



**David L Sackett: Interview in 2014 and 2015**

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## Preface



When I told my friends (and anyone else who asked) about my metastatic cholangiocarcinoma, it sparked requests for interviews about my career, beliefs, and outlook from several journals, institutions, and individuals.

I dislike 'on the spot' interviews, certainly didn't want to keep repeating myself for different interviewers, and was concerned that I'd miss mentioning important events and people in 'live' interviews. So I made a counter-proposal to these requests: send me your questions, and I'll collate, combine, and compose a single set of written responses to them. This document is the result.

My hero, Brian Haynes (he was one of my 1<sup>st</sup> mentees in 1972, and now I'm 1 of his) agreed to edit the emerging document. In addition, to make sure it is rational and coherent, he is part of the group who have monitored my intellectual function along the way (because folks in the end-stage of my cancer often develop Alzheimer-like hepatic encephalopathy).

The interview questions fell into 2 series, each having 4 logical 'Sections:'

An historic flow of experiences and progressing ideas

- I. The Making of a Clinical Epidemiologist: 1934 – 1967.
- II. McMaster Medical School: 1967 – 1994.
- III. The Oxford Years: 1994 – 1999.
- IV. Back Home to Irish Lake: 1999 –

And a series of transcending matters:

- V. My Career as a Clinician.
- VI. My Career as a Clinical Trialist.
- VII. My Career as a Clinical Epidemiologist.
- VIII. Summing Up.

In whatever I have accomplished I am indebted to hundreds of students, colleagues, and teachers, and my constant fear is that I've failed to name some of them and acknowledge their help and friendship in this document. I ask for their forgiveness.

Finally, a few prior interviews might shed additional lights on aspects of interest:

1. A 1979 oral interview about starting the McMaster medical school, taken 12 years after my appointment as the Foundation Chair of Clinical Epidemiology and Biostatistics there. Source:

McMaster University Health Sciences Library.

2. An interview *Profiling the EBM Man* by an Oxford medical student. Source: Hobson J. Profiling the EBM man – Professor Sackett. *Student BMJ* 1998;6:75-6.

3. A 2009 television interview, taken when I received the Gairdner-Wightman Award. Source: <https://www.youtube.com/watch?v=Nbd--s2dFY0>

4. A series of 2014 television interviews about the past, present, and future of EBM, organized by the *British Medical Journal* and the *Journal of the American Medical Association*. Sources: <http://ebm.jamanetwork.com/index.html> and <http://ebm.jamanetwork.com/bios.html> and <http://ebm.jamanetwork.com/extended-sackett1.html>.

5. A 2015 interview by Alison Rose. (forthcoming)

### Editor's Preface

David Sackett created the text of this interview, with leavening and editing from Barbara Sackett, over a period of 124 days during the latter part of the course of his illness with cholangiocarcinoma. Dave sent his responses to the final set of questions and edits on May 8, 2015, and was admitted to hospital for end-of-life care on May 11, dying on May 13.

David Sackett was truly remarkable by any measure, and I feel very fortunate to have had his teaching, mentoring, collaboration and friendship from the beginning of my career. Many can say the same, as a key facet of his genius was engaging others in the mission of finding and disseminating scientifically robust answers to questions about the cause, diagnosis, course, prevention and management of health problems.

If there are any questions arising from the text, I would be happy to try to answer them ([bhaynes@mcmaster.ca](mailto:bhaynes@mcmaster.ca)), but please bear in mind that, except for this preface, I just took care of the commas and formatting: virtually all the facts, wisdom, and words are vintage David Sackett.

Brian Haynes  
McMaster University

## Career Thumbnail

David L. Sackett OC, FRSC, MD, MDHC, ScD, FRCP (Canada, London, Edinburgh).  
Professor Emeritus, McMaster University, Hamilton, Ontario, Canada.

After training in internal medicine, nephrology and epidemiology, David Sackett re-coined the term “clinical epidemiology” and began his 1<sup>st</sup> career (age 32) as the founding Chair of Clinical Epidemiology & Biostatistics at McMaster University’s new medical school. In his 2<sup>nd</sup> career he began to design, execute, interpret, monitor, write and teach about randomized clinical trials, an activity that continues to the present, some 200 trials later. His 3<sup>rd</sup> career was dedicated to developing and disseminating “critical appraisal” strategies for busy clinicians, and ended when he decided he was out of date clinically and returned (at age 49), in his 4<sup>th</sup> career, to a 2-year “retreading” residency in Hospitalist Internal Medicine. His 5<sup>th</sup> and 6<sup>th</sup> careers were largely clinical, as Physician-in-Chief at Chedoke-McMaster Hospitals, and as Head of the Division of General Internal Medicine for the Hamilton region. In 1994 a Chair was created for him at the University of Oxford, where he took up his 7<sup>th</sup> career as foundation Director of the National Health Service Research & Development Centre for Evidence-Based Medicine, Consultant on the Medical Service at the John Radcliffe Hospital, Foundation Chair of the Cochrane Collaboration Steering Group, and Foundation Co-Editor of *Evidence-Based Medicine*. Retired from clinical practice in 1999, he began his 8<sup>th</sup> career by returning to Canada and setting up the Trout Research & Education Centre, where he reads, researches, writes and teaches about randomized clinical trials. Along the way, he has published 12 books, chapters for about 60 others, and over 300 papers in medical and scientific journals.



## Section I: The Making of a Clinical Epidemiologist: 1934 – 1967

### Chapter I-1: Where did you grow up, and what were you like as a kid?

Born in 1934, I grew up in a small, semi-rural suburb of Chicago, the 3<sup>rd</sup> son of a bibliophile mother and artist-designer father. I remember our large Victorian house as filled with love, neighborhood kids, border collies, bagpipe and classical music, and books for every age and interest. My eldest brother became a Madison Avenue publishing magnate and the 2<sup>nd</sup>, a Stone Age archaeologist who became Chair of Anthropology at UCLA.

Because everything is ‘normal’ to a naïve kid, I enjoyed friendships with both black and white kids in our integrated schools, but raised no objections to my hometown’s racially segregated housing until my later civil rights days. I look back on my childhood as a happy time in a happy family.

I was a prototypical geek: far taller and skinnier than my classmates, my baseball aspirations shattered by monocular vision from severe amblyopia, my shyness exacerbated throughout 8 years of dental braces, and out of commission for half of my 12<sup>th</sup> year from polio and a post-polio leg contracture.

In retrospect the polio was a blessing, for not only did my forced initial inactivity create a life-long voracious reader, but my subsequent rehab included running which, as it improved from grotesque to merely ungainly, won me spots on my high school track and cross-country teams, my 1<sup>st</sup> rich and lasting friendships, individual and team trophies, recognition by schoolmates, and increased self-confidence. I even received 2 nicknames: “Sack” from my friends, and “The Heap” from my cross country coach (because I finished most cross-country races after crashing at least once).



An enthusiastic student, I loved school, and couldn’t stop talking, joking and punning about it, especially in class, especially when I was supposed to be silent. After banishing me to the hall for much of grade 2, my teacher told my mom “Your boy will wind up either President of the United States or hung in a village square.”





And the Dean of Boys at my high school complained that it was difficult to consult my file when recommending me for academic awards because most of its contents were ‘Misconduct Slips.’

My predilection for marching to a different drummer also emerged around this time. The church my family attended delayed baptism until adolescence, and thus offered me the opportunity to redress my long-held grudge that I hadn’t been given a middle name at birth. Both my brothers and everybody else in my confirmation class had one, and a Catholic chum even had 3! I began to ruminate over a perfect one for me: as it happened (or, as Vonnegut subsequently wrote, as it was *meant* to happen), my oldest brother was a freshman at Lawrence college, and the current damsel I was unsuccessfully trying to impress had a little brother named Larry. Accordingly, when our minister approached me with the holy water and whispered, “What’s your name, my son,” I blurted out “David *Lawrence* Sackett” and was baptized thus. My dad was quietly amused, my brothers found it hilarious, and my mom wouldn’t speak to me for weeks.

My childhood interest in performance music saw me through piano lessons (where I was more interested in my teacher’s goiter and stridor than in theory and practice), playing the clarinet in our grade school orchestra, playing a rhythm guitar in an unsuccessful high school band, and – throughout all these – singing (1<sup>st</sup> as the youngest-ever member of the SPEBSQSA<sup>1</sup> and later as the leader and baritone of a locally popular barbershop 6: *Five Mellowtones and a Monotone*).



In my enthusiasm for learning I completed high school a year before my mates but, at 16, I felt too young to go away to college. So I stayed on another year, taking enough science and choir to maintain my eligibility for the cross country and half-mile teams. When I won a combined academic scholarship and part-time job from a college in upstate Wisconsin at age 17, I headed north.

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<sup>1</sup>Society for the Preservation and Encouragement of Barber Shop Quartet Singing in America.

## Chapter I-2: Tell us about your college education, what you learned there that you used later, and how it led you to choose a medical career.

All 3 Sackett boys (and their wives-to-be) attended Lawrence College, a small (750 students) 'land-grant' school in Appleton, Wisconsin. Noted for providing an excellent liberal arts education (its 1<sup>st</sup>-year 'great books' course included Plato's *Republic*, Marx's *Communist Manifesto*, von Frisch's *Bees*, and *Huckleberry Finn*), Harvard recruited our president to become theirs during my freshman year.

The 1<sup>st</sup> thing I learned there anticipated the decades-later findings of cognitive psychologists<sup>2</sup> about ephemeral short-term memory, vital long-term associative memory, and the futility of trying to transfer the former to the latter by underlining textbooks, borrowing notes from classmates, and all-night cramming (that lesson cost me a 'D' in philosophy).

The 2<sup>nd</sup> complementary thing I learned was that, by recreating in my own words, drawings and diagrams, the lectures, texts, microscope slides and dissections I encountered in a course in vertebrate embryology and morphology, I achieved the transfer to long-term associative memory that brought not only great enjoyment of the science but 'straight As' thereafter.

From college onwards I've taken the sophisticated and complex notions I've had to master and broken them down into bits that are so small and simple that I can grasp them individually. I then reassemble the bits that build on and enrich each other in a step-wise fashion and describe them, applying the elements of style of Strunk and White<sup>3</sup>, the editorial lessons I learned on my 1<sup>st</sup> sabbatical in 1974-5 from David Sharp when he was Deputy Editor of the *Lancet*, and a sense of humor nourished by Kurt Vonnegut (*Cat's Cradle*, *Slaughterhouse Five*, *Breakfast of Champions*, and beyond). The resulting talks, essays and books are clear enough for even a schoolboy to understand<sup>4</sup> simply because they have been prepared by a perpetual schoolboy.

In my 3<sup>rd</sup> year at Lawrence I began to think beyond individual courses to eventual careers, and was torn between field zoology (the sea lamprey had migrated up the St. Lawrence to decimate Great Lakes fisheries, and I was absorbed in studying the behavior of one I had captured) and physiology (beginning with the fascinating properties and power of osmosis, and progressing to intriguing surgical experiments in parabiosis). I'd little exposure to or interest in statistics, and none to epidemiology or RCTs beyond *Arrowsmith*<sup>5</sup>.

From discussions with my teachers and friends I realized that I could extend my interest in physiology to not only better understand it, but also to combat its derangements in disease, if I

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<sup>2</sup>Norman GR, Sackett DL. Clinician-trialist rounds: 24. Modernizing your introductory graduate course in clinical trials. Part 1: Commonsense meets evidence. *Clin Trials*. 2014;11:681-4.

<sup>3</sup>Strunk W, White B. *The Elements of Style*. New York: Macmillan. 1972.

<sup>4</sup>In *Cat's Cradle*, the 'Father of the atomic bomb' was quoted: "Any scientist who couldn't explain to an eight-year-old what he was doing was a charlatan."

<sup>5</sup>Originally published in 1925, it is now available as: Lewis S. Arrowsmith. New York: Penguin Group, 1998.

became a physician. Barbara Bennett agreed to join and support us both in this adventure, we got engaged, and I started looking for a medical school I could afford to attend.

### Chapter I-3: Tell us about medical school. What happened there, and how did it shape your later career?

There were five 4-year medical schools in Chicago in 1956, each carrying a nickname that described not only its students but their overwhelming male makeup (my entering class of 182 included just 6 women). Northwestern was the “Rich boys’ school,” Loyola-Stritch was the “Catholic boys’ school,” Chicago Med was the “Jewish boys’ school,” U of Chicago was the “Genius boys’ school,” and the U of Illinois was the “Poor boys’ school.” Needless to say, I sought a scholarship at the U of Illinois. I was successful, reduced my tuition and fees to \$500 per year, and began my medical studies.

In those days the 1<sup>st</sup> year of pre-clinical courses (anatomy, histology, biochemistry, and physiology) were notorious for ‘washing out’ large numbers of aspiring physicians, so much so that Barbara and I had previously decided to postpone our marriage until I’d survived or succumbed to that 1<sup>st</sup> year. She returned to her home in Minneapolis, and after learning typing and speedwriting, she so impressed the group of surgical and autopsy pathologists who had recruited her as a medical secretary that they financed her additional coursework in anatomy and medical terminology.

For my part, I applied my college-perfected strategy of transferring short- to long-term memory (at least long enough to do well in final exams) by re-writing and re-drawing the contents of every course in my 1<sup>st</sup> year. This required 18-hour days, ‘all-nighters’ on Thursdays, and confining my ‘time-off’ to Saturday nights (40 years later, the contrast with the far healthier, but equally efficacious study schedules of my McMaster and Oxford students was unnerving). I earned high grades, but although I shared my re-writes with my 2 roommates, 1 washed out and the other had to repeat the year.



We married shortly after that 1<sup>st</sup> year ended, and not only did Barbara obtain a steady job in the university hospital’s Department of Pathology but, as a result, we were eligible for a ‘0-bedroom’ flat in a safe apartment in the slum that surrounded the medical school (it was a dangerous neighborhood, and 1 noon-hour a neighbor rescued Barbara from an attempted kidnapping in front of our building). We survived on Barbara’s salary and her genius at designing and sticking to budgets, augmented by the \$500 I earned in my 3<sup>rd</sup> year as an anatomy ‘prosector’ (entering the gross anatomy lab Sunday, Tuesday and Thursday nights and carrying out ‘model’ dissections for the 1<sup>st</sup> year students to replicate the following mornings) and similar-sized summer research stipends. Barbara stopped working at the start of my 4<sup>th</sup> year (just after we exercised our eligibility for a 1-bedroom flat)

when we welcomed the 1<sup>st</sup> of our 4 sons, and I supported our growing family as a ‘Medic,’ running an emergency room and 4-bed overnight ward for 5 nights and 1 weekend a month at a large steel mill, across the state border in Indiana.

The 2<sup>nd</sup> pre-clinical year was less stressful to us survivors, despite a fearsome course in gross and microscopic pathology from a department that focused our attention wonderfully by giving us ‘final’-style exams every 2 weeks.

It was in my 2<sup>nd</sup> year microbiology course that Dr. Robert Pumper, a virologist, began stopping by my lab bench and talking with me, not just about microbiology, but about my career directions and aspirations. When I expressed my interest in tissue culture, he gave me space and my own equipment in his lab, taught me the relevant theory and practice, and arranged a summer fellowship for me to test my idea (generated during my visits to a sanitarium for children with fulminating rheumatic carditis) of developing a line of mouse myocardial cells that might react selectively with serum from children with acute rheumatic fever. Along the way Dr. Plumper regularly tested my ideas, methods, and career aspirations, protected me from his Chair (who disliked medical students), brought me into the final steps of his novel work in growing vaccinia virus in serum-free media, and awarded me junior authorship on the resultant report in *Nature*<sup>6</sup>. Thus, I had my 1<sup>st</sup> experience in *‘The process whereby an experienced, highly-regarded, empathetic person (the mentor) guides another [usually younger] individual (the mentee) in the development and re-examination of their own ideas, learning and personal and professional development’*<sup>7</sup> that, 54 years later, Sharon Straus and I would explore in a sextet of *Clinician-Trialist Rounds* in the journal *Clinical Trials*<sup>8</sup> and in our 2014 text on mentoring.<sup>9</sup>

My 3<sup>rd</sup> and 4<sup>th</sup> years of clinical rotations were both exhilarating and doubly disappointing. On the one hand, I loved working with and for impoverished patients on the wards of Chicago’s impoverished Cook County Hospital as they taught me the presentations and progress of previously untreated and often untreatable disease.

On the other hand, I was dismayed by how little of the content I’d mastered in my 2 pre-clinical years was useful to me at the bedside. Although bits of physiology and pharmacology were relevant, even they were taught in isolation, without clinical context. Justification for my dismay arrived with the internist George Miller<sup>10</sup>, who was just then setting up one of the world’s 1<sup>st</sup> ever Medical Education Research Units at my school. His 1<sup>st</sup> study administered the 1<sup>st</sup> year anatomy final written exam to 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> year medical students, interns, surgical residents, and attending surgical faculty. *I was the only person beyond a few 2<sup>nd</sup> year students who passed the exam* (due, no doubt, to my working nights as an anatomy prosector)! All my classmates flunked it, but not as badly as the 4<sup>th</sup> year students, who performed not as badly as

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<sup>6</sup>Pumper RW, Sackett DL. Multiplication of Vaccinia virus in serum-free and serum-containing cell cultures. *Nature*. 1960;185:123-4.

<sup>7</sup>Oxley J, Fleming B, Golding L, Pask H, Steven A. Mentoring for doctors: enhancing the benefit.

[www.academicmedicine.ac.uk/uploads/Mentor1.pdf](http://www.academicmedicine.ac.uk/uploads/Mentor1.pdf)

<sup>8</sup>Straus SE, Sackett DL. Clinician-Trialist Rounds 8-11 on the structure and function of effective mentoring:

Part 1: Why every clinician-trialist needs to get mentored. *Clin Trials*. 2011;8:765-7.

Part 2: Linkage, resources, and academic opportunities. *Clin Trials*. 2012;9:127-30.

Part 3: The structure and function of effective mentoring: Advice and protection. *Clin Trials*. 2012;9: 272-4.

Part 4: The essential attributes of an effective mentor. *Clin Trials*. 2012;9: 367-9.

<sup>9</sup>Straus SE, Sackett DL. *Mentorship in Academic Medicine*. Chichester: BMJ Books, 2014.

<sup>10</sup>Remembering George Miller. <http://cores33webs.mede.uic.edu/dme/warp/bulletins/May99/george.html>

the interns, who performed not as badly as the surgical residents, who performed not as badly as the surgical faculty. My skepticism about the readiness of basic science departments to integrate their content into clinical context was cemented by the response of the basic science Chairs to George's report: they immediately voted, not to revise their courses, but to cancel the budget of his Med Ed Research Unit!

My 2<sup>nd</sup>, and much greater, disappointment arose from the unsatisfying justifications I received from my seniors for their therapeutic decisions. They ranged from:

1. That's how we've always done it.
  2. That's how I was taught to do it.
  3. That's how this month's Attending Physician insists we do it.
  4. That's how 'the Bible' (in those days, a several-years-old edition of Harrison's Textbook of Medicine) says we should do it.
  5. That's how the pathologists said we should do it ('it takes about 5 weeks for fibrous tissue to form a firm scar across a myocardial infarction, so keep them at bed rest for at least 30 days').
  6. That's how the 'experts' say we should do it ('your patient's blood pressure of 240/120 is required to maintain their proper brain perfusion, and lowering it will cause a stroke, so leave it alone').
5. Don't talk back! Just do it!

This 2<sup>nd</sup> disappointment primed me for caring for the patient who not only changed my requirements for therapeutic decisions but also set the course for my subsequent career. As I reported 50 years later in a contribution to the James Lind Library<sup>11</sup>:

*"I was a final-year medical student on a medical ward, where a teenager with 'infectious hepatitis' (now called hepatitis A) was admitted to my care. He presented with severe malaise, an enlarged and tender liver, and a colorful demonstration of deranged bilirubin metabolism that made me the envy of my fellow clerks. However, after a few days of total bed rest his spirits and energy returned and he asked me to let him get up and around.*

*In the 1950s, everybody 'knew' that such patients, if they were to avoid permanent liver damage, must be kept at bed rest until their enlarged liver receded and their bilirubin and enzymes returned to normal. And if, after getting up and around, their enzymes rose again, back to bed they went. This conventional wisdom formed the basis for daily confrontations between an increasingly restless and resentful patient and an increasingly adamant and doom-predicting clinical clerk.*

*We clinical clerks were expected to read material relevant to the care of our patients. I wanted to understand (for both of us) how letting him out of bed would exacerbate his pathophysiology. After exhausting several unhelpful texts, I turned to the journals. PubMed was decades away, and the National Library of Medicine had not yet begun to help the Armed Forces Medical Library with its Current List of the Medical Literature. Nonetheless, the Armed Forces Medical*

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<sup>11</sup>Sackett DL (2008). A 1955 clinical trial report that changed my career. JLL Bulletin: Commentaries on the history of treatment evaluation ([www.jameslindlibrary.org](http://www.jameslindlibrary.org)).

Library directed me to a citation in the *Journal of Clinical Investigation* (back in the days when it was a real clinical journal).<sup>12</sup> Reading this paper not only changed my treatment plan for my patient. It forever changed my attitude toward conventional wisdom, uncovered my latent iconoclasm, and inaugurated my career in what I later labeled 'clinical epidemiology'.

The paper introduced me to Tom Chalmers, who quickly became my hero and, a decade later, my friend. Tom was a US Army gastroenterologist in the Korean War, and had become involved in a major outbreak of 'infectious' hepatitis among American recruits. The application of conventional wisdom on enforced bed rest was keeping affected soldiers in hospital for about two months and requiring another month's convalescence. Tom wrote: "This drain on military manpower, along with more recent [short-term metabolic] observations suggesting that strict bed rest might not be as essential as heretofore thought, emphasized the need for a controlled study to determine the safety of a more liberal regimen of rest and less prolonged hospitalization."

Employing what I increasingly came to recognize as 'elegant simplicity', Tom and his colleagues allocated soldiers who met pre-defined hepatitis criteria at random either to bed rest (continuously in bed, save for one trip daily to the bathroom and one trip to the shower weekly), or to be up and about as much as the patients wanted (with no effort made to control their activity save 1-hour rests after meals) throughout their hospital stay. The time to recovery (as judged by liver function testing) was indistinguishable between the comparison groups, and no recurrent jaundice was observed.

Armed with this evidence, I convinced my supervisors to let me apologize to my patient and let him be up and about as much as he wished. He did, and his clinical course was uneventful.

My subsequent 'clinical course' was far from uneventful. I became a 'trouble-maker', constantly questioning conventional therapeutic wisdom, and offending especially the sub-specialists when they pontificated (I thought) about how I ought to be treating my patients. I had a stormy time in obstetrics, where I questioned why patients with severe pre-eclampsia received intravenous morphine until their respirations fell below 12 per minute. I gained unfavorable notoriety on the medical ward, where I challenged a consultant's recommendation that I should ignore my patient's diastolic blood pressure of 125 mm Hg "because it was essential for his brain perfusion".

Tom Chalmers, along with Ed Fries (who answered the question about whether diastolic blood pressure should be ignored) and Archie Cochrane, became my role models.

In the year that the paper by Tom Chalmers and his colleagues was published there were only 347 reports of randomized trials. Ten years later, after lots more clinical (internal medicine and

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<sup>12</sup>Chalmers TC, Eckhardt RD, Reynolds WE, Cigarroa JG, Jr, Deane N, Reifenshtein RW, Smith CW, Davidson CS. The treatment of acute infectious hepatitis. Controlled studies of the effects of diet, rest, and physical reconditioning on the acute course of the disease and on the incidence of relapses and residual abnormalities. *J Clin Invest.* 1955;34:1163-1235.

nephrology) and methodological (US Public Health Service and Harvard School of Public Health) training, I began my 1<sup>st</sup> RCT.



#### Chapter I-4: Tell us about your internship, (1<sup>st</sup>) residency, and sub-specialty training. What happened there, and how did it shape your later career?

Entering my senior year in medical school (1959), I'd decided to become an internist, and was encouraged to visit the prestigious internships in New York and Boston. I thought I might become a better consultant if I had the additional experience in surgery, obstetrics, gynecology, emergency medicine, and even pediatrics provided by a 'rotating' internship. However, only 'straight' full-time internal medicine internships were available at the fancy Eastern centers (1 of my interviewers dismissed rotating internships as 'quaint'), so I applied (successfully) for a rotating internship back home at the University of Illinois Research & Education Hospital.

My internship met all my expectations. The surgical specialties gave me enough OR time to see patients' operative pathology and integrate it with my histories and physical exams and the associated imaging, and the surgeons were delighted to assign me the responsibility and learning opportunity for sorting and managing our patients' associated medical problems (calling 'teaching consultations' whenever I desired) and ordering and administering their IV fluids. The Emergency Room rotation taught the 'sorting out' of undifferentiated patients and the techniques of minor surgery, with quick access to the other specialties. Although our intern's schedule was rigorous (36 hours on, 12 off), and the pay pitiful (\$90 per month), our camaraderie was high and an interest-free loan of \$900 from the Merck Drug Firm saw us through the year and the birth of our 2<sup>nd</sup> son.

My medical rotation confirmed my career choice, and when my resident was off for several weeks with pneumonia, the Chair of Medicine, Harry Dowling, promoted me to resident-pro-tem and, with close monitoring from him, let me run the service. Thus, I gained a 2<sup>nd</sup> mentor, who helped me identify and confirm my interest in academic internal medicine and sponsored me in my successful application for a 1<sup>st</sup> year of medical residency at the U of Illinois Research & Education Hospital.

Although my overall performance had been very good, I had also made mistakes for which I learned to apologize to both patients and colleagues. The worst 1 (for which I also apologized 55 years later in the BMJ<sup>13</sup>) was failing to recognize that the hyper-resonance to percussion I'd found in a young woman with a wheeze was, in fact, "Skodatic resonance" above an early pleural effusion due to her lymphoma.

Medical Residents earned the princely sum of \$150 per month and, with another interest-free loan of \$900 from the Merck Drug Firm, carried our growing family through another year (our 2<sup>nd</sup> son was born on its 1<sup>st</sup> day). And the reduced night call (1 in 4) gave us more wonderful family time.

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<sup>13</sup>Sackett DL. My greatest mistake: Skoda's fool. BMJ. 2004;329:1494.

