

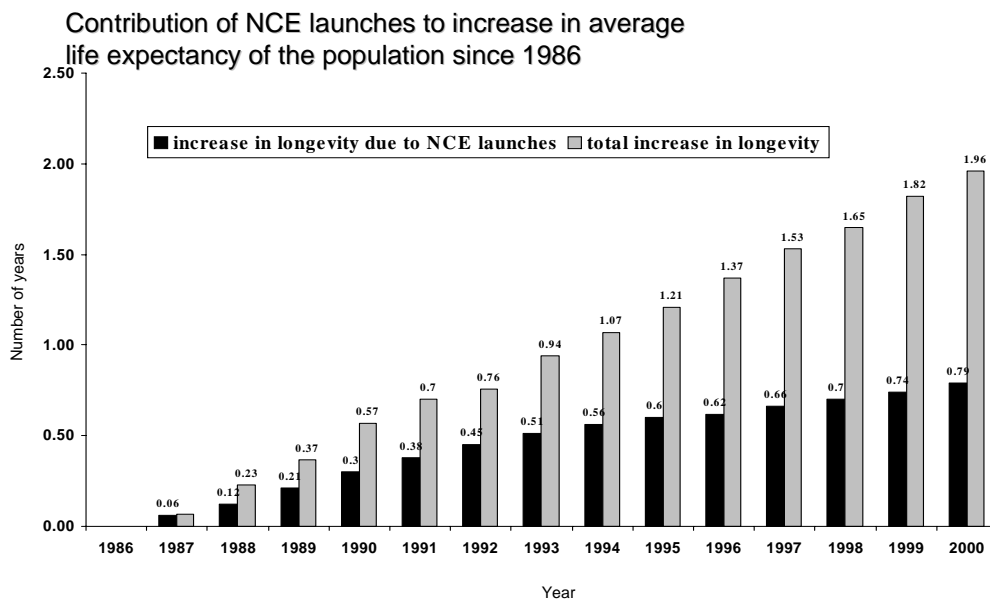
Value Proposition for New Drug Use

Terry Montague, March 2003

Cost-effectiveness

Health and drug investments can produce value for money beyond the healthcare system. For example, drug use that reduces time lost from work and improves productivity is an important effect for the society as a whole. From this societal view, new drug technologies can be defined as effective within any given patient population when their clinical and economic benefits exceed their costs.

In clinical terms, the relation between new drugs and improved outcomes is very well illustrated by the figure below,



an analysis of data from 52 countries, which reveals: an increase in life expectancy between 1986 and 2000 averaging 1.96 years; and, the introduction of new drugs accounted for 40 percent of the longevity increase (**Lichtenberg FR**. Pharmaceutical knowledge-capital accumulation and longevity, in: *Measuring Capital in the New Economy*, eds. C Corrado, J Haltiwanger and D Sichel, *University of Chicago Press*, forthcoming).

The weight of other available evidence strongly and consistently supports the link between new drug use and improved longevity and quality of life (**Cutler D, McClellan M**. Is technological change in medicine worth it? *Health Affairs* 2001; 20: 11-29; **Analysis Group/Economics**. The value of pharmaceuticals in Canada 2003; http://www.canadapharma.org/Industry_Publications/Value_Medicine/; **Lichtenberg FR**. Are the

benefits of newer drugs worth their cost? Evidence from the 1996 MEPS. *Health Affairs* 2001; 20: 241-51; **Lichtenberg FR**. Pharmaceutical innovation, mortality reduction, and economic growth. National Bureau of Economic Research Working Paper No. 6569; forthcoming in: *The Economic Value of Medical Research*, Murphy and Topel eds, University of Chicago Press, 2003).

In purely economic terms, also, the weight of data demonstrates new drug development to be a valuable proposition for any society. Based on US data, the national impact of the positive health benefit of increased longevity is estimated to produce economic growth that is twice as large as unadjusted growth (**Nordhaus W**. The Health of Nations: Irving Fisher and The Contribution of Improved Longevity to Living Standard, Cowles Foundation Paper No. 1200, Yale University, September 1998; in: *The Economic Value of Medical Research*, Murphy and Topel eds, University of Chicago Press, 2003).

While, in dollar terms, it is difficult to define a line below which all products are cost-effective and above which they are not, there is some gradient which may define what we, as a society are willing to pay. The recent analysis of Lichtenberg, outlined in the above figure, revealed the cost per life-year saved from launch of new drugs between 1986 and 2000 to be very low - about \$4500.

