

Spiralling Medical Costs: Why Canada Needs NICE Medicine

Escalade des frais médicaux : le Canada pourrait tirer profit des lignes directrices du NICE



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Abstract

Healthcare spending in Canada has grown rapidly in recent years, especially for drugs. This paper discusses the causes of the problem and makes policy proposals. Conflicts of interest (COIs) are a frequent occurrence in medical research and lead to bias. Published studies, especially in the area of clinical trials on drugs, are much more likely to produce findings favourable to the drug when funded by the manufacturer. Bias can occur by various means, including inappropriate study design (such as giving a placebo to control subjects rather than an existing drug) and selective publication of results. COIs also frequently occur with clinical practice guidelines. High-priced (particularly new) drugs are often marketed by inappropriate means. Drug costs in Canada could be greatly reduced if doctors prescribed lower-cost alternatives where appropriate (therapeutic substitution). Proposals are made for changes in the regulatory agencies responsible for the approval of drugs, drug marketing and post-marketing surveil-

lance. In addition, a new regulatory agency is proposed that would examine the value of drugs and medical devices in terms of clinical effectiveness and cost-effectiveness. Such an agency would set the rules for therapeutic substitution and would determine which medical interventions can be used based on agreed cost-effectiveness criteria.

Résumé

Les dépenses en santé ont connu une croissance rapide au Canada au cours des dernières années, surtout pour ce qui est des médicaments. Cet article examine les causes du problème et propose des politiques. Les conflits d'intérêts sont chose courante dans la recherche médicale et entraînent des biais. Les études publiées – en particulier dans le domaine des essais cliniques portant sur les médicaments – sont beaucoup plus susceptibles de parvenir à des conclusions favorables au médicament lorsque ces études sont financées par le fabricant. Les biais peuvent se manifester de diverses façons, y compris une méthodologie inappropriée (comme, par exemple, donner aux sujets-témoins un placebo au lieu d'un médicament existant) et une publication sélective des résultats. De plus, des conflits d'intérêts surviennent fréquemment avec les lignes directrices sur la pratique clinique. De nombreux médicaments coûtent excessivement cher et sont souvent commercialisés par des moyens inappropriés. Le coût des médicaments au Canada pourraient être considérablement réduits si les médecins prescrivaient des solutions thérapeutiques moins coûteuses lorsque possible (substitution thérapeutique). On propose des changements à apporter aux organismes réglementaires responsables de l'approbation, de la commercialisation et de la surveillance post-commercialisation des médicaments. On propose également de créer un nouvel organisme réglementaire qui serait chargé d'examiner la valeur des médicaments et des appareils médicaux tant du point de vue de leur efficacité clinique que de leur rapport coût-efficacité. Un tel organisme mettrait en œuvre la substitution thérapeutique et déterminerait quelles interventions médicales peuvent être utilisées d'après les limites de dépenses convenues.



Introduction

Whenever the subject of cost escalation in medicine arises, attention often turns to the United States, where spending increases have outstripped those in Canada. But spending on medicine in Canada has also grown rapidly in recent years, as it has across most of the Western world. In Canada, healthcare spending per capita by the government (in constant dollars) has almost doubled over the last 30 years (CIHI 2005a), while drug spending increased 150% between 1985 and 2002 (CIHI 2005b). These num-

bers reveal not only the rapid pace of inflation in medical costs, but also that drug costs are central to the problem. This paper discusses the causes of this problem and makes policy proposals.

Problems in the Reliability of the Medical Literature

COIs are a frequent occurrence in medical research and lead to bias in various ways (Fraser 2007). If bias is introduced, it can affect any stage of a clinical study, including its design, the types of subjects used, the collection of the data and the reporting and publication (or non-publication) of the results. The main focus here is in the design and conduct of randomized, controlled, double-blind clinical trials (RCTs).

