manage patients afterward (with lifestyle advice and oral therapy[3,4]) is potentially huge.

The prospect of targeted screening (as supported by Lyon and associates) warrants consideration. Screening tools with different predictive abilities (75% to 80% sensitivity and 50% to 76% specificity[5,6]) are available, which could be used anywhere in the community. These tools take into account major risk factors such as family history, exercise levels, age, body mass index, waist circumference, dietary habits, medication history and history of dysglycemia; however, they perform poorly as standalone tests.[7]

A 2- or 3-stage screening test (e.g., the combination of a questionnaire and random capillary blood glucose testing, which yields 58% sensitivity and 94% specificity[8]) might be a more efficient use of resources, ensuring that OGTTs are not performed unnecessarily. Other combinations of near-patient tests and scoring tools that might be used in community settings should be studied, similar to the successful assessment in local pharmacies of people at risk of hypertension.[9] It would be entirely possible, using a mixture of community-based measurements such as scoring tools for diabetes risk, fasting capillary blood glucose readings and near-patient testing of hemoglobin A_{1c} to target individuals who should undergo an OGTT. This might reduce the potential burden on both laboratories and family physicians.

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References

1. Lyon AW, Larsen ET, Edwards AL. The impact of new guidelines for glucose tolerance testing on clinical practice and laboratory services. *CMAJ* 2004;171(9):1067-9.
2. Harris MI, Klein R, Wellborn TA, Knuiman MW. Onset of NIDDM occurs at least 4–7 years before clinical diagnosis. *Diabetes Care* 1992;15:815-9.
3. Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *Lancet* 2002;359(9323):2072-7.
4. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle and metformin. *N Engl J Med* 2002;346 (6):393-403.
5. Rolka DB, Narayan KM, Thompson TJ, Goldman D, Lindenmayer J, Alich K, et al. Performance of recommended screening tests for undiagnosed diabetes and dysglycemia. *Diabetes Care* 2001;24:1899-903.
6. Lindstrom J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care* 2003;26(3):725-31.
7. Engelgau MM, Narayan KMV, Herman WH. Screening for type 2 diabetes. *Diabetes Care* 2000;23(10):1563-80.
8. Peters AL, Davidson MB, Schriger DL, Hasselblad V. A clinical approach for the diagnosis of diabetes mellitus: an analysis using glycosylated hemoglobin levels. Meta-Analysis Research Group on the Diagnosis of Diabetes Using Glycated Hemoglobin Levels [published erratum appears in *JAMA* 1997;277:1125]. *JAMA* 1996; 276:1246-52.
9. Kaczorowski J, Karwalajtys T, Chambers L, Levitt C, Dolovich L, McDonough B, et al. Community strategies to monitor high blood pressure among older adults [abstract]. Pharmacy Practice Research Symposium; 2002 Feb 1; Toronto.

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Clinical trial budgets

In May 1991, Ian Rusted chaired a 2-day workshop sponsored by the National Council on Bioethics in Human Research (now the National Council on Ethics in Human Research) entitled "Ethics of Clinical Trials for Research Ethics Boards."[1] The participants were representatives of the pharmaceutical industry, the Medical Research Council of Canada, Health and Welfare Canada and the Royal College of Physicians and Surgeons of Canada, as well as members of research ethics boards from across Canada.

On reading the viewpoint by Lorraine Ferris and David Naylor,[2] the spirited response by Salim Yusuf[3] and the rebuttal by Ferris and Naylor,[4] I experienced a sense of déjà vu: the points of view expressed in this exchange mirror the conclusions of the 1991 workshop. Unfortunately, although the Tri-Council drafting committee had access to the workshop recommendations for financial accountability and conflict of interest, they were not incorporated in the Tri-Council policy statement.[5] The authors and *CMAJ* are to be commended for revisiting the subject.

At the heart of the matter are issues critical to both patient care and clinical research. Both of these activities are dependent upon public trust, which must be earned through openness and integrity.