Optimal prescribing

"Optimal prescribing is the level of prescribing that leads to the best patient outcomes" - is a good definition and goal, conceptually.

However, there are some significant impediments to attaining the goal.

First, there are enormous gaps, or patterns of under-prescribing, in many important diseases, from about 50 percent for cardiac diagnoses, to probably more than 90 percent for osteoporosis. Moreover, these care gaps are significantly larger for older and female patients, despite the evidence of greater efficacy in such higher risk patients (**McAlister FA, Taylor L, Teo K, Tsuyuki RT, Ackman ML, Yim R, Montague TJ, for the Clinical Quality Improvement Network (CQIN) Investigators**. The treatment and prevention of coronary heart disease in Canada: do older patients receive efficacious therapies? *J Am Geriatr Soc* 1999; 47: 911-8).

These prescribing gaps, determined by repeated audits, are also supported by survey data of physicians showing similar lower rates of intention-to-treat for females and older subjects (**Taylor LK, Teo KK, Cox J, Tymchak W, Tremblay G, Ashton T, Alter D, Montague T**. Contemporary physician attitudes and practice patterns in acute myocardial infarction – results of a large Canadian survey. *Can J Cardiol* 2000; 16 (Suppl F): 156F).

A second conundrum is these practices and intentions occur in the face of other data demonstrating physicians, across all specialties, rate the literature evidence as the overwhelming influencing factor in their prescribing decisions, with age of the patient the second most important consideration (**Taylor LK, Teo KK, Tymchak**

W, Cox J, Alter D, Ashton T, Tremblay G, Montague T. Treatment differences in elderly patients: insights from a large Canadian survey on contemporary physician attitudes and practice patterns in acute myocardial infarction. *Can J Cardiol* 2000; 16 (Suppl F): 157F).

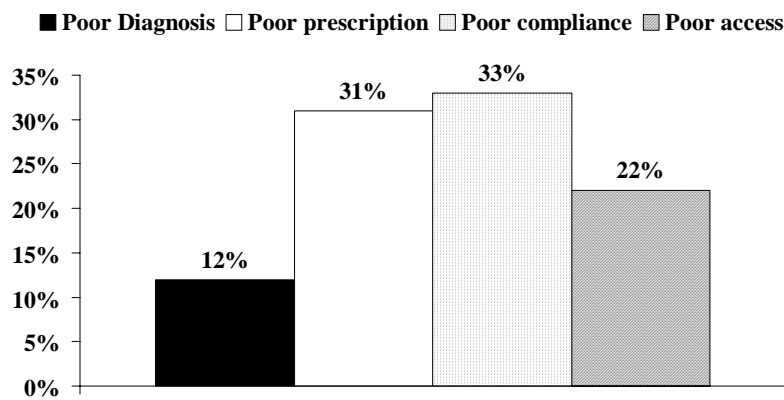
Thus, there is dissonance not only between the efficacy evidence and practice patterns, but also between what prescribers report as principal influences driving prescribing decisions. Under-treatment remains the great issue for the major disease burdens and, despite the problems of prescribing behavior outlined above, it can be attacked and improved (**Montague T, Cox J, Kramer S, Nemis-White J, Cochrane B, Wheatley M, Joshi Y, Carrier R, Gregoire J-P, Johnstone D**, for the ICONS investigators. Improving cardiovascular outcomes in Nova Scotia: ICONS, a successful public/private partnership in primary health care. *Hosp Quart* 2003 (In Press).

Current Barriers to Optimal Prescribing

Tugwell and colleagues predicted, many years ago, the most important barriers to the optimal population use of proven therapies would likely be one, or some combination, of: poor diagnosis, poor prescribing, poor compliance or poor access (**Tugwell P, Bennet KJ, Sackett, Haynes RB.** The measurement iterative loop: a framework for the critical appraisal of need, benefits, and costs of health interventions. *J Chron Diseases* 1985; 38: 339-51).

