Drug policy trials can be randomised

Randomised drug policy trials are feasible, and they may produce results in a short time, which are likely to concord with observational evaluations. Schneeweiss and colleagues (p 560) compared results of studies investigating the health effects of a new reimbursement policy for nebulised respiratory drugs. The randomised policy trial and an observational time trend analysis had similar results. Randomised policy trials provide rigorous results almost as soon as the data become available, avoiding the time delay caused by identifying controls and adjusting for confounding.

POEM*

Fondaparinux is as effective and safe as unfractionated heparin for pulmonary embolism

Question Is fondaparinux as safe and effective as unfractionated heparin for treating pulmonary embolism?

Synopsis Fondaparinux (Arixtra) is an inhibitor of factor Xa. Although it's not a low molecular weight heparin, it's similar in that it's given by subcutaneous injection and does not require monitoring of anticoagulation. Alternatives to unfractionated heparin are widely used for treating deep vein thrombosis, but they are less widely used for pulmonary embolism because of concerns about efficacy. In the current randomised controlled trial (non-blinded), 2213 adults with a pulmonary embolism were randomised to either unfractionated heparin titrated to an activated partial thromboplastin time between 1.5 and 2.5 or fondaparinux given by subcutaneous injection. The average age was 62 years and 55% were women. Randomisation and allocation concealment were appropriate, groups were similar at baseline, analysis was by intention to treat, and outcomes were reviewed (although not initially assigned) by a blinded monitoring committee. Fondaparinux was given as a single daily injection of 5 mg for patients weighing less than 50 kg, 7.5 mg if they weighed between 50 and 100 kg, and 10 mg if they were heavier than 100 kg. Patients were started on warfarin as soon as possible and treatment with unfractionated heparin or fondaparinux continued for five days and until warfarin was therapeutic for at least two days. Patients were followed up for three months; the primary outcome was recurrence of venous thromboembolism. At the end of the study period, there was no significant difference in any of the primary or secondary outcomes: recurrent venous thromboembolism (3.8% for fondaparinux *v* 5.0% for unfractionated heparin), major bleeding (2.0% *v* 2.4%), non-major bleeding (5.7% *v* 8.4%), and death (5.2% *v* 4.4%). One in seven patients treated with fondaparinux were treated as outpatients for at least part of the time, the majority for at least three days. This was an industry sponsored trial, and four of the authors are employees of the company that makes fondaparinux.

Bottom line Fondaparinux is similar in effectiveness and safety to unfractionated heparin in treating pulmonary embolism. Although more expensive, it offers the advantage of dosing without attention to the extent of coagulation, and offers the possibility of outpatient treatment for selected patients.

Level of evidence 1b (see www.infopoems.com/levels.html). Individual randomised controlled trials (with narrow confidence interval)

Matisse Investigators. Subcutaneous fondaparinux versus intravenous unfractionated heparin in the initial treatment of pulmonary embolism. *N Engl J Med* 2003;349:1695-702.

* Patient-Oriented Evidence that Matters. See editorial (*BMJ* 2002;325:983)

Editor's choice

"Doctor, come quickly. There's been a nuclear incident"

A friend of mine was recently late for the opera because he was preparing south London's plan for a nuclear attack. Despite living south of the Thames I don't think the plan justified missing the first bars of Turandot. But imagine the phone going in the middle of the night and a voice saying: "Doctor, can you come quickly? There's been a nuclear incident." Would you have any idea how to respond? The evidence suggests you wouldn't, which is why it might be a good idea to read our clinical review on the subject (p 568).

Unintentional and unexpected radiation incidents have so far been rare, with 134 deaths from 420 incidents worldwide between 1944 and 2002. Typically people find shiny metallic objects, put them in their pocket, and take them home—failing to realise that the objects are radioactive. The fear now is of a terrorist attack—the explosion of a "dirty bomb" or the dispersal of high activity radioactive sources through air conditioning, subways, drinking water, or food. Hundreds or thousands might die.

Symptoms of radiation sickness come in phases. With higher doses the phases come more quickly and last for a shorter time. Nausea, vomiting, weakness, and fatigue are followed by infection, bleeding (from gums and nose), and gastrointestinal symptoms. Doctors may misdiagnose radiation sickness as food poisoning or infection. Radiation may also cause injuries to skin, but these may evolve over months.

Doctors who identify a radiation incident should start by controlling the spread of radioactivity. A differential blood count will help assess the severity of exposure. Contaminated clothing should be removed, and the patient might be showered. If after exposure the patient doesn't vomit then outpatient surveillance may be enough. Vomiting within one or two hours probably requires admission to a haematology ward, while vomiting within an hour accompanied by other symptoms means care in a centre of radiopathology.

We are, of course, much more used to radiation as a useful diagnostic tool, and medical tests are the largest manmade source of radiation exposure. In most affluent countries medical sources of radiation were one fifth of natural radiation in 1987 but equal to it by 1997. We are, argues Eugenio Picano, overdoing it (p 579): "long term risks are not being weighed against the immediate short term benefits."

Several letters attempt to weigh the importance of a paper on the the long term effects on cognitive function of infants who had skin haemangiomas treated with radiation (p 581). The findings are probably relevant to computed tomography. One paediatrician told me that this was the most important paper in paediatrics in five years, while others don't think the findings relevant to today. A letter from authors at the National Radiological Protection Board suggests that the brain dose from computed tomography may be as high as those seen in the study. We are seeking further guidance for readers.

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