TEXT OF P2P SUBMISSION ON NEW WAYS OF TESTING MEDICINES

Consultation on the International Council for Harmonisation Guideline E20 for adaptive clinical trial design

Submitted to the Medicines and Healthcare products Regulatory Agency
via required Excel template

Submission from Pupils 2 Parliament, a project gathering schoolchildren's views for government consultations and parliamentary committee inquiries.

These general points came from three consultation focus groups with a total of 68 primary and secondary school pupils in the UK.

Pupils were concerned that group selection criteria are very likely to miss important selection criteria relevant to outcomes that might emerge during a trial. They identified seemingly irrelevant factors such as blood group, height, weight, hair colour, mental health, strength, general state of health, existing and recent medication, allergies and food intolerances as examples. They however favoured using a set of initial selection criteria to balance groups over solely random selection and large group size.

They wished the requirements to strongly state that all trails should actively seek possible unexpected criteria that might emerge as affecting outcomes and side effects, and to assess whether different dosages might be relevant to different effects and side effects.

Pupils were by a small majority in favour of adapting a controlled trial once started, principally to respond to emerging potentially relevant subject selection criteria or test different dosages. There was a preference however for the alternative strategy of conducting a new trial concurrently with the first to cover the adaptation(s), and for major and urgent trials running a series of trials with staggered starts, allowing for adaptations to trials without changing the original trial.

Pupils were strongly against ending a trial early once a significant main finding had been achieved, on the grounds that this maximises the risk of missing emerging relevant factors.

Pupils strongly supported requirements for blind trial design and for both long term follow up and replication, by different researchers, of all controlled trials.

In relation to risk, it is important to note that as 'naïve commentators', pupils were less concerned about control groups potentially 'missing out' than about potential harms to treatment groups.

It is also significant that the children themselves spontaneously identified "does it work?", "is it safe?" and "does it have side effects?" as the three primary research questions for medical trials.

Pupils raised a concern that even in an emergency, medication under trial should not be prematurely put into production before the completion of the relevant trials, as it would be

difficult and expensive to destroy all stocks and prevent its 'leakage' into use if subsequently not approved for general use.

Pupils wished E20 to identify the risk that some subjects might have an allergy to a component of a placebo.

Some also raised the question of whether taste of a placebo might affect the placebo effect in a control group, and advocated research into this question.

Pupils strongly advocated that the E20 should routinely require testing all medications for potential effects on mental health.

Some pupils raised the need to monitor and taken into account in trials whether certain medications or their side effects might affect third parties such as family members or carers.

In tests involving children and young people, age is likely to be a sensitive factor, and narrow age ranges need to be used as subject matching criteria given the speed of development in children.

There should also be a requirement to take especial care in testing not only outcomes but side effects in relation to younger children for any medication potentially for use with children, and for use of long follow up when considering medication for use with children.

Finally, asked to consider the placebo effect, pupils spontaneously recommended E20 reference to the risk that during trials, subject behaviour (such as personal hygiene behaviour or precautions against infection) might be significantly changed by the reassurance of believing that you are potentially being protected by the medication under trial, affecting outcomes and needing to be monitored between trial groups. One pupil group termed this the 'complacency effect'.

Roger Morgan
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