Women, children, and other patient populations frequently excluded from the most influential clinical research trials

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A Sunnybrook Health Sciences Centre study today released in the Journal of the American Medical Association indicates that certain patient populations are routinely being omitted from the clinical research carried out and published in high impact journals and that this could have serious implications for the validity of the trials' results.

The groups that were most commonly excluded from randomized controlled trials (RCTs) include women of child bearing years, children, the elderly and those with common medical problems. Multicenter clinical trials investigating medications seem to be most often associated with extensive exclusions.

"The problem with excluding certain groups is that it prevents the trials' results from being truly applicable to the population of patients we treat each day," says Dr. Robert Fowler, the study's senior and corresponding author, an Internal Medicine and Critical Care physician at Sunnybrook Health Sciences Centre. "It begs the question, are we focusing only upon a small subgroup of patients that have the best chance of demonstrating effectiveness of a new drug, or all those who will actually be exposed to the drug in clinical practice?"

Certain groups are not included because clinical trials with narrow and homogeneous populations can be smaller, shorter, more efficient, and less expensive. However, these short-term benefits come at the loss of validity in clinical practice.

"Groups such as children and pregnant women have been excluded from clinical trials as a result of reflexive unease about studying therapies in this population. The downside is that we know very little about the safety and effectiveness of many medications for such groups, and physicians are forced to use older drugs or prescribe new ones with trepidation," says Dr. Fowler, Assistant Professor of Medicine, University of Toronto. "People are excluded simply because they have been in the past; assumptions about outcomes are made before they are even proven."

The study determined that pharmaceutical companies have an increased reluctance to include certain populations in their trials. The authors found patients in drug trials were frequently excluded due to their age, gender, common medical problems, and even their socio-economic status, often with limited justification. This may mean that they select participants they know will do well, and have a minimum of side-effects; unfortunately not what will occur in the general population. This may in part explain why drugs are subsequently pulled from the market due to 'unanticipated side-effects' – the drugs were never studied in the patient population that will receive them. Their testing is often internally valid, but externally invalid.

"Not only are we putting patients at risk of serious side effects by not testing a well-rounded sample of the population," says Dr. Fowler. "We are also limiting the unexpected good that a trial could do for people at risk. For example, the anti-HIV drug AZT was not tested on pregnant women for a long time due to fears about its side effects. Ultimately it was found that the drug was good for both mother and baby – it could actually prevent HIV transmission to the baby."

To arrive at their conclusions, the researchers reviewed 283 articles that were randomly selected from a pool of 4827 trials in the highest impact medical journals, spanning a 12-year period from

January 1, 1994 – December 3, 2005. The exclusions and inclusions of each trial's subjects were also classified according to whether they were strongly, potentially or poorly justified.

The study, sponsored by the Ontario Ministry of Health and Long-term Care, suggests that each clinical trial's inclusion and exclusion criteria be clearly listed in a table so that clinicians could more clearly evaluate the applicability of the results to other patients, and also serve as a reminder of the need to consider all groups when designing and reporting clinical trials.

"It is important for investigators to make clinical research as relevant to as much of the population as possible," says Dr. Fowler. "This includes children and adults, females and males, and the sick as well as the healthy."

About Sunnybrook Health Sciences Centre
Sunnybrook Health Sciences Centre is transforming health care through the dedication of its more than 10,000 staff members who provide compassionate and innovative patient focused care. An internationally recognized leader in women's health, academic research and education and an affiliation with the University of Toronto distinguishes Sunnybrook as one of Canada's premier health sciences centres. Sunnybrook specializes in caring for newborns, adults and the elderly, treating and preventing cancer, heart problems, orthopaedic and arthritic conditions and traumatic injuries.

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