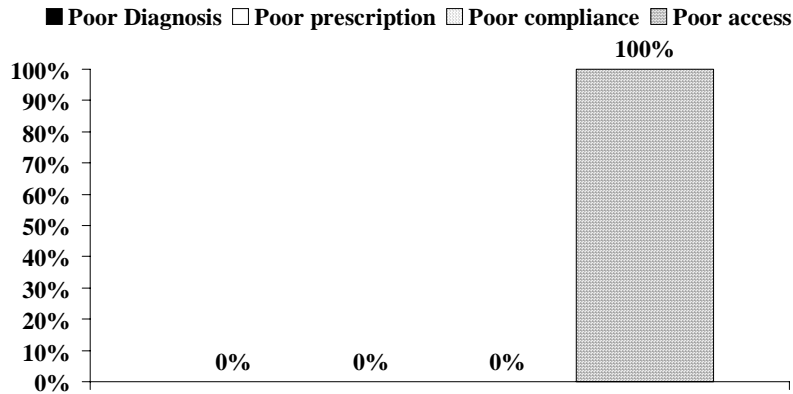
However, it does seem to depend on which seat one occupies at the health care table as to how one ranks of relative importance of the four factors producing the acre gap and impeding optimal care and outcomes realization. The two next figures illustrate these divergent views of stakeholders.

Physicians' And Nurses' View



Montague. *ACCC Audience Survey*, Halifax, NS, April 1999.

Consumers' View



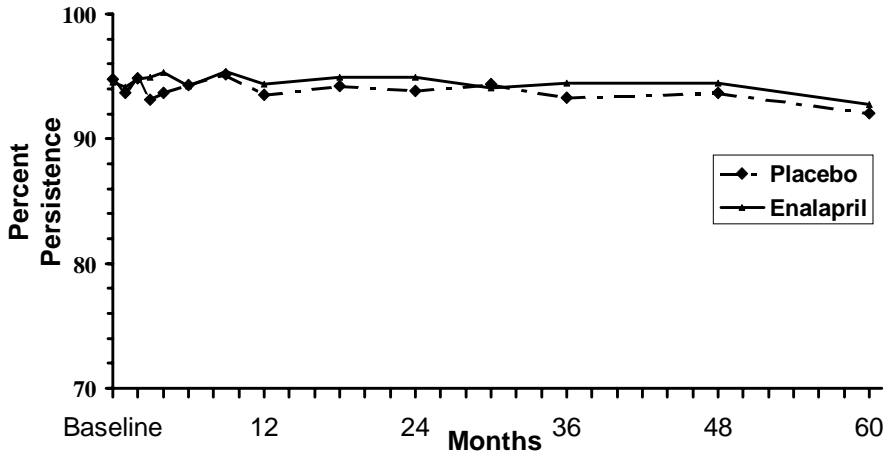
Montague. *Kiwanis Club Audience Survey*, Montreal, QC, March 2000.

The bottom line: all the barriers to optimal care and outcomes are important and all can be addressed successfully.

In particular, the contribution to the overall care gap from patients not persisting with proven therapies remains under appreciated, incompletely understood in terms of causation, and ineffectively addressed in terms of solution. It occurs in all major diseases and the cost to society from the lost opportunity is enormous. On average, patients persist with their drugs, as prescribed, for about six months, even in high risk cardiac settings.

However, the data from large clinical trials suggests this is not necessarily so. For example, as indicated in the figure below, during the SCAT trial (the Simvastatin/enalapril Coronary Atherosclerosis Trial), two drugs were taken by >400 high-risk patients for >four years, with compliance rates >90 percent (Teo K, Burton J, Buller C, Plante S, Catellier D, Tymchak W, Dzavik V, Taylor D, Yokoyama S, Montague T, on behalf of the SCAT Investigators. Long Term Effects of Cholesterol Lowering and Angiotensin-Converting Enzyme Inhibition on Coronary Atherosclerosis: The Simvastatin/Enalapril Coronary Atherosclerosis Trial (SCAT). *Circulation* 2000;102: 1748-54).

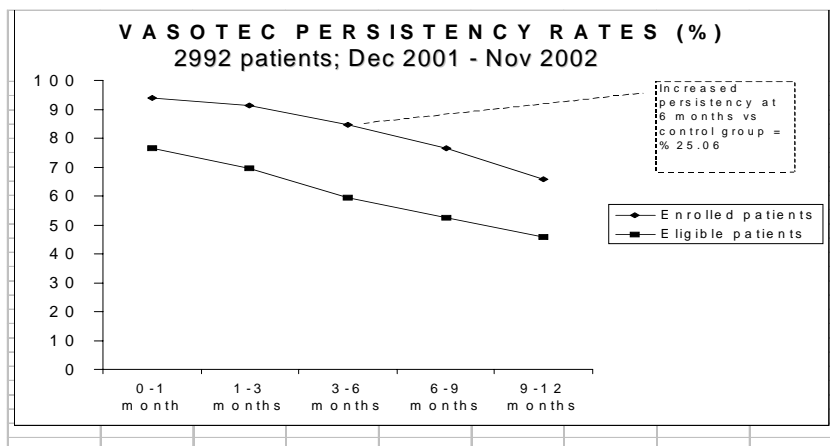
Compliance In The Trials' World



SCAT. *Circulation* 2000; 102: 1748-54.