It was an exhilarating year, full of patient-centered learning enhanced by the slowly increasing body of RCT evidence to inform my clinical decisions (but, alas, not enough to prevent disputes with my Attending Physicians when I wanted to treat moderate and severe hypertension). Among my emerging fascinations were renal countercurrent mechanisms and fluid-electrolyte balance, and I had just about memorized D.A.K. Black's beautiful book on the kidney<sup>14</sup>. How fortuitous, then, mid-way through that year, to be paged by Robert Kark, the brusque Chief of the Hepato-Renal Service who'd cared for me when I'd passed my 1<sup>st</sup> cystine stone as a 4<sup>th</sup>-year med student, calling me to his office with a cryptic message: "It's not your kidneys, but your career that I'm concerned about." I didn't know that he'd been monitoring my performance as an intern and medical resident, and was 'gob-smacked' when he offered me a sub-specialty resident post and a National Institutes of Health Research Fellowship for the following year. The fit with my growing interest in nephrology and renal physiology was perfect, and by accepting his offer I gained my 3<sup>rd</sup> mentor.

With my salary tripled and night-call eliminated, we moved to a suburban townhouse and rejoiced in a more normal family life-style and the 1<sup>st</sup> of our 6 family dogs. The Hepato-Renal Unit was an exciting and international place, staffed with bright German basic biochemists, superb UK-trained South African clinicians who had recently introduced percutaneous renal biopsy to North America and taught us how to perform them, a brilliant Italian pathologist who introduced us to their improved interpretation through thin-sectioning, and a bright, collegial gang of Fellows from Peru, Quebec, South Africa, and the US. Clinical renal-metabolic practice was both fascinating (including serving a full clinic of patients with Wilson's disease) and frustrating (although we could meticulously follow the pathologic and clinical course of the hundreds of lupus nephritis patients who came to us for help, there were no modern drugs or RCTs to guide our offers of therapy, and we agonized over their rapid deterioration on high doses of prednisone).

Our Fellows' joint project was the introduction of hemodialysis to Chicago, and each of us pursued our individual research interests as well. I combined my interest in renal tubular physiology with my cystinuria by attacking the tubular resorption of amino acids. I immediately confronted a major bottleneck in the time and effort required to identify which amino acids were failing to be (normally) reabsorbed and therefore appeared in the urine: in those days it took 2 days of 2-directional paper chromatography of a patient's urine to identify them. I wondered whether replacing the passive migration of amino acids in chromatography with their forced migration along an electrical field might speed the process, and succeeded in shortening their 2-day identification to 2 hours<sup>15</sup>.

On the basis of this success, my mentor encouraged and sponsored me for a move to the NIH for a PhD and a career in renal tubular transport. I was drafting my PhD proposal in October

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<sup>14</sup>Black DAK. Renal Disease. Philadelphia, F.A. Davis Co., 1962.

<sup>15</sup> Sackett DL. Adaptation of monodirectional high-voltage electrophoresis on long papers to the rapid qualitative identification of urinary amino acids. J Lab Clin Med. 1964;63:306-14.

1962 when Russian intercontinental ballistic missiles (ICBMs) were discovered in Cuba and the U.S. government immediately began drafting my generation of physicians for 2 years of national service.

At a stroke, my circumstances had radically changed. An external event over which I had no control had closed my chosen career path, at least for the next 2 years. Looking back 50 years later, I re-read the philosophic debate on whether changing circumstances make the person, or whether changing circumstances reveal the person who was already there. In retrospect, given the often radical differences between my multiple roles (in rough chronological order: renal tubular physiologist, classical epidemiologist, clinical epidemiologist, foundation Chair and curriculum designer at a new medical school, clinical trialist, designer and chief of a graduate program in clinical practice research methods, expert in medication adherence, 'critical appraisal' developer and author, Chair of both the opening and final (clinical) phases of a medical school curriculum, 'retreading' medical resident, physician in chief at a university hospital, chief of general internal medicine for a region, designer and chief of an advanced medical residency program, foundation Chair and developer of a UK/European Centre for EBM, developer and host of an international residential series of clinical epidemiology research workshops, and author of a regular column for clinician-trialists in a leading clinical trials journal), all of which I enjoyed and succeeded in, I guess they 'revealed the person who was already there'.

In 2 further events over which I had no control, the government allocated me to the U. S. Public Health Service (USPHS), and the medical resident I'd replaced as an intern came back to visit me along with his boss, Warren Winkelstein Jr., a classical ('big-E') epidemiologist who was looking for a USPHS recruit to join his unit at the Chronic Disease Research Institute in Buffalo. We both successfully petitioned the USPHS, and Barbara and I and our 2 sons moved there in July 1963.

## Chapter I-5: Tell us about your time in the U. S. Public Health Service. What happened there, and how did it shape your later career?

Mistakenly fearful about moving from the ‘friendly’ Midwest to Buffalo in the ‘aloof’ east, in 1963 our family of 4 settled quickly into a manse in a welcoming eastern suburb of Buffalo. The ‘big-E’ classical epidemiology group there, led by Warren Winkelstein Jr, had just entered the analytic phase of their large, population-based hypertension survey, and by adding me to the team analyzing these data, gently introduced me to the strategies and tactics of descriptive and analytic epidemiology and frequentist biostatistics. Michel Ibrahim arrived a few months later with his fresh epidemiology PhD, Bill Elsea emerged from the Peace Corps to take a senior post at the health department, and we and our families began a warm friendship and mutual education that continue to this day.

The team pointed me to a pair of textbooks that would help me understand the relevant methods. I had trouble getting excited over Brian MacMahon’s epidemiology text<sup>16</sup> (although he proved a wonderful mentor 4 years later), but loved the clarity and friendly style of Austin Bradford Hill’s 7<sup>th</sup> edition of his *Principles of Medical Statistics*<sup>17</sup>, which by now included a riveting section on clinical trials, and – shortly thereafter – his seminal paper on sorting out causation vs. association<sup>18</sup>.

Fearful of losing my clinical and bench research skills, I also sought out the Chair of the Department of Medicine, Evan Calkins, and he responded with great interest and generosity (foretelling his mentorship during my immediate post-USPHS career).

I experienced 2 related revelations during that 2-year tour of duty. First, my bench research into the tubular transport of amino acids (‘tho I’d continue it at a low key for the next 3 years) began to lose its excitement and bedside relevance to my 1<sup>st</sup> love of clinical medicine. Second, and in parallel, my growing understanding of the strategies and tactics of population-oriented epidemiology and biostatistics made me wonder whether they might be redirected to individual patient-encounters and improve my diagnostic abilities, my prognostic predictions, and my selection and application of therapeutic interventions.

These latter wonderings received a huge boost when I encountered Alvan Feinstein’s paper applying Boolean algebra to the diagnosis of acute rheumatic fever in my latest copy of the *New England Journal of Medicine*<sup>19</sup>. I wrote him a fan letter explaining my embryonic ideas, and his encouraging response initiated an association, friendship, and occasional collaboration that survived for 30 years.

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<sup>16</sup>MacMahon B, Pugh TF. *Epidemiologic Methods*. Boston: Little, Brown, 1960.

<sup>17</sup>Hill AB. *Principles of Medical Statistics*. 7<sup>th</sup> edition. London: Lancet, 1961.

<sup>18</sup>Hill, AB. The environment and disease: association or causation? *Proc R Soc Med*. 1965;58:295–300.

<sup>19</sup>Feinstein AR. Boolean algebra and clinical taxonomy: I. Analytic synthesis of the general spectrum of a human disease. *N Engl J Med*. 1963;269:929-38.

Warmly welcomed into Warren's team, as we analyzed their recent blood pressure survey they opened my eyes to defects in the precision and accuracy of blood pressure measurement (including dramatic end-digit preferences) and how to overcome them with random-zero sphygmomanometers, lessons I applied 29 years later when I launched The Rational Clinical Examination in JAMA<sup>20</sup>. And, as my mentor, Warren guided me as I tracked down, appraised, and described the determinants of aortic atherosclerosis<sup>21</sup>.

Warren taught me a crucial lesson in the manners and style of manuscript review when he asked me to co-referee a paper he'd been asked to assess. I criticized it in the rough, tough style I'd learned from basic science reviews of my own previous work, but *Warren sent it, unedited, directly to the authors!* They wrote back, thanking me and agreeing with my criticisms, but asking me why I needed to be so nasty, disdainful, and condescending in my choice of words. I was mortified, and not only apologized but radically revised my approach to subsequent manuscript reviews:

1. I began to state my concerns in the form of direct questions for the authors, not conclusions for the editors ("Is it possible that the loss of so many participants might have biased your conclusions about efficacy?" rather than "The authors are fatally naive about the possible effects of selective withdrawal of participants on the validity of the entire study.")
2. Thirty years before it became common practice, I sent a copy of these questions (but not my overall conclusion) directly to the authors<sup>22</sup>, along with the request: "If you think I've been unfair, or have simply missed the boat, please contact me."<sup>23</sup>

I maintained my clinical skills by working in a 'healthy aging' screening clinic: speaking with, examining, and ordering and interpreting a host of tests among the elderly for the early detection of possible diseases. But as I lessened my ignorance about the natural history of the chronic diseases I was pursuing, and learned more about the power of the RCT to distinguish useful from useless or even harmful interventions for them, I became increasingly sceptical about what I was doing. With permission and encouragement from its director, I carried out a primitive (by Cochrane standards) literature review, on the basis of which the clinic was closed, and I embarked on a decades-long scrutiny of whether screening and early diagnosis did more harm than good.<sup>24, 25</sup>

I came to realize that Buffalo was the early stamping ground for some of the leading North

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<sup>20</sup>Sackett DL, Rennie D. The science of the art of the clinical examination. JAMA. 1992;267:2650-2.

<sup>21</sup>Sackett DL, Winkelstein W Jr. The epidemiology of aortic and peripheral atherosclerosis. A selective review. J Chronic Dis. 1965;18:775-95.

<sup>22</sup>A practice that got me fired by a few journals and into the 1<sup>st</sup> of several arguments with Arnold Relman at the New England Journal of Medicine.

<sup>23</sup> This 2<sup>nd</sup> element rescued a revised Ms. from Hal Sox when the editors mistakenly sent me his original Ms. instead of its revision. When Hal received his copy of my 2<sup>nd</sup> review regretting that he hadn't responded to the questions I'd asked earlier, he telephoned me and we rescued his publication.

<sup>24</sup>Sackett DL, Holland WW. Controversy in the detection of disease. Lancet. 1975;2:357-9.

<sup>25</sup>Early Diagnosis. In: Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical Epidemiology. A Basic Science for Clinical Medicine, 2<sup>nd</sup> Edition. Boston: Little Brown, 1991.

American epidemiologists and statisticians, and Warren (who went on to a Chair and the Deanship at Berkeley) introduced me to them and helped me benefit from their works, friendship, and 'fatherly advice' as I developed my ideas about clinical epidemiology. In his early 30s, Abe Lilienfeld (later named "the father of contemporary chronic disease epidemiology") had generated a standardized questionnaire that afterward captured the sociodemographics, environmental and dietary exposures, and health habits of every patient admitted to the Roswell Park state cancer hospital there. Milt Terris, the physician-epidemiologist who later was Chair of that department at the New York Medical College, had been in Buffalo in the 1950s and introduced a problem-based epidemiology course for its medical students. Shortly before my arrival, Irwin Bross (previously a key contributor to auto crash injury studies) came to head the Biostatistics Unit at the Roswell. And the statistician Marvin Zelen, later Chair at the Dana Farber Institute and the Harvard School of Public Health, arrived for a decade in Buffalo just as I returned there from my year in Boston.

Warren took me to annual epidemiology meetings, introduced me to these and other 'greats' (Jerry Stamler, Al Tyroler, Walter Holland<sup>26</sup>, Bill Miall, Stoney Stallones, Bill Kannell, et al) and added me to their 'round table' lunches, dinners, and evening discussions, especially at the cardiovascular epidemiology meetings<sup>27</sup>. I was stunned by how much friendlier and supportive people they were than the academic medical 'greats' I was introduced to at the big clinical research ('Atlantic City') meetings.

In a splendid 'triple-play' of mentorship, Warren linked me with Irwin Bross, showed me Abe Lilienfeld's exposure profiles on every admission to the Roswell, and introduced me to John Pickren, their autopsy pathologist. Because Roswell patients gave consent for their autopsies on admission, John was able to remove, grade and freeze the aortas of every patient who died there. We quickly realized that we could usefully describe the relationships between smoking, alcohol, and aortic atherosclerosis, and my new friends generously appointed me Principal Investigator of the effort. With a delightful combination of good science and great collegiality (a lesson for the future!), John happily and reproducibly graded atherosclerosis severity (blind to questionnaire results) on an ordinal scale that Irwin patiently and generously taught me (via 'ridits') how to transform to interval data of far greater discriminatory muscle. We submitted its positive results to the New England Journal of Medicine, and my education was further enhanced when its Editor in Chief, Franz Ingelfinger, appointed himself its referee and opened a series of rigorous but friendly exchanges with me about how to improve its clarity and presentation. Intrigued by the usefulness of scale transformation, he had me write an accompanying educational editorial about that, and closed our correspondence with a

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<sup>26</sup>It was Walter who nominated me for my Chair at McMaster.

<sup>27</sup> These were the days before epidemiology was recognized as a useful discipline by the big academic cardiology centers, and smoking was still rampant (especially among statisticians). We met in the dead of winter in Chicago (Bill Miall regularly sported frost-bitten ears by meetings' end), and Jerry Stamler was hooted down when he introduced a motion that smoking (which often obscured slide presentations) not be permitted during scientific presentations.

beautiful, brief note: “Dear Sackett, I think the piece<sup>28</sup> is ready to go. I read it in bed last night and didn’t fall asleep.” (It was a pre-publication draft of this paper that satisfied the scientists at McMaster that I might be worth the risk of an appointment.)

By the end of my 2-year USPHS appointment we’d added a 3<sup>rd</sup> son to our family, and I’d started planning the next phases of my search for a career as a clinical epidemiologist. First, I wanted a final year of clinical training in internal medicine. Second, I wanted to round out my ‘book learning’ in epidemiology and biostatistics, and to at least decrease my ignorance about computers.<sup>29</sup> I went to Buffalo’s charismatic Chair of Medicine, Evan Calkins, for advice about the former.

Evan reinforced the friendly encouragement he’d shown me 2 years earlier, told me he’d already recruited a Chief Resident, and offered me a 2<sup>nd</sup>, combined clinician-educator post (‘Chief Teaching Fellow’) that would not only round out my clinical training but also would let me explore how I might inject my evolving ideas about clinical epidemiology into patient care, bedside teaching, grand rounds, and the morning report. I decided the appropriate sequence was clinical 1<sup>st</sup>, followed by classroom, accepted Evan’s exciting offer, and gained another mentor.

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<sup>28</sup>Sackett DL, Gibson RW, Bross ID, Pickren JW. Relation between aortic atherosclerosis and the use of cigarettes and alcohol. An autopsy study. *N Engl J Med.* 1968;279:1413-20.

<sup>29</sup>The Harvard School of Public had a single, Hollerith card, Fortran-driven computer at this time, and the PC wouldn’t be available for another 15 years.

## Chapter I-6: Tell us about that 3<sup>rd</sup> year of post-graduate clinical training in Buffalo. What happened there, and how did it shape your later career?

My 1965-66 year as Chief Teaching Fellow ('Super-Chief' medical resident) for Evan Calkins in Buffalo consolidated both my clinical training and my aspirations for becoming a clinical epidemiologist. We continued to live in the manse, and we completed our family with a 4<sup>th</sup> son, and a German shepherd-cross, a pair of rabbits, and a short-lived crow. I'd maintained my clinical skills in the well-aging clinic I served during my 2 years in the USPHS, and I'd kept up with all the clinical journals, so bedside rounds and discussions resumed seamlessly.

I worked with a very bright and energetic group of 30 interns (many from 'Ivy League' medical schools) and an outstanding Chief Resident, Chris D'Amanda. Although all my interns were stationed at the Buffalo General Hospital downtown, I also attended grand rounds at the Roswell Park State Cancer Hospital across the road (where James Holland had initiated historic, heroic treatments for childhood leukemia) and the Buffalo Veterans Administration Hospital out near the University.

By chairing 'morning report' on all our medical in-patients I identified the most promising opportunities for bedside and small-group teaching. For the former, I tried out tactics for identifying, understanding, and correcting observer variation and disagreements in the clinical examination (e.g., retinal vein pulsation as an indicator of intracranial pressure); and for the latter, challenging the 'complete history and physical' by demonstrating the impact of doing the physical exam before taking the history, and by providing us with only the patient's chief complaint, constructing a differential diagnosis list, and then arguing about the best, next, single piece of history, physical exam, or laboratory evidence that would shorten that list.

Not all my educational efforts were appropriate. To teach my housestaff to avoid costly but unnecessary lab tests, at 1 of their 'grand rounds' I asked an intern to describe the end-of-life care he had given a terminal cancer patient who was well-known to our service. After praising his compassionate care, I took a strip off him in public for the unnecessary lab bill he'd run up on the patient's last day. I took him aside later to apologize, but he remained quiet and wary of me for months thereafter. Although lots of senior clinicians still practice 'education through humiliation'<sup>30</sup>, I rejected it from that day forward.

Evan Calkins gave me a book for Christmas that secured my interest in clinical epidemiology. In *Controversy in Internal Medicine*<sup>31</sup>, clinical experts of the day (including Evan) paired off to debate each other about whether or how to treat the major maladies of the day. It solidified my dissatisfaction with the standards of evidence practiced by my betters.

The book's introduction admitted the problem and advocated its exposure: "The fact remains that in the practice of medicine strong opinions are held and taught in the absence of adequate

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<sup>30</sup>Detsky AS. The art of pimping. *JAMA*. 2009;301:1379-81.

<sup>31</sup>Ingelfinger FJ, Relman AS, Finland M, eds. *Controversy in Internal Medicine*. Philadelphia: Saunders, 1966.



data, and to discourage open controversy in such areas is to gloss over their foundations of ignorance.” On the other hand, 1 potential discussant read my mind when he objected: “Just in an era when medicine is trying to take the ‘great leap forward’ and have some kind of an idea of approach, control, programming and experimental design – this is the precise moment when this sort of promulgation of prejudice seems unfortunate.”.

And my hero Tom Chalmers, in commenting on the evidence presented by the proponent and opponent of blood-letting for hemochromatosis, exposed the fallacy of the ‘selective review’: “Each has naturally cited the research which best fits his thesis rather than that which does not. About 10 per cent of the references are in both papers.” To my chagrin, I had to admit that I had just committed that same sin in my recent ‘selective review’ on the determinants of aortic atherosclerosis<sup>32</sup>. I vowed both to mend my ways and to seek a formal education in applied research methods.

My increasing interest in and excitement about applied clinical research was matched by a corresponding decrease in my attitudes toward my basic bench research into amino acid tubular transport. Finally, recognizing that my 1<sup>st</sup> love of bedside clinical practice would enhance the former but retard the latter, I shut down my lab.

Barbara having announced, “One more year of school, and that’s it!”, I explored several graduate programs, settled on Harvard, and won admission to their School of Public Health.

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<sup>32</sup>Sackett DL, Winkelstein W Jr. The epidemiology of aortic and peripheral atherosclerosis. A selective review. J Chron Dis. 1965;18:775-95.

## Chapter I-7: Tell us about your time in Boston. What happened there and how did it shape your later career?

The 'G-I Bill' (an educational support program for veterans of compulsory service in the U.S.A.) provided tuition, books, and a living allowance, and these funds, generously supplemented by Evan Calkins back in Buffalo, made it possible for us to rent a house in Newton Center (with its renowned public schools for our 2 older sons). Our cracker box house was so small that Barbara was able to kick a football over it, and our 4 boys semi-grudgingly shared the same bedroom (in an upper and lower bunk bed and two cribs).

After 2 weeks in a cottage at Bar Harbor while taking Victor McKusick's summer course in genetics (and getting captivated by the prose and presence of the statistician Tony Murphy), we settled in and I paid my respects to the Harvard School of Public Health. Brian MacMahon (a classical 'big-E' epidemiologist renowned for his work in breast cancer) was then the Chair of Epidemiology at the Harvard School of Public Health; he kindly took me under his wing.

After quizzing me about my unusual career objectives, he both set me up in a spacious office and suggested that I *not* pursue an MPH. Instead, he advised me to take all the epidemiology and biostatistics methods courses offered at the School of Public Health, consider taking other relevant courses offered at the university (e.g., demography) and at the Massachusetts Institute of Technology (e.g., computers), and rely on him to award me any remaining credits required for an M.Sc. under the heading of 'research'.

I leaped at his kind offer, spent half my time mastering the methods courses, and then branched out, enjoying the demography course, being humiliated by my 12-year old fellow students in an M.I.T. course in Fortran-4, taking part in an infectious disease seminar series, and attending Medical Grand Rounds around Boston.

Having previously met Bill Kannel, the head of the Framingham Heart Study, I also drove 40 miles out to visit him at the Study and, to my pleasant surprise, drove home with an unpaid night job as 'Clinical Examiner 054'. Thus began that year's best (and funniest) educational experience. When Dr. Bill Castelli (who looked and spoke like W.C Fields) 1<sup>st</sup> met me, he humorously challenged: "Are you going to be 1 of those 'big-E' epidemiologists at Harvard or are you going to be 1 of us 'little-E' epidemiologists out here in the real world?"

Framingham turned out to be a wonderful site for pursuing my education in the precision and accuracy of the clinical examination. Designed in the 1940s, its clinical measurement methodology was a decade ahead of its time. However, to my mind in 1966, some of its methods were behind the times. For example, before I measured a participant's blood pressure, I was supposed to consult their chart and examine several of the blood pressures measured earlier that day by others. And, if, *but only if*, I thought they had angina pectoris, I had to seek a 2<sup>nd</sup> opinion from another examiner; those I considered angina-free never received a 2<sup>nd</sup> opinion (all of which pitted good manners against good methods: what was I to say to a fellow examiner/colleague/friend I reckoned had mis-diagnosed angina?).

In an effort to bring local attention to the problem of observer variation, I asked 1 of the study radiologists to review 100 chest films for the presence of aortic calcification (a candidate risk factor for myocardial infarction). Of course, I couldn't tell him until afterward that they were the same 50 films, scrambled and passed by him twice. Although my study design was wise, I foolishly underestimated the offensiveness of my positive results to its 'expert' subject. His outrage at the prospect of being exposed left me with the distinct impression that a publication of its results would be the last 1 of my career, so I 'ate' it. However, I remained in the good books of the rest of the Framingham team, and subsequently collaborated with them in study of 'assortative marriage' to determine whether Framingham women tended to marry Framingham men with similar coronary risk factors (they did<sup>33</sup>).

At the school of public health, my fondest learning occurred over everyday lunches in the library, listening to and later joining in discussions and debates with Brian MacMahon, the statisticians Robert Reed and Janet Worcester, and the epidemiologists Manning Feinleib, Theo Abelin and Olli Miettinen. Olli briefly adopted me when I became the 'scribe' for the students taking his course in population genetics, was both kind and rough with me in individual sessions about experimental design, and pounded into my head the importance of specifying the 'study question' so precisely that the methods used to answer it became immediately obvious.

I also took an elective course in designing epidemiology I curricula for health professional students. I spent the 1<sup>st</sup> half of the course 'venting my spleen' about the irrelevant, off-putting traditional classroom epidemiology courses that not only focused on issues in public health of no interest to 95% of medical students, but also ignored issues in the clinical exam (accuracy and precision) and therapeutics (deciding whether a treatment did more good than harm) that were both highly relevant and could be made highly interesting. Challenged by our teacher, Ascher Segall, to design an alternative course that would ignore the former and teach the latter, I began to think about clinical 'cases' that might be introduced into classroom settings to illustrate and solve relevant clinical problems in precision, accuracy, and efficacy.

The year in Boston confirmed and more clearly defined my thoughts about what I decided to call "clinical epidemiology"<sup>34</sup>, a term that deserves more explanation.

The term "clinical epidemiology" was introduced by John Paul (who was born in 1893 and died in 1971), an infectious disease internist who was appointed head of the Section of Preventive Medicine in Yale's Department of Medicine in 1940. In his president's address to the American Society for Clinical Investigation in 1938 (when it was still an organization with broad interests that included intact humans), he proposed clinical epidemiology as a "new basic science for

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<sup>33</sup>Sackett DL, Anderson GD, Milner R, Feinleib M, Kannel WB. Concordance for coronary risk factors among spouses. *Circulation*. 1975;52:589-95.

<sup>34</sup>Sackett DL. Clinical epidemiology. *Am J Epidemiol*. 1969;89:125-8.

*preventive medicine*” in which the exploration of relevant aspects of human ecology and public health began with the study of individual patients.”<sup>35</sup> Dr. Paul wrote the 1<sup>st</sup> book bearing that title<sup>36</sup> and offered the 1<sup>st</sup> course in clinical epidemiology for undergraduate medical students. However, his concept of clinical epidemiology had a population rather than individual patient orientation in which he described the role of the clinical epidemiologist as being “like that of a detective visiting the scene of the crime” who then “branches out into the setting in which that individual became ill”. Thus, the procedure in his course for 3<sup>rd</sup> and 4<sup>th</sup> year Yale medical students was to “start the student at the bedside and lead him gradually *away from it*”. And Alvan Feinstein was proposing his own definition of clinical epidemiology, again including a public health perspective.

I described what might comprise a ‘clinical epidemiology unit’ back in Buffalo to my mentor Evan Calkins. Once again, he generously offered me space, a research assistant, and ‘rations and quarters’ and we headed back ‘home’ to Buffalo, where yet another cataclysmic event over which I had no control arrived in the form of a letter from John Evans, who was starting a new medical school 70 miles away in Canada.

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<sup>35</sup> Paul JR. Clinical epidemiology. J Clin Invest. 17, 539-41.

<sup>36</sup> Paul JR. Clinical epidemiology. Revised Edition. Chicago: University of Chicago Press, 1966 .

## Section II: McMaster Medical School: 1967 – 1994

### Chapter II-1: Why did you move to McMaster University in Canada in 1967?

Barbara, our 4 boys and I were very happy to be back in Buffalo after our year in Boston, and I was just getting down to work. I started to set up a 1500-square-foot Clinical Epidemiology Unit at the county charity hospital, was beginning to plan how I might teach both bedside clinical medicine and classroom epidemiology, and was doing my background reading for my 1<sup>st</sup> ever RCT (to determine whether treating systolic blood pressures  $\geq 160$  in elderly women and men lowered their risk of fatal and non-fatal cardiac and cerebrovascular events).

