Of course, one could also
submit that the decisions on study design were made by individuals whose beliefs and
values were similar to those of the industry or other affiliation in the first place; since, by
the same token, studies funded by groups like Pharmacare or HMO’s, which have a
vested interest in finding the older, cheaper drugs to be as good or better, also make
decisions on study design and inclusion/exclusion criteria. Neither group can confidently
be identified as benevolently impartial, and both groups (unsurprisingly) tend towards those types of evaluation and trial method that are most likely to bolster their own position. Again, one is loathe to point fingers or lay blame, however the message for patients, especially, and clinicians, secondarily, is one of extreme caution. No matter how well-meaning or well-designed, studies are weighted along theoretical grounds towards finding those answers that most closely match institutional concerns, not those posed by patients or practitioners. *Caveat emptor* would seem as broadly applicable here as anywhere else.

Medical editors and others have suggested that greater transparency is key (Jefferson & Demicheli, 2002, 281); since “none of us is blessed with knowledge of our own motivations and mental mechanisms” (Smith, 1998, 292). But, in this age of burgeoning commercial opportunities and subtle industry-academy collaborations in everything from baby formula to pharmaceuticals, is more transparency necessarily the solution? The term transparency seems somewhat glib, implying as it does that merely adding information—more research, studies, databases, Royal Commissions and web pages—would make for better and more accurate analysis of outcomes. While the recent idea of posting all studies, at their inception, on a central web database and reporting results regardless of outcome or publishing status, could well facilitate researchers’ ability to track studies (*Economist*, 2004), given the sheer amount of literature there already is, how reasonable is it to assume that this will be of genuine value to anyone other than researchers?
Transparency, much like equivalence, is a vague term that lacks clarity and rigour and sidesteps fundamental questions of belief, process, definition or boundary. For, as Vandenbroucke’s analysis of homeopathy versus calcium channel blockers showed, our beliefs are the drivers for the facts we seek. They determine the value we then place on the observed results, and researchers, like the rest of the world, more easily perceive what they believe to be true and what they expect to see. Bias in terms of research topic, or what problems are deemed worthy of study, is also difficult to spot. Short of a Vulcan mind meld there is little recourse against belief or value systems. Vandenbroucke writes that even randomized clinical trials show a “willingness to please” (Vandenbroucke, 1998, 2003).

Bias may be overt or covert: it may consist of a series of minor exclusions (something one simply considers irrelevant) from the data or the research questions; it may be an inability to note information that conflicts with one’s own ideas about what ought to happen; it may be a faulty secondary analysis or a general rounding out of awkward numbers. Fundamentally, we are all disposed to focusing on what we think matters (Vandenbroucke, 2003). This lack of attention to things outside one’s current focus or experience is true inter- and intra-culturally, and it seems unlikely that calls to greater professionalism will appreciably alter its existence, for culture not only determines what we study but how we interpret and evaluate the results of that study.
Culture Clashes

In a rare cross-country comparison of medical practice throughout parts of the west, Medicine and Culture, the late medical writer Lynn Payer wrote that practices that go against the cultural grain are often rejected or dismissed out of hand. American medicine, in particular, is based on the appeal of the active, she suggested, be it a sentence, medical treatment or life in general. The primary focus is on progress, advancement, change: doing things. Any research that confirms that cultural worldview is therefore more readily accepted:

Even when American medicine leans toward the “gentle” therapies it does so using aggressive language, and the word “aggressive” is used so often regarding the screening, diagnosis, and treatment of diseases that one suspects it confers a particular psychological satisfaction. When American blood pressure experts announced [alternatives to drug therapy for hypertension], they urged that non-drug therapies such as diet, exercise, and behavior modification be “pursued aggressively”. (Payer, 1996, 126)

An American study which found gently-handled premature infants to have fewer complications, Payer wrote, did not result in recommendations for gentler treatment of neonates but merely called for more research. Had that study seen the light of day in France, which is doubtful since few countries read any other country’s research (28), its recommendations might perhaps have been followed – the French, while taking just as many drugs and being just as enamoured of treatment as North Americans, veer towards a less overt approach. For instance, recommended doses of common pain relievers like
acetaminophen (Tylenol) in France are roughly half what they are in the United States, Canada and Britain (Payer, 66).25

Furthermore, even within medicine, different specialties differ in ways that could be considered cultural. A comparison of recommendations for the treatment of prostate cancer, published in JAMA, noted that clinical judgement differed widely depending on what type of specialist one consulted. When approximately one thousand American urologists and radiation oncologists were asked what they would personally do if they were diagnosed with prostate cancer, 79% of urologists said they would choose a major surgical approach (radical prostatectomy) while 92% of radiation oncologists would opt for radiation treatment (external beam radiotherapy), a less invasive therapy. Patients could therefore expect radically different diagnostic recommendations and opinions as to what constitutes optimal management depending on which specialist they consulted (Fowler, McNaughton Collins, Albertsen, Zeitman, et al., 2000, 3217). Yet both groups of doctors agreed that surgery was far more likely to produce severe side effects, e.g., incontinence and sexual dysfunction. The authors point out that fewer than 25% of doctors in either specialty would recommend “expectant management” or watchful waiting even though patients appear to have an essentially normal life expectancy without aggressive treatment. Interestingly, when patients are asked their preferences and are

25 Of course culture is also fundamental to our understanding of the mechanism of disease. The Chinese idea of chi that western practitioners perplexedly acknowledge does work (at least with the more or less accepted practices of acupuncture and chi qong – which even Kaiser Permanente, the biggest HMO in the US, subsidizes for certain conditions) deals with pathways or “meridians” that simply do not match any known circuitry in western anatomy books. So is anatomy “real”? Is chi?
given comprehensive information on possible risks, the majority opt to do nothing and wait to see what develops (3222).

Pharmacoeconomic analyses utilizing statistical information gleaned from groups to make recommendations or to create guidelines also involve a culture clash of sorts. The logic of large numbers is not predictive of individual care, no matter how biologically plausible – and data, as Vandenbroucke discussed in his provocative lecture, are also subject to different influences. In the end, evidence-based reasoning begins “with the preconceived idea from which the experiment follows” (Vandenbroucke, 1998a:S-15). It is difficult, furthermore, for institutions to accurately reflect the values and ethics of the often diverse constituents they serve, particularly given the tension which exists between equity and efficiency (Maxwell, 2002, 1543). Yet individual patients are, in the end, the endpoint of all medicine and they are the ones to suffer the consequences should rules, guidelines or treatment recommendations be flawed or incomplete.

**Patients Deserve Better**

Until a few short years ago, hectoring articles in medical journals declared hormone replacement therapy or HRT (a bizarre term since increasing the level of hormones that are naturally waning is hardly a “replacement”) a necessity for any post-menopausal woman at risk of heart disease. “What’s the matter with cardiologists?”
scolded a Montreal epidemiologist in a 1999 *CMAJ* editorial (Grover, 1999, 42). In that same issue, researchers (Wise, Stewart, Liu, & Abramson, 1999) had noted that contrary to recent “Canadian and US guidelines” which advocate the use of HRT to “protect women with cardiovascular disease from secondary events”, only some 21% of women seen in a Toronto hospital cardiology clinic were documented users of HRT (Grover, 42). Of course since then the evidence has shown estrogen to be risky, even dangerous in some instances. But even without supporting data, such blithe disregard on the part of guideline writers for individual women’s values, symptoms — or their physical, psychological, emotional or financial tolerance of daily hormone treatment (or any daily medication) — would seem to suggest that group recommendations matter more than patients and that authoritative (or authoritarian) expert evaluations trump individual choice. This blind spot is rarely addressed in the glowing reports on evidence:

> Because evidence-based medicine ascribes the values inherent in its outcome measures, which commonly ignore the values most important to patients, its role in resource allocation and health services management must be recognized as that of a tool, able to enlighten decisions, but not as a standard by which decisions about the allocation of health care resources and crafting research agendas and priorities are made. (Culpepper & Gilbert, 1999, 831)

When patients are asked for their opinion, they often prove to be quite conservative and well cognizant of the vagaries of expert advice, as Canadian epidemiologists found in one of the rare studies that actually asks patients what *they* 24

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24 In all fairness to Dr. Grover and his hectoring, he attributed both women’s and doctors’ reluctance for HRT to “a healthy skepticism about medical dogma” and to the fact that at the time the evidence was entirely population-based and epidemiologic.
think. Blood pressure guidelines from different organizations were presented to a “random sample of 94 family physicians and 146 hypertensive patients” in Ottawa and Edmonton. However “well established” the efficacy of antihypertensive therapy might have been in the researchers’ minds, patients (to the researchers’ astonishment) overwhelmingly opted either for the lower doses or no drug therapy whatsoever “even when presented with risk profiles that would qualify for treatment under the Canadian Hypertension Society Guidelines”. Barring a very small sub-group (15% to 26% depending on the scenario) who wanted anti-hypertensive drugs no matter what, the majority of patients (up to 74%) differed sharply with doctors as to when they should take drugs. Patients’ “correlation with physician preferences”, the researchers wrote without irony, was “less than ideal” (McAlister, O'Connor, Wells, Grover, & Laupacis, 2000, 407).²⁵

Patients understand only too well that they are the ones who bear the brunt of it when experts become too enamoured of their own pet theories. They hear the list of potential side effects at the end of the American drug advertisements and usually read the sheet the pharmacist gives them. Patients also know they are the ones with the bother and expense of buying drugs and the ones to suffer adverse drug reactions. Yet, even in this ostensibly enlightened age, the very people most affected by clinical guidelines and policy decisions are rarely, if ever, consulted nor particularly central to the process. There is minimal research on how they might feel about said guidelines – or even the topics of

²⁵ Of course those patients who wanted the drugs might have had personal reasons for their choice, such as a family member having died of cardiac disease, versus faith in the guidelines.
There is, in fact, often a wide gulf between the agenda of the patient and that of the researcher (Tallon, Chard, & Dieppe, 2000), and, since there is little reason to believe that today's medical dogma will not become the basis for tomorrow's class action suit, it would make sense to revisit what passes for "fact" and examine those unbending guidelines to which the individual must adapt rather than the other way around. Unlike the climbing of Everest, apparently undertaken because the mountain was there, the mere existence of tests or screens or drugs cannot be considered sufficient reason to engage in them. Times and technologies may have changed but the inherent fragility of the human body has not.

Uncovering patients' opinions is neither expensive nor difficult - a simple questionnaire or interview will suffice. Charles Wright and his colleagues at the Centre for Clinical Epidemiology and Evaluation at Vancouver Hospital examined "small-area variations in the rates of elective surgical procedures" by asking 138 surgeons and 5313 patients who had undergone one of six surgeries (a total of 6274 operations) for feedback. Patients filled out health-related quality-of-life (HRQOL) forms pre- and post-surgery. Some surgeries, such as cataract removal, did not appear to appreciably affect patients' quality of life; while others, like hip replacements, offered massive and obvious benefits. Most surgeons, the authors dryly commented, "were not enthusiastic about this kind of evaluation" (Wright, Chambers, & Robens-Paradise, 2002, 461), yet such simple pre- and

26 Participatory Action Research (PAR) has emerged, slightly, in the social sciences but has not penetrated into medicine (White, Suchowierksa, & Campbell, 2004). Few medical researchers have even heard of PAR.
post-surgery questions (which cost approximately twelve dollars per patient) go a long way towards including patient values and opinions.

Wright et al. were "disappointed" by the lack of interest exhibited by many of the surgeons who seemed unaware that patient self-reports are "a more valid measure" than their own impressions (465). Equally important, factors that matter to patients such as mobility and recovery can be uncovered with such studies. The authors suggest that the "wide range of severity of symptoms and disability for which elective surgery was recommended raises questions about the appropriateness of some procedures" (465) (my emphasis). One might also question the expectations that individuals might have about the benefits of surgery and the general lack of discussion, medically, socially and generally, on the possibility of negative results (or how long it takes for post-surgical problems to abate and benefits to become noticeable). Incorporating quality-of-life assessments in clinical practice could well facilitate doctor-patient communication and "heighten physicians' awareness" of what their patients might be expecting and experiencing with only a "modest" investment of time and personnel (Detmar, Muller, Schornagel, Wever, & Aaronson, 2002, 3027).

The extreme focus on, and centrality of, the randomized clinical trial in recent years, however, has lessened interest in other kinds of research, be they simple evaluations, such as the one described above, or observational studies, case histories or repeated therapies observed on one person (n of one). Yet these can be important,

*27 Versus roughly $800 for a cataract surgery according to the 2004 BCMA fee schedule.
according to an article in *The Lancet*, for identifying “large adverse effects of treatment on infrequent outcomes (i.e., rare but serious side-effects) that are not likely to be related to the indications or contraindications” of the treatment of interest (MacMahon & Collins, 2001, 455). Such information, which can assist in generalizing from clinical trials to clinical practice, is often of great interest to patients. Currently such research is often relegated to second-class status in comparison to the RCT, yet most treatments, write Collins and MacMahon in a follow-up article, have a serious down side, and “most claims for big improvements turn out to be evanescent”. The reliable assessment of “more moderate effects of treatment on major outcomes” – which are more realistic – requires unbiased studies that control error and include “large numbers of deaths or some other relevant outcome” to be meaningful, but at present medicine lacks these studies, which has “led to many premature deaths and much unnecessary suffering” (Collins & MacMahon, 2001, 373).

Furthermore, few studies are conducted to examine low-tech interventions that strongly affect patients’ lives and which patients report they would like more information on, such as physiotherapy, massage, exercise, rest, complementary therapies, diet advice and the like (Rogers, 2002, 96). Although lip service is paid to the “centrality of the biopsychosocial” model, it would require “academic, political, scientific and social will to change the emphasis and content of medical research and education” (White, 2000, 1905) (my emphasis). In addition, patients truly value good communication – far more than most health professionals and policy-makers realize. The lack of “adequate, good quality information is the most frequent complaint” patients have, writes British patient advocate
H. Thornton, a frequent contributor to British medical journals. The "reality of the intense commitment brought by involved consumers" can come as "a shock" to health professionals "when it impinges on areas hitherto believed to be sacrosanct to the medical profession" and requires "people of maturity, vision, sensitivity, humility and tenacity" (Thornton, 2001, 73). Thornton calls for patient involvement at early stages and in the design of research trials so that hypotheses and protocols may be made more relevant to patient needs. Another British advocate, Jean Robinson, who was instrumental in the formation of Britain’s Association for Improvements in Maternity Services (AIMS), also urges caution:

Too many research projects come to a premature and unsatisfactory end, not because statistical analyses show that it is unnecessary or unethical to continue, but because they were ill-conceived and badly planned in the first place. It is both unethical and wasteful to use patients as research material in such projects. (Robinson, 1994, 1473)

It would appear that many studies (and too many policy decisions based on those studies) consider patients and their wishes an unaffordable luxury – or worse, as irrelevant. Yet "patients and healthy volunteers continue to participate in research that may be of limited clinical value", not realizing that their participation may never be noted or used, particularly given the sheer number of "underpowered" clinical trials (Halpern, Karlawish, & Berlin, 2002, 358).

28 I found this to be true in my own medical writing career. Almost all the patients I interviewed were eager to pump me for information on everything from hormones to surgery.
Dialogue with patients is consistently undervalued within the research and scientific community, yet communication is more than a mere abstraction for patients and may affect outcomes. A Swedish study that examined the effects of bad news (about cancer) on patients found that “the physician’s communicative style affects the patient’s psychological adjustment and satisfaction with the care she/he receives” as well as the extent to which subsequent advice is trusted and followed. Patients value “contact and continuity” and good information and require time to absorb complicated medical input (Salander, 2002, 726). Inconsistency upsets patients and, “simply stated … information about treatment relieves the diagnostic burden” (728). In fact, the style of communication and the presentation of information can matter more than the information itself: often doctors’ “humaneness” matters as much to patients as technical competence (Mead, Bower, & Hann, 2002, 285).

How well and how fast patients recover is also associated with subjective feelings: A systematic review by a group of Toronto researchers found that the relationship between patients’ recovery expectations and health outcomes was “consistent with evidence that feelings and perceptions may profoundly affect biological disease processes through behavioural and non-behavioural mechanisms” (Mondloch, Cole, & Frank, 2001, 177). The same group of researchers compared injured workers’ recovery expectations with outcomes and noted that expectations provided “useful information on

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29 A physician who had read one of Mrs. Robinson’s letters to The Lancet simply couldn’t believe she was a lay person given her “degree of scholarship and understanding”. Clearly, he thought, the letter must have been written for her “by a doctor with an extensive knowledge of the literature”. Some “wee cowering timorous obstetrician, sheltering behind the skirts of the Chairman of the Patients Association,” suggested Mrs. Robinson in her mischievous response (Robinson & Cox, 1975, 1242).
the complex process of recovering from work-related soft-tissue injuries” (Cole, Mondlock, & Hogg-Johnson, 2002, 749). The more positive workers returned to work sooner and felt better faster, even with the severity and nature of their injury factored in. Other influences on recovery time were previous experience, vicarious learning, verbal persuasion and social support (Mondloch et al., 2001, 177). How patients feel matters medically.

Zelda Di Blasi and her colleagues examined these subjective feelings or “context effects” in a review published in *The Lancet* and also found them of therapeutic importance. What struck them most, however, was the lack of interest in such types of research and the dearth of studies:

Vast amounts of energy and resources have been spent to advance diagnostic tools, and pharmacological and surgical treatment. The lack of attention to the more humane aspects of care, alongside increased specialization and shortened consultation time, could have ... affected our understanding of its effects. (Di Blasi, Harkness, et al., 762)

On a pragmatic note in this litigious age, it is noteworthy that there were significant differences in “communication behaviors” between physicians who were sued and those who were not; a study published in *JAMA* identified “specific and teachable” communication styles which were associated with fewer malpractice claims (Levinson, Roter, Mullooly, Dull, & Frankel, 1997, 553). It is not even necessary (or relevant) that clinicians genuinely care about communication, as sociologist David Mechanic bluntly states, but merely that they have and use the necessary “interactive tools”: 
We can, however, develop organizational skills that help people behave like good people and avoid incentives and systems that result in adverse events. … Such social technologies must build on the exercise of technical and interpersonal competence, and a willingness to be an advocate for patients’ needs while also responsible in the use of limited resources. (Mechanic, 2002, 466)

Neither funding nor research interest, however, tends to be available for such non-quantifiable aspects of care and patients’ feelings only seem to matter in a negative sense, namely their conforming with treatment recommendations. As a JAMA review of RCT’s which examined regimens designed to increase “patients’ adherence to prescribed medications” (often called compliance) points out:36

Such regimens fulfill theoretical, physiological, and empirical considerations about optimal care, while ignoring practical patient-centered concerns, such as the nature, nurture, culture, and stereotyping of the patient, and the inconvenience, cost, and adverse effects of the treatment. Indeed, low adherence with prescribed treatments is very common. Typical adherence rates for prescribed medications are about 50%, with a range of 0% to more than 100%. (McDonald, Garg, & Haynes, 2002, 2868)

**Adding Nuance**

Yet in the end, it is the patient who determines what drugs or treatments s/he will consent to and, by extension, what costs the system will incur. As a survey of visits to a Toronto family medicine clinic found, “the mean number of visits increased with worsening self-perceived physical and mental health” (my emphasis). Patients’ “perceptions of their own health” were associated with “frequency of use of health care

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36 The terms “adherence” or “compliance”, with their coercive overtones, are themselves somewhat disquieting.
services” (Finkelstein, 2000, 45). Perhaps cost-cutting enthusiasts should look again.

Similarly, oncologists in the United States who studied terminally ill cancer patients noted that patients’ own estimation of their chances were the primary influence on the treatments they chose (Weeks, Cook, O'Day, & Petersen, 1998, 1712). “Enhanced communication”, the researchers suggest delicately, could perhaps help patients make better and more informed choices and diminish suffering at the end of life:

This suggests that it may be quite possible both to maintain patient hope and to provide sufficient prognostic information so that patients would be able to make treatment decisions consistent with their underlying values. (1713)

It is often assumed that the “objective” measurements of dysfunction or disease are more valid than what patients say or feel, yet, in a longitudinal survey of patients beginning a new therapy for chronic arthritis, researchers concluded that patients’ “retrospective perceptions of change” consistently measured change more accurately than lab results (Fischer et al., 1999, 1159) and this resulted in higher compliance with treatment, greater satisfaction and generally helped in maintaining a continuum of care (1162). Other observers and clinical researchers have also found patient perspectives important, in particular “as an aid to complex patient management” (Bausell et al., 2000).

Patients, furthermore, perceive illness (and invisible biomarkers such as cholesterol readings or blood pressure) very differently and there is “often a discrepancy between seemingly objective biological or imaging data and the patient’s symptoms or functioning” – for example between individuals’ serological results and their own sense of wellbeing in rheumatic disease or low back pain (Fischer et al., 1157). Yet few
researchers or policy experts seem aware that patients' instincts are quite good when it comes to the success of various treatments, as good as that of physicians much of the time (Lee, Fairclough, Antin, & Weeks, 2001, 1034). It often seems as though they have forgotten that there are real people out there to whom their conclusions apply — and that any risk resulting from their decisions is borne by the patient, not the decision-makers themselves. This disconnect is rarely addressed.

Moral hazard is a term used in economics (and which will be discussed at greater length in a later chapter). It is an off-shoot from the language of insurance and is used to describe the dangers of decision-makers not being subject to the consequences of their actions. Equivalence and the guidelines and regulations derived from them qualify as moral hazard issues: Few people involved in the many studies, reports, evaluations and other aspects of validating and regulating the material on equivalence would themselves suffer the consequences of their decisions. It is doubtful whether anybody at a research centre, pharmaceutical company, university or government agency would have to switch to a lower-priced medication if the reference drug did not suit them. Neither are they in a position to actually see, or have to deal with, any unhappy or sick patients.31

This dissertation uses equivalence as a starting point for questions requiring research and discourse with depth, breadth and quality — versus the reductive models so common today. Over the past decades, as our options in medicine have increased, expert and institutional voices have become louder, deafening even; meanwhile, patients and

31 Plus, if anyone gets sued it is the doctor and nurse, not the administrator or researcher.
those subject to what Foucault called “the medical gaze” seem to be consigned to silent sidelines. So while it is perhaps true that, at present, cost-cutting formulary restrictions based on therapeutic equivalence might seem like a valid health policy route, they nevertheless represent an approach to health and health care that is technocratic and reductionist. Such institutional and policy directives and guidelines have become so common, however, that personal, social, cultural, political, economic, linguistic and other narratives of illness have begun to appear incidental. Yet medicine, which has been called both an art and a science, a practice as well as a form of analysis and research, lends itself particularly well to the separation of its theoretical and empirical elements. It would not be that giant a step to broaden the context in which it is practiced and discussed. In her weighty, feminist-inspired analysis of scientific method and practice, *Science as Social Knowledge*, Helen Longino argues that it is possible to apply social analysis to science while considering both context and empiricism – moving from what she calls:

...the negative goal [of] rejecting the idea of value-free science [to] a positive one, developing an analysis of scientific knowledge that reconciles the objectivity of science with its social and cultural construction. (Longino, 1990: 215)

In other words, to create a model that contains scientific and biomedical questions but also shades in the contextual, social, cultural and other values and ideas which play a part in medical practice.

There is more to health than medicine. How else to explain differences in health and longevity between the wealthy and the poor? Canadian women have a life expectancy at birth of 81.8 years; a woman in sub-Saharan Africa anywhere from 31 to
49.9 years (Economist, 2003). Even in a developed country such as Canada, poverty is a leading cause of illness, for example, cardiovascular illness (Williams, 2002). It is not merely the fact of poverty that affects illness but the size of the gap between rich and poor. As Hadler writes:

There is an incontrovertible relationship between socioeconomic status (SES) and longevity. But do not be misled into assuming the SES is simply a measure of income status. Longevity is more dependent on how poor you are relative to those who are advantaged in your particular ecosystem. The greater the gap in income between rich and poor (the “Robin Hood index”) across states in the United States, for example, the greater the decrease in longevity of the poor. (Hadler, 2004, 11)

That socioeconomic and educational status are major determinants of health is currently a minor aspect (at best) in the terminology of medicine, which is dominated by narrow discussions on risk factors for cardiac disease, or when and how to screen for cancer, versus the impact one’s overall well-being or general circumstances might have on one’s health. Asking whether this drug or treatment reduces cholesterol or blood pressure, and which is “equivalent” to another, is hardly on par with asking what made this individual sick in the first place. The latter could well involve broad questions of housing; work; social, educational and clinical support; breathable air; reduced pesticide and fewer chemical residues and a host of other factors; the former relies on technical and statistical analyses derived from broadly comparable groups given a drug or other treatment.

32 Or even if they are sick. Pursuing symptomless individuals in order to prevent potential future illness is a peculiar perspective on treatment – one specific to our time. More on this in later chapters.
Rules, guidelines and policies, therefore, not only affect the way we perceive and frame the problems we have in health care but are instrumental in creating borders and a sense of what "fits" diagnostically and therapeutically. Much like the term equivalence itself, the implication is that, at its root, medicine is quantifiable and manageable.

Arnowitz (1998) writes:

Proponents of practice guidelines assume that variation in medical practice generally reflects poor quality care, as is generally held to be true in industrial production. The success and practicality of such guidelines, typically formulated as an algorithmic approach to patients with a specific problem, ultimately depends on the degree to which clinical reality can be adequately understood as a set of uniform and predictable encounters between patients suffering specific ailments and physicians who apply specific diagnostic and therapeutic technology and practices. (184) (my emphasis)

People are not units of production and we all intuitively grasp that, yet we rarely question the authority or logic of the thrust of medical discourse as it has evolved.

Equivalence, an easy term with little drama to it, juxtaposes our gaze from the patient, the person, their suffering and their life circumstances to the illness, condition, syndrome, diagnosis and the medical intervention commonly prescribed, the treatment trajectory embarked upon. In that process, patients (and clinicians) are marginalized; patient characteristics shunted to the side and dismissed as "context effects"; the doctor-patient relationship and the specific circumstances of the sick individual consigned to the "placebo effect". This dissertation maintains that these contextual elements – social cultural, personal and medical – deserve greater focus than they currently have and ought, at the very least, to be included in the discussion.
Medicine lacks strategies for integrating subjectivity and doubt and our policy decisions reflect this. Even Herodotus, *circa* 400 BC, recognized that the patient-doctor relationship mattered and that the it was not only the medicine given but the whole atmosphere in which therapy was instigated that made a difference (Di Blasi, Harkness, Ernst, Georgious, & Kleinjen, 2001, 357). We may be light years away technologically and scientifically from the ancient Greeks, yet our essential humanity has not changed. This work introduces qualitative, philosophical and complex questions into a single policy concept, therapeutic equivalence, and argues that current enthusiasms for numeric reasoning and reductionist thought have unduly de-emphasized the human, social and cultural dimensions of illness and medicine. At the centre of this work – as at the heart of medicine itself – is concern for patients and the diminishing value placed on them as individuals, their values and expectations, as well as a lack of respect and understanding for the myriad uncertainties and ambiguities fundamental to medical practice.
II. On Cost, Classification and Class

Perhaps the most fundamental dilemma facing modern medicine is contained in the notion that health resources can be rationed on the basis of cost. Obviously, health resources are scarce and there is a need to use them wisely. But can the ancient injunction to ‘do no harm’ be equally and simultaneously applied to the patient, the taxpayer and society as a whole, without one or other coming off the worse for wear? (Thomas, 1999, 535)

Medical “facts” reside in complex surroundings where multiple explanations and ambiguities abound both in their application and interpretation. Yet over the last decades, writes physician and author Alvin Tauber, we have witnessed a widening gulf between medicine’s technocratic advances (somewhat quantifiable ones such as efficiency, efficacy, cost-benefit analysis) and human concerns such as ethics, sociology, politics, culture and psychology (e.g., the relationship between doctor and patient, the appropriateness and value of interventions, and so on). The “debate is a classic case of rationing and risk taking”, finding a balance between what is available and funded and what can reasonably be excluded without creating undue risk. All too often both “proponents and critics base arguments about policy on fragmentary data, unclear facts, and incompletely described outcomes” (Tauber, 1999, 18).

At present, the most compelling narrative driving Canadian and many other national health systems concerns spiralling costs, with the focus often on drugs, the
fastest-growing segment of health care expenditures. Yet even the widespread use of economics to evaluate drugs, what UBC health economist Robert Evans has called the "pseudo-discipline" of pharmacoeconomics, has not appeared to appreciably decrease expenditures. But, as Evans cynically notes, "There are a lot of drugs, and there is a lot of money, so the 'field' is booming." Evans criticizes pharmacoeconomic analyses because they overlay a "procedural solution" onto what is "fundamentally a structural problem" (Evans, 1995, 59), however most observers, such as the editors of JAMA who devoted an entire issue to pharmacoeconomics, reluctantly concede that pharmacoeconomics, appropriate or not, is here to stay (Rennie & Luft, 2000, 2158).

The Business of Drugs

Worldwide spending on pharmaceuticals in 2002 exceeded $400 billion (US), and if, as "optimists" in the drug industry foresee, current trends continue, global expansion will continue at a rate of roughly 10% annually (Taylor, 2003, p. 408). In Canada, drugs now represent the second largest category of health expenditures after hospital services (Schneeweiss, Soumerai, Glynn, et al., 2002, 737), yet experts warn that the forecasting of pharmaceutical costs is complex and merely examining present or past numbers is insufficient for accurate extrapolations. Observers of the pharmaceutical industry note that future medications will probably not have the same staying power or widespread markets as current ones, and that business models "underpinning the mainstream

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33 In Canada, somehow even more expensive medical technologies (MRI's, CT scans, mammography) do not seem to engender the same kind of dismay. Whether that has to do with our cultural reverence for machinery or how we perceive value is an interesting social question.
pharmaceutical industry since the 1950s will have to be restructured” (Taylor, 408).

Advances in genetics and immunology are also cited as reasons for future drugs and therapeutic models being fundamentally different; for instance, advances in pharmacogenetics might make it possible to target drugs more accurately through genotyping (identification of a person’s genes). Depending on chromosomal genes reflecting inherited characteristics, drugs could, in theory, be tailored to improve drug concentrations, absorption, distribution, metabolism and elimination, leading to more effective, patient-specific drugs – which would no doubt be quite expensive. (This type of genetic research is not the same, incidentally, as the disease-specific mutation testing which has received a great deal of publicity and which refers to altering the gene believed to be responsible for a single-gene disease, e.g., sickle-cell anaemia or Huntington’s.)

What pharmacogenetics would rely on would be “polymorphisms in drug metabolism enzymes and drug target genes” (Roses, 2000, 1360), or disease-specific markers within a single individual. Already some women with breast cancers whose pathogenesis is estrogenic have been identified as a specific group to be targeted and, conceivably, further refinements could pinpoint the hormonal mechanisms more subtly and considerably reduce adverse drug reactions (Meyer, 2000).

The current increases in drug spending, according to the American Society of Health-System Pharmacists, can – somewhat obviously – be attributed to several factors, from numbers of users, to days of therapy and/or dose per day of therapy. Growth in prescription drug expenditures has nevertheless “moderated after years of significant increases” (Hoffman, Vermeulen, Hunkler, & Hontz, 2004, 145) (my emphasis). At
present, patent expirations and fewer genuinely innovative drugs partly explain this, but
the decline is also attributable to regulatory efforts and moves to increase cost-sharing
between patients and insurers. As a result, over the last decade, much, if not most, of the
payment has been shifted away from institutions and onto the patient (Hoffman et al.,
145), who may choose not to take that drug for personal or financial reasons. (Also, if
paid for out-of-pocket, that cost would no longer appear as a health care expenditure.)
The Canadian Institute of Health Information (CIHI) estimated in 2003 that of the $577 that
the average Canadian spent on drugs, public drug benefit programs paid $209, the
private sector kicked in $152, and $216 was paid out of pocket. So it is not actually drug
expenditures which are less but the amounts health care plans will pay (CIHI, 2003),
though, as a commentary in The New England Journal of Medicine (NEJM) points out,
this carries a high social cost:

The soaring cost of prescription drugs has caused two interrelated
problems – the expense for those who can afford to pay for them and the
limited access to medications for those who cannot. (Steinbrook, 2002)

This tends to be most severe for the elderly and for those with chronic illnesses, as a
report from the Manitoba Centre for Health Policy explains:

High-cost users (of drugs) were more likely ... to have underlying chronic
physical conditions which required medication therapy. Forty percent of
high-cost users had hypertension, 25% had diabetes and 6% had peptic
ulcer disease. ... They were also more likely to have mental health
conditions... High-cost users were also higher consumers of other health

34 According to data from the Romanow Report some 300 million prescriptions are filled in Canada each year
(though that does not necessarily mean that these drugs are taken). According to the Canadian Pharmacists
Association, we may know how much we spend on drugs but not how much we are “wasting” (Romanow, 2002,
194).
care services. They had a greater number of physician visits, were hospitalized more often and stayed in hospital for a longer duration. (Kozyrskyj, 2005, ix)

The same report adds that 40% of high-cost users had more than one major medical condition and over 85% used six or more medications. Overall, this group generally also (predictably) had poorer health outcomes (ix).

Recent History

When Medicare was introduced in Canada during the post-war years, and later expanded in the sixties and seventies, drug therapies were not the major issue so much as acute and hospital care. Drug therapies consisted of a few analgesics (pain medications), antibiotics, cardiac medications, a few anti-psychotics and a handful of other remedies, some of which are no longer prescribed. Others are used differently, as social definitions and dimensions of both illness and treatment have altered with time. For instance, amphetamines are no longer prescribed as diet aids or “pep” pills but are given to children diagnosed with attention-deficit-hyperactivity disorder (ADHD). The drug industry was young fifty years ago, since it was only in 1897 that Germany’s Felix Hoffman added a few atoms to a substance extracted from willow bark and created aspirin – and Bayer, a small dye-maker, became the first modern pharmaceutical company (Carr, 1998, 3). Today even a cursory glance at the Health Canada web page devoted to drugs reveals hundreds of sub-groupings of antibiotics, anti-spasmodics, anti-virals, and a host of other anti’s. Similarly, the Canadian Pharmacists Association Compendium of Pharmaceuticals and Specialties (CPS), the big blue book released
annually to medical professionals and used as the major Canadian drug reference, is in its 39th edition at nearly two thousand pages. Containing information on everything from anti-rejection drugs for solid organ transplant recipients to aspirin, the weighty CPS delineates what the drug is, what it does along with dosing and side effects.

Pharmaceutical policy in Canada is set both at the federal and provincial levels. Intellectual property rights (patents) and the “initial approval and labelling” of prescription drugs is federal, while the provinces hold jurisdiction over, and are responsible for, funding. According to Anis:

One key failing of the system is that the federal government is almost completely insulated from the impact of its policies because, although it regulates drug prices, it does not buy any drugs. In contrast, provincial governments have no jurisdiction over market competitiveness or pricing, yet end up paying for most of the drug expenditures incurred. (Anis, 2000, 523)

There is currently enormous variation inter-provincially in terms of how (or whether) patients are reimbursed for drugs. Outside the extended health insurance provided by many employers, Newfoundland and Saskatchewan cover the fewest number of drugs (yet include more drugs in their formularies than any other province) while BC and Ontario have the closest ratio of covered to non-covered drugs. Based on data from 2000, the last year for which comparable data are available, CIHI reports that the proportion of prescribed drugs financed by the public sector varies from 32.1% in Prince Edward Island to 53.7% in BC (CIHI, 2003). But, as costs rise across the board, more

\[35\] Literally. The CPS must weigh at least five kilos.
restrictions will no doubt be initiated and patients will find themselves responsible for increasing portions of their drug bills. The integration of private with public insurance seems to be the primary predictor of formulary exclusions (Anis, Guh, Rahman, & Wang, 2001) and provincial governments, which tend to subsidize the cost of prescription drugs primarily for seniors or people on social assistance, are as happy to shunt costs onto the individual as are private insurers in the United States and elsewhere. And if the Romanow report recommendation of a nation-wide drug plan forges ahead, cost-containment issues around drug reimbursement will be front and centre of the health care debate for years to come.

**Drugs of the Future?**

For the last five years or so gene therapies and their extraordinary possibilities have been the glamorous *leitmotif* in many discussions on what the future holds pharmacologically. So what of those magnificent new gene therapies whose virtues have been extolled by magazines, newspapers, television and radio shows as the Genome Project drew to a close in 2001? It turns out they may not be quite the panacea they were thought to be. As David Melzer and Ron Zimmern of Cambridge University point out in the *BMJ*:

In the public imagination genetic science has already brought us close to a world in which tests and cures are available for most diseases. The immediate prospects are, however, decidedly more prosaic.... The genes that play a part in the pathogenesis of most common disorders are for the most part as yet unidentified and their role ill understood. Individually their predictive value is low, and at present there is little to suggest they will have any greater clinical value than more conventional physiological
risk markers. We believe, as do others, that the arguments for “genetic exceptionalism” – for treating genetic information and tests as somehow special – are not compelling. (Melzer & Zimmern, 2002, 863)

They question both the medical and social benefits of allowing genetic technologies in a climate in which the borders of disease have become grey and blurry:

Over time, the tendency has been to expand diagnostic and treatment boundaries, and to include in the “disease” category people with milder manifestations of pathology and lower levels of risk. Genetic tests for markers that may not result in symptoms for half a century or more could be new examples of a process of premature medicalisation – of attaching the “disease” label before it has been established that prevention or treatment is clearly beneficial. Treating the presence of a genetic marker as though it were the clinical disease can be very unhelpful. In haemochromatosis, less than 1% of homozygotes for the responsible genetic variant develop frank clinical manifestations. (863)

But once a technology has been developed, particularly one that has had as much fanfare as the Human Genome Project, it is natural for people to want to exploit it commercially – and, given the enormous investments these genetic advances have required, the claims tend to be more grandiose and exuberant than most. Sober critics suggest that even should the ethical and social problems be dealt with, gene therapies are unlikely to be of clinical interest since current theories and techniques are too crude to deal with the complexities of disease. Gary Nabel of the US National Institutes of Health compares the hype around genetics to the enthusiasm with which monoclonal antibody techniques were greeted in 1975. The early promise of these techniques was slow to

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36 A disease in which individuals develop abnormally high levels of iron in the blood stream.
37 With the discovery of radioactivity came similar claims of miracle drugs, but they lost their lustre as the lethal effects of radioactivity began to be felt. The death of American tycoon E.M. Byers in 1932 from radium poisoning ended the hype (Melzer & Zimmern, 864).
materialize and fraught with technical problems. “Worse,” writes Nabel, “it became evident that the first-generation antibodies derived from mouse hybridomas were themselves subject to immune responses that limited the efficacy and duration” of their therapeutic effect (Nabel, 2004, 136). In other words, human immune systems reacted to the mouse-engineered substances, further demonstrating just how individual and idiosyncratic living organisms are. Nabel suggests gene therapies will encounter similar difficulties (137) but holds out more hope for immune modulation (vaccines, e.g.) that, conceivably, could lead to treatments for cancer, Alzheimer’s, even atherosclerosis (138).

Research into HIV and AIDS has stimulated long-dormant research into the immune system and it seems biologically plausible that modulating and “retraining” immune responses could solve some chronic problems, many of which are auto-immune in origin (e.g., rheumatoid arthritis, lupus, MS, diabetes, Addison’s Disease and so on). We may, in future, even be able to “desensitize” transplant recipients to donor organs, reducing the need for strong (and expensive) immune-suppressant drugs (Baxter & Lane, 1999, 35) such as cyclosporine. Whether this would be financially feasible is another story. Unlike current “blockbuster” drugs such as antidepressants (e.g., the selective serotonin reuptake inhibitors, or SSRI’s, like Prozac and its ilk), the cholesterol-lowering statins or antihypertensive treatments, newer drugs may have to be narrowly targeted compounds intended for relatively small groups of patients. For years there has been talk of a cancer vaccine, for instance, but using an individual’s own tumour markers to create

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38 The process involves fusing B-cells from the spleen with dividing cancer cells to create an antibody-generating “hybridoma”. Monoclonal antibodies were used for David, the “Bubble Boy” with SCIDS, and have been used
an "antigen" of sorts would be highly specialized and expensive and it is difficult to imagine who, other than the very wealthy, might be able to afford it.

Already, even without individually tailored genetic or immune therapeutics, corporate, social, economic and political factors have affected the productivity of brand name pharmaceutical firms. Large mergers in recent years have led to sharp reductions in research and development, and observers note that "productive lines of inquiry have been abandoned because their projected benefits failed to meet the expectations of incoming accountants" versus the "hopes of incumbent medical researchers" (Taylor, 2003, 408).39

Drug companies’ major reliance on the United States as a primary market (nearly half of all global earnings in pharmaceutical sales come from the United States) may also backfire, as Americans realize – and react to – the fact that they are paying more for drugs than any other country.