And, we have recently realized that compliance could be improved in the real world, in part by borrowing some ideas from the trials' world, namely patient education. In the figure below, pharmacist-directed and third party-provided, patient education was the primary intervention driving the improved compliance.

Compliance Improvement



Health Inform 2003.

Possible Strategic Solutions

A partnership/measurement disease management strategy could be implemented in one, or more, diseases immediately. As Roy Romanow has recently said, in reference to the ICONS model, this approach is: "ensuring that people have access to the right, evidence-based treatment at the right time, by the right provider, .. substantial savings can be realized through fewer or shorter hospital stays and,... will lead to better overall health outcomes, such as increased longevity, higher quality of life and greater productivity" (Commission on the Future of Health Care in Canada, Montreal, 27 March 2002).

Disease management can be defined, simply as: a focused application of resources to drive desirable health outcomes. This general framing allows for many specific variations to be gathered under the definition and, in this context, disease management is not a new concept. However, as indicated, the modern use of the term often refers to a patient-centred approach for the prevention, diagnosis, therapy, and monitoring of disease/health states, and considers drug and non-drug therapy, stakeholder and patient education and coordination of resources across the whole healthcare system.

Other characteristics of current programs include: a shift away from isolated inputs and controls, toward a systems view with integration of components geared to improving the health of whole populations. The working premise is: care and outcomes can be better!

The type of disease management program of which I have the most experience can be characterized as the partnership/measurement model, also referred to as patient health management (**Montague T, Sidel J, Erhardt B**, et al. Patient health management: a promising paradigm in Canadian healthcare. *Am J Man Care* 1997; 3: 1175-82). The key features of this model are broad, community-based partnerships and use of repeated measurement and feedback of practices and outcomes to generate a continuous quality improvement loop, particularly to ensure more appropriate prescribing. Heretofore, the most advanced case study of the model is the ICONS (Improving Cardiovascular Outcomes in Nova Scotia) project (**Montague T, Cox J, Kramer S, Nemis-White J, Cochrane B, Wheatley M, Joshi Y, Carrier R, Gregoire J-P, Johnstone D**, for the ICONS investigators. Improving cardiovascular outcomes in Nova Scotia: ICONS, a successful public/private partnership in primary health care. *Hosp Quart* 2003 (In Press).

The benefits of these types of disease management programs are:

To The Health System

- More appropriate use of drugs / services
- Improved health outcomes
- Increased cost-effectiveness
- Increased measurement / accountability

To The Investment Climate

- Direct investment in research
- Knowledge export opportunities
- Database and infrastructure attracts new investments
- Sense of partnership: government, hospitals, community
- Healthier population / workforce

One particularly attractive disease state choice would be to tackle diabetes as a model for comprehensive and continuous primary care delivery, because:

- it is a very large and expanding disease burden, spans several important disease states, all with large gaps in prescribing and compliance
- pre-symptomatic molecular diagnosis of susceptibility, for aboriginal or MODY forms, would allow efficient targeting for primary prevention
- and, specific molecular diagnosis may also allow more specific therapy for secondary prevention

To optimally favour success in such an endeavour one key ingredient is that MoH be engaged as a partner at the outset. As Sarah Kramer, co-chair of ICONS and the Chief Information Officer for the Department of Health of Nova Scotia, responsible for ensuring valid information is available to support sound health care decision making from the bedside to the Cabinet table, points out: " A key component of the design of ICONS as a research project was the engagement of the Department of Health as an original partner. This facilitated government understanding of the purpose and objectives of the project, in the short term, and meaningful buy-in, in the long term. Moreover, it provided an avenue for communicating ongoing results, as opposed to the less viable, but more usual, method of presenting final results as a *fait accompli* in a risk-averse environment." (Montague T, Cox J, Kramer S, Nemis-White J, Cochrane B, Wheatley M, Joshi Y, Carrier R, Gregoire J-P, Johnstone D, for the ICONS investigators. Improving cardiovascular outcomes in Nova Scotia: ICONS, a successful public/private partnership in primary health care. *Hosp Quart* 2003 (In Press)).