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References

1. Bioethics when undertaking clinical trials. In: Ethics of clinical trials for research ethics boards: proceedings of a national workshop. *NCBHR Communiqué* 1991;2(2):19-23.
2. Ferris LE, Naylor CD. Physician remuneration in inudstry-sponsored clinical trials: the case for standardized clinical trial budgets [editorial]. *CMAJ* 2004;171(8):883-6.
3. Yusuf S. Randomized clinical trials: Slow death by a thousand unnecessary policies? [editorial]. *CMAJ* 2004;171(8):889-92.
4. Ferris LE, Naylor CD. Rebuttal [editorial]. *CMAJ* 2004;171(8):892-3.
5. *Tri-Council policy statement: ethical conduct for research involving humans*. Ottawa: Medical Research Council of Canada; Natural Sciences and Engineering Research Council of Canada; Social Sciences and Humanities Research Council; 1998. Available: www.ncehr-cnerh.org/english /code_2/ (accessed 2005 Jan 5).

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We commend Salim Yusuf for his reply[1] to the call by Lorraine Ferris and David Naylor[2] for additional monitoring of clinical trials. Yusuf's point on the increasing complexity of regulation for clinical trial research is well taken, as is the point that complying with complex regulations creates significant costs. Although one of us (J.A.C.D.) has previously argued against an excessive reliance on clinical trials,[3] it is clear that they represent the modern gold standard. Given this reality, it is essential that we not choke off this important type of research.

Increasing costs through the requirement to deal with nontransparent and complex regulations actually makes it harder for independent researchers to do research. We have recently seen the consequences of restricting clinical trials to large drug companies[4] rather than independent academic investigators. It would seem more appropriate to have well-trained auditors who could iden-

tify and rectify mistakes rather than merely increasing the burden of paperwork for researchers.

Ferris and Naylor rightly argue that their proposed measure is a reasonable addition to clinical trial monitoring in and of itself.[5] However, too many individual straightforward and reasonable measures can result in a whole that is anything but. We agree with Yusuf that the correct direction is to reduce overhead costs and paperwork in the hope of making clinical trials more accessible.

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References

1. Yusuf S. Randomized clinical trials: Slow death by a thousand unnecessary policies? [editorial]. *CMAJ* 2004;171(8):889-92.
2. Ferris LE, Naylor CD. Physician remuneration in inudstry-sponsored clinical trials: the case for standardized clinical trial budgets [editorial]. *CMAJ* 2004;171(8):883-6.
3. Delaney JA. The best type of trial [letter]. *CMAJ* 2004;170(12):1772.
4. Dyer O. GlaxoSmithKline faces US lawsuit over concealment of trial results. *BMJ* 2004;328 (7453):1395.
5. Ferris LE, Naylor CD. Rebuttal [editorial]. *CMAJ* 2004;171(8):892-3.

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Is topical treatment of osteoarthritis site-specific?

The topical treatment of osteoarthritis has until now been left to the questionable domain of patent medicines and television advertising. Arthur Bookman and associates[1] are to be congratulated for bringing some science to the area through their placebo-controlled study of topical diclofenac. However, like all good trials, this study raises other questions.

The authors state that topical treatment is site-specific but do not present data in support of this assertion. The appropriate control to determine site specificity would be topical application of diclofenac to an unaffected site. It is unlikely that a lipid-soluble agent dissolved in ethanol would travel from the skin to the joint without first being absorbed by veins or the lymphatic vessels and then entering the systemic circulation. A previous study, in which one of the authors participated, showed that topical diclofenac is in fact absorbed and metabolized.[2] Poor bioavailability may be enhanced by periarticular inflammation, but this has not been demonstrated either.

Nonetheless, because of the pharmacokinetic profile of topically applied diclofenac, which avoids the peaks and valleys associated with toxicity, this route may be superior to oral administration. If the efficacy of topically applied diclofenac is related to the systemic level of the drug, Bookman and associates[1] may have discovered a new ultra-low therapeutic range for non-steroidal agents, much like low-dose acetylsalicylic acid (ASA) in other situations. In this respect it would be interesting to know if concomitant use of low-dose ASA affected outcome.

The 2 placebo groups in this study enjoyed a benefit that was both clinically and statistically significant. Again, it is not known if the placebo effect is site-dependent, but it would seem that use of placebo creams should be continued in experimental design and considered in clinical practice.

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References

1. Bookman AAM, Williams KSA, Shainhouse JZ. Effect of a topical diclofenac solution for relieving symptoms of primary osteoarthritis of the knee: a randomized controlled trial. *CMAJ* 2004; 171(4):333-8.
2. Hui X, Hewitt PG, Poblete N, Maibach HI, Shainhouse JZ, Wester RC. In vivo bioavailability and metabolism of topical diclofenac lotion in human volunteers. *Pharm Res* 1998;15(10):1589-95.

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