We had scarcely unpacked when I received a letter from John Evans, the foundation Dean of a new medical school at McMaster University in Hamilton, Ontario, a steel town of 300,000 located 70 miles northwest of us in Canada. Education is a provincial (not national) responsibility in Canada, and Ontario had decided to open its 5<sup>th</sup> medical school at McMaster, already a strong natural science university (it had the 1<sup>st</sup> university-based nuclear reactor in Canada). Having heard about me from Walter Holland, John said he wanted my opinions about departments and courses in community, social, and preventive medicine.

Abundant in both my ignorance of Canada and in my disinterest in moving, and mindful of my novice-status as an academician, I viewed his invitation as an interesting, 1-day holiday from my 'real job' in Buffalo. Having consented to the interview only because it would have been discourteous to turn them down, I made no attempt to 'sugar coat' my answers to the 1<sup>st</sup> 2 questions John Evans posed at that visit:

Q1: *"What sort of Department of Social, Community, and Preventive Medicine should we have at this new medical school?"*

A1: "None! Unless every department insists on taking responsibility for the social, community, and preventive issues that are relevant to them, you could never have a department of SCPM big enough to generate any useful improvements in health care."

Q2: *"What sort of course in epidemiology & biostatistics should we teach our medical students?"*

A2: "None! Unless clinically relevant bits of epidemiology and biostatistics are integrated into instruction in clinical skills, clinical pharmacology, therapeutics, and into every clinical rotation, an isolated course in epidemiology and biostatistics would be as awful as it is everywhere else, the students would hate the faculty, and vice versa."

I didn't know that they'd already reached these same conclusions! The Chair of Psychiatry was already placing most of his faculty out in community agencies, and the Chair of Pediatrics was already teaching mums of injured hemophiliac kids how to store and inject Factor VIII to prevent hemarthroses and hospitalizations. And, they'd already decided not to have courses in epidemiology *or anything else*, but to provide self-directed, tutorial-based, clinical problem-

based learning in which medical students would track down, master, and integrate information across the entire range of pre-clinical and clinical disciplines.

In short, John mistook a hip-shooting novice for a sage, and we set out on a wide-ranging conversation about medical education and health care. As we spoke, I became very impressed with both the depth and breadth his interests, understanding, and novel ideas. He was a *clinical cardiologist*, a former (like me) *bench researcher* (into the use of fatty acids as an energy source by endocardial cells), a *'public-healther'* with ideas about how to improve the organization and distribution of health and social services, a *consummate politician* who had won over both a major university and a provincial government to his cause, an *educational innovator* (proposing a revolutionary problem-based, self-directed learning approach to medical education), and a *charismatic leader* who was recruiting a remarkable group of young academicians. Moreover, he had a warm, welcoming personality and was clearly smart as hell.

After 2 hours I headed back home, thinking that John was the smartest person I'd ever met, deeply impressed by what was going on in Hamilton, and wondering if Buffalo (where I was committed) could ever match it. I didn't expect to hear from him again.

To my surprise, within a week I received a letter, summarizing our 1<sup>st</sup> meeting and inviting both me and Barbara (who did not want us to move from Buffalo) to visit. When we arrived at John's office, he ignored me and won Barbara over during a warm, lively conversation about her interests and ideas, terminated only when his wife, Gay, arrived to take Barbara to lunch and a tour of the area. We all soon became fast friends and have remained so.

In short order I met the half-dozen newcomers to McMaster and the local leaders who were welcoming them there. Bill Spaulding, a senior Toronto general internist with a revolutionary vision of how medical students ought to learn, had arrived as Dean for Education. He immediately made me an ex-officio member of the education committee; he wrote the definitive description of our program 10 years later<sup>37</sup>. Fraser Mustard, already an internationally-renowned platelet and thrombosis researcher, had arrived as Dean for Research. He began by grilling me about my clinical epidemiological research methods and results. Once satisfied, he won me over with his commitment to organizing and financing research within carefully structured problem-centered programs that spanned wet labs through patients to populations. The town's 3 leading internists, Bill Walsh, Bill Goldberg, and Jack Sibley, had not only welcomed the idea of a new medical school but had joined it in senior positions, exemplifying a better 'town-gown' relationship than any other I've ever encountered, before or since.

It was a prosperous time for centenary Canada and Ontario, and these visionary people and developing programs at McMaster were being provided with abundant resources (generous 'hard-money' faculty and staff salaries, lots of seed-money, and a new building with 40-acres of

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<sup>37</sup>Spaulding WB. Revitalizing Medical Education; McMaster Medical School; The Early Years 1965-1974. Philadelphia: Decker, 1991.

floor space<sup>38</sup>). Moreover, pre-existing hospitals were competing to provide both temporary and permanent space and facilities for new faculty, departments, and programs.

As joining McMaster started becoming a serious career option, I met with my mentor Evan Calkins. Not only did I seek his advice, but because he had done so much for me, I felt I could not leave Buffalo so soon after my return without his approval. He responded at 3 levels. First, he gently suggested that I was being 'snowed' by the Canadians, who would never fulfill their grand promises to so junior an academic. Second, to confirm his suspicions, he drove to Hamilton to confront John Evans and find out 'what was really going on.' Third, he returned to tell me that, contrary to his suspicions, I'd been offered a serious, once-in-a-life-time opportunity to work with an outstanding group of academics to revolutionize medical education and health research and, although he'd hate to see me go, I'd go with his blessings.

A quick series of additional visits and family discussions led both sides to conclude that McMaster held too much promise and was going to be too much fun for us to stay away. My appointment as foundation Chair of the Department of Clinical Epidemiology and Biostatistics was confirmed by the University Senate a few days before my 33<sup>rd</sup> birthday. Provided with abundant temporary space, a professional assistant, a Departmental Manager, and a hunting license for a biostatistician and a 2<sup>nd</sup> clinical epidemiologist, I began 'commuting' a couple of days per week, and we moved to suburban Hamilton in August of 1968.

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38 Zeidler EH. Healing the Hospital. McMaster Health Science Center: Its Conception and Evolution. Toronto: Zeidler Partnership, 1974.

## Chapter II-2: What did McMaster mean to you and your career?

I could not have achieved anywhere near as much, with anywhere near as wonderful colleagues and students, and with anywhere near as much fun, at any other institution in the world. (Indeed, when I turned down Chairs at the most prestigious universities in America and England, one of them sent a team of investigators to Hamilton to find out why. When I showed them what I was able to do at McMaster, they agreed with my decision to stay home.)

I attribute my happy, productive time at McMaster to 8 of its qualities:

### 1. Leadership:

I've never encountered a more gifted, fair, imaginative, collaborative, and effective group of leaders anywhere else. We all worshipped our foundation Dean, John Evans. Our foundation Dean for Research (and John's successor), Fraser Mustard, a world-class basic scientist in blood platelets, insisted that his and other basic research had to extend to patients and communities to be worthy. Our foundation Dean of Education, Bill Spaulding, was both a master clinician and a visionary around matters of medical education whose innovations have been taken up at other medical schools around the world. We had similarly outstanding foundation Chairs in the key departments of Anatomy: Jim Anderson, Pediatrics: Al Zipursky, Psychiatry: Nate Epstein, and Medicine: Moran Campbell. With so few of us, we and our spouses helped each other wine and dine prospective recruits and their partners, and our families became very close.

### 2. Organization:

First, we avoided a bottom-heavy set of basic science departments by arranging for relevant contributions from like-minded members of pre-existing departments across campus. Second, a department's faculty size, rations, and quarters were determined by their contributions to multi-departmental programs of education, service, and research. Some outside 'experts' came by later and told us we were practicing 'matrix management.' Reflecting our unpretentious and light-hearted attitudes, we replied that our model was simply a "Centralized Hierarchy of Organization and Administrative Services" (CHAOS).

### 3. Colleagues:

Vital to my/our success was the willingness of world-class biostatisticians and clinical epidemiologists to not only share our goals but to lead us in achieving them. The biostatisticians Gary Anderson from the USA, Mike Gent from ICI Pharmaceutical and the University of Bradford in England, Charlie Goldsmith from Flin Flon, Manitoba arrived early on, soon followed by Gerry Hill from Statistics Canada, Robin Roberts from England, Charlie Dunnett from Abbott Laboratories in the USA, Wayne Taylor from Canada, Harry Shannon from



Oxford and the Universities of Birmingham and London, Stephen Walter from Yale, and most recently Lehana Thabane from Lesotho and Janice Pogue from Canada. They have excelled, not only in their content expertise but in their ability to put it to powerful, great use in both collaborative research and inspiring graduate education.

Early clinical epidemiology recruits were Walter Spitzer (who later was recruited to a Chair at McGill) and Gene Vayda (who later was recruited to a Deanship at the University of Toronto) both arriving from Alvan Feinstein's training program at Yale. Because Alvan had been such an encouraging mentor-at-a-distance to me in the previous few years, we were able to capture him for an extended sabbatical as Canada's 1<sup>st</sup> National Health Visiting Scholar. Always a tough task-master, he brought a rigor to our methodological discussions and early research, although he later regretted that we had devoted so much of our energy to randomized trials.

We recruited outstanding clinical epidemiology graduates from our DME program into our department, and they have taken on leadership posts in research and education: the 1<sup>st</sup> of these was Brian Haynes, an internist diabetologist, followed in successive generations by Peter Tugwell (a rheumatologist who soon thereafter became Chair of our department and later the Chair of Medicine at the University of Ottawa), George Browman (an oncologist who later chaired our department), Gordon Guyatt (who coined the term 'evidence-based medicine' and leads its continuing development), Deborah Cook (a general internist/intensivist who created our 1<sup>st</sup> nation-wide consortium carrying out ICU-based trials), PJ Devereaux (a cardiologist who is a world-leader in trials of the efficacy and safety of perioperative interventions among non-coronary patients), and Maureen Meade (a principal investigator in key ICU trials).

And we have benefitted greatly from the 'multiplier effect' of DME graduates whose home bases are in other McMaster Departments. The shining example here is Jack Hirsh, a world-class thromboembolism researcher (often with Mike Gent) who went on to Chair our Department of Medicine. Jack not only took our DME courses, but also steered a number of his recruits to our DME program, often making it a prerequisite for their academic appointments: in thromboembolism, Clive Kearon and Marc Crowther are shining examples. Another is the neonatologist Jack Sinclair, who brought rigor to the evaluation of NICUs, and Murray Enkin in obstetrics.

And DME graduates are role-models in several other areas of excellence at McMaster: Vic Neufeld as Dean of Education, Anne Holbrook and Mitch Levine in pharmacology and therapeutics, Hertzell Gerstein in diabetology, Mark Levine (who now Chairs our new Department of Oncology), Roman Jaeschke in intensive care, Sonia Anand in cardiology, Peter Szatmari in psychiatry (Canada's expert in autism and now Chief of the Child and Youth Mental

Health Collaborative between the Centre for Addiction and Mental Health and the Hospital for Sick Children in Toronto), Jim Nishikawa in internal medicine, and Mike Walsh in nephrology.

And Salim Yusuf, the cardiologist-trialist from Oxford and the NIH who heads McMaster's Public Health Research Institute and is currently President of the World Heart Association, is both a leader in, and advocate for, clinical epidemiology.

Last but by no means least, the Chairs of all McMaster's clinical departments have recruited clinical epidemiologists like Andy Oxman and been openly supportive of their and our efforts.

#### 4. Resources:

Ontario was a very prosperous province when we started, and the credibility of our leaders and our programs with the high-quality provincial and federal mandarins who controlled it meant money was never a limiting factor during our 1<sup>st</sup> several years. For example, we were able to support our statisticians with medical school (rather than much lower university) salaries, and never had to beg for funds for our repeated acquisition of additional space and service for our expanding department. Indeed, our common view was that the only limitation on our freedom to innovate was our imaginations.

#### 5. Resource allocation by program, not department:

In appointing me, the university senate authorized a faculty contingent of 2 clinical epidemiologists and a statistician for my department, to be reassessed after 6 years. However, in the medical school (described in Chapter II-3: How (on earth!) did you convince McMaster to agree to the 10-fold expansion of CE&B), we allocated faculty to departments to meet the needs of multi-departmental programs of education, research and service. With full-time and cross-appointments we quickly became the largest department in Canada, permitting us to take on whatever challenges and opportunities we desired.

#### 6. The town-gown relation:

Our town-gown relationship was the best I've ever encountered. Hamilton already had a vigorous post-graduate program underway before we arrived, and area physicians were vocal advocates for the new medical school. Of the three leading internists in town, two immediately took senior university posts and the 3<sup>rd</sup> remained a powerful advocate and supporter. The same phenomenon occurred in several other clinical departments.

We reciprocated their welcome. For example, our foundation Chair of Medicine made an appointment with every internist in town, went to their offices, exchanged ideas and expectations with them, and ended the visit by offering every one of them a part-time faculty post (virtually all accepted).

Area physicians quickly opened their offices and wards to our medical students, and continued to do so even after one of us documented that, when learners were present, their billings were sharply reduced. Perhaps the most compelling evidence of a positive town-gown relationship was when the Hamilton Academy of Medicine (the local medical society) elected one of us, an 'outsider' from (ugh!) Toronto, to become their President.

#### 5. Short tenure for Chairs:

If we adopted long appointments to Chairs, our lack of experience and youth (I was 32, and our average age was less than 40) presented potential problems for both the university and ourselves. If we turned out to be 'turkeys,' the university would be stuck with us at a stage that required far better leadership. Conversely, if we had multiple career goals, we shouldn't be stuck in an administrative post that prevented us from pursuing them.

We solved this by limiting appointment to Chairs for 3 years, renewable just once. Indeed, I successfully petitioned to reduce my 2<sup>nd</sup> term to 2 years, so 5 years after my original appointment I was able to give far more time and attention to my interests in research and teaching.

#### 6. Sabbatical policies and financial support:

We instituted a liberal sabbatical system in which faculty were not only encouraged to take sabbaticals every 6<sup>th</sup> year, but also provided generous financial support for them to take them. For example, I was provided with 75% of my previous year's base salary, and 50% of my previous year's clinical billings. With plentiful external travel grants from governments and foundations, I regularly obtained sabbatical support at 110% of my previous year's income. These sabbaticals were invaluable for both faculty and their families. See Chapter VIII-6 to learn how we spent our three.

#### 7. Support for clinical retreading:

At age 49 I decided that I was out of date clinically, and after discussions with one of my mentors (the senior internist at my hospital, Bill Spaulding), requested permission to spend 50% of my time for the next two years in a 'retreading' medical residency. My Chair and the Deanery agreed and supported me, my mentor arranged both my clinical rotations and my assessments, and I wound up with renewed competency and enthusiasm and certification by the Royal College of Physicians and Surgeons of Canada (who immediately placed me on their Council). I soon became Chief of Medicine at my hospital.

#### 8. Simply being at the right place at the right time:

As McMaster's reputation grew, it was offered opportunities to participate in unique and world-changing initiatives. For example, in the early 1980's INCLIN (International Clinical Epidemiology Network) selected McMaster to become one of three educational centers for

aspiring clinical epidemiologists from the developing world<sup>39</sup>. Peter Tugwell, then our Chair, offered me, Wayne Taylor, and Eileen Wang the opportunity to host and mentor aspiring colleagues from the West China Medical School in Chengdu. We met and grew to honor their venerable leader Luo Duchan, taught and mentored several students (most notably Wang Jialiang, Liu Zhenlo, and Wang Juesheng), and spent several mind-blowing Aprils with them in Chengdu, lending a hand with their rapidly growing research and education programs and immersing ourselves in their rapidly changing culture.

I close by repeating my opening conclusion: I could not have achieved anywhere near as much, with anywhere near as wonderful colleagues and students, and with anywhere near as much fun, at any other institution in the world.

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<sup>39</sup> Halstead SB, Tugwell P, Bennett K. The International Clinical Epidemiology Network (INCLIN): a progress report. *J Clin Epidemiol.* 1991;44:579-89.

### Chapter II-3: How (on earth!) did you convince McMaster to agree to the 10-fold expansion of CE&B (from 4 to 40 faculty)? What were the key ingredients of the 'growth formula'?

It's true that the McMaster University senate designated a start-up faculty of just 2 clinical epidemiologists and a statistician for our department, to be reassessed after 6 years. However, when the gang of us who actually started the medical school began by setting down our objectives, we decided that departments were simply resources of special knowledge and expertise whose size would be determined – not by senatorial proclamation or politicking – but by the needs of multi-departmental program of education, research and service. Moreover, our foundation Dean of Research (Fraser Mustard, a dynamic and internationally renowned thrombosis researcher) led us to form and execute the policy that, for a research program to receive space, money, and faculty, it had to attack a problem in human biology and health care across its entire spectrum, from basic biology through treatment discovery through intervention trials and on to the assessment of the organization and effectiveness of its relevant health care.

Our tiny department (me, Gary Anderson [who set up a main-frame but friendly computer more than a decade before the 1<sup>st</sup> primitive PCs were born] and our 2 half-time statisticians, Mike Gent and Charlie Goldsmith), quickly became consumed as willing collaborators and co-investigators in several fledging research programs.

Our effectiveness had 3 consequences. First, colleagues seeking to establish new research programs regularly lobbied for 'more of those CE&B guys' to join their core-memberships. Second, clinicians in these new programs frequently decided that they wanted graduate training in clinical epidemiology for themselves, emerging both as cross-appointees in our department and role-models for aspiring academic clinicians in their home clinical departments. World-class examples here are Jack Hirsh in thromboembolism and Jack Sinclair in neonatal intensive care. Third, our expanding graduate program began to attract brilliant graduate students who went on to dazzling careers in academic medicine (e.g., Brian Haynes developed medical informatics, Gordon Guyatt developed EBM). As a result, our fledgling department grew exponentially, and in 2014 I understand that its full-time and cross-appointed faculty now number 158.

## Chapter II-4: Tell us about the educational programs you created at McMaster

Although I fostered 6 educational innovations at McMaster, their evolution and success (and, more recently as my department expanded, their initial conceptualization) would not have occurred without the great ideas and efforts of my colleague-comrades.

When I began at McMaster in 1967, all my educational efforts went into the 3-year undergraduate M.D. [UGMD] program<sup>40,41</sup>, as follows.

Principles: Guided by the genius William Spaulding (the internist-Dean of Education), we of the education committee quickly agreed on 3 principles:

1. It must be self-directed, clinical problem-based, and tutor-supported, with the objective of teaching our students how to teach themselves forever after.
2. Students must be selected for their personal qualities, with no course pre-requisites and little attention to age or prior marks.
3. Another genius, Moran Campbell (a clinical physiologist-respirologist and foundation Chair of the Department of Medicine) convinced us that the focus must be on *education* (intellectual preparation for clinical medicine), not *training* (in medical procedures, as their mastery is central to post-graduate training).

### #1: Phase I of the Undergraduate Medicine Curriculum:

I chaired, and tutored in, the opening 4 months of McMaster's undergraduate MD program. I had some wonderful collaborators, and notable among them were a contemporaneous and a future star. The contemporaneous star was Jim Anderson, foundation Chair of anatomy, who created a spacious, friendly environment, filled part of it with a galaxy of morphological educational resources, invited the other disciplines to add theirs to the milieu, and role-modelled problem-based learning. The future star was Lynn Franks (now Lynn Johnston), in her 1<sup>st</sup> job as an artist, adding humorous illustrations to our slide-tape lectures that could be checked out and viewed day-and-night; a decade later she inaugurated her syndicated comic strip *For Better or For Worse*.

Strategies: We began by drafting 16 'biomedical problems' (BMPs) describing patients whose diseases, illnesses, and predicaments provided an introduction to human structure, function, and responses to stimuli, accompanied by relevant diagnostic imaging, lab results and therapeutic prescriptions. Each draft-BMP was reviewed by 18 'resource groups' (anatomy, behavior, biochemistry, pathology, physiology, primary care, women-in-medicine, etc. ) who proposed revisions to bring out important issues in their domains, and labeled the key educational resources that best transmitted their associated principles and facts. The revised BMPs, plus the tabulated 'resource group' inputs, provided the backbone of Phase 1.

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<sup>40</sup> Spaulding WB. Revitalizing Medical Education: McMaster Medical School: The Early Years: 1965-1974. Hamilton, ON: B.C. Decker Inc., 1991.

<sup>41</sup> Leeder SR, Sackett DL. The medical undergraduate program at McMaster University: learning epidemiology and biostatistics in an integrated curriculum. *Med J Aust.* 1976;2:875, 878-80.

Tactics: Entering medical students and faculty tutors (the latter coming from any department and emerging from a 'tutor training program') were randomized into 'tutorial groups' of 5 students and 1 tutor, each with access to a family physician's practice and educators/ educational resources (e.g., gross and microscopic anatomic materials and slide-tape lectures available 24 hours a day) from every discipline. A typical week would begin with the students opening a fresh BMP and listing all the questions it raised about the patient ("What's vertigo?/ 3+ pitting edema?/ rales?/ atrial fibrillation?/ heart failure?/ digoxin?/ a furosemide injection?/ why hadn't he kept his doctor appointments and taken his medicine?" etc., etc.) They would then, with gradually decreasing reliance on their tutor, consolidate their questions into operable sets of issues to pursue in structure, function and response to stimuli, and organize their week. Meeting most every morning, they would get together to share what they'd found, test their progress toward understanding and explaining their BMP patient, decide what they still needed to find out, what they'd learned and wanted to learn from their Family Physician, and what they wanted to accomplish at their next tutorial. When they concluded that they had 'solved' a BMP, they presented their solution to the tutor, who listened, explored, and challenged their solution (calling on content experts as necessary). The tabulated 'resource group' issues and resources, which had accompanied the BMP in a sealed envelope, could be opened by consensus at any time. Early in Phase 1 they might be opened at the conclusion of the 1<sup>st</sup> tutorial on a BMP; by mid-Phase 1, they would be opened as part of the evaluation of a BMP's 'solution' (to see how well students had progressed in identifying key issues and in finding the 'best' resources on their own); delightfully, by the end of Phase 1 many tutorial groups left the envelope unopened.

Outcomes: Our bizarre new med school was viewed as a risky place to learn medicine (indeed, one skeptical applicant was accepted both by us and a sister med school, accepted both offers, and commuted between us until he was exposed almost half-way through Phase 1; he left McMaster, and dropped out of medicine at the end of his 1<sup>st</sup> year). After initially attracting lots of students who were inadmissible elsewhere (over 35, no post-secondary education, lousy grades, no pre-med science courses), our graduates quickly became recognized as superior house officers, clinicians, and academicians, our applications soared, and women quickly comprised well over half of our students.

## #2. Phase 6 of the Undergraduate Medical Curriculum:

Six years later, I became Director of all Clerkships in the McMaster MD program. Positives about this job were to witness and recognize the enormous, selfless contributions of clinicians and hospitals to the program (both in Hamilton and when we were invited to add clerkships in Northern Ontario), and the marvelous performance of our medical students. Among a typical entering class of 100 students, 90 would sail through the program without interruption. Nine would briefly stumble, collaborate in setting up and completing individualized remediation programs, and complete their MD on time. However, 1/100 would be found to lack the personal qualities required for an effective clinician, and the negative thing about my job was having to confront and remove them from the program.

#3. A Graduate Program in Clinical Epidemiology and Health Care Research Methods: One weekend in 1970 (when our inaugural medical class had just completed their 1st year of our 3-year program) , Dean John Evans took me for a walk and – after congratulating me on my department’s success in infecting the rest of the faculty with a clinical epidemiological approach to applied health research – urged me to start an MSc graduate program. He even had a name for it: Design, Measurement, and Evaluation, and by Monday I had drafted its entry and degree requirements, courses, and the resources required to pull it off.

Two of its central features distinguished it from existing Canadian graduate programs. First, since the applicants we wanted to serve included busy early- and mid-career clinicians, it had to offer not only 1-year (July through June), concentrated (‘sabbatical’) immersions but also multi-year, part-time (‘one-course-at-a-time’) options to the degree, as well as a 3<sup>rd</sup> option to take just 1 or a few courses. Second, we had to confront the incompatibility between our primary 1-year MSc option and the then-standard Canadian MSc degree-requirement of a completed research project, given our conviction that any research project worth doing (e.g., a solid determination of the reproducibility and accuracy of a diagnostic test, the value of a prognostic marker, or the usefulness of a therapeutic intervention) required between 2 and several years to do well. Our solution was propose a high-quality research *protocol* as a satisfactory product for our MSc degree, and we were able to gain the approval of both university and provincial certification authorities for our proposal (the latter group briefly lifting their embargo on new grad programs to accommodate us).

We launched our 2-stream program (Clinical Epidemiology for clinicians, and Health Care Research Methods for non-clinicians) within a year. Our 1<sup>st</sup> Clinical Epidemiology grad student (Alec Macpherson, a gifted psychiatrist who later served as a pioneering Medical Officer of Health for Toronto) and I co-designed the courses and contents of both streams: 6 courses comprising an introductory pair in epidemiology and biostatistics (led by our recently recruited outstanding statisticians, Mike Gent, Charlie Goldsmith, and Gary Anderson), followed by a 1<sup>st</sup> research protocol that was reviewed by faculty (and by another student when the full program was underway). The Health Care Research stream was initiated the following year by Larry Chambers (who went on to a path-finding career that recently included a ground-breaking cluster randomized trial of a community-based intervention that both improved health and reduced hospital costs<sup>42</sup>) and Cam Voelker. These 1<sup>st</sup> grad students’ theses developed the key outcome measures of physical, social and emotional function that were used by Walter Spitzer in the 1<sup>st</sup>-ever randomized trial showing that nurse-practitioners can provide effective care to 80% of the problems that arise in primary care<sup>43</sup>.

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<sup>42</sup> Kaczorowski J, Chambers LW, Dolovich L, Paterson JM, Karwalajtys T, Gierman T, Farrell B, McDonough B, Thabane L, Tu K, Zagorski B, Goeree R, Levitt CA, Hogg W, Laryea S, Carter MA, Cross D, Sebaldt RJ. Improving cardiovascular health at the population level: A 39 community cluster-randomized trial of the Cardiovascular Health Awareness Program (CHAP). *BMJ*. 2011;342:d442 doi:10.1136/bmj.d442

<sup>43</sup> Sackett DL, Chambers LW, MacPherson AS, Goldsmith CH, Mcauley RG. The development and application of indices of health: general methods and a summary of results. *Am J Publ Hlth*. 1977;67:423-8.



