

trials and in a field-at-large (eg, publication bias) might invalidate both direct and indirect estimates.

Making sense of the composite evidence of half a million clinical trials is a daunting task. To make things worse, direct evidence is often lacking for the most important questions. How much can we exploit disparate indirect comparisons to fill these evidence gaps? Should we discredit old or seemingly irrelevant data? Can we judge clearly what is old and what is irrelevant in randomised evidence? Should we abort indirect syntheses and start from scratch? These questions need to be addressed carefully on a case-by-case basis. Deciding when the clinical trials mesh is a mess is not easy.

*John P A Ioannidis*

Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina 45110, Greece; and Department of Medicine, Tufts University School of Medicine, Boston, Massachusetts, USA  
jioannid@cc.uoi.gr

I declare that I have no conflict of interest.

- 1 Glenny AM, Altman DG, Song F, in collaboration with the International Stroke Trial Collaborative Group. Indirect comparisons of competing interventions. *Health Technol Assess* 2005; **9**: iii-iv, 1-134.
- 2 Piaggio G, Elbourne DR, Altman DG, for the CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. *JAMA* 2006; **295**: 1152-60.
- 3 Ioannidis JP, Polycarpou A, Ntais C, Pavlidis N. Randomized trials comparing chemotherapy regimens for advanced non-small cell lung cancer: biases and evolution over time. *Eur J Cancer* 2003; **39**: 2278-87.
- 4 Bloomfield P, Hodson EM, Craig JC. Antibiotics for acute pyelonephritis in children. *Cochrane Database Syst Rev* 2005; **1**: CD003772.
- 5 Bucher HC, Guyatt GH, Griffith LE, Walter SD. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol* 1997; **50**: 683-91.
- 6 Panidou ET, Trikalinos TA, Ioannidis JP. Limited benefit of antiretroviral resistance testing in treatment-experienced patients: a meta-analysis. *AIDS* 2004; **18**: 2153-61.
- 7 Caldwell DM, Ades AE, Higgins JP. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ* 2005; **331**: 897-900.
- 8 Lumley T. Network meta-analysis for indirect treatment comparisons. *Stat Med* 2002; **21**: 2313-24.
- 9 Chou R, Fu R, Huffman LH, Korthuis PT. Initial highly-active antiretroviral therapy with a protease inhibitor versus a non-nucleoside reverse transcriptase inhibitor: discrepancies between direct and indirect meta-analyses. *Lancet* 2006; **368**: 1503-15.
- 10 Yazdanpanah Y, Sissoko D, Egger M, Mouton Y, Zwahlen M, Chene G. Clinical efficacy of antiretroviral combination therapy based on protease inhibitors or non-nucleoside analogue reverse transcriptase inhibitors: indirect comparison of controlled trials. *BMJ* 2004; **328**: 249.
- 11 Yeni PG, Hammer SM, Hirsch MS, et al. Treatment for adult HIV infection: 2004 recommendations of the International AIDS Society-USA Panel. *JAMA* 2004; **292**: 251-65.
- 12 Song F, Altman DG, Glenny AM, Deeks JJ. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *BMJ* 2003; **326**: 472.
- 13 Ioannidis JP, Evans SJ, Gotzsche PC, for the CONSORT Group. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; **141**: 781-88.

## Caesarean section: the paradox

See [Articles](#) page 1516

In today's *Lancet*, Carine Ronsmans and colleagues present strong evidence for inequalities in access to caesarean sections in developing countries.<sup>1</sup> Their thorough analysis of data from Demographic and Health Surveys in 42 low-income and middle-income countries, comparing caesarean section rates in quintiles of wealth, showed that women of low income received significantly fewer interventions compared with the highest. However, fewer caesarean sections do not necessarily mean lower health-care quality.

The appropriate range for the caesarean section rate in a country remains a matter of debate.<sup>2-5</sup> The recommended lower limit ranges from a minimum of 1% to an optimum target of 5% to avoid death and severe morbidity in the mother.<sup>2-4</sup> Although these figures are good estimates based on complication rates in the mother<sup>2,3</sup> and on historical data,<sup>4</sup> whether the frequency of intervention is enough to prevent avoidable perinatal deaths is unknown. The best known recommended upper limit is 15%, suggested by WHO.<sup>5</sup>