Reference Pricing and Therapeutic Substitution

All prescription and many over-the-counter drugs on the market today are considered to be members of certain existing drug classes, but determining class inclusion is no simple matter:

The criteria for membership in a class vary from class to class. For some, specific biochemical properties such as the ability to block a particular enzyme system may be the defining characteristic .... For others, the effects of a drug on the organs of animals may be required. The oestrogens (with varying degrees of success) in other immune-suppressed individuals.

39 Drug companies are now some of the largest financial entities in the world. The drug company Pfizer, for instance, is larger than Sweden (Freemantle, 865).
are defined by their ability to induce uterine growth and vaginal epithelialisation in rodents. Certainly, this broad and heterogeneous approach to the grouping of drugs has many advantages and is useful for teaching, drug development, and marketing. (Furberg, Herrington, & Psaty, 1999, 1202)

As pragmatic as this classification system might sound, the authors, all frequent clinician commentators on therapeutic equivalence and reference pricing, warn that simple membership in a class fails to address many salient points such as potency and unrelated drug actions such as the pharmacodynamics of the drug or its actions on the body. (Pharmacokinetics, or how an individual’s physiology interacts with and responds to the drug rarely figures in the discussion.) There is generally little, if any, agreement as to what constitutes a class effect. The U.S. Food and Drug Administration (FDA) uses class labelling when “all products within a class are assumed to be closely related in chemical structure, pharmacology, therapeutic activity, and adverse reactions”, however, as Furberg et al. point out, this “close” relationship is neither defined nor clear (1202). Canada simply assumes “therapeutic class” in its regulation and acceptance of new drugs by comparing “breakthrough or substantial improvement” with median prices in seven countries: France, Germany, Italy, Sweden, Switzerland, the UK and the US (Anis, 2000, 524).

Opinions differ as to what constitutes a drug class. Clinicians, manufacturers, and purchasers vary in their valuations of a drug’s safety, efficacy or cost-effectiveness compared to others in its class (McAlister, Laupacis, Wells, Sackett, & for the Evidence-Based Medicine Working Group, 1999, 1371). Typically, different agents used for the treatment of the same condition have slightly different actions and “the ultimate test of
the usefulness of a drug or device depends on the determination of outcomes”, which are often not apparent until the drug has been in circulation for many years (Sobel & Furberg, 1997, 1661).

Until recently, drug substitution referred to generic drugs. The therapeutic substitution of one drug for another within a set class was only introduced in the nineties (Anis, 2000, 525). These types of programs, often called reference-based pricing, use the available literature on drug class information as their basis for restricting access to certain medications – often the newer and more expensive ones – within a class. The practice originated in the Netherlands and Germany and spread to a few other western countries including Norway, Australia, and New Zealand. France considered but did not initiate the program; Norway briefly did start a reference program but quietly discontinued it (Furniss & Zammit-Lucia, 1997; Panel, 2002). In the United States, the majority of HMO and acute care hospital settings use restrictive formularies, purchasing only certain drugs within a certain class. The only Canadian province to have officially initiated reference-based pricing (now called the reference drug program or RDP) is British Columbia, although Nova Scotia has a program called the Special Maximum Allowable Cost Program, which is somewhat similar but only restricts two types of drugs – H2 antagonist gastric drugs and non-steroidal anti-inflammatories or NSAIDS.

The RDP in BC began in October of 1995 on a limited scale, with the same two types of drugs as the Nova Scotia program, then expanded to five categories in January 1997. The program limits “the reimbursement for a prescribed drug to the cost of the lowest priced product within the same class of drugs deemed to be therapeutically
equivalent" (Grootendorst & Holbrook, 1999, 273). It was one of several concurrent cost-cutting measures introduced in BC at the time (others were the generic drug program and a trial prescription format which allowed patients to test small quantities of a new prescription before buying a full supply). The RDP now applies to five drug classes: NSAIDS, primarily used to treat the pain and inflammation of arthritis; histamine-2 receptor antagonists, more commonly called H2 blockers, which reduce gastric acid; oral nitrates (commonly used for angina) and two types of antihypertensive or blood-pressure lowering drugs, angiotensin-converting enzyme (ACE) inhibitors and calcium-channel blockers. After announcing the first two categories very quickly and with minimal discussion, the Ministry of Health Pharmacare program subsequently softened its stance somewhat and created certain exemptions with the three latter categories: Diabetics and asthmatics under the care of a specialist were excluded from automatic substitution of the reference drug and prescribing for patients with chronic conditions was left to the discretion of the prescribing physician. This was sensible since often there are enormous problems for people with chronic illnesses, often prescribed multiple medications, when a sudden change is made to their existing drug regimen.

The RDP policy in British Columbia has generated what a CMAJ editorial politely calls “considerable debate” (Grootendorst & Holbrook, 1999, 273), with pharmaceutical companies, in particular, but also patients, doctors, pharmacists and seniors’ groups speaking out against, even as others (e.g., BC Persons with AIDS Society) expressed support (Hilton, 2002). The right-of-centre Fraser Institute has taken a stance against the RDP on principle; they charge that reference-pricing tilts prescribing towards older,
cheaper drugs with more adverse effects, ultimately shifting costs from one program (Pharmacare) onto others (acute care and physician visits). They also charge that it negatively affects research and development and accuse RDP proponents of devious statistical subterfuge (Graham, 2003). Meanwhile, the left-leaning Centre for Policy Alternatives has reacted favourably to the RDP (Cassels, 2002), maintaining that pharmaceutical companies wield huge power within medicine, and policies such as the RDP are a rational counterbalance to corporate marketing and PR efforts. The group does balance out their position by recommending that more consultation be undertaken with health professionals and suggest that projected savings be weighed carefully against social costs (16).

From a more neutral position it is difficult to determine how well the RDP has done. Certainly the policy did save money, at least at the outset, but whether the savings were across the board or program-specific is less clear. Determining what general societal impact, if any, the policy has had, furthermore, is complicated and difficult to glean from existing data since there has been very little interest in asking patients about their experiences – or determining whether or not their overall health or quality of life has been affected. Shortly after the RDP was begun Victoria researchers Neena Chappell and colleagues at the Ministry of Health did conduct a telephone survey in 1997, contacting a randomly-selected group of 1699 elderly patients to ask them about the RDP (then called the RBP or reference-based pricing) – but only 19% of the respondents had even heard of the program and only an undistinguished 60.1% knew the correct answer to half the questions posed (Chappell, Maclure, Brunt, & Hopkinson, 1997, 122). Nearly a third
(27.5%) refused to participate in the study (118) and less than a tenth (7.9%) knew the correct answer “over 85 per cent of the time” (122-3).\textsuperscript{40} The one noteworthy result was neither administrative nor policy-oriented but personal and clinical: Some 92% of respondents expressed confidence in their physician as a source of information and 85% expressed trust in their pharmacist (128). Not surprisingly, those seniors who were on the medications restricted through the reference program had greater “concerns” about the policy (Chappell et al., 1997, 123). Mystifyingly, given the responses they received, the researchers concluded that “patients overwhelmingly accept, and the majority support, government’s efforts to change their Pharmacare policies” (129) (my emphasis). More interesting (to this researcher) was the finding of a “mismatch” between clinicians’ and seniors’ “perceptions of the need to give and receive information on prescription drugs” (130), which would seem indicative of the genuine desire on the part of patients for high-quality, trustworthy information.

A more recent telephone survey of 265 Kaiser Permanente (a large and generally well-regarded HMO in the US) members in California suggested that patients are, by and large, amenable to restrictions provided they are given choices and allowed input. This study found that 60% of Kaiser patients would be willing “to switch their current allergy or hypertensive medication to a less expensive formulation” if (1) their doctor recommended it, (2) if they could continue with their current drug if they so chose, and (3) if the formulary alternative actually worked for them (Nair, Ganther, Valuck, et al., 2002, 44) (my emphasis). In other words, patients are reasonable and quite willing to be

\textsuperscript{40} There were only six questions and answers could be “true”, “unsure” or “false”.

flexible so long as they can maintain personal autonomy, have sufficient and appropriate
information and are given a choice in the matter. Therefore, introducing some flexibility
and better or at least sufficient communications into such policies would make them more
successful. It is somewhat difficult to understand precisely why these restrictions are
currently not bolstered by better communication strategies or why, given the many
communications specialists at various institutions, good communication is not the norm.

The Data on the BC Reference Drug Program (RDP)

The one, modest patient survey on attitudes towards the RDP cited above is
heavily outnumbered by quantitative studies, which there are in abundance. Harvard
School of Public Health epidemiologist Sebastian Schneeweiss, a frequent commentator
and researcher on pharmaceutical cost-containment, and his colleagues, including one at
Pharmacare, analyzed thirty-six months of claims data for the 119,074 patients over age
sixty-five who took ACE inhibitors in BC for a period of three years, two years before
and one year after reference pricing was implemented for that category of drugs.41
Results, published in the CMAJ, showed a “sharp” decline (29%) in the use of “non-
referenced ACE inhibitors” (in other words nearly a third of people opted not to pay
anything out of their own pockets and took the cheaper drug), which translated into a “net
savings of $6 million in the first year in the elderly (population) alone” (Schneeweiss,
Soumerai, & Maclure, 2002, 126). This was “conservatively” extrapolated to mean a $6.7

41 During the early nineties BC also initiated PharmaNet, a computerized pharmacy record of all prescriptions filled
in BC, which facilitated such types of numeric research.
million savings in the cost of antihypertensive medications in the first year — which, the authors say, is a higher savings rate than most pharmaceutical policies. These savings, furthermore, took place "without unintended outcomes on patient health status or use of expensive services", which one assumes means that people didn’t generally get any sicker or end up in hospital more often (126). Verification for this sweeping statement was derived numerically by counting the number of physician visits, elective admissions to hospital and emergency room admissions, and derived from "a health status measure based on a weighted sum of dispensings of specific classes of prescription medications" during the six-month period after the RDP program was instigated (Schneeweiss, Soumerai, Glynn et al., 2002, 739). This "health status measure" is not explained.

A subsequent letter from John Graham of the Fraser Institute accused Schneeweiss et al. of "failure to observe negative health consequences" since "the majority (of people affected) chose to pay the difference" between the insured and uninsured drugs themselves:

The resulting lack of statistical power meant that a 19% increase in hospital admission for "switchers" in the 2 months after implementation ... was considered insignificant. (Graham, 2003)

The matter of patients versus statistics also concerned UBC health economist Aslam Anis, who disputed Schneeweiss and colleagues’ findings in the CMAJ. The researchers had noted that although there had been a ten percent decline in the use of antihypertensives, this figure was not statistically significant. Anis retorted (in a letter) that "regardless of statistical significance, the decline was real” (Anis, 2002a), a point
statisticians often gloss over. Anis charged that identifying therapeutically equivalent medications may well be impossible in the absence of solid evidence, which is lacking to date (Anis, 2002b, 763) – and savings in drug costs may be offset by increases in other areas of the budget such as hospital admissions and doctors’ visits. More important, it is often the poor and elderly who are disproportionately affected by such policies (Horn et al., 1998; Marshall, Grootendorst, & Holbrook, 2002; Marshall, Grootendorst, O’Brien et al., 2002; Tamblyn et al., 2001). Furthermore, restrictive formularies tend to target newer and more expensive drugs, which may be more easily tolerated, and it is conceivable that patients would lose out on the medical benefits of newer drugs (Lichtenberg, 2001, 242).

Is the premise that individuals have the capacity to make rational choices about which drugs to use or abandon under restrictive formularies in fact true? Robyn Tamblyn and her colleagues at McGill University’s Department of Medicine and Department of Epidemiology and Biostatistics reasoned that if not, short-term attempts to save money would be offset by future “downstream” costs of potentially preventable illness. Using a study design similar to that of Schneeweiss et al., these researchers analyzed cost-sharing prescription drug data from 93,950 elderly persons and 53,333 adult welfare recipients in Quebec (from a 1996 attempt to legislate mandatory drug insurance for all residents), publishing their results in JAMA (Tamblyn et al., 2001, 421). Checking monthly drug use and conducting cohort studies to determine the impact of the policy “on the rates of adverse events and ED (Emergency Department) visits associated with reductions in use of essential and less essential drugs”, Tamblyn and her colleagues found that drug use in both elderly persons and social assistance recipients did indeed drop – but there were
consequences. There were “significantly higher” rates of adverse events and ED visits for those people who reduced their essential drug use and adverse events nearly doubled, from 2.0% to 3.9%. The researchers concluded that:

Increased cost sharing had the desired effect of reducing the use of less essential drugs but also the unintended effect of reducing the use of drugs that are essential for disease management and prevention. (427)

Precisely which drugs (for what conditions) were reduced could not be measured through the study’s design, nevertheless the researchers wrote that even though they could not “confirm that reductions in essential drug use led to a deterioration in health status”:

We believe this is a plausible explanation ... Consumers may not have the information needed to make wise decisions about necessary treatment. We estimate that for elderly persons alone, the drug policy reform in Quebec may result in 7000 additional adverse events per million annually... Our results suggest that more stringent cost-sharing pharmaceutical cost containment policies in other parts of Canada and the United States may contribute to avoidable illnesses. (428) (my emphasis)

Susan Horn, of the University of Utah’s Institute for Health Outcomes Research, has also found positive and significant associations between formulary limitations in drug class and resource utilization “significantly greater for elderly patients after controlling for severity of illness and other variables” (Horn et al., 1998, 1105). Horn, who has long been a critic of formulary restrictions at the 81% of American HMO’s which use them,

42 The study used expert evaluations to determine “essential” and “less essential” drugs. Insulin, all cardiac drugs, aspirin, anti-virals, antidepressants and the majority of drugs were considered “essential”; only a handful of stomach and sedative drugs were considered “less essential” (Tamblyn et al., 422).
writes that when providers “encourage or require therapeutic substitution, i.e., substitution of a related but chemically different compound in the same therapeutic class”, these actions could have consequences greater than the sum of the parts:

When access to reimbursable medications is restricted, elderly patients may be at higher risk for suboptimal therapy or adverse drug reactions than are younger patients. This is therapeutic modification with potential clinical significance far beyond mere substitution. (1105)

Similarly, commenting on New Zealand’s reference-based pricing program, cardiologist Merlin Thomas maintains that therapeutic substitution is a “cost shifting exercise rather than a cost saving one”, moving “the cost of appropriate care [to] high risk patients”, who are forced to pay more for effective treatments. More generally, costs shift to the health care system as a whole which is made to carry “the consequences of sub-optimal therapy” (Thomas, 1999, 443). Stephen Soumerai, also at Harvard, who collaborated with Schneeweiss on some RDP studies, came to a similar conclusion after examining Medicaid claims when the state of New Hampshire limited schizophrenic patients’ access to psychotropic drugs in 1994 – noting a sharp increase in the use of health services, emergency and clinic visits (Soumerai, McLaughlin, Ross-Degnan, Casteris, & Bollini, 1994):

Our data suggests that important changes in health policies affecting vulnerable populations should be implemented under close scientific scrutiny [or] at the very least undergo careful evaluation before their widespread adoption... [Yet] political factors often predominate at such times... (655)
To assume, in any event, that drugs are equivalent on the basis of class may be a fundamental error, according to McGill University epidemiologist, Chantal Bourgault. With her colleagues in Saskatchewan, Bourgault used retrospective data to check differences between ACE inhibitors using data from residents aged between forty and seventy-nine who had begun treatment for hypertension with one of the three most frequently prescribed drugs. The researchers found that:

After treatment was initiated patients on captopril were dispensed more medications on average, with an overall rate of 18.6 prescriptions per patient per year (v. 16.4 and 14.7 for enalapril or lisinopril users respectively); they were admitted to hospital more often, and they made more visits to GP’s and specialists....This suggests that ACE inhibitors may not be therapeutically equivalent. (Bourgault et al., 1999, 255)

This lends credence to those critics who charge that there are complexities in drug therapies that class distinctions cannot address – although whether this is also an argument for unlimited access to new drugs is debatable. The humble aspirin has been found equal if not superior in some instances to some newer drugs and the more recent selective serotonin reuptake inhibitor (SSRI) antidepressants have not necessarily been found to be more effective than the old tricyclic (TCA) ones (Parker, 2001, 95).

Frank Lichtenberg, an economics professor at Columbia who analyzed some 23,000 patient records from the Medical Expenditure Panel Survey (MEPS) in the US, has concluded that newer drugs are superior to older ones “because they reduce medical expenditures, increase longevity, and improve overall quality of life” (Lichtenberg, 2003, 16). Studying the association “between the use of newer medicines and morbidity (illness), mortality, and health spending” by matching patient records with the year the
drug(s) they were taking was approved, his research noted that people on newer drugs died in fewer numbers and lost fewer work days than those on the older medications. Lichtenberg concluded that drug research, unlike other types of technical progress, benefits the less fortunate more (18):

If a drug approved by the FDA in 1987 is replaced with one approved in 1997, the direct cost of the newer drug would be about $18 per prescription higher than the older one. The switch to the new drug, however, would reduce the use and cost of other medical services such as hospital stays, office visits, home health care and outpatient visits. Reduced utilization of these nondrug medical services would save approximately $71 per year, which is about 4 times as much as the increase in drug cost. (16)

Susan Horn, using with the same MEPS data, also found an association between the “use of newer asthma drugs and lower overall drug costs and fewer PCP [Primary Care Provider] visits” and, like Soumerai, she also noted more psychiatric complications when psychiatric medications were restricted (Horn, 2003; Horn, Sharkey, & Kelly, 2001).

In recent years there have been advances and refinements in drug therapies for many conditions from diabetes and epilepsy to inflammatory bowel as well as certain types of cancer. If caught early enough, the ravages of a heart attack and some types of stroke can be reversed with a genetically engineered drug (tissue-plasminogen activator or tPa). Newer drugs for rheumatoid arthritis may slow the course of the illness if they are given early and, overall, many newer drugs seem to be better tolerated and have fewer side effects and drug interactions. Often, it is those people on multiple drugs (i.e., those with chronic illness) who benefit most from drug “refinements”. Simply measuring the numbers of side effects, as drug comparisons often do, does not adequately reflect their
severity or their relative importance to patients. For example, ranitidine is a slightly newer H2 blocker than cimetidine (which the BC reference program has approved), yet Vancouver General Hospital (which has their own restrictive formulary, independent of Pharmacare) prefers ranitidine, even though it is slightly more expensive. Ranitidine has fewer drug interactions and is more easily tolerated by hospitalized patients (private communication, Dr. Robert Hewko, March 2004). For sicker patients this is a major issue. The old tricyclic antidepressants did work for depression, but patients often refused to take them because the side effects were so unpleasant – and they were lethal in large doses. Given that one of the primary risks of depression is suicide, this presents a major problem. It is possible, at least in some instances, that we do get what we pay for.

Early appraisals of overall savings from the RDP had been quite optimistic – one study noted a 38% or roughly $10 million drop in total expenditures “from $23.9 million the year before implementation to $14.8 million the year after” (Narine, Senathirajah, & Smith, 1999, 286), but an evaluation by the Auditor General and the Ministry of Health in 2002 found that the Ministry’s estimates of cost-savings attributable to the RDP in the year 2000 were actually $11.8 million (Panel, 2002, 13). However, indirect costs, e.g., the increased administrative burden on pharmacists and doctors and the extra time spent, were not addressed. The Panel warned that savings would decline to some $7.6 million annually were the RDP to remain “static” and as “patents expire and generic products

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43 The Therapeutics Initiative newsletters, for example, compares numbers of side effects.
44 Based on consideration of submissions from some forty-six groups.
enter the market" (13). In adding this caveat the Ministry evaluators were in agreement with the policy literature where the general consensus is that any sudden shift in reimbursement schedules creates a major change at the beginning, then gradually loses impact as people adapt to the policy. BC has proven no exception. By 1998 the increase in Pharmacare’s costs returned to pre-RDP levels of approximately 15% a year (Schneeweiss, Maclure, Dormuth, & Avorn, 2002, 1250). Given that an earlier, 1998, report on appropriate drug use by the Office of the Auditor General in BC had said that between 1989 and 1994 drug spending in BC had doubled, from 10% to 21% (Morfitt, 1998, 21), one can surmise that the RDP did indeed slow expenditures, even in the absence of concrete evidence. However whether this lowering of costs was true across the board, or merely applied to drugs, the current data cannot answer.

The central ethical question, however, is whether certain groups, such as seniors and the poor, are unfairly affected by restrictive drug policies and here it becomes both complicated and abstruse. Merely analyzing statistical data provides no specifics and clinicians, who are in a position to know more about what goes on with patients, rarely collect information systematically or publish. Laudably, Schneeweiss et al. in their large CMAJ study of ACE inhibitors did “focus on the most vulnerable patient groups”, namely the elderly and the poor, and found that (predictably), low-income patients were the most likely to switch to the no-cost (to them) medication. Anis writes:

45 Originally, the savings from the RDP were said to be some $50 million, but these savings were wrongly attributed to the RDP when they resulted from a different program (the Limited Coverage Drug Program restricting proton pump inhibitors, used by patients with severe gastric problems).
Reference-based pricing affected demand in a manner that led to an 11% decline in the use of ACE inhibitors. Furthermore, it also caused a 10% decline in the use of all antihypertensives. Since it is already well known that hypertension is undertreated, further declines in drug use by patients with hypertension is not good news. A more in-depth investigation of these effects is urgently needed. (Anis, 2002b, 763-4)

Low-income patients, furthermore, the ones most prone to cardiovascular disease (Williams, 2002), were also most likely to quit taking hypertensive therapy altogether, although the numbers, relatively speaking, were not large – only three percent of the patients studied or 1,093 patients (Schneeweiss, Soumerai et al, 2002, 743). Nevertheless, that still translates into some eleven hundred people with potentially negative sequelae, since “data based on processed prescription claims” cannot answer questions about health outcomes (Anis, 2002a) or inform as to the impact on quality of life.

"Me-too"

While drug selection might not appear to greatly affect outcomes when one is examining data for a short time, the stakes may be higher when the drug treatment is intended to thwart long-term complications or disease development, since evidence of efficacy or safety may not become apparent for many years. As clinicians and formulary critics Furberg and colleagues write, “If a drug within a particular class lowers the occurrence of a disease by 30% and another drug lowers occurrence by 20%, physicians and patients
need to know that before they embark on a long-term treatment plan” (Furberg et al., 1999, 1203). That information is, at present, nonexistent:

The optimum source of comparative information on preventive effects is head-to-head comparisons of efficacy, safety, and cost, in large randomized trials. Unfortunately, such information on efficacy, safety, or cost-effectiveness of new drugs is not required by the FDA and most other regulatory agencies and rarely provided by drug companies. ... There are major financial disincentives for drug companies to invest in costly comparative trials. The number of individuals needed to show that a new drug is equivalent to an established one generally exceeds the number needed to find the efficacy of a drug compared with a placebo. (Furberg et al., 1999, 1203)

Comparability is no simple matter. Researchers define their own pre-set limits and these often differ from study to study and researcher to researcher. The flood of “me-too” drugs with weak documentation during the past decade (beta blockers, ACE inhibitors, statins, calcium antagonists, all of which treat hypertension) illustrates this strategy, which involves marketing based on class effect rather than evidence from comparative clinical trials (Furberg et al, 1999, 1203). In other words, marketing trumps research as far as the manufacturer is concerned, and that lack of long-term data, needed by policy makers when deciding which drug to pay for, can potentially negatively affect patient health.

Drugs have multiple effects and these, whether “overt or occult”, may effect either beneficial or deleterious changes regardless of whether they are assessed or evaluated (Sobel & Furberg, 1997, 1662). The authors employ an eye-catching example to illustrate the point:

46 Of course more to the point is what the incidence and risk of the condition is to begin with. A 20% reduction of an
As an extreme example, consider arsenic, cyanide, endotoxin, and snake venom, all of which lower blood pressure. Obviously, none qualifies as a therapeutic agent. Occult as well as overt multiple and diverse actions of drugs make it incumbent on clinicians to recognize that the validity of inferences about the clinical consequences of the use of any given agent to induce a specific pharmacologic effect will depend not only on the extent to which it affects the targeted biological phenomenon but also on the extent to which all of the actions of the agent have been defined and the extent to which all affect the entire organism. (1662)

On the other hand, since a high percentage of newer drugs are old ones slightly tweaked, one could argue that such “me-too” drugs are being increasingly advertised (not only to doctors but to the general public) as genuine improvements.47

The proliferation of similar drugs within a single class from the perspective of the drug companies, of course, is highly positive, reflecting “pharmacodiversity” and assisting clinicians in finding the right drug for each individual, allowing for dose and delivery variations and representing improvement and choice. (Many doctors and patients might well agree with this.) Alternative agents are useful “in cases of treatment failure” and create a “backup in case an agent is withdrawn from the market”, and they represent “incremental innovations” that often save money on hospital stays, surgeries and side effects (Wertheimer, 2002). The bald truth is that while newer drugs may be more refined and better tolerated (particularly for those with chronic illnesses), unscrupulous variations on a theme abound in pharmaceutical research. Most of these are intended primarily for patent protection and higher sales in western countries (Angell, 2000). One company, for

already low risk is no big deal. More on this later.

47 So perhaps the truly subversive question that one ought to address should be on the appropriateness of the widespread use of all drug classes.
instance, has slightly reformulated an antidepressant and has marketed it for pre-menstrual depression, now cleverly and pseudo-medically referred to as “pre-menstrual dysphoria”. Similarly, antihypertensive or gastric drugs are given minor molecular alterations, patented and marketed as an innovation for fast-food gobbling westerners. Drug companies do not tend to be interested in developing drugs for tropical diseases such as malaria which affect the developing world, generally preferring to target their products to those who can best afford it. Pragmatically speaking, however, patients are a diverse and different group, and greater drug choice does tend to mean that individuals needing pharmacotherapy are better able to find a drug which suits their physiology and particularities. Again, the question is whether all of these drugs are needed or whether we might not be better served by a research, regulatory and medical community more focused on helping us determine, however vaguely, what medical necessity might entail.

In a slight twist on “me too”, Schneeweiss et al., the researchers who originally examined the BC Pharmacare data, also made some minor modifications to their product and released a new version. Taking eighteen months’ worth of the data they had analyzed earlier for the CMAJ, they submitted their work to the prestigious New England Journal of Medicine – but, in the American publication, perhaps in an attempt to be more culturally appropriate, their tone is studiedly impersonal. No mention is made of “vulnerable” patient groups and they merely write that “analyses of patient subgroups” as defined by “low income, a high chronic disease score, or diagnosis of coronary heart disease, heart failure, or renal failure did not show any group-specific effects of the policy (RDP)” (Schneeweiss, Walker et al., 2002, 824). Group-specific effects are neither
defined nor elaborated on. In sharp contrast to the warmer tone taken in the Canadian article, the impersonal style continues with a reference to individuals who have entered a nursing home being considered a “one time” admission to hospital (statistically) since those “patients almost never returned to the community” (Schneeweiss, Walker et al., 2002, 823) – which is rather a chilling comment, however true it may be.4

This difference in tone may not appear to count for much in the grand scheme of things (particularly when one reads the impressive statistics and elegant descriptions of the “Poisson regression models” the numbers were subjected to), but it does indicate the extent to which these researchers (and pharmacoeconomics in general) can distract themselves from the fact that their numbers refer to a person: someone’s friend, aunt, grandfather, colleague. These researchers found that the positive aspects of restricting certain drugs within a class outweighed the negative: that these policies save money without “adversely affecting health outcomes” and with no “severe negative side effects” such as hospital or long-term care admissions or mortality being attributable to the RDP (Schneeweiss, Maclure et al., 2002, 1250). Similarly, after listening to forty-six submissions by various community and professional groups, the Panel appointed by the BC Auditor-General concluded that the RDP “offers an effective way of controlling some Pharmacare costs”, with conservative estimates of savings being $12 million in the year 2002 alone (Panel, 2002, 13). They did suggest that the effects of the program on patients

48 Throw-away lines like this always make one wonder what the real story is – and what, if any, impact the new drug policy had on these individuals who made that “one time” entry into long-term care.
be examined, particularly with respect to hypertension (and presumably those ACE inhibitors Schneeweiss et al. had studied), and “independently evaluated” (80).

**Communication Matters**

Such recommendations, not uncommon in group reviews of medical practice, are almost always expressed in the passive, “agentless prose” sentence structure that technical, scientific, regulatory and medical language utilizes to create the illusion of abstraction and distance, suggests David Locke, emeritus professor of English at the University of Florida. Locke writes that this language, in which “science conducts its business … is a studiedly impersonal one, designed to emphasize its vaunted objectivity” (Locke, 1998, 1). Yet since Heisenberg, 20th century science has acknowledged that there is no such thing as an immaculate perception and no true means of separating the observer from the observed. Locke adds that it is not merely the “opacity” of the official voice that grates but the unappealing picture it paints of practitioners. Writing in *The American Scholar*, Locke considers it one of the paradoxes of our time, that even as science has penetrated deeper into our lives, the “chill dehumanization” of its representation of our modern world generates greater distrust:

> When judged by their language scientists seem cold, dispassionate, disengaged from everything we feel puts life in our days. (Though we may not penetrate far into the jargon, we hear enough to be able to characterize the voice that is speaking over our heads.) … The official voice of science is not a voice to comfort us in the long night. (Locke, 1998, 2)

49 To some extent this also explains many physicians’ dislike of reference pricing; they see patients, not statistics.
Of course that is not the only language of science. From Darwin to Einstein to current writers (some cited here), many scientists and researchers take communication seriously. In medicine, such care is not only useful but essential from a clinical perspective:

“Linguistic care is needed not only for crisp communication but also for insightful assessment of cause/consequence relationships and, in particular for the therapeutic efficacy of drugs,” write Sobel and Furburg, adding that “wisdom” and good science are necessary to determine the extent to which policy decisions can be inferred from the results of “mechanistic” studies (Sobel & Furberg, 1997, 1662). Simply recording what happened (e.g., usage data, numbers of hospitalizations) is rarely sufficient to understand what effects a policy decision might have. Furthermore, no matter how “universally satisfactory” and efficient science may be in seeking answers to questions about what happens in the world, one must not “deliberately set aside” what “makes human life worth living”, writes physicist John Polkinhorne (Polkinhorne, 1996, 3). Even the most austere of scientists, he points out, even the greatest “apostles of an extreme and unrelenting material reductionism”, live rich lives that encompass a myriad of factors from human interactions to humour and love – and it ought not be unreasonable for us to expect at least some consistency between their work and their lives.50 He adds that science “furnishes humanity with great resources of power”, but since “it does not trade in wisdom” we are also left with ecological and human disasters “for which technology has provided the catalyst” (4).

50 He adds: “The context of science is the human context .... Science by itself is not enough even to describe the pursuit of science itself” (Polkinhorne, 2).
A different kind of disconnect appears in the affiliations of many researchers who write on reference pricing. With minor exceptions, those arguing for formulary restrictions tend to be funded by those paying the costs; those against have ties, however tenuous, to the pharmaceutical industry. This does not, *ipso facto*, render their findings invalid or unsound, but, as a *JAMA* editorial points out, these “lurking biases” do merit notice (Browman, 2001, 1510) since they will often have an impact on conclusions.

**The Trouble with Convenience**

Drugs can be splendid therapeutic interventions; they can dramatically improve a person’s quality of life, mobility and ability to function. Additionally, since drugs have become the treatment of choice for many conditions and diseases, it can be argued that they reduce emergency room or doctor visits and the need for more costly and complicated treatments such as surgery. As Mechanic writes:

> New technologies need not drive up costs. The most successful new technologies can substitute for invasive, costly and inferior approaches, and potentially reduce expenditures for treating an episode of illness. (Mechanic, 2002, 462)

For example, since the advent of acid-reducing medications (H2 blockers), gastric surgery for ulcer has been greatly reduced, and since the newer migraine medications have come on the scene, fewer migraine sufferers end up in emergency rooms for hydration and morphine. On the other hand, when any drug or technology falls into general use, its use tends to spread and increase:
Reducing the costs of care for episodes of care does not necessarily reduce aggregate cost if the improved technology attracts more professionals and clients to it, and substantially increases the incidence of use. (462)

When a drug is easy to take it tends to expand out of the domain of those with major manifestations of disease – which is when its scope widens and side effects and costs mount up. For instance, when only those people depressed to the verge of suicide took antidepressants, the negative effects were slight, but when anyone even slightly gloomy is added, the numbers go up, costs rise and side effects commensurately increase. All drugs have side effects, some of them quite dire, and it is when the original complaint is less threatening than the side effects of the therapeutic that problems develop – medically, socially, financially.

In addition, drugs may well be useful and necessary, improving many people’s quality of life, but pharmaceutical companies are hardly charitable organizations. Their primary goal is to make money, sometimes through questionable tactics. When, as a society, we focus on drug therapies to the exclusion of all else, research attention is deflected away from low-tech, old-fashioned interventions that often provide complementary and sometimes equal amounts of relief for the elderly and those suffering from chronic ailments (and also from basic research into disease). Pain clinics, massage, assistance with daily living, therapy and personalized advice, particularly when coming from a nurse or dietician, can provide major benefits to chronic disease sufferers, yet these are seldom studied or analyzed (Rogers, 2002, 100). In the grand scheme of 21st century values such things do not seem glamorous or exciting enough to deserve our
attention – neither are they the focus of corporate funding, and, at a time when other sources of funding have largely dried up, this can be problematic.

Hardest hit by pharmaceutical restrictions are those same patients who benefit most from pharmaceutical innovation, the chronically ill and those with the most severe symptoms. This patient group is disproportionately affected by the high price of pharmaceuticals – as well as being least able to pay. In Manitoba, for instance, the annual average cost for prescription drugs was $35, but some 40,000 Manitobans with health problems had drug costs that exceeded $1,500 a year. The total cost to Manitoba Pharmacare for these people was approximately $112 million or nearly half (44%) of the total cost ($256 million) of the public plan (Romanow, 198). The fundamental concern, then, is whether all these many drugs that do so many things from lower cholesterol to reduce inflammation are essential and necessary for so many people – or whether we have generally become a society too emotionally attached not only to the “quick fix” but to the idea of equity: if a drug or technology is available to one, then it should be available to all, without regard to degree or extent of dysfunction.

On the other hand, how do we decide on the cut-off? How sick is sick “enough” to qualify for intervention? As a society, how much do we value cost-savings – and will the fact that drugs are expensive mean that we turn away people with chronic problems which we are now better able to control? These are not questions with simple answers. They require ethical examination and critical thought. Social and cultural beliefs in the medico-pharmacologic model run deep, however, and even with the many, inherent ambiguities, uncertainties and flaws in our understanding of how and why drugs work,
most drug policies rely on naïve faith in the evidentiary underpinnings of pharmaceutical therapy for known, measurable medical conditions – along with the medical necessity of pharmacotherapy (and other technologies and interventions). This in turn creates an environment (academic, policy, social) where the discussion revolves around the drugs or technologies themselves and the extent to which we use, misuse, abuse, over- or under-use them. Rarely in the medical, economic or even sociological literature is there any serious examination of the basic premise, namely that pharmaceutical or other interventions are the logical (and necessary) solution, and even less often are questions raised regarding the context, method, criteria or processes used to make those determinations. Politicians and journalists bemoan the horror of waiting lists for various procedures and technologies (such as MRI’s for example), yet the necessity of the technology is rarely questioned. Yet there is good evidence that MRI’s are of little or no benefit to the majority of patients with back or knee problems (Hadler, 2003), which is often what they are used for. Many (especially older) specialists are highly skilled at diagnosis through the most old-fashioned technology of all, a detailed patient history. But we worry about the lack of MRI’s, not rushed consultations or physicians’ skills. Our remuneration systems reflect this bias. At present such topics are glaringly absent in the discourse on medicine and health care – so much so that questioning the necessity of more technology seems absurd. Yet history shows that most medical interventions and technologies do not stand the test of time.

In particular, it remains to be seen whether our current obsession with prevention and proactive health will be found to be useful, as will be discussed in detail in a later
chapter. It is one thing, after all, to seek medical treatment, undergo tests or surgery or take drugs when one is sick or injured – when the option is between death or massive dysfunction and some medical intervention – but what of the many symptom-less individuals modern medicine has a tendency to chase down? What does one do when one feels fine but some test or screen shows elevated blood sugar or cholesterol that is said to require treatment? What is being treated here, the person or the number? From reference-pricing to cancer screening, modern medicine is rife with guidelines, directives and rules. One could question whether such directives are appropriate, ethical or even sensible.

**Outcomes or Narratives?**

According to the late Yale physician Alvan Feinstein, who entered medical school in 1948 and whose experience with medicine encompassed over half a century, some twenty years ago a major shift occurred in medicine, one which relegated patients and their problems to a secondary position and elevated disease modalities (Feinstein, 2002, 472). The diverse approaches to clinical care thus converged into a taxonomy that divided health care into three components: structure (the institutions and personnel involved in medicine); process (what is actually done); and outcomes (what happens). These classifications not only tilted attention away from patients but had an impact on how doctors practice medicine (472):

The legendary “old-fashioned” doctor may not have been quite as splendid as portrayed in the legend, but the doctor’s concern and “iatrotherapy” were often the only treatments that were effective. … [Now], conversation with the patient can often be avoided or reduced greatly if the clinician orders certain approved procedures in “preventive care”. In the days when
“workups” were planned mainly in response to pertinent symptoms, the clinician had to talk to the patient to learn about the symptoms. Today, however, many activities in screening or prophylaxis (prevention) are accepted as appropriate for anyone in an eligible demographic group, regardless of symptoms. (Feinstein, 2002, 475)

As health care interventions increased and guidelines, evidence, benchmarks and other standardization techniques proliferated, a certain depersonalization took place and individual narratives lost ground to the generalities of the life situation or identification of the pathology. Feinstein wrote that this often could take place through routine orders and “with little more communication than handing the patient a written pamphlet” (on quitting smoking, exercise, diet, blood pressure, etc.) – which may seem like excellent practice on a quality assurance form, but cannot be considered good medicine:

Such symptoms as pain, dyspnea [difficulty breathing], distress, and diverse manifestations of disability, which are often particularly important for patients, may be neglected because they are not part of a disease to be “cured”. The neglect also occurs because relief or comfort may be regarded as an “interpersonal” component of therapy, rather than a specific target that can be cited and appraised just as distinctly as a laboratory or morphologic abnormality. (475)

Patients bring their own experience of illness to the consulting room: “episodes of sickness are important milestones in the enacted narratives of patients’ lives”. It is this narrative which provides “meaning, context and perspective” for the person’s predicament. It defines “how, why and in what way he or she is ill” (Greenhalgh & Hurwitz, 1999, 48). What we increasingly experience as patients, however is the invisible hand of institutional directives and consensus reports (perhaps prompted by cost considerations) whereby treatment is not driven by our own story and experience but by
abstract precepts decided elsewhere by nameless, faceless people who usually have nothing whatsoever to do with clinical care. For example, if one happens to pertain to the category of "menopausal woman", then bones are a consideration. If the patient is a male of a certain age, then it is prostate antigens or cholesterol which must be measured and therapy initiated if the numbers warrant. And so on.

The extent to which such guidelines may be said to be "objective" is also questionable, given the influence that drug company marketing has on their development. As an editorial in the CMAJ rhetorically asks: "How do we detect the influence of industry sponsorship on clinical practice guidelines, consensus conferences, narrative and systematic reviews and continuing professional development?" (Editorial, 2002). For example, six out of nine experts from the American Heart Association who picked alteplase as their drug of choice for acute stroke received money from the manufacturer, Genentech — and over "59% of experts writing clinical practice guidelines reported ties (honoraria, consulting contracts, equity, etc.) with the manufacturers of the drugs they recommended" (Choudhry, Stelfox, & Detsky, 2002, cited in CMAJ). Even if those particular recommendations are genuinely best, such ties connect the therapeutic process to corporations and institutions, not individuals and illness.

Pain, disability and illness, which are what medical sociologist Renee Fox calls a "panhuman occurrence", do not correspond well to quantitative measures (Fox, 1989). They are private, personal and contain a wealth of different meanings depending on who we are and where and how we live. It is our narratives which allow us to ground them in reality and help us make sense of them:
Not so long ago, doctors knew (without having to be told) that the lives of their patients were intelligible narratives; now that the market has started dismantling the framework which made those lives intelligible, the cues need to be made explicit. (Bamforth, 2001, 1361)

With illness it is that narrative, that experience we want to understand and affect. No group or society can be said to be free of illness and anywhere in the world those individuals professing not to have been ill a day in their lives are few and far-between. When doctors listen to their patients they are acting as “ethnographers, historians and biographers” who are asked not only to understand the disease but its context, both personal and social (Greenhalgh & Hurwitz, 49). All cultures have developed some means of dealing with ill-health and keeping citizens well, and providing access to medical care is a primary concern for modern politicians, although geography tends to determine content. African countries, for example, are preoccupied with AIDS and parasitic diseases, while cardiac disease and cancer top the list of western countries’ concerns. Surely such an intensely human, cross-cultural experience deserves more careful scrutiny, broader perspectives and different templates than those used in export policies, trade rules or other forms of government activities.