Doctors are often paid large sums to recruit patients for clinical trials; this practice may lead to the enrollment of patients who are not really eligible (Angell 2004). Another way in which COI in patient recruitment can distort the conduct of trials

is through the selection of patients who are more likely to react positively to the drug. Bodenheimer (2000) suggested that by selecting patients who are younger and healthier and who have milder symptoms of the disease, a drug will likely appear to be more effective and show

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fewer side effects than might be the case in the actual target population. For example, Rochon et al. (1998) noted that in major trials of non-steroidal anti-inflammatory drugs (NSAIDs), only 2.1% of the participants were over 65 years old, even though the principal users of these drugs, and those who are likely to have more serious side effects, are the elderly. Another possible design flaw in RCTs is that drugs are often tested for relatively short periods of time.

Drug companies commonly test new drugs against placebos (Rothman and Michels 2003), thus maximizing the chance that the new drug will appear effective. However, this practice can cause systematic bias. If the control group were given an existing drug, the trial might reveal that the new drug is, in reality, no better than, or even inferior to, the existing drug. In Canada, under the Tri-Council policy, placebo treatment of controls is not usually permitted. However, much of the marketing of drugs in Canada is based on the results of clinical trials done in other countries; the results typically show only that the drug is better than a placebo, not that it is superior to an existing treatment.

Predictably, the above problems in the design of clinical trials are more likely to lead to unreliable results when COIs are also present. How common is this situation? In a study of the scope and impact of financial COIs in biomedical research, Bekelman et al. (2003) found that approximately one-quarter of researchers have industry affiliations, and roughly two-thirds of academic institutions hold equity in start-up companies that sponsor research undertaken in those institutions. There is considerable evidence that such close financial relationships have a strong impact on the results of clinical trials. Several investigations over the last decade or so have reported that when studies of new drugs or other medical products are funded by drug companies, the results are appreciably more likely to favour the new product than when funding comes from other sources (Bekelman et al. 2003; Bhandari et al. 2004; Lexchin et al. 2003; Perlis et al. 2005).

One means by which pharmaceutical and other companies manage to transform their funding for RCTs into such high levels of “success” is by the selective publication of results. This practice was documented in a review of 38 published RCTs of selective serotonin reuptake inhibitors (SSRIs) that were sponsored by drug companies (Melander et al. 2003). Over half the studies contributed to two or more publications each, and studies showing significant effects of drugs were published more often than studies with non-significant results. Many publications ignored negative results.

This problem is exemplified by the episode concerning celecoxib (Celebrex[®]), a COX-2 selective NSAID (Schafer 2003). Although the full data set was available, only partial results of the clinical trial of the drug were published. These results, based on six months of data, indicated that the drug causes lower rates of stomach and intestinal ulcers than two existing drugs used for treating arthritis. Following publication of the trial results, celecoxib became a “blockbuster” drug. However, the full year of data revealed that it is no safer than existing arthritis drugs. These latter data had been available on the FDA website but had been excluded from publications. The fact that eight of the study’s authors were paid medical consultants for Pharmacia, which funded the study, and the other eight were company employees, underscores the problem with COI.

After RCTs have been published, their significance is interpreted. Here again, COIs have an impact (Jorgensen et al. 2006). For example, Stelfox et al. (1998) reviewed 70 reports in order to examine the links between doctors’ published support of the use of calcium channel antagonists to treat high blood pressure and their financial relationship with drug manufacturers. These researchers reported that among authors who supported the use of this class of drugs, 96% had received funding from drug manufacturers, while those who criticized their safety were much less likely (43%) to have financial ties.

Another important area where COI is involved is in the preparation of clinical practice guidelines (CPGs). Choudhry and colleagues (2002) examined 44 published

guidelines. They reported that 87% of authors had some form of interaction with the pharmaceutical industry, while a mere 2% declared a financial relationship with the drug company and none declared any potential COI.