The graduate program burgeoned, was quickly taken up by dozens of faculty from other departments (exemplified by the world-leader in thromboembolism research, Jack Hirsh), and soon became a pre-requisite in the recruitment of new faculty who aspired to carry out clinical research, both at McMaster and other universities<sup>44</sup>, especially after it expanded to offer PhDs. Its local and visiting faculty in 2014 numbered >175 and is just 1 of 5 graduate programs currently offered by the department at McMaster.

#### #4. The Fellowship Program in General Internal Medicine:

Because Canadian primary care is already provided by well-trained 'Family Physicians' with 2-3 years of post-graduate training, Canadian 'general internists,' are consultants with up to 5 years of post-graduate training who provide 'hospitalist' and office-based secondary care to patients with multiple and undifferentiated illnesses<sup>45</sup>. When I became Head of General Internal Medicine (GIM) for the McMaster Region in 1990, a major opportunity arose for developing an innovative educational program for them and competing with the other medical subspecialties for senior residents. Having recently received a provincial Trillium Award of \$500,000, and in collaboration with Dr. Deborah Cook, a brilliant GIM-intensivist-clinical trialist, we designed a GIM residency. It offered relevant courses from the 'DME' program described in #3 above, individual mentoring, a wide range of clinical placements, and a weekly 'academic half-day' for the presentation and discussion of clinical cases and evidence on the clinical usefulness of relevant diagnostic, prognostic, therapeutic and rehabilitative maneuvers. Finally, it took all GIM Fellows to annual meetings of their U.S. counterparts.

We were surprised by our success in competing with our sub-specialty colleagues for high-quality residents, and recruited some wonderful young people. Weekly half-days were both rigorous and fun, and our 'graduating' Fellows were snapped up by academic departments and community hospitals, making important contributions in both settings.

#### #5. Critical Appraisal of the Clinical Literature:

By the late 1970s, I had the notion that some of the DME content could be taught to practicing clinicians to help them become better practitioners by better understanding and managing the medical literature they encountered. Peter Tugwell and Brian Haynes enthusiastically agreed, and with animated support from the Chair of Medicine, Jack Laidlaw<sup>46</sup>, the trio of us started teaching the basic principles of critical appraisal to medical residents in 1978. The residents not only showed up and learned, but became threatening to some of the faculty, and we eagerly responded to the latter's requests for their own (separate) sessions. This program rapidly spread through the other clinical departments, and often lit fires of interest among residents who went on to enroll in our DME program. Along the way, it was bolstered by a non-randomized trial conducted by the DME graduate student Kathryn Bennett that demonstrated

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<sup>44</sup><http://www.fhs.mcmaster.ca/hrm/>

<sup>45</sup>For a further explanation of Canadian General Internal Medicine, see the *Canadian Journal of General Internal Medicine*.

<sup>46</sup>Hilariously, Jack initially preferred the term 'critical thinking,' but quickly reverted following vigorous complaints from his bench researchers who deeply resented the implication that this notation rendered them 'noncritical' thinkers.'

considerable improvements in critical appraisal skills among experimental, but not control, medical students<sup>47</sup>.

We started publishing background papers to support this educational program, 1<sup>st</sup> on the clinical examination<sup>48</sup> and soon thereafter in a broader series on how to read clinical journals<sup>49</sup> and how to interpret diagnostic data<sup>50</sup> that were consolidated in the 1<sup>st</sup> edition of our clinical epidemiology text<sup>51</sup>.

Brian Haynes, Peter Tugwell and I then established the program of annual international 'Critical Appraisal of the Medical Literature Workshops' for colleagues around the world who wanted to learn how to do it. They were run in 2 tiers, 1 for newcomers who wanted to learn the basics of Critical Appraisal, and a 2<sup>nd</sup>, advanced tier for colleagues who already knew the basics and wanted to learn how to teach them to others. In the latter, each participant set a teaching scenario for themselves, with the rest of the group role-playing the recipients of their teaching efforts and providing feedback on how they did and how they could do it better.

Thus began the series of events that led to the early 1990s proposal for a shift to Evidence-Based Medicine.

#### #6. Evidence-Based Medicine:

By the early 1990s we began to extend the Critical Appraisal concepts to include clinical decision making for and with individual patients. This was labelled Evidence-Based Medicine by our former graduate student, Gordon Guyatt, who subsequently led its development at

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<sup>47</sup> Bennett KJ, Sackett DL, Haynes RB, Neufeld VR, Tugwell P, Roberts R. A controlled trial of teaching critical appraisal of the clinical literature to medical students. *JAMA*. 1987;257:2451-4.

<sup>48</sup> Department of Clinical Epidemiology and Biostatistics, McMaster University.

Clinical disagreement I: how often it occurs, and why. *Can Med Assoc J* 1980;23:499-504, and  
Clinical disagreement II: how to avoid it and learn from one's mistakes. *CMAJ*. 1980;123:613-7.

<sup>49</sup> The "How to read clinical journals" series:

I. why to read them and how to start reading them critically. *CMAJ*. 1981;124:555-8.

II. To learn about a diagnostic test. *CMAJ*. 1981;124: 703-10.

III. To learn the clinical course and prognosis of disease. *CMAJ*. 1981;124:869-72.

IV. To determine etiology or causation. *CMAJ*. 1981;124: 985-90.

V: To distinguish useful from useless or even harmful therapy. *CMAJ*. 1981;124:1156-62.

<sup>50</sup> The "How to interpret diagnostic data" series:

1. How to do it with pictures. *CMAJ*. 1983;129:429-432.

2. How to do it with a simple table (part A). *CMAJ*. 1983;129:559-64.

3. How to do it with a simple table (part B). *CMAJ*. 1983;129:705-10.

4. How to do it with a more complex table. *CMAJ*. 1983;129:832-5.

5. How to do it with simple maths. *CMAJ*. 1983;129:947-54.

6. How to do it with more complex maths. *CMAJ*. 1983;129:1093-9.

<sup>51</sup> Sackett DL, Haynes RB, Tugwell P. *Clinical Epidemiology: A Basic Science for Clinical Medicine*. Boston: Little, Brown, 1985.

McMaster and beyond<sup>52</sup>, including the successor to the workshops (rebranded the Evidence-Based Clinical Practice Workshop<sup>53</sup>), followed shortly by my move in 1994 to a Chair in the Nuffield Department of Medicine at Oxford and the creation of the Centre for Evidence-Based Medicine there. That phase of my career is the subject of Section III of this Interview.

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<sup>52</sup> Evidence-based medicine working group. Evidence-based medicine: a new approach to teaching the practice of medicine. JAMA. 1992;268:2420-5.

<sup>53</sup> <http://ebm.mcmaster.ca/>

## Section III: The Oxford Years

### Chapter III-1: Why did you move to Oxford in 1994?

It was a case of a breath-taking opportunity presented to a contented, 59 year-old academic physician then working in a post-revolutionary institution. McMaster was 25 years old, and although it was (and still is) the best medical school in the world, with the best people and programs, the radicalism of the mid-60s was waning, most of its founders had moved on to other institutions, my mentees were thriving on their own, I had done everything I had wanted to do there, and the undergraduate MD education program had become too conservative for my liking.

It was against that background that I was contacted by the charismatic revolutionary Dr. (now Sir) Muir Gray, a former Glaswegian surgeon who was then the UK National Health Service Head of Research and Development for the Oxford and East Anglian Regions of England. Brimming with resources to match his interests in introducing EBM to the UK and Europe, he challenged me to visit Oxford, talk with whomever he and I wanted, and generate a report on whether and how somebody like me might lend a hand in developing EBM there and beyond.

Oxford was already the home of 2 of the world's most creative and important units, the Clinical Trials Service Unit (led by Richard Peto and Rory Collins with their outstanding colleagues Mike Clarke and Colin Baigent) and the emerging Cochrane Collaboration (conceived and led by Iain Chalmers).

My interest piqued, I spent a whirlwind week in Oxford, interviewing 73 people in 4 days and nights, writing all night on Thursday (in part to show them that I hadn't slowed down at 59) and delivering my report at 0500 on Friday morning. In it, I described how, and with whom, programs of education, clinical care, and research could incorporate the strategies and tactics of EBM to improve clinical and health care.

I returned to Canada and Muir set to work recruiting the people and resources necessary to accomplish our shared goals. He received strong support from Sir David Weatherall, Regius Professor (Oxford's 'Dean' of Medicine), John Bell (a former Canadian Rhodes Scholar who never went home), the Nuffield Professor (Oxford's 'Chair' of the Department of Medicine), Dr. (now Sir) Iain Chalmers, the genius who was launching the Cochrane Collaboration, Sir Richard Doll, and others, and sent me his proposal for the academic, organizational, and financial arrangements that could achieve our shared goals.

While he was doing that, Barbara and I weighed the pros and cons of pulling up stakes in Canada and moving to England for up to 10 years. It was a tough decision, mitigated by an already welcoming group of old Oxford friends, my pledge (which I kept!) to leave the hospital at 6 PM when I wasn't on service and plans for both of us to return to Irish Lake each summer. We found a wonderful 6 bedroom house in North Oxford (which we remodeled and added central heating, and where we hosted up to 40 visitors a month!) with a large English garden (>

50 rose bushes) and easy access to Port Meadow, the Thames, the colleges, and a host of enchanted pubs, with the Cotswolds a short drive away. Because my maternal grandfather was born in Glasgow, permission to immigrate was granted within a month, and we moved across in July 1994.

I was given a Chair and appointed Professor of Clinical Epidemiology in the Nuffield Department of Medicine, and their flagship John Radcliffe Hospital became the home of the *UK National Health Service Research and Development Center for Evidence-Based Medicine*.

Barbara soon became engrossed in advanced studies in Architectural History and Methods of Local History, and volunteered in the 'Ephemera' Section of the Bodleian Library. We both biked to concerts at the Sheldonian, bought a Rover for longer trips, and I commuted between home, the hospital, and colleges (mine became Magdalen) on a series of 3 motorcycles (the 1<sup>st</sup> was stolen and the 2<sup>nd</sup> lost its brakes), protected by a helmet and distinctive purple coverall. Quick (1 hour) trains to London Paddington were frequent for meetings, theatre, and my membership at the Athenaeum (where we opened membership to women).

We settled in and got to work.

## Chapter III-2: Tell us about the Centre for Evidence-Based Medicine.

Our Oxford Centre for Evidence-Based Medicine was located in the heart of the Department of Medicine's action at the John Radcliffe Hospital. Muir Gray effected the remodeling and furnishing of 2 adjoining offices (and later, the remodeling of a large Men's loo and shower facility to include an additional office for 2 CEBM Fellows). The original staff comprised a Senior Research Associate, Gordon Dooley, and a Research Assistant, Jayne Edwards. Gordon soon moved on to a more senior post at an innovative software group affiliated with the Cochrane Collaboration, and was succeeded by Douglas Badenoch. And, after 2 years Jayne became a PhD student in Oxford's Pain Research Unit, succeeded by Olive Goddard, who became our invaluable Administrator, ably assisted by Bridgett Burchell.

The Centre's remit was 2-fold:

1. To promote the teaching and practice of evidence-based health care ('EBHC') throughout the UK and Europe.
2. To effect the creation of formal graduate education in the conduct of randomised controlled trials and systematic reviews at the University of Oxford.

At its inception, with a team of just 3 of us, we thought that these goals might take a decade to establish. However, with the unflinching encouragement and support of Muir Gray and the enthusiasm and hard work of a worldwide array of >200 colleagues who unselfishly joined the centre, we surpassed these goals by the end of our 4<sup>th</sup> year:

- a. We had published 6 EBHC textbooks (one in 5 languages and another in 2), and chapters for more than a dozen clinical texts.
- b. In collaboration with Brian Haynes back at McMaster, we began the journal *Evidence-Based Medicine* (soon published in 5 languages with a circulation of >50,000), and assisted with 2 EBHC journals in other health care disciplines, nursing and mental health.
- c. We had created and distributed > 400 copies of user-friendly software (the "CATMaker") for critically appraising the clinical literature.
- d. We were running inter-connected websites containing both educational and immediately clinically applicable resources that were receiving > 10,000 hits per day.
- e. We had created and launched EBHC educational programs for undergraduate students and post-graduate trainees in internal medicine, surgery, pediatrics, obstetrics & gynecology, psychiatry, general practice, nursing, occupational therapy, critical care, and midwifery.
- f. We had established a nation-wide consortium in how to practice and teach EBHC that ran workshops in 3 languages (English, German, and Spanish) for more than 5,000 participants.
- g. We had helped colleagues across England create Centres of Evidence-Based Mental Health, Child Health, Pathology, Dentistry, Surgery, Nursing, and Practice & Policy.

h. We led and participated in the creation of Oxford-based graduate programs in Randomized Trials and Systematic Reviews (led by Doug Altman, whom we helped recruit to create Oxford's Centre for Statistics in Medicine), and in Evidence-Based Health Care.

Both our productivity and our fun received great boosts from 2 Fellows who joined us from Canada. Sharon Straus, a recently qualified internist/geriatrician from Toronto (and now Professor of Medicine and Director of the Division of Geriatric Medicine in Toronto) brought her boundless energy and imagination to a 3-year fellowship with us, quickly took on our contribution to the EBM journal, became a role-model EBM bedside teacher and innovator, designed and carried out several studies on the accuracy of the clinical exam and on how to incorporate patient-values into decisions about their health care, became co-author (now lead author) of the Oxford Texts on EBM<sup>54</sup>, and initiated a series of discussions and reviews around mentoring that led to our jointly-authored book *Mentorship in Academic Medicine*<sup>55</sup>. Finlay McAlister spent a year with us from Edmonton, and both collaborated and led research into the clinical examination and its bedside instruction.

The Clinical Tutor in Medicine, William Rosenberg (now the Richard Cristin Chair of Hepatology University College London and Joint Head of the Centre for Hepatology at UCL) provided invaluable advice and creative input to our early work, and Scott Richardson (now Associate Dean for curriculum at the Athens campus of the Georgia Health Sciences University) brought his enthusiasm and imagination with him to a sabbatical where he introduced a series of imaginative and effective teaching strategies to our group.

At the risk of omitting the names of some of the other key Oxford collaborators (to whom I now apologize) I want to acknowledge the unselfish contributions of Clive Adams, Neil Bacon, Chris Ball, Amanda Burls, Martin Dawes, Lelia Duley, Maureen Forrest, John Geddes, Carl Heneghan (then a med student, now Director of the Centre), Nick Hicks, Tony Hope, Rod Jackson, Tim Lancaster, Klim and Ann McPherson, Henry McQuay, Ruairdh Milne, Andrew Moore, Judy Palmer, Julie Parkes, and Bob Phillips.

Although it was not formally within the Center's remit, my highlight each week was a Wednesday morning walk with Iain Chalmers, ostensibly to effect the incorporation of the Cochrane Collaboration (I chaired the inaugural Steering Group). But our themes, discussions, and arguments had no boundaries, and comprised many of the most exciting and challenging issues in determining the effects of health care.

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<sup>54</sup> Straus SE, Richardson WS, Glasziou P, Haynes RB. Evidence-Based Medicine. How to Practice and Teach EBM. 3<sup>rd</sup> edition. Edinburgh: Elsevier, Churchill Livingstone, 2005.

<sup>55</sup> Straus SE, Sackett DL. *Mentorship in Academic Medicine*. Chichester: Wiley/Blackwell/BMJ Books, 2014.

### Chapter III-3: How did you incorporate EBM into your clinical practice, teaching, and research in Oxford?

#### Structure:

The in-patient medical care at the John Radcliffe Hospital was provided by teams comprising a highly trained Registrar or Senior Registrar (the latter might be in their 30s), a Senior House Officer in their 2<sup>nd</sup> or 3<sup>rd</sup> year of post-graduate training, a pair of House Officers (equivalent to a North American straight medical intern), and up to 6 medical students, all overseen by a consultant physician who changed each month. To maximize my opportunities to learn and teach, after my 1<sup>st</sup> 'go' I took on 2 teams at a time, twice a year, equivalent to 4 months of in-patient service per year. My Fellows Sharon Straus and Finlay McAlister joined me, as did sabbaticant Scott Richardson, Visiting Professors, often the Research Librarian Anne Eisinga (nee Lusher), and occasionally elective Registrars who wanted to integrate their training with ours (e.g., from Radiology).

#### Function:

When operating as a double-team, we were on 'take' for ten 12-hour periods per month. On an average 'take' we would see 25-30 patients. During our 'post-take' rounds of up to 6 hours, 1 or 2 were provided terminal care, we'd be able to 'top up' and release 2 or 3 more, and we'd admit 24, for a total in-patient census of about 240 patients per month. We met each weekday when we weren't on 'take,' saw the sickest and most problematic patients together, and reviewed each of the rest in our 'Rounds Room,' teaching and learning as we went, and then splitting off into different learning sessions (e.g., auscultation with a 6-person stethoscope) for the different levels of learners (these latter sessions grew to about 50 hours of supplemental teaching per month).

At month's close, I took the team, plus some local 'celebrity' physicians and scientists, to a delightful dinner-celebration at a renowned Chinese restaurant.

#### Our Teaching:

Our teaching followed from our setting down of 'what EBM is and what it isn't' in the BMJ<sup>56</sup>. Accordingly, the unique educational strategies and tactics we employed in this practice comprised:

##### 1. *Immediately available evidence-based resources:*

Over previous years I had generated and maintained summaries (with citations) of the most valid evidence on the accuracy of key elements of the clinical exam and diagnostic tests, on

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<sup>56</sup>Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ. 1996;312:71-2.



valid prognostic markers, and on the efficacy and safety of specific treatments. Carried with me in a monster loose-leaf 'Red Book' (updated prior to each month on service), I would haul them out during post-take rounds to speed (and often correct) decision-making, increasing the efficiency as well as appropriateness of our initial care (copies were made and distributed after the round). Every student was expected to contribute at least 1 new item to the Redbook during their month on service.

### *2. Educational Prescriptions:*

When decisions were not urgent, the learner caring for the patient would be given (increasingly at their own request) an original document (I'd keep a copy) that specified a question about diagnosis, prognosis or therapy, what the learner was expected to answer about it, and the time that that answer was to be provided as a 'Critically-Appraised Topic' to the rest of the team. Filling an Educational Prescription was greatly enhanced when our Centre's Douglas Badenoch created a web-based CATMaker<sup>57</sup> that produced a standardized summary that could be distributed and added to the Redbook.

### *3. Midway and End-of-Month Evaluations:*

We met as a group at the start of the month, discussing how the team would work, presenting my expectations, and identifying everyone's learning objectives.

At 2 weeks I met individually with each learner and:

- asked them how they thought they were doing,
- asked them how they thought I was doing, and how I could be more helpful to them,
- told them how I thought they were doing, and, for any deficiencies, how they'd need to improve by month's end,
- asked them what they still hoped to learn by month's end, and how they'd accomplish this.

This was an entirely new experience for most of them, as most had not been through such an evaluation previously (and certainly not one in which they'd been asked to evaluate faculty!).

By the end-of-month evaluations, all had overcome their deficiencies and were performing satisfactorily. Indeed, 3 or 4 would have performed so well that I handed them a letter, recommending them for whatever subsequent job they might seek; to my surprise, about half of them became tearful, stating that no one had ever told them before that they were really good (a tragic manifestation of the British pedagogic axiom that telling a learner that they were really good would make them really lazy thereafter).

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<sup>57</sup><http://www.cebm.net/catmaker-ebm-calculators>

Our Research to Validate our Teaching:

1. *Were we practicing evidence-based medicine in the 1<sup>st</sup> place?*

In my 1<sup>st</sup> month on service, our House Officer Jonathan Ellis challenged me with this question, and I showed him how to answer it for us. At the time of the discharge or death (or still on the ward at month's end) for every patient admitted that month, we achieved consensus on both their primary diagnosis and our primary treatment for that diagnosis. We then traced that treatment into the current clinical literature and again reached consensus on whether it was derived from randomized trials, from convincing non-experimental evidence (so strong that subjecting patients to a placebo-armed randomized trial of it would be unethical), or lacking support of either sort.

This study, published quickly in the *Lancet* under Jonathan's lead authorship<sup>58</sup>, generated 2 striking results. First, and in contrast to the conventional wisdom of the day that only 10% of interventions were 'evidence-based,' we documented that 53% of our patients' primary treatments were backed up by RCTs (with a further 29% from convincing non-experimental evidence, and with just 18% lacking substantial evidence). Second, we discovered that 21 of the 28 RCTs supporting our evidence-based care were already in my "Red Book", available to the team during the post-take round when these patients were admitted.

We included these results in our orientation of every subsequent clinical team, setting the goal of improving on them. In addition, their publication stimulated a replication of our study by colleagues from several other locations and specialties.

2. *Can teaching EBM skills change practice in a community hospital?*

To justify our broader mission, we needed to know whether EBM could be practiced away from the university 'hot-house.' Accordingly, our CEBM Fellows Sharon Straus and Finlay McAlister, greatly assisted by Chris Ball, an early medical student convert from Oxford, went to a 465-bed District General Hospital in Staffordshire, provided their consultants and house staff with evidence-based summaries for their most frequently applied treatments, used 7 of their regularly scheduled conferences to conduct a 7-session EBM course, installed EBM resources on the PCs in their medical wards, and handed out copies of our EBM text<sup>59</sup>. Their before-after study<sup>60</sup> documented that patients became statistically significantly more likely to receive RCT-validated treatments that were of statistically significantly higher validity.

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<sup>58</sup>Ellis J, Mulligan I, Rowe J, Sackett DL. Inpatient general medicine is evidence based. *Lancet*. 1995;346:407-10.

<sup>59</sup>Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. *Evidence-Based Medicine: How to Practice and Teach EBM*. 1<sup>st</sup> edition. Edinburgh: Churchill Livingstone, 2000.

<sup>60</sup>Straus SE, Ball C, Balcombe N, Sheldon J, McAlister FA. Teaching evidence-based medicine skills can change practice in a community hospital. *J Gen Intern Med*. 2005;20:340-3.

### *3. Can a busy medical service participate in international research into the validity of the clinical examination?*

Despite the importance of the clinical examination in achieving accurate diagnoses, its elements have rarely been rigorously evaluated for their accuracy. For example, of the 32 signs of obstructive airways disease we found in medical texts and journals, only 1 had been the subject of an independent, blinded comparison with a reference standard among an appropriate spectrum of consecutive patients; and even there, the number of examining clinicians was just 2, and the number of patients just 164<sup>61</sup>. Citing the need for large, simple studies of the clinical examination<sup>62</sup>, our Fellows Finlay McAlister and Sharon Straus employed the web to recruit 46 investigators in 20 groups in 14 countries who, within a month, performed independent, blind comparisons between 1 bit of clinical history and 3 clinical signs and spirometry in 309 patients; they documented that the area under the receiver operating characteristic curve for these combined features was 0.86; that the likelihood ratios for obstructive airways disease was 220 when all were present, and 0.13 when all were absent.

Along the way, our team members learned both about the problem and how to incorporate its solution into a busy in-patient medical service.

### *4. Can we search for and obtain high-quality evidence at (or at least close to) the bedside?*

Although clinicians reported needing about 5 bits of evidence about diagnosis, prognosis, therapy, or prevention for every inpatient they cared for when we were getting underway in Oxford, they seldom had the time and energy to hike off to their medical library to find it. Could we overcome this barrier?

Operating in the pre-Wi-Fi, -iPad, -iPhone era, and with great help from Anne Eisinga<sup>63</sup>, we attempted to answer this question by loading a massive trolley, the 'evidence cart'<sup>64</sup> with our Redbook, a cable-connected searching computer, CD-ROM, EB texts and journals, our JAMA series on the Rational Clinical Examination<sup>65</sup>, the rapidly evolving Cochrane Library, a projector and a portable screen.

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<sup>61</sup>Holleman DR Jr, Simel DL, Goldberg JS. Diagnosis of obstructive airways disease from the clinical examination. *J Gen Intern Med.* 1993;8:63-8.

<sup>62</sup>McAlister FA, Straus SE, Sackett DL for the CARE-COAD1 Group. Why we need large, simple studies of the clinical examination. *Lancet.* 1999;354:1721-4.

<sup>63</sup>Straus S, Eisinga A, Sackett DL (2015). What drove the Evidence Cart? Bringing the library to the bedside. *JLL Bulletin: Commentaries on the history of treatment evaluation* ([www.jameslindlibrary.org](http://www.jameslindlibrary.org)).

<sup>64</sup>Sackett DL, Straus SE. Finding and applying evidence during clinical rounds: the "evidence cart". *JAMA.* 1998;280:1336-8.

<sup>65</sup>Sackett DL, Rennie D. The science of the art of the clinical examination. *JAMA.* 1992;267:2650-2.



Too large to trundle around our wards, we kept it in our 'Rounds Room' and taught our team how to use it to 'fill' both the educational prescriptions we gave them and the ones they created for themselves. To our pleasant surprise, to address their questions not already answered by other Cart contents, they successfully carried out 90% of their searches, 52% of which confirmed their current or tentative diagnostic or treatment decisions. However, 25% of their searches gave them a new diagnostic skill or directed them to a new diagnostic skill, additional test, or management decision. Moreover, 23% of their searches corrected a previous clinical skill, diagnostic decision, or treatment selection.

Even more telling was what happened when we took the Cart away. In just 2 days they reported needing evidence on 41 occasions, but left the ward to find it only 5 (12%) times.

Armed with our experiences and this evidence, I set out to introduce EBM at Universities and District General Hospitals throughout the UK and Europe.

A brief note on my other clinical teaching at Oxford:

I learned that a group of 1<sup>st</sup>-year medical students in 1 of the colleges were disillusioned and discouraged by their inability to see the relevance of their basic science courses and their goals of becoming competent clinicians. In response, Sharon Straus and I took them on, and held evening sessions with them (both in their hallowed college halls with medieval choristers singing in the background) or up at our hospital. Adapting the approach we'd used at McMaster with 1<sup>st</sup>-year students, we presented our Oxford malcontents with patient-scenarios, x-rays, and other diagnostic data and challenged them to explain what was going on in terms of their emerging understandings of the basic sciences. The sessions recaptured the enthusiasm of most, were fun for all, and gradually expanded to include students from other colleges. Similarly, I occasionally took on an entire 1<sup>st</sup> year class for 3 hours, presented them with a 'stercoraceous<sup>66</sup>' confused man with a big belly, and showed them how they could form and test diagnostic hypotheses and proceed from mystification to spontaneous bacterial peritonitis within 1 morning.

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<sup>66</sup>Smelling of shit, which certainly got their attention.

## Chapter III-4: Tell us about bringing EBM to District General Hospitals throughout the UK and beyond.

Once I had sorted out how best to conduct post-take rounds in Oxford, and had collected a series of complaints and misunderstandings about EBM, I started responding to invitations from District General Hospitals throughout the UK.

I negotiated 1-day visits in which I would:

### 1. Conduct a post-take round on the previous day's admissions:

In these bedside rounds with the house staff, I would identify each patient's most useful history; demonstrate relevant, quick, and resource-saving clinical findings (e.g., retinal spontaneous venous pulsation as a means to rule-out suspected, clinically important, raised intracranial pressure); explore observer variation in identifying key physical findings; refine their differential diagnoses; and challenge them about their evidence-base for their initial treatments. I carried my Red Book of previously critically-appraised clinical evidence, and confirmed that 1 of more of its summaries (which we later copied for the team) were relevant to each patient. The objectives here were both to demonstrate bedside-EBM and to establish that their visitor was a competent, hands-on clinician (news that I hoped they'd spread to the rest of the hospital).

### 2. Conduct Medical Grand Rounds to identify and dispel myths and misunderstandings about EBM:

I'd begin by asking them what they thought about EBM. After a slow start, they typically would identify (and I'd write on the board) the 'usual' 20+ questions, criticisms, and 'beefs' about EBM that were currently in circulation. I'd then give them a 20-minute slide-assisted lecture defining EBM, addressing these questions, and addressing their criticisms. I'd close with an open discussion in which they'd typically exhibit at least changes of heart and often enthusiasm about getting EBM resources and education going at their hospital. I'd pledge our help in getting these going. It was at this point that some of their senior clinicians, quiet to this point but not wanting to be left behind in the new wave, would relate personal experiences in which they'd already successfully practiced EBM on individual patients.

### 3. Hold meetings with whoever wanted to discuss how to get EBM going at their hospital:

These meetings identified the local 'movers and shakers' who became prime candidates for our EBM Workshops and for membership in our Centre.

As word of them spread, invitations soared, and soon I was making 1 or more trips a week to UK general hospitals. I reckon I made over 200 of these visits by the time I left Oxford.

Once the CEBM program was established in England, I began to collaborate with colleagues in the Nordic Countries and Europe (taking advantage of Europe's short distances and excellent, frequent trains and planes<sup>67</sup>). Workshops and seminars were held in Finland with Marjukka Mäkelä, in Denmark with Lars Lassen and Finn Børlum Kristensen, repeatedly in Oslo with Andy Oxman's group, in the Netherlands with Harry Buller, in Germany with Gerd Antes, in Italy with Alessandro Liberati, and in South Africa with Merrick Zwarenstein and my hero Jimmy Volmink. My last formal lecture about EBM was in the spring of 1999, in Krakow, in support of Roman Jaeschke's EBM initiatives in Poland (following which my local hosts took me to their salt mine).

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<sup>67</sup>For example, I once held a teaching round in Oxford 1 morning, chaired a symposium in Copenhagen that afternoon, held a working dinner in Basel that evening, gave a lecture in Berlin the following noon, and was home in Oxford for dinner. And my 'frequent traveler' interview appeared in the British Rail magazine.

### Chapter III-5: How did Britain respond to your Introduction of EBM?

As described in the preceding chapters, the response of medical students (Bob Phillips and his classmates put on their own EBM Workshop), post-graduate trainees (the Chair of Medicine told me that growing numbers of applicants for our house jobs listed working with me as their motivation), and individual clinicians throughout Britain and Europe was wonderfully enthusiastic and supportive. But the initial response of the British medical ‘establishment’ was so negative, condescending, and dismissive that I was often miserable for the 1<sup>st</sup> year and a half of my time there.

The establishment considered EBM an affront to their omniscience and authority, and dismissed it as both ‘old hat’ (“everybody’s already doing it”) and a “dangerous innovation, perpetuated by the arrogant to serve cost cutters and suppress clinical freedom.” It was labelled “impossible to practice,” “could be conducted only from ivory towers,” “cookbook medicine,” and “restricted to randomised trials and meta-analyses.” Rather than take me on, a fellow-professor right in Oxford published nasty criticisms of 2 of our younger advocates in a ‘Socratic dissent’<sup>68,69</sup>. Another Oxford colleague, learning that I planned to videotape my forthcoming Grand Round on ‘Observer Variation in Evaluating a Patients with Dysphagia,’ wrote a letter of protest to the Chair of Medicine, stating that I was attempting to destroy the tradition of confidentiality in Oxford’s most cherished hall. And to top it off, an unsigned editorial in the ‘leading’ British and Commonwealth journal, the *Lancet*, appeared under a title that employed the discriminatory Jim Crow rhetoric typical of the Southern USA: “*Evidence based medicine: in its place*”<sup>70</sup>.

Led by Muir Gray, my friends did their best to support and reassure me through this difficult time. And I acquired a new champion in Richard Smith, the Editor-in-chief at the British Medical Journal. Reassuring me that we were on the right track, he opened his journal to us and proposed that we write a counter editorial, defining precisely what EBM *was* and *was not*. Published in January 1996<sup>71</sup>, we defined EBM (“requiring *both* individual clinical expertise and the conscientious, explicit, and judicious use of current best evidence [of any design] in making decisions about the care of individual patients”), and showed that it was possible in routine clinical practice, could not be “cookbook,” and wasn’t limited to RCTs and meta-analyses.

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<sup>68</sup>Grahame-Smith D. Evidence based medicine: Socratic dissent. *BMJ*. 1995;310:1126-7.

<sup>69</sup>As was my practice when my mentees were attacked by senior professors, I hauled the author into my office, told him what I thought of his behavior, and threatened to throw him down the stairs if he ever repeated it. He didn’t.

<sup>70</sup>Unsigned Editorial: Evidence based medicine: in its place. *Lancet*. 1995;346:785.

<sup>71</sup>Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn’t. *BMJ*. 1996;312:71-2.

I credit this editorial (which has received over 10,000 citations to date) with initiating a sea change in the opinions of all but the most reactionary of the British establishment. Destructive criticism plummeted, constructive criticism rose, and their participation in what we were doing soared (see Chapter III-2 for how our 10-year goals were achieved in 4 years).

My spirits lifted, I got on with my work.



## Chapter III-6: Why did you leave Oxford and return to Canada in 1999?

The reasons were 6:

1. We had exceeded all the Oxford EBM Centre's objectives:

As documented in Chapter III-2, with far more EBM Center members than we'd anticipated, we had created more books, more journals, more EBM software, more workshops, more EBM educational programs for students and house staff, and more widespread interest in EBM than we could have imagined when we started in 1994. Both graduate programs were underway, and excellent EBM centers in other disciplines had been launched.

2. I was about to stop practicing bedside medicine:

I'd long been convinced that the judgement of acute-care, bedside internists began to deteriorate at age 65, and had long since resolved not to join them.

3. I was increasingly dissatisfied with my role of EBM 'Expert':

I had long held the view that 'experts' inevitably became detrimental to the fields of their expertise, for 2 reasons. First, their opinions and pronouncements about their field carried a far greater persuasive power than they deserved on the basis of evidence alone. Second, subconsciously (if not consciously), experts' acceptance or rejection of new ideas about their field (presented in the grants and manuscripts they were asked to referee) were influenced by the extent to which these new ideas challenged their prior expert pronouncements.

For these reasons, I had 'resigned' from the field of compliance research back in the early 80's<sup>72</sup>. Matters were even worse for me as the EBM expert: I was considered a nice guy, and colleagues who disagreed with my views were worried about hurting my feelings. Shortly after our return to Canada I published my resignation from EBM in the BMJ<sup>73</sup>, and with the exception of these interviews, I haven't refereed, written, or lectured about EBM since.

4. I'd become ambivalent about Oxford remaining 'the' Centre for EBM:

With so many excellent EBM centres being developed elsewhere, I wondered whether their continuing development might be stifled by the presence of a 'flagship' centre at Oxford. However, if I was leaving Oxford, any decision about the future of the Oxford EBM Centre had to be up to those who remained, not to me, and I had to get out of their way. Fortunately, the world-class clinical epidemiologist Paul Glasziou soon arrived in Oxford on sabbatical, and was appointed Head of the Centre shortly thereafter. And at the time of this writing, the Centre is in the dynamic hands of Carl Heneghan, who'd been one of our student members back at its beginnings.

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<sup>72</sup>Sackett DL. Second thoughts. Proposals for the health sciences--I. Compulsory retirement for experts. *J Chronic Dis.* 1983;36:545-7.

<sup>73</sup>Sackett DL. The sins of expertness and a proposal for redemption. *BMJ.* 2000;320:1283.

5. We missed Canada:

We regarded the Canadian culture as more integrated, and were drawn homeward to it.

6. We missed our family and friends and our Irish Lake paradise:

We were homesick.

So, after a series of touching public and private farewells, we came home in the spring of 1999.

## Section IV: Back Home to Irish Lake: 1999 – 2015

### Chapter IV-1: Why did you start the Trout Workshops, and what were they about?

Shortly after settling back home, requests started pouring in for me to give weekly lectures, tutoring, and regular seminars at McMaster, the University of Toronto, and the University of Western Ontario. However, our home, up on the Bruce Peninsula (that separates the main body of Lake Huron from Georgian Bay), was a 5 to 7 hour round-trip from these universities. It just didn't make sense to drive for 6 hours in order to teach for just one.

On the other hand, we mused, might it make sense to have learners come up to us? Our cottage on Irish Lake (a 20-acre, spring-fed, trout-stocked lake from which we'd banned gasoline) could sleep 9 (to accommodate our 7 grandchildren who came for "Camp Irish Lake" each summer). And, just 700 meters through the adjacent forest, our country house included a large solarium that could serve as a classroom. Barbara enthusiastically offered to feed us all from her new, expanded kitchen, and we sent a prospectus to friends and colleagues around the world.

The key elements of Trout Workshops were 8:

1. Our objective was to help clinical epidemiology graduate students and new faculty increase their mastery of some principles, strategies and tactics of clinical-practice research into (especially) therapy, but also into diagnosis, prognosis and etiology; and to help them grapple with the challenges of career development and academic success in clinical-practice research.
2. Trout Workshops were held 3 times a year: January, May and October.
3. Applicants from any country submitted their protocols, from which I would select 6, designate them "Trout Fellows," and engage in a vigorous exchange of comments and criticisms about their protocols prior to the Workshop.
4. Trout Fellows found their ways to our cottage, settled in, and trekked to our house for dinner and an evening session of orientation and brief presentations of their (previously circulated) protocols.
5. During the next 2 days, each Trout Fellow chaired and controlled 2 general sessions in which they raised, discussed, argued about, and resolved the methodological issues that needed solutions if their protocols were to succeed. I contributed an occasional summary or example, but they did most of the work.
6. Meals and informal sessions were spent responding to Fellows' questions and concerns about career development, work-life balance, mentoring, and any other topics they wished to raise.

7. And 1 afternoon was open for exploring the lake (in its liquid or solid state) and countryside, and being introduced to rowboats, swim rafts, kayaks, snowshoes, ice skates and a nearby tavern.

8. Tuition was free (we paid for the Workshops through the fees I collected as an expert witness taking on big Pharma).

Between October 1999 and October 2006, we held 17 Trout Workshops for over 100 Trout Fellows from 5 continents. Our Fellows' feedback reported >80% success in getting their protocols funded and underway, and agreed with us that the Workshops were both intellectually stimulating and enormous fun. New friendships flourished among the Fellows, and I continue to meet and correspond with dozens of them.

## Chapter IV-2: Why did you start the Clinician-Trialist Rounds, and what were they about?

When the Society for Clinical Trials (SCT) was formed in 1979, its President, Curt Meinert, invited me to join. I politely refused. The SCT was a gathering place for ‘true believers’ in the RCT, whereas I was laboring in the contentious battlefields of frontline clinical medicine where the RCT had to contend with tradition, ‘1<sup>st</sup> principles’, experts, and special interest groups in deciding which treatments ought to be provided to our patients (PubMed yields only 2,478 ‘hits’ for ‘randomized trials’ that year, compared to 31,645 for 2014). I reckoned the meetings I ought to attend were the big annual clinical research meetings where I could debunk non-RCT approaches to determining best treatments. Rather than meet with the converted at the SCT, I devoted my efforts to my invited address on RCTs for the annual meeting of the premier North American clinical research establishment<sup>74</sup>.

By the time we returned to Canada from Oxford in 1999, the RCT had gained acceptance (however grudgingly) among frontline clinicians and decision-makers, and I was delighted to join the SCT and immerse myself in its friendly membership, wonderful science, and annual get-togethers. However, it didn’t have very many clinician-trialists in its membership, and Dr. Yves D. Rosenberg of the NIH and I agreed to try to increase their interest and numbers in the Society.

My contribution to our effort, supported wonderfully by Steve Goodman, the then-Editor of the Society’s journal, was to offer a regular column (each 1 short enough [<2000 words] to be digested ‘at a single sitting’). Applying the format of the traditional ‘medical grand round,’ each *Clinician-Trialist Round* begins with a ‘Case’ in which a clinician-trialist (often at the start of their career) faces a problem, either with an RCT they are designing or conducting or with their career-development. The discussion briefly summarizes either the available evidence or the opinions we gathered from a world-wide net of trialists, and closes with a resolution of the case.

Steve Goodman introduced the series thus<sup>75</sup>:

*“Courtesy of the inimitable David Sackett, we are inaugurating a new column devoted to career advice for the clinician-trialist, a career path that has become increasingly difficult for many of the reasons that Sackett attempts to address in this series. You will see that the tone and content of the column, like its author, are informal, irreverent, wise, but overall, real. He talks about the life and career management skills that are needed to foster success in this field, in which clinician investigators are desperately needed to assure that clinical trials are asking the*

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<sup>74</sup>The American Federation for Clinical Research, the American Society for Clinical Investigation, and the Association of American Physicians.

<sup>75</sup>Goodman S. On making clinical trials possible. *Clin Trials*. 2010;7:621.

*right questions, but professional, economic, and social pressures are making it increasingly difficult for them to choose this path. While Sackett's advice will make the biggest difference for those early in their careers, this non-early-career trialist can testify that it is never too late to receive it. Sackett has all the bona fides to offer such advice, but more importantly, an endless wellspring of good humor and a passionate commitment to nurturing the next generation of clinician researchers. I welcome him to our pages, and look forward to his jovially serious wisdom over at least the next year."*

At the time of this writing in 2014, 27 Clinician-Trialist Rounds (often jointly authored) had been published:

- 1: Inauguration, and an introduction to time-management for survival. Clin Trials 2010;7:749-51.
- 2: Time-management of your clinical practice and teaching. Clin Trials. 2011;8:112-4.
- 3: Priority setting for academic success. Clin Trials. 2011;8:235-7.
- 4: Why not do an N-of-1 RCT? Clin Trials. 2011;8:350-2.
- 5: Cointervention bias – how to diagnose it in their trial and prevent it in yours. Clin Trials. 2011;8:440-2.
6. Testing for blindness at the end of your trial is a mug's game. Clinical Trials. 2011;8: 674 – 6.
7. Mentoring – Part 1: why every clinician-trialist needs to get mentored. Clin Trials. 2011;8:771-3. (with Sharon Straus)
8. Mentoring – Part 2: The structure and function of effective mentoring: linkage, resources, and academic opportunities. Clin Trials. 2012;9:127-30. (with Sharon Straus)
9. Mentoring – Part 3: The structure and function of effective mentoring: advice and protection. Clinical Trials. 2012;9:272-4. (with Sharon Straus)
10. Mentoring – Part 4: The essential attributes of an effective mentor. Clin Trials. 2012;9:367-9. (with Sharon Straus)
11. When your grant gets turned down. Part 1: remorse, anger and reconciliation. Clin Trials. 2012;9:447-9. (with Peter Szatmari)
12. When your grant gets turned down. Part 2: Resurrection. Clin Trials. 2012;9:660-3. (with Peter Szatmari)
13. Ways to advance your career by saying "no" Part 1: Why to say "no" (nicely), and saying "no" to email. Clin Trials 2012;9:806-8. (with Andrew Oxman)
14. Ways to advance your career by saying "no". Part 2: When to say "no," and why. Clin Trials. 2013;10:181-7. (with Andrew Oxman)
15. Ways to advance your career by saying "no". Part 3: How to say "no," nicely. Clin Trials. 2013;10:340-3.
16. Mind your explanatory and pragmatic attitudes! – part 1: What? Clin Trials. 2013;10:495-8.
17. Mind your explanatory and pragmatic attitudes! – part 2: How? Clin Trials. 2013;10:633-6.

18. Should young (and old!) clinician-trialists perform single-arm Phase II futility trials? Clin Trials. 2013;10:987-9.
19. Faux pas or fraud? Identifying centers that have fabricated their data in your multi-center trial. Clin Trials. 2014;11:128-30. (with Janice Pogue)
20. Shouldn't 'trialists-in-training' rotate through RCT-clerkships? Clin Trials. 2014;11:263-6.
- 21: The presenting complaints, diagnoses and treatments of mentorships in trouble. Part 1: Dysfunctional mentorship meetings. Clin Trials. 2014;20:376-9. (with Sharon Straus)
- 22: The presenting complaints, diagnoses and treatments of mentorships in trouble. Part 2: Abuses of power. Clin Trials. 2014;11:508-11. (with Sharon Straus)
- 23: When an RCT's Data Center Report drowns vital information in seas of data: Where's Waldo? Clin Trials. 2014;11:601-4. (with Janice Pogue)
24. Modernizing your introductory graduate course in clinical trials. Part 1: Commonsense meets evidence. Clin Trials. 2014 Dec;11:681-4. (with Geoff Norman)
25. Designing an evidence-based introductory graduate course in clinical trials. Part 2: Applying the evidence to your RCT course design. Clin Trials. 2015;12:91-3. (with Geoff Norman)
26. Sabbaticals. Part 1: Should I take a sabbatical? Clin Trials. 2015;12:174-6. (with Sharon Straus)
27. Sabbaticals. Part 2: I'm taking a sabbatical! How should I prepare for it? Clin Trials. 2015;12:29. pii: 1740774514567970. [Epub ahead of print] (with Thomas Stelfox and Sharon Straus)

The Rounds dealing with mentoring have been incorporated into the book *Mentorship in Academic Medicine* that Sharon Straus and I published in 2014<sup>76</sup>.

Feedback via letters, email, and conversations has been uniformly positive (but who would write to me complaining that they hated the series?).

Writing them (especially with co-authors) has been enormous fun.

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<sup>76</sup><http://www.mentorshipacademicmedicine.com/>

### Chapter IV-3: Why did you (and your mates) become satirists?

I attribute this to the effect of day-long ‘reunion’ hikes along the Thames with Andy Oxman and Iain Chalmers, good English beer, suppressed anger, the Christmas BMJ (which invited humorous papers), and an amalgamation of our Canadian-American-Norwegian-English senses of humor.

Despite great progress (CONSORT and its progeny, registration of RCTs, etc), there was still plenty wrong with how RCTs were manipulated and how trialists were messed about by their bosses. These problems were included in the panoply of topics we discussed during our jaunts. Although we’d already contributed to the serious literature about these problems, we decided that it would be fun to collaborate in the use of humor, irony, mockery, exaggeration, derision, ridicule, scorn, and caricature to expose and criticize them and their perpetrators.

Authorship (sometimes including Dr. Trine Prescott, a clinical geneticist from Oslo) shifted with our interests and other commitments. I contributed to 3 of the rants<sup>77,78,79</sup>, some of which were re-published (sometimes translated<sup>80</sup>) in other journals. Two examples will supply both the flavor of our rants and readers’ responses to them.



**HARLOT** satirized the greed and manipulation by those who profit from distorting the conduct, analysis and interpretation of RCTs by forming a new company to help them achieve their nefarious objectives. Andy and I authored the piece (Iain declined to be a co-author because he maintained he hadn’t earned it, not because of any dividends that might accrue from the enterprise, which explains the ‘Where’s Wally/Waldo’ visage on the conspirator to the left of the closing figure).

<sup>77</sup> Oxman AD, Chalmers I, Sackett DL: A practical guide to informed consent to treatment. *BMJ*. 2001;323:1464-6.

<sup>78</sup> Sackett DL, Oxman AD. HARLOT plc: an amalgamation of the world’s two oldest professions. *BMJ*. 2003;327:1442-5.

<sup>79</sup> Oxman, A. D, Sackett, D. L, Chalmers, I., Prescott, T. E. A surrealistic mega-analysis of redisorganization theories. *J R Soc Med*. 2005; 98:563-8.

<sup>80</sup> Sackett DL, Oxman AD. Prostit S.A.R.L.: La fusion des deux plus vieux métiers du monde. *Prescrire*. 2004;24:302-6.



Our offerings included:

1. *E-Zee-me-Too Protocols* with selective, non-systematic reviews, substituting placebos for established effective treatment, unconcealed allocation to ensure better prognoses in "experimental" patients, "mini-max" manipulation of the competitor's product, incorporating irrelevant surrogate and composite end points, and "shifting the goal posts" for "superiority" and "non-inferiority";
2. immediate RCT approval (including uninformed consent) from our *Ethics Are Us* outlets in most shopping malls;
3. *RATs (Research Administration Teams)* who would add efficacious co-interventions to (just) your product, and carry out both unblinded outcome assessments and repeated interim analyses;
4. a *Find the Pony Statistical Unit* who would carry out subgroup analyses until they found a statistically significant one that favored your product and over-interpret any indeterminate results in your favor;
5. a *SAFE (Say Anything For a Euro)* panel of experts who would laud your product, write guidelines endorsing it, and referee any manuscripts about it;
6. assembling a *SCUM (of Sick Celebrities to Use in the Media)* to get onto talk shows, into gossip magazines, and at the front of parades on any issue;
7. a *PPCT (Pay the Piper and Call the Tune)* of journalists to monger your disease and laud your product in the lay media;
8. an *RCAF (Rabid Citizens Against Facts)* of secretly funded 'patient action' groups that would attack any counter-evidence that exposes your product as useless or harmful;
9. a squad of *SHARKS (Striking horror and Retreat through Killer Solicitors)* who would threaten nay-sayers and drug-review boards with frivolous but expensive SLAPP (Strategic Lawsuit Against Public Participation) law suits;
- 10, ff. and so on, including rescue packages for executives who are caught cheating, etc.

The responses to HARLOT (in the BMJ Rapid Response column, emails, and letters) were many and humorous, and culminated in its translation and publication as '*Prostit S.A.R.L.*' in the French journal *Prescrire* noted above.

Our '*surrealistic mega-analysis of redisorganization theories*' included both justifications for it:

- There is need to hide the fact that an organisation has no reason to continue to exist.
- It has been 3 years since the last reorganisation.
- A video conferencing system has just been purchased out of an employees' retirement fund.
- The CEO's brother is an organisational consultant.
- The auditor general's report is about to be released.

-and indicators of a successful redisorganisation:

- All the good people have left or become catatonic.
- Inept people have been given tenure or its equivalent.
- Important decisions have been postponed or are being made on a whim-to-whim basis.
- Resolutions have been mistaken for solutions.
- The number of administrators has at least doubled.
- Vast resources have been diverted from patient care, research and education and spent on relocating and refurbishing executive offices and supplying them with the flashiest business machines.
- Administrators' office windows point toward, not away from, nearby mountains, lakes, and oceans.
- Large consultancy fees have been paid to relatives by blood or marriage (hence HARLOT's recruitment program).

- all of which formulated the ABCD of any successful redisorganisation:

- **A** minimum amount of thought has gone into a maximum amount of change.
- **B**rownian motion has been mistaken for progress.
- **C**oincidence has been mistaken for cause.
- **D**ecibels have been mistaken for leadership.

And we closed with advice for well-functioning enterprises who wanted to avoid being redisorganised:

- Fake it, and only make it look like you are redisorganising yourselves.
- Schedule (but don't hold) countless meetings.
- Plagiarise, photocopy and distribute (on coloured paper) strategic plans lifted from out-of-town redisorganizers.
- Rename traditional sporting and social events "team-building."
- Get on with doing your job.

Reactions to our redisorganization rant were both frequent and remarkably consistent: "I

laughed until I cried, realized it was all true, and then *really* cried.” And the United Nations Staff Association republished it in its newsletter!

We enjoyed the reactions to our rants, but our real fun was in the process of discussing, debating, and writing together.

## Section V: My career as a Clinical Epidemiologist

### Chapter V1: What or who inspired you to think that epidemiology could be useful for studying clinical problems and improving health care? What and who encouraged or discouraged you?

The evolution of these thoughts and actions can be traced through several prior chapters of this interview:

Chapters I-3 (med school) and I-4 (post-grad medical training) describe both my growing dissatisfaction with the evidence that was being applied to guide the diagnostic and therapeutic decisions of those days, and my great (but unsophisticated) attraction to the RCT as the best way to decide about therapy. My views were tolerated but not encouraged at this stage of my career.

Chapters I-5 (US Public Health Service) and I-7 (Boston) describe my growing understandings of classical epidemiology and biostatistics, my emerging thoughts on how they might be applied to individual patients, and my decision to appropriate<sup>81</sup> the term 'clinical epidemiology' to describe this new way of thinking. As reported therein, my views were now encouraged, especially by Warren Winkelstein, Evan Calkins, and Brian MacMahon.

But the proof of this pudding occurred at McMaster, exemplified in Mike Gent's and my collaboration with Jack Hirsh and his world-class thromboembolism group. Our growing understanding of ways to extract greater information from diagnostic test results<sup>82</sup> led to a series of landmark papers on the diagnosis of potentially lethal deep vein thrombosis by signs and symptoms, impedance plethysmography, blood tests, and ultrasound. And our growing sophistication in RCTs led to a landmark series of trials in the prophylaxis, immediate and long-term treatment, and prognosis of these patients. These studies set the standard of care for these patients around the world.

Clinical epidemiology had proven its usefulness, at least to us!

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<sup>81</sup>As noted previously, the term "clinical epidemiology" was 1<sup>st</sup> introduced by John Paul, an infectious disease epidemiologist, in 1938 [Paul JR. Clinical epidemiology. J Clin Invest. 1938;17:539-41]. However, his concept of clinical epidemiology had a population rather than individual patient orientation and was designed to "start the student at the bedside and lead him gradually away from it."

<sup>82</sup>Sackett DL. Interpretation of diagnostic data: 6. How to do it with more complex maths. CMAJ. 1983;129:1093-9.