It has been said that even at its scientific best, medicine is always a social act and “even the most evidence-crazed doctors” must translate “biostatistical truths into accounts that make sense to others” (Elwyn & Gwyn, 1999, 186). Even in this analytical and technological age the clinical encounter remains more than the sum of its parts. But our discourse on medicine has become sparse and lacking in the terminologies associated with pain and illness, often to the point where clinicians or researchers seeking to add
them in are considered revolutionary.\textsuperscript{51} Over the last decades as health care has grown and has been turned into an "industry" of sorts, even being referred to as such, medicine has become politicized, institutionalized and shaped by terms more common to the boardroom than the clinic. From "clinical governance" to "quality assurance", many terms and ideas focus on means, not ends, and "betray [their] origin in business management theory" (Campbell, 2001, 55). One can argue that this was inevitable as medicine expanded and became more expensive, but is it truly in health institutions' best interest "to maintain the denial of uncertainty" and act as though better systems will lead to better care? Or is it that acknowledging ambiguity "challenges the prevailing power structure" (Hall, 2002, 218)? Does this tacit agreement between clinicians and policy makers genuinely address the needs of patients (218) or does it marginalize those clinicians who genuinely try to care for patients as individuals – and make a mockery of patient care? The zeitgeist of medicine is currently driven by many concerns, only one of which is medical. Whether the subject of discussion is therapeutic equivalence or any other type of recommendation based on information from large groups and statistics, factors other than the question of "disease" or ill-health propel the debate.

Our expectations and beliefs are affected by many things, from economics to the media, advertising and the corporate agenda as well as our socio-cultural reverence for technology and high-tech tools and our belief in the value of being proactive. Within this

\textsuperscript{51} For example, the work of Dr. Jerilynn Prior, a Vancouver endocrinologist studying the role of the hormone progesterone in menopause. She is attempting to incorporate women's feelings and experiences on menopause into her research and has largely been ignored by the medical and research community (personal communications, Drs Prior and Tom Elliott, 1998).
environment, governments, professional groups and even patients have begun to believe that the only appropriate route to good care lies in evidence, experts and the clinical guidelines derived thereof, be that reference pricing on an institutional level or more finite ones emanating from professional organizations dictating methods on detecting and treating osteoporosis, heart disease, breast cancer and so on. Yet clinical guidelines can be problematic – and possibly hazardous for the individual.

**Rules, Guidelines and Recommendations**

Clinical guidelines (also called clinical practice guidelines or CPG) have been called a “memory machine of facts and instructions”, but, as with many aspects of memory, they seem to be more about “promise than outcomes” (Hoey, 2001). Guidelines, which are said to “improve the quality of care received by patients” (Woolf, Grol, Hutchinson, Eccles, & Grimshaw, 1999, 527), became prominent around the same time as quality assurance programs and other such institutional initiatives. Patients, seen in much the same light as clients or customers are to business, were said to be deserving of good, standardized care leading to improved health “outcomes”, a word with strong bureaucratic overtones:

Guidelines that promote interventions of proved benefit and discourage ineffective ones have the potential to reduce morbidity and mortality and improve quality of life … [and] improve the consistency of care… Patients with identical clinical problems receive different care depending on their clinician, hospital, or location. Guidelines offer a remedy, making it more likely that patients will be cared for in the same manner regardless of where or by whom they are treated. (Woolf et al., 527)
Which sounds absolutely splendid – at least until one realizes that patients are not a homogenized group but individuals, with different ages, values, problems and tolerance for everything from pain to degree of intervention. Precisely how treating them as identical units in an assembly line could be an improvement on anything is something of a mystery. Furthermore, since no illness presents in exactly the same way in two people, no symptom perceived identically, the term "outcomes" is ambiguous in the extreme. Would it refer to numeric results of medical tests or to patients subjective sense of well-being? Functionality and ability to return to work? Perhaps differences in care have more to do with differences between people than incompetence.

Even the most enthusiastic of guideline proponents admit there are problems. Guidelines can be simply wrong, based on "lacking, misleading or misinterpreted" evidence or subjectivity (Woolf et al., 529). What drives guideline writers may not necessarily be patient benefit but other motives, such as controlling costs, serving "societal needs" or protecting special interests (529). Since guidelines consist of a distillation of multiple studies and viewpoints, they may also be oversimplified and incomplete. In addition, many guideline writers have connections to the pharmaceutical industry (Morin et al., 2002). Researchers in Birmingham, England, examined "composite outcomes, in which multiple end points are combined" in a number of original published reports in high-profile medical journals and found the conclusions to be "inadequate" and the clinical trials themselves to be often "arbitrary" (Freemantle, Calvert, Wood, Eastaugh, & Griffin, 2003, 2554). Composite outcomes, they write, must
"sensibly be added together" yet many studies do not seem to adhere to this simple injunction. Clinical advice emanating from such distillations can therefore be misleading:

The differing interests of sponsors, licensing authorities, and interpreters become manifest. Sponsors are attracted by the hoped-for gains in statistical precision to improve their chances of a positive trial and the increase in the use of composite outcome measures is largely due to their acceptance by licensing authorities. The latter might argue that their role is to ensure that [pharmaceuticals] .. have an effect, yet they have a role in the manner in which sponsors are permitted to market their products (as a result of the evidence provided). (Freemantle et al., 2558)

This, they add, is generally unsatisfactory since the shortcomings of guidelines may literally be “lost in the small print” (2558).

An examination of drug therapy clinical practice guidelines in Canada drew only lukewarm praise, at best, for the quality of the reporting. Of the 217 guidelines studied, only one (fairly irrelevant) criterion, which identified the agency responsible for the drafting of the guideline, was met 100% of the time. In terms of the appropriateness and applicability of the guidelines, results were poor: the highest score was 4.1% and only 14.7% of the guidelines met half or more of the twenty criteria defining the development process. Worse, only 12.9% of the guidelines could be said to have any “explicit statement of how patient preferences should be taken into account” (Graham et al., 2001, 159) (my emphasis). Clearly this was not a priority. It would seem that quantity takes precedence over quality much of the time. A Dutch enquiry on the translation of evidence into good clinical practice criticized the abundance of guidelines – in 2000 there were over 2200 guidelines in the United States – and the researchers expressed concerns about
the potential conflicts between the "art" and "science" of medicine and pondered whether "the scientification" of medicine had gone too far (Gill, 2001, 307).

Reference pricing and other restrictive formularies are prototypical applications of guidelines by a government or other body which has the power to restrict drug use through payment plans. Currently there seems to be a "political enthusiasm" for the development and use of such guidelines, even as, paradoxically, there are "fewer healthcare issues that have a sound research evidence base" (Rycroft-Malone, 2001, 238) and few patients to whom the evidence cleanly applies. As two UK psychiatrists point out with respect to their own patients:

Most of the randomized knowledge-base in psychiatry consists of trials, produced or funded by the pharmaceutical industry, and designed to meet licensing requirements, rather than the needs of UK clinicians. Difficulties begin when extrapolating these data to the real world, because patients whom we would recognise from our own practices would never make it into these trials … Difficulties continue when we find that the success or otherwise of treatment has been judged using complex rating scales that are never used in the real world, the results of which are difficult to interpret. The situation might be improved if trialists asked simple questions, such as whether patients feel any better, or recorded whether a drug kept patients out of hospital or in housing or out of trouble with the police. … The research that might form the evidence-base of truly valid and relevant guidelines has yet to be conducted, and is unlikely to be conducted until real world evidence of clinical and cost-effectiveness (not just efficacy) is demanded by drug licensing bodies. (Adams & Gilbody, 2001, 292)

Family doctors commonly express the same complaint:

Several characteristics of general practice provide obstacles to answering questions with RCTs. About 40% of all new disorders in general practice do not evolve into conditions that meet accepted criteria for a diagnosis. The preferred management of undifferentiated disorders is "watchful
waiting”, a step that requires a trusting relationship …. (Rosser, 1999, 661)

One of the cheapest interventions of all, in other words, doing nothing and keeping an eye on the problem. But, in a culture that increasingly values intervention über alles and sees drug treatment as an inalienable right, the solution to the problems of guidelines has become more guidelines. Ironically, groups attempting to counter the pharmaceutical industry’s influence often use that industry’s data for many of their conclusions. Putting the weight of a Ministry of Health or HMO behind such initiatives then gives these guidelines heft – when they may be just as buffeted about by winds of culture and economics and be prone to as much error as anything else. As Stephen Lewis, in his role as Adjunct Professor of Health Policy at the University of Calgary, writes in the CMAJ:

Perhaps we should blush twice and upgrade our expectations in line with the appraisal instrument criteria (of clinical practice guidelines). Our collective response to the evidence that practitioners only rarely follow guidelines, and sometimes think they do when they don’t, is to produce more guidelines rather than rethink the whole enterprise. (Lewis, 2001, 180)

Lewis adds that he was personally involved in various federal and provincial committees on health services “that sought to address the cacophony” of guidelines, but nothing came of it but “turf battles, parochialism and flagging will” (180). This has not seemed to dim organizational enthusiasm for guidelines, which may also function as “rationing tools” allowing clinicians to withhold treatment from certain populations, whether based on age or social or family status (Giacomini, Cook, Streiner, & Anand, 2001).
Even more troubling than the rationing element is the fact that guidelines operate on a different sphere from normal clinical care and may be in conflict with “the perceived needs and expectations of patients and physicians” (Beaulieu, Hudon, Roberge, & Pineault, 1999, 519). Medical practice “depends on the interactions between a physician and a patient” (520) and guideline writers rarely seem to appreciate this. Perhaps, as a CMAJ editorial suggests, we need “dynamic, ‘living’ guidelines that grow along with science and experience” (Hoey, 141). Or perhaps the time has come to completely rethink our approach, whether the guidelines are alive or not.
III. Research and Clinical Uncertainties

Uncertainty abounds in clinical medicine. Remarkable scientific advances in the last 40 years have allowed clinicians to help patients survive many life-threatening illnesses, yet strong cultural beliefs suggest that medicine’s powers are much broader than they really are. In fact, most symptoms that people experience are self-limiting, requiring nothing more than the body’s intrinsic self-corrective process. Many medical interventions have no firm scientific basis and often do not substantially alter the natural history of disease. The overzealous pursuit of certainty and control has contributed heavily to unnecessary health care costs and, paradoxically, has often left patients feeling less confident about their health. (Quill & Suchman, 1993, 109)

Contrary to the popular perception of medicine – particularly media coverage of medical advances, which are either trumpeted as “breakthroughs” or verge on the alarmist, incomplete, or downright inaccurate (Bartlett, Sterne, & Egger, 2002, 81) – uncertainty is integral to medicine. For reasons ranging from individual physiology, disease aetiology and process, social factors or just serendipity, it is never possible to predict precisely which intervention will work, when and for whom or how a disease or condition will manifest within a single individual.

Since the nineteenth century and the ascendancy of the scientific method, the primary means for reducing medical uncertainty has been through comparisons and by reviewing alternate modes and methods of treatment. Typically, the intent has been to
ascertain superiority of one course of action over another. Since the 1950’s, the standard approach to this comparative evaluative methodology has been the randomized (double-blind, placebo-controlled) clinical trial, or RCT, which, for drugs, has become a basic requirement for the Health Canada and FDA drug approval process. *Prima facie*, this “gold standard” of research, as the RCT is often called, has great appeal as it aims to provide “robust information about the effectiveness of medical interventions” and drug therapies, even though it does not always result in useful clinical information (Rogers, 2002, 96). Furthermore, simply because a study is a randomized clinical trial does not automatically make its findings useful or usable (McAlister, Straus, & Sackett, 1998, 488). A fundamental flaw with most RCT’s is that they frequently fail to provide much of the information needed to make therapeutic decisions – primarily due to their lack of comparative information and the difficulties inherent in ascertaining “relative effectiveness” or the extent to which one agent can be considered superior or equal to another, whether in terms of efficacy, toxicity or price (Ray, Griffin, & Avorn, 1993, 2029).

In recent years, partly due to pressure from funding bodies no longer willing to pay higher prices for newer drugs, and as drug and treatment options have multiplied, equivalence trials, which attempt to demonstrate that two treatments are essentially the same, have been added to the research repertoire. These generally are an attempt to demonstrate therapeutic equivalence (also called bioequivalence) on one, measurable, surrogate end point such as blood pressure or cholesterol. Less frequently, bioequivalence
has been tested on multiple endpoints, a practice which has increased somewhat in recent years (Freemantle et al., 2003; Quan et al., 1999).

**The Uncertainty Principle**

Both types of study, superiority or equivalence, depend on the “uncertainty principle”. This is not Heisenberg’s famous maxim stating that the mere act of observation alters the observed phenomenon (although, as Vandenbroucke remarked, this could also be applied to clinical trials), but refers to “a fundamental ethical and scientific principle” in conducting randomized clinical trials stating that there must be “substantial uncertainty about … the relative value of the treatment being assessed” (Djulbegovic & Clarke, 2001, 1206). There must, in other words, be genuine doubt on the part of the clinical community as to the “relative merits” of a treatment (Shapiro & Glass, 2000, 834). Uncertainty can range from slight to maximum ignorance; the latter is also known as “equipoise”, although there has been some discussion as to what degree of uncertainty equipoise refers to and at what point the term can appropriately be used.\(^2\)

The trial is designed to reject the null hypothesis by showing that there is a difference between the treatments. Since the null hypothesis can never be proven, but only rejected, alternative hypotheses (ie, that one treatment is better) are not assessed directly, but are accepted if the probability that the observed results obtained by chance is less than some predetermined level of statistical significance. (Djulbegovic & Clarke, 1206-7)

\(^2\) Some researchers refer to “theoretical equipoise” that requires that evidence supporting two treatments be balanced exactly, versus “clinical equipoise” which means lack of consensus within the expert community (Shapiro and Glass, 834). I prefer to use the old-fashioned term “uncertainty” and be done with it.
In other words, one enters a trial with a statement of some kind, for example that drug X will affect physiology in such and such manner (presumably in a curative fashion), with the null hypothesis stating that there is no difference. After giving the drug to a certain percentage of an agreed-upon group and a placebo (or, rarely, the standard treatment) to the other portion of the group, researchers then decide whether differences between the two groups are purely coincidental (there will, after all, always be differences between people) or due to the effects of drug or treatment X.

Equivalence trials are the mirror image of this process: the null hypothesis is that the two treatments are different, but researchers are fairly certain (or hoping) they will be proven wrong and that the two courses of treatment are, in fact, the same, or close enough to be considered equivalent. Interpretation is always tricky. Once the results are in, a key question is whether the intervention was effective or not, and, as oncology researchers Benjamin Djulbegovic and Mike Clarke warn in a JAMA editorial, this can be problematic (and somewhat bewildering): “Absence of evidence [of a difference] must not be confused with evidence of absence [of a difference],” they write, and observing a lack of difference between the two treatments “cannot automatically be used as evidence of equivalence” (Djulbegovic & Clark, 1207). However pragmatic it might seem, it is simply not good methodology. Cardiologists Elliott Antman and James Ferguson agree that indirect comparative evidence is “fraught with hazard” and can be potentially misleading due to “apples-to-oranges” comparisons – due to “differences between trials in patient populations, inclusion criteria, management algorithms, and end-point definitions” (Antman & Ferguson, 2003, 2605). Relying on meta-analyses to distill the
vast amount of information rarely suffices either, as these may be subjective and often rely on studies too disparate to be accurately compared.

In an editorial aptly titled “Absence of evidence is not evidence of absence”, Phil Alderson, an associate director of the UK Cochrane Centre53 points out in the *BMJ* that inadequate sample sizes and confidence ratios (or the extent to which one can confidently state one’s research results were not due to chance) may skew the end results:

Statements implying that an intervention has no effect (or is equivalent) might actually discourage further studies by giving the impression that the question has been answered. (Alderson, 2004, 476)

Consequently, an intervention that does in fact protect against infection may not be used, or an intervention that is viewed as having no effect may in fact be harmful (477).

Is it ever appropriate to claim that no differences exist and that there is genuine equivalence? Alderson says no since some uncertainty will always exist.54 But he adds that since we do need some rules for deciding when we are reasonably certain “that we have excluded an important benefit or harm”, it is best to decide, in advance, on some threshold “for what size of effect is clinically important in that situation” (Alderson, 477).

These thresholds, often called “limits of equivalence”, in essence decide the top and bottom point between which equivalence can be assumed – which is also problematic.

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53 The Cochrane Centre is an international repository of so-called best medical practices, based on reviews of randomized clinical trials, available on a central database (and now on the web). Begun in 1992 at Oxford University, it is the namesake of Archibald (Archie) Cochrane, an advocate of scientific medicine. (It is important to note, however, that Cochrane himself was not a clinician.)

54 Djulbegovic and Clarke (2001) write: “If there were no uncertainty, there would be no clinical research. It’s that simple. It is that simple, and the resolution of uncertainty should be the main purpose of clinical trials.” (1206) One could argue, however, that in their zeal to reduce uncertainty some researchers may ignore clinical relevance.
Who decides? At what point should these limits be drawn? Should there be different limits for different groups of patients or different outcomes? And to what extent has equivalence simply become a matter of ease and expediency? Given the difficulties that exist in demonstrating differences in the effects of two drugs, particularly if their effects (e.g., lowering blood pressure) are similar, “it is perhaps not surprising” that focus has turned to ways of determining “whether drugs have ‘equivalent’ effects, yet how equivalence is defined remains of course a matter of opinion” (Hampton, 2002, 2811).

Usually, the first drug of any completely new class “has a reasonable chance of leading to a significant improvement in outcome”; whereas later drugs rarely lead to improvements of “comparable magnitude”. Which is not to say that they may not have other advantages: they may, for instance, have fewer side effects, be easier to administer or be more easily tolerated by patients, or be cheaper (Hampton, 2811). Alderson suggests that, given some precautionary tactics, it is possible to have some measure of assurance:

Firstly, considering results of a particular study in the context of all available research which considers the same question can increase statistical power, reduce uncertainty, and thus reduce the confusing reporting of underpowered studies. … Secondly, researchers need to be precise in their interpretation and language and avoid the temptation to save words by reducing the summary of the study to such an extent that the correct meaning is lost. Thirdly, journals need to be willing to publish uncertain results and thus reduce the pressure on researchers to report their results as definitive. We need to create a culture that is comfortable with estimating and discussing uncertainty. (Alderson, 477) (my emphasis)
Therein lies the rub. No matter how lofty or sensible the rules, in practice most trials contain substantial ambiguities and uncertainties which are open to interpretation. Even those studies which might appear to conform to Alderson’s criteria, at least insofar as they have been peer-reviewed and published (often in quite prestigious journals), are often not as unequivocal as they seem, and, as Alderson points out, the bias is towards a “positive and optimistic interpretation of the effects of new drugs and other interventions” (Alderson, 477). Clinicians and managers then reflect this metaphoric positive “rounding out” of the process, adding their own biases and blind spots to their appraisals and recommendations (Muir Gray, 1999, 1551). These are further codified through guidelines and policy decisions, and, finally, it is patients – oblivious to the layers of uncertainty involved in the process – who end up bearing the consequences, believing in those authoritative sources who have assured them that “this is what the literature says”.

**Decoding the Evidence**

The recent arguments favouring the use of evidence-based medicine in clinical practice and in policy decisions attempting to affect clinical practice make several assumptions, not the least of which is that the evidence from randomized clinical trials *can* be extrapolated to clinical practice. However, in a random assessment of 266 RCTs (of which twenty-seven were picked as being relevant to clinical practice), reviewers at the Clinical Epidemiology Unit at the Ottawa Health Research Centre found that authors of RCTs published in major medical and internal medicine journals “do not consistently
provide their own interpretation of the clinical importance of their results” and “often do not provide sufficient information to allow readers to make their own interpretation” (Chan, Man-Song-Hing, Molnar, & Laupacis, 2001, 1197) (my emphasis). This, Chan et al. write, indicates that the interpretation of results “has traditionally emphasized statistical significance rather than clinical importance” (1197). Other researchers go so far as to suggest that future medical historians will decry our current fashion of reporting research findings:

They will encounter what might be described as a cognitive dissonance: a disconnection between the increasing sophistication of the design [and the swelling cost] of these studies and the apparent lack of care – disastrous in some cases – with which they have been reported. (Moher, Altman, Schulz, Elbourne, & The CONSORT Group, 2004, 349)

This is not an inconsequential problem since, as integral as statistics might be to the data analysis process, it is their context and interpretation which make them applicable to clinical practice and therefore to individual patients, which is, one assumes, their raison d'être. Without that broader context they are, in the words of Hillaire Belloc, “the victory of sterility” over all that matters.

Context, however, has increasingly lost out to process and “clinical trials have progressed from an art to a science” over the last fifty years, writes a UK cardiologist in an article in Statistics in Medicine wittily titled “Size isn’t everything” (Hampton, 2002, 2807). Once fairly straightforward attempts at answering a clinical question, many trials today have become massive multi-centre operations involving thousands of patients with professional researchers and statisticians on hand to “emphasize the importance of trial
size in ensuring that ‘correct’ answers are obtained” (2807). But when a truly good
treatment appears for a disease – fruits high in vitamin C like oranges and lemons for
scurvy, streptomycin for tuberculosis – the smallest of trials will suffice. Large trials are
only needed to demonstrate small effects, writes Hampton, and these may often be
misleading, hiding undesirable effects of individual drugs with large numbers (2807).
Trials have become larger and more complex as treatments have became more similar,
with “relatively minor effects” on disease, which is why it is always important to keep in
mind that chance always plays a large part in differences observed between groups of
people:

What we now accept is that we can place quantified limits around the
difference between the treatments which indicates the range in which a
“real” result lies. There will, however, always remain a possibility that a
particular result is a random occurrence and we often underplay that
likelihood; the improbable coincidences of every day life are real even
though the chance of them actually happening are, in statistical terms,
remote. The desire to establish the reality of small differences between
treatments has led to a progressive increase in the size of clinical trials,
and we have learnt that large trials have many intrinsic problems.
(Hampton, 2807)

Large trials are expensive and time-consuming; patients are difficult to find and recruit,
and errors increase commensurately. “The larger the trial, the less data about individual
patients that can be collected,” writes Hampton (2808). This, in turn, means that results
are less relevant to clinical practice and to individual patients. In many instances,
“statistically significant results may not be clinically important and, conversely,

As the late science and science fiction writer Isaac Asimov used to say, given the complexities of the universe,
what would really be weird was if nothing weird ever happened.
statistically insignificant results do not rule out completely the possibility of clinically important effects” (Chan et al., 1197).

Chan and his colleagues do not define “clinically important”, but, given the vast social, personal, economic, political, cultural, and even domestic consequences of illness and treatment, the term deserves greater examination and weight. Furthermore, given that “drug interventions have been studied more extensively than non-pharmacologic interventions” (van Weel & Knottnerus, 1999, 917) due to their relative simplicity (and highly motivated drug companies), clinical importance – defined or not – often loses out to expedience. Factors that matter to patients, be it efficacy, ease of use, side effect profile, long-term risk, quality of life, freedom from pain and disability or simply feeling better (which one would think should matter), seem to have taken a back seat to statistics and this “techno-scientific” perspective within medicine, pharmacology and epidemiology as well as pharmacoeconomics and health policy decision-making. This often minimizes patient concerns (or ignores them altogether) and glosses over the risks inherent to all medical interventions, including, or perhaps especially, medication.

Risk is most often perceived as an “objective phenomenon” which can be mathematically or algorithmically expressed, thereby providing information on causality, safety, and dosage. The idea is that risk may be quantified; its causes mapped out and its incidence limited (Corrigan, 2002, 497). But it is patients who subjectively carry any risk there might be, and this “black boxing” of human factors, as philosopher of science
Bruno Latour proposed in a different context\textsuperscript{56} (Latour, 1987, 3), sidesteps individual and human factors – from physiology and side-effect profile to personal psychology and values. This is Belloc’s victorious “sterility”, amplified as researchers simplify messy human aspects by allocating surrogate end points or biomarkers (numbers representing a state of health or ill-health, in other words) as stand-ins for larger, inferred clinical results.

Even without such shortcuts around individual idiosyncrasies, translating research findings into clinical practice presents major difficulties and contains huge ambiguities. Understanding the “minimal clinically important difference” or MCID as it is called in epidemiological circles, is no easy matter. The MCID is defined as the smallest treatment effect “that would result in a change in patient management” (one assumes a positive one) taking into account “side effects, costs, and inconveniences” (Chan et al., 1197). It is, in other words, an intervention with a greater positive aspect than a negative one, a move with the cost-benefit ratio tilted towards the benefit side, enough so for most reasonable people to conclude that it is worthwhile. But again, who decides what has value?

To use David Eddy’s analysis, having opened the first black box – the evidence – the second black box – the preferences – will need to be opened in public. (Muir Gray, 1999, 1551)

\textsuperscript{56} Latour borrowed “black box” from cyberneticians, who, whenever “a piece of machinery or a set of commands is too complex” simply draw a box around it to indicate that all they need to know is “input and output”, not the inner workings (Latour, 1987, 3).
The problem is that it rarely is opened in public and evidence-based medicine can be said to drastically curtail patient choice insofar as it rarely includes outcomes “such as the nature and incidence of side effects which may be considered minor by researchers”, or takes into consideration patient characteristics and circumstances. Traditionally, the practice relies on “biomedical markers” rather than consequences that patients value (Rogers, 2002, 97). Too often research reflects professional interests and enthusiasms, yet it is difficult for an impartial observer to understand precisely why patient input should not play a deciding (or even a minor) role. It is, after all, for patients’ ostensible benefit that all research is undertaken.

It is also important to note that “participants in clinical trials are seldom representative of the general population” and are, with rare exceptions, healthier, younger (perhaps even prettier), not to mention of higher socio-economic status (Mant, 1999, 743). Extrapolating from this group to patients in general to achieve “conscientious, explicit and judicious use of current best evidence” (Sackett et al., 1996, 71), which is how evidence-based medicine is defined, presents major problems. Additionally, the research itself can be shown to have design and methodological flaws, since many, if not most, trials utilize a comparison of the new drug or treatment with a placebo rather than comparing it to other possible and existing treatments. The relevant question clinically is one of relative effectiveness, or the “efficacy, toxicity, and cost of the new drug as compared with those of alternative agents” (Ray et al., 1993, 2029) – and, importantly, whether there are adequate data to guide choices among therapeutic alternatives, which is what doctors and patients want to know. Clinical trials, however, are seldom able to
answer this question, and, as the number of reviews and analyses on research increase exponentially, most clinicians struggle to apply the results of studies that do not seem relevant to their patients and practice:

We face the problem that criteria for internal and external validity may conflict. Clinical studies are usually performed on a homogeneous study population and exclude clinically complex cases for the sake of internal validity. Such selection may not, however, match the type of patients for whom the studied intervention will be considered. Medical practice is often confronted with patients presenting several problems. Older patients and women are under-represented in clinical trials and patients with comorbidity [more than one disease], a common phenomenon at older ages, are generally excluded. Evidence from patients selected by referral cannot easily be generalised to patients seen in primary care with less severe or early stage clinical pictures. And some important needs for evidence are almost ignored. For instance, while drug trials usually provide evidence about starting drug treatment, doctors are increasingly confronted by patients taking multiple long term medications but have no proper data on evidence based drug cessation. (Knottnerus & Dinant, 1997, 1109)

Knottnerus and Dinant make a plea for “medicine-based evidence” that encompasses the broader spectrum of real life instead of increasingly sophisticated trials that are large, expensive, and provide results that are vague and untrustworthy.

How studies are funded, furthermore, often correlates with whether or not the findings are positive (Als-Nielsen, Chen, Gluud, & Kjaergard, 2003, 921), and there is a certain arbitrariness to clinical trials – the “same trial may be considered positive or neutral on the basis of decisions concerning the statistical design – and treatment effect

Internal validity refers to the extent to which a study establishes “the cause-and-effect relationship between the treatment and the observed outcome” and ideally is based on logic and not statistics (Slack & Draugalis, 2001, 2173). External validity refers to the clinical applicability of the study and the extent to which it can be generalized to individuals outside the study.
measures may be diluted” by other considerations (Freemantle et al., 2003, 2556). For the vast majority of patients, therefore, the evidence simply does not apply:

Clinical trials often include patients within a certain age group and with certain clinical characteristics; in the real world patients are less well-defined and do not fit the inclusion and exclusion criteria of the trial. In order to obtain a “clean” answer, the designers of trials usually attempt to include patients with a single disease; in practice patients frequently have multiple problems involving multiple therapy. Clinical trials, by their nature, tend to include low-risk patients, and when registers are maintained … it is clear that the trial’s results only apply to a very small proportion of the generality of patients. (Hampton, 2002, 2812)

When patients excluded from a trial (because they were too sick or had too many things wrong with them, the typical physician roster) are followed over time, their outcomes are almost always worse than those of patients in a clinical trial:

Patients included in a series of thrombolytic trials in Nottingham had a considerably lower fatality rate (24 per cent compared with 37 per cent at four years) than those who were given a thrombolytic but who did not fulfill admission criteria of the trial. (Patients given no thrombolytic at all had the highest fatality rate: 60 per cent.) … The inclusion and exclusion criteria of clinical trials lead to the trials recruiting younger and more mobile patients who can attend follow-up and patients free of other diseases and patients who are not being treated with multiple drugs. The results of the trial therefore apply only to those low-risk patients, which makes the application of “evidence-based medicine” very difficult in the real world. (Hampton, 2812)

A further problem is that for any given area of research it is impossible to know how many studies “have been conducted and never reported” (Williams & Garner, 2002, 9).

Unfortunately, at this stage, researchers are still in thrall to the randomized clinical trial, which has entered the medical lexicon as a standard bearer for scientific, objective, and value-free medical knowledge. The president of the UK Royal College of
General Practitioners has even called evidence-based medicine "the new deity in medicine" (Mant, 743). But the "paradox of the clinical trial is that it is the best way to assess whether an intervention works yet is arguably the worst way to assess who will benefit" (744). One could, conceivably, require larger and larger trials that include every possible sub-group of patient – or, at the other end of the spectrum, call for an infinite series of "N = one" trials – but these are not feasible, affordable, or, ultimately, useful.

**Bradford Hill and Post-war Exuberance**

Contrary to the current hype, which makes the clinical trial sound as though it is a pure scientific method which has existed for eons, the RCT has only been around in its present form since the 1940's, although it is popular to ascribe similar evaluative techniques to historical figures, the book of Daniel in the Bible being a particular favourite.58 Furthermore, writes medical historian Marcia Meldrum, the RCT is "not a theory in itself, but a technology, a method encompassing several concrete practices" resting "on implied theoretical assumptions" and understood "through a mathematical statement about probability" (Meldrum, 1994, 6). In its simplest form the RCT allows the researcher to decode that "mathematical" statement to construct a conclusion that ought, in the best of all possible worlds, to have meaning for the patient, namely that the drug or treatment is effective and safe or more effective and safe than an alternative – or,

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58 Daniel convinced a palace official to let him conduct a "pilot study" to examine the effects of a vegetarian diet on the court, which traditionally dined on rich food and wine (Daniel 1:15).
perhaps, doing nothing at all, although that is rarely suggested, modern western medicine being the active enterprise it is.

The randomized clinical trial came into prominence in the euphoric years after World War II, during a period when technology, pharmacology and medical innovation seemed limitless. War has always been an excellent stimulus for medicine – the Napoleonic Wars led to sharper (sorry) surgical techniques, particularly amputation, as well as to the concept of triage and ambulances. The American Civil War accelerated the acceptance of anaesthesia and created the first documentation on epidemiology and on the care of surgical patients, while the brutal wounds of World War I led to improved burn techniques, plastic surgery and blood transfusion, and also ameliorated the understanding of the psychological impact of war, battle fatigue and post-traumatic stress (Duffin, 2000, 233). Even the Trojan War in ancient times resulted in some medical advances, notably analgesia (pain relief). But the 20\textsuperscript{th} century saw such extraordinary changes that it seemed for a time as though technology could solve \textit{everything}. So prevalent was faith in technology's potential benefits, whether machines or processes (scientific, bureaucratic, managerial, social), that by the 1990's patients were being hurled down "treatment trajectories" that would have been unthinkable even a few decades earlier (Mechanic, 2002, 459). Evidence and evidence-based medicine, therefore, took on enormous importance as governing bodies of one kind or another sought to set limits on new and expensive medical interventions. Within that repertoire, the randomized clinical trial has constituted a kind of counter-balance to market and socio-
cultural forces, yet, ironically, the RCT itself was one of those promising post-war technologies which epitomized the use of logic, mathematical algorithms and progress.

Streptomycin was the first drug to be systematically tested in this way, primarily because so little of the drug was available that A. Bradford Hill, the physician manqué turned researcher and statistician who had long attempted to quantify medical treatment, managed to convince Britain’s Medical Research Council to agree to a “rigorously planned clinical investigation with concurrent controls” to treat pulmonary tuberculosis.⁵⁹

The pioneering study, comparing streptomycin with conventional treatment [bed rest], got under way in January, 1947. (Patients were randomly allocated but the study was not blinded.) ... Post-enrolment mortality indicated a clear advantage of the new treatment (4 deaths before the end of six months among 55 patients who received streptomycin versus 14 fatalities among 52 patients who were treated with bed rest). The need for a control group in this study was underlined by the finding that impressive clinical improvement was seen in 13 patients treated by bed rest alone. Important limitations of streptomycin treatment were also disclosed: the emergence of streptomycin-resistant strains of tubercle bacilli...; serious toxic effects of the new drug on vestibular function...; and the drug appeared to have little effect on the chronic fibro-caseous forms of tuberculosis. (Silverman, 1998, 99-100) (my emphasis)

The streptomycin trial was based in part on Hill’s belief that statistics were relevant to medicine, which he had eloquently expressed in 1937 in his seminal book, *Principles of Medical Statistics* – a book which was one of the most “influential textbooks on medical statistics in this century” (Vandenbroucke, 1998a, S14). Hill revised the text until his death in 1991, which coincided with the 12th and final edition, by

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⁵⁹ What little was left over of the drug was used to treat two invariably fatal forms of the infection, military and meningeal TB.
which time Hill had been knighted and had become synonymous with the RCT. In retrospect the book is said to have its “one-sidedness” and, as it contains no references, can leave the reader second-guessing the source of his teachings (S15). Interestingly, with the passage of time and perhaps as a result of realizing the extent to which his ideas were being misapplied, Hill’s reverence for numbers and statistics dimmed somewhat and by the 9th (1971) edition, Hill was cautioning that the pre-eminence of the statistical method should not mean “a blind or exaggerated faith in, or reliance upon, techniques” (Horton, 2000, 3152). He even pondered on informed consent and whether the streptomycin study would even have been possible had patient consent been an issue – and expressed dismay at the rising trend to shift “consent-giving responsibility” onto the shoulders of patients “who cannot really be informed or know what weight relatively to put on the technical information provided” or to properly understand the risks and benefits involved (Silverman, 1998, 100).

As Richard Horton, the high-profile editor of The Lancet relates, this constituted a definite shift in tone from earlier editions where Hill had extolled the virtues of numeric data and had exhorted statisticians “to rise from their humble place” (3151). By 1961 Hill even went so far as to suggest that randomized clinical trials should be designed “to promote rather than hinder the traditional method in medicine of acute observation of disease by the clinician at the bedside” (Horton, 2000, 3152), and, in a 1965 lecture, exhorted his audience to “relax and reflect”, since any belief that the RCT is the “only” route to medical truth would not only mean that the pendulum had swung too far but that “it had come right off its hook” (Enkin & Jadad, 1999, 297). By 1984, Hill had added the
rider that “at its best” a clinical trial “shows what can be accomplished with a medicine under careful observation and certain restricted conditions” and tiredly warned that similar results would not invariably or necessarily be observed when the medicine passed into general use (Horton, 3152).

Yet equivalence, a pragmatic concept used in policies designed to affect general practice and use, relies crucially on evidence from clinical trials. Does this mean that there is an inherent fallacy contained within the idea of therapeutic equivalence? External validity – or the ability to generalize from study results to the population of patients at large – has indeed become a major problem as clinical trials have proliferated, which could perhaps explain the indifference that many physicians demonstrate for the heavy-handed persuasion tactics emanating from evidence (no matter how much university-based research groups would prefer it to be otherwise.)

The mechanistic and often autocratic approach favoured by so many guideline writers and researchers (often indicating a blithe obliviousness to clinical realities) makes the application of evidence at the bedside complex, difficult and ambiguous. Ideally, the clinical research on which treatment decisions are based “refer to methodologically strong clinical trials examining the impact of therapy on clinically important outcomes” (Bucher et al., 1999, 771) – such as not dying from TB. But in contrast to Hill’s clear prose and pointed clinical bent, at present, even though “the ultimate goal” of the

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60 *JAMA*, since the late nineties, has run a series of “User’s Guides” in which evidence-based researchers painstaking instruct physicians on how to “translate” evidence from clinical trials into clinical practice. These articles are long, complicated, abstruse and mind-numbingly dull. How a practicing physician could even manage to find the time to read these much less apply them to each patient boggles the mind.
research and guidelines appears to be “the identification of therapies which can prolong life and/or alleviate suffering” (Lonn, 2001, 497), the majority of research topics seem less concerned with patients and more interested in signs, biomarkers and surrogate end points.

**Surrogate End Points**

Conducting research that genuinely answers the broad questions of health and disease is immensely complicated, presents enormous logistical difficulties and requires time, resources and infinite creativity. Methodological problems are substantial. Answering clinical questions requires long-term patient follow-up, large sample sizes and diverse and varied patient populations. A common solution, therefore, has been to substitute surrogate end points for the targeted benefit; in other words, cardiac or AIDS or cancer drugs are not tested over time by measuring overall morbidity and mortality. Rather, biomarkers are used as proxies for long-term well-being. What is measured and studied (and assumed to be a reliable indicator) is blood pressure or cholesterol for heart function; bone density for skeletal strength; CD4 cell counts for HIV-AIDS, tumour shrinkage as a measure of cancer remission and so on. It is now commonplace to take a laboratory measure and assume that it is an accurate reflection of whatever it is that is being studied (Fleming & DeMets, 1996, 605). These measures are called surrogate end points, and whether they are lab findings or physical signs, they are assumed to be clinically meaningful endpoints that measure “directly how a patient feels, functions, or survives” (Bucher et al., 771). Only occasionally, for example in the Cardiac Arrhythmia
Suppression Trial (CAST) which tested drugs that suppressed ventricular arrhythmias, is the real endpoint — sudden death — studied. (In this case the hypothesis was that the intervention, drugs, would prevent sudden death after a heart attack. But they did not and, in fact, patients who were on placebo did far better than those in the treatment arm.) (Echt et al., 1991, 781).

There is much debate as to the utility of surrogates — or biomarkers as pharmacologists and statisticians call them; nevertheless most researchers seem to feel that, judiciously used, surrogates “have a definite and important role in the development of new therapies” and, if wisely applied, are vital to biomedical research (Lonn, 2001, 507). Suggestions vary as to how this “importance” may best be measured. Since “surrogate endpoints in clinical trials are biological markers or events observable earlier than the clinical endpoints” such as death or major dysfunction, they are quicker and more expedient. The “proportion of treatment effect”, or PTE, captured by a surrogate is “intended to address the question of whether trials based on a surrogate end point reach the same conclusions as would have been reached using the true endpoint” (Cowles, 2002, 811). This PTE measure is then assumed to provide the certainty needed to make assumptions for clinical care.

The word surrogate comes from the Latin and means to “elect or ask in place of”. It has been suggested that the name itself “entails a hint of disreputability, evoking

Most large trials, especially of cardiac drugs, have catchy acronym titles like HOPE (Heart Outcome Prevention Evaluation) and PROGRESS (Perindopril Protection Against Recurrent Stroke Study). One suspects these catchy acronyms were thought up by catchy PR people.
images of distorted motherhood” (Wittes, Lakatos, & Probstfield, 1989, cited in Lonn, 498). Toronto cardiologist Eva Lonn provides a more functional description:

Investigators use surrogate end points when the endpoint of interest is too difficult and/or too expensive to measure routinely and when they can define some other, more readily measurable endpoint which is sufficiently well correlated with the first to justify its use as a surrogate. (Lonn, 2001, 498)

Surrogate end points must be “biologically plausible” (Ballantyne, 2001; Orloff, 2001) and “feasible” at the tissue, cellular and molecular level (Kelloff et al., 2000). For drug approval purposes, according to FDA physician Robert Temple:

A surrogate endpoint or marker is a laboratory measurement or physical sign that is used in therapeutic trials as a substitute for a clinically meaningful endpoint that is a direct measure of how a patient feels, functions or survives and is expected to predict the effect of the therapy. (Temple, 1999, 790)

Patients (and by extension medical researchers, or so one supposes) do not really care about the surrogate per se; it is “a benefit only to the extent that it causes or predicts an improved outcome” (Temple, 790). Surrogates may also be used to measure toxicity and drug safety, although they may only be used for direct risk assessment if they are “critical to the mode of action” (Renwick & Walton, 2001, 97).

