# Cost-effectiveness of outpatient parenteral antibiotic therapy for children with cellulitis

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Outpatient parenteral antimicrobial therapy (OPAT) is a method for delivering intravenous antimicrobials in outpatient settings, and this delivery method is an alternative to inpatient care.[1,2] Although this approach is not commonly used in children because of the perceived risks of infections and complications, it is gradually gaining importance and has been used for the treatment of several infections. Previous studies[3-6] have shown that OPAT leads to a reduction in admissions and in duration of hospital stay, and that it is cost saving compared with inpatient care. OPAT has also been shown to reduce the risk of hospital-acquired infections, which are a contributory factor to antimicrobial resistance.[7]

In their study in *The Lancet Infectious Diseases*, Laila Ibrahim and colleagues[8] assessed the cost-effectiveness of OPAT (with 50 mg/kg intravenous ceftriaxone once daily) versus standard hospital care (with 50 mg/kg intravenous flucloxacillin every 6 h) for the treatment of moderate or severe cellulitis in children. The analysis assumed a societal perspective and was conducted alongside the Cellulitis at Home or Inpatient in Children from the Emergency Department (CHOICE) randomised controlled trial.[9] To our knowledge, this is the first study to investigate the cost-effectiveness of OPAT in children with cellulitis. Ibrahim and colleagues showed that OPAT costs less (mean difference in cost to the hospital per patient episode –AUS$1809, 95% CI –1324 to –2295; mean difference in cost to the family per patient episode –$410, –312 to –508) and is more effective (quality-adjusted life year [QALY] difference 0·0006, 0·0004 to 0·0008) compared with standard hospital care. Their results suggest that the use of OPAT to deliver intravenous antimicrobials in outpatient settings should be adopted more widely for the management of children with moderate or severe cellulitis. However, a possible limitation of the study relates to the artificial nature of the single-site trial, which limits the generalisability and external validity of the findings. The authors, however, attempted to address this issue with sensitivity analyses.

A fundamental issue associated with economic evaluation studies in children relates to how health-related quality of life is measured. The study by Ibrahim and colleagues included participants aged 6 months to 18 years, and it used the Child Health Utility 9D (CHU9D) questionnaire[10] to derive QALYs. The advantage of using the CHU9D questionnaire for economic evaluations is that it is preference-based and can be used to generate QALYs. However, this measure might not be valid for all participants included in the study, such as those younger than 5 years. It is therefore suggested that economic evaluations of this sort consider other health-related quality of life measures in addition to the CHU9D. Also, the study understandably used proxy completion of the CHU9D (ie, by parents or guardians) for younger children (aged 6 years or younger) and self-completion for older children (older than 6 years), which raises questions relating to consistency and proxy bias.[11]

Ibrahim and colleagues did not include the cost of antimicrobial resistance in their cost-effectiveness analysis. The importance of including such estimates in economic evaluation studies that consider antibiotic use has been highlighted by a few studies.[12,13] Although there is substantial uncertainty and several practical issues associated with the estimation of this cost, it is important that studies such as that by Ibrahim and colleagues are encouraged to account for the cost of antimicrobial resistance within economic evaluations. Doing so will ensure that there is an assessment of the effects of the different treatment pathways on antimicrobial resistance, and it will also ensure that sub-optimal policy recommendations are avoided. However, accounting for the cost of antimicrobial resistance would require additional research into how these costs are estimated and included within economic evaluations.

Although the findings by Ibrahim and colleagues represent an important first step in determining the cost-effectiveness of OPAT compared with standard hospital care for children with moderate or severe cellulitis, it is possible that the single-centre trial and artificial environments might restrict the generalisability and external validity of the findings. We recommend that additional studies are undertaken in other settings to determine the cost-effectiveness of OPAT for children with moderate or severe cellulitis.

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# Time for *Helicobacter pylori* eradication

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Gastric cancer is the third leading cause of cancer death in the world with more than 1 million cases per year and almost 800 000 deaths. Approximately half of the cases occur in east Asia,[1] including Taiwan, the site of a large clinical trial presented by Jyh-Ming Liou and colleagues in *The Lancet Infectious Diseases*.[2] Because *Helicobacter pylori* in high-risk countries is the pre-eminent cause of these malignancies, *H pylori* screen-and-treat programmes have received considerable attention as a potential cost-effective approach to eliminating the gastric cancer scourge.[3] *H pylori* treatment trials support this approach, with meta-analyses indicating that screen-and-treat programmes could prevent approximately 35% of gastric adenocarcinomas[4] while simultaneously reducing transmission and the overall infection burden.

Despite this promising research, screen-and-treat programmes are few and far between, even in countries at highest risk, because of the high prevalence of infection; in some high-risk countries, almost the entire adult population older than 50 years is infected. The prospect of treating such a huge proportion of the population with multiple, relatively broad-spectrum antibiotics, when only a small percentage (<5%) will go on to get cancer,[5] is both logistically daunting and microbiologically worrisome. Because of the complexities of such programmes, in 2014, a Working Group of the International Agency for Research on Cancer simultaneously put its foot on both the gas and the brake of screen-and-treat programmes.[6] Although overall, the Working Group was enthusiastic about eliminating *H pylori*-induced cancers, major concerns were raised about whether screen-and-treat-programmes would lead to induction of antimicrobial resistance in either *H pylori* or other resident flora, and about deleterious alterations in host microbiomes that might persist after treatment. Additional concerns were raised about weight gain with *H pylori* eradication and increases in oesophageal adenocarcinoma, asthma, and other conditions. The Working Group concluded that more research needed to be done to balance risks and benefits before pushing forward with broad screening and treatment programmes.

The paper by Liou and colleagues[2] provides support, although muted, for screen-and-treat programmes. The investigators compared the effects of three treatment protocols (clarithromycin triple therapy, clarithromycin quadruple therapy, and bismuth quadruple therapy) on the gut microbiome, on antimicrobial resistance in *Escherichia coli*, and on metabolic parameters including weight. The first of these treatments, which showed the least disruption of the microbiome, is unlikely to be an effective treatment strategy in much of the world, owing to high prevalences of clarithromycin resistance.