Although these figures are based on theoretical

estimates, we agree with the main idea behind the recommendations: that the appropriate range for caesarean section rates should be defined through an outcome-based approach. Caesarean section is a surgical intervention to prevent or treat life-threatening maternal or perinatal complications, and the appropriate rate should be associated with the lowest attainable maternal and perinatal morbidity and mortality.<sup>6</sup> Researchers from two observational ecological studies,<sup>6,7</sup> which included developing countries, assessed the association between caesarean section rates and mortality and morbidity in mothers and neonates. Both studies recorded no reductions in maternal and neonatal mortality and morbidity when frequency of caesarean section was more than 15%. Moreover, an increased rate of intervention was associated with higher mortality and morbidity in mothers and neonates.<sup>7</sup> Therefore, new evidence seems to confirm what was suggested 20 years ago.<sup>5</sup> For the health of both the mother and the neonate, and until further research gives new evidence, a frequency of between 5% and 10% seems to achieve the best outcomes, whereas a

## The printed journal includes an image merely for illustration

Panos Pictures

Woman undergoes caesarean section in hospital in Sierra Leone

rate of less than 1%, or of higher than 15%, seems to result in more harm than good.

In sub-Saharan countries and southern Asian countries, Ronsmans and colleagues found that the caesarean section rate in the poorest women was less than the minimum recommended frequency of 1%. This finding is consistent with those of other analyses<sup>8</sup> from the same databases, which showed that only 5–20% of births in these countries were attended by a skilled birth attendant. Ronsmans and colleagues estimate that the current situation contributes to about 80 000 maternal deaths a year. We think that no more research is needed. The current situation is mainly an economic problem that is costing thousands of lives.<sup>19</sup>

On the other side of the Atlantic, the situation is quite different. Ronsmans and colleagues show that in Latin American countries, poorer women again have a lower rate of caesarean section than do those of higher income. However, in most countries analysed, the frequency of caesarean section in the poorest women ranged from 1% to 15%, whereas the rate in at least 40% of the population was more than 15%. Paradoxically, and only for caesarean section rates, poorer women receive health care of better quality than those of higher income.

This finding is consistent with those of other rigorous studies in Latin America,<sup>7,10</sup> which show that caesarean section rates at hospitals in public health-care systems (in which women from the lowest socioeconomic

groups are attended) is lower compared with that at social-security and private hospitals. In countries such as Argentina, Brazil, Chile, and Mexico, the caesarean section rate in the poorest women has probably exceeded the upper threshold of 15%.<sup>10</sup> We estimate that 1.5 million unnecessary caesarean sections are done every year in Latin America,<sup>7,10</sup> causing about 100 maternal deaths and 40 000 cases of neonatal respiratory morbidity, and probably increasing the occurrence of preterm births and neonatal mortality.<sup>7,11,12</sup>

Now is the time for research in Latin America, where there are many complex reasons for this increasing trend. Recent attempts to reduce the number of unnecessary caesarean sections have resulted in only small decreases,<sup>13</sup> and original interventions are needed. Although urgent action is needed in sub-Saharan Africa, measures to prevent what is already occurring in Latin America should also be a priority.

\**Fernando Althabe, José M Belizán*

Perinatal Research Unit, Montevideo, Uruguay (FA); and Institute for Clinical Effectiveness and Health Policy (IECS), Buenos Aires, Argentina (JMB)  
althabef@gmail.com

We declare that we have no conflict of interest.

- Ronsmans C, Holtz S, Stanton C. Socioeconomic differentials in caesarean rates in developing countries: a retrospective analysis. *Lancet* 2006; **368**: 1516–23.
- Dumont A, de Bernis L, Bouvier-Colle MH, Breart G. Caesarean section rate for maternal indication in sub-Saharan Africa: a systematic review. *Lancet* 2001; **358**: 1328–33.
- De Brouwere V, Dubourg D, Richard F, Van Lerberghe W. Need for caesarean sections in west Africa. *Lancet* 2002; **359**: 974–75.
- Ronsmans C, Van Damme W, Filippi V, Pittrof R. Need for caesarean sections in west Africa. *Lancet* 2002; **359**: 974.
- Anon. Appropriate technology for birth. *Lancet* 1985; **2**: 436–37.
- Althabe F, Sosa C, Belizán JM, Gibbons L, Jacquerioz, F, Bergel E. Caesarean section rates and maternal and neonatal mortality in low-, medium-, and high-income countries: an ecological study. *Birth* (in press).
- Villar J, Valladares E, Wojdyla D, et al. Caesarean delivery rates and pregnancy outcomes: the 2005 WHO global survey on maternal and perinatal health in Latin America. *Lancet* 2006; **367**: 1819–29.
- Population Reference Bureau. The wealth gap in health. May, 2004: [http://www.prb.org/Content/ContentGroups/Datasheets/TheWealthGapinHealth\\_Eng.pdf](http://www.prb.org/Content/ContentGroups/Datasheets/TheWealthGapinHealth_Eng.pdf) (accessed Sