

Pediatric clinical trials registry

Although the need to register clinical trials in a publicly accessible register has been considered for years,^{1,2} it has only recently become a major issue. After the much-publicized situation regarding withheld data on the use of selective serotonin reuptake inhibitors in children, various groups, including the International Committee of Medical Journal Editors (ICMJE),³ have acted to increase awareness of the need for trial registration and to put pressure on pharmaceutical companies to register all trials.

Although a single, all-inclusive, worldwide register would be optimal, disciplines such as pediatrics need special attention. The well-known difficulties of conducting studies in young patients, along with the limited economic returns to pharmaceutical companies for pediatric drugs, have led to a scarcity of pediatric studies and therefore a scarcity of knowledge about drug safety and efficacy in children. The lack of scientifically evaluated medicines for children has been recognized as an area that requires correction.^{4,5} Legislation to increase the number of clinical trials for children has been introduced in the

United States⁶ and is planned for Europe. To facilitate pediatric research, promote more network-based studies and identify areas where research is needed, an international register of clinical trials of drugs in children (both planned and under way) has been established, the DEC-net (Drug Evaluation in Children) register (www.dec-net.org).

Researchers, health professionals, sponsoring agencies and the public will be able to search DEC-net for information on trials specific to children. The register, supported by the European Union and currently operating as a 3-year feasibility study, was activated in 2004 and is run by groups of researchers from 4 countries: Italy, France, Spain and the United Kingdom.⁷ It fits the criteria outlined by the ICMJE,³ is available free of charge, allows for data correction and updating, and is designed for use by the general public as well as health care professionals. The DEC-net register is the only pediatric, population-oriented trial register set up to receive information from a variety of sources (ethics committees, national health agencies, universities, national and international medical societies, hospitals, physicians, industry and spontaneous reporters). The register complies with the criteria of the *meta*Register of Controlled Trials

(an international register of registers run by Current Controlled Trials; see <http://controlled-trials.com/mrct>), to allow future collaboration.

We agree with the ICMJE that clinical trial registers will be most useful if they are designed to include all possible trials from any country in the world. For pediatric research, the DEC-net register meets this goal.

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Cardiovascular risk in patients with type 2 diabetes

There is no doubt that aggressive control of common risk factors is of paramount importance in the management of diabetic patients with atherosclerotic disease to prevent cardiovascular morbidity and mortality. In assessing management of such patients, Lauren Brown and associates¹ identified the study cohort between 1991 and 1996 and followed the patients until 2000; however, the evidence for the standard therapies they evaluated (regarding antiplatelet agents,² angiotensin-converting enzyme [ACE] inhibitors³ and statins⁴) did not become available until at least 2000. In other words, evidence published during or after the year 2000 was applied to data collected up to 2000; thus, it is no surprise that management was suboptimal relative to current recommendations.

It would have been preferable for the authors to have used the 1998 guidelines for management of diabetes⁵ in evaluating the care provided to these patients. I acknowledge that their findings would probably have been similar, as it takes a few years to implement such guidelines (by which time they may have been changed or be undergoing revision). None of the therapies listed above was strongly recommended for cardiovascular protection in the 1998 guidelines. In fact, the UK Prospective Diabetes Study,⁶ published at the same time, highlighted the importance of effectively controlling both blood glucose and blood pressure to improve microvascular and macrovascular complications and did not favour one agent over the other (β -blocker versus ACE inhibitor).

Since then, however, evidence has accumulated, and the 2003 Canadian

guidelines⁷ make appropriate recommendations about these therapies.

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Lauren Brown and associates¹ observed low use of therapies with proven benefit for the prevention of

cardiovascular events in patients with type 2 diabetes, both with and without atherosclerotic disease. We are conducting a similar study analyzing use of acetylsalicylic acid (ASA), statins, β -blockers and angiotensin-converting enzyme (ACE) inhibitors (or equivalent) in a cohort of 407 high-risk patients attending the Lipid/Cardiovascular Risk Reduction Clinic at St. Paul's Hospital in Vancouver. These patients have a history of vascular disease (coronary, peripheral or cerebral) with or without diabetes.

Data on the patients' lipid profile and use of the 4 medications at the time of the initial visit to the clinic (between 1984 and 2004) and their most recent visit (between November 2003 and July 2004) have been collected (Table 1). The use of these medications will also be prospectively evaluated at the next scheduled visit.

We are also trying to examine differences in medication use in a subgroup of 178 patients with diabetes from the same cohort: 54 with established coronary artery disease (CAD) and 124 without clinical evidence of CAD. Preliminary data were obtained from the most recent follow-up visits (with an average of 60 months between the first and the most recent visit). We found no significant differences in the use of ASA and statins between the 2 groups; however, the rate of treatment with β -blockers and ACE inhibitors was significantly higher among patients with CAD than among those without CAD. Although the difference in β -blocker use was not unexpected, we

Table 1: Use of proven cardioprotective agents in a cohort of high-risk patients: preliminary results

Agent	No. (and %) of high-risk patients n = 407			No. (and %) of diabetic patients* n = 178		
	First visit n = 407	Most recent visit n = 402	p value	With CAD n = 54	Without CAD n = 124	p value
ASA	194 (48)	302 (75)	< 0.001	39 (72)	81 (65)	0.22
Statins	158 (39)	328 (82)	< 0.001	44 (81)	99 (80)	0.80
β -Blockers	108 (27)	127 (32)	0.11	23 (43)	13 (10)	< 0.001
ACE inhibitors	143 (35)	284 (71)	< 0.001	45 (83)	80 (65)	0.012

CAD = coronary artery disease, ASA = acetylsalicylic acid, ACE = angiotensin-converting enzyme.

*Data obtained during most recent visit.