

key objective over the next two or three years is to create a dynamic environment for research and development within which doctors can work with suppliers and others on the new electronic services, can continue to innovate after the initial services have been delivered, and can, if necessary, take part in decisions to amend or stop unsuccessful developments.

Staff working on the programme face a dilemma, however. How can they retain the advantages of the central procurement arrangements while at the same time encouraging localism? The answer may be for Connecting for Health, the agency responsible for the programme, to become a regulator. The agency could stop directing implementation centrally and could become responsible for encouraging good working relationships between suppliers and clinicians. In this way the agency would retain its role in monitoring compliance with multibillion pound contracts while letting clinicians and suppliers get on with development. It would also have an ongoing role in protecting the wider public interest on matters such as patient confidentiality. This arrangement might help

to allay some clinicians' natural fears that their concerns will not be taken into account in the rush to computerisation.

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Antipyretic drugs for children

There's still not enough evidence to support prescribing paracetamol and ibuprofen in combination or alternately

Fever is common in children¹ and can cause distress, parental anxiety, and—in some parents—“fever phobia.”² Rationales for treating childhood fever include relieving distress (allowing the child to sleep, rest, or feed) and lowering temperature, often in the hope of reducing the risk of febrile convulsions. Non-pharmacological treatments include loosening clothing, reducing the ambient temperature, and encouraging the child to take fluids. The pharmacological options are paracetamol and ibuprofen, and parents commonly give both drugs to a child with fever.³ But should these drugs be used together, or alternately, and for which children, and at what dose and frequency? Advice is inconsistent, leading to confusion and frustration among parents, nurses, and doctors.

Both drugs are licensed and widely purchased over the counter in Europe for children: sales in 2004 were £128m for paediatric ibuprofen and £277m for paracetamol (€186m and €403m, \$233m and \$504m; personal communication, Boots Healthcare International). Paracetamol and ibuprofen exert their effects at differing points in the pyrogenic pathways,⁴ so synergistic action is plausible.

We searched Medline (1966 to March 2006), the Cochrane database, and our own databases and found three studies comparing a combination of paracetamol or ibuprofen with separate use.⁵⁻⁷ The first studied 89 children admitted to hospital in India with axillary temperatures greater than 38.5°C.⁵ Children received ibuprofen 10 mg/kg singly or in combination with paracetamol 10 mg/kg, each three times daily. The paracetamol-ibuprofen combination was more effective than paracetamol alone from 0.5 hours to 2 hours and less effective from 10 hours to 24 hours, but the

temperature differences amounted to less than 1°C and were not statistically significant.

The second study randomised 123 children presenting to a UK emergency department with tympanic temperatures $\geq 38^\circ\text{C}$ to receive paracetamol 15 mg/kg or ibuprofen 5 mg/kg, or both, and measured tympanic temperature at one hour.⁶ The investigators defined a clinically important temperature difference as $\geq 1^\circ\text{C}$. Although they found a statistically significant difference ($P=0.023$) between all treatments, the temperature difference between the groups receiving combined treatment and paracetamol only was 0.35°C and between those receiving combined treatment and ibuprofen only was 0.25°C. The confidence intervals exclude the original target difference of 1°C and so, if the 1°C threshold is accepted, the study was able to rule out a clinically important difference at one hour. Neither the Indian nor UK studies measured symptoms associated with fever.

The third study randomised 464 children presenting to Israeli ambulatory care centres with rectal temperatures of $\geq 38.4^\circ\text{C}$ to receive paracetamol 12.5 mg/kg every six hours or ibuprofen 5 mg/kg every eight hours or both alternating four hourly.⁷ Irrespective of their intervention group, all children received a double loading dose of either paracetamol or ibuprofen. Rectal temperatures and distress scores were measured (at times determined by the parents) three times daily for three days and the thermometry outcome used for the analyses was the maximum temperature recorded. The investigators found differences lasting three days in temperatures (range 0.8°C to 1.1°C, all $P<0.001$) and distress scores (all $P<0.001$) between the alternating and monotherapy groups.

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The children in these studies were probably more unwell than most febrile children managed at home. Collating the evidence is limited by inconsistent doses and thermometry methods, and only one study measured the children's discomfort.⁷ The Indian study suggests there is no advantage in using both drugs rather than one, but it may have been underpowered. The UK study helps our understanding of early treatment effects, but not those beyond one hour. The Israeli study is difficult to interpret because half the children in the monotherapy groups received both medicines in the first 24 hours and parents determined the timing of thermometry and recording of distress scores.

Evidence on safety is also limited. Renal failure is associated with the use of ibuprofen in dehydrated children,⁸ and the combination of both drugs may, in theory, cause renal tubular necrosis as ibuprofen inhibits the production of renal glutathione, which detoxifies and prevents the accumulation of a nephrotoxic metabolite of paracetamol.⁹ However, two studies have shown no difference in renal function comparing combined with separate use,^{5,7} and the website of the Committee on Safety of Medicines has no reports of adverse events.¹⁰

There are other important gaps in the evidence. Most surprisingly, there is an absence of evidence of effectiveness for monotherapies compared with physical methods of reducing fever or placebo.¹¹ Furthermore, future research should measure the outcomes that are important to parents—namely, symptoms associated with fever.

The definition of a clinically useful difference in temperature after treatment is debatable and, given that the maximum times for antipyretic activity differ for paracetamol and ibuprofen, the timing of measuring the difference in temperature is crucial to the validity of the comparison. The best method to ensure fairness is continuous thermometry, which generates an average time spent under a fever threshold after treatment and has been used in one study to date.¹² More research using maximum therapeutic doses, continuous thermometry and measuring symptoms associated with fever is under way (www.controlled-trials.com/isrctn/trial/0/26362730.html), but until such evidence is available, the role of combined antipyretics is uncertain.

Given that the absence of evidence from trials is at odds with strongly held parental beliefs in many cases,

and given the desire among parents and clinicians to do something when faced with febrile children, it seems churlish to conclude that combined treatment should be withheld from all children. But parents should be advised to use the minimum treatment necessary. Using two drugs always has some disadvantages: increased risks of overdosing, underdosing, and adverse effects; increased costs; greater medicalisation and—in this case—an associated risk of exacerbating fever phobia.

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Psychological interventions for treatment of adult sex offenders

Treatment can reduce reoffending rates but does not provide a cure

Sexual offending is a public health issue and a social problem. Medical practitioners might assume from the volume of work published on treatments for sex offenders that clinically effective treatments are available. Indeed, psychological treatment is often mandated in the sentencing decision for sexual offenders. Yet the effectiveness of treatments is debated, and evidence for the efficacy of sex offender treatment programmes is often too readily accepted uncritically.¹

In conducting a Cochrane meta-analysis on the effects of such psychological interventions we found nine trials that were well conducted in terms of randomisation, blinding, loss to follow-up, and analysis.² These included randomised controlled trials with a total of 567 male offenders, 231 of whom were followed up for a decade.

The results indicated that studies on behavioural treatments were too small to be informative, although statistically significant improvements were recorded