Theoretical or laboratory indications aside, the basic truth is that drugs always have multiple effects – and even the safest drug may be dangerous for a minority of patients. Focusing merely on one positive (or negative) action ignores the multiplicity of
action involved in pharmacodynamics – and completely ignores pharmacokinetics as it is simply too difficult to measure. As the University of Chicago’s Thomas Kramer writes:

Drugs have effects on the body. That is why we give them to patients. Our goal is to have the effect of the drug be therapeutic. Generally speaking, drugs have two kinds of effects: therapeutic effects and side effects. It is, to a certain extent, a value judgement, however, whether a particular effect of the drug is a side effect or a therapeutic effect. (Kramer, 2003)

It is not unknown, for instance, for a drug to be developed and approved for a particular symptom, only to be found more effective for something completely different. For example the drug Viagra, which is marketed for “erectile dysfunction”, was originally developed as a cardiac drug.

The main purpose of clinical trials during the drug development process is to weed out those drugs whose side effects or toxicity overwhelm their therapeutic impact. When surrogate end points are used to determine safety and efficacy, however, the multiplicity of drug actions can be obscured by the focus on perceived benefit as measured by the surrogate, thus muddling the situation and making interpretation tricky:

In theory, for a surrogate end point to be an effective substitute for the clinical outcome, effects of the intervention on the surrogate must reliably predict the overall effect. In practice, this requirement frequently fails. (Fleming & DeMets, 1996, 605)

The authors add that a measurement of a drug’s efficacy is merely an indication of the ability of the drug to treat whatever condition it is indicated for and is not a statement of tolerability since even sophisticated statistical models cannot accurately pinpoint the treatment effect of a new therapy.
Many decisions about effectiveness are dictated not only by methodological requirements but are based on the “assumptions, interests and values of the researchers (Rogers, 2002, 98). The estimates of a treatment effect:

of a new therapy under investigation explained by its effect on the surrogate is extremely variable, with point estimates varying largely based on different assumptions made for the experimental conditions. (Lonn, 499) (my emphasis)

For patients, many of the decisions made during this process result in “a narrowing of focus or judgement” (Rogers, 2002, 97), as the question which can reasonably be answered is tailored and reduced to fit the experimental parameters. Researchers, like everyone else, create experiments in which they are likely to observe what they anticipate seeing, and as a result “both investigators and publishers” tend to enthusiastically report studies in which large treatment effects on surrogates are demonstrated. Meanwhile, they fail to “report negative or even modest treatment results” (Lonn, 503). This publication bias – frequently commented on but never parsed or analyzed within the discussion or commentary sections of actual studies – often leads to an overestimation of treatment effect with imprecise treatment recommendations even for biologically plausible events.62

In addition, merely focusing on a positive effect is inadequate clinically as other drug actions and side effects may well become harmful in the long run as the drug comes into widespread use and is used for a wider and more diverse population. This is particularly

62 Missing or censored data, whether it consists of “informative censoring” (“censoring that depends on the variable of interest”) or incidental censoring – such as patients dropping out – can also introduce bias. It is suggested that when there is a sizable amount of missing data “it may be most appropriate to avoid drawing any conclusions from the study” (Lonn, 504), but this laudable idea rarely makes it into practice.
problematic if the drug is primarily given to asymptomatic individuals, as is often the case with cardiac drugs.

In the mind of two American cardiologists, “a certain linguistic erosion” has crept into research pertaining to such drugs:

In studies of antihypertensive agents, we determine what happens to systolic and diastolic blood pressure, cardiac output, peripheral vascular resistance, and other pathophysiological variables in the context, of course, of patients stratified with respect to the etiology, duration, and severity of hypertension and target organ involvement. In mechanistic studies, the dependent variable of interest is a biological phenomenon (i.e., in this case, blood pressure), which is, in turn, dependent on specific physiological determinants such as cardiac output and peripheral vascular resistance. If hypotheses that elevated blood pressure causes vasculopathy [which in turn] causes mortality are valid, inferences regarding long-term outcomes that are predicated on the basis of the antihypertensive effects of a given drug will be valid. (Sobel & Furberg, 1997, 1661)

On the other hand, if the hypotheses are inadequate or overly simplistic or simply wrong and the pathology of the heart is determined by “covariates of blood pressure rather than by blood pressure itself”, or “by a common ancestral phenomenon that influences blood pressure in parallel”, and if cardiac disease is influenced by unrelated factors we do not yet understand, then the inferences will be weak or wrong (Sobel & Furberg, 1661). In other words, we are reasoning on the basis of a correlation, assuming that blood pressure must be a cause of cardiac disease, but we could be wrong. And therein lies the rub.

Truth in medicine is often elusive, and current theories and fashions do not always accurately reflect what is really going on. Merely “being on the causal pathway does not itself constitute surrogate validity” (Schatzkin, 2000, 887). Even when we are examining the “how” (versus the “why”), when a phenomenon occurs that scientific methods are
said to clarify (Sutter, 2000, 338), teasing out accidental associations and correlations from genuine biological and physiological causes is complicated and messy.

**The Downside of Surrogate End Points**

There is some concern on the part of researchers that long-term studies using surrogate end points may be misleading because of “missing data” (Agewell, Fagerberg, Berglund et al., 2001, 305) and the inability of surrogates to “capture all the therapeutic benefits and potential adverse effects a drug will have on a diverse patient population” (Lesko & Atkinson, 2001, 347). This is particularly worrisome given the unfortunate and extensive “history of quite plausible surrogate markers giving the wrong answer” (Schtazkin, 887). For instance, as was mentioned earlier, agents that suppressed ventricular arrhythmias (a kind of irregular heartbeat that is associated with an increased risk of heart attack) were assumed to prevent adverse cardiac events; yet the very opposite was found: Suppressing arrhythmias was found to *increase* mortality, an unexpected finding which led to “the deaths of tens of thousands of patients” (Bucher et al., 1999, 773). Similarly, CD4 cell counts proved useless as a surrogate marker in predicting the development of AIDS, even though they seemed to make sense at the time.

In HIV-AIDS, as the virus advances, the quantity of CD-4 cells, a subset of immune system T-cells, decline. Researchers, therefore, theorized that increasing CD4 cell counts would halt or slow the progression of the disease. Unfortunately, CD4 cell counts turned out to be incidental to the progression of AIDS, as the Concorde Trial in the early 1990’s demonstrated. Some 1749 asymptomatic HIV-positive patients were
randomly assigned to receive immediate or deferred treatment with the drug zidovudine (AZT) which was believed to increase CD4 cell counts. One group received the drug as soon as they were diagnosed HIV-positive; the other, after full-blown AIDS had developed. During a three-year follow-up, zidovudine did indeed slow the decline of CD4 cell counts, as predicted, but not only did the patients' health not commensurately improve, but some twenty more patients died in the early treatment group.

Biostatisticians Thomas Fleming and David DeMets of the University of Washington write:

Time of progression to AIDS-related complex, AIDS, or death was essentially unaffected (175 events in the immediate zidovudine treatment group compared with 171 in the delayed zidovudine group). For death alone, the results actually favored the delayed ... treatment group (95 compared with 76 deaths). The early pressures to use zidovudine treatment in asymptomatic persons with HIV were not supported by these longer-term clinical events. (Fleming & DeMets, 1996, 607)

Since correlation is never proof of cause, the substitution of surrogate end points in clinical trials is potentially dangerous as well as theoretically problematic. Current theories may be found to be spectacularly wrong. For example, does high cholesterol cause cardiac disease or is it merely an incidental association? Do blood pressure drugs actually prevent heart attacks because they lower blood pressure or because they have some other, as-yet-unidentified, effects such as reducing inflammation and effecting protective changes on the arterial wall as Sobel and Furberg and other cardiac researchers have suggested (Gerstein, 2000, 253)? We assume it is the former, but at this stage we simply do not know.
The list of studies and theories using plausible-sounding surrogate end points which were unable to predict other, unintended effects of the therapy goes on. Sodium fluoride, which stimulates bone formation and increases bone mass, came into widespread use two decades ago because it was believed to prevent osteoporosis in postmenopausal women. Even though it had not been officially approved, the general belief was that anything that fortified bone would be effective in preventing osteoporosis and the subsequent bone breakage which only too often leads to disability and early death.\textsuperscript{63} The compound did indeed do what it was supposed to do, namely increase bone mass, but breakages and fractures increased (seventy-two compared with twenty-four broken bones in the placebo group). It turned out that sodium fluoride did make bones harder, but it also made them more brittle (Fleming, 610), much in the same way some nail polishes and hardeners do. In this instance the multiplicity of treatment effects (or the complexity of physiology) were not taken into account, only the perceived benefit. Later studies proved equally inconclusive, leading one group of researchers to conclude that “bone mineral density as a surrogate end point has shown an inconsistent relationship to osteoporotic fractures”. Ironically, low-tech interventions such as calcium and vitamin D, which did not increase bone density, did seem to lead to fewer fractures (Bucher et al., 1999, 776).

Surrogate end points may also have false-negative results, which means that promising and effective treatments are discarded prematurely. This was demonstrated in a

\textsuperscript{63} “There will always be plausible interventions for which no evidence is [yet] available, but that in itself is no reason to withhold the intervention.” Or so many researchers think. (van Weel & Knottnerus, 1999, 917) In other
trial of chronic granulomatous disease in children. Children with this disease have a compromised immune system in which macrophages, a particular type of “eater” cell present in the immune system, identify and target microorganisms but cannot generate the oxygen “burst” necessary to eliminate them. This results in recurrent, serious, often life-threatening infections.

Interferon-gamma was considered to have therapeutic potential because of its anticipated ability to increase superoxide production and kill bacteria. The initial design of a placebo-controlled trial specified that patients who were randomly assigned to the control group would receive placebo for an interval so brief that only an evaluation of the effect of interferon-gamma on the surrogate end points (superoxide production and ability to kill bacteria) would be possible. Before its initiation [luckily], the trial was redesigned to enable longer-term assessment of treatment effects on the true clinical outcome, that is, the rate of serious infections. ...Interferon-gamma produced a significant 70% reduction in the rate of recurrent serious infections [with] no detectable effect on the surrogate end points. (Fleming & DeMets, 610)

Obviously, the how, the mechanism of action of interferon-gamma on the macrophages had not been understood. Perhaps the macrophages have nothing to do with it at all.

Fleming and DeMets mildly conclude by suggesting that “effects on surrogate end points often do not predict the true clinical effects of interventions” (613). In the end it is unclear whether this is due to a lack of understanding of disease causal pathways not mediated through the surrogate end point or whether the intervention has unintended and/or positive mechanisms that have not been recognized or anticipated. Either way, the use of surrogate end points merits caution – yet surrogates are almost invariably the rationale used in policies on equivalence.

words, even though we’re not sure, it’s fine to practice our theories on unsuspecting patients.
Surrogates as Part of the New Drug Approval Process

Too often the literature on surrogate end points does not sufficiently “distinguish between the effort to validate a surrogate end point as a risk factor and the use of a surrogate end point to evaluate a new therapy” (Psaty et al., 1999, 788). In the latter instance, surrogates perform fairly well in screening for “promising” new therapies through “evaluation of biological activity in preliminary phase 2 trials” (Fleming & DeMets, 611) and can guide decisions as to whether or not an intervention is promising enough to warrant further investigation. However, if the surrogate study is not a prelude to further examination of true process and is merely an exercise in generalizing from one drug to another (as is common in equivalence trials), problems can result. The sheer convenience of surrogate end points can result in too-quick acceptance of new therapies, even though ideally “results obtained with surrogates should be regarded as preliminary and necessitate definitive studies” (Ray & Sarkar, 1999, 894).

Surrogate end points, furthermore, often are the basis for drug approval, solidifying the often-untested assumption that the risk factor is the “real” problem when it may be a mere association or archetype. In coronary artery disease, for instance, both the medical and lay literature glibly cite the mantra of risk factors – high blood pressure and cholesterol levels, diabetes, obesity and smoking – as the primary focus points. The logical extension is that it is the risk factor itself which is the problem and changing it,

Psaty et al. (1999) write that “paradoxically, surrogates are most likely valid where least needed”, the so-called “me-too” drugs which are not as necessary to the clinical repertoire given that other, equally efficacious drugs already exist.
e.g., quitting smoking or losing weight or lowering blood pressure, is tantamount to decreased morbidity and mortality from cardiac disease. The “logical appeal and the formal structure of deduction” makes this reasoning attractive: “a risk factor causes morbidity and mortality, and the intervention reduces the risk factor level, therefore, the intervention will reduce the risk of morbidity and mortality” (Psaty et al., 786). But as the authors argue, this is “argument by analogy”, not empirical evidence. The fact that a new drug appears to reduce the level of a biomarker (e.g., a blood pressure or lipid level reading) provides no proof that this translates into any genuine health benefit.

Take, for example, the issue of excess weight, often considered a major risk for heart disease, which, as Psaty and colleagues describe, backfired badly:

An editorial on the pharmacotherapy of obesity [in The New England Journal of Medicine no less] illustrates the argument: in the context of discussing the association between appetite suppressant drugs and primary pulmonary hypertension, the editorialists used observational evidence on the association of body mass index with mortality and translated data on weight loss in a small, short-term trial of dexfenfluramine into an estimate of lives that could be saved by long-term drug therapy for obesity. The US Food and Drug Administration approved dexfenfluramine on the basis of this same surrogate end point argument [no doubt encouraged by the many people who were desperately looking for an easier, quicker weight loss method]: “the potential health benefits of anorectic drugs outweigh their risk when considered against the health hazards of obesity.” (Psaty et al., 786)

The FDA (and the NEJM) turned out to be spectacularly wrong. Dexfenfluramine was a potent stimulant that dangerously affected heart muscle and a number of people died

Some (rare) authors distinguish between risk factors and risk markers, with the former being considered in the causal pathway and the latter, not (Morley Sutter, personal communication, November 2004).
before the drug was withdrawn. Has this obvious and fundamental flaw in the drug approval process and its underlying “risk factor” rationale deterred anyone? Not to date. Blood pressure and blood sugar and cholesterol levels continue to be used as biomarkers in clinical trials and for drug approval even though trial results are often inconclusive, complex and yield equivocal results. “Randomized clinical trials are not tests of particular risk factors or mechanisms of therapies,” warn Psaty et al., “They are always trials of particular interventions, often specific drugs in particular doses.” (788) Their long-term impact on large populations remains ambiguous, and caution is called for in extrapolating from their conclusions.

Some investigators suggest that the only exceptions to this should be treatments for highly aggressive and often fatal diseases such as cancer and AIDS, where alternatives are minimal. In these instances the medical and regulatory community has a “justified concern about delaying potentially lifesaving interventions” (Lonn, 2001, 497) and, in this era of patient activism, media attention and corporate-assisted lobbying, regulators and researchers are often under considerable pressure to speed through decisions:

In addition to these arguments of ethics and convenience, the most relevant clinical endpoints may occasionally be extremely difficult to measure accurately (for example, cause-specific death) and in certain circumstances, even “ultimate” endpoints, such as survival, may be misleading. The issue of “competing risks” when survival is the endpoint, has been raised in cancer research, as in long-term trials a substantial proportion of the study population might be expected to die of causes unrelated to the disease under investigation, cause-specific death may be difficult to establish and thus an earlier intermediate endpoint might actually provide a more precise estimate of the treatment effect. (Lonn, 497)
Ideally, then, there is a balance between primary endpoints and clinically-relevant events, i.e., those events which patients generally want to avoid such as disability and early death, and the use of the more expedient surrogate outcomes or biomarkers. But the use of “continuous surrogate end points such as blood pressure in RCT’s has become popular” and gained wide acceptance without sufficient analysis of what the ultimate point of the research might be – or any real understanding of whether or not the surrogates are “valid as proxies for clinically important outcomes” (McAlister et al., 1998, 488). Given that it is evidence which is the basis for therapeutic equivalence, this gap is fundamental to the argument around formularies and reference pricing. For, as McAlister et al. wearily point out, even with the gold standard RCT, “all that glitters is not gold” (489).

Claims of Equivalence and the Evidence

Data based on surrogate end points is commonly used to make assumptions about different drugs within a single class and in determining therapeutic equivalence:

Conceptualizing the issue in terms of “the surrogate end point” – drug effects on risk factor levels – unfortunately encourages easy extrapolation from one drug to another drug even though the mechanisms of action, the adverse effects, and the effects on clinical end points may differ markedly between drugs or drug classes. (Psaty et al., 788)

This type of conclusion, based on comparison and analogy, means that the “net health effects of the untested drug are simply assumed to be the same as the net health effects of the tested drug” (my emphasis). Yet one, or even many, trial(s) from a single drug class provides minimal information on the surrogate’s validity since “the evaluated therapy
may in fact work through a mechanism completely independent of the surrogate” (788). Validation of a surrogate as a genuine risk factor is best done with data from multiple trials using drugs from a variety of drug classes, thus enabling observers to confidently state that this or that surrogate is actually part of the disease process; yet common practice is to extrapolate from one class of drugs to another. This is especially true when the perspective is regulatory, since guidelines, by their very nature, are extrapolations and generalizations. But even assuming that drug class divisions as they now are defined are genuine and will stand the test of time, making the jump to equivalence seems more a leap of faith than science, particularly given the haphazard ways in which claims for equivalence are presented.

True understanding of what can reasonably be substituted for something else can be mystifying for the prescribing physician – and totally bewildering for patients – and clinicians frequently disagree with statisticians and researchers as to what constitutes equivalence (Hampton, 2813). At the 9th annual congress of the International Headache Society in Barcelona, Fred Sheftel, a neurologist from the United States, complained that prescribing information based on current data using different endpoints is completely inadequate for prescribing and illustrated the point with the available information on migraine drugs:

Take this scenario: triptan A [the triptans are the relatively new class of migraine drugs, e.g., Imitrex®] claims 75% response rate; triptan B claims 51% adjusted placebo rate; triptan C claims two-hour pain free of 44%; triptan D offers complete pain relief of 34%; and triptan E offers adjusted complete response – according to the International Headache Society Definition – of 28%. What is the primary care doctor to do? What are you
to make of these figures? Ideally I’d like all companies to make their endpoint two hours pain free and no recurrence. (Johnston, 1999, 9)

Placebo-based data, which most RCT’s provide, is also problematic. According to the neurologists at the congress described above, all the new migraine drugs (rizatriptan, sumatriptan, and eletriptan) claim superiority over their competitors, but it is difficult to find any clinically relevant difference between them. In the end what matters to patients and clinicians is that an individual patient can tolerate the drug and obtain pain relief, and that initial prescribing requires data is presented in ways that matter to patients suffering from the condition or disease in question. “Although in clinical trials we present data usually based on a single attack, our patients will invariably use these medications over multiple attacks,” added neurologist Richard Lipton, yet this data is rarely, if ever, presented or made clear in the literature (9).

Clinically relevant or not, references to equivalence studies have multiplied in the medical literature in the last fifteen years. A cursory Medline search reveals a mere fifteen mentions of “therapeutic equivalence” or “therapeutic equivalency” between 1967 and 1987, with the earliest reference appearing in 1976. The numbers jump between 1988 and 2003 where equivalence is cited 766 times. (It would seem that there simply were not enough potentially equivalent drugs on the market prior to 1976 to warrant study.) While the majority of these references deal with the bioequivalence of generic drug substitutions, a little over a third analyze therapeutic equivalence and within-class substitutions of one drug for another. Physician-researchers at the Yale School of Medicine, William Greene and colleagues, attempted to assess “the justification and
support for claims of clinical and therapeutic equivalence in medical journals" by analyzing 1209 citations from Medline between 1992 to 1996, excluding non-original, pure laboratory and nonhuman research. This left a scant eighty-eight eligible papers. Of those, they found that “quantitative distinctions” regarded as “equivalent” ranged “from 0% to 76% for proportionate differences” – a wide range by any standard (Greene et al., 2000, 715). Who would buy an appliance or a food or anything else where up to three-quarters of it might not correspond to what one actually expected it to be? The researchers write that claims of therapeutic equivalence “may not be reviewed with the same quantitative rigor” (as other studies) and that in the majority of the articles analyzed (67%) equivalence was declared “after a failed test for comparative superiority” (717). In other words, the researchers had intended to show one treatment was better than another, and when they could not, opted instead for equivalence – equivalence as consolation prize. The authors conclude that:

Many studies of clinical equivalence do not set boundaries ... [and] claims of “difference” or “similarity” are often made not by thoughtful examination of the data but by tests of statistical significance that are often misapplied or accompanied by inadequate sample sizes. (Greene et al., 715)

Thus, it seems that a new drug or treatment may often be considered equally effective to another while bestowing some other benefit (e.g., being cheaper or easier to use) through faulty logic, poor methodology or misleading or misapplied conclusions. This evaluation then enters the realm of the literature where it is used as a basis for guidelines, policy recommendations and, eventually, clinical decisions.
As Furburg and Psaty point out, drugs marketed and approved under the rubric of a single class, e.g., ACE-I inhibitors, used for a single indication such as “hypertension”, are promoted and prescribed with the tacit assumption that all ACE-I inhibitors similarly reduce “cardiovascular complications of hypertension, that they convey health benefits to patients with congestive heart failure or vascular disease, or that the recommended dosages for the ACEI’s are optimal or equipotent” (Furberg & Psaty, 2003, 2608). Yet the existing data do not support this view. At this stage, for instance, only ramipril and the data from the HOPE – Heart Outcome Prevention Evaluation – study demonstrated a link between an ACE-I antihypertensive drugs and a reduced risk of all-cause mortality. Two other ACE1 inhibitors, quinapril and perindopril in the recommended dosages had no effect on subsequent risk of stroke or coronary events (Furburg & Psaty, 2608).

Extrapolations are not accepted by regulatory agencies like Health Canada, yet clinicians, policy makers, managers and others in positions to affect drug choice are free to use whatever drug (and whatever evidence) they decide might be best for whatever indication they deem fit. Furburg and Psaty continue: “Many forces, such as marketing and restricted formularies, represent challenges” such as over-interpretation and misapplication of the concept of “class effect” as well as the implication that all members of a drug class are interchangeable (2609) – with the implication that equivalence has been proven. Over-enthusiastic marketing exacerbates the effect. How well patients’ interests are served by this evidentiary and regulatory nonchalance is questionable. Even the FDA appears “troubled by how the class effect concept is handled in the
marketplace”. According to the same two cardiologists and their colleagues, in an earlier article:

> After a claim by Novartis in a television advertisement that fluvastatin sodium (Lescol) is similar in effectiveness to other cholesterol-lowering agents including prevastatin (Prevachol), lovastatin (Mevacor), and simvastatin (Zocor), and that the only difference between these agents is cost, the FDA issued a warning letter to Novartis which concluded that Novartis’ advertisement was false or misleading and lacking in fair balance in violation of the Federal Food, Drug, and Cosmetic Act” (sic). (Furberg et al., 1999, 1203)

The authors add that they “would be interested to know the criteria used by the FDA to generate this letter” and what follow-up it might have generated (1203).

Overall, comparative information to guide clinicians in their treatment of individual patients is conspicuously lacking, as though all that matters is the symptom, sign, surrogate end point or measurable pathology and its potential alteration by the therapy or drug.

We sometimes talk loosely about the outcomes of a treatment or the cost-effectiveness of a treatment as though they were properties of the treatment. They are not. The outcomes, and therefore the cost-effectiveness of a treatment, depend critically on the characteristics of the patient to whom the treatment will be applied. In similar fashion ... the outcomes of a treatment will also depend on the specific features of the treatment, such as a particular drug regimen or screening frequency. Thus when we talk about the cost-effectiveness of a treatment we are really talking about the cost effectiveness of a very specific treatment for a very specific set of indications – what we might call a “treatment/indication”. (Eddy, 1996, 182)

The focus on outcomes, surrogates, and risk factors is not confined to cardiac disease; although cardiac drugs certainly are in the limelight more than others at present. Non-
steroidal anti-inflammatories, or NSAIDS, drugs like naproxen and ibuprofen, which are primarily used to treat the pain and inflammation of osteoarthritis (which most of us will experience as we get older), are similarly lumped into large generalized categories with vague medication-related data and little, if any, reference to the patient. As a commentary in the *NEJM* points out:

[Nearly] 70 million prescriptions for NSAIDS were filled in 1991 (3.8 percent of all prescriptions) at a cost of about $2.2 billion. The use of NSAID's increases with age....NSAIDS frequently have adverse effects in elderly patients, the most serious of which is a three- to five-fold increase in the rate of hospitalization for and death from peptic ulcers. In this population approximately 30 percent of ulcer-related hospitalizations and deaths are attributable to NSAIDS ... result[ing] in direct costs of at least $1 billion (US) per year .... Despite the frequent use and serious toxicity of NSAIDS, several important questions have not been adequately answered. First, what is the efficacy of potentially safer alternatives...? Acetaminophen, mild exercise, and weight reduction may have comparable effectiveness for many patients with osteoarthritis, the indication for NSAIDS in the majority of elderly patients. Second, are currently recommended doses optimal? Lower doses may have adequate efficacy with a reduced risk of toxicity. Third, is there justification for the widespread use of the more expensive NSAIDS (like Celebrex and Vioxx) which may cost 12 times as much as ibuprofen? ... The lack of such data underlies [how few] incentives there are to address these fundamental questions. (Ray, 1993, 2030)

Fundamental they may be, but these are questions that are complicated to study and difficult to answer.

The ambiguities from patients' (and clinicians') perspective do not stop there. Ostensibly minor issues such as dosage also present problems. For example, findings for high-dose and low-dose diuretic therapy (also used as a treatment for high blood
pressure) "were not the same even though both therapies came from the same drug class" (Psaty et al., 1999, 787). It was, in fact, the low dose regimen that seemed to provide the most benefits – thereby going against the cultural grain that "more" is better. The "health outcomes of blood pressure reduction appear to depend not only on the type but perhaps also on the dose of the drug" (787) (my emphasis). The sheer number of pharmaceutical products on the market make such concerns vital for patients, yet there is little information to assist with decision-making or evaluation within a clinical setting. Perhaps, like the types and topics of research we engage in, our thinking on which (and how much we need of) treatments also needs to evolve.

**Old-style Thinking**

As our medical knowledge expands and our options increase, "our traditional groupings of drugs have become, to a large extent, obsolete" (Antman & Ferguson, 2003, 2604). For example, there are currently nine calcium-channel blockers approved for use; these can be sub-divided into five general groups on the basis of chemical structure, yet the "voltage-sensitive" ones have been further classified as L, N, or T on the basis of their ability to sense cardiac electrical function. "Any attempt to lump all calcium channel blockers into a single class is an oversimplification and obscures important observations with therapeutic consequences" (2604). But head-to-head comparisons of drugs within a class are rarely done given the pharmaceutical companies’ unwillingness to subject their drugs to such potentially damaging analysis. Researchers point to the "the complexity of..."
the evidence we must consider before deciding whether calcium channel blockers as a
class, or any individual calcium channel blocker, are deleterious or beneficial to the
overall health of patients" (Califf & Kramer, 1998, 1529). And that is merely one single
class of antihypertensive drug among many.

Regulatory utility often dictates the asking of circumscribed questions in
randomized clinical trials, yet the answers provided do not necessarily inform patient or
clinician choice. Knowing that “anti-inflammatory substances are better than placebo” is
useful information, but not as useful as comparisons between the whole range of possible
interventions (Rogers, 2002, 98). These could include non-drug therapies such as exercise
and massage or low-tech therapies such as the application of hot packs or even posture. In
addition, simply knowing that a treatment is successful a certain percentage of the time
does not allow us to make any reasoned judgements as to whether this is in fact the best
option or an effective treatment for any particular person, or even any particular “class”
of patients with a specific problem, at least not unless we know the success rate of the
alternatives (98). For a serious, life-threatening condition even a small chance may be
acceptable as long as it is better than zero – one could well be willing to take risks, even
with an untested treatment. But add in a high chance of severe side effects or a small
chance of spontaneous resolution, and one’s course of action becomes less clear-cut – and
it is here where individual patients’ perspectives, values and life choices ought to matter
as much as any research or statistical (group or institutionally-derived) evidence. As two
Dutch family physicians write:
Adequate medical care always includes the combination of the disease and the personal dimension, but in general practice the personal dimension offers a particularly rich potential for intervention. With the RCT methodology of evidence-based medicine, the convention is to ignore the consequences of the personal dimension, and instead to focus on the assessment of evidence exclusively in terms of the disease intervention. (van Weel & Knottnerus, 1999, 917)

Individual choices require time, attention and a discussion and acceptance of the uncertainties involved, and generally speaking we tend to dislike that. We prefer unequivocal answers and spurious accuracy, even where none exists. Disliking uncertainty, nevertheless, is insufficient cause to ignore the complexity of physiology and the variations in individual patient values, perspectives and needs.
There is no doubt that we have made notable progress in fighting certain diseases, but increasingly we appreciate that simple changes in sanitation, diet, and lifestyles have had more dramatic effects on public health than more highly touted advances.... It is difficult to state in clear categorical terms the cost/benefit relationships for resources spent on basic research [and] the data that would allow an assessment of how scientific and technological achievements translate into a higher quality of health care or objective health criteria are difficult to obtain. Without this information, there is a general sense that we are not quite sure what we are paying for... and the public... is clamoring for a better justification of health care costs. (Tauber, 1999)

Studies claiming equivalence have a common perspective, namely, that whatever effect or difference is being studied is not “sufficiently large to ‘matter’” (Greene et al., 2000, 719). But what matters to whom and why? Who decides? Although we like to believe there is clarity and objectivity in medical data which qualified experts are able to deconstruct (or construct), the reality of medical knowledge is that there are huge gaps and ambiguities in evaluating what evidence there is. In a powerful CMAJ commentary entitled “Dancing with the porcupine”, a group of distinguished persons eloquently express this concern and point out that, inevitably, “institutional imperatives are bound to conflict” given the stark differences between various interested parties and their
positions, be they drug companies, health care managers or administrators, clinicians, researchers or patients, all of whom have differing viewpoints with respect to what “matters” (Lewis et al., 2001, 783). Research, even that gold standard randomized clinical trial, suggest these commentators, cannot be called neutral: it can “serve or subvert the public interest” (783). Furthermore, one could ask what the “public interest” even is and who gets to decide, since, ultimately, it is essential to know from whose point of view value is being measured. For that matter, one could question what is meant by the “public”, with or without its interest in, or relationship to, medical research, and ponder whether this heterogeneous entity actually finds experts’ reasoning compelling.

Decisions made in the public realm around health and medicine, whether on reference-based pricing, equivalence or anything else, are based – or so we, the people to whom the decisions apply, assume – on expert advice and recommendations using a judicious blend of sense, sensibility and science. There is, one hopes, reference made to social and societal benefits as well as concern about cost – but in the end, as individuals, our concern is access: the availability of good clinical care when most of us need it. Anything making this possible can then be said to be the “best” or the most “efficient” alternative(s), providing the greatest benefit for the largest number of people. How efficiency is defined, however, depends largely on the position and perspective of the evaluator.

67 Including the health economist Steven Lewis; geneticist and ethics commentator Patricia Baird; recent Order of Canada recipient economist Robert Evans; ethicist Francoise Baylis, etc.
Economics and Efficiency

From an organizational (institutional, government, public policy) perspective, a system (in this case the medical system) consists of a “nexus of contracts, treaties, understandings” and other transactions (Milgrom & Roberts, 1992, 20). These exist in order to maximally satisfy what individuals want and need – while factoring in cost. This is how efficiency is defined. The reference drug program of BC reflects this notion of efficiency: the intent is to provide more people with the drugs they need by restricting general access, ergo efficiency. Nevertheless, as Stanford economists Paul Milgrom and John Roberts, authors of an influential economics textbook on organizations, write:

The efficiency or inefficiency of a choice is always relative to some specific set of individuals whose interests are being taken into account and also to some specific set of available options. This is important to remember. It is distinctly possible that a particular choice from a given set of alternatives will be efficient relative to the interests of a given group of people, but not when some larger affected group is considered. ... Thus, in applying the concept of efficiency it is necessary to be clear about whose interests are counted and what alternatives are considered to be feasible. (22) (my emphasis)

Given that it is not ordinary individuals’ perceptions, concerns or desires driving research questions (Litva, Coast, Donovan, & Eyles, 2002; Rogers, 2002) but the enthusiasms of researchers, drug companies, managers, administrators, health economists, academics, hospitals, think tanks and so on, at what point could one safely state that these concerns intersect with patients’?
The most commonly used criterion in distributive economic (and public health) analyses is practical and pragmatic, to “compare alternative allocation of resources” (Milgrom & Roberts, 22-3). Implicit is the budgetary subtext of preventing costs from spiralling out of control and the need for financial restraint. Yet inherent to any research undertaken quantitatively to assess the “value” of drugs and therapies are tacit assumptions, with inherent qualitative values driving them. As Milgrom and Roberts prosaically write, therefore, “to note that an allocation is efficient is hardly to recommend it on ethical grounds”. In medicine, various stakeholders’ values are reflected not only in the subjects of study and which diseases, conditions or illnesses are deemed worthy of examination but, just as fundamentally, in where the boundaries are drawn between health and illness. These underlying beliefs are rarely referred to much less defined, questioned, or analyzed, and, as physician-ethicist Nuala Kenny explains, there are dramatic discrepancies between points of view, narratives and the understanding various groups bring to the table:

The experts are concerned with information, evidence, outcomes and incentives. The public discourse is concerned with wait lists, access to doctors, emergency rooms, hospitals and technology and the need for more money in the system. Are the experts wrong? Is theirs an “ivory tower” view divorced from the “real” experience of health care? Do the politicians and the public not know or understand the facts regarding the determinants of health [e.g., socio economic status], efficient health care and evidence of benefit? Grappling with these competing and often conflicting diagnoses of what is wrong with our health care system is essential if we are to make truly informed choices. (Kenny, 2002, 4)

68 The efficiency principle in economics is the working hypothesis that “organizations and institutional arrangements that persist” are those which are the most efficient. “Efficient” is negatively defined as an allocation or organization or contract where “there is no feasible alternative that everyone finds to be at least as good and at least one person strictly prefers” (Milgrom & Roberts, 1992, 598).
In medical terms, Kenny adds, the popular story could be considered a “deficiency disease”: not enough nurses, doctors, hospitals, MRI’s, home care, drugs, hospitals to “do all the good things for Canadians that we should be doing” – and the common answer is the one we often hear in commercials and advertisements, “more” (Kenny, 30). Yet unlike many things one can (more or less) safely want more of (houses, friends, books, music, good will), with medicine there is far-reaching agreement that there can, indeed, be too much of a good thing. As health economists Robert Evans and Alain Enthoven, among others, point out, “Increasing medical inputs will at some point become counterproductive and produce more harm than good” (Moynihan & Smith, 2002, 859). Where that point might be, of course, is case-specific and debatable, nevertheless the fact remains that medical spending needs to be seen in context:

Presumably no one wants to keep cutting back on education, the arts, scientific research, good food, travel, and much else as we spend more and more of our resources on an unwinnable battle against death, pain, and sickness. … And do we in the rich world want to keep developing increasingly expensive treatments that achieve marginal benefits when most in the developing world do not have the undoubted benefits that come with simple measures like sanitation, clean water, and immunization? (Moynihan & Smith, 859)

At present the ratio of medicine to education, social services and other government-funded programs is, to a large extent, a hodge-podge that has simply added more interventions, technology, and screening or other forms of care as they have become available and socially valued (for example the burgeoning use of CT scans or mammograms), while choices made on screening, the delivery of care and administrative options have often been politically motivated (such as closing hospitals in favour of care
that is "closer to home"). As medical costs have increased, cutting costs has also become a priority and this is where evidence-based medicine has made its mark, as governments and health planners "find the notion of allocating health resources on the basis of evidence attractive" (Kerridge, Lowe, & Henry, 1998, 1151).

Evidence provides a systematic framework for comparing treatments and inclusion/exclusion criteria, with the underlying philosophical framework being utilitarianism (Kerridge et al., 1151). This approach, also called consequentialist or teleological, corresponds almost exactly to the idea of efficiency in organizational economics and is believed to equitably produce the most good (or at least the least ill) for the greatest number. Hence, reference-based pricing and drug substitution schemes are an attempt at using evidence and expert recommendations to restrict payment of expensive drugs for some, in order to allow a larger pool of people to have access to similar (or "equivalent") medication. This practice, according to philosopher J.J.C. Smart, a proponent of utilitarianism, writing in *An outline of a system of utilitarian ethics*, is both reasonable and appeals to people's sense of fairness. "The suggested method of developing normative ethics is to appeal to feelings, namely of benevolence, and to reason, in the sense of conceptual clarification and also of empirical enquiry." (Smart, 1973, 40) Evidence-based medicine, therefore, allows for policies that represent a practical example of utilitarianism and/or economic efficiency – i.e., the most good for the most people according to what the evidence tells us works, which is appealingly simple and defensible from an institutional and broad-brushed perspective.
Additionally, in this era of checks-and-balances, the concept has a comforting ring of scientific truth about it. After all, if we can demonstrate via randomized clinical trials that a certain drug, intervention or therapy produces a quantifiable (and presumably desirable) result, it is relatively simple to argue convincingly that it ought to be paid for. This practical aspect of utilitarianism, the idea that the worth of an action can be assessed by the measurement of its consequences, is nevertheless ethically problematic:

Firstly, many important outcomes cannot be adequately measured or defined. [For example, quality of life is an intensely personal issue that even the most detailed questionnaire cannot accurately measure.] Secondly, it is often unclear whose interests should be considered in determining outcomes. Thirdly, consequentialism (or utilitarianism) may lead to conclusions that are … unethical from other points of view. These criticisms may equally apply to evidence-based medicine. (Kerridge et al., 1998, 1151) (my emphasis)

Furthermore, evidence, by its very nature, covers only a small slice of life; it is incapable of encompassing complexity or the multi-factorial aspects of health and illness and often only observes those aspects which are controllable and easily studied such as drugs and surgery (and which someone has opted to study – and fund).

The alert reader will have noted that whether one approaches the question from either discipline, economics or ethics, the basic question remains one of perspective. Even the most cursory analysis reveals multiple stakeholders, from professional groups, governments and institutions to patients, families, communities and the general public (people who are not sick at this time and whose only real interest in the medical system is that it exist). Deciding between these competing claims almost invariably tilts away from individuals and towards generalized institutional and organizational concerns.
Furthermore, “values which may be easily quantified in economic terms often require comparison with values which are not quantifiable” (Kerridge et al., 1152), creating the dilemma of either leaving out those aspects which cannot be quantified (as is often done in cost-utility or cost-benefit analyses) or else attaching some kind of numeric value to them (as in health-related quality of life scores or pain scores), which is not only reductionist but may be misrepresentative or downright wrong.⁶⁹

Evidence-based medicine when used as a basis for policy also involves the concept of efficacy (results, in other words: does the intervention bring about the expected result?) and is not equipped to handle context and other matters of individual interest. Pain clinics, for instance, which teach patients various strategies to manage chronic pain, have been demonstrated to matter to patients and improve functionality and quality of life, yet when pain is quantified (“On a scale of one to ten, your pain is an X?”) their impact often seems negligible and statistically insignificant. As a result many pain clinics have been shut down including one in Vancouver. Quantitative questions are not equipped to handle complex, qualitative human factors:

Evidence based medicine may therefore introduce a systematic bias resulting in allocation of resources to those treatments for which there is rigorous evidence of effectiveness (evidence that the treatment “works”), or towards those for which there are funds available. (Kerridge et al., 1153)

⁶⁹ Although some values and desires remain constant over time, most of us change with our circumstances and situation.
Often, this tilts funding towards pharmaceutical agents, which the drug companies want to sell and are willing to subsidize research into, or finite interventions such as surgery which are more easily studied. Framed in this manner, it then becomes a short conceptual step to move from considering an intervention "without substantial evidence" as one that is "without substantial value" (1153). Yet the (meagre) literature on chronic disease, palliative or geriatric care, pain control and other such aspects of ill-defined health problems overwhelmingly suggests that such non-quantifiable aspects of care can be of vital importance to the individuals affected – particularly when there is no cure.

A further problem is that the bias towards evidence may distort the doctor-patient relationship:

The physician’s priority is to act in the best interests of the patient, acknowledging fully the importance of the patient’s own values and perception of his or her health and decisions regarding it. … Although evidence-based medicine is a tool that might help weigh options available to a patient, it usually provides little or no guidance with regard to the tailoring of options to the priorities and circumstances of the individual patient. However when evidence-based medicine is used to evaluate health care decisions and resource allocation, it becomes a potent force that transforms the physician into an agent of the health service and the patient into a consumer. (Culpepper & Gilbert, 1999, 831) (my emphasis)

No sane observer would suggest that we do away with randomized clinical trials or evidence-based medicine altogether; nevertheless it behooves us to delve more deeply into their ethical and social implications and consider what they leave out as well as what they are capable of telling us.
Metaphors of Care and Cure

Whatever the delivery method or underlying philosophy – allopatic or complementary medicine, prescriptive or prophylactic, evidence-based or folkloric – the underlying definitions and dichotomies (sick/not sick, at risk/safe) rely crucially on how we define individual states of health and illness, and, by extension, presuppose some form of assessment. In policy decisions such as those dealing with therapeutic equivalence, these become fundamental. However, given that it is next to impossible to have even two people agree on what constitutes “pain”, much less illness or disability, as well as the enormous variability and uncertainty inherent to medicine, how can we be confident that these definitions and assessments are sound and that our beliefs around them are correct?

It is academically and personally obvious that there are two competing views of health, one that is subjective, “internal” and based on one’s own perceptions and feelings, and another which is “external” (or top-down), relying on observations made by outsiders, doctors or pathologists (or anyone who is not the person/patient). These contrasting views, writes the Nobel-prize winning Cambridge economist Amartya Sen, may certainly be combined (a good clinician or researcher would no doubt care about both), but there exists a fundamental gulf and “major tension” between evaluations based on these two perspectives (Sen, 1999). Given this fundamental gap, how can framers of public policy, managers, hospital administrators, or funding agencies hope to truly

This criticism on how the doctor-patient relationship can be distorted also holds true for direct-to-consumer drug
formulate approaches that make sense without obtaining some *qualitative* sense of what is wrong? The mere fact of operationalizing, creating rules and guidelines, requires that one put aside such considerations in favour of statistical, numeric and population generalities – if for no other reason than practicality, since these are less mutable, variable and confusing.

There are, at any given time, “a large pool of bodily symptoms available” which can be attributed to a host of factors from normal fatigue or stress to medication side-effects or illness (Barsky, Saintfort, Rogers, & Borus, 2002, 623), and there is considerable “tension between the complex narrative a patient brings” and “a doctor’s understanding” (or manager, health board, College, HMO or insurance company’s agreement with that understanding) of what is really going on “as formulated in a diagnosis or an idea about pathology” (Launer, 1999, 117). Which account more closely corresponds to the “truth”, such as it might be, and what is deemed acceptable is neither static nor well-defined but fluid, dynamic, changeable – depending on where one is geographically, historically, culturally, socially, personally. As a result, policy makers rely on a consensus as to what a particular illness or condition consists of and agree to agree on what should be done about it. Unfortunately this may well become a *reductio ad absurdum* – accepting too easily as a basis the idea that physiology and pathology are

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71 Even a single individual might assess the same symptom – dizziness, for example – quite differently from one day to the next, depending on what had gone on before (such as a friend dying of cancer or having had a fall down the stairs the previous day, making one hypervigilant).
simply two sides of the same coin, distinguishable numerically via surrogate end points or biomarkers.

This process follows along the same philosophical and socio-cultural lines as much of the rest of western thinking. As Foucault argued over thirty years ago in *The Birth of the Clinic*, as medical discourse became increasingly allied with the observational techniques of the burgeoning sciences in the 19th century, the body became "part of nature and thus part of the project to identify and classify the workings of nature" (cited in Hardey, 1998, 39). From the microscope and stethoscope to Roentgen's x-rays through to current sophisticated, sensitive imaging techniques, medical and clinical questions gradually came to be considered an archeological expedition of sorts, seeking to unearth physical signs associated with disease rather than a true probing of an individual's pain, illness and suffering. All too often, biomarkers and symptoms which are observable and quantifiable are therefore assumed to be causative when they could well be incidental correlations; interactions between symptom, sign and pathology are considered linearly and as a straightforward relationship that experts (as well as patients) can decode analytically through tests, technology, deductive reasoning and logic. This biomedical model ignores the experience of illness and reduces broad, human, qualitative aspects of ill-health in ways we collectively seem reluctant to face. "Our period in human history has located illness in an objective, scientific, physical account that regularly assigns medical science and technology a heroic role," writes Kenny (77). That heroism, reflected as it is in our television shows and news items extolling the virtues of this and that piece of genetic research, surgical or pharmaceutical advance, furthers a common
idea of medicine as one reflecting an epic struggle against the forces of entropy, chaos and disease.

Such ideas hanker back to maps and voyages of discovery – and cartography is perhaps the most compelling “tool-metaphor of technoscience”, as argues philosopher of science Bruno Latour (Latour, 1987, 244). It is not unusual to hear medical news expressed in metaphors that mirror geographic discoveries as though human physiology were simply another terrain waiting to be conquered. The journal Science described the Genome Project, for instance, in a special issue devoted to this apparently mythic journey as “Mapping Terra Incognita (Humani Corporis)”, a story that simply reverberated with narratives on “freedom, the free world; democracy; and, inevitably, the free market” (Haraway, 1997, 167). Naturally most of us, especially the media, were swept along with the majesty of the concept and the extraordinary possibilities of the gene “revolution”.

Metaphors such as these might seem trivial, mere words dreamt up by bored editors or drug company public relations staff attempting to spice up their subject, but they fundamentally and vitally shape our thinking, affecting how we perceive and value those aspects of life they refer to. Whether mythic, military, or market-related, wrote George Annas in a seminal piece in the NEJM a decade ago, metaphors and analogies create conceptual frameworks which allow us to understand and experience one thing in terms of another and play “a central role” in how we “construct our social and political reality” (Annas, 1995, 745). They provide the scaffolding on which we hang whatever mutable ideas on health or disease we might have and penetrate and mould our ideas on the subject. At present, one of the strongest metaphors of medicine is one of conflict: the
war on cancer, drugs that battle disease, the fight against flu or bacteria, strengthening our body’s immune defenses. This negative sense of disease-as-enemy is powerful but what truths it might contain are negligible. Even bacteriologic or viral disease, which can be argued to have as its original cause an “external” microbial cause, is not purely caused by the organism since only a fraction of infected persons actually develop TB or even a cold. Immune-compromised, malnourished, deprived, fragile or stressed hosts are far more likely to succumb to a parasite or bacterium than their healthy, well-fed, well-off, relaxed counterparts. “The strength of a cause,” explains epidemiologist Kenneth Rothman in the medical text, Epidemiology, “necessarily depends on the prevalence of other causal factors that cause disease”, be they inherent (genetic) or environmental (Rothman, 2002, 11). These act in concert within a certain time and place to create the foundations for disease. It is naïve, writes Rothman, to attribute disease to any single cause however compelling the notion might be (12-13).

Popular culture, however, enhances this external view of illness as an alien intruder or enemy to be fought and tamed, even as it inundates us with breathless news on medical advances and miraculous new therapies. In this it is ably assisted by the press who trumpet new and magical cures with little discussion or understanding of the limitations and uncertainties involved (Leibovici & Lievre, 2002), leading to the expectation that there will be results, treatments, a “cure”, once the problem is identified. Unfortunately, and all too often in the real world, disillusion and disappointment set in.

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What is rarely considered is the extent to which a “strong” immune system, for instance, can be damaging. Some of the worst and most deadly diseases – lupus, scleroderma, MS – emanate from our very own body’s “defenses”
when patients, families, and other affected individuals realize just how vague and complex most illnesses are, how many long-term consequences and side effects most therapies have and the extent to which it is individuals themselves who must adapt to and understand their own physiologic processes — in particular with chronic diseases.

**Chronic Illness**

Even though they receive far less airplay than dramatic life-threatening conditions requiring chemotherapy or a double transplant (hardly the panacea most people think it is, involving as it does a lifetime of immune suppressant drugs and valetudinarianism), chronic diseases, in fact, are the true scourge of our times, accounting for the majority of social and financial costs related to illness. It has been estimated that a mere three chronic conditions, diabetes, asthma, and depression, account for over $61 billion (US) in "annual direct medical costs" — even without factoring in adjunct costs such as work time lost and reduced quality of life (Weingarten et al., 2002, 925). An earlier study, conducted at the Institute for Health and Aging at the University of California which analyzed data from 1990 found even more alarming figures: Ninety million Americans live with chronic conditions, thirty-nine million with more than one, resulting in direct costs of $425 billion and $234 billion in indirect costs (Hoffman, Rice, & Sung, 1996, 1473). The authors add that, contrary to common perception, the majority of people with chronic conditions are neither disabled nor elderly. In this context the going rogue and attacking our own organs and systems.
medical model (find the underlying problem or pathology and remove it, change it, fix it, make it better) is woefully inadequate.

Chronic illness includes auto-immune disorders such as rheumatoid arthritis, multiple sclerosis (MS), lupus, psoriasis and the like; idiopathic pain (pain whose origin is unclear and is considered a maladaptive physiologic response to an injury or trauma of some kind); painful conditions such as osteoarthritis, migraine, post-traumatic injuries from back pain to knee problems and various and sundry physical problems (some of them even caused by medical intervention), even cardiovascular disease and some cancers – to name a few. Here, an entire, and burgeoning, population of patients exists for whom the vast majority of the clinical trials, the scientific methods, the cut-and-dried formulae do not cleanly apply (if they can be said to cleanly apply anywhere). To be sure, there are some newer medications and treatments, ranging from sonar therapies for joint pain to drugs that reduce inflammatory processes in rheumatoid arthritis which are improvements on older ones, but, by and large, for most chronically ill patients, getting better involves a kind of psychological, medical, social and physiological détente and consists, in essence, of learning to manage and live with the multiplicity of factors that make up their illness and treatment with a range of therapies, drugs and life strategies. This typically requires patients' direct involvement in everything from stress and life management to medication and other interventions.

With asthma, for instance, researchers from the University of Alberta found that it was the “patient’s own perception of how well their disease is controlled” and their assessment of its impact on their daily lives that determined their medication (steroid)
use, not so-called objective tests of lung function (Johnston, 2002). Asthma severity, in other words, had more to do with patients’ self-management strategies and their own adaptation strategies than quantitative, measurable criteria. Similarly, diabetic patients “involved with self-management” programs had improved blood pressure and to some extent were better able to control their blood glucose (Warsi, Wang, LaValley, Avorn, & Solomon, 2004, 1641). In almost all chronic diseases, from Crohn’s (also known as inflammatory bowel) to chronic pain, MS to osteoarthritis, patients and doctors must balance out medical factors, medication and psychosocial elements for optimal care.

Teaching patients these adaptive techniques has, in some instances, fallen to disease management teams and programs, developed in recent years, which involve assisting patients to change their lives in everything from diet and attitude to physical therapy, physiotherapy, physically administering hot or cold packs, rest, pacing oneself, even cognitive and behavioural therapy. Integrating these practices within standard medical therapies has often been quite effective, but while the standardization and delivery of such chronic-disease management has garnered some interest (to some extent because there might be some financial gain to be had in providing such services to HMO’s in the US), these low-tech interventions tend to lie beneath the research and regulatory radar and have rarely, if ever, been the subject of clinical trials or other research.73

73 This area of medicine also contains the most interdisciplinary interest.
A meta-analysis of some of these disease management programs concluded with the ubiquitous pleas for more research and stressed that, since "existing studies do not directly compare interventions", less is known about what works than seems reasonable (Weingarten, 927). Randomized clinical trials rarely study such "soft" interventions and generally there is little, if any, institutional or corporate interest in how people learn to adapt to chronic illness (or what medicine can do to help them). Yet for every pain clinic closed and every multi-disciplinary team disbanded to save paltry amounts of money, thousands if not hundreds of thousands of patients discover that, for them, the medical model is not only inadequate and ineffective but that so-called quaint old-fashioned methods, low-tech interventions and slight adjustments can make the difference between functionality and disability.\(^74\) So it would seem that even though we barely understand, at present, what constitutes normal physiologic functioning, much less the aetiologies (causes) and processes of pathology, for patients, acquiring a sense of autonomy and control, chipping away at symptoms with a variety of interventions from drugs to exercise and understanding states of mind as well as social and psychological factors has genuine value. As Sir William Osler, perhaps the most famous clinician-healer in western medical lore, said over a hundred years ago: It is not only the disease that matters but the patient with the disease.

\(^74\) Weingarten et al. (2002) write that to their knowledge theirs is the "first comprehensive attempt to evaluate the effectiveness" of these chronic illness programmes. One assumes they did (and the editors of the BMJ required) a literature search. This points to a serious lack of interest in a subject of enormous interest to symptomatic individuals (versus asymptomatic ones with elevated blood pressure at possible risk of something down the road). This seems to indicate a major focus with "risk factorology", as ethicist Daniel Callahan calls it, or Hilaire Belloc's victory of sterility over what truly matters.
What Is Health?

Health – which one can vaguely assume is more or less the polar opposite of “disease” – is commonly and glibly defined in the lofty, idealized terms set out over half a century ago by the WHO: “Health is a state of complete physical, mental and social well-being, not merely the absence of disease or infirmity.” (WHO, 1947, cited in Hardey, 1998, 28) Naturally it would be delightful were anyone to ever attain this extraordinary state of total well-being; unfortunately, only a scattered few could be considered healthy by this utopian definition. A more pragmatic vision is offered by medical sociologist Michael Hardey in The Social Context of Health:

Patients suffer “illness”; physicians diagnose and treat “disease”… illnesses are experiences of disvalued changes in states of being and social function: diseases are abnormalities in the structure and function of body organs and systems. (Hardey, 29)

This is somewhat better, more grounded and less abstract, but still problematic. What is (and how would one define) “abnormal”? How are values assigned so as to allow certain changes to be considered “disvalued”? Even the term “experience” is ambiguous, relying as it does on individual and social judgement and what the person remembers, considers important and thinks to notice, be they doctor or patient.

Biological science does not and cannot distinguish between health and disease writes physician Lester S. King in a thought-provoking essay; it merely concerns itself with the “interaction between living organisms and their environment” (King, 1981, 107). Health and disease, better or worse, sick or well, are irrelevant – all that can be said with
certainty is that these interactions are multiple and complex, forming an “integrated system which we can arbitrarily divide” into an “external” component (e.g., light, heat, percentage of oxygen in the air, micro-organisms in the food and water, etc.) that “induce changes in … the ‘internal’ environment”. These may include crude anatomical structures or more delicate processes involving inter-cellular fluids, glandular secretions or changes in fibre or muscle or electrical activity (107). Medical science studies the internal and seeks to find connections to the external. A bacterium, therefore, may be found to induce immunologic changes (and a “disease” under the right circumstances), while other environmental factors such as lack of food or water may lead, respectively, to starvation and dehydration. Any one of a number of external influences ranging from the weather to one’s physical environment can alter one’s internal makeup, be it a communicable disease (catching the flu from someone sitting behind us in an airplane) to developing mesothelioma after working with asbestos – or, more tragically and quickly, stepping on a landmine or falling down a cliff. We are fragile creatures whose equilibrium can easily be overset by any number of outside forces. Sociologist Renee Fox quotes microbiologist Rene Dubos from 1959:

The very process of living is a continual interplay between the individual and his environment, often taking the form of a struggle resulting in injury or disease. The more creative the individual, the less he can hope to avoid danger, for the stuff of creation is made up of responses to the forces that impinge on his body and soul. (Fox, 1989, 182)

Ignoring, for a moment, the more obvious value-laden expressions in the above (is an individual whose only job option is to work in a mine where he is exposed to asbestos being genuinely “creative”?), observers can therefore infer that medical scientists study
the interplay and connections between the external and the internal; isolate relevant conditions that affect the organism and create hypotheses and boundaries (e.g., normal versus abnormal) to describe them. These parameters and classifications can then be used to generate solutions (therapies, drugs, treatments). The sheer number of those relevant conditions, connections and possible reactions make the process extraordinarily complicated, which is why our analyses ought to be broad-brushed and general. What is relevant for one person might not be significant for another. As King writes:

If everyone had the same sort of liver or the same sort of pancreas, investigations would be a lot simpler. But they don’t. Clearly, this “total environment” of which we speak is not identical for all people. Science tries to isolate as many discrete factors as possible. Some will apply to virtually all humans without exception, others may concern only a small fraction of the total population. Science, in studying reactions within the total environment, cares not a whit about “health”. (108)

In fact, disease is purely an arbitrary designation and is not, in any way, essential to the discussion (109). What science does care about are irregularities and differences which are duly noted, studied, researched and commented on:

We call these examples of disease. But as Sir Clifford Allbutt clearly stated “disease is a state of a living organism (sic)... the disease itself contains no elements essentially different from those of health, but elements presented in a different and less useful order.” One combination, configuration, or pattern is succeeded by another. One is more “useful” than another. (King, 108) (my emphasis)

75 Surgeons are only too well aware of this every time they operate.
76 A contemporary of the famous Canadian physician Sir William Osler, Thomas Clifford Allbutt (1836-1925 – later Sir) was a British physician and inventor of medical devices. (He invented the modern thermometer – replacing an older version that was a foot long and took twenty minutes.) Allbutt was known for his clinical observations, outlined in his eight-volume book, Systems of Medicine.
Which brings in yet another ambiguous term to plague us: “useful”.

The conceptual models making up modern medical thought are quite eclectic and include the biological, physical and behavioural:

Biology is its cornerstone, but the phenomena which medicine deals with are both too complex and too individuated to be confined to a purely biological analysis, or to any single explanatory theory. The theoretical framework within which medical thought is hung is made up of congeries of conceptual schemes, linked by their common object of study and the style of the reasoning that they share. Null hypothesis, experimental, and probability reasoning are brought to bear on what is observed, manipulated, and analyzed, within a structure of thought that also entails various forms of systematic reductionism. (Fox, 183)

Current research and medical literature lionizes randomized clinical trials, quantitative methods and statistical reasoning, considered safeguards – the guardians of specificity, the Chinese lions at the gate, protecting us from our own tendency towards sloppy thinking and subjectivity, bringing us closer to clarity and genuine understanding. But ordinary statistics, quantitative methods in general, cannot judge any part of the data referring to disease, illness or pathology, merely note what is different. The reader will recall from the previous chapter that science does not make value judgements and cannot tell us whether something is “better” or “worse”, it is simply a method of inquiry that provides information as to the relative truth of our null hypothesis based on our experimental conditions. As epidemiologist Miettinen writes in the CMJ:

Perhaps the most fundamental tenet of praxeiology (the theory of human action) bearing on scientific arts such as those of modern medicine is this: “science never tells a man how he should act; it merely tells a man how he must act if he wants to attain definite ends”, as “ultimate decisions, the valuations and the choosing of ends, are beyond the scope of science”. So
an orientational concern in the theory of medicine is, Who is the decision-making 'man'? We still hear a lot about doctor's orders, but is it not that at issue is the client's health, that it is his/her valuations and ends that matter? (Miettinen, 2001d, 1327)

When we apply scientific methodology to a medical question, we already have in mind an idea of health and disease and of what the ends are – in other words, what constitutes pathology and what does not. In many cultures, for instance, seeing visions and hearing voices was (and is) considered a great honour for it means the seer had been blessed by the gods and could see what others could not. In contemporary western culture, visions are neither benign nor honourable; they indicate psychosis and severe mental illness treatable with anti-psychotics. Convention and the character of our knowledge determine what we value and how we classify health and disease.

A Question of Borders

It is important to digress briefly and to point out that regardless of the apparent arbitrariness of the definitions of pathology and physiology, it would be equally, if not more, reductionist and ridiculous to suggest that the practice of medicine is a mere game of chance, a simple whim or opinion buffeted about by the strong winds of fashion, belief and opinion. Since antiquity physicians and others have noted clusters and patterns that correspond to malaise and sickness. There are aggregates of symptoms and similarities

77 Devotees of the medical model will protest that to use mental illness as an example of the arbitrariness of diagnosis and pathology is neither fair nor accurate; since mental illness consists almost entirely of arbitrary designations. But, as will shortly be demonstrated, even heart disease is not as certain a category or diagnosis as one might think, nor is it devoid of social, historical and cultural influences.
that are “deemed painful, or disabling, and which, at the same time, deviate from either
the statistical norm or from idealized status” (King, 112), and these, over time, remain
consistent and observable regardless of socio-cultural boundaries. Pain in or around the
right lower quadrant of the abdomen, often accompanied by nausea, vomiting, fever and a
high white blood cell count, spell out the features of acute appendicitis, which, if left
untreated, almost always results in death. Migraines, which are severe debilitating
headaches often accompanied by gastric disturbances and an extreme sensitivity to light
and sound, run in families and were identified hundreds, if not thousands, of years ago. The
wear-and-tear of osteoarthritis is visible in skeletons and sculptures from many
centuries ago (although rheumatoid arthritis appears to be a recent phenomenon, not seen
in older European painting or literature, which has led some observers to suggest that its
origins are microbial and North American). There are, in other words, many examples of
finite clusters of symptoms that one could consider deviations from health. Where
problems arise is in specifics and how the borders are drawn in disease classification and
treatment – and, by extension, in the policies and guidelines which are put in place to
shape and restrict medical practice (as is done with reference pricing).

The “quantitative research paradigm of medicine” represents, at best, a “confined
access to clinical knowledge” maintains Norwegian physician Kirsti Malterud in The
Lancet. It incorporates “questions and phenomena that can be controlled, measured,
counted, and analysed by statistical methods” (Malterud, 2001a, 397). As prevalent as

78 The Roman emperor Justinian (483-465) was said to seek migraine relief by pressing his head to a magic pillar in
Istanbul.
these methods have become, few clinicians will rely solely on such data to make a diagnosis, or, for that matter, to come up with a treatment. The task of the physician is not just to understand the disease but to understand the patient. Unfortunately, although there are methods and criteria for understanding disease, there is as yet no parallel clinical method for this understanding:

The difficulty for medicine as a discipline is maybe not that this subjectivity is happening, but that the medical research tradition lacks strategies for the study of interpretative action, its dynamics and its consequences. [It has been suggested] that modern medicine is flawed because of a refusal to accept that results of research are outcomes of interpretation. (Malterud, 397)

Clinicians therefore must rely on observation, intuition, experience, shortcuts known collectively as heuristics.

**Heuristics**

Writing in the *Annals of Internal Medicine*, American physician Clement McDonald suggests that health care could profit from an exploration of the heuristics that physicians adopt, since it is erroneous to assume that “medical decisions are driven by established scientific fact”. He therefore suggests that “a set of heuristics explains how physicians make decisions because available biologic evidence is not sufficient”, and given that so much more seems to go into the medical decision process:

Angioplasty became a multibillion-dollar industry long before a single randomized trial or epidemiologic study had shown its benefits. Large numbers of MRI units were purchased during the first 5 years of their clinical availability, before any data were available to show that MRI was preferable to the diagnostic alternatives. (McDonald, 1996, 56)
We all engage in the mental shortcuts that heuristics provide, at least to some degree. One of the simplest is Occam’s razor, which, simply stated, means the most straightforward solution is usually the best. Medical students are advised: “When you hear hoof beats think horses, not zebras.” Common conditions are, by definition, common and the rare disorders studied in medical school are not the ones most physicians encounter in clinical practice. Another common heuristic is Sutton’s Law – Sutton was a bank robber who explained that he robbed banks because “that’s where the money is” (57). Physicians also utilize extrapolation, personal experience and advice from colleagues; they retain memories from their training or conferences they have recently attended along with a host of other mental shortcuts that McDonald suggests can lack critical analysis (58). Heuristics are most often used in situations of greater uncertainty, where they can potentially lead to error, according to New Zealand physician and educator Katherine Hall:

When uncertain, clinicians are more likely to frame their responses about likelihood in broad, “symbolic” descriptions of likelihood, such as “possibly” or “probably” rather than use precise percentages. This is despite evidence which shows such broad, “qualitative” expressions of probability are open to widely divergent interpretation by people (both patients and clinicians) … and creates obvious difficulties for the notion of informed consent. (Hall, 2002, 219)

Consensus and using the available evidence are thought to be “constructive” ways of reducing uncertainty, she adds, yet, overall, the evidence can only advise as to what the limits of medical knowledge are and becomes “inefficient and unwieldy” when attempting to answer questions having to do with “technical uncertainty” (219). McDonald also warns against excessive reliance on so-called objective data, which often
only reveal toxicities and negative side effects of drugs or other treatments after they have been in use for some time, and cautions against the too-rapid adoption of new technologies – part of the common “don’t just stand there do something” heuristic. Too often how a product is actively marketed and the perceived “immediacy of its benefit” also affect how and whether a new technology is used. But “a diagnosis is not a prerequisite to treatment”, warns McDonald (60), no matter how insistent the social clamour (or personal tendency) towards action might be.

Heuristics tend not to have a good reputation among proponents of more “scientific” forms of medical reasoning, nevertheless observers point out that they often result in accurate predictions (particularly when clinicians are experienced) and may well “reflect a highly adaptive and efficient response” to the uncertainties of the real world of medicine (Hall, 219) and the ambiguities inherent to pathology.

Physiology and Pathology

In the simplest theoretical terms, physiology pertains to normal functioning while pathology refers to abnormal functioning – except that one is only intelligible by reference to the other. To illustrate the point, King79 relates a personal story:

I recall a very precise young physician who asked me what our laboratory considered the normal hemoglobin level of the blood [with the particular technique we used]. When I answered, “Twelve to sixteen grams, more or less,” he was very puzzled. Most laboratories, he pointed out, called 15 grams normal, or perhaps 14.5. He wanted to know, if my norm was so

79 The 1981 book (Concepts of Health and Disease) in which King’s essay appears does not specify precisely who Lester S. King is, but, from this quote, one assumes he is a haematologist.
broad and vague, how he could possibly tell whether a patient suffered from anaemia, or how much anaemia. I agreed that he had quite a problem on his hands, and that it is a difficult thing to tell. So difficult, in fact, that trying to be too precise is actually misleading, inaccurate, stultifying to thought, and philosophically very unsound.” (King, 109) (my emphasis)

The zealous young physician then wanted to know why King didn’t take a hundred or so “normal” individuals, determine their hemoglobin by the method in question, and use the resulting figure as the norm:

This, I agreed, was a splendid idea. But how were we to pick out the normals? The obvious answer is, just take one or two hundred healthy people, free of disease .... But that is exactly the difficulty. We think of health as freedom from disease, and disease as an aberration from health. This is traveling in circles, getting us nowhere. (109)

Implicit in this idea of normal-is-healthy or healthy-is-normal is a transposition of metaphors and concepts using an internal and personal classification of health to determine an external one and vice versa. Yet, as King wryly points out, we have all known or heard of people who seemed perfectly healthy, had periodic checkups which they passed with flying colours and were subsequently found to be riddled with disease:

In other words, it is possible that an individual may have an undiagnosed organic disorder and not experience any symptoms, or if they do experience symptoms, these may not be recognized as such and explained away. The tensions between “top-down” (external) and “bottom-up” (internal) approaches to defining health reflect broader theoretical and methodological debates. (Hardey, 1998, 39)

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80 One supposes actually talking to patients, looking at them (anaemic people being notoriously wan) and taking a detailed history was Out Of The Question.
Furthermore, even individuals considered "sick" (with cancer, rheumatoid arthritis, etc.) will often answer in the affirmative when asked if they are in "good" health, suggesting that a diagnosis or label is not the sole arbiter of a person's own sense of how "normal" or "well" they feel. Health is therefore more than mere absence of illness and encompasses a considerably larger range of social functioning (39).

This is the inherent complexity, the perplexing factor, as discussed in the previous chapter on surrogate endpoints. Precisely which clusters of signs and symptoms belong together? Which ones constitute a discrete disease process – and which ones, out of a compendium of possible symptoms, are related aetiologically and physiologically? What symptoms are on the disease "pathway" and which ones are incidental or idiosyncratic? Which ones should we care about and try to control? From a "confusion of phenomena and relationships", we are in the awkward position of having to pick those which are inconsequential or accidental in order to discover what is "essential" (King, 113). It is testament to the human spirit that we are continually convinced that whatever we choose at this period in history is closest to the "truth" – since we are, only "too ready to assume our penetration into the real nature of things" (113).

Thus Bartlett, in the year 1844, said, "It is only within a few years that we have been furnished with a means of distinguishing, with clearness and certainty, between pleurisy and pneumonia, but these two diseases have always been as distinct from each other as they now are." (113-4)

In other words, the truth was always there, whether we saw it or not, just waiting for us to stumble upon it. Of course today, pleurisy is considered merely a symptom, an inflammation of the pleura or the membranes of the lung, which, according to Taber's
Medical Dictionary, "may be primary or secondary; unilateral, bilateral, or local; acute or chronic; fibrinous, serofibrinous, or purulent" (Taber, 1977). What it is not is a disease, whether distinct from pneumonia or not, and naturally it is somewhat embarrassing to realize what a faux pas the venerable Bartlett made.

The history of medicine, writes King "is the history of distinguishing one condition from another" (114). One could further add that the history of medicine abounds with hypotheses and descriptions based on then-relevant models of knowledge, which, like Bartlett's pleurisy, have subsequently been denied, disproved or merely fallen into disfavour. From the ancient Greek attribution of all disease to the misalignment of the four humours to later descriptions that have sunk into oblivion, it has not always been a simple matter to disentangle even one ostensibly simple illness, measles, from smallpox, German measles, scarlet fever, or what was called "fourth disease" (Arnowitz, 12). Contrary to what most people think, medicine remains rife with unanswered questions and confusion as to what constitutes a discrete disease entity, whether the diagnosis is Lyme Disease, fibromyalgia, cardiac disease or cancer. What a cardiologist would refer to as damaged or fibrotic heart tissue descending downwards towards the stomach a gastroenterologist will call retro-peritoneal fibrosis – and, according to each of their specialties, neither would be wrong. The mere fact of detecting prostate cancer in a seventy-year-old man is, we are gradually realizing, quite normal. Most of these men are

81 Does anyone even remember that until the 17th century people largely believed, as did the Romans, that air ran through our veins? Or that a man called John Brown came up with the "Brunonian" system of disease – which, simply stated, divided all disease into "asthenic"(weak) and "sthenic" (strong), for which one either prescribed a stimulant or a sedative? That prior to Joseph Lister operating rooms were filthy?
far more likely to die with the disease than of it. So while prostate cancer might well be present, it is not a problem per se and overzealous screening in all men over a certain age may well create problems of over-detection (Draisma et al., 2003, 868). Even deciding on how best to pursue a particular line of research consists of a long string of questions, with countless lines, threads and avenues of inquiry dropped or forgotten, until and unless they are needed. For example, with the discovery of antibiotics, a promising line of research begun in the 19th century on bacteriophages, viruses that destroy bacteria, was abandoned. In recent years, as antibiotic-resistant strains of bacteria have begun to proliferate, especially in hospitals, some biotech companies have begun to research phage therapies again.

Transcending the misattributions, mistakes and blind alleys is the point of view, an “important and influential” one, that “diseases have an independent reality” (King, 114). This perspective, that diseases are specific entities which simply manifest themselves differently in different individuals, is considered “ontological”. It stands in contrast to the view dubbed “holistic” or “physiological” that stresses individuals and their adaptation – physical, psychological, social – to their environment (Arnowitz, 8). The ontological view currently dominates medical research and thought. It is therefore believed that it is not our concepts or definitions or social understanding of disease or illness that give them substance, but that, like trees or clumps of dirt or a piano bench, they simply exist. We simply have to discover them, figure out where their edges are, define them. The physician, researcher and essayist Lewis Thomas exemplified this view when he wrote that there have always been diseases we did not understand, but that many
have gone from “blank mysteries to approachable scientific problems” which, ultimately, the right mix of “the right kind of research and a certain amount of luck” can solve (cited in Fox, 1989). At the time of Thomas’s writing this was very much a reflection of the hope of the time; however it would seem that today this concept is problematic, inasmuch as disease cannot be considered a pure material entity such as a piano bench but a linguistic label we give to a collection of human complaints.82

Currently, disease categories are given substance not merely through verbal connections between patients and clinicians but through “scientific” means such as laboratory tests and technological devices that ground them in ostensibly physical and physiological anomalies and pathologies. Nevertheless, writes King, when we ask “what is a disease” we are “thus led into metaphysical difficulties”. He adds, with that literary charm so rare in current scientific and technical writing:

Some persons, who may, perhaps, be the most sensible among us, prefer to ignore the difficulty. But it never does any harm at least to stare a difficulty boldly in the face. We can always hurry along and ignore it later. (115)

So, hurrying right along, the problem then transmutes into a metaphysical one, raising troubling questions as to how and to what extent we can trust these patterns which have been identified as pathological, abnormal, or “diseased” and the extent to which we can rely on definitions which use the ontological status of those clusters and relationships. Do

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82 Yet Lewis Thomas understood better than most the ambiguities and complexities that are involved in the evolution of knowledge and science. He merely felt that science, for all its flaws, was the best (and only real) solution. “At the moment we are an ignorant species,” he wrote, “flummoxed by the puzzles of who we are, where we came
these truly cleave to that Platonic ideal in which the “real” or the “permanent”, however ephemeral, nevertheless has genuine substance, transcending place or time? It may change in tone with the seasons, but grass remains, at its essence, green. Round remains spherical and we can point to various phenomena as being as permanent and unchanging in their essence as they were thousands of years ago. But is that also true of illness?

**Metaphysical Conundrums and other Problems**

Much as we may want and require a diagnosis, a label on which we can hang whatever cluster of symptoms we are suffering from, the connection between the two is tenuous at best. As a British family physician writing in the *BMJ* reminds us:

> General practitioners, like all clinicians, are under pressure to make a diagnosis – under pressure from our training, from managers, from the journals that bombard us with information, and from institutions like the royal colleges … Yet a diagnosis is actually no more than a linguistic construct. (Launer, 1999, 118)

King resolved this conundrum by suggesting a loose framework of signs and symptoms, within which, he felt, we could approach and organize “crude experience” in ways that roughly correspond to what we know and which will allow us to deal with “everyday events” in the most “satisfactory” way possible – one with “utility” – not only in the clinical sense of taking care of patients but intellectually, allowing us to “assimilate new discoveries and observations” (King, 116).

from, and what we are for. It is a gamble to bet on science for moving ahead, but it is, in my view, the only game in town” (Thomas, 1985, 21).
By keeping our labels flexible, then, we can recognize uncertainty while practicing clinical medicine and engaging in research. Diabetes, accordingly, becomes a loose classification corresponding to a physiologic pattern in which insufficient insulin is secreted by an individual pancreas (or is secreted but does not produce its usual effects), leading to deterioration and decay of vital organs and death, should this pathological state continue. (Presumably there have always been diabetics, but prior to Banting and Best’s discovery of insulin there simply was no classification system to identify what ailed them or why they died.) Where this runs into problems (and as King explained to that eager young physician) is in terms of degree and extent. How do we decide on the cutoff, and what to include or exclude? How did we go from Type I diabetes and total insulin dependency to such large numbers of people being told they have or are at risk for Type II diabetes? Are these accurate or have the goalposts – the inclusion/exclusion criteria – been moved through factors unrelated to medicine?

Several august panels, speaking for equally august professional bodies, are convinced that we can, and therefore should be more liberal with the [diabetes] cut-off. Consequently, the cut-off is progressively lowered by consensus. It follows that the prevalence of Type 2 diabetes is escalating. ... The public health world is alarming us about yet another epidemic it is helping to create simply by changing the labeling rules. Screening programs are advised. And, in parallel with the reasoning for treating Type 2 diabetes, meticulous management of blood sugar is called for, in this case resorting to pills designed to increase the efficiency of the patients' own insulin responsiveness. (Hadler, 2004, 50)

Hadler adds that this “hot spot of pharmaceutical development” ranks with the cholesterol-lowering statins and anti-hypertensive agents, where only too often “the advisers to the medical associations and the panel members (the same ones advocating
the tighter cut-offs) often have financial ties to the marketplace, one way or another" (51). It is, indeed, interesting, to say the least, to observe how we have managed to achieve such stunning numbers as we now see quoted with respect to risk factors for heart disease, such as blood pressure and cholesterol, diabetes and so on.

An article in the on-line journal Medscape Cardiology (funded by the pharmaceutical firm Astra Zeneca) cites the numbers we read so often with respect to coronary artery disease (said be the "leading killer" of both men and women), affecting nearly thirteen million Americans alone and resulting in a million deaths a year (Jones, 2004). Similarly, an article in the NEJM firmly states that "on the basis of ... current national guidelines" some "36 million people in the United States should be taking a statin" to lower cholesterol, but "only 11 million are currently being treated" (Topol, 2004, 1562) (my emphasis). The figures worldwide are even more daunting according to the NEJM article: "More than 200 million people meet the criteria for treatment, but fewer than 25 million take statins." The tone is chiding and verging on the horrified, yet at present cholesterol-lowering statin drugs "already account for the largest prescription drug expenditure in the United States, at $12.5 billion (US) a year" (1562) (my emphasis).

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83 The UK Prospective Diabetes Study, published in The Lancet, found that intensive therapy for Type 2 diabetes did not result in any advantage to patients. "No decrease in heart attacks, strokes, or important peripheral vascular disease," writes Hadler. And no decrease in diabetes-specific mortality (Hadler, 53).

84 I am always tempted to ask what the murder weapon is.

85 As a physician at an ethics conference I attended dryly pointed out, formerly people simply died. Today, everyone dies in hospital of cardiac disease. No doubt this has an appreciable impact on the statistics.
So are these millions of asymptomatic people, whose “disease” consists of biomarkers measuring different kinds of naturally-occurring blood lipids (HDL and LDL cholesterol), victims or pioneers? Is high cholesterol a genuine disease, a dangerous risk factor, worthy of medical intervention – or is it irrelevant? Is it as “real” and “permanent” as Plato thought the colour green was, or have we allowed institutional and market forces to dictate the (ever shrinking) edges of what we consider to be within the range of “normal” individual physiology?

Many physicians and researchers are adamantly against measuring and medicating cholesterol, stressing that its connection with heart disease is correlation and not cause. There is, furthermore, research suggesting that higher cholesterol levels may actually “protect against infections and atherosclerosis”, the very problem high cholesterol is said to exacerbate (Ravnskov, 2003, 927). A Finnish research paper published in the BMJ, found that levels of the “good” HDL cholesterol increase with alcohol intake; yet alcoholics are not protected against heart disease, on the contrary, they often die of it (Salonen, 2003, 1082). Along the same lines, one could argue that chemotherapy and severe weight loss ought to be cardioprotective since they reduce cholesterol, but they are not – and would be just as ill-advised therapeutically as would be using arsenic or cyanide to reduce blood pressure. So, are these remarkable expenditures on cholesterol-lowering drugs reasonable and necessary, or is it clever drug company marketing, sophisticated manipulation of statistical information and over-enthusiastic reporting on the part of medical researchers and the media?
A British physician wearily suggests that it would be a good idea for us to find means of ensuring that "statistics are better understood by journalists and the general public" given the enthusiasm with which results from research papers "are splattered across the news media" and disseminated. "I have the impression," he writes, "that much government policy is driven by those who read headline medical information without really understanding it" (Rivers, 2002, 864-5). Perhaps utilitarian concepts and our desire for quantification – not to mention our dislike of uncertainty – have conspired to create an "emerging orthodoxy" that boxes us into tight-fitting categories from which we can no longer extricate ourselves. Add that to our belief that numbers don't lie, and the concurrent constraints of our metaphors and technology, and it is only a short conceptual step to a point where we are no longer able to distinguish markers, lab findings, test results and biomarkers from genuine disease (Williams & Garner, 2002, 10). Or perhaps there are other forces, including those emanating from the market and macro-economic considerations of cost (10), which conspire to create the practice of medicine as we know it: less relevant, more intrusive, less personal and more removed from the healing arts than it perhaps ought to be.

\[56\] An article on medical education suggests that experienced physicians find it easier to express uncertainty and that uncertainty in medicine is most easily resolved through action (Hall, 2002, 217). The same cultural tendency Payer spoke of in *Medicine and Culture*. 
Ethical Considerations

From an ethical (and compassionate) perspective, suggests ethicist Edmund Erde, it is essential to clarify this dilemma and to reassess from time to time, taking care not to confuse a biomarker or laboratory result with genuine human welfare:

Welfare is the *general* condition enabling any relatively independent person of any age, in any era, culture, or circumstances to function well and happily. Many separate elements of welfare are necessary for it to be realized. None alone is sufficient. Trying to specify welfare's elements produces platitudes: “It is better to be alive, sane, pain-free (and comfortable in other ways), strong, healthy, whole (including having good hearing, sight, all limbs working, etc.), free, wealthy, attractive, well-liked, and smart than the opposites.” Fine-grained specifications such as “It is better not to have blood pressure above 135 over 90” or “It is good to have investments in IBM” do not describe welfare. Rather they state markers, predictors of welfare or indicators of it. Medicine is the science that specifies the fine-grained markers of bodily welfare. It also concerns ways of bringing abnormal values into normal range and even defines tests of being alive and dead. (Erde, 1998, 528)

As Erde emphasizes, an over-focus on the specificity of markers can blinker us to context. We must take to heart, he says, Aristotle's warning “not to seek answers that are more precise than a field of inquiry allows”(527). Or, as Einstein said, we ought not try to solve problems using the same ideas that created them in the first place. Consider, for example:

...the sense of conflict that arises over the issue of feeding an anencephalic baby or adjusting the blood gases of someone about to die. To refrain in these situations is not to refrain from pursuing welfare. It is to refrain from pursuing a *marker of welfare*. Treating the marker when welfare is not expected is ... “treating the numbers”, not “treating the person” (Erde, 528). (my emphasis)
Currently western medicine in general, and North American practice in particular, is quite enchanted with treating the numbers, whether it's blood pressure or blood sugar or cholesterol. Technologically-driven, top-down assessments of welfare trump the internal view. Consider “Marty”, a patient that physician Robert Arnowitz describes in Making Sense of Illness:

Marty, a 50-year-old business executive who smokes and has mildly elevated blood pressure, had been taking nitroglycerine and other medications for angina pectoris for the past three years. He described his chest pain alternatively as indigestion and a pressure, often related to exertion but also occurring after meals. The pain was sometimes relieved with rest but more often by burping. After a particularly severe episode, he was admitted to hospital to “rule out myocardial infarction”, that is, heart attack. He did not have a heart attack and subsequently underwent coronary angiography which revealed ‘clean’ (normal) coronary arteries. He was told he did not have angina pectoris and discharged. (Arnowitz, 1998, 5)

In earlier years, writes Arnowitz, nobody could have taken his diagnosis away from Marty: his subjective experience of pain was all that determined angina pectoris, but “in this case, a priority given to the way a disease is experienced by a patient is in conflict with the belief that a specific, measurable, and visible anatomic abnormality is the best way to define disease” (5). And, as counter-intuitive as it may seem in this age of medicalization and belief in the might and advance of medical progress and technology, even something as obviously medical as a heart attack has dynamic definitions and changes with the times. Fifty years ago, Marty would simply have been told that he had a heart attack. He would have had a heart attack. He would have had a chronic illness, angina. Today, he has nothing, no matter how uncomfortable and distressed he might be.
Who is to say that a person’s own sense of what is wrong or what is transpiring within his or her body is any less authentic than those of clinicians and caregivers? To ethicist Erde, such denial of a patient’s suffering is both disrespectful and unethical. “The enduring self,” he writes, “has a sense of continuity with its past and future, a sense of having a story it is living” (Erde, 530). That narrative, that ethical story, is not simply centred around end-of-life care, reproduction or stem cells, as ethics is so often assumed to be, but encompasses all aspects of illness and medical intervention and must include the person at the centre, the patient (and his or her family and social network and circumstances). Even were we to assume that Marty’s pain were psychosomatic – and caused by psychological and psychiatric factors rather than purely physiological ones – it is nonetheless real: pain is pain, whatever the cause. Psychosomatic pain simply emanates from the “mind” and not the body. As for the boundaries between physiology and psychology, is there anyone in the medical profession (or any other) who can confidently delineate where these are or create precise borders that transcend patient differences?