### Chapter V-3: How did you get into medicolegal work, and what has it meant to you?

Medicolegal work found me in the early 1980s when 1 of my medical students gave my name to a prominent Toronto lawyer who then challenged me to help him sue a major drug manufacturer on behalf of a woman who had suffered a disabling stroke while taking their oral contraceptive. The challenge was attractive for 6 reasons: the company had already bullied her and brushed off her request for a few thousand dollars to pay off her modest mortgage; they boasted that they had never lost a suit like hers in Canada; I was aware of some promising evidence on stroke risks from their drug; putting that evidence together could provide a great experience for an elective student, Dr. Ruth St. Amand; my lawyer's keen mind was hidden beneath an engaging imperialistic, bombastic personality; and both of us would work for free so that the entirety of any settlement would go to the victim. In short, it would be worthy, educational, and fun (indeed, I quickly named him "Lumpy" and he named me "Cigar-thief"). By restricting my testimony to cohort studies (thus avoiding cross-examination around my earlier published criticisms of case-control designs, and armed with drug inserts from the U.S. (which warned users about stroke risks) and Canada (which did not!), we won the case and a subsequent appeal and our plaintiff was awarded several hundred thousand dollars.

Learning of our success, shortly thereafter a branch of Health and Welfare Canada asked me (once again, 'pro bono') to help them prosecute a group of flim-flam artists who were descending on unsuspecting farmers 'to test the safety of their well water.' Knowing the high calcium content of rural 'hard water,' the charlatans would scare the farmers and their families by adding the Sulkowitch reagent to it and, before their eyes, precipitate a scary white cloud (or even clot) of calcium oxalate. In shocked tones, the charlatans would scare the hell out of the farmers by telling them that their water was likely to give them cancer, gall stones, kidney stones, arthritis, hardening of the arteries, cataracts, etc., etc., but that they could prevent and cure these disasters by immediately purchasing an obscenely overpriced water distiller that the 'testers' happened to have brought with them. Fueled in part by righteous indignation, a junior colleague, Larry Chambers, and I combed the Medline of the day for evidence that 'hard' water caused, or distilled water cured, these maladies. At the conclusion of our courtroom documentation of the absence of such evidence, the defense refused to cross-examine me, abandoned the case, and their defendants were put out of business. (Twenty years later, while strolling through exhibits at an International Plowing Match in rural Ontario, I spotted a suspicious pair of salesmen who were flogging water distillers to the passing farm families. Fearing that I'd 'blow' my cover and get into a shouting match with them, I hid outside and made Barbara go back and talk to them to see if they were the same outfit making the same claims – they weren't, and didn't!)

I found these cases worthy (little guys taking on and beating up big guys), educational (working with junior colleagues and smart lawyers to identify and convert scientific evidence to courtroom evidence), exciting (my courtroom battles of wits with defense lawyers), and therefore great fun. However, my increasing clinical responsibilities precluded taking on more of them until I retired from clinical practice at age 65 when we returned from Oxford in 1999.

By then, both my motivation and the ‘rules of engagement’ had changed. We were living on Irish Lake and I was resisting cordial invitations to commute weekly for 6-8 hours in order to teach for just 2 hours at McMaster and the Universities of Toronto and Western Ontario. As described elsewhere (see ‘Trout Workshops’), Barbara and I proposed an alternative educational contribution in the form of thrice-yearly 3-day residential “Trout Workshops” to be held at Irish Lake. Because it was not in our nature to make money from serving learners, there was no tuition fee, and we were scrimping to make them possible.

Requests for my medicolegal input had changed, too. They were now coming from large legal firms with deep pockets, conducting multiple class-action suits against big Pharma and major manufacturers. To my former criteria for taking on a case on behalf of injured patients I now added a new one: whether the law firm would pay me enough to support our Trout Workshops. Fortunately, several were willing to do so, and they made it possible for us to support the lodging, feeding, and education of 106 Trout Fellows.

But this generation of litigation became less and less evidence-based and therefore much less fun. Pre-trial ‘discoveries’ by defense lawyers became nit-picking 8-hour interrogations in search of inconsistent language I might use to describe consistent evidence, and courtroom cross-examinations became ‘team-tag’ assaults from beavies of lawyers who delighted in introducing sight-unseen ‘new’ and invalid evidence designed to unnerve and exasperate. Science became progressively replaced by ‘show-business,’ and I eventually joined the growing numbers of expert witnesses who were willing to provide written depositions but refused to appear in court. Finally, when we sold our house/eating place/classroom, stopped our Trout Workshops, and moved full-time to our cottage, I quit accepting invitations to do all medicolegal work.

Finally, to illustrate the opportunities for fun in testifying, even late in the game, I close with a ‘Walter Mitty-come-true’ episode from a southern U.S. courtroom: The ‘clean-up’ lawyer in a tag team had just handed me a paper (I’d never seen before), claiming that it was an RCT proving the harmlessness of the drug in dispute. I signaled my lawyer, who immediately requested a recess, during which I studied the paper and established that it was not an RCT. When court reconvened and I demonstrated his error, he stated: “Well, I could take several more days and show you dozens more papers on this topic, but the jury would probably want to lynch me.” I replied, “I would welcome that.” He replied, “Well, we could meet after the trial and go over these papers together.” I replied, “No, I meant that I would welcome the lynching.” [Pandemonium, gavel pounding, “Order in the Court!” etc.]

## Section VI: My career as a Clinical Trialist.

### Chapter VI-1: Why did the RCT become the primary focus of your career<sup>83</sup>?

I suppose this process began when I came to the University of Illinois College of Medicine in 1956 where, despite its well-deserved high reputation, a recent therapeutic scandal was smoldering (and occasionally bursting into flames). Its university Vice-President-Director and famous physician-physiologist, Dr. Andrew Ivy (a renowned g-i physiologist who had represented the American Medical Association at the Nuremberg Nazi Doctors Trial and subsequently became Executive Director of the National Advisory Cancer Council and a director of the American Cancer Society), had recently been accused of fraudulently defending the efficacy of a quack cancer remedy, Krebiozen (which turned out to be simple creatine)<sup>84</sup>. Although none of my teachers (some of whom were involved in attempts to resolve the dispute) ever spoke of the scandal, there was an atmosphere of skepticism toward authority figures around the place that fostered iconoclasm.

For example, by 1959 I had become a final-year medical student, and I once found myself responsible for a teenager who had been admitted to a medical ward with hepatitis (this episode is described in detail elsewhere, both in my answer to the question: Tell us about medical school. What happened there, and how did it shape your later career?, and in an essay I wrote for the James Lind Library<sup>85</sup>). After a few days of enforced total bed rest – the standard management of the condition - his spirits and energy returned and he asked me to let him get up and around. I felt I needed to have a look at relevant evidence to guide my response to his request. I went to the library and came across a remarkable report<sup>86</sup> of a meticulously conducted randomized trial had made clear that there was no good evidence to justify requiring hepatitis patients to remain in bed after they feel well. Armed with this evidence, I convinced my supervisors to let me apologize to my patient and encourage him to be up and about as much as he wished. His subsequent clinical course was uneventful.

Gathering momentum, during my post-graduate training in internal medicine, the better I became at diagnosing my patients' illnesses, the more frustrated I became at my profession's collective ignorance about how I should treat them, or whether I should treat them at all. I was already caring for patients at McMaster when the practice of treating 'peptic' ulcers by freezing

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<sup>83</sup> Sackett DL (2015). Why did I become a clinician-trialist? JLL Bulletin: Commentaries on the history of treatment evaluation (<http://www.jameslindlibrary.org/articles/why-did-i-become-a-clinician-trialist/>).

<sup>84</sup> Ivy AC. [Krebiozen](#). Science. 1951;114:285-6.

<sup>85</sup> Sackett DL (2008). A 1955 clinical trial report that changed my career. JLL Bulletin: Commentaries on the history of treatment evaluation ([www.jameslindlibrary.org](http://www.jameslindlibrary.org))

<sup>86</sup> Chalmers TC, Eckhardt RD, Reynolds WE, Cigarroa JG, Jr, Deane N, Reifenshtein RW, Smith CW, Davidson CS. The treatment of acute infectious hepatitis. Controlled studies of the effects of diet, rest, and physical reconditioning on the acute course of the disease and on the incidence of relapses and residual abnormalities. Clin Investig. 1955;34:1163-1235.

stomachs came into question<sup>87</sup>, and prior to 1967<sup>88</sup>, the ‘experts’ advised against treating symptomless diastolic blood pressures <130 mm Hg).

Contemporary therapeutics was mostly based on clinical observations of treatments applied by expert clinicians. But I came to the conclusion that there were 4 things wrong about the way they were using their clinical observations in those days to decide whether a treatment did more good than harm; more precisely, I was worried that these 4 ‘wrongs’ destroyed our ability to make ‘fair comparisons’ of the effects of different treatments. The validation of these worries both initiated and reinforced my decision to devote most of my career to RCTs.

Worry #1: I became worried that clinicians might preferentially give new treatments to patients with better prognoses.

One of my ‘rotations’ as a 1st year medical resident was the Admitting Clinic, where I evaluated referrals from all over Illinois (who were seeking the free care we could provide) to determine whether they would be ‘good teaching cases’ for the medical and surgical services at our Research and Educational Hospital. My surgical resident colleague taught me that they had 2 ‘general surgery’ services, and that they evaluated innovative operations by performing them on the ‘A Service’ (where he scrubbed) while continuing to perform standard operations on the ‘B Service.’ Although a perfect setting for randomization, when we examined a patient and found them suitable for one of their comparative studies, my surgical colleague decided where they went. Over time, I became convinced that he was preferentially admitting eligible surgical patients with sounder hearts, healthier lungs, and higher hematocrits to receive the new, promising operations on his ‘A Service.’ Thus sensitized, I began to pay more attention to the therapeutic recommendations for new, untested treatments I received from my medical attendings and consultants, and again concluded that, within the same illness, it was my healthier patients whom they considered ‘good candidates’ for the latest, untested treatment.

It was decades later that Iain Chalmers introduced me to the most telling confirmation of this 1<sup>st</sup> concern. In New York City in the 1930’s, babies born into households that included members with pulmonary tuberculosis were at high risk of dying from the disease before their 1<sup>st</sup> birthdays. Although the BCG vaccine was already in use and touted to protect such infants, a New York City public health team that included Margaret Sackett<sup>89</sup> was skeptical about these claims and therefore carried out 2 BCG ‘trials.’<sup>90</sup> In the 1<sup>st</sup> ‘trial,’ public health physicians were assigned batches of at-risk newborns and told: “vaccinate half of them.” The results were spectacular: the risk of dying before their 1<sup>st</sup> birthday was reduced by 80% among vaccinated babies.

In the 2<sup>nd</sup> “trial,” however, the decision about whom to vaccinate was taken out of the

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<sup>87</sup>Bunker JP, Barnes BA, Mosteller F. Costs, Risks, and Benefits of Surgery. New York: Oxford University Press, 1967.

<sup>88</sup>Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension: Results in patients with diastolic pressures averaging 115 through 129 millimeters of mercury. JAMA. 1967;202:1028-34.

<sup>89</sup>I do not know whether we are related, but I herewith claim to be her long-lost nephew.

<sup>90</sup>Levine MI, Sackett MF. Results of BCG vaccination in New York City. Am Rev Tuberc. 1946;53:517-32.



physicians' hands and was determined by 'drawing lots,' generating a fair comparison of BCG efficacy. The results were no less spectacular, but in this case quite 'negative:' the risk of dying before their 1<sup>st</sup> birthday was identical between vaccinated and non-vaccinated babies.

This presented the opportunity to determine how the physicians in the 1<sup>st</sup> trial (told to "vaccinate half of them") made the decision to vaccinate some babies but not others. This inquiry revealed that they were more likely to vaccinate babies who were headed for wealthier, less crowded households whose family members had less severe tuberculosis. The BCG-inoculated babies had better prognoses before they were vaccinated!

Thus, clinicians often do preferentially treat patients with better prognoses. And, that's why our RCTs employed the 'fair comparison' strategies of random allocation and concealment (from treating clinicians) of the treatment that was destined to be given to the patient they were considering enrolling onto an RCT<sup>91</sup>.

Worry #2. I became worried that compliant patients might have better prognoses, regardless of their Rx.

My 1<sup>st</sup> 5 clinical years as student and post-graduate trainee gave me the opportunity to observe and contribute to the care of a few hundred patients, and I'd kept an irregular list of their treatments, clinical courses and outcomes folded into my copy of Harrison's medical text. As they accumulated, 2 perplexing conclusions emerged. First, I was surprised to discover that only about half of my patients regularly refilled their prescriptions and took their medicine (it was already 'common knowledge' that we physicians were poor compliers, but we'd naively thought our patients were much better). Some of them simply disappeared, and those that returned to clinic continued their poor compliance despite our exhortations and often succumbed to their illnesses.

Second, the rest of my patients who refilled their prescriptions on time and appeared compliant not only had better prognoses, but appeared to achieve them regardless of whether my treatments were supported by strong evidence (e.g., the early trials in complicated severe hypertension), on the one hand, or by little or no evidence (e.g., the contemporary treatments for coronary heart disease), on the other. Looking more closely, I noted that they also were less likely to be smokers, heavy drinkers, or overweight. Finally, and harking back to my 1<sup>st</sup> 'worry,' they often were the patients whom my seniors picked as 'good candidates' for new, untested treatments.

On the basis of the foregoing, I began to worry whether high compliance might be a 'marker' for rosier prognoses, regardless of therapy. Confirmation of this 'worry' had to wait for compelling examples of this phenomenon in analyses of placebo groups in RCTs. For example, when the 1960's Coronary Drug Project<sup>92</sup> randomized myocardial infarction survivors to

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<sup>91</sup>Sackett DL. The tactics of performing therapeutic trials. In: Haynes RB, Sackett DL, Guyatt GH, Tugwell P. Clinical Epidemiology. 3<sup>rd</sup> Ed. How to Do Clinical Practice Research. Philadelphia: Lippincott Williams & Wilkins, 2006. P 86.

<sup>92</sup>I had entered patients into this trial when I was a house officer in Buffalo in 1966.

placebo or 1 of several of that decade's lipid-lowering agents, they were hard-pressed to find a drug that worked. For example, the 5-year mortality for participants randomized to clofibrate (20%) was no better than for those randomized to placebo (21%)<sup>93</sup>.

Their hopes rose when they noted that a 3<sup>rd</sup> of clofibrate-assigned patients were taking less than 80% of their assigned meds, and they decided that a better measure of clofibrate's efficacy would be to compare the mortality of clofibrate non-compliers with that of the majority who were taking 80% or more of their clofibrate. The results were (temporarily) encouraging: good 'adherers' to clofibrate had substantially lower 5-year mortality than did poor adherers to clofibrate (0.15 vs. 0.246; RRR = 39%; P = 0.00011).

However, the hero-statistician of the trial, Paul Canner, carried out a similar analysis for participants who did and didn't take their placebos and showed an even greater compliance 'effect' on mortality (0.151 vs. 0.282; RRR = 46%; P = 0.00000000000000047). The NNT to save another life by faithfully taking the placebo was 10! And, in a major contribution to our (?non-) understanding of the 'compliance-effect,' they documented that the increased risk of death among poor placebo compliers could not be accounted for by the measures one might insert into a 'propensity score,' in this case 40 baseline characteristics associated with 5-year mortality. After this 'propensity score correction,' the RRR of 46% only fell to 36%, and the P-value from 0.00000000000000047 to a still-overwhelming 0.00000000073.

The investigators concluded: "These findings and various other analyses of mortality in the clofibrate and placebo groups of the project show the serious difficulty, if not impossibility, of evaluating treatment efficacy in subgroups determined by patient responses (e.g., adherence or cholesterol change) to the treatment protocol after randomization."

Compliant patients do have better prognoses, regardless of their Rx (as long as it isn't inherently toxic). And that's why our RCTs have employed the 'fair comparison' strategies of unobtrusive compliance measures, intention-to-treat analyses<sup>94</sup>, and keeping track of everybody who enters them<sup>95</sup>.

Worry #3. I became worried that patients who liked their Rx might report better outcomes unrelated to the true efficacy of their treatments.

As clinical clerks on the internal medicine service, we were encouraged to read the Journal of the American Medical Association and the New England Journal of Medicine. For example, in

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<sup>93</sup>Influence of adherence to treatment and response of cholesterol on mortality in the coronary drug project. N Engl J Med. 1980;303:1038-41.

<sup>94</sup>Thus, 'per-protocol' analyses confined to compliant patients are inherently invalid, and I consider them nefarious when carried out by folks who know better.

<sup>95</sup>I recently toted up the losses-to-follow-up among the >12,000 participants from trials in which I was a PI or co-PI and they amount to 0.4%. On the other hand, Michael Walsh and colleagues have documented that over 50% of 'positive' RCTs in leading journals have losses to follow-up that exceed the fragility of their positive result (Walsh M, Srinathan SK, McAuley DF, et al. The statistical significance of randomized controlled trial results is frequently fragile: a case for a Fragility Index. J Clin Epidemiol. 2014; 67:622-8).

May of 1959 we learned from JAMA about the 1<sup>st</sup> few successful cardiopulmonary resuscitations and how the active ingredient in the Sabin polio vaccine rapidly spreads throughout an institutional population, and the NEJM told us how to select patients for 'definitive' surgery for their duodenal ulcers and how we could obtain rapid polio immunization by injecting 10 mL of the Salk vaccine.

But the paper in the NEJM that made the greatest, lasting impression on me was the report from a surgeon, Leonard Cobb, and his colleagues who had randomized a group of patients who were so seriously limited by angina that the majority were unemployed.<sup>96</sup> Randomized to what? In the decade before their RCT, thousands of angina pectoris patients had undergone the 'miracle operation' of internal mammary artery ligation (based on the theory that blood previously coursing down these arteries would be partially redistributed to the coronary circulation). As reported in Readers' Digest for July 1957<sup>97</sup>: "complete or partial relief from the pain that accompanies the major types of heart disease has been obtained in nearly 80% of the several hundred operations performed to date." This simple operation (done under local anesthesia in just a few minutes) became so popular that I was suggested: "It is, perhaps, surprising that between 1955 and 1960 there were still patients with angina whose mammary arteries were not ligated." Indeed, all 3 patients I had examined with incidental intercostal scars claimed their operations had improved or relieved their angina. Thus, although Cobb's RCT "subjects were informed of the fact that this procedure had not been proved to be of value. . . many were aware of the enthusiastic report published in Readers' Digest."

Cobb's trial patients had their internal mammary arteries surgically exposed (while screened from their vision). After a ligature had been loosely placed around these arteries, the surgeon was handed a "randomly selected envelope" which contained a card instructing him either to tie off the arteries, or to remove the loose ligature and leave them alone. Thus, the patients had neither the choice nor the knowledge of whether their arteries were ligated.

During their 3-15 month follow-up by physicians who were blind to whether trial participants been ligated, some spectacular results were documented: for example, Case #4, previously unable to work because of his angina, reported almost instant relief and was able to return to work. In fact, however, his arteries had not been ligated. On the other hand, "The average improvement was 32% for the ligated patients and 43% for those whose internal mammary arteries were not ligated." The trialists concluded: "Bilateral skin incisions in the 2<sup>nd</sup> intercostal space seem to be at least as effective as internal-mammary-artery ligation in the therapy of angina pectoris."

Although internal mammary ligation rapidly disappeared after this and a 2<sup>nd</sup> RCT, this "positive expectation bias" has continued to haunt attempts to critically appraise therapeutic fads to the

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<sup>96</sup>Cobb LA, Thomas GI, Dillard DH, Merendina KA, Bruce RA. An evaluation of internal-mammary-artery ligation by a double-blind technic. N Engl J Med. 1959;260:1115-8.

<sup>97</sup>Ratcliff JD. New surgery for ailing hearts. Readers' Digest. July 1957:109-12.

present day, as we continue to debate the efficacy of ‘liberation therapy’ for patients with multiple sclerosis.

Patients who like their Rx do report better outcomes unrelated to the true efficacy of their treatments. That’s why our RCTs employed (whenever possible, and it’s possible more than detractors might think) blinding of trial patients to their treatments, ‘hard’ outcomes such as total mortality, and the ‘blind’ adjudication of softer outcomes.

Worry #4. I was worried that clinicians who liked their Rx might report spuriously better outcomes among patients who received them.

The internal mammary ligation fiasco also hardened my worry that physicians writing prescriptions might be as guilty of over-reporting their favorable effects as the patients who filled and consumed them. Although the James Lind Library<sup>98</sup> notes that the need for the blind assessment of treatment effects was emphasized 2 years before I was born<sup>99</sup>, the hardest evidence that clinicians who like their Rx report spuriously better outcomes comes from far more recent RCTs.

For example, in a promising placebo-controlled Canadian RCT of weekly plasma exchange, prednisone, and cyclophosphamide among patients with multiple sclerosis, 2 sets of neurologists were asked to determine treatment responses at 6, 12, and 24 months<sup>100</sup>. Neurologists who were blind to the treatments reported no difference in outcomes among the treatment groups at any time. However, unblinded neurologists reported statistically significantly improved outcomes for patients receiving triple therapy at all 3 follow-up assessments.

Clinicians who like their Rx do report spuriously better outcomes. That’s why our RCTs blind outcome assessors whenever we can, draw conclusions from ‘hard’ outcomes if possible, and blindly adjudicate softer outcomes.

Finally, some 40 delightful years later, as I witness the emerging era of Comparative Effectiveness Research and propensity scores, I haven’t encountered convincing examples in which the proponents of observational studies of efficacy have developed strategies and tactics for avoiding or overcoming these 4 worries that have forced me into hard RCT labor for the past 48 years. Indeed, I’m curious as to how they will (and could) tell whether they’ve avoided or solved them.

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<sup>98</sup>This treasure trove of reports and resources on the fair comparison of treatments can be found at: <http://www.jameslindlibrary.org/>

<sup>99</sup>Martini P. *Methodenlehre der Therapeutischen Untersuchung* (Methodological Principles for Therapeutic Investigations). Berlin: Springer, 1932.

<sup>100</sup>Noseworthy JH, Ebers GC, Vandervoort MK, Farquhar RE, Yetisir E, Roberts R. The impact of blinding on the results of a randomized, placebo-controlled multiple sclerosis clinical trial. *Neurology*. 1994;44:16-20. Reprinted as a Classical Article in *Neurology*. 2001;57(12 Suppl 5):S31-5.

## Chapter VI-2: What is the biggest surprise you've had in doing research?

My biggest surprise occurred at the end of 1 of our earliest RCTs (indeed, the 1<sup>st</sup> RCT ever funded by the Canadian Medical Research Council). It nurtured my growing interest in bias, caused lively disagreements with some of my RCT-friends, and ultimately led to a change in the CONSORT guidelines for reporting RCTs.

We were just finishing a 26-center pan-Canadian 'double-dummy' factorial RCT of aspirin, sulfinpyrazone, both or neither, in preventing stroke or death among patients who'd recently suffered a transient ischemic attack (TIA, or threatened stroke) we reckoned was due to blood platelet emboli. We had shown, for the 1<sup>st</sup> time, that aspirin (but not sulfinpyrazone) reduced the risk of stroke and death among these patients. We were elated with our primary results and already dreaming of a lead article in the *New England Journal of Medicine*.

There were just a few odds and ends to attend to. One of them was to follow the advice of the RCT texts of the day and, before we gave them the trial results, applied an end-of-study questionnaire to our collaborating neurologists to confirm that our efforts to keep them 'blind' had been successful. Our 'double-dummy' design had randomized their patients to both active drugs, to active aspirin and placebo sulfinpyrazone, to placebo aspirin and active sulfinpyrazone, or to both placebos. Consequently, when we asked our neurologists which regimen they thought each of their patients had received, they would have guessed correctly for 25% of them on the basis of chance alone. Any big increase in this rate of correct responses would be worrisome, and a statistically significant difference would suggest that our attempts to blind them had failed.

As I described 30 years later in a Clinician Trialist Round<sup>101</sup>, "I felt the bullet enter my heart" when our co-PI statistician tracked me down on the ward to tell me that our clinicians' correct guesses were, indeed, statistically significantly different from 25%. The biggest surprise I've had in doing research was his report that their guesses were statistically significantly wrong!

The penny dropped when he showed me their predictions (obtained at that same time, before we'd broken the treatment code for them) about the efficacy of our 2 study drugs. They'd got that wrong, too! Most of them predicted that aspirin would be worthless but sulfinpyrazone would be effective. Thus, with a 'prior' belief that sulfinpyrazone was effective, when a patient fared well throughout the trial it was clinically sensible for their neurologist to suspect that they were on it. Similarly, if a patient suffered a stroke during the trial, it was clinically sensible for their neurologist to suspect the double placebo or the aspirin they thought was probably worthless. Our end-of-study test for blindness was exposed as a test for (incorrect) hunches about efficacy! We successfully explained these results to the *New England Journal's* Editor (if

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<sup>101</sup>Sackett DL. Clinician-Trialist Rounds. 6. Testing for Blindness at the End of Your Trial is a Mug's Game. *Clin Trials*. 2011;8:674–6.

not to 1 persistently confused referee) and encouraged a series of RCTs into ever more effective antiplatelet therapies<sup>102</sup>.

I revisited this phenomenon 29 years later after some old and new friends examined collections of RCT reports and lamented that less than 10% of them included tests for blindness. Again proposing that these tests were shaky, I now had 'back-ups,' not only from other trialists (Stephen Senn had argued: "The whole point of a successful double-blind trial is that there should be un-blinding through efficacy."), but, most important, from the folks who created and maintain the CONSORT Statement on how to report randomized trials have now come to this same conclusion: "Regardless of the ultimate success of blinding, tests of the success of blinding might actually be tests of hunches on harms, side-effects, or efficacy." Accordingly, they revoked their previous recommendation to report "how the success of blinding was evaluated," and: "In CONSORT 2010, we have removed mention of how the success of blinding might have been evaluated."

Finally, understanding this phenomenon reinforced and expanded my understanding of bias: we blind our RCT participants and clinicians to avoid or at least minimize 3 threats to fair comparisons: the contamination of the comparison group with the experimental treatment, the unequal application of an efficacious co-intervention to experimental and comparison participants, and the consciously- or unconsciously-biased reporting of trial outcomes that occurs when participants or their observers know the treatment allocation of the participants they are assessing.

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<sup>102</sup>The Canadian Cooperative Study Group: A randomized trial of aspirin and sulfinpyrazone in threatened stroke. N Engl J Med. 1978;299:53-9.