Another key ingredient, I believe, to success of initiatives such as ICONS is the access environment for physicians prescribers and patient consumers is as non-restrictive as possible. Or, in other words, for disease management to be most successful all barriers to optimal care are addressed including diagnosis, prescribing, compliance and access.

How should cost-effectiveness be balanced with optimizing patient care?

In answering this question, I refer back to the definition and data on cost effectiveness, above. Briefly, the evidence suggests that innovative drugs are very cost effective and enhancing their evidence-based use and accountability via partnership/measurement disease management programs produces an optimal return on investment (Montague T, Cavanaugh S, Skilton K, Szabo G, Sidel J,

Gregoire J-P. Drugs, health and the economy: investment, innovation, outcomes, growth. *HealthcarePapers* 2002; 3: 63-69).

In addition, I would like to deal a bit with the concept of incremental innovation. I believe there are a couple of very important fundamental truths that are often overlooked.

First, to the best of my knowledge, all innovation advances are incremental, built on previous increments. This is true of even what we may consider, with retrospection, seminal, or "breakthrough" events, as for example, the delineation of the double helix structure of DNA, or the description of the Theory of Relativity. Einstein and Watson and Crick developed their views standing on the shoulders of others.

This is certainly true in the pharmaceutical arena, as repeated econometric analyses have shown (**Lichtenberg FR.** Pharmaceutical innovation, mortality reduction, and economic growth. National Bureau of Economic Research Working Paper No. 6569; forthcoming in: *The Economic Value of Medical Research*, Murphy and Topel eds, University of Chicago Press, 2003).

It is important, as well, to remember that with regard to pharmaceuticals "incremental innovations are evolutionary, not duplicative" and, moreover, from a strictly cost viewpoint, new drugs in existing classes tend to be priced at a discount to what is already available, because of competitive pressures within the market (**Wertheimer A, Levy R, O'Connor T.** Too many drugs? The clinical and economic value of incremental innovations. In: *Investing in health: The social and economic benefits of health care innovation* 2001; 14: 77-118; and, **DiMasi JA.** Price trends for prescription: pharmaceuticals: 1995-1999. Analysis prepared for the Department of Health and Human Services Conference on pharmaceutical utilization and costs, August 2000).

Perhaps the most appropriate way to summarize the value proposition inherent in this question is: the value in drug innovation is "newness", not "firstness" or "sameness".

What if optimal care of the patient is not cost-effective?

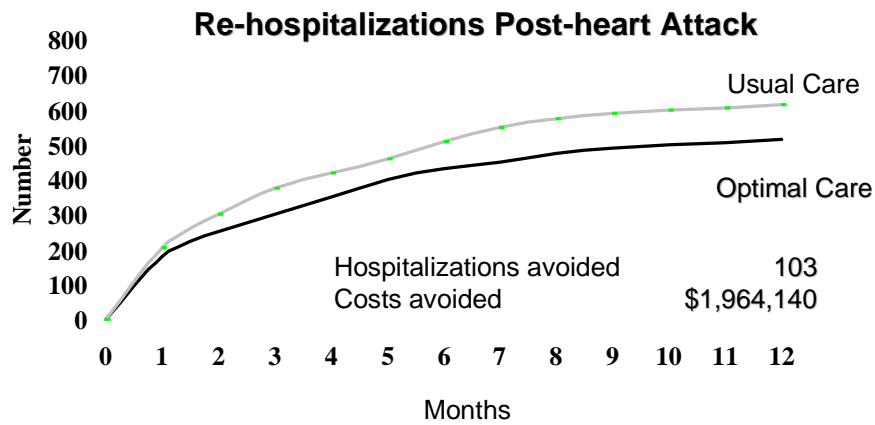
This eventuality is difficult to conceive, at least based on the summary of clinical and economic data outlined above.

What if the strategies for changing practice are not cost-effective?

Based on my experience, for large burden of illness diseases, like CV or diabetes, where there are frequent clinical end points to measure and efficacious therapies to improve outcomes, this is a very unlikely eventuality.

For example, in ICONS, the infrastructural and operating costs of ICONS were about 1.2 million dollars/year and the incremental costs of increased use of ACE inhibitors in patients with heart failure was .32 million dollars. However, based on the anticipated reductions in re-hospitalizations for this high-risk patient group, secondary to the increased use of ACE inhibitors, 3054 hospital days were avoided with net cost avoidance >3 million dollars.

We saw a similar net cost savings in a trial of an optimal post-heart attack patient management trial done in Calgary, as shown in the figure below.



Edworthy. *Can J Cardiol* 1998; 14 (Suppl F): 113F.