The needs of each patient are different, requiring individual professional assessment, and are often multiple, requiring application of skills of different disciplines. The social, economic and biological contexts of each patient result in varying outcomes. It is questionable whether one can ever have simple causality in human relationships. (Williams & Garner, 2002, 11)
Treating the Numbers

Social and cultural factors, however, appear to have converged today in beliefs not only with respect to disease entities and classifications but on prevention and health promotion. It is not uncommon to hear glib statements on how we should be spending more on prevention than we do – or hear individuals speak of being “proactive” about health care. But, as evidence-based medicine guru David Sackett points out in a *CMAJ* article, such health promotion maneuvers warrant far more scepticism than they hitherto have:

Preventive medicine displays all 3 elements of arrogance. First, it is *aggressively assertive*, pursuing symptomless individuals and telling them what they must do to remain healthy. … Second, [it] is *presumptuous*, confident that the interventions it espouses will, on average, do more good than harm to those who accept and adhere to them. Finally, preventive medicine is *overbearing*, attacking those who question the value of its recommendations. (Sackett, 2002, 363)

Sackett’s article refers to the pomposity of the proponents of “hormone replacement therapy” prior to the data from the Women’s Health Initiative (a study of over 16,500 women randomized to receive either placebo or estrogen plus progestin), which was stopped early when it became clear that “the participating women’s risk of cardiovascular disease went up, not down on active therapy” (363). It could, however, easily be expanded to include a host of other routinely-recommended suggestions, from lowering cholesterol and various types of “preventive” screening such as mammography and bone scans to routine PSA testing (for prostate cancer) or even the full-body MRI’s (or “preventive health scans” according to an ad in the Yellow Pages) now privately offered
by various clinics – claims which can be said to be semantically and medically questionable.87

How, then, should the ostensibly preventive aspects of screening be conceptualized? It is clear what it means to have a complaint, go to the doctor (or emergency room or clinic) seeking a diagnosis and relief. We understand how a physical examination and consultation may be simultaneously comforting and yet contain uncertainties and dilemmas. The question is how we arrived at a stage where a mammogram is considered good “preventive” care – to the point where not having one is somehow suspect or even subversive (and even women’s “advocacy” groups strongly recommend them for women over forty). As epidemiologist Olli Miettinen writes in the CMAJ:

Is it (screening) application of an initial diagnostic directed to a particular illness in the absence of any overt manifestations suggestive of that illness, and thus the pursuit of very uncertain, almost tentative “rule-in” (versus ‘rule-out’) diagnosis …? Or, is screening itself an intervention, as it is now commonplace to claim? (Miettinen, 2001c, 1220)

Dictionary definitions don’t help – suggesting as they do that screening is merely examining a specific part of an individual or a group to detect the presence or absence of a certain disorder – so we must turn our attention towards the ideology of screening which, as Miettinen points out, is to achieve “a diagnosis of latent illness with a view to early intervention” (my emphasis). A negative result, therefore, will result in the

87 A CMAJ editorial points out that what few people know is that the practice of giving estrogen at menopause originated with a single person, Robert Wilson, and his book: Feminine Forever, in 1968. The publicity for the book was paid for by the drug company Wyeth-Ayerst (Hoey, 2001).
cessation of any further efforts and a “clean” bill of health,” whereas a positive one will lead to more extensive intervention with ruling-in of the illness “the final alternative possibility” (1220). But is this useful or effective from either an individual or a community perspective? Or even a medical one?

Just as there now prevails the medically – and logically – alien idea that application of a diagnostic in ordinary diagnosis is an intervention, so there is, even more eminently, the idea that screening is an intervention. In cancer screening taken to have the useful property of having effectiveness of reducing “mortality” – quite arbitrarily defined – from the cancer. (1220)

By this standard, the discovery of x-rays, which were and are a means of identifying pulmonary tuberculosis, could be considered an effective intervention (read therapy) – versus streptomycin, which actually cures TB in most instances – which makes no sense. Yet few of us stop to consider that simply because a diagnostic is sophisticated and high-tech (and cool) doesn’t make it a cure. Identification, no matter how detailed, is hardly a solution to a problem.88 A real medical intervention, suggests Miettinen elsewhere, is not invoked for the purpose of knowing but to change the future for the better through its intended effect (Miettinen, 2001b, 1059). An intervention comes between the disease and its natural conclusion; screening merely highlights what the disease is. Is it our fear of uncertainty or belief in medicine’s magical power that has us confuse these disparate activities?

88 As King explained, an absence of signs and symptoms does not necessarily mean one is disease “free”.
89 Extraordinarily, patient advocacy groups also push screening as though it is part of “the cure”. For instance, as I write, a massive “Run for the Cure” for breast cancer plans to use half the money raised for a new mammography unit. How this is part of a “cure” eludes me.
A further and highly relevant aspect of screening is that few, if any, patients are ever accurately informed of the uncertainties, ambiguities and risks inherent to many of them. We often hear of the benefits to mammograms or x-rays or CT scans, yet few of us even realize the high doses of radiation these tests involve or the hazards they may contain for susceptible individuals. Neither are we told of the frequency of error with screening. Depending on the test, the expertise of the person analyzing the results, the care with which the lab handles results and individual patients and their physiology, different screening procedures can result in false positive or negative results in ranges anywhere from 74% to 96% of the time for mammograms, to 75% of the time in colorectal screening (Hadler, 2004, 71, 84). Even reading the results of an ultrasound or a lowly x-ray depends on the skill (and bias) of the radiologist (Eddy, 1996, 12), but in our zeal for medical and linguistic mastery of this scourge we call illness, we set aside doubt and believe in the experts.

In this, we are ably assisted by our institutions. The Office of Technology Assessment in the United States, for instance, has “quite cavalierly adopted the view that diagnostics, too, are invoked to change the course of health” for the better and that “therefore they too are interventions” (Miettinen, 2001b, 1059). Precisely what this might mean is unclear, for, as Sackett reminds us, disease prevention or risk reduction (e.g., health promotion and screening) is neither cost-effective nor applicable across the board. Many factors, from socio-economic status and employment to genetics affect individual susceptibility to illness, and when prevention guidelines are wide-ranging many more people will undergo the procedure (a proportion of them suffering adverse effects) than
will ultimately benefit. Relatively small numbers of people from a population perspective are ever likely to encounter specific health problems (associated with high cholesterol, e.g.), whatever the hype around them might be. In addition:

The effectiveness of prevention and promotion efforts depends on the size of the group at risk relative to the size of the population that has to be targeted for the intervention. Even a very modest intervention becomes very expensive when applied to large populations. (Mechanic, 463) (my emphasis)

**Presumptive Preventive Care**

A group of researchers in Reykjavik, Iceland, writing in the BMJ, ask whether "opportunistic disease prevention" (i.e., routine screening), or the concept of risk factors, has any role to play in the basic clinical encounter and ponder whether such interventions should take precedence over an individual's reasons for visiting a doctor in the first place (Getz, Sigurdsson, & Hetlevik, 2003, 499). Physicians and other health professionals, however, have been so inculcated with guidelines and instructions on what they should be doing to keep their patients healthy that it is not unheard of for patients to visit their doctor in order to ask about a specific complaint, such as a knee injury or a cough, and come out clutching multiple requisition forms for everything from blood tests to mammograms.

The model of family doctor as advisor on prevention was developed in 1979 "in an influential article" by Stott and Davis (Stott & Davis, 1979, cited in Getz et al., 498), that delineated four possibilities inherent in the doctor-patient encounter. These range from the management of presenting problems (what the patient came for in the first
place) to the modification of help-seeking behaviour and discussion of continuing
problems to "opportunistic health promotion". At the time the latter did not amount to
much and could be considered technically feasible or even ethically justifiable. Today,
however, when choices range from invasive (and risky) CT scans requiring dye injections
to other complicated procedures involving everything from high doses of radiation to
hard tubes wound into various orifices (which can slip and tear other organs), the picture
is more complicated:

As authoritative researchers advocate lower thresholds for intervention,
asymptomatic people are more likely to be labelled as at risk and needing
medical intervention and follow-up. (Getz et al., 498)

Not only can this be unduly intrusive, expensive and difficult from a practical point of
view, but, from a patient and societal perspective (not to mention cost), this can become
problematic, leading to important ethical concerns with respect to iatrogenesis and health
as well as informed consent:

Preventive medicine – that is initiatives to improve health among people
who are currently free of symptoms – is fundamentally different from
curative medicine, which is offered to patients who seek medical help. The
two disciplines imply different promises and have different obligations to
the individuals whose lives they modify. (Getz et al., 498)

As Sackett tersely pointed out, these ostensibly preventive measures (many of which
have little good evidence in their favour) could be called presumptive and even unduly
assertive, particularly given the widespread lack of awareness both on the part of patients
and many health professionals of their imperfections and inadequacies, the number of
false positive/negative results and the variability and range of “normalcy” – not to mention the inadequacy of many tests’ predictive qualities.

Passive advice with respect to prevention, such as calls for accident prevention or avoidance of high-risk behaviour (wearing bicycle helmets, not smoking), rarely has serious adverse effects and is usually relatively benign. Other interventions, however, such as screening and “risk classification for the purpose of selective preventive interventions, dietary intervention and prophylactic drug treatment”, such as long-term drug therapy to reduce cholesterol or blood sugar, may well be hazardous and have serious side effects (Marshall, 1996, 1493). Lipid-lowering drugs such as the statins, for instance, may cause rashes or nausea or, more seriously, a fatal myositis, a “deadly destruction of muscles” (Hadler, 40). Granted, this deadly effect occurs only rarely, but whenever greater numbers of people take a drug the incidence of even rare side effects increases. So can it even be possible to justify the possible iatrogenic consequences medically, legally, ethically?

The fundamental distinction between active and passive therapy is simple and most of us have no problem distinguishing between an individual voluntarily seeking out medical counsel versus its dubious health promotion counterpart – well people exhorted through guidelines and institutional decrees of one kind or another to take tests or scans or drugs – particularly when this advice is based on moot premises such as drug company promotions and media hype. But so entrenched have ontological ideas around illness and health become (as well as the evidence on which they are based), so institutionalized and solid, that more often than not we think and speak of “health” and “disease”, screening
and treatment, sick and well, as facts of life: irrefutable, solid, real and not the often vague ideas and linguistic constructs they frequently are. Constructs, furthermore, that shift with the times and whose boundaries are, strictly speaking, only matters of human decision-making and consensus/convention, given weight only through expert say-so, statistics and endless repetition. And while not without some merit, at least from a policy or population perspective, this perspective can be severely limiting and problematic for the individual:

This monolithic view .. simplifies the continual negotiation and shifting balance in medical research, clinical practice, and social thought between ontological and holistic orientations. In the twentieth century, the appeal of ontological models of disease, even in the domain of acute, infectious disease has been tempered by questions about individual predispositions to disease (in the discussion around genes for instance) and the social, nonspecific basis of dramatic trends in disease morbidity and mortality. For example, epidemiologists and others recognized early in [the 20th] century that in a polio epidemic a significant percentage of the population may become infected, yet only a small fraction develops symptoms and an even smaller fraction, paralysis... Similarly [it has been pointed out] that the decline of tuberculosis mortality in this century has been a constant one, seemingly uninfluenced by the introduction of specific public health approaches and clinical interventions such as isolating infectious individuals and treating with antibiotics the silently infected (even though it has not stopped public health officials and clinicians for claiming the credit) … (Arnowitz, 1998, 9) (my emphasis)

The processes by which we recognize, name, classify and find meaning in illness fluctuate with time and knowledge, Arnowitz adds, and classifications are dynamic and fluid, changing with the tides of politics, society, culture and technology (9).
Increasingly, market forces also play their part, especially since there seems to be a good deal of money to be made "from telling healthy people they're sick" (Moynihan, Heath, Henry, & Gotzsche, 2002, 886).

Even without delving into the ontological objections to the prevention model, health promotion is neither uniformly successful nor does it always accomplish what it sets out to do. As an editorial in the *BMJ* reminds us, "health is not a unidimensional concept" and "despite professional belief in the power of medical authority to kindle change", attempts to encourage or coerce changes in behaviour may even increase resistance and fail abysmally if failing to take into account "sensitive and practical approaches to individuals" – particularly if such "wellness" efforts are undertaken without an appropriate understanding of the wider environment and socio-cultural world within which individuals function (Stott, Kinnersley, & Rollnick, 1994, 972). The authors end with a reference to the "hollow rhetoric" of those who focus too little on context and ignore the risk patients face from over-exuberant medical interventions, when numbers, biomarkers and surrogate end points are the focal point. Many prevention strategies "aim to create opportunities that allow individuals and communities to make healthy lifestyle choices" yet this is a complicated and ill-defined process dotted with many pitfalls.

Furthermore, healthy people are rarely motivated by threats of long-term risks (McPherson, 2001). Sadly, neither are institutions or policy makers.

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*90 Mortality from coronary artery disease (CAD) in men (age 45-64) has similarly declined in the US, Canada, Australia and New Zealand after peaking in the late '60s/early '70s. In a controversial theory, James Le Fanu suggests in the *BMJ* that the progression of CAD in the west has followed a course eerily similar to that of a microbe – irrespective of health promotion efforts around blood pressure and cholesterol. Tellingly, nobody appears interested in researching this further (Le Fanu, 2002) and Le Fanu has been ridiculed.*
An epidemiological study (a prospective general population survey) in Scotland conducted to study the limits of health promotion messages at the individual level noted:

Recognition of behavioural risk factors has been incorporated into lay epidemiology of heart disease as an element of “coronary candidacy” – the kind of person who “should” or “should not” develop heart disease. Highly visible risk factors, including a person’s tobacco consumption, weight, levels of activity, and diet are invariably invoked in both retrospective explanations of past coronary events (particularly fatal heart attacks) and in discussions of the likelihood of future events. The candidacy system, however, is also recognized as fallible and incorporates the observation that “it never seems to happen to the people you expect it to happen to.” Violations to candidacy are noted .... At the high end of the spectrum attention focuses on the “unwarranted survivor”, graphically characterized as “Uncle Norman,” who lives to a ripe old age flaunting advice on coronary health. (McConnachie, Hunt, Emslie, Hart, & Watt, 2001, 1487)

Six thousand and sixty-eight men were allocated to high or low “visible risk” groups based on two risk factors, weight and smoking, yet the researchers found that other, invisible factors such as poor respiratory function, diabetes, previous coronary heart disease and socio-economic deprivation (for the men at low visible risk) and height and cholesterol level (among men at high visible risk) modified the visible risk factors. The researchers concluded that “health promotion messages would be more credible if they discussed anomalies and the limits of prediction” at an “individual level” (1487). For us to genuinely understand what risks might apply generalities do not suffice, neither do statistics or percentages.

These general messages on risk factors may even have a negative impact. British sociologists Helen Lambert and Hilary Rose have found that the many media messages on cholesterol adversely affected how individuals diagnosed with hyperlipidemia, a
genetic inability to metabolize lipids such as cholesterol, understood and managed their condition, particularly at the outset. The researchers found that the unrelenting media messages on cholesterol and coronary artery disease actually interfered with these patients' ability to understand and explain their illness to others – including to the medical profession – and created barriers to their understanding the familial/genetic nature of their illness (Lambert & Rose, 1998). Lambert and Rose also found that ordinary people often have a far more sophisticated and subtle understanding of medicine and medical messages than experts gave them credit for. This research “challenged” the view that the public somehow experiences “decontextualized knowledge” on which they are “deficiently cognizant” (81).

**Informed Consent: When the Numbers are the Message**

Just as tone, content and placement of information affects individuals’ understanding of illness, how numeric data is presented also affects perceptions of therapeutic effectiveness and risk. Both professionals and patients make different choices depending on how statistical information is stated; percentages, in particular, are overwhelmingly compelling (Gigerenzer, 2002, 135). For example, an older man might be interested to hear about a therapy that promised an 18% reduction in the relative risk of dying from colorectal cancer; yet that same person would probably think twice when
told that “one’s lifelong risk of not dying from colorectal cancer is 99.34% if you are screened and 99.20% if you are not” (Getz et al., 499). 91

These perceptual phenomena are potentially important in health care where numeric data must be interpreted by clinicians, patients, and policy makers alike. Psychology thus meets epidemiology in the continuing debate about the best summary measures to describe the quantitative outcomes of clinical studies. (Naylor, Chen, & Strauss, 1992, 916)

Larger percentage differences, add Naylor et al., are “impressive”; yet a 25% relative risk reduction “can be reported whether the absolute event rates in the two arms are 40% and 30% or 4% and 3%”. The numbers needed to treat or NNT – in other words the (estimated) number of people who would need to be treated to prevent a single adverse outcome or event – is a somewhat more accurate measure of effectiveness, however much this number may reflect the ambiguities and possible biases of the original study. The NNT figure, however, does at least provide a reasonably comprehensible context for the statistics provided and allows for personal decision-making in a way that percentages do not. For example, if one is told 10,000 asymptomatic individuals would need to take pravastatin (a cholesterol lowering drug) to prevent some 245 cardiac events in the future (and 9755 people would see no benefit at all), one might well decide to abstain (Freemantle & Hill, 2002, 864). Numbers-needed-to-treat can also be very convincing, for example only fourteen people would need to be given the drug tPA, post stroke, for one person to show improvement or even have some of the stroke damage reversed (personal communication, Dr. Anthony Woolfenden, January 2000). However, as Hadler

91 Based on Kronborg et al. (Kronborg, Fenger, Olsen, Jorgenson, & Sondergaard, 1996).
points out, there is no guarantee that these numbers will ultimately have anything
whatsoever to do with the individual patients or doctors actually involved:

[As] for the NNT, if the result of the trial is marginal, say a 1 per cent
improvement in survival in one year, why should I be offered the
supposition that I will save 1 life for every 100 people I treat for a year?
(Hadler, 216)

Much of the time these subtleties do not even crop up, as patients or clinicians rarely
even know the NNT of a treatment or test and are bombarded with significant-sounding
percentages. Even less common is the inverse of the NNT, a number that has only
recently come into circulation, the numbers-needed-to-harm or NNH.

The relative risk reduction figure, expressed as a percentage, is, unfortunately, the
most common since it is powerful and compelling and drug companies and media love it.
Patients then undergo tests and procedures believing they know the odds which makes a
mockery of informed consent, a problem on many levels. Furthermore, the professional
who offers the test is responsible – legally, ethically, personally – for ensuring that the
person undergoing the test understands what the test is about, and genuine informed
consent presupposes “an understanding of the limitations” of whatever course of action is
being advised (Getz et al., 499) (my emphasis). Yet few people even know that the tests
they take even have limitations – witness the lives destroyed by false positives on AIDS
or cancer tests (and the inverse, false negatives). With the advent of genetic tests this
problem becomes even more pronounced, as the tendency for asymptomatic individuals
to be labelled “sick” increases, yet, as we saw earlier, merely possessing a genetic marker for many conditions does not necessarily mean anything.

Informed consent, whether for screens, treatment or to enter a clinical trial (or for a genetic test) contains both an administrative and ethical dimension. Often, the administrative and legal part, the consent form, is the only one given any consideration when it is, in fact, the latter which is more to the point. Few people genuinely understand the degree of uncertainty (and risk) there can be in tests or treatments; neither do most individuals appreciate the interpretive difficulties inherent to results from mammograms, ultrasound or even the humble x-ray. Communication presents further ethical concerns: subtle persuasion tactics may well verge on coercion given the vast gulf in both power and understanding between patients and health care professionals. Patients often struggle with terms and concepts that seem commonplace to the medical staff – and even “helpful” analogies can confuse as well as inform. Responsibility for their understanding, nevertheless, resides in the medical profession, for, as Tauber writes, “Medicine is fundamentally a moral commitment”, in other words, the care of the person. Medical ethics is not merely “judicial directives, risk management, and academic debate” (Tauber, 2002, 562). Practitioners and policy makers need to appreciate this.

92 Women commonly believe, according to Dr. Susan Love in an old PBS film on breast cancer, that mammograms reduce breast cancer by 95% when, what is said is that mammograms detect up to 95% of cancerous tumours.
Utilitarianism, Moral Hazard and the Greater Good

From an institutional and public policy perspective, however, percentages and other numeric forms of expression take precedence over personal ethics and risk. Although many institutions originally emerged as a result of political and social factors, their professional exigencies demand ostensibly dispassionate distance, not ambiguity or doubt.93 Even that archetypal locus of medical intervention, the hospital, is a complex bureaucracy with an “elaborate systematic division of labor and a high degree of specialization of expertise, responsibilities, rights, and authority” whose “manifold statuses, roles, and offices” are hierarchical and governed by “impersonal rules and rule-like norms” (Fox, 1989, 145). Furthermore, hospitals, health boards, ministries of health, professional organizations, and other institutions such as the Medical Services Plan or Pharmacare, by their very nature, require benchmarks and standards in order to function collectively. Even within the relatively simple Canadian single-payer system it would not be possible to adopt public policy and develop fee schedules and budgets if there were no mechanism for delineating what procedures and treatments are possible.94 These require diagnostic criteria as well as fairly precise disease definitions and boundaries, and, by extension, what ought to be done about them and what type of treatment(s) are called for.

93 For example, the American Medical Association was formed in the 19th century to act as a professional lobby “and to preserve and advance standards”, but was also a means of protecting doctors “from the financial threat and personal success of their ‘unorthodox’ colleagues, the homeopathics, eclectics, …and midwives” (Duffin, 2000, 120).

94 In the fractured American system this process becomes even more difficult as individual physicians must set their own fees which they subsequently submit to HMO’s and Medicaid and so on. Canadian physicians moving to the US often find this process extremely daunting (Baxter, 1996).
This model of medical practice, which through consensus, evidence and discussion has evolved over time into what is familiarly known as “standard” (or sometimes “best”) practice, has, at its ethical root, the concept of utilitarianism, discussed earlier with respect to its similarities to economic efficiency.

Originally articulated by the philosopher John Stuart Mill in the 19th century, utilitarianism judges or assesses the rightness or appropriateness of an action through its results; its normative ethics thus entail engaging in actions that result in the most “good” for the largest number of people. Of course the question then becomes exactly what is the common good and who decides. Proponents maintain that in order to develop norms and standards it is essential to rely on expert judgements and not, as “moralists” would have it, the ordinary person, who is “frequently irrational” (Smart, 1973, 39). Experts are the people best able to make the broad choices needed to determine the “greater good” since, from a utilitarian position, the “moral value of any action always lies in its consequences” (Williams, 1973, 79). Of course this may conflict with the people to whom the decisions apply – might, at times, even trample on their civil liberties or be at odds with their personal wishes. An expert panel or health board or some other group may decide that a woman who has just delivered a baby should go home forty-eight hours later, but new mothers might disagree. Group protocols might call for PSA testing for men over fifty, yet some men might want one at forty, or seventy – or never.

Health guidelines based on utilitarian principles are thus subject to the same fallacies as medical research based on large populations using surrogate end points: there is little or no understanding of process, variability, uncertainty. Neither is there much
attention given to the possibility that not everything considered good or necessary today will be seen that way tomorrow. From an ethical and philosophical standpoint utilitarianism contains disquieting similarities with some biomedical research, with its statistical conclusions based on homogenous groups that exclude difficult patients or anomalies. The focus on markers and measurable outcomes (with its attendant tendency to sidestep individual patient concerns), furthermore, can easily become inflexible and dictatorial, especially if too rigidly applied. The late philosopher Bernard Williams, an opponent of utilitarianism, compared this ideology to colonial rule (Williams, 138), where conquerors attributed all that was good and noble to their own culture, which they then used as justification for any number of unpleasant, even totalitarian, practices. Williams, like Kuhn in his analysis of science, also felt that utilitarianism naturally tended toward the facile and the known, obscuring the new and original:

Just as in the natural sciences, scientific questions get asked in those areas where experimental techniques exist for answering them, so in the very different matter of political and social decision weight will be put on those considerations which respected intellectual techniques can seem, or least promise, to handle. (Williams, 148)

Williams added that since utilitarianism does not interest itself in the agent so much as in actions or results, "it essentially involves the notion of negative responsibility" (95). Not only do policy makers not have to live with any negative consequences of their decisions, being at such a remove from patients, but they themselves are often exempt from some of the more onerous effects of their policies.
That same point is made by economists Milgrom and Roberts in their discussion of moral hazard, a term used in insurance to describe the fact that protection and insurance actually change the behaviour of the person who is covered. They refer to this as a form of "postcontractual opportunism":

The term moral hazard originated in the insurance industry, where it referred to the tendency of people with insurance to change their behavior in a way that leads to larger claims against the insurance company. For example, being insured may make people lax about taking precautions to avoid or minimize losses. (Milgrom & Roberts, 167)

In other words:

Moral hazard problems may arise in any situation in which someone (who may be a supplier, a customer, an employee, or anyone else) is tempted to take an inefficient action or to provide distorted information (leading to inefficient actions that are not in the best interests of the largest number) because the individual's interests are not aligned with the group interest and because the report cannot easily be checked or the action accurately monitored. (168) (my emphasis)

Moral hazard is not usually thought of in reference to policy-makers; rather it tends to refer to the individual, whose interests are not considered to be aligned with the larger group, or society in general. Individuals, whose real motive is assumed solely to be personal gain, will, according to this notion, inevitably opt for maximum personal benefit without consideration for general consequences. So, persons with zero-deductible fire insurance will carelessly set fire to their sofa since they know insurance will replace it and will not concern themselves with the higher premiums this will translate into for everyone else. In medicine, this adversarial stance implies that patients, aided and abetted by doctors who are of course the real gatekeepers, will want for themselves any available
test, scan, treatment or drug regardless of what it might mean for everyone else. Services, therapies and drugs (even numbers of doctors and nurses), therefore, must be rationed and controlled.

The flaw in this argument is twofold. Not only does it present humanity in its most unattractive light, using a minority as the basis, but it ignores the fact that individuals also operate in the same social world as those experts and policy makers and share their values and beliefs. No doubt there do exist some (rare) careless firebugs who enjoy setting fires and for whom a no-deductible fire insurance policy translates into happy (and "free") incendiary practices, but for the vast majority of people a fire in their living room is hardly a day in the park. Insurance tends to be seen as a necessary precaution, but most people do not enjoy having their home go up in flames (or their belongings stolen or damaged). By the same token, it can be safely said that the vast majority of people do not like or enjoy being sick or having to seek medical care.

Medical care is not a commodity (Evans, 1984). It is, at best, a solution to a problem nobody wants, namely ill-health and disease. Medical procedures are neither amusing nor fun (nobody gives up a holiday in the sun to check themselves into hospital for surgery), and only rare, disturbed individuals seek them out. Yet this peculiarly pessimistic view of human nature assumes that not only can individuals not be trusted to know what is best for them, particularly when there are numerous choices available, but maintains that strict guidance and restrictions are needed to keep people in line, which is utilitarian morality verging on medical colonialism.
With restrictive formularies, both criticisms of moral hazard can be applied. First, there is the notion of non-engagement: Those who are in a position to draft policy do not themselves bear the consequences of the decisions they make – it would be highly unusual for an expert or policy maker not to be in a position to pay whatever was necessary if they felt it necessary to take a non-referenced drug. Furthermore, this group does not have any direct dealings with the people who might suffer the consequences of their decisions. Distressed patients will not show up at their offices or phone them on a weekend to complain of side effects; neither will they have to check that patient into hospital should something dire happen. The experts are not then, in Milgrom and Roberts’ phraseology, aligned with the group for whom they are making decisions. Second, the basic assumption that individuals will automatically opt for the most expensive drug, treatment or therapy if left to their own devices does not stand up to scrutiny. Patients simply want to feel better. Taking “designer” drugs does not provide cachet or status. Most people neither know nor care the vintage of the drugs they use. Provided the drug works without too many side effects they are happy to take cheaper drugs (Nair et al., 2002). Furthermore, patients are frequently far more conservative than experts give them credit for and far less willing to take drugs than guideline writers and researcher-physicians think (McAlister et al., 2000). Yet this pessimistic view of human function reflects a common theme in health economics, and economics in general:

Economics is, at root, the study of incentives: how people get what they want, or need, especially when other people want or need the same thing. Economists love incentives. They love to dream them up and enact them, study them and tinker with them. The typical economist believes the world has not yet invented a problem that he cannot fix if given a free hand to design the proper incentive scheme. His solution may not always be pretty
– it may involve coercion or exorbitant penalties or the violation of civil liberties – but the original problem, rest assured, will be fixed. An incentive is a bullet, a lever, a key: an often tiny object with astonishing power to change a situation. (Levitt & Dubner, 2005, 20)

Furthermore, and this is an important point, however much they may believe in the accuracy and sense of the policies and restrictions they recommend, experts often rely on data which may be distorted, incomplete, ambiguous and lacking in nuance. Much of the drug research done in recent years has been subsidized by the pharmaceutical industry and (understandably, given its source) has been more focused on the benefits of treating risk factors and surrogate markers than on health. Yet:

Information from EBM is being used to encourage minimalist purchasing in the name of science. This pseudoscience may lead to rationing and the non-purchase of care that clinical judgement says is useful. (Williams & Garner, 10)

In addition, over-focusing on drugs and technologies deflects attention from other types of care that patients might want and need, such as lifestyle advice on nutrition, diet, pain control or physiotherapy and exercise, topics on which, generally, little research has been done (Rogers, 2002, 96). Williams and Garner point out that there are drugs which may not work for everyone but which are effective for sub-groups of patients – so why not allow three-month trials of these “to discover those individuals who will benefit” (Williams & Garner, 11) rather than banishing them outright? Another solution might be to create more “organic” and flexible policies which incorporate the ambiguous and shifting definitions of illness as patients define it (11). But patients really are not at the core of this discussion – neither, for that matter, are health professionals.
Milgrom and Roberts suggest a variant on involving patients when they describe "moral hazard in agency situations" (Milgrom & Roberts, 1992, 190), what the doctor-patient is in economic terms. (Patients cannot themselves have access to prescription drugs, neither do they have sufficient knowledge to make informed choices, it is the doctor therefore who is the "agent" of the deed. The principal, the patient, must therefore have the agent intervene — prescribe — in order to have access to the drug or treatment.) They suggest that the principal agents, or patients as they are more commonly known, be given the freedom to effect choice. This would not be possible in many medical scenarios (nobody can do their own surgery), but could be feasible with drugs if patients were given access to good information (and time with their doctors or a nurse or pharmacist to talk about it). At the very least, patients could be provided with the available choices (outside of emergency situations) and information on risks and benefits and allowed to consult with their clinician more effectively. Given the value that Canadians place on their health care system and its sustainability, it stands to reason that if more of us knew the prices of drugs and were aware of the various choices and consequences (including social and financial ones), many more of us would choose to at least begin with the cheaper, older drugs. Then, if these did not work or had onerous side effects, we could move "up" to the newer, more expensive ones. The one exception would be people with chronic illness who take multiple medications and for whom drug interactions can be a major problem. This group might well opt for caution and start with the most "refined" alternative possible. (Given that many chronic sufferers could end up in hospital as a result of a drug interactions, this still would be a savings given what even one day of acute care costs.) Even making the relative prices of drugs more easily available to
patients and doctors could well result in marked savings: people who feel included in
decision making are more vested in the results – as countless employee incentive
programs have demonstrated. In short, merely giving people rules and directives to
follow – be they patients or doctors – does not tend to engender helpful or cost-effective
behaviour and trying to do one-dimensional good more often than not translates into one-
dimensional harm (private communication, John Fountain, May 2005). As medical
sociologist David Mechanic writes:

There are many pressures to achieve technical rationalization of health
care but ... any re-engineering must be attentive to socio-cultural factors,
values and psychosocial processes. Whatever the technologies, medicine
depends on the quality and credibility of interpersonal relationships
between clinicians and patients and the organizational forms that support
them. (Mechanic, 2002, 466)

Creating policies that incorporate patient wishes and autonomy, illness narratives
and the complex nature of individual illness would require, however, a major shift in
direction and attitude. In our age of burgeoning medical possibilities, expanded
technology and over-reliance on institutions, groups and experts, this is somewhat
difficult to envisage. Nonetheless, there are good reasons to at least make the attempt.
V. Medicine or Medicalization?

The rise in the prevalence of reported disability in our population is, partly, the result of modern medicine—taking into account that we now live with diseases from which we used to die—but is also related to a rise in expectation of what it means to be "healthy".... We have to ask whether in our enthusiasm for biomedical science, or knowledge, we have not lost sight of the need for wisdom in how it is applied.


For centuries medicine has been the art and science of healing, along with the practice of bringing comfort and succour to the sick. But what does it mean today to be "sick", particularly if invisible and asymptomatic markers such as being HIV-positive or having high cholesterol are included in the term? How can a country like Canada, with its entrenched concepts of public health care, come to terms with medical "necessity" and timely intervention during an epoch when everything—from education and travel to work, communication and even food—has become so broadly technological, corporate, institutional?

Health and illness, once obvious subjective states, have expanded to include a vast array of screening and test results as well as complicated and ethically complex interventions such as transplants and pre-emptive surgeries based on genetic testing. Within this framework, then, can we truly state that policies such as reference pricing
genuinely decrease pharmaceutical expenditures or are they short-sighted, finger-in-the-dyke solutions which, by narrowly defining dysfunction and delineating boundaries around subtle clinical problems, exacerbate the very problem(s) they are intended to solve? Psychologist Leon Festinger established many years ago that codifying (and remunerating people for) actions that occurred naturally would not only alter the behaviour in question but the values surrounding it (Zimbardo, 1985, 582). In pharmaceutical terms, this implies that simply creating a set of rules under which certain medications will be reimbursed can itself change people’s perceptions of the value and necessity of pharmacotherapy. Yet at present we seem more bogged down with questions as to what health care technologies are or are not, can and cannot provide, than questioning their implications or considering the tacit beliefs driving them. Whether it is the actual “machine” kind of technology (such as CT scans or machines to measure bone density), administrative and managerial technologies (a national Pharmacare program or better drug-approval processes) or infrastructure and personnel like hospital beds, operating rooms and nurses, it seems that in our collective minds the mechanics of health care have overwhelmed its primary purpose: namely, shielding us from the devastating and potentially catastrophic effects of illness and injury. Machinery, in particular, has attained iconic status, as anything with a digital screen and a technician at its controls would appear to generate extraordinary reverence and an overweening sense of entitlement with respect to access.

Health, however, cannot be a “right”, for, as the French philosopher Michel Foucault wrote:
It is clear that there is no sense in talking about a “right to health.” Health — good health — cannot arise from a right. Good and bad health, however rough or fine the criteria used, are facts — states of things and also states of consciousness. And even if we correct for this by pointing out that the border separating health from sickness is in part defined by the capacity of doctors to diagnose a sickness, by the sort of life or activity of the subject, and by what in a given culture is recognized as health or sickness, this relativity does not preclude the fact that there is no right to be on this side or that of the dividing line. (Foucault, 2003, 73)

We may not overtly talk about this “right to health”, but there is nevertheless much attention given to access to various “means” of health and the paraphernalia and services that we now include in the health care matrix — even as focus increasingly shifts from the prosaic facts of illness and its often devastating personal consequences onto waiting lists and access to technology or operating theatres.

Ironically, the higher our expectations of medicine and the greater the number of diseases and conditions we are able to control, manage or cure, the less satisfied we appear to be, even though most Canadians are healthier and live longer than ever before. The question then is whether our conceptual models of health and health care reflect something even vaguely resembling reality or whether other powerful influences, from pharmaceutical advertising to the edicts handed down from consensus groups and others professing to decode the evidence for us, have hijacked and confused the point.

**The Paradox of Health**

Canada consistently rates high on traditional international measures of health such as longevity and infant mortality, which like the incidence of many childhood diseases and other measurable elements of ill-health, have decreased dramatically. Yet Canadians,
like Americans and Britons, report “more frequent and longer-lasting episodes of serious, acute illness now than they did 60 years ago” (Kenny, 2002, 75). Canadian normative data suggest that mean Canadian scores on self-reported mental and physical illness hovers around the fifty per cent mark, hardly a ringing endorsement. Predictably, younger people have higher estimates of their own general health, but, as of one’s forties, perceptions of physical functioning and general health decline (Hopman et al., 2000).

Perceptions, however, do not occur in a vacuum and are always relative. “People’s evaluations of their quality of life are made within horizons of possibilities,” explain epidemiologists at the University of Nottingham. These relate to identity and are shaped by factors such as “social class, age, sex, ethnic group, sexuality, disability, and personal biography”, incorporating the ideological spheres within which each individual operates:

The result is that someone with an experience of poor health who has low expectations might not evaluate the experience (of poor health) as having an impact on their quality of life because their expectations are correspondingly low. Conversely, someone who has generally good health might experience a significant impact on their quality of life from a relatively minor illness (such as the flu or tonsillitis) because they have high expectations. (Carr, Gibson, & Robinson, 2001, 1241)

This has “profound implications”, write Carr et al., for health policy and decisions on prioritizing and planning, particularly in this age of reverence for polls and questionnaires. Merely listening to what people report on a superficial level (as any attempt at quantifying opinion must do) ignores the not inconsiderable social and cultural
expectations behind the beliefs around personal health – as well as how medicine itself is perceived within the socio-cultural environment:

We recognize that health, well-being and happiness are somehow related. Health, however, is neither necessary nor sufficient for happiness.... We understand strong, sometimes overwhelming desires to avoid all injury, illness, disease, disability and death. These fundamental desires have always moved humankind … [but] are experienced in a very particular way by Canadians today. We expect that life will not be burdened with disease and that death will be deferred. (Kenny, 77)

Kenny charges that the dominant model is now biomedical and, as a result, “mechanistic and reductive”, as disease definitions and boundaries have changed and treatment options have expanded and multiplied (77).

A comparison of two communities in India by the respected economist Amartya Sen demonstrates just how large a part beliefs, expectations and social conditions play in health and health care use. The state of Kerala, which has the highest literacy and longevity rates in India, also reports the most morbidity and sickness. When compared to another Indian state, Bihar, whose medical delivery systems are “woeful”, personal measures of health run “almost fully in the opposite direction” to actual life expectancy and other outcome measures (Sen, 2002, 861). Feeling healthy somehow seems to depend on not knowing what could go wrong, suggests Sen, and “a person brought up in a community with a great many diseases and few medical facilities may be inclined to take certain symptoms as ‘normal’ [even] when they are clinically preventable” (861).