An important aspect of evaluating a treatment is to estimate its cost-effectiveness, and even here COI may exert a major impact. This situation was well demonstrated in the case of statins for treatment of patients at relatively low risk for coronary disease. When the investigators who published the estimates were funded by government or universities, then the cost of statins, relative to benefit achieved, was around twice as high for lower-risk patients than when the funding came from the pharmaceutical industry (Franco et al. 2005). This finding strongly suggests that the drug manufacturers have exerted undue influence so that published estimates make statins appear to be cost-effective for millions of extra potential patients. Similar findings have been reported with respect to numerous other drugs (Baker et al. 2003; Bell et al. 2006).

The evidence documented above reveals a systemwide problem related to corporate sponsorship in the whole research and publication process. As a result, new products of dubious value are often reported in the medical literature as being superior to existing products, and are then marketed, usually at a much higher price than the older product. The evidence is especially strong with regard to drugs. The likely result is that doctors will change their prescribing habits in directions that serve the profits of the drug industry rather than the health of their patients (Kassirer 2004).

Pricing of Drugs

The pharmaceutical industry typically charges high prices for its products. It attempts to justify this practice by exaggerating the benefits of new drugs, as discussed above, while claiming that high prices are essential to pay for the high costs of research and development, a claim that is also greatly exaggerated (Goozner 2004; Light 2007).

A major activity of the pharmaceutical industry is the production and marketing of “me-too” drugs. These are chemical variations of existing drugs. Indeed, according to an independent European review, only a tiny fraction of all new drugs have the potential to offer an important therapeutic gain over existing drugs (*Prescrire International* 2003).

The Marketing of Overpriced Drugs and the Need for Therapeutic Substitution

An integral part of the “business plan” of the pharmaceutical industry is intensive marketing of drugs, often by inappropriate methods. There is ample evidence that great effort is expended to promote the sale of drugs that maximize profit (Balay-Karperien et al. 2007; Angell 2004; Abramson 2004). As a result, society pays high prices for

drugs that are often no better than cheaper alternatives.

Cassels and Lexchin (2007) examined the 10 most costly drugs prescribed in Canada, based on budgetary impact. Their findings show that expenditures would be reduced by up to 45% if doctors switched to lower-cost alternatives (therapeutic substitution). As these drugs represent \$2.2 billion of the \$18 billion spent in 2004 on prescription drugs (Morgan 2005), some one billion dollars a year is wasted. If therapeutic substitution were applied to many prescribed medicines, several billions more in savings would be achievable. Supporting evidence for this conclusion came from a study that revealed that 80% of the increase in drug prices in Canada in recent years was due to new, high-priced, patented, me-too drugs (Morgan et al. 2005).

One example is rosuvastatin (Crestor®). While it has been shown to lower blood cholesterol, its effect on risk for heart disease and its safety profile have never been tested in a long-term trial. Despite this shortcoming, and costing 50% more than

generic statins, rosuvastatin has achieved 10th spot in Canada for all drugs, based on value of sales. This position was achieved, in part, by heavy advertising, including frequent direct-to-consumer advertising (DTCA) on American TV (which can be seen by viewers in Canada, although the impact of such viewing is not known). The

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TV ads do mention that the drug has not actually been shown to prevent heart disease, but this point is unlikely to be noticed by most members of the target audience. An editorial in *The Lancet* demanded that AstraZeneca, the manufacturer, "... desist from this unprincipled campaign" (*Lancet* 2003).

A similar problem is seen with drugs for hypertension. The pharmaceutical companies have achieved considerable success in persuading doctors to prescribe calcium channel blockers and angiotensin-converting enzyme inhibitors: three of these drugs are among the top 10 most costly drugs prescribed in Canada (Cassels and Lexchin 2007). Yet, enormous cost reductions could be achieved by using diuretics.

The most effective way to implement therapeutic substitution is by way of government policy. In Canada, this approach could also be applied to employer-sponsored drug plans. The approach has been adopted, with some success, by governments in several countries (Cassels and Temple 2007). One such program was implemented in British Columbia in 1995: the Reference Drug Program (RDP). It was applied to only five classes of drugs. The rationale behind RDP is simple: if there is no evidence that

a newer, more expensive drug is therapeutically superior to a cheaper treatment, then the program funds the least expensive alternative first.