### Chapter VI-3: Tell us about your involvement in Data Safety Monitoring Boards and what you've accomplished in creating and improving them?

I've been involved with Data and Safety Monitoring Boards (DSMBs) in 3 different ways, corresponding to 3 stages of my career: as a student, a supplicant, and a chair.

1. As a 'student': In my 3<sup>rd</sup> year of post-graduate training in internal medicine in Buffalo in 1965, I admitted patients to the Coronary Drug Project Trial. It was an RCT of several drugs thought likely to reduce the recurrence of heart attack among men who'd survived a 1<sup>st</sup> one. DSMBs weren't yet standard practice in that era, and because some of the drugs were potentially harmful (indeed, estrogen was found to increase recurrences), the emerging trial results were reviewed by the trial's investigators! My hero and future friend Tom Chalmers pointed out what a terrible idea this was<sup>103</sup>, and DSMBs gradually came into being.

2. As a 'supplicant': 20 years later I was a co-principal investigator in the NASCET RCT that tested expert surgical endarterectomy to see whether it prevented fatal and severe strokes among patients with symptomatic high-grade carotid stenosis.<sup>104</sup> Following discussions among all the investigators and statistical colleagues elsewhere, our superb biostatistician Wayne Taylor designed and applied statistical 'warning' rules for the efficacy of the operation ( $P < 0.001$  in each of 6 clinically relevant subgroups every month for 6 months). DSMBs had become standard practice, and Wayne and I were designated to give our confidential interim results to the 1 created for our trial. However, we were deeply dissatisfied with its composition, for it included individuals whom we felt might harbor financial or intellectual conflicts of interest. We simply did not want to give them early, uncertain results. Accordingly, and with crucial support from its biostatistical member, Byron Brown Jr., they agreed to remain 'in the dark' about trends unless and until they met our warning rule.

DSMB meetings soon followed a predictable pattern: they began cordially during reports about recruitment, follow-up, data completeness and quality, but exploded when Wayne and I limited our confidential interim report to a single sentence: "The statistical warning rule has not been triggered." Predictable members of the DSMB blew up, demanded detailed interim subgroup results, and threatened to fire us unless we provided them; Wayne and I countered by threatening to resign rather than give in; and Byron Brown led the cooling-off process to the point of grudging acceptance of our report.

Fortunately, our warning rule was triggered shortly before scheduled meetings of not only the DSMB and Steering Committee, but also an international neurosurgical society. Our detailed report led both the DSMB and the Steering Group to declare the trial's positive result on a Thursday afternoon, and the Principal Investigator publicly announced its results that evening. The next day, the National Institutes of Health prepared a 'Clinical Alert' for general dissemination and a recently-recruited control patient underwent carotid endarterectomy.

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<sup>103</sup>Redmond CK, Colton T (Eds): Biostatistics in Clinical Trials. Hoboken: Wiley, 2001. P 241.

<sup>104</sup>North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial Effect of Carotid Endarterectomy in Symptomatic Patients with High-Grade Carotid Stenosis. N Engl J Med. 1991;325:445-53.

3. As a 'DSMB Chair': Over the past decade, during which there have been thoughtful books<sup>105</sup> and syntheses<sup>106</sup> concerning DSMBs (many now call themselves Trial Monitoring Committees or TMCs) I have chaired several DSMBs. I've certainly not perfected the enterprise, but I have introduced 3 'terms of reference' to the ones I've chaired:

First, we never stop the trials we serve; surely that is a decision for folks who know the target disorder and its treatment far better than the DSMB, and I consider it not only arrogant, but stupid for us to make a unilateral decision. Rather, we unblind the Principal Investigator and discuss the findings with her. This policy has invariably led to additional urgent follow-ups, data clean-ups, adjudication completions, and the like, included in confirmatory analyses. Although my DSMB charters include plans for resolving disagreements between us and the PI, I've never had to invoke them.

Second, my rules for the eligibility of DSMB members are stricter than most. I prohibit not only direct financial interests (employees or stockholders of drug and device makers) but also institutional (read NIH) and academic-reputational (spoken or published proponents or opponents) interests.

Third, I discourage giving combined (experimental and control event rates combined into a single figure) interim results to the investigators, as both thought experiments and real-world experience has taught us that the same, 'rosy' interim combined event rate can be generated by an intervention that is useful, useless, or harmful.

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<sup>105</sup>Ellenberg SS, Fleming TR, DeMets DL. Data Monitoring in Clinical Trials: A Practical Perspective. Hoboken: Wiley & Sons, 2003.

<sup>106</sup>Clemens F, Elbourne D, Darbyshire J, Pocock S; DAMOCLES Group. Data monitoring in randomized controlled trials: surveys of recent practice and policies. Clin Trials. 2005;2:22-33.



## Section VII: My career as a Clinician

### Chapter VII-1: What role has providing patient care played in your career?

When I designed my Clinical Epidemiology Unit in Buffalo in 1966, patient care was at its center: *“Clinical epidemiology is the application, by a physician who provides direct patient care, of epidemiologic and biometric methods to the study of diagnostic and therapeutic processes in order to effect an improvement in health. A clinical epidemiologist is, therefore, an individual with extensive training and experience in clinical medicine<sup>107</sup> who, after receiving appropriate training in epidemiology and biostatistics, **continues to provide direct patient care in [their] subsequent career**”<sup>108</sup>.*

Providing patient care has remained the source of most of my research ideas and educational efforts ever since. For example:

1. Probing my repeated failures to control my hypertensive patients’ blood pressures with drugs led to the realization that the most common cause was not faulty pharmacology but low compliance with their prescribed meds. This evolved into a 20-year collaboration (soon led by Brian Haynes) in RCTs of compliance-improving strategies<sup>109</sup>, co-authoring 2 books<sup>110</sup>, leading multiple symposia, and co-authoring a host of papers in peer-reviewed journals.

In the course of this work, we documented that getting labeled ‘hypertensive’ doubled absenteeism and decreased levels of psychological well-being among Canadian steelworkers, even when no antihypertensive drugs were prescribed.<sup>111</sup> No surprise that these sobering findings were unpopular among our more interventionist colleagues to the South; when our RCT of ‘mastery learning’ about hypertension found no effect on compliance<sup>112</sup>, the U.S ‘dean’ of hypertension told me our results were “scientifically impeccable but socially unacceptable,” and when attendees at the annual gathering of the hypertension clan in Washington DC where we’d reported the labeling effects were asked for suggestions for ‘next year’s meeting,’ a voice from the back shouted: “Tell those goddam Canadians to stay away from our meetings.”

2. Familiar with the presentation, clinical course, treatment, outcomes, and patient behavior of the gamut of disorders that I cared for, I became a valued methodological collaborator in

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<sup>107</sup> Later expanded when colleagues from the other health professions excelled as clinical epidemiologists.

<sup>108</sup> Sackett DL. Clinical epidemiology. Am J Epidemiol. 1969;89:125-8.

<sup>109</sup> Haynes RB, Sackett DL, Gibson ES, Taylor DW, Hackett BC, Roberts RS, Johnson AL. Improvement of medication compliance in uncontrolled hypertension. Lancet. 1976;1:1265-8.

<sup>110</sup> Haynes RB, Taylor DW, Sackett DL, eds. Compliance in Health Care. Baltimore: Johns Hopkins University Press, 1979.

<sup>111</sup> Haynes RB, Sackett DL, Taylor DW, Gibson ES, Johnson AL. Increased absenteeism from work after detection and labeling of hypertensive patients. N Engl J Med. 1978;299:741-4.

<sup>112</sup> Sackett DL, Haynes RB, Gibson ES, Hackett BC, Taylor DW, Roberts RS, Johnson AL. Randomised clinical trial of strategies for improving medication compliance in primary hypertension. Lancet. 1975;1:1205-7.

dozens of RCTs whose expert clinician-Principal Investigators lacked methodologic expertise. My clinical expertise regularly identified elements in recruitment, treatment, follow-up, and outcome assessment that required protocol modifications to both avoid bias and increase precision (and get the damn protocol funded!).

3. The NNT (the “number-needed-to-treat” with an intervention to prevent 1 more event) and its derivatives were conceived in our Coronary Care Unit 1 day by Andreas Laupacis and me when he was on sabbatical at McMaster and I was rotating through the Unit during my ‘retreading’ residency in internal medicine. The Chief of Service cornered me, complaining that my teaching of critical appraisal to ‘his’ house officers had led to the overtreatment of ‘his’ low-risk post-MI patient with a beta-blocker. They insisted that its 1-year relative risk reduction (RRR) for recurrent MI of 30% demanded treatment, whereas he insisted that the patient was at so low a risk of MI recurrence (he reckoned about 2%) that he would simply suffer unnecessary and significant treatment side-effects for an insignificant benefit. Talking our way through his case, Andreas and I juggled that 2% risk of recurrence with that 30% RRR and came up with an interesting (to us) but not intelligible (to other clinicians) absolute risk reduction (ARR) of  $[(2\%) \times (1-0.3)]$  or 0.014. But a few seconds of head-scratching and doodling revealed that the inverse of this ARR ( $1/0.014 = 71$ ) told us the number of these low-risk MI patients we’d need to treat with a beta-blocker to prevent 1 more MI within a year was 71 (compared with just 17 high (20%) risk patients). We quickly decided that the clinically most useful way to describe this was ‘the Number Needed to Treat’ (NNT) for a given time to prevent 1 more event,’ and the Chief was able to resolve his dispute with his housestaff through reason rather than rank. Robin Roberts helped us understand its statistical properties, and we published the result in the *New England Journal of Medicine*<sup>113</sup>. Richard Cook (a statistician who had briefly joined my clinical service) exposed our hilarious mistakes in bedside calculations as we tried to adjust published data to fit the risks and responsiveness of our individual patients and showed us easy ways to avoid them<sup>114</sup>; subsequent Fellows at McMaster started an international flurry of other “Number Needed to X” for screening, examining, poking, prodding, diagnosing, etc people and patients for other useful purposes<sup>115</sup>. Finally, Sharon Straus made the giant leap of showing us how to incorporate our individual patient-risks with our patient-values about the relative severities of the bad outcomes a treatment might both prevent and cause. The result is the highly useful ‘likelihood that we might help vs. harm you with this Rx.’<sup>116</sup>

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<sup>113</sup>Laupacis A, Sackett DL, Roberts RS. An assessment of clinically useful measures of the consequences of treatment. *N Engl J Med.* 1988;318:1728-33.

<sup>114</sup>Cook RJ, Sackett DL. The number needed to treat: a clinically useful measure of treatment effect. *BMJ.* 1995;310:452-4.

<sup>115</sup>Sauve MD, Sauve JS, Sackett DL. Number needed to treat; the next generation. *Clin Invest Med* 1993;16:B1.

<sup>116</sup>Straus SE. Individualizing treatment decisions. The likelihood of being helped or harmed. *Eval Health Prof.* 2002;25:210-24.

4. When I chaired the 1<sup>st</sup> phase of the undergraduate M.D. program at McMaster in 1973, we decided to implement our problem-based, self-directed education program by presenting our students with 'packages' that described the presentations, clinical and laboratory findings, social situations, and clinical courses of 16 patients across the spectra of age, gender, social class, and organ system. Based on my clinical experiences, I drafted each of these packages and polished them with inputs from 16 basic and clinical departments and interest groups (e.g., Women in Medicine).

5. By bringing departmental non-clinical colleagues into the daily work of my in-patient clinical team (and with permission from the nursing staff), I provided them 1<sup>st</sup>-hand exposure to the content, context, and chaos of acute in-patient medicine. The 1<sup>st</sup> cluster comprised a statistician and 2 health economists, and we agreed to publish both our independent 'Roshomon' observations of the experience and our combined appraisal of its value<sup>117</sup>. Each 'side' benefitted from the other: they reported gaining greater understanding of front-line acute care medicine; the statistician showed us a much quicker way to determine which of 4 drugs we were giving to a critically-ill patient were doing more good than harm (stopping 2 at a time, rather than 1); and the health economists helped me begin the process of clarifying the 'terms of engagement' between docs looking after sick patients and economists looking after global health resources that culminated in a dinner at the House of Lords in London and giving the 1966 Annual Lecture to the Office of Health Economics at the Royal College of Physicians on The Doctor's (Ethical and Economic) Dilemma<sup>118</sup>.

This same clinical context was, of course, vital as we introduced the strategies and tactics of both 'Critical Appraisal'<sup>119</sup> and 'Evidence-Based Medicine at the bedside and in the clinic.'<sup>120</sup> 'Educational Prescriptions' for finding and appraising the best evidence about a patient's diagnosis, prognosis, and therapy were perfected in that milieu, and it was there that we showed in 1998 that hauling a behemoth 'evidence-cart' (soon replaced by ever-smaller, faster hand-helds) around the wards permitted my housestaff and students to 'fill' over 16 educational prescriptions on the ward in the same time that it took them to fill just 1 by trekking to the hospital library only 2 floors beneath our wards<sup>121</sup>.

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<sup>117</sup>Walter SD, Hurley JE, Labelle RJ, Sackett DL. Clinical rounds for non-clinicians: some impressions. *J Clin Epidemiol.* 1990;43:613-8.

<sup>118</sup>Sackett DL. *The Doctor's (Ethical and Economic) Dilemma*. London: The Office of Health Economics, 1996.

<sup>119</sup>Bennett KJ, Sackett DL, Haynes RB, Neufeld VR, Tugwell P, Roberts R. A controlled trial of teaching critical appraisal of the clinical literature to medical students. *JAMA.* 1987;257:2451-4.

<sup>120</sup>Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ.* 1996;312:71-2.

<sup>121</sup>Sackett DL, Straus SE. Finding and applying evidence during clinical rounds: the "evidence cart". *JAMA.* 1998;280:1336-8.

6. It was Educational Prescriptions about the precision and accuracy of bedside observations that forced us to confront the sorry state of evidence about the precision and accuracy of key elements of the clinical exam. For example, we discovered that ‘experts’ had proposed 37 signs for diagnosing chronic airflow limitation at the bedside (a common possibility among our patients in Oxford), but that only a handful had undergone rigorous evaluation for their reproducibility and validity. Moreover, most validation studies involved a handful of clinicians and a few dozen patients. Sharon Straus and Finlay McAlister, 2 fellows at the Oxford Center for EBM, took on this challenge and combined their clinical expertise with the power of the internet and created a worldwide consortium of clinicians<sup>122</sup> who enrolled over 300 patients within a month, and showed that laryngeal height, but neither laryngeal descent nor wheezing, were valid markers for a FEV1/FVC ratio less than the 5<sup>th</sup> percentile (adjusted for patient height, age, and sex)<sup>123</sup>.

7. Finally, in 2010 I initiated *Clinician-Trialist Rounds* in each issue of the journal *Clinical Trials*. Each of the 26 *Rounds* published to date begins with a ‘case’ that describes an RCT in trouble,<sup>124</sup> an educational opportunity,<sup>125</sup> or a career challenge facing a young clinician-trialist.<sup>126</sup> My clinical career has been invaluable in creating both the style and substance of these columns.

Perhaps the best evidence I can present on the importance I placed in maintaining my clinical competency, not only as a clinician but as a researcher and educator, is that, at age 49, I began a 2<sup>nd</sup> 2-year ‘retreading’ residency in internal medicine.

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<sup>122</sup>McAlister FA, Straus SE, Sackett DL. Why we need large, simple studies of the clinical examination: the problem and a proposed solution. CARE-COAD1 group. Clinical Assessment of the Reliability of the Examination-Chronic Obstructive Airways Disease Group. Lancet. 1999;354:1721-4.

<sup>123</sup>Straus SE, McAlister FA, Sackett DL, Deeks JJ. The accuracy of patient history, wheezing, and laryngeal measurements in diagnosing obstructive airway disease. CARE-COAD1 Group. Clinical Assessment of the Reliability of the Examination-Chronic Obstructive Airways Disease. JAMA. 2000;283:1853-7.

<sup>124</sup>Sackett DL. Clinician-Trialist Rounds. 5: Cointervention bias – how to diagnose it in their trial and prevent it in yours. Clin Trials. 2011;8:440-2.

<sup>125</sup>Sackett DL. Clinician-Trialist Rounds. 20. Shouldn't 'trialists-in-training' rotate through RCT-clerkships? Clin Trials. 2013;11:263-6.

<sup>126</sup>Szatmari P, Sackett DL. Clinician-Trialist Rounds. 12. When your grant gets turned down. Part 2: Resurrection. Clin Trials. 2012;9:660-3.

## Chapter VII-2: How “evidence-based” are the treatments you have received and prescribed for medical disorders?

The vector here follows the growth and ascendancy of the RCT. On the one hand, the contractures I developed from polio at age 12 were par-boiled with wet towels and diathermy as per Sister Kenny’s non-experimental pronouncements, 2 years before the MRC published their trial of streptomycin for pulmonary TB, the very first RCT to be published in the British Medical Journal. On the other, my nonvalvular atrial fibrillation at age 64 was nicely controlled by amiodarone, the RCTs for which also correctly warned me about my subsequent possible need for thyroid replacement.

Two of my mentor-heroes, Archie Cochrane and Kerr White, used to argue whether the percent of medical interventions that were evidence-based was 5% or 10%, but as a clinician it has always seemed to me that they had chosen the wrong denominator: surely it should be patients, not maneuvers.

Accordingly, on Day #1 of my 1<sup>st</sup> month ‘on service’ at the John Radcliffe Hospital in Oxford in 1995, the House Officer who challenged me with this question was shown how to answer it prospectively for our admissions that month. At every in-patients’ discharge or death, our team identified the main treatment we’d offered them for the main disorder that caused their admission. He found that over 50% of our patients had received main treatments that had been validated in RCTs, giving him a 1<sup>st</sup>-authored publication in the Lancet, giving a grand boost to my teaching of EBM at the bedside, and initiating a flurry of similar audits of other clinical services at other institutions.

## Section VIII: Summing Up

### Chapter VIII-1: To what do you attribute your success?

Although self-assessments are always imperfect and sometimes deluded, I think my 'success' has been the result of the following 10 determinants:

1. A series of external events, over which I had absolutely no control, that forced fundamental changes in my environment and opportunities. The 1<sup>st</sup> was being drafted into the U.S Public Health Service as a result of the Cuban missile crisis in 1963,<sup>127</sup> the 2<sup>nd</sup> was being offered the founding Chair at a new med school in Canada in 1967<sup>128</sup>, and the 3<sup>rd</sup> was being offered the founding directorship of Europe's 1<sup>st</sup> Centre for Evidence-Based Medicine in 1994<sup>129</sup>.
2. I think I possessed the ability to identify a very broad spectrum of ways that I might respond to these opportunities, many of which eluded the visions of other folks (I looked at what others looked at, but saw what others didn't see).
- 3 and 4. I also think I possessed the abilities to both identify young people with star-potential to join me in responding to these opportunities and to mentor them to stardom (and, in the process, follow 2 elements of my life-philosophy: 'be loyal to people, not institutions'; and 'serve the young').
5. The enduring, loving support, encouragement, and understanding of Barbara and our 4 sons.
- 6 and 7. The willingness of a few senior colleagues from afar (exemplified by Mike Gent) to buy into my ideas and not only realize but improve them, and the devotion of a series of wise and effective professional assistants.
8. An insuppressible capacity for finding and injecting fun into everything I did (sometimes to the distress of others).
9. The ability 'to become what I pretended to be'. This one requires further explanation: At age 32, I became the founding Chair of a new and novel department at a new and novel medical school. I had completed my internal medicine training less than a year earlier, had written only 1 (unsuccessful) research grant, and was lead author on just 2 refereed publications. But I had 2 things in abundance: intense fear about my new job and intense selfishness when it came to my academic ambitions. I was terrified that no one would want to join my department, that I would never be successful in obtaining research grants or space or other departmental resources, and that I would be so busy keeping the department afloat that I would never have

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<sup>127</sup>This event was quickly followed by a 2<sup>nd</sup> in which my former resident introduced me to Warren Winkelstein Jr, who was looking for a USPHS draftee to join his epidemiology unit in Buffalo.

<sup>128</sup>The Department of Clinical Epidemiology & Biostatistics at McMaster University in Hamilton, Ontario.

<sup>129</sup>The National Health Service Research & Development Centre for Evidence-Based Medicine at Oxford University.

time to achieve my academic ambition of becoming a principal investigator, lead author, and famous researcher.

However, I was raised in optimistic post-WW II times in an optimistic family, and had achieved an optimistic recovery from childhood polio. Moreover, I had had enough clinical experience to realize that it was important to behave in different ways around different sorts of patients if I was to help them: formal and respectful for quiet elderly maiden-ladies (as was my nature), but pretending to be rough and blunt around gruff steelworkers and stevedores.

I decided to try to transfer this insight and behavior to my new and frightening post. I began to pretend to be an ideal departmental Chair: fearless, unselfish, and happy to achieve my academic ambitions through the successes of others, not myself. I put on a convincing performance. My colleagues in our rapidly growing department marveled at my incurable optimism as we applied for research funds, more space, and more staff. Moreover, I appointed my junior colleagues to leadership roles as we dared to launch the 1<sup>st</sup>-ever randomized trials of the nurse-practitioner, of aspirin for transient ischemic attacks, and of compliance-improving strategies in hypertension. Although I wrote much of their grants and often guided them in executing these studies, they became the lead authors, not me. Over the next decade this pretended unselfish behavior started to become natural to me. It was my changing values that made it unconsciously normal for me to relegate myself to junior authorship and, indeed, to take my name off of papers when I thought my presence on it might reduce the credit and advancement given to my junior colleagues.

Nowadays I deserve my reputation for fearlessness and unselfishness. I have become what I earlier only pretended to be. Along the way, I became enchanted by the writings and worldview of Kurt Vonnegut Jr., and found a chilling confirmation of what I had done in his book *Mother Night*<sup>130</sup>.

10. Finally, writings, mentees, colleagues, family and friends provide me all the validation and recognition I have ever needed. I have twice 'resigned' from fields when I reckoned my comfortable 'expert' status was retarding their development (compliance research in 1981<sup>131</sup> and EBM in 1999<sup>132</sup>), have turned down high-profile Chairs when I reckoned their prestige outweighed their potential, and have declined honorary degrees when I knew of at least 1 person I thought deserved them more than I did (on those rare occasions when I have succumbed to the latter, I typically open my acceptance remarks with the phrase "I am blessed with colleagues whose opinion of me is higher than my own").

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<sup>130</sup>[http://en.wikipedia.org/wiki/Mother\\_Night](http://en.wikipedia.org/wiki/Mother_Night)

<sup>131</sup>Sackett DL. Second thoughts. Proposals for the health sciences--I. Compulsory retirement for experts. *J Chron Dis.* 1983;36:545-7.

<sup>132</sup>Sackett DL. The sins of expertness and a proposal for redemption. *BMJ.* 2000;320:1283.

My lack of pretentiousness is not only beneficial for others, but also offers benefits closer to home:

- a. It prompts me to give credit and prominence to deserving others (e.g., by removing my recognized name from their early-career manuscripts, thus freeing them from my shadow);
- b. It immunizes me against that ghastly disease of egomania that causes such dreadful behavior in many experts who, like fading stand-up comedians, feel only as good as their last performance, and trod on others (especially the young) as they desperately try to maintain pre-eminence.
- c. It frees me from the burden of having to defend a former, abandoned field from its critics, whether they be thoughtful or kooky; indeed, it frees me from even having to read or acknowledge their criticisms. It is a delight to ignore them.



## Chapter VIII-2: What role has collaboration played in your career?

I credit all of my scientific and educational achievements to collaboration (evidence: I've never run a course on my own or been sole author of any book or journal publication, save an occasional invited editorial or letter).

In clinical practice research, I don't know anybody who has all the knowledge and skills required to generate a valid, clinically useful result. Indeed, in the 3<sup>rd</sup> edition of our clinical epidemiology book I wrote: "If you don't start looking for a biostatistician co-principal investigator the same day that you start formulating your study question, you are a fool, and deserve neither funding nor a valid answer." I reckon the modal composition of co-PIs in my research have included at least 1 biostatistician, at least 1 expert front-line clinician, a pair of clinical epidemiologists, and other experts (economists, behaviorists, etc) as necessary, each accompanied by one or more students.

The same holds for the design and creation of a successful department, education or research program, medical school, or public organization that purports to serve the public health (epitomized by the "unselfish collaboration" of the Cochrane Collaboration).

My successful collaborations have had 4 elements. First, their objectives had to promise important contributions to new knowledge and, ultimately, better patient-care. Second, my collaborators had to be not only knowledgeable but enthusiastically energetic. Third, we really had to like each other and enjoy not only working but also playing together (for several years our faculty, staff, and graduate students ran away Wednesday noons for a couple of hours of co-ed ice hockey [no lifting the puck, and body checking only between consenting adults] followed by a visit to a local pub).

Fourth, unselfish collaboration had to be rewarded by sharing the credit; a typical RCT provided invited lectures and lead authorships all across the collaboration as various members presented and published not only its primary results but generated additional talks, papers and theses of their own about the methodologic innovations they developed to pull it off, substudies, biologic and clinical implications, and reviews (ultimately systematic). As a result of such transparent recognition and reward, we avoided (or at least minimized) envy between colleagues, as every collaborator's CV and recognition flourished. Professional envy over colleagues' successes (e.g., publications, recognition, awards) has destroyed many a collaboration, and even some departments. Envious persons exhibit 'harmful behavior' in that they are less likely to share information with a 'successful' colleague or to cite their work, are more likely to put them down in public or spread gossip about them, and are less likely to contribute to collaborations or to improve their own performance<sup>133</sup>.

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<sup>133</sup>Can envy be a virtue? Taming the green-eyed monster at work.  
<http://knowledge.wharton.upenn.edu/article/can-envy-virtue-taming-green-eyed-monster-work>. 10 June 2014.

### Chapter VIII-3: You've been reinventing yourself periodically and list 8 careers. What is that all about?

There have been 5 reasons for changing my career:

1. Unforeseen opportunities that suddenly and unexpectedly arose and looked like too much fun to pass up. This applied to offers from McMaster in 1967 and from Oxford and the Cochrane Collaboration in 1994.
2. Resignation from expert status. Because of my conviction that 'content' experts do more harm than good, I quit compliance research in 1982 and stopped writing and talking about EBM in 2000.
3. Realization of a deficiency. In 1983 I was keen to teach our emerging ideas about 'critical appraisal' at the bedside. However, I reckoned that my effectiveness as a bedside clinician had become 'out-of-date' since my residency training in the 1960s. Fortunately, I was able to become a 2-year 'retreading' medical resident, validated in 1985 by the Royal College of Physicians and Surgeons of Canada.
4. Logical progression. After my retreading medical residency, it was a logical progression for me to become Physician-in-Chief at the McMaster University Medical Centre.
5. Boredom. After being Physician-in-Chief for a few years, I simply became too bored to continue, found an excellent replacement, and resigned.