These variations also held true in an examination of Glasgow residents, which found that even though people living in deprived areas were more vulnerable to heart
disease than those in affluent ones (and were well aware that they were at higher risk), those same individuals were nevertheless less likely to seek medical advice (Richards, Reid, & Watt, 2002, 1308). Various factors were involved, such as fear of hospitals and what the doctor might say, diagnostic confusion relating to comorbidity (e.g., diabetes, which increases the risk of cardiac disease) and low expectations of treatment. In addition, people in the deprived area “reported greater exposure to ill-health”, which allowed them to minimize and normalize their symptoms. There was also greater identification with high risk groups, giving “rise to a belief that they were overusing medical services” (1308). The authors concluded that social and family norms and past experience played a major role in how these individuals perceived their own health status:

Respondents from the deprived area were more likely to report negative experiences of health care and to have lower expectations of health care. The quality of interactions was determined by the degree of social alignment between the doctor and the respondent, the degree to which knowledge about health was shared in the consultation, and the extent to which respondents felt at fault for their health problems. (1309)

Individuals who share a common background, language and value system inevitably are able to communicate better. They speak the same language, understand the same metaphors, have similar experiences. The elderly, Aboriginals, immigrants or the poor often perceive the world differently than health professionals, and often it is these same groups who are medically (and otherwise) marginalized. In terms of reference

95 Recent initiatives to increase medical school graduates from northern communities and from different cultural backgrounds could be a positive force in closing this gap.
pricing and therapeutic equivalence, this also explains why people in lower socio-
ecoconomic groups are more likely to quit taking medication altogether when they are told
to switch to a cheaper one; not only are their values at odds with those of the experts, but
they may not find the explanation(s) compelling or comprehensible. (Even well-educated,
younger, better-off individuals complain that medical explanations can leave them in the
dark. Add that to the problem of class and background and communication clashes can
become even more divisive.)

Socio-economic status is not only predictive of health-related behaviour but of
health in general. According to American rheumatologist Nortin Hadler in The Last Well
Person: How to Stay Well Despite the Health Care System:

A lifetime tottering on the edge of poverty is a lifetime likely to be mean,
often discouraging, sometimes desperate – and also short. What is it about
a compromised socioeconomic states (SES) that is so malevolent?
Multiple psychosocial factors have emerged from the studies of relative
poverty. Some of these factors operate from conception, but the majority
derive from the loss of self-respect and the resentment, if not hostility, that
results from the sense of abject vulnerability associated with and imposed
by poverty. (Hadler, 2004, 166)

Modern life also makes us vulnerable and presents its own hazards, from the ever-present
humming, buzzing, interactive contraptions many of us live with (or cannot live without)
to “ecosystems that can perturb our biology” and create biohazards of which we are
frequently unaware (166), present in everything from the air we breathe to the food we
eat. The health care industry itself can be seen “to be both a solution to environmental
decline and as a problem” (Jameton & Pierce, 2001, 365), not only in terms of creating
more pollution and waste, but in subjecting individuals to toxic substances and radiation which they might otherwise not have been exposed to.

Nevertheless, challenges to everyday coping are increasingly being conceptualized in medical terms. Present-day western culture predisposes us, particularly when overwhelmed, to transform our distress into “idioms of physical distress” (Hadler, 167) which appear to be a more acceptable narrative to us and to those around us than those referring to personal or psychosocial dysfunction. From sleep disturbances, general malaise or depression to musculoskeletal disorders such as repetitive strain injury or backache, the preferred framework is one of illness rather than psychic or psychological (or even social or economic) distress. Such misconceptions, suggests Hadler, “have misled the occupational health and safety agenda for over sixty years” (167). It would seem that medicine, and health care, have become the repositories of much of our 21st century angst. Health professionals, often against their will, must handle some of the more negative aspects of life that others – and perhaps we ourselves – are reluctant to face. Yet few of us perceive medicine (and medical care) in its complicated clinical, social, cultural, ethical and economic entirety. We are far more prone to being swept along the compelling currents of medicine itself (as tests lead to more tests; drugs lead to more drugs to treat the side effects of the first ones) or to being lulled by the powerful stories flowing from the media or the market which tell us that the solutions to our distress lie in medicine: drugs, surgery and other such interventions.

Perhaps, as medical sociologist David Mechanic suggests, it is our cultural and societal templates and our beliefs and values which are at the root of our dilemmas in
medicine, along with our tendency to elevate (read: romanticize) concepts around "self-improvement, autonomy, strength, personal initiative, technology and progress" (Mechanic, 2002, 459). These lead us to believe that by staying healthy, promoting healthy initiatives, being proactive and taking active charge of our health, doing more, we can somehow "win" in the health sweepstakes, perhaps even cheat age and death. Within this context, writes Mechanic, innovations in medicine and technology can "take patients on treatment trajectories that are difficult to control" (Mechanic, 459). Disturbingly, it is no longer unusual for an ailing, older individual who refuses further invasive medical treatment to be considered lacking in competent judgement (private communication, Robert Hewko, May 2004). Yet these ideas are relatively recent and owe more to the prevailing economic and socio-cultural paradigms of the day than many of us realize:

The development and uses of medical technology are shaped by faith in marketplace competition, technological progress, activism, choice and consumerism. This constellation of values has resulted in very rapid growth and dissemination of hardware and related procedures whose costs pose significant financial dilemmas. In response, a range of management technologies [reference-based pricing, e.g.] have been developed to restrain the excesses of intervention but, because they are counter to many prevailing values and interests, they have led to much tension and a social backlash. Resolving these rationing tensions – which are rarely acknowledged as such – is a major challenge in American medical care and in much of the world. (Mechanic, 2002, 459)

Informed and affected by dominant economic concepts such as globalization, competition, free trade and an assumed, collective, inalienable, right to cheap goods and ready access to energy and other resources; seduced by the paradigm of the self-reliant
individual, only held back by his or her own limitations, health is only too often perceived (primarily in the United States but also throughout the developed world) as an extension of the better life to which we can all aspire and often feel entitled. And at times it seems as though we really do believe that good health, and the health care system which will ensure we attain it, is just another commodity, like cheap oil or power at the flick of a switch – even though medicine cannot be considered in the same “class” as other goods and services. Untrammelled medical enthusiasms can result in misdiagnoses, unnecessary labelling and harm to us as patients – and no amount of “proactive” care or healthy living is guaranteed to prevent illness.97

The late Yale physician Alvan Feinstein attributed this medicalization to the “redefinition” of scholarship in medicine as well as the path taken by the research community, notably the National Institutes of Health in the US, after the second world war:

Medical work contains two sets of fundamental scientific challenges: in biological explication to understand mechanisms of disease, and in predictive clinical intervention to treat (or prevent) disease. The NIH’s research and grant policies, however, confined the focus of basic science to explicatory mechanisms. The subsequent basic research led to magnificent advances in pathophysiology, in molecular biology, and in the development of new technology, but an appropriate [basis] was not developed for the clinical task of evaluating the technology and appraising the therapeutic interventions. (Feinstein, 2003, 241)

96 One could add that these beliefs are underscored with a reverence for youth and vitality that easily misattributes to ageing problems that frequently appear in earlier years.

97 People who become seriously or chronically ill often do not merely become (justifiably) upset at being ill, but may feel personally betrayed. Particularly if they ate well, exercised and did everything they were told was good for them. Nobody had prepared them for the unpredictability of illness: People who never smoked do get lung cancer; marathoners can drop dead of a heart attack, and nice people do get sick.
In other words, focus moved away from the patient and towards disease.

**Symbolism and Meta-messages**

The cheapening impact of an impersonal medical machine on western society (and the culpability of the medical establishment) was the subject of two slight volumes, *Medical Nemesis* and *Limits to Medicine*, written nearly fifty years ago by the eccentric philosopher (and theologian) Ivan Illich, who blamed the ascendancy of medicine for most of western society’s problems. Illich felt that, even by the 1960’s, medicine had overstepped its bounds to become a latter-day narcotic, designed more to assuage and mitigate negative life experiences than to comfort or heal:

> Medical civilization is planned and organized to kill pain, to eliminate sickness, and to abolish the need for an art of suffering and of dying. This progressive flattening out of personal, virtuous performance constitutes a new goal which has never before been a guideline for social life. Suffering, healing, and dying … are now claimed by technocracy as new areas of policy-making and are treated as malfunctions from which populations ought to be institutionally relieved. (Illich, 1976, cited in Fox, 1989, 36) (my emphasis)

Sociologist Talcott Parsons expressed similar sentiments (albeit less harshly), writing that individuals lose autonomy and power as they fall prey to the power of institutionalization – which is, in essence, a covert form of social control. Distinguishing between people’s roles, which reflected the “participation of an individual in a social system” and their tasks, which were more private and “differentiated” (Parsons, 1981, 60), Parsons concluded that “relevant aspects of the value system have come to be institutionalized” and that by placing illness within a larger context of socio-cultural
“deviance” (57) we have created an unrealistic and unattainable ideal of health. This, in turn, has had an insidious effect on how we perceive our roles within the world we inhabit:

To be ill is thus to be in a partially and conditionally legitimated state. The essential condition of its legitimation, however, is the recognition by the sick person that to be ill is inherently undesirable, that he therefore has an obligation to “get well” ... The balance of health and illness comes to be bound up with the balance of control of the motivation of individuals in their relation to the society as a system. (70)

By extension, organizational and institutional policies or guidelines serve as a covert form of social control, a subtle form of coercion that relate to a person’s “commitment to the values of the society” (64). Illness thus places the individuals in a position of duty and highlights their responsibility to the collective:

[Another] important implication of institutionalization of the roles is that being categorized as ill puts the individual in the position of being defined as “needing help” and as obligated to accept help and to cooperate actively with the agency which proffers it. The role of illness, that is to say, channels those categorized as belonging in it into contact with therapeutic agencies [and is therefore involved] in both negative and positive mechanisms of social control. (71)

This reflects and reinforces the notion that people are only valuable for their roles and the contribution they make to society and its institutions – which illness and disability interfere with. Parsons wrote that even as medicine “evaluated and institutionally recognized” illness and health, among other states or conditions (62), it had an effect on
the individual as well as the culture at large. In this he compared medicine to religion, which also defined states of “ritual impurity” (68).

Another thinker who compared the strictures and structures of medicine to religion was Foucault, who considered the moralistic overtones of the “medical model” to be reminiscent of Christianity. Foucault wrote that the act of medicine required that one “show one’s wounds in order to be cured” – much as “one appeases one’s judge by confessing faults” in Catholicism (Foucault, 163).

The modern Western state has integrated into a new political shape an old power technique that originated in Christian institutions. We can call this power technique “pastoral power.” (131)

For Foucault, the power exerted by institutions over the individual clearly was neither balanced nor reciprocal, it was not “a relationship between ‘partners’” but a “way in which some act on others” (137). This latter observation, or the extent to which individuals are at a disadvantage in their dealings with the medical system, has also been a theme in medical ethics, although it has been pushed out of the spotlight at present by themes of reproduction and genetic and stem cell research.

Whatever the underlying symbolism or sociologic metaphor we might pick to describe how medicine affects individuals’ roles in society, what is obvious is that, for a range of reasons, medicine has increasingly been asked to step up to the plate when other

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98 Parsons stopped short of extreme criticism of the United States, which he was describing. Illich was less tactful and lambasted medical institutions and the forms of acculturation they engendered, particularly in comparison to “traditional” cultures which he felt confronted pain, impairment and death far better.
social and community connections fail, whether it is protection from an abusive environment or support during significant milestones during the life cycle from birth and death to menopause. Many philosophical, anthropologic, sociologic and even political discussions of medicine glibly blame this enmeshing of medicine and social functioning on the medical establishment, who are said to benefit by gaining power and control. This may well be true in some instances, but a great deal of the time the medical profession is a reluctant participant in the social dramas of our lives. As an editorial in the *BMJ* plaintively asks, who is ultimately responsible when the physician is asked to deal with a sick ninety-two year old woman who refuses to eat, but whose sons insist the hospital check for “depression, brain tumour, rare diseases”? The doctor, meanwhile, “talks in terms of old age, her home, her own room” (Leibovici & Lievre, 2002, 866).

From emotionally fraught scenarios, such as end-of-life care or possible genetic defects detected *in utero*, physicians, nurses and other clinicians (as well as lawyers and administrators) are being pulled into conflicted situations with alarming regularity, somehow having become the arbitrators of messy ethical questions – and the ones to blame when things go wrong. Leibovici and Lievre write that this shift towards the institutional solution and medicalization not only affects the people concerned but has consequences for the medical profession as a whole:

[Such] aspects of medicalisation make doctors miserable. The bad things of life: old age, death, pain, and handicap are thrust on doctors to keep families and society from facing them. Some of them are an integral part of medicine and accepted as such. But there is a boundary beyond which medicine has only a small role. When doctors are forced to go beyond that role they do not gain control: they suffer. (866)
Along the same lines, a qualitative study from the Université de Montreal which examined physicians’ perspectives on the often-mentioned problem of over-prescribing psychotropic medications to the elderly found that the physicians had "a patient-centered" approach and often used these medications to help their patients adapt to the unfavourable circumstances they often found themselves in:

Physicians see ... patients as having difficulty dealing with change in many aspects of their lives (e.g., decreased health status and autonomy, death of spouse, loss of friends and relocation) and a high level of psychological suffering. Moreover, many physicians described in-house conditions that isolated elderly residents and exacerbated their anxiety and suffering. Often these retirement buildings, described as "ghetto-like," are located far from centres of activity.... Most physicians described a very strong attachment of many of their patients, women in particular, to anxiolytic drugs ... and many [physicians] felt it would be more detrimental for the patients' health not to prescribe. In their view psychotropic medication helps the elderly patient remain functional. (Damestoy, Collin, & Lalande, 1999, 144)

It would seem that in many instances, as community and social ties have fallen prey to increasing fragmentation, urbanization, cost-control measures and globalization, it is the structures and institutions of medicine that have gained power, sometimes to a point where they overtake all individual will, whether that of patient or clinician. Health and pharmaceutical policies such as reference pricing exacerbate this trend towards institutionalization and depersonalization, adding to the problem of prescribing the right drug for the patient. These institutionally-defined parameters not only place the patient under an obligation to accept help, as Parsons described, but go even further by describing the nature of the "deviance", giving it meaning and legitimacy. Ultimately, when medical decision making is at a distance from the patient, our perceptions of health
and illness are altered and our concepts of normalcy, distorted – even as potentially harmful results and iatrogenesis may result.

**iatrogenesis** and Error

Clinical iatrogenesis, or medical error, has been the subject of much discussion and study in recent years and is said to consist of both errors of commission and omission which result in harm to patients. These range from the ordinary and statistically expected (e.g., surgical complications or problems with anaesthesia), to missteps and mistakes, such as being prescribed the wrong dose or type of medication, and rare occurrences such as having a life-threatening reaction to the contrast dyes used in CT scans. All medical investigations and treatments carry some risk and patients rarely fully comprehend the consequences of many procedures. Surgery, for example, is often seen as a solution to pain or dysfunction, a means of eliminating whatever is “causing” the problem. Yet many surgeries, back surgery for instance, can result in excessive fibrosis (scar tissue build-up) at the site, which can become problematic and result in dysfunction. In general, the more complicated the intervention, the higher the likelihood of hazard, be it at an individual, institutional or policy level.

Policies and cost-cutting measures create their share of problems as well, and it is inevitable that someone, at some point, will sue a Ministry of Health for harm done as a result of a drug or other therapy being withheld in order to control cost.
Estimates of medical error in Canada are said to range from 16.6% of all admissions to hospital, of which 51% were considered "preventable", to 18% or more, according to the National Steering Committee on Patient Safety in their 2002 Report, *Building a Safer System: A National Integrated Strategy for Improving Patient Safety in Canadian Health Care*. The Committee also cited the dramatic figures from the much-quoted US Institute of Medicine Report, *To Err is Human*, which maintained that between 44,000 and 98,000 Americans die each year as a result of medical errors (Wade et al., 2002, 1). The US data implied that "more Americans are killed every six months than died in the entire Vietnam War", with some observers comparing "the alleged rate to three fully loaded jumbo jets crashing every other day" (Hayward & Hofer, 2001, 415). The hyperbole and emotive language notwithstanding (there are, by definition, hazards and risks associated with any illness or intervention; even the simplest of surgeries has risks; drugs have adverse effects), the fact that people can be hurt by a medical intervention is not new. What has drastically changed, however, is the availability and amount of technology and its rationale, not to mention the lengths to which it can presently be taken therapeutically, diagnostically and even administratively.

At times the disconnect between expert/researcher and patient/clinician takes on a surreal quality. Take, for example, a group of researchers comparing Alberta’s rates of cardiac catheterization (an invasive diagnostic procedure to “measure” the extent of damage in cardiac disease) to that of the United States who concluded that Alberta’s rates

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iatrogenesis, from the Greek *iatros*, or physician, plus genesis, originating in, refers to disease or dysfunction caused by medical examination or treatment. The term usually refers to errors of commission although many
were “suboptimal” (Graham et al., 2005, 35). What these competitive researchers failed to mention was the risk, pain and time involved, the resources needed and the sheer ambiguity of the test’s benefits. Critics charged that the higher rates of catheterization in the US have led to “a 2- to 3-fold increase” in surgery (with its attendant risks), with little evidence of benefit (Natarajan, Gafni, & Yusuf, 2005, 50). (This of course stands to reason, since the more you look for so-called “abnormalities”, the more likely you are to find them.) They added that these tests are often over-used in American (insured) patients “for whom the trade-off between relative benefits and harms” may be “marginal” and that harms far outweigh the possible benefit. Furthermore, not only is catheterization difficult (the procedure is done under anaesthetic) and painful, but common risks include “life-threatening bleeds” as well as any other risks the anaesthetic might entail (50) (my emphasis).

Would patients opt for this test were the potential dangers appropriately communicated? Would anybody even need to consider the expense (or have to go to the time, bother and expense of creating cost-cutting guidelines) if patients were actively involved and consulted? Patients, as we saw earlier, tend to be conservative and hesitant of extreme treatments. It is not, then, patient enthusiasms driving the procurement and expanding use of the vast majority of painful, risky technologies such as catheterization and colonoscopy. On the contrary, it is everything from research, such as this Alberta

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100 Colon cancer – and “early” detection through a painful colonoscopy – has had some high-profile media proponents in recent years, yet there is little evidence that the (older, cheaper, easier and flexible) sigmoidoscope (that doesn’t penetrate as high up into the colon) is any less effective (Hadler, 72).
study suggesting our rates are somehow inadequate, to media reports, television
dramatizations of heroic interventions in acute care (where little ever goes wrong) and
celebrity endorsements (for colonoscopies, e.g.), as well as the overwhelming attention
paid to, and our cultural reverence for, fancy, high-tech interventions. As Mechanic
writes:

In cultures that promote activism, individuals have much difficulty doing
nothing when told they may have a potentially deadly disease [such as
cardiac disease]. Thus, patients and their doctors move along a trajectory
of interventions despite the absence of evidence that intervention is
worthwhile. . . . We typically focus on the new, exciting and expensive
technologies, but most of the encounters in medical care systems are more
or less routine depending on small-scale technologies such as laboratory
tests [and] . . . the use of simple surgical interventions and drugs....
(Mechanic, 2002, 464)

Mechanic illustrates the point by relating that his 97-year-old mother’s “able neurologist”
wanted a CT scan to check for “early (sic) intervention of Parkinson’s Disease”, which
would make zero difference to her care but was an automatic response and “a desire for
information interesting to know even if it will not affect care” (464) (my emphasis).

**Social and Cultural Iatrogenesis**

From a more general perspective, the ascendency of labelling as medical what had
formerly been considered a life or social problem results in a type of thinking that Illich
called “social iatrogenesis”. This, as Kenny only semi-ironically writes, is clearly
demonstrated in psychiatry:
... where ... all of the seven deadly sins in the Christian vocabulary – the moral failings of pride, covetousness, lust, anger, envy, gluttony and sloth – now have a diagnosis .... Medicalization has occurred both for deviant behavior – madness, alcoholism, hyperactivity, eating disorders, child abuse – and for natural life processes – sexuality, childbirth, child development, menstrual problems, aging and death. (Kenny, 89)

The result is not only a discourse which revolves around “medicalese” and medicalization but an ever-greater number of seemingly healthy people becoming candidates for medical intervention of one kind or another:

Numbers-created diseases like high blood pressure, high cholesterol levels, sensory integration disorder and fat density ratios keep changing their statistical definitions. The reason for this is that causal connection rather than only statistical correlation is lacking and treatment of these statistical diseases does not appreciably influence outcome. More and more people keep being pushed into these disease categories as a result. (Clements, 2002)

Clements, an ethicist and physician, cites attention-deficit and hyperactivity (ADHD) disorder, baldness, shyness, post-traumatic stress and grief as areas pulled into the medical matrix as well as normal developmental stages such as menopause and ageing.

Unfortunately, such designations have consequences. When we are called “ill” and told we need help, as Parsons pointed out, our entire identity and sense of self undergoes a swift transformation. A label might, of course, seem like a minor price to pay for life-extending care, such as emergency bypass surgery or dialysis, but what of those ambiguous problems such as high cholesterol or slightly elevated PSA levels which may

\[101\] A good question for patients to learn to ask is, “How will this affect the clinical picture?” Merely knowing the precise location of a damaged organ often has no impact on treatment. And is risky.
or may not mean anything? Such cases may lead to permanent and life-altering consequences: Hadler writes that even if concerns with respect to the medical necessity of cholesterol-lowering drugs turn out to be unfounded, it has been known “for twenty years that many people feel stigmatized once they are diagnosed as hypercholesterolemic” or having high cholesterol (Hadler, 42). Having a health problem makes one vulnerable, vaguely “abnormal”, which, in a society that values health, vigour and accomplishment, could easily result in one “disappearing” or being banished from “the ranks of the well forever” (42). Terms like “disabled” or even “sick”, as the late sociologist Irving Zola demonstrated, create extreme personal and psychological difficulties when used as nouns; they affect social roles and psychological health (Hardey, 40). So, if illness or disability is culturally presupposed to be wrong or abnormal in some way, as it so often is, how can a person who is ill or disabled consider themselves in any meaningful or positive light?

Only rarely do we hear of those early, painful, adaptive stages of illness, particularly onerous soon after diagnosis. Adapting to Parkinson’s or diabetes, asthma, heart disease or cancer is a huge adjustment personally, socially, financially and otherwise. In a study of recently diagnosed patients with heart failure – admittedly a potentially serious condition (which most chronic conditions ultimately are) afflicting three to five million people a year in the United States – researchers noted that it was not “objective circumstances” which had the strongest impact on “our evaluations of life events but our perceptions of those events” (Stull, Starling, Haas, & Young, 1999, 285). In other words, the label could be as or more debilitating than the condition itself, and
patients and families need information, counseling, education and support in order to adapt. Yet a British qualitative study of the same condition noted that many patients felt their needs for information and communication were not being met (Rogers et al., 2000, 607). Patient needs for information may seem irrelevant in our evidence-based, technology-dominant model of medicine, but patient perceptions have profound personal, social, cultural, economic, medical and life consequences.

Illich referred to this last category of consequence as “cultural iatrogenesis” and blamed it for the “destruction of traditional ways of dealing with and making sense of death, pain, and sickness” ((Illich, 1976, cited in Smith, 2002). We often mock Hollywood’s obsession with appearance, cosmetic surgery or “extreme makeovers”, but rarely appreciate the extent to which this creeping, cultural, celebrity-endorsed medicalization affects us all – along with our values and notions of normalcy.102 Generally speaking the process is cleverly camouflaged, in part because the process has been slow and, writes Kenny, masked as a natural outflow from the progress of science and technology. Medical, genetic, surgical and pharmacologic advances are perceived as advances to help those in need, the result of “important altruistic and benevolent goals” such as the relief of suffering (Kenny, 89).103 But this belief frequently obscures the cultural indifference we demonstrate, politically, culturally, institutionally, towards the more prosaic aspects of ill-health, from mental health problems in the prison population...

102 As evinced by our ho-hum attitude to such things as breast enlargements or other cosmetic surgeries handed out as prizes in contests or clubs.
103 Yet millions of people die of malaria, AIDS and TB while we investigate ways of enhancing sexual satisfaction or come up with better ways to get rid of wrinkles.
Ageing – A Double-edged Sword

Ageing has come under great medical and pharmaceutical scrutiny in recent years. Journal articles and advertisements target the perceived deficiencies of the old as companies have become aware of the huge marketing potential this demographic represents. Yet even as we over-focus on the perceived problems of age, from hormone and cardiac deficiencies to cognitive or mobility problems, many of the fundamental problems are sidestepped or ignored outright. It is therefore important to make the distinction between the medicalization of old age and the mistaken idea that simply because old age is natural “the diseases that accompany it are also natural and should be excluded from medical attention” (Ebrahim, 2002, 862). If a condition or illness were merely due to ageing it would be universal and common in people of all cultures and races. Currently nothing fits that description, barring a slight deterioration of bone mass (and even that is being questioned) and some ocular degeneration (Mulley, 1997, 1161). Even hearing loss, which people in developed countries consider a normal part of the ageing process tends to be due to exposure to noises our species has not evolved to tolerate, be it the high-pitched sounds of jet engines, the blare of leaf blowers or long exposure to loud music through headphones.
At present the primary attitude of medical professionals with respect to age is often to focus on bodily functions (or dysfunctions), betraying "a narrow but safe biological bias" (Horton, 1997, 1156), with little appreciation of the diversity of the population in question. Horton quotes John Kenneth Galbraith at age eighty-five:

Our scheduled physical and probable mental decline must be accepted. What is less necessary is that we be reminded of it every day. "Are you still walking?" "Still writing, I see." "Are you still interested in politics?" "Still enjoying life?" "I see that you still read the medical journals." This is the omnipresent still syndrome. Alas, that so many good scholars should have failed to identify and condemn it. (Galbraith, 1994, cited in Horton, 1997, 1156)

In medical parlance, ageing is of course not a disease per se but tends to fall under the vague phrase "at risk", a term connected to our liking for risk factors and the phraseology of insurance. For, as we age, we are more prone to cancer, Parkinson's or Alzheimer's Disease, diabetes, heart disease, bone fractures and so on. Age is therefore another "risk factor", much as weight and cholesterol are for cardiac disease. As American geriatrician (a rare breed of doctor in North America) Jason Karlawish relates in an award-winning essay for The Lancet:

At a recent national geriatrics meeting, a youthful physician gave a talk entitled: "Successful clinical components in managed care for the frail elderly". The speaker showed slides of pathways and networks, and spoke of relative risks and odds ratios. Disease management. At question time, an elderly physician stepped forward ... and announced, "This isn't medicine ... This is economics." ... As physicians, the meaning of what we do no longer comes from a common understanding of a "natural order" and a language that separates "disease" from "health". Instead we are fast learning a new language, the language of risk. Our patients are not patients because they have disease, but because they are "at risk". (Karlawish, 1997, 1833)
The comment about economics is apt; many attitudes around the medicalizing of old age and other transitions can be considered an elaborate subterfuge to reduce costs, even though it many ultimately have the opposite effect (along with many negative social consequences). As British professor of clinical epidemiology, Shah Ebrahim, writes:

> In the past decade the problems of elderly people have been “de-medicalised” by the movement of patients from hospitals into nursing homes, where their health care has been substituted by social care. The warehousing of frail elderly people in nursing homes is the result of medical disinterest and political ideology and has led to a social model of care in which medicine is denied a role ... Concerns about the medicalisation of old age may hide a desire to reduce costs. (Ebrahim, 2002, 862)

Nevertheless, whether the elderly are categorized as “at risk” or shunted onto social programs ill-equipped to handle them, how we perceive age has changed dramatically in recent years. As Karlawish explains:

> Compare textbooks of today with those of 30 years ago. There is dementia, systolic hypertension of the elderly, osteoporosis, and the latest disease – the loss of lean body mass called sarcopenia. The remark made by a senior cell biologist at a US National Institute on Aging meeting best expresses this change: “Once I thought I understood the distinction between ageing and disease. Now I plainly confess I no longer do”. In sum, the elderly are a major public health concern because, despite all the talk of “natural ageing”, ageing has become a disease. (Karlawish, 1833)

A disease, furthermore, in which medicine is only desultorily interested, and then primarily as a collection of symptoms. In North America, in particular, age does not merit any special attention. Although there are more geriatricians than there were a decade
ago, this part of the world generally undervalues clinicians who specialize in the problems of the elderly, particularly when compared to countries like Great Britain:

While the British spend much less on health care than do Americans ... their allocation of what they do have emphasizes to a much greater extent this “caring” as opposed to “therapy”. Britain is generally recognized to be ten to fifteen years ahead of Canada and the United States in geriatric medicine. The British medical system may not provide old people with high tech treatments, but it will give them a geriatrics specialist and possibly even a psychogeriatrician. When Dr. Thomas Pickering wrote to the BMJ pointing out there were as many psychogeriatricians in Britain as there were cardiologists — a mistaken priority in his opinion, since he felt cardiologists could do more medically... — a spate of responses followed, nearly all of them suggesting that life in America had corrupted his priorities.  

A geriatrician who is, himself, in the throes of dealing with an infirm, ageing father, writes, with much cynicism and sadness, that not only is geriatric care “time-consuming, excruciatingly detail-oriented professional piecework”, but it is not “sexy” when one can opt for a career “lasering the grunge out of blocked arteries”, “suck out the fat, prop up the sags, botox the wrinkles” or even “snap in new knees or hips” (Winakur, 2005, 1068).

There are nevertheless good ethical and excellent medical reasons for appropriate diagnosis and timely treatment of older individuals – not merely in terms of the elderly being treated as well as any other patient group but in terms of recognizing that older persons have special and specific problems with medicalization, e.g., over-prescribing,

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104 The last time I wrote an article on geriatrics, which was about six years ago, BC had five geriatricians.
105 Britain opts for care versus cure in many instances. Stroke rehabilitation, for instance, is much better organized and delivered much more competently with home care nurses, dieticians, occupational therapists and physiotherapists dispatched to the home. I am unaware of any studies comparing long-term survival and functionality between the two regions, but my guess would be that even if there are not massive differences in quantity, quality of life is greatly enhanced.
infection as a result of excessive hospitalization, the inappropriate use of tranquillizers as a means of restraint and other such hazards (Ebrahim, 862). Elderly patients are disproportionately prone to suffer from clinical iatrogenesis and preventable adverse events, in part because of the clinical complexity of their care. A large proportion of the geriatric population experiences “permanent disability or death as a result” of this neglect or prejudice (Thomas & Brennan, 2000, 743). In many ways this is to be expected given the dearth of data on fragile older bodies and a research and social climate that cuts off participants to clinical trials at the age sixty-four – if it doesn’t ignore them altogether (Lee, Alexander, Hammill, Pasquali, & Peterson, 2001). Yet it is the elderly population who is most likely to be prescribed those same drugs being researched, not healthy forty-year-old men.

Additionally, the fragmented care that specialized medicine tends to provide (a nephrologist to treat the kidney, a cardiologist to treat the heart) frequently results in multiple drugs being given to older patients, with the side effects of one being treated by another. The increasing popularity and preponderance of so-called multi-disciplinary “disease management” teams handling specific conditions such as diabetes or heart disease could exacerbate this. Although often little more than a “marketing” or “packaging” device – since managing chronic illness is as old as medicine itself – this means of delivering care has increasingly been taken on by pharmaceutical companies.

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106 There is a somewhat of a similar problem with paediatric medicine – not only are children not included in clinical trials, but their organs, which are still developing, have a very different physiology from adults. For instance children are more vascular than adults so topical medicines will enter the bloodstream faster. At the other end, older patients metabolize drugs more slowly so “normal” dosage can become toxic or lethal. Psychiatrists, for
looking to expand. The danger is that such programs may undermine primary care and the individual attention patients need (Bodenheimer, 1999, 1203).

Such “carving out” of disease management inevitably puts guidelines ahead of ethics and generalities ahead of personal care, creating enormous potential for the over-use of pharmaceuticals. Indeed, a recent US retrospective cohort study of 765,423 patient records from patients over sixty-five expressed concern for the “common use of potentially inappropriate drugs” (Curtis et al., 2004, 1621). The authors noted that although elderly persons were likely to have co-morbidities and concurrent medical problems, problems of drug interactions and drug safety were not addressed and that the “evidence base” for prescribing for the elderly was “weak” (1621).

Although the way we treat old age (or the possible dysfunction or disability associated with age) can be a “powerful marker of the health of a society” and “should not be stigmatized as a waste, a burden on society” (van Weel & Michels, 1997, 1159), it is also important to stress that the “elderly” are not a homogeneous group but are different and idiosyncratic individuals:

From a physiological standpoint ageing is best characterised as progressive constriction of each organ system’s capacity to maintain homeostasis in the face of challenge. This gradual decline … begins in the third decade and occurs in each organ system independently of changes in other organ systems and is influenced by diet, environment, and personal habits as well as by genetic factors. From this concept it follows that individuals become more dissimilar as they age, belying any stereotype of age; that an abrupt decline in any system or function is always due to

instance, tell me that lithium toxicity in older bipolar patients is common.
disease rather than "normal ageing"; that "normal ageing" can be attenuated by modification of risk factors such as increased blood pressure ... and that "healthy old age" is not a paradox ... (Resnick & Marcantonio, 1997, 1157) (my emphasis)

In any event, chronological age is a "poor marker of vitality and ability to benefit from treatment" (Ebrahim, 262) and it is not possible to generalize or make predictions based on age – any more than we can predict which gene will lead to illness (except Huntington’s) or which child will grow up to win the Nobel prize. There are, however, (reasonably) effective treatments for cataracts, hearing impairment, angina, osteoarthritis, impotence, depression and other common conditions, including, sometimes, dementia and forgetfulness, which could have a neurologic, metabolic or toxic origins and ought no more be ignored in the elderly than in anyone else. It is, incidentally, a myth that the elderly are a major drain on the system and that their care costs a great deal; it is functional status (how well one feels and is able to cope with life) that predicts costs to the health care system (Pollicino & Saltman, 2000).

Disease Mongering or Useful Classification?

What of those ephemeral "lifestyle" conditions discussed earlier? Are these newer disease classifications genuine or are pharmaceutical firms (and others) engaged in Illich’s "social iatrogenesis"?

107 The ageing of the population is often cited as a scare tactic in Canadian health care; yet currently only some 13% of the Canadian population is sixty-five or over – and by the year 2010 that percentage will have only reached 15% (Economist, 2000). Hardly a terrifying percentage.
Some forms of medicalising ordinary life may now be better described as
disease mongering: widening the boundaries of treatable illness in order to
expand markets for those who sell and deliver treatments. Pharmaceutical
companies are actively involved in sponsoring the definition of diseases
and promoting them to both prescribers and consumers. The social
construction of disease is being replaced by the corporate construction of
disease. (Moynihan et al., 2002, 886)

Many of the illnesses considered under the rubric of social iatrogenesis ("social phobia",
erectile dysfunction, baldness), suggest Moynihan et al., along with some recent
diagnostic categories for which drugs have become available such as osteoporosis and
irritable bowel syndrome (IBS), could be considered drug company “sponsored” diseases
which have entered the medical lexicon without attracting sufficient critical scrutiny:

Within many disease categories informal alliances have emerged,
comprising drug company staff, doctors, and consumer groups. Ostensibly
engaged in raising public awareness about underdiagnosed and
undertreated problems, these alliances tend to promote a view of their
particular condition as widespread, serious, and treatable. Because these
“disease awareness” groups are commonly linked to companies’
marketing strategies, they operate to expand markets for new
pharmaceutical products. Alternative approaches – emphasizing the self
limiting or relatively benign natural history of a problem, or the
importance of personal strategies – are played down or ignored. (886)

Although many patient or advocacy groups and clinicians enter into these alliances with
honourable motives, what few of them appreciate is the limited nature of their own area
of specialization or how it fits in with the larger picture. In theory, government policies
protect us from such professional or corporate enthusiasms, yet groups who set policy are
no more exempt from general socio-cultural beliefs or economic trends than patients or
doctors.
It is, nonetheless, shortsighted to exclusively fault the drug companies and their marketing, although in recent years these have become disturbingly influential. The entire drug regulatory system in industrialized countries consists of a placid collusion involving government, doctors and nurses, patients, medical journals and pharmaceutical companies. Because authorities need detailed information on drugs before they can be approved (on quality, consistency, dose, impurities, stability, colorants, contaminants, additives) and need to know what impact a drug will have on the organism (toxicity, absorption, metabolism, distribution, excretion), drug firms engage in a two-pronged effort, first in-house and then through clinical trials. Early work is done in vitro and in the lab, but research is then commissioned, often through multi-centre trials, with real people. Inevitably, the company developing the product has a dominant role, which it maintains throughout the process, even as it “funds the study, designs the protocol, chooses the investigators, and, in many instances is involved in the collation, interpretation, and reporting of data” (Collier & Iheanacho, 2002, 1406).

Pharmaceutical companies are the single biggest sponsor of medical research and thus the “largest generator” of related information. In some countries, including Canada and the United States, they are the “only realistic source of such support” (Collier & Iheanacho, 1407). Recognizing the enormous influence that journals have – particularly the more prestigious ones such as the New England Journal of Medicine, The Lancet, BMJ, CMAJ or JAMA (which are often also summarized in the media) – creates a massive push to ensure positive results are published and subsequently disseminated. Positive findings are always more likely to see the light of day than neutral or negative
ones, and, since drug companies want their products to be seen in a favourable light (and, naturally, their stock prices to rise), it is “especially helpful” if the article is published around the time the product is launched (1404). Later, some of those same physicians, nurses, and patients who were involved in the pre-marketing trials become involved, often naively, with the drug company’s promotional and marketing efforts, acting as “expert” voices throughout the process. Meanwhile, the media are inundated with information and they, in turn, flood the public with “news” stories on the prevalence and dangers of the “new” (or old, hitherto unidentified or poorly understood) disease and the now-available therapy.

Over time, often with grants and other support from drug companies, conferences and consensus panels are convened, delineating the condition (e.g., osteoporosis) and creating guidelines as to what should be done about it. Toronto researchers have found that there is “considerable interaction” between drug companies and authors of clinical practice guidelines and that, on average, the major interaction consists of financial support from the drug companies for their efforts (Choudhry et al., 2002, 612). Rarely is this appropriately disclosed, even in medical journals (in any event, few people read the “competing interests” section following a long series of recommendations preceded by hundreds of references). From this ostensibly objective process there evolves a complicity of sorts, whether conscious or unconscious, of various interested parties – however much each group may be convinced of their own benevolent motives:

Patients and their professional advocacy groups can gain moral and financial benefit …. Doctors, particularly some specialists, may welcome the boost to status, influence and income that comes when new territory is
defined as medical… [and] companies manufacturing mammography equipment or tests for prostate specific antigen (among others) can grow rich on the medicalization of risk. Many journalists and editors still delight in mindless medical formulas, where fear mongering about the latest killer disease is accompanied by news of the latest wonder drug. Governments may even welcome some of society's problems – within, for example, criminal justice – being redefined as medical, with the possibility of new solutions [and the chance of shunting some of the costs away from their own departments and onto another]. (Moynihan & Smith, 2002, 859)

But this may not necessarily be an appropriate or realistic appraisal of what the risk of a particular medical disorder or condition might be.

This widening of the inclusion criteria creates additional social, medical and personal problems. As Parsons noted, institutionalized social control can result in the unnecessary labelling of individuals and iatrogenic consequences as well as increased cost. Resources may be diverted from other, perhaps more or equally serious problems which are simply not, at that time, in the limelight. Easy generalizations, glib statements and vague assertions on various diseases and conditions become blurred into “fact” through repetition and authoritative statements. Where a peer-reviewed journal might conclude that the evidence suggests drug X might be beneficial in treating condition Y under certain circumstances, this can become a statement of fact in a newspaper or non-profit organization brochure. As more people then come to believe they must be tested – and treated – for high cholesterol or impending osteoporosis or colon cancer, medical system usage and the amounts spent on drugs and technology will increase as will burgeoning anxieties around the inadequacies of health care. For example, if “one in nine” women will get breast cancer, as we are so often told, then access to mammography becomes as pressing a problem in most people's minds as basic research
into the causes and nature of tumour growth or broader questions of why (or whether) breast cancer has become so prevalent to begin with.\textsuperscript{108}

From a communications perspective these information strategies (or what some might call propaganda) are skilful and subtle, as “groups and/or campaigns are orchestrated, funded, and facilitated by corporate interests, often via their public relations and marketing infrastructure” (Moynihan, Heath & Henry, 886). The process draws in and on mainstream media as well as professional and lay groups, starting with minor noise, an advertisement or two, the odd article placed in a newspaper, magazine or television program and gradually building up to a crescendo that eventually descends into the buzz of “common” knowledge. Eventually, these half-truths become accepted as known statistical truths, repeated so often that they exist, hermetically sealed off from discussion, as unquestioned statements. Statements such as “one in four” women past menopause has osteoporosis or “cholesterol causes heart disease” have become so prevalent that they are widely quoted – and accepted – without reference. Take the case of osteoporosis, which went from being a little-understood, rarely diagnosed disorder to being perceived as an ubiquitous, overriding problem.