Drugs and Regulatory Agencies

Drugs are regularly approved for use but are later found to have a far less favourable risk–benefit profile than was claimed at the time of their approval. Unfortunately, the ability of regulatory agencies to act effectively is limited by the reliability of the information they are given: like computers, it is a case of “junk in, junk out.” An important part of the problem is the bending of the rules in the design, conduct and publishing of drug trials. But we cannot be optimistic about major improvements while pharmaceutical companies have a strong financial incentive to corrupt the system. Accordingly, a strong case can be made for the establishment of independent agencies to carry out clinical trials of new medical products, especially drugs. However, for reasons of cost, such agencies would have to be international in scope. While it is easy to argue for the advantages of such agencies, there are certain to be many obstacles to overcome in their establishment.

Furthermore, there is much evidence of a lack of vigilance by the regulatory agencies responsible for approving new drugs (Lexchin 2007). The problem extends to serious deficiencies in the post-marketing surveillance of drugs. Lexchin (2007) proposed a radical reform in the regulatory approach.

Implementing Cost Controls in Medicine

Based on current trends, it is highly predictable that medical costs, especially drug costs, will continue their upward spiral for years to come. Contributing factors include the aging of the baby boomers, the rapid pace of development of new (and expensive) medical technologies and the ever-rising cost of drugs. This situation requires bold policy initiatives. New policies related to drugs, as proposed in this paper, would help to reduce the problem. But much more is required. One approach is to set limits on the maximum permitted cost of medical expenditures, expressed as dollars per quality-adjusted life-year (QALY).

The great advantage of measuring the real cost of medical interventions on the basis of dollars per QALY is that this method allows a direct comparison of medical interventions that extend life and those that improve its quality. Thompson and Temple (2007) proposed a twin set of cost limits: a medium-term goal of US\$50,000 (C\$59,000) per QALY and a lower limit of US\$27,000 (C\$32,000) as both an ideal limit and a longer-term goal. They emphasize that these figures are very rough estimates and therefore open to debate. Such limits should be used as guidelines for public funding of medical practice. I propose that Canada set a medium-term goal of C\$59,000 per

QALY, to be achieved within five to 10 years, and a lower limit of C\$32,000 as both an ideal limit and a longer-term goal, to be achieved within 10 to 15 years.

The country that appears to come closest to implementing such a policy is the United Kingdom. The National Institute for Health and Clinical Excellence (NICE) examines the value of drugs and medical devices in terms of both clinical effectiveness and cost-effectiveness. This agency is independent of government and releases detailed reports. Drugs or devices costing above about US\$31,000 to US\$46,000 per QALY are likely to be rejected (Henry et al. 2005; Pearson and Rawlins 2005).

Conclusion

There are serious deficiencies in the approval of drugs, the regulation of their marketing and their post-marketing surveillance. COI is the root cause of many of the problems. Two new types of regulatory agencies are required, with both types being free of COI and having both independence and the required resources. One type of agency would carry out both clinical trials of new medical products, especially drugs, and post-marketing surveillance. Because of the high costs involved, such an agency would have to be international.

The other proposed new regulatory agency would be modelled on NICE. It would be established and funded by the Canadian government but would work independently. It would examine the value both of drugs and of medical devices in terms of clinical effectiveness and cost-effectiveness. As part of its mandate, it would set the rules for therapeutic substitution. By this means, governments and other bodies that pay for drugs can be advised as to how to obtain the best value for money and avoid paying for more expensive drugs that are not therapeutically superior. The proposed agency would also be given guidelines by government that public funding of drugs and medical procedures would be allowed only where the cost does not exceed an agreed limit, expressed as dollars per QALY. By this means, society would have a clear understanding that it should spend on healthcare only what it deems it can afford. Such a policy would also help ensure that limited funds are directed to where they can achieve the most benefit, rather than allocating them based on pressure by industry, its lobbyists and other special-interest groups.

The proposed agency already exists in an underdeveloped form as the Canadian Agency for Drugs and Technologies in Health (CADTH; www.cadth.ca). However, in its present form, CADTH lacks the authority we see in NICE, and is therefore failing to achieve the necessary impact.

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REFERENCES

- Abramson, J. 2004. *Overdosed America: The Broken Promise of American Medicine*. New York: HarperCollins.
- Angell, M. 2004. *The Truth about Drug Companies: How They Deceive Us and What to Do about It*. New York: Random House.
- Baker, C.B., M.T. Johnsrud, M.L. Crismon, R.A. Rosenheck and S.W. Woods. 2003. "Quantitative Analysis of Sponsorship Bias in Economic Studies of Antidepressants." *British Journal of Psychiatry* 183(6): 498–506. Retrieved June 13, 2007. <<http://bjp.rcpsych.org/cgi/content/full/183/6/498>>.
- Balay-Karperien, A., N.J. Temple and J. Lexchin. 2007. "The Marketing of Drugs: How Drug Companies Manipulate the Prescribing Habits of Doctors." In N.J. Temple and A. Thompson, eds., *Excessive Medical Spending: Facing the Challenge*. Oxford: Radcliffe Publishing.
- Bekelman, J.E., Y. Li and G.P. Gross. 2003. "Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review." *Journal of the American Medical Association* 289(4): 454–65.
- Bell, C.M., D.R. Urbach, J.G. Ray, A. Bayoumi, A.B. Rosen, D. Greenberg and P.J. Neumann. 2006. "Bias in Published Cost Effectiveness Studies: Systematic Review." *British Medical Journal* 332(7543): 699–703.
- Bhandari, M., J.W. Busse, D. Jackowski, V.M. Montori, H. Schunemann, S. Sprague, D. Mears, E.H. Schemitsch, D. Heels-Ansdell and P.J. Devereaux. 2004. "Association between Industry Funding and Statistically Significant Pro-Industry Findings in Medical and Surgical Randomized Trials." *Canadian Medical Association Journal* 170(4): 477–80.
- Bodenheimer, T. 2000. "Uneasy Alliance – Clinical Investigators and the Pharmaceutical Industry." *New England Journal of Medicine* 342(20): 1539–44.
- Canadian Institute for Health Information (CIHI). 2005a. *Preliminary Provincial and Territorial Government Health Expenditure Estimates, 1974–1975 to 2004–2005*. Ottawa: Author.
- Canadian Institute for Health Information (CIHI). 2005b. *Drug Expenditure in Canada: 1985–2004*. Ottawa: Author.
- Cassels, A. and J. Lexchin. 2007. "Potential Savings from Therapeutic Substitution of Ten of Canada's Most Dispensed Prescription Drugs." In N.J. Temple and A. Thompson, eds., *Excessive Medical Spending: Facing the Challenge*. Oxford: Radcliffe Publishing.
- Cassels, A. and N.J. Temple. 2007. "Paying for What Works: The Reference Drug Program As a Model for Rational Policy Making." In N.J. Temple and A. Thompson, eds., *Excessive Medical Spending: Facing the Challenge*. Oxford: Radcliffe Publishing.
- Choudhry, N.K., H.T. Stelfox and A.S. Detsky. 2002. "Relationships between Authors of Clinical Practice Guidelines and the Pharmaceutical Industry." *Journal of the American Medical Association* 287(5): 612–17.
- Franco, O.H., A. Peeters, C.W. Looman and L. Bonneux. 2005. "Cost Effectiveness of Statins in Coronary Heart Disease." *Journal of Epidemiology and Community Health* 59(11): 927–33.
- Fraser, J. 2007. "Conflict of Interest: A Major Problem in Medical Research." In N.J. Temple and A. Thompson, eds., *Excessive Medical Spending: Facing the Challenge*. Oxford: Radcliffe Publishing.
- Goozner, M. 2004. *The \$800 Million Pill: The Truth Behind the Cost of New Drugs*. Berkeley: University of California Press.

