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Such end points give extra statistical power but often overemphasise the outcomes with least importance to patients

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PICTURE OF THE WEEK

A child walks out after surgery in the flying eye hospital in Mumbai, India, last week. The world's only flying eye hospital is on a two week mission to India to perform free surgery and train hundreds of eye care personnel in a country that has the world's largest number of blind people.

THE WEEK IN NUMBERS

4 Days of improved oxygenation in patients with acute lung injury who were given nitric oxide (**Research p 779**)

1.8 million Child deaths a year from diarrhoea (**Editorial p 755**)

50% Reduction in sexually transmitted infections if prostitution were legal and regulated in the UK, according to unsubstantiated claims by chairman of the BMA's public health committee (**News p 790**)

48 hours Maximum weekly working time in Europe (**Feature p 770**)

49.10 World Health Assembly resolution to destroy the smallpox virus, in 1999, balked at by Russia and the US (**Head to Head p 774**)

THE WEEK IN QUOTES

“Trialists [should] restrict their use of composite end points to end points of similar importance to patients”

Research p 788)

“Interventions were effective in reducing diarrhoea even without improved sanitation” (Research p 782)

“In the light of modern science . . . [Hippocrates and Galen] killed much more often than they cured” (Letter p 762)

“Extravagant and obvious self destructiveness . . . at least lend to the vacuity of their existence the patina of drama” (Between the Lines p 803)

“The risk of mothers passing HIV to their babies can be reduced simply and cheaply” (News p 763)



ON THE COVER

Smallpox: is it time to destroy the virus?

See Head to head, p 774

COVER IMAGE: CDC/SPL

PLUS

In this week's BMJ careers

Busmen's holidays

Drug companies are not that bad

Diploma in critical care medicine

Fifteen minute interview with a sailing shrink

EDITOR'S CHOICE

Caveat emptor

If you read only one thing in the *BMJ* this week, it should be the article by Ferreira-González and colleagues, with its accompanying editorial (well, that makes two things). Rory Watson's article on whether Europe will achieve a 48 hour week is important (p 770), as is the related article on how to make shift work more bearable and less damaging to health (p 777). Doug Kamerow's "Yankee Doodling" (p 776) is highly deserving of your time, as are the smallpox debate (p 774), the clinical review on post-traumatic stress disorder (p 789) and this week's medical classic—*La Belle Dame Sans Merci* (p 803). But Ferreira-González et al's systematic review (p 786) is like a great big "caveat emptor" sign hanging over the portal of the world's most influential clinical trials.

What they've done is to look at how trials use composite end points—for example, combining rates of death, myocardial infarction, and revascularisation when comparing two treatments. This is standard practice and quite legitimate: composite end points reduce the number of patients needed in any trial and can give a sense of the overall clinical impact of a treatment. But this practice becomes a problem if the component parts of the composite end point differ widely in their importance to patients, and if the less important end points (treatment failure, for example) are much more common than the more important ones, such as death. Ferreira-González and colleagues found this to be the case in most of the cardiovascular trials published in six leading journals. They say that readers could be misled into believing that a new treatment reduces deaths when it doesn't. Clearly, such a conclusion would be gold dust to the marketing of a new drug.

In their editorial, Freemantle and Calvert (p 756) say that the current system of drug regulation tends to encourage both the use of composite end points and the addition of death to those composites. To help people interpret trials correctly, they suggest a health warning that makes it clear which parts of a composite end point were affected by the new treatment and which were not.

Drug regulation, and how it could be improved, was at the heart of discussions in Rome last month at a meeting organised by Italy's pharmaceutical agency, AIFA. Representatives of industry argued that drug licensing and reimbursement decisions were too slow and inconsistent across Europe and worried about the lack of incentives to innovate. Academics argued that "speed to market" must be secondary to proper evaluation of a new drug, including head to head comparisons against current best treatment. Silvio Garattini, chairman of AIFA's research committee, called for more independent, publicly funded evaluations of new drugs. Garattini is behind Italy's revolutionary 5% tax on drug marketing expenditure, which funds independent trials and has set a standard for other countries to follow.

The meeting was an attempt to move beyond confrontation to constructive dialogue with the pharmaceutical industry. In the same spirit, the *BMJ* will be running articles over the next few months exploring drug development, licensing, evaluation, and marketing. We all want safe, effective, innovative drugs. The question is how best to achieve that.

Fiona Godlee, editor fgodlee@bmj.com

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