#### Chapter VIII-4: What was the funniest/craziest thing that you experienced in your career?

Being offered a Chair at McMaster when I was 32, 1 year out of my chief medical residency, with no research grants and only 2 1<sup>st</sup>-authored publications (on irrelevant subjects).

Their foundation Dean, John Evans, wrote me a letter, briefly describing the new school and inviting me to come up for an exchange of ideas. I had never heard of McMaster, much less John Evans, my family and I were happy in Buffalo, and I wasn't looking for any other job. I consented to the interview only because McMaster was located just 70 miles away and it would have been discourteous to turn them down.

Nonetheless, I made no attempt to 'sugar coat' my answers to the 1<sup>st</sup> 2 questions John Evans posed at my 1<sup>st</sup> visit:

Q1: *What sort of Department of Social, Community, and Preventive Medicine should we have at this new medical school?*

A1: *None!* ("Unless every department insists on taking responsibility for the social, community, and preventive issues that are relevant to them, you could never have a department of SCPM big enough to generate any useful improvements in health care.")

Q2: *What sort of course in epidemiology & biostatistics should we teach our medical students?*

A2: *None!* ("Unless clinically relevant bits of epidemiology and biostatistics are integrated into instruction in clinical skills, clinical pharmacology, therapeutics, and into every clinical rotation, an isolated course in epidemiology and biostatistics would be as awful as it is everywhere else, the students would hate the faculty, and vice versa.")

I didn't know that they'd already reached these same conclusions! The Chair of Psychiatry was already placing most of his faculty out in community agencies, and the Chair of Pediatrics was already teaching mums of injured hemophiliac kids how to store and inject Factor VIII in order to prevent hemarthroses and hospitalizations. And, they'd already decided not to have courses in epidemiology *or anything else*, but to provide self-directed, tutorial-based, clinical problem-based learning in which medical students would track down master, and integrate information across the entire range of pre-clinical and clinical disciplines.

In short, they mistook a hip-shooting novice for a sage, and offered me the job.

## Chapter VIII-5: Were sabbaticals important to your career?

When we set up the medical school at McMaster, we recognized the importance of sabbaticals and not only enshrined them in our policies but also established rules for their financial support: 75% of one's university base salary and (at each clinical department's discretion) >50% of one's previous year's billings. Generous 'top-up' funds were available from provincial, national, and foundation fellowships, so that our family income was well-maintained without having to ask for financial support from our hosts.

My 3 full-year sabbaticals were vital not only to my career-success, but to our family.

Sabbatical 1: London, UK (pre-PC and email)

We spent 1974-5 with all 4 sons in London, on a courtesy appointment with Walter Holland (who had nominated me to McMaster 7 years earlier) at St. Thomas's Hospital Medical School. Renting a rickety Commer camper-van, we spent our 1<sup>st</sup> 2 months unforgettably introducing ourselves to the people, places, and histories of Belgium, the Netherlands, Germany, Lichtenstein, Switzerland and France. Returning to a townhouse just north of Primrose Hill, with the boys enrolled in multinational neighborhood schools and Barbara volunteering at both as well as attending art school, I began riding my bicycle each weekday into central London (through Oxford and Picadilly Circuses, around Trafalgar Square, down Whitehall, and crossing the Thames on Westminster Bridge) to the department's Lambeth building where I met, learned from, and bonded with Doug Altman and some wonderful Aussies (Les Irwig and Steve Leeder) over hour-long scampi-and-chips lunches. A high point was a leisurely visit at Rhoose Farm with Archie Cochrane.

Escaping the obligations (my mentees and colleagues were already full collaborators in our trials back home, and seamlessly took them over) and frenetic pace of McMaster (in that halcyon pre-email era, having my letters forwarded by sea rendered 90% of them irrelevant by the time they reached me 6 weeks later), I had time for reflection and unhurried self-assessment.

The more time I spent reading the brisk, brief, frank, clear writing styles of my British clinical (e.g., Douglas Black) and methodologic (e.g., Austin Bradford Hill) heroes, the greater my dissatisfaction with my North American lethargic, long-winded, fuzzy, and ambiguous offerings. I set out to shorten, tighten, clarify and enliven mine by studying Strunk and White's *Elements of Style*<sup>134</sup> and by writing/rewriting under the benevolent tutelage of David Sharp, then Deputy Editor of the Lancet. For example, David started with my 50-word summary sentence from one of our compliance trials: '*Through a comprehensive, multi-media array of educational resources,*

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<sup>134</sup> Strunk W, White B. *The Elements of Style*. New York: Macmillan, 1972.

*experimental patients mastered information about the definition of hypertension, its effects on health, target organs, and life-expectancy, the ability of anti-hypertensive drugs to overcome or reverse these effects, and the importance of high-compliance with these anti-hypertensive drugs.'* As an alternative, he gently suggested, "Dave, why don't you (reduce it by 80% and) just say: *"Our patients learned a lot about high blood pressure?"*".

I then worked on my evolving short, succinct, informal writing style in a series of Lancet articles with my host on whether and how screening might do more harm than good, and to editing and writing a book on the work that Brian Haynes and I and a growing group of investigators had done on the magnitude, determinants, and treatment of low compliance with therapeutic regimens.

In the process, I realized that I needn't 'go to the office' and 'do science' every day, and that my time was often better spent at 1 of London's excellent libraries, or at the National Gallery or the British/Tate/Transport/War Museums, or at my writing desk back home.

And I had the unfettered time to think about future paths for my career, and developed the germ of an idea about how clinicians might think more usefully about evidence on the diagnosis, prognosis and treatment of patients (that my friends and I subsequently helped to develop into 'critical appraisal').

But we also seized school-break opportunities for family adventures: Christmas skiing in Austria, spring meandering by car from Casablanca through Fez to Marrakesh and Tangier, and biking to Brighton with our 2 older sons.

The benefits to my emerging career should be evident above. Perhaps more striking were the benefits to our family, as described by 1 of our grown sons as he looked back 35 years at being dragged off to a sabbatical year in London, UK when he was 15:

*"Sabbaticals were brilliant and very important for both the kids and the family. I will always consider it one of the greatest opportunities you ever gave us.*

*As kids, you never wanted to go. The 1<sup>st</sup> couple of months are hard. After that, you never want to leave. The next 10 months go by too fast."*

*There are 4 elements that were of extraordinary value:*

*1. A chance to strengthen family bonds. Putting a family in a situation where they are in unfamiliar territory means that they have to stick together and rely on each other to a much greater extent.*

2. A chance to spend more time with the physician/parent whose schedule at home doesn't always allow for as much time as anyone would like.

3. The chance to immerse yourself in the culture of a different society: this creates a level of confidence and an ability to adapt that cannot be replicated, a critically important skill.

4. A chance to develop a level of understanding and empathy with other cultures that teaches you that there are DIFFERENT ways of looking at the world that are just as legitimate as your own.

*Coming home is hard, as it is for most any "ex-pat." You have become used to being 'unique', and when you come home that goes away and you miss it for a while."*

Coming home from this 1<sup>st</sup> sabbatical was harder for me than for the rest of my family. I experienced mood-swings, and my family noticed that, although I began our weekends in a good mood, I grew quieter and short-tempered by Sunday evening. After several weeks, I realized the cause: my loss of freedom of choice over how I had spent my days on sabbatical. I decided to reclaim Mondays for my own, spent them in a dedicated room near the library with no 'phone, answered no mail, attended no meetings, but spent the entire day writing for publication. Not only did my mood and disposition improve virtually overnight, but my publication rate soared, and I subsequently maintained this policy for myself and recommended it to my colleagues and mentees<sup>135</sup>.

Sabbatical 2: Dublin, Eire. (still pre-PC and email)

We spent 1981-2 in Dublin with our 2 younger sons (whose older brothers were at universities back in Canada), on a courtesy appointment with James McCormack at Trinity College Dublin.

Friends had found a 'garden flat' (Irish for 'basement apartment') for us in a Victorian mansion along embassy row in Donnybrook, and although we were a short bicycle ride from the River Liffey and the heart of the city, we immediately bought a grotesquely pink Hillman Hunter auto and spent most of the summer exploring the Irish coast and inland and getting to know its remarkable and friendly people, interrupted by a side-trip to the island of Aegina in the Saronic gulf near Athens.

The boys happily enrolled at Sandymount School, quickly joined a young people's social club, and enjoyed the Dublin teenage nightlife. Barbara, who had become expert in the development of research questionnaires and the training of interviewers since our 1<sup>st</sup>

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<sup>135</sup>Sackett DL. Clinician-Trialist Rounds. 1: Inauguration, and an introduction to time-management for survival. Clin Trials. 2010;7:749-51.

sabbatical, explored opportunities for formal research training and quickly became a full-time graduate student at Trinity. As a result, we happily exchanged roles and I stayed home to 'run the house'.

Adapting to this role-reversal led fortuitously to an innovative agreement with my host that I used (and later taught others to apply) during this and my 3<sup>rd</sup> sabbatical: I had them select the 1 day each week in which I would arrive early, teach their graduate students, give seminars, review protocols and manuscripts, lunch with whoever was around, meet with whomever they wished, and provide any other service they desired. But the other 6 days were all mine, both to run the house and to pursue my own interests.

They picked their seminar day for my appearances, so I got to know all of them and discuss and debate our common interests. I gave a few seminars that provoked useful debates, and reviewed their ongoing research. It was also the day of a challenging biostatistics course for their grad students, so I met with them immediately afterwards to demystify and consolidate its practical essentials. They could count on me to show up that day, and I could count on them to ignore me on the others.

Those other days were spent in uninterrupted, unhurried sessions of writing and reflecting on my future. It was there, in collaboration with Brian Haynes and Peter Tugwell back at McMaster, that I drafted (in longhand – the PC was just aborning) a 1<sup>st</sup> edition of our clinical epidemiology text. And, as I wrote about how clinicians might improve their clinical skills, I became increasingly dissatisfied with my own (with all my other commitments and duties at our new medical school, my clinical practice had become restricted to exotic forms of secondary hypertension). This discomfort was to lead to my taking up a 2-year 'retreading' residency in internal medicine shortly after we returned home.

In the meanwhile, weekend jaunts to the countryside in the 'pink panther' continued, and our older sons joined us for a winter holiday in the Canary Islands.

Thirty years on, our 3rd son summarized his advice about sabbaticals thus:

*If you're thinking about a sabbatical, and you're wondering how your kids will do with it, follow the same rules we did. They worked for us, twice. Make sure they can speak [your native language] at school and don't need neck ties. Make sure you can get around town without a car. Take as many opportunities as you can to experience life both as a tourist and as a local (you should have plenty of time to do both). You'll be glad you did it, and so will your kids, even if they don't tell you.*

Sabbatical 3: Oxford UK, Sydney Oz, and Auckland NZ. (PCs in hand!)

All the boys off on their own, Barbara and I split our 1989-90 sabbatical between Oxford (9 months) and Australia-New Zealand (3 months), the latter on a Simm's Royal College Visiting Professorship. From our Oxford base we immediately purchased a wonderfully eccentric Citroen 'deux chevaux,' auto, mastered the single-lane roads of the Cotswolds, and explored the length and breadth of England-Scotland-Wales. Week-ends were spent exploring local history and regional countrysides with a welcoming walking group.

Affiliation with Nuffield College brought cordial and illuminating sessions with Sir David Cox, and a welcome from the Clinical Trials Service Unit led to discussions held at varying degrees of passion with Richard Peto (after 1 of which he apologized in writing!) and at normal temperatures with Richard Doll, Rory Collins and Mike Clarke. I came to treasure their brilliance and friendship. I also spent time in the Nuffield Department of Medicine at the John Radcliffe Hospital and with some of their medical students.

Wary about the resilience of the portable computers of the day, I'd brought 2 with me (indeed, one died and wound up a boat anchor back in Canada) and took the lead in generating the 2nd edition of our clinical epidemiology text, this time with Gordon Guyatt joining Brian Haynes and Peter Tugwell as co-authors.

Having escaped the continuous, relentless demands of Physician-in-Chief at the university hospital back in Hamilton, I had time to think about possible futures, and began to wonder whether the assessments of evidence we'd achieved through 'critical appraisal' could be carried 1 more giant step forward and translated into actions that clinicians and patients could employ at the bedside. (Carried home, our group – especially Gordon Guyatt – eventually succeeded in this translation and named it 'evidence-based medicine.')

We spent January through March in the antipodes of Australia and New Zealand, giving a flurry of presentations scheduled by our host and friend Les Irwig, but also finding time for a week at Heron Island on the Great Barrier Reef and a get-away on the breath-taking Kepler Track at the bottom of New Zealand's southern island.

Once again, a sabbatical had provided vital free time to think, write, and ponder my future, all in unhurried contact with stimulating old and new friends, new places, and new perspectives.



## Chapter VIII-6: Why is mentorship so important to you?

I define 'mentoring' as 'a process whereby an experienced, highly regarded, empathetic person (the mentor) guides another (usually younger or more junior) individual (the mentee<sup>136</sup>) in the development and re-examination of their own ideas, learning, and personal and professional development. The mentor, who often (but not necessarily) works in the same organization or field as the mentee, achieves this by listening or talking in confidence to the mentee."<sup>137</sup>

Mentorship is important to me for 2 reasons:

1. The mentorship I received was vital to my own career development.
2. My mentees report that my mentorship of them was vital to their career development.

It turns out that the scant evidence-base supports my contentions. When Sharon Straus systematically reviewed the relevant literature for our 2014 book *Mentorship in Academic Medicine*<sup>138</sup>, we summarized it thus:

1. Academic clinicians who got mentored report greater career satisfaction.
2. Academic clinicians who are mentored get more research grants.
3. Academic clinicians who are mentored report more protected time for scholarly activities and produced more publications.
4. Academic clinicians who are mentored are promoted more quickly.
5. Academics who are mentored are more likely to stay at their academic institutions.
6. Academic clinicians who are mentored report a greater belief in their ability to succeed in academic medicine ('self-efficacy').

Even scantier evidence supports the conclusion that mentoring is good for mentors as well. Surveys have reported that mentoring can reinvigorate their interest, lead to personal and professional growth, create satisfaction from helping to solve mentees' problems, from being able 'to give back', from providing support, from seeing their mentees develop, and from having the opportunity to use their mentoring experiences to reflect on their own careers and skills.

But this evidence wasn't around during the decades in which I did most of my mentoring, so how did I justify it back then? After several years of mentoring and observing its (usually) successful and (occasionally) unsuccessful results, I became convinced that the determinants of success as an academic (defined in terms of principal investigatorship, lead authorship,

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<sup>136</sup>In the literature, *protégé* is a term that is sometimes used interchangeably but I find this term pater/maternalistic.

<sup>137</sup>Standing Committee on Postgraduate Medical and Dental Education. Supporting doctors and dentists at work: An enquiry into mentoring. 1998. [www.mcgl.dircon.co.uk/scopme/mentor5.pdf](http://www.mcgl.dircon.co.uk/scopme/mentor5.pdf).

<sup>138</sup> Straus SE, Sackett DL, Eds: *Mentorship in Academic Medicine*. Oxford; Wiley Blackwell BMJ Books, 2014.

promotion, tenure, career awards, honours, power, and reputation) were not “academic” (defined in terms of intelligence, theoretical understanding, mastery of a body of knowledge, and teaching skills). Some clinician-investigators fail because they are crazy. Others fail because they lacked minds that were “prepared” to generate important questions based on their clinical observations. However, the range of their intelligence was so compressed at the top of the scale that even if it were an important determinant, my attempts to correlate it with success were doomed. Furthermore, academic failure was common among those who did and didn’t understand the theory and know the facts, and were and weren’t excellent teachers. Their ability to generate novel, imaginative hypotheses did play a role in the academic success of basic researchers I followed, but this rarely applied in patient-based and clinical-practice research (where the hypotheses usually are common knowledge and often originate with patients). Finally, I’m confident that nobody will seriously argue that being a nice person is a prerequisite for academic success.

What, then, did I identify as the determinants of academic success for the clinician-investigators I mentored? As described in our book on mentoring and in the *Clinician-Trialist Rounds* I ran in the journal *Clinical Trials*, I concluded that they were three: mentoring<sup>139</sup>, priority-setting<sup>140</sup>, and time-management<sup>141</sup>.

In practice, I incorporated the latter 2 into my mentoring functions:

*“The most important element of time-management for the academic success of individuals in a ‘research’ faculty stream is setting aside and ruthlessly protecting time that is spent writing for publication. When on-service, your total attention can be paid to the needs of your patients and clinical learners. No time is spent writing, travelling, attending meetings, or teaching non-clinical topics. When “off-service,” however, your time and attention should shift as completely as possible to research and non-clinical teaching.”*

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<sup>139</sup> Straus SE, Sackett DL. Clinician-Trialist Rounds: Mentoring – Part 1: Why Every Clinician-Trialist Needs to Get Mentored. *Clin Trials*. 2011;8:771-3.

Mentoring – Part 2: The Structure and Function of Effective Mentoring: Linkage, Resources, and Academic Opportunities. *Clin Trials*. 2012;9:127-30.

Mentoring – Part 3: The Structure and Function of Effective Mentoring: Advice and Protection. *Clin Trials* 2012;9: 272-4.

Mentoring – Part 4: The essential attributes of an effective mentor. *Clin Trials*. 2012; 9: 367-9.

Mentorships in Trouble. Part 1: Dysfunctional Mentorship Meetings. *Clin Trials*. 2014;11:376-9.

Mentorships in Trouble. Part 2: Abuses of Power. *Clin Trials*. 2014;11:508-11.

<sup>140</sup> Sackett DL. Clinician-Trialist Rounds. 3: Priority setting for academic success. *Clin Trials*. 2011;8:235-7.

<sup>141</sup> Sackett DL. Clinician-Trialist Rounds. 1: Inauguration, and an introduction to time-management for survival. *Clin Trials*. 2010;7:749-51.

Clinician-Trialist Rounds. 2: Time-management of your clinical practice and teaching. *Clin Trials*. 2011;8:112-4.

*“At least once every 6 months, you must generate 4 lists:*

*List #1: Things you’re doing now that you want to quit.*

*List #1a: Things you’ve just been asked to do that you want to refuse to do.*

*List #2: Things you’re not doing that you want to start doing.*

*List #3: Things you’re doing that you want to continue doing.*

*List #4: Strategies for improving the balance within your lists by shortening Lists #1 and #1a (quit and refuse) and lengthening List #2 (start) over the next 6 months.”*

The scope of my mentoring both widened and became more refined with time, and eventually took the form that Sharon Straus and I described in our book<sup>142</sup>. Key additions were:

- greater organization of mentorship meetings, goals, and documentation of progress,
- duplicate, ‘blind’ reviews of manuscripts and grant applications,
- protecting my mentees from “dys-opportunities”,
- organized (rather than ad hoc) coaching on their presentations,
- organized responses to their rejected grant applications and manuscripts, and
- mentoring for promotion and job prospects.

Since medical school, I credit much of my success (and fun!) to having been mentored by over 20 individuals (progressively younger than me!), and continue to be mentored as I respond to this interview.

Over the past 46 years I reckon I have mentored over 300 aspiring academics, some for as little as a year and others for decades. It has been the most fulfilling element of my career.

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<sup>142</sup>Straus SE, Sackett DL, Eds: Mentorship in Academic Medicine. Oxford; Wiley Blackwell BMJ Books, 2014.

## Chapter VIII-7: What are your most important contributions; which make you feel the proudest?

I'll leave it to others to judge my most important contributions.

For my part, the ones that make me feel the proudest are 3:

1. The brilliant young people I taught and mentored, who have gone on to great academic and clinical success and who have taught and mentored the next generation of brilliant young people, who also have gone on to great academic and clinical success and who have taught and mentored the next generation of brilliant young people, ad (I hope) infinitum.
2. My "Positive Skepticism" that didn't stop at simply tearing down the iconic conventions that were dictating 'sufficient clinical evidence' and 'proper medical education,' but replaced them with sounder approaches that continue to evolve.
3. My ability to translate, demystify, explain, promote, and popularize research methods for answering clinically relevant questions for 2 main audiences:
  - health/health care researchers (especially clinicians)
  - health care practitioners (of any persuasion)

## Chapter VIII-8: If you could have done one thing differently in your career, what would it be? What regrets?

Two regrets:

1. I would have struck a healthier work-life balance earlier in my career. It took 3 sabbaticals for me to realize that, a la Parkinson's Law, I had been inefficiently expanding the time I spent working on academic tasks to the 90-100 hours per week I could stay awake, cloistered in my hospital and home offices. My family paid for it (despite occasional family excursions and sabbaticals). By my 7th career at Oxford, I'd mastered how to complete even more academic tasks in only 50 hours per week (almost none of it after 6 PM except when I was running a clinical service).

2. I would have refused to spend my 5th career as Chief of Medicine at the McMaster Hospital. To be fair, 20% of it was both worthy and fun, immersed in bedside care and teaching, devoted to improving patient care (establishing a rapid-response General Internal Medicine Consult Service that, inter alia, took over the pre- and post-op care of emergency orthopedic patients), rescuing a suicidal colleague, working with brilliant interns and residents (the pair of Chief Residents who came to us from Ireland met me every morning with their 1-word summary of the state of the medical service: either 'grand' or 'desperate.')

But 80% of the job was miserable, trying to meet increasing patient needs and increasing faculty demands with decreasing beds and money, and especially in spending far too much time disciplining a few misbehaving and thoroughly unlikeable consultants ('you can pick your friends but not your sub-specialists') who threatened to sue me for defamation of character when I documented their bad behavior or varied their privileges.

## Chapter VIII-9: What else would you like to say?

During my 7<sup>th</sup> career I spent an insightful week in Colombia, much of it in white-knuckle forays careening along narrow dirt roads through its spectacular mountainous countryside. In addition to my life frequently passing before my eyes, my hosts (who had just started to debate whether and how they might introduce clinical epidemiology at their med school) repeatedly asked me for a similar reflection on my several careers and a description of the philosophic principles that had guided them.

Borrowing Stoney Stallones' definition of epidemiology as "what epidemiologists do," I reflected back to see whether I could identify persistent, recurring "dos" across my several careers that might reflect such underlying principles. I found 3:

### 1. Be loyal to people rather than to institutions.

By loyalty to people I mean carefully selecting colleagues and students who share your concepts of honesty, scientific rigor, social responsibility, and fun, and then supporting them through both the good and bad times that occur during any academic career. Your loyalty is tested when these persons speak out against current scientific or clinical dogma, and when their dedication to the public good leads them to take unpopular stands on social issues.

Here are 2 examples of what I mean: In the 1<sup>st</sup>, my loyalty to persons led me to defend (and shoulder some of the criticism directed toward) colleagues whose research was described as "scientifically impeccable but socially unacceptable" because it disproved the efficacy of current "expert" clinical practice. On another occasion, it led me to take on some of the storm of criticism directed toward a junior colleague when I implemented his proposal to keep drug representatives away from our students. In both cases, I was willing to sacrifice, at least temporarily, my "popularity" and reputation in order to remain true to my colleagues.

Furthermore, in both of these examples I had to reject loyalty to institutions. In the 1<sup>st</sup> case, I damaged the reputation of the "hypertension establishment," and in the 2<sup>nd</sup>, retaliation by the drug industry was judged to have reduced their willingness to sponsor research at our medical school. I could not serve both my people and my institutions.

On the other hand, in order to serve the public, institutions must constantly change to meet society's changing needs and challenges. But, because their resources (space, money, faculty posts, etc) are limited, for them to give resources to new ventures usually forces them to take some away from existing ones. Established departments lose faculty positions, established research groups lose accommodations and access to bridge-funding, and the further growth of established, effective academic programs is restricted. Loyalty to their public mission forces institutions to treat loyalty to individual people as a lower priority. Institutions simply cannot be loyal to all their members, all the time.

The failure to recognize this institutional necessity often leads to crushing disappointment among its members, especially toward the end of their careers. For example, after decades of “loyal service” to one’s institution, to then be denied a departmental Chair, a program directorship, or even the simple preservation of research space because they are being redirected to a new program, is an awful blow.

In summary, to maintain loyalty to individual people, one must inevitably sacrifice loyalty to institutions. Likewise, to meet the changing needs of society, institutions must inevitably sacrifice loyalty to individual people. I have chosen the former path, and never regretted it.

## 2. Serve the young.

Loyalty to persons, though often expressed in the support of colleagues of equal rank, is epitomized in serving the youngest individuals who are just beginning their academic or professional education or training. At its highest level, it comprises the provision, by an already successful and secure academic, of 4 services to the young. First, providing the resources (space, equipment, supporting personnel, salary and travel supplements) that are required for launching a career, all given freely and without obligation. Second, providing opportunities (but not demands) in the form of a systematic examination of everything that crosses one’s desk for its potential contribution to the scientific development and academic advancement of the young. Third, providing frequent, unhurried, and safe opportunities for the junior colleague to think their own way through their choices of educational experiences, areas of concentration, the scientific and methodological challenges in their individual projects, the pros and cons of embarking on a particular program of research with a particular set of collaborators, and their development as social beings. As before this advice is offered as reflections on their choices from a senior colleague, not as orders to be obeyed. Fourth, the protection of the young from needless academic buffeting and from the bad behavior of other academics. This includes organizing the vigorous debate of their ideas, research designs, data, and conclusions in supportive settings, and proving the vigorous defense of their career development against the actions of jealous colleagues. The name often given to these 4 services: resources (but not obligations), opportunities (but not demands), advice (but not orders), and protection, is mentoring. Not only has mentoring been found to be key to academic success for the 1 who receives it, but it also increases the reputation and professional satisfaction of the 1 who provides it.

## 3. You become what you pretend to be.

I’ve discussed this 3<sup>rd</sup> principle in Chapter VIII-1 (To what do you attribute your ‘success’?).

### Editor's Postscript

Dave Sackett died May 13, 2015, from his cancer. He loved to teach and support students in any way possible. The David L Sackett Scholarship Fund has been established in his honor. Donations can be made to McMaster University in his memory at this [link](#).