- Henry, D.A., S.R. Hill and A. Harris. 2005. "Drug Prices and Value for Money. The Australian Pharmaceutical Benefits Scheme." *Journal of the American Medical Association* 294(20): 2630–32.
- Jorgensen, A.W., J. Hilden and P.C. Gotzsche. 2006. "Cochrane Reviews Compared with Industry Supported Meta-analyses and other Meta-analyses of the Same Drugs: Systematic Review." *British Medical Journal* 333(7572): 7827.
- Kassirer, J.P. 2004. *On the Take: How Medicine's Complicity with Big Business Can Endanger Your Health*. Oxford: Oxford University Press.
- Lancet*. 2003. "The Statin Wars: Why AstraZeneca Must Retreat." Editorial. *Lancet* 362(9393): 1341.
- Lexchin, J. 2007. "Drug Regulation: Two Paradigms in Conflict." In N.J. Temple and A. Thompson, eds., *Excessive Medical Spending: Facing the Challenge*. Oxford: Radcliffe Publishing.
- Lexchin, J., L.A. Bero, B. Djulbegovic and O. Clark. 2003. "Pharmaceutical Industry Sponsorship and Research Outcome and Quality: Systematic Review." *British Medical Journal* 326(7400): 1167–70.
- Light, D.W. 2007. "Pricing Pharmaceuticals in the USA." In N.J. Temple and A. Thompson, eds., *Excessive Medical Spending: Facing the Challenge*. Oxford: Radcliffe Publishing.
- Melander, H., J. Ahlqvist-Rastad, G. Meijer and B. Beermann. 2003. "Evidence B(i)ased Medicine – Selective Reporting from Studies Sponsored by Pharmaceutical Industry: Review of Studies in New Drug Applications." *British Medical Journal* 326(7400): 1171–73.
- Morgan, S. 2005. "Canadian Prescription Drug Costs Surpass 18 Billion Dollars." *Canadian Medical Association Journal* 172(10): 1323–24.
- Morgan, S.G., K.L. Bassett, J.M. Wright, R.G. Evans, M.L. Barer, P.A. Caetano and C.D. Black. 2005. "'Breakthrough' Drugs and Growth in Expenditure on Prescription Drugs in Canada." *British Medical Journal* 331(7520): 815–16.
- Pearson, S.D. and M.D. Rawlins. 2005. "Quality, Innovation, and Value for Money. NICE and the British National Health Service." *Journal of the American Medical Association* 294(20): 2618–22.
- Perlis, C.S., M. Harwood and R.H. Perlis. 2005. "Extent and Impact of Industry Sponsorship Conflicts of Interest in Dermatology Research." *Journal of the American Academy of Dermatology* 52(6): 967–71.
- Prescrire International*. 2003. "A Review of New Drugs and Indications in 2002: Financial Speculation or Better Patient Care?" Editorial. *Prescrire International* 12(64): 74–77.
- Rochon, P., P.B. Berger and M. Gordon. 1998. "The Evolution of Clinical Trials: Inclusion and Representation." *Canadian Medical Association Journal* 159(11): 1373–74.
- Rothman, K.B. and K.J. Michels. 2003. "Update on Unethical Use of Placebos in Randomised Trials." *Bioethics* 17(2): 188–204.
- Schafer, A. 2003 (October). "Bad Rx – Big Pharma and Medical Research." *CAUT Bulletin*: A13.
- Stelfox, H.T., G. Chua, K. O'Rourke and A.S. Detsky. 1998. "Conflict of Interest in the Debate over Calcium-Channel Antagonists." *New England Journal of Medicine* 338(2): 101–6.
- Thompson, A. and N.J. Temple. 2007. "The Cost of Medical Care." In N.J. Temple and A. Thompson, eds., *Excessive Medical Spending: Facing the Challenge*. Oxford: Radcliffe Publishing.