**How osteoporosis became famous**

Osteoporosis is authoritatively said to take “its toll” on women over fifty.\textsuperscript{109}

According to an article in *The New England Journal of Medicine*, this group has a “40

\textsuperscript{108} In fact a woman has a *lifetime* risk of one in nine for breast cancer, which is not at all the same thing. A younger woman’s risk of breast cancer – in the absence of a family history – is miniscule.
percent lifetime risk of an osteoporotic fracture” (Strewler, 2004, 1172). Translated into normal human terms, this means that four out of ten American women over the age of fifty might have a fracture of the hip, wrist or some other bone at some point during the remainder of their (projected) lives. Strewler’s next sentence, however, is a total non sequitur, should one care to examine it closely:

One woman in three and one man in nine older than 80 years of age will sustain a hip fracture at some point, and 15 to 20 percent of these patients will die from attendant complications. (1172-3) (my emphasis)

Which sounds very impressive, until one is reminded that average life expectancy in the United States is seventy-seven – or, if one is opting for what one medical statistician calls “spurious accuracy”, 76.9 – years (Rifkin, 2004), which would make these eighty-year-olds already somewhat of an actuarial anomaly. In any event, compared to what? Expressing these figures in terms of a probability (or what is called relative risk) makes it difficult to ascertain, particularly since the reference group is unclear.

As health economist Gerd Gigerenzer explains in his illuminating book *Calculated Risks*, it makes far more intuitive sense to think in terms of frequencies rather than probabilities and percentages (Gigerenzer, 2002, 41). If we deconstruct these numbers then, what the frequencies translate into is as follows: Out of 100 American men and women over the age of eighty, forty-four will be at risk of sustaining a hip fracture. Of these forty-four, six to nine could die. Up to seven times that number, thirty-five to

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109 Whereas the data focuses primarily on women over sixty.

110 Suddenly the stakes are thirty years higher and we are talking of people over eighty.
thirty-eight individuals, will be just fine, even after that hypothetical fracture (since only fifteen to twenty per cent are at risk of death). In any event, in this already hardy older group, the majority – well over half or fifty-six men and women – will have no fractures at all. Hardly stop-the-presses headline news.

Furthermore, logic dictates that among the eighty- and ninety-year-olds who end up in hospital for any reason there will be some deaths. Many elderly people are fragile and have multiple conditions and co-morbidities, from arthritis and diabetes to cardiac disease and low-grade cancers. Why should osteoporosis or a hip fracture be any different? But these definite-sounding numeric odds are not only impressive and frightening, they are also the rationale for drug intervention at age fifty (with drugs which became widely available some twelve years ago). Should we be wary when we realize that the article on which Strewler bases his commentary, a research study reported in the same issue of the *NEJM*, is “sponsored by Merck Research Laboratories”, the makers of one of the most widely prescribed osteoporosis drugs on the market (Bone et al., 2004)? It would seem so. It would also seem that those who accuse drug companies of disease mongering have a strong point. The more troubling and subtle implication, however, is that bone density and osteoporosis are neatly and inversely correlated – trivializing the complexity of physiology and implying that our understanding is more advanced than it is. The subtext is also that the risk of bone degeneration is a serious matter, as worthy of consideration and health care resources as other disorders, and that bone density scans and pharmacologic intervention are the only medically sensible solution. Reading the

111 Private communication, medical statistician Jonathon Berkowitz, March 1998.
numbers cited above at face value, most readers, whether doctors or patients, would likely agree.

Brian Lentle, a radiologist at Vancouver General Hospital, puts osteoporosis in perspective in a *CMAJ* editorial and writes that both men and women after the age of thirty “lose bone at a rate of approximately 0.5 to 1% yearly” (Lentle, 1998, 1261). There is “considerable individual variation” (an important and often glossed over point) and, by and large, this loss is not problematic unless it results in “fragility fractures”, a broken bone in other words, often after a fairly minor fall or trauma. The WHO defined, “for epidemiological purposes”, normal bone density as within one standard deviation from the “young adult reference mean” (in other words, old bones are compared to young ones and found wanting) and low bone mass or osteopenia as more than one standard deviation below. Anything above 2.5 is classified as osteoporosis. Unfortunately, “these definitions have often come to be used as intervention thresholds, a purpose for which they were never intended” (1262) (my emphasis). Lentle suggests that “osteoporosis and bone measurements have each become a focus for different world views”:

It could be argued that osteoporosis is simply part of aging and that treating it amounts to “medicalizing” the menopause. Others are afraid that bone measurements will cause undue concern in people found to have low bone mass. Such people may paradoxically avoid exercise for fear of fracture. Another perspective is the impending time, when, because of changing demographics, far too many hospital beds will be occupied by people undergoing surgery for osteoporotic fractures unless preventive measures are taken. (1261)

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112 The WHO meeting which defined “the bone density of young white women” as the standard against which older women of all ethnicities should be compared was also funded in part by drug company money according to the BC Office of Health Technology Assessment (Moynihan, 889).
Whatever the worldview, using a surrogate end point such as a bone density measurement as a stand-in for fracture risk requires compelling proof, and the use of densitometry, or bone density scanning, is controversial. In Alberta the health technology assessment office has spoken out against the practice and their counterpart in BC has recommended that it not be used in “well women” (Lentle, 1261). In the past, bone density has not been found to make a difference to fractures, which are of course known to be risky. In earlier years, sodium fluoride was the drug in question for osteoporosis, except, as Bucher and colleagues at the Evidence-based Medicine Working Group at McMaster write in JAMA:

Although sodium fluoride was found to increase bone mineral density at the lumbar spine by 35% over 5 years more vertebral and nonvertebral fractures occurred in the intervention group than in the placebo group (163 and 72 in 101 women with sodium fluoride vs 136 and 24 in 101 women with placebo). … Inferences on the basis of unchanged bone density may also be problematic. A study of calcium and vitamin D in the elderly showed virtually no change in bone density, but a reduction in the fracture risk of approximately 50% (Bucher et al., 1999, 773)

But non-drug or simple dietary interventions such as taking calcium and vitamin D rarely command the same attention (or money and research) as pharmaceutical interventions, no matter how much individual clinicians may counsel their patients on diet and exercise.

The extent to which the drug companies are culpable in exaggerating the dangers of osteoporosis became a newsworthy item in Australia, when the organizers of “healthy bones week” came under fire for making “exaggerated and misleading claims”, as was reported in the news segment of the BMJ on-line:
The false claim that more women die from osteoporosis than cancer was a distortion of another “fact” being promoted by Osteoporosis Australia, co-sponsor of healthy bones week with Dairy Australia, that mortality in women from hip fracture “was greater than the incidence of all female cancers combined”. According to Dr. Donohoe [a government advisor on false claims who described the claim as “patent rubbish” and “a bare-faced lie”] this is a meaningless statement because it compares the death rate in a particular group of women (older ones) who are at higher risk anyway … Professor David Henry, from the University of Newcastle, New South Wales, said it is like comparing apples and donkeys. (Moynihan, 2003)

But comparing apples and donkeys is what we increasingly do with medical statistics. And while it is true that our misconceptions are ably encouraged by the pharmaceutical industry, it is also clear that as a society we are all too eager to believe in the numbers, the power of technology (fancy machines that test bone mineral density), the idea of being active, proactive, and engaging in prevention. Moreover, unlike baldness or sexual dysfunction or even “social phobia” which one can reasonably trust most people do appreciate are more of a want than a genuine medical need, osteoporosis is ethically complex, being inexorably allied metaphorically with “weak” bones and breakage. Whether this is the result of clever marketing and media hype or general naivety is irrelevant to some degree since these ideas have not only had an impact on the lay public but on professionals and governments (Moynihan, 889).

Expert, serious, weighty advice has resulted from these perceptions on osteoporosis, such as the 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. Much in the same way as guidelines on

111 Military metaphors abound in medicine where “weak” is usually synonymous with “bad”. Yet with the immune system, for instance, too strong can equal auto-immune disease.
hormones for post-menopausal women stressed cardiovascular health as the primary
reason for taking hormones, at least prior to the Women’s Health Initiative study, these
guidelines focus throughout the first twenty-two pages on drug interventions. Then, in the
last three pages – just prior to the references, a section few people will read – brief
mention is made of calcium and vitamin D intake, the importance of developmental
factors and exercise and diet. (Brown & Josse, 2002, S22) Yet clinicians rarely absorb
“multipage publications” produced by organizations or national groups, as an analysis of
hypertension guidelines noted, and, in fact, the longer and more involved the guidelines,
the less likely they are to be read or followed (McAlister, Campbell, Zarnke, Levine, &
Graham, 2001, 519). In any event, in terms of osteoporosis, if conclusions are truly to be
based on the evidence, the best intervention would be to ensure that young people get
enough calcium in their diet and get enough exercise. As Anna Day of the Departments
of Medicine and Health Policy in Toronto writes in an editorial comment in the CMAJ:

The results of the WHI [Women’s Health Initiative on hormones at
menopause] should make us evaluate whether we are targeting and
funding primary prevention efforts appropriately. If the risks of hormone
replacement outweigh the benefits, what are the options for women who
hope to avoid the fractures associated with osteoporosis? Recent studies
demonstrate that the risk of osteoporosis is related to the peak bone mass
achieved in the teens and twenties. Primary prevention of osteoporosis
could therefore consist of ensuring that teenagers and young adults
maximize their bone mass with appropriate exercise and diet. (Day, 2002,
361)

Yet generally our attention remains focused on how many bone scan machines we need
and can afford and whether or not government or insurance will reimburse us for the
procedure or the drugs – as our popular culture and media reflect and encourage our fascination with technology and drugs.

**The Truth According to TV**

Physiology and its complex workings (whether diseased or healthy) tends not to be fun or sexy. It is far more exciting and dramatic to look for ways to “correct” one’s genetic structure or find some terrific new miracle drug or technology, particularly when so many headlines suggest these are just around the corner. Few people appreciate the extent to which newspapers and other media exaggerate, under- or over-report medical news and emphasize the sensational and experimental. Most medical news is disease-oriented and this results in people often overestimating the dangers of less-common conditions. A British longitudinal study on newspaper reporting of 1193 medical studies found that bad news was more likely to be highlighted, particularly on women’s health, reproduction, and cancer (Bartlett, Sterne & Egger, 2002, 81). Media coverage of medical and health information has also been criticized for:

- attributing too much certainty to research findings, for premature representation of findings as breakthroughs, and for being alarmist, incomplete, or inaccurate. [Also]: journalists seek health stories that will seize readers’ attention and ... tend to present issues using straightforward, stereotyped themes, sometimes contradicting early reports about the same issue (81).

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114 There seems little understanding that “genes” reflect not only our original chromosomal “programming” but that there is ongoing cellular regeneration and death which the environment – what we eat, breathe, experience – affects.
Headlines seem to be designed to grab attention (for example, the ever-shifting news with respect to coffee or other common foods or beverages “causing” cancer). The researchers also found that “randomized trials were substantially less likely to be covered in newspapers than observational studies” and that papers had a ghoulish preference for bad news:

Thus, newspapers reported the finding that the risk of acute myeloid leukaemia is increased in cockpit crews and that childhood acute lymphoblastic leukaemia is linked to a chromosome translocation event in utero, whereas they ignored a reassuring study that failed to show an association between exposure to ultrasound during pregnancy and lymphatic or myeloid childhood leukaemia…. We are concerned that many aspects of medical research are not well represented in newspapers. (83-4)

But newspapers reflect the society they are in – as do other media. For example, while a Canadian study found that survival rates for adult in-patients following cardiac or respiratory arrest had not “changed markedly in 40 years” and that of 247 heart attacks (and subsequent cardiopulmonary resuscitation or CPR) only twenty-eight people left hospital (with a fair number, 15.2%, experiencing a “significant enough decrease in function ... that they were no longer deemed able to fully care for themselves”), television dramas beg to differ (Brindley, Markland, Mayers, & Kutsogiannis, 2002, 345). Network hospital dramas (ER, Chicago Hope, and Rescue 911) depict “exciting” cases of CPR often performed on young victims of violence and often zero in on “amazing, often miraculous” rescues (Baer, 1996, 1604). Whereas in real life CPR is most often
performed on elderly patients with cardiac disease, on television shows nearly two-thirds (65%) of patients are teenagers, children, or young adults, with some 75% walking away unscathed (1604). Is it any wonder our expectations of medicine are warped?

There do seem to be some slight cultural differences. An observational study of British medical dramas, reported in the *BMJ*, found that “although the reasons for resuscitation are more varied and more often associated with trauma than in reality”, the overall success rate was “nevertheless realistic” (Gordon, Williamson, & Lawler, 1998, 780). Still, the British observers of television dramas did point out:

The context within which issues around resuscitation are shown on television will affect how the viewer perceives the event .... The average television viewer is exposed to a wide variety of television medical images, of which the programmes under study here are but a small part. News programmes, documentaries, other dramas and films all frequently portray cardiopulmonary resuscitation, and may have an equivalent or greater influence than the dramas we have studied. Indeed, the American series *Baywatch* is one of the most widely watched television programmes in the world, and, we are told, frequently features resuscitation, which is nearly always successful. (782)

Resuscitation is only the tip of the iceberg. Even a cursory glance at ostensibly sophisticated programs such as PBS’s *Nova* demonstrate the extent to which the “magic” of medicine and the allure of technology supersede the more pedestrian and messy human aspects of medicine. From post-surgical disability to medication side effects, or any other lingering after-effects of tinkering with bodies whose physiology does not correspond to

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115 Years ago Dr. David Suzuki was quoted as saying that 100% of newspaper accounts of medical and scientific news were wrong. At the time I thought he was exaggerating.
our fast-food, 24/7 ideas of what constitutes a “reasonable” time frame for healing, it is not the messy consequences of illness that capture our attention but the dramatic and extraordinary. Newspaper coverage of new drugs in Canada rarely provides information on potential harms or side effects (Cassels et al., 2003, 1133), and, in general, the cumulative effect of media reports propel us towards the magic of medicine, not its prosaic realities. Unfortunately, believing in magic, as the late media critic and writer Neil Postman wrote in Technopoly: The Surrender of Culture to Technology, is problematic insofar as our attention is misdirected to the “what” rather than the “why” and, during that process, “evokes wonder rather than understanding” (Postman, 1993, 94). This has serious social (and financial) consequences, for when our social narratives become over-involved with medical technologies, and the tools and strategies of medicine are held in greater thrall than even our own subjective experiences of illness and recovery, we “become blind to the ideological meaning of our technologies” (94). As a result we construe our world in ways which run parallel, or even counter, to what our senses, minds and values tell us and do not intersect with the reality of illness.

This disconnect is no mere abstraction; it has important personal and socio-cultural consequences and is implicated in our worries on health care. Yet we rarely seem to understand that culture is one of the major determinants of how medicine is practiced. As Postman explains:

Although the US and England have equivalent life-expectancy rates, American doctors perform six times as many cardiac bypass operations per capita as English doctors do. American doctors perform more diagnostic tests than doctors do in France, Germany, or England. An American woman has two to three times the chance of having a
hysterectomy as her counterpart in Europe; 60 percent of the hysterectomies performed in America are done on women under the age of forty-four. American doctors do more prostate surgery per capita than do doctors anywhere in Europe and the United States leads the industrialized world in the rate of cesarean-section operations – 50 to 200 percent higher than in most countries. When American doctors decide to forgo surgery in favor of treatment by drugs they give higher dosages than doctors elsewhere. They prescribe about twice as many antibiotics as do doctors in the United Kingdom and commonly prescribe antibiotics when bacteria are likely to be present, whereas European doctors tend to prescribe antibiotics only if they know that the infection is caused by bacteria and is serious. (Postman, 94)

This American “cowboy” mentality has honest, historical roots. As the ironic Oliver Wendell Holmes – who had spent time in England – rhetorically asked:

How could a people which has a revolution once in four years, which has contrived the Bowie knife and the revolver … which insists in sending out yachts and horses and boys to outslay, outrun, outfight and checkmate all the rest of creation; how could such a people be content with any but “heroic” practice?¹⁶ (Payer, 1996, 127)

From the outset, American life and, by extension, its medicine and medical research have been in thrall to the idea of progress (and American exceptionalism), driven by a fundamental belief that technology and quantification is inherently superior to human abilities. This reduces or eliminates the need for “intellectual struggle”, wrote Postman, since machines (and numbers) appear to dispel “complexity, doubt and ambiguity” (93). Quantification has the added bonus of standardizing our perceptions and

¹⁶ Dr. Benjamin Rush, one of the signers of the Declaration of Independence, believed that “one of the hindrances to the development of medicine had been an ‘undue reliance upon the powers of nature in curing disease’, a thesis he blamed on Hippocrates”. Rush further believed that American diseases, like the American people, were meaner and tougher than their European counterparts (Payer, 128).
simplifying complex phenomena and allowing us to make tables, plot graphs and otherwise create visually and intellectually pleasing shortcuts.

Canada does not share the same history and culture as the United States, but we have admired and emulated the best of American culture, or so we believe. So, perhaps for us the more appropriate question ought to be whether we should follow the tactics of American medicine or make a concerted effort to determine what medicine and health care mean to us as a society and culture – not only as a delivery model but as a practice. Perhaps, as Romanow, Rifkin and others have suggested, we should ponder more on our similarities to Europeans. What does seem clear is that if present trends continue, medical care will increasingly become more technology-driven and systems- or guidelines-oriented, active (even intrusive) and, by extension, expensive (Postman, 95).

Disease, ill-health, pain and distress do not correspond well to numbers however much we may wish them to. Although it is may be necessary to set some parameters and guidelines, it is also important to acknowledge that medicine involves people, individuals with complicated narratives, specific socio-economic circumstances, geography and culture. An urban professional will have different needs and problems than a rural farm worker; an elderly Chinese-Canadian woman will not have the same issues as a refugee child from Guatemala. Canada is a diverse country with pockets of extreme ill-health in desperate need of good public health (e.g., poorer Aboriginal reserves) and areas of robust good health (such as the well-off residents of Richmond, BC). Rarely is socio-economic background incidental; on the contrary it is vitally allied to health (Hadler, 12). Reductionist policies that do not appreciate the interconnectedness of health with other
social needs are doomed to fail, as are any discussions on health care that do not at least comprehend that biomarkers and risk factors are only the tip of the iceberg and that illness cannot be understood in terms analogous to the faulty function of a flawed machine (Charon, 2004). Tests and screening and high-tech interventions may be able to describe what is common (and therefore inferred to be “normal”), but they are pale reflections of the real world which is diverse, variable and unpredictable. Furthermore, too many medical technologies currently contain disquieting connections to the marketplace – not exactly noted for its ethical bent or capacity for self-analysis.

Given that it is individual people who experience and are affected by illness, there seems no logical reason not to balance out the heavy institutional (corporate, government, etc.) influences with at least a modicum of patient input, be it into the topics of research, guideline formation, health policy or anything else designed to streamline and “improve” medical care – particularly since it is individuals who run the risk of side-effects, over- or under-investigation and iatrogenesis, not groups. Bringing patients into the world of medical research and policy-making would naturally take time, money and effort, but so do randomized clinical trials and the convening of expert committees to draft consensus reports and guidelines. What it would require, however, is an understanding and appreciation that patients have something to offer – and a major shift in paradigm and perspective.
Some Patient Perspectives

A study in the north of England (Newcastle) which involved “patient-consumers” in guideline development found there to be “good reasons for taking consumer involvement seriously”, not the least of which was for professionals and experts to understand the vagaries of clinical care and its effects on patients.117 The researchers used workshops and one-on-one meetings with patients and incorporated a patient advocate into group guideline development discussions. The researchers found that involving patients was neither onerous nor awkward; they also found it to be illuminating in the extreme, although some cases (the workshop in which the technical elements of qualitative and quantitative drug research were discussed, for instance) were somewhat resource intensive. Patient input was blunt, outspoken and practical. For example, on asthma guidelines:

Patients were often critical about the treatment they had received for their asthma. Some expressed a lack of confidence in clinicians, and there were several examples of patients having received conflicting information from different clinicians. They also felt they were not always listened to, which led to examples of inappropriate clinical decisions. Furthermore patients complained about the lack of adequate information: “people go in and out of the hospital without being told what is happening”; “there is no one to ask questions from”. (van Wersch & Eccles, 2001, 12)

Asking patients their opinion could easily lead to improved communication (so often cited as essential to good care) and better, more comprehensible procedures not only for asthma but any chronic disease. For example, in this research, patients explained

117 Nowhere is the insidious impact of business language and practice on medicine more obvious than in the burgeoning and insidious use of the term “client” or “consumer” for patient.
that they often used an inhaler’s colour as identification (and they all knew exactly when and how to use each one) and were more comfortable using a drug’s brand name (analogous to using the term “Tylenol” rather than “acetaminophen”); but health professionals seemed to feel it necessary to use the “chemical” names of the drugs as reflected in the guidelines, thereby leading to unnecessary confusion (12). This is not something that would seem particularly vital to the experts, but clearly to patients it matters. Generally speaking, patients were most attracted to information on self-management and patient-centred education than in “external” solutions. (Sadly, these also generate the least amount of research.) Interestingly, having patients present did not change the content of these particular guidelines in any major way (15) and what changes there were appear to have been more in tone and perspective than content – probably because these researchers only included guidelines that directly involved clinical care.

Experts express reservations about lay input insofar as it is felt that the public lacks the education and knowledge to assess complex subjects. The public is also said to be too “subjective” (Litva et al., 2002, 1825). Yet even Nature, whose primary interest is in scientific and technological advances and not clinical medicine or how science affects people, conceded in an issue on biotechnology and genetics that those who have been involved in “public participatory events … remark on the (to them) unexpected way” in which individuals are able to comprehend the key aspects of the discourse (Nature, 2000). Involving patients in administrative, bureaucratic or managerial aspects of medicine could well add an important dimension to the discussion at hand, adding nuance and breadth as well as potentially deal with over-use of the system. Consumers make
unique contributions particularly in terms of integrating users’ views with research findings (Oliver, Milne, Bradburn, & Buchanan, 2001, 27) and are often focused on questions of ethics, consent and risk. No matter how well intentioned, merely applying guidelines and evidence is paternalistic. It is important to address patients’ values regarding treatments and possible outcomes as well as involving them in decision making (Edwards, Jacobson, Elwyn, & Mowle, 1999, 151).

Another British study (one can see a pattern forming here) consisting of nineteen interviews growing “out of a collaborative interest in public participation and priority setting” in health planning identified three levels of decision making (Litva et al., 2002, 1827-8) in which patient participation could improve health care delivery:

- At the health system level (location and delivery of services);
- At the program level, the determination of funding (particularly of specialist services);
- At the individual level (who should have access and which patients would most benefit from a particular treatment).

Strikingly, in all these studies there was strong agreement that public consultation added a dose of common sense and was an excellent source of creative problem-solving. The desire for public involvement had to be genuine, however, as many individuals expressed a strong dislike of tokenism:

It is lack of information and lack of honesty about what the intention is … and if you’re going to have the public having input, then it’s got to be accepted and some notice taken of it. It’s not a bit of good having ‘Oh well, we’ll have a meeting and invite the public and then just ignore any of the things they ask for.’ And I think this is what we all get cynical about,
isn’t it? [someone murmurs agreement] No-one really takes any notice ….
(Litva et al., 1831)

Although there were variations as to the extent to which patients stated they might wish to become involved, the general feeling was that public involvement in health care decisions would be positive (versus individual patient care which everyone felt was a doctor-patient matter). Litva and colleagues concluded, as did other authors, that the public has much to contribute, particularly at the system and program level (Litva, 1825). Most medical writers and health professionals who have spent any time talking to patients would agree.

There is often a wide mismatch between the “agenda” of the research community and the research “consumer”. A British study on osteoarthritis of the knee found that the published and unpublished research on interventions was dominated by surgical (238 or 26%) and pharmaceutical (550 or 59%) interventions, whereas patients chose education and advice as their primary choice (Tallon et al., 2000, 2037). This discrepancy was in line with other such studies. The authors concluded that reasons for this disconnect included commercial funding bias, vested researcher interests and a lack of consumer involvement. They also cited publication bias as 94% of studies “provided a positive conclusion” (2040). Patients do not share researcher enthusiasms and often outcomes highlighted in the research literature are of little interest to patients (Edwards, Elwyn, Smith, & Williams, 2000. 152). Patient-participants place a high value on continuity of care and stress that medicine should respect individual patients’ wishes, which they understand must be context-dependent:
Consumers felt that the aim of consultations should not be participation per se, but rather the professional should seek involvement to the level that the consumer desires. Furthermore, consumers were aware that their own desire for involvement would vary from one situation to another. (Edwards et al., 155)

Patients do not place as high a value on numeric and the other “objective” outcomes so prized by researchers and government agencies; rather, they value feeling understood and reassured (157). Most important, patients want accurate, or at least honest, descriptions of risk and negative aspects of treatments and interventions. Far too many clinical trials gloss over adverse effects of treatment or side effects of drugs (Williams & Garner, 9). In short, communicating risks should not only be central but must involve an honest exchange between patients and doctors (Edwards, Elwyn, & Mulley, 2002, 827): “The two way exchange about information and opinion is important if decisions about treatment are to reflect the attitudes to risk of the people who will live with the outcomes” (827) (my emphasis). Conversely, what this also means is that patients need to take on greater responsibility and learn to live with greater uncertainty.

This may lead to “informed dissent” (a somewhat pejorative term), which may in turn produce tensions between what is perceived to be good for populations and what individuals perceive to be good for themselves. We may need to accept that increased involvement of patients (and risk communication as a means towards this) may therefore be based more on values than on evidence. (Edwards, 2003, 691)

Given the weight most researchers place on evidence, tilting funding and attention towards values, communication and individual choice could be a hard pill to swallow. Nobody likes to cede power and authority. This is no doubt why risk evidence rarely
includes psychosocial outcomes, although these matter to patients (Godolphin, 2003, 692).

Ironically, shifting focus away from patients – and towards bigger and better institutional directives that tacitly imitate corporate tactics – has not made a dent in health care expenditures. On the contrary, we do more, spend more and generally feel less satisfied with our access to health care than ever before, even as our discourse and model of health care becomes increasingly abstract, technology-driven and sparse. Perhaps it is time to reexamine our priorities, language and perspectives.

**A Tale of Two Commissions**

In April 2002, then-prime minister Jean Chretien convened the Commission on the Future of Health Care in Canada and asked Roy Romanow, the former Saskatchewan politician, to “engage Canadians in a national dialogue”. Thousands of people turned up over an eighteen-month period “from sea-to-sea” to speak to the Commission (Romanow, 2002). Clearly the interest, the motivation, was there to embark on “the road to renewal” for health care, this “public good” and “national symbol” (xviii). Yet the result of this extensive dialogue, *Building on Values, The Future of Health Care in Canada*, was an uninspired (and uninspiring) document that would not have been out of place at a bank or business school. With language as clichéd and sterile as any corporate financial report, and an obsessive focus on drugs and technologies (with absolutely no realization that the administrative and management changes advocated also constitute technologies), this publication did not bode well for health care, our so-called “national symbol”, and its
renewal. Yet only a scant ten years earlier there still appeared to be some realization that the human and humane aspects of medicine do merit notice – suggesting perhaps that it is not too late to change course.

The 1991 BC Royal Commission Report (*Closer to Home*), for instance, contained moving narratives and evocative language and gave the reader the definite sense that the commissioners’ understanding transcended medicine’s techno-scientific aspects. Compare the 1991 Report with that of 2002 on a single topic, educating the public. The older report stated:

One of the five principles of Canadian health care is that all medically necessary care will be provided without financial barriers. But, as the commission has been told on a number of occasions, for this principle to be upheld, the public must use the health care system responsibly. We agree, and we also believe that the vast majority of people do try to use the system responsibly, and that it is a small group of exceptions who are noticed by practitioners because they are unusual. However, to use the system responsibly and appropriately, the general public must have enough information on which to base their decisions to seek care. (Seaton, 1991, B-112)

Contrast this with the later effort and the section on “Information, Evidence and Ideas” which suggested, as “directions for change”:

Leading-edge information, technology assessment and research are essential foundations for all of the reforms outlined in subsequent chapters of this report ... To take full advantage of the potential of information, evidence and ideas in the health care system, the necessary information infrastructure must be in place. This requires action on three important fronts: putting essential information management and technology systems in place, improving our ability to assess and manage the potential benefits of health care technologies, and expanding our applied research base across the country. (Romanow, 2002, 76)
No longer even acknowledging that there might be human beings to whom that leading-edge technological assessment refers, the 21st century solution would seem to consist of a "personal electronic health record for each Canadian", a "pan-Canadian electronic health record framework built onto provincial systems" that "harmonize" privacy policies and support "health literacy" through an "electronic health information base" to link patients to "properly researched, trustworthy and credible" health information (77).

Even without waxing lyrical about the contrast in writing and focus, the socio-cultural shift is jarringly obvious. This linguistic shift mirrors the political and economic developments of the recent past and is reflected in the science, the evidence and the questions we ask of medicine – as well as the answers we look for. As Fox Keller writes:

> If, as I have been arguing, the ways in which we talk about scientific objects are not simply determined by empirical evidence but rather actively influence the kind of evidence we seek [and hence are more likely to find], we must consider other factors if we are to understand the strength and persistence of the discourse … (Fox, 34)

This dissertation has argued that these “other factors”, and the policies based on them, are neither inevitable or natural, merely hidden in our socio-cultural norms, values and avoidance of uncertainty. To some extent, they operate in a circular fashion, determined by the perspective and purview we bring to the questions and extending to the tone and content of the writing and discourse – and vice versa. Oddly, although we are not oblivious to the many factors, from economic or socio-cultural models to media reports, which shape the ways we perceive our world, we largely seem to have capitulated, accepting that they simply “are”. We tamely concur, therefore, that expenditures,
particularly those that cannot be quantified and measured, are suspect and accept expert-
and group-driven solutions. This worldview is continually at play in our apocalyptic
vision of rising health care costs. Yet if we leave the US out of the comparison, Canada
spends roughly the same amount on health care per capita as other wealthy nations,
somewhere between 8% and 10% of GDP, and the vast majority of patients do receive
timely, appropriate care, contrary to the panicked cries to the contrary.

Restrictive policies such as those based on therapeutic equivalence assume that
current levels of expenditure are unsustainable and the only solution lies in restricting
access. Yet whether considered from its evidentiary basis, as a guideline, linguistically or
as a defining element of what constitutes good care for an existing medical condition, the
term equivalence and its policy off-shoots demonstrates a disquieting lack of breadth,
little understanding of clinical care and no acknowledgement of the complexities of
physiology. Primary reliance is on a static and one-dimensional definition of health and
disease, one as fallible and reductionist as the one used in corporate models and as
lacking in subtlety. It would seem that reference-based policies are an imperfect solution
at best and a reductionist shortcut at worst, fraught with inconsistencies and
contradictions. Disproportionately, those affected by such policies are the
disenfranchised, the elderly, the poor and the fragile who are most likely to need (and
benefit from) medication. Therapeutic equivalence over-values end points and
biomarkers over physiology and process, assumes certainty where none exists and,
perhaps most critically, operates on the belief that current ontological disease
classifications will stand the test of time.
Nevertheless, given that drug costs have risen rapidly, in Canada as in other countries (Moulton, 2002), policy makers find themselves in a bit of a quandary, especially since pharmacotherapy, being finite, lends itself better to rules and guidelines than physician services or hospital care. This dissertation has suggested that the problem is not with the analysis but the position and perspective. It does not require bigger and better algorithms or more complicated data – but is inherent to the quality of the discussion. All too often both corporate promotional efforts and efforts made to counteract them (such as reference pricing) treat medical advances as metaphorically analogous to electronics or telecommunications which is patently inappropriate. Patients are not consumers or clients, and they do not choose to have heart surgery or a colonoscopy: they do it because they feel they must. Marcel Proust wrote that “for each ailment that doctors cure [as I am told they do occasionally succeed in doing], they produce ten others in healthy individuals by inoculating them with that pathogenic agent a thousand times more virulent than all the microbes – the idea that they are ill” (Proust, 1992). Today it is not merely doctors but a host of institutional voices joining in the clamour – even as we bandy around terms like equivalence and evidence as though they refer to things, not ideas.

Equivalence, like so many of the terms and concepts casually used, is a verbal and medical shortcut. It has its uses but also has potential to do harm and adversely affect health and health care. It would seem sensible, therefore, rather than perpetually focusing on the what (drugs, diseases, conditions, treatments, tests) that we occasionally pause to examine the broader questions: the why and how. Rather than always questioning why
there is never enough to go around – never enough MRI’s, mammography units, doctors, hospital beds, cancer clinics – ask on occasion why we need so many of them in the first place – counter pharmaceutical companies’ marketing with our own, ask our own unique questions and go beyond the most “frequently asked” ones cited on pamphlets and websites to matters of social and environmental consequence. The multiple influences on medicine, from economics, linguistics, history, sociology and personal and cultural narratives (including corporate influences) cannot make us take our medicine. Should we, as patients, researchers, clinicians, observers and citizens demand better information and pay closer attention, focus could be shifted away from institutions and towards ethical discourse and education. Remuneration incentives could be altered so that patient-clinician interactions are valued and paid for – versus passive acceptance of the status quo and continual complaint. Perhaps, most important, we could regain the fundamental understanding that medicine is not confined to its technologies and genuinely move towards a medicine that looks towards the future.

Epilogue

Western medicine changed irrevocably with the discovery of antibiotics. Suddenly it was possible for medicine to actually do something for people who were deathly ill and could die, from tuberculosis, infection, sepsis. That paradigm – effective curative pharmacotherapy – has had a lasting socio-cultural impact on our collective

118 Drug company tactics are open to all. Why could the Therapeutics Initiative or other groups not use their expertise (and a fraction of their budgets) to punch holes in the gung-ho, drug-happy culture the pharmaceutical companies
medical psyche, and today that idea has converged with other factors, from technology, mass communications, open borders and global trade to create fundamental changes in the authority and systems of medicine, from research to practice. The result has been a medicine that is stunningly effective at times (particularly for many acute problems and trauma) and remarkably ineffectual at others, notably with respect to chronic illness, screening and cancer. It has also become increasingly expensive, although when viewed as a portion of GDP it has remained reassuringly constant.

This work has examined a single concept, therapeutic equivalence, used in one small aspect of health policy, to point to the massive complexities, the towering edifice of assumptions, the multiplicity of social and cultural beliefs, upon which even this one simple policy relies. The purpose has not been to find a "culprit" or to assign blame but to discover the patterns which have converged to create our dilemmas in present-day health care and policy. As we have seen, from the many ambiguities contained within the data and statistical process to the difficulties in classifying pathology; from the uncertainties of the clinical process to the idiosyncrasies of the patient, medical decision-making rests on a myriad factors, many of them unknown (and perhaps unknowable). However, by the middle of the 20th century, the institution of medicine (not clinical practice) had "gained professional dominance in the halls of policy and had taken on a mantle of cultural authority" – creating a "health care industry" larger than life and more powerful than any of the individuals involved (Hadler, 2004, 202).

are taking pains to foster rather than always focusing on creating more "rules" for patients and clinicians to follow?
Too many ostensible solutions, therefore, such as reference-based pricing, tend to be blunt instruments, based on tenuous concepts such as therapeutic equivalence, and are wielded by expert groups relying on rules, guidelines, protocols and other strategies at a distance from the patient. The problem, overuse of prescription drugs, is real, but the solution lacks finesse. It presents pathology and pharmacotherapeutics as one-dimensionally as the drug company marketing it is meant to address. As researchers in Montreal, examining the over-prescription of psychotropic medications for the elderly from a physician perspective, suggest in the *CMAJ*:

> The inappropriate prescribing and use of medications is a complex matter that involves more than one professional body. … There appears to be a need to improve physicians’ communication skills so that they can respond more appropriately to patients’ requests for medication. … Other strategies should be considered… Promoting links between physicians and community pharmacists is one option that might alleviate the relative isolation of physician in these [nursing home] settings. Thus, a multifaceted intervention strategy should result in long-term modification of inappropriate … prescribing. (Damestoy, Collin, & Lalande, 1999, 145) (my emphasis)

Solutions, as these authors point out, are possible. They would, however, require will and understanding: understanding of the multiple layers of meaning and history and the will to tackle the issue with flexibility, humility, critical thinking and deep communication. These qualities are not typical of our age, better characterized as impatient, self-important and rigid.

Patients – ostensibly the focal point of all medicine – have never been as oblivious to the uncertain inner workings or processes of therapeutics as they are today. Yet patients are the ultimate cost-savings weapon if insurers and governments would but
realize it. Patients, on the whole, tend to be conservative, wary of over-medicalization and generally suspicious of over-exuberant claims. Imagine what a force they could be with good information and if professional groups, the media, governments, universities and other groups so eager to bemoan the problems of medicine actually used a fraction of their budgets to disseminate some of the doubts and questions discussed here. We have at our disposal today extraordinary means of communication, from blogs and satellite radio to old-fashioned print. Professional groups, governments, disease advocacy groups, even patients could engage in the discussion. Also vital are training and educational initiatives and shifts in remuneration systems. After all, if we value something we pay for it – and right now it is clear that patient communication and education are not high on the list of priorities. As for the expert groups and economists, too many seem focused on coming up with incentives to change behaviour they do not seem to understand. It is simplicity itself to criticize clinicians for over-prescribing, missing diagnoses, ignoring patients, not communicating – and entirely more complicated to attempt to find genuine, ethical solutions.

The crux of the matter is that, as in bioethics, both the problems and potential solutions are multilayered, complex, and messy, which is anathema in the present climate where neat, quantifiable rules or protocols are preferred. Yet imagine a landscape in which policy makers and other observers actually understood and were sympathetic to the problems of medical problem-solving and worked with medical professionals rather than

\[119\] Nearly half of all internet queries in 1997 concerned medical information (Frymoyer & Frymoyer, 2002, 101); no doubt it is as much or more today. Certainly the number of sites devoted to medicine has increased.
at thwarting them – and understood the wisdom and value of interacting with patients and
the need for good information. After all, if one could discuss one’s concerns regarding a
painful knee with a trusted health professional who took the time to explain that, with or
without an MRI, that knee would get better in a few months (or deteriorate, in which case
surgery could become necessary), perhaps that particular technology would not always
top the list of concerns. Conversely, imagine an environment in which cardiologists were
encouraged (and paid) to discuss heart function and the chronic, long-term nature of heart
disease with their patients versus being boxed into doing procedures or handing out
drugs. It is entirely conceivable that fewer individuals would be on those endless waiting
lists. Or, imagine if children’s hospitals ran television advertisements to raise money not
just for fancy machines but for innovative ways to provide prenatal health and long-term
social programs to help keep children (and families) healthy – socially, environmentally,
holistically. Surely, with time, things could change and more of us would realize that the
discussion on health and illness needs more than reductionist talk of disease, diagnosis
and types of treatment.

Many problems attributed to medicine are, in fact, social and economic. As
outlined earlier, socio-economic status (as well as a clean environment, breathable air,
good food, drinkable water) affect well-being and almost always those who are better-off
lead healthier lives. Yet public health officials seem fixated with flu pandemics and
infected cows rather than what circumstances could lead to the proliferation of an
epidemic to begin with (or how the conditions and feed of farm animals might contribute
to illness). Pockets of Canadian society contain disproportionate degrees of disease and
dysfunction, from diabetes and asthma to AIDS and TB. These areas need addressing, urgently, even if some hospital does not get to buy the latest high-tech microwave for prostate cancer. Yet our discourse seems fixed at the level of scarcity, technology, wait lists and “magic” – in language that seems designed to obscure everything from research to risk.

In the end, we cannot change the tenor of the times, globalization, trade agreements, the internet, the advance of technology or the way things have evolved over decades. What we can do is work with these forces to question, speak out and demand better – whether we are patient or clinician, policy expert or researcher, working or retired, sick or well. The bulk of medicine consists of human interaction and is, at heart, quite simple. Yet our default image for modern medicine is inevitably some complicated machine with a fancy monitor and neat graphics, headed by a person wearing a white lab coat. Such images further the idea that medicine has advanced beyond all recognition (it has not); that technology is the answer (it rarely is) and that the individual is merely there to be acted upon, which is neither true nor safe. There is more to medicine than disease and diagnostics and neither technology nor data and statistics are, ultimately, the solution. The answer, as Shakespeare said so many years ago (dear Horatio), lies not in our stars but in ourselves – which, fortunately, we are better able to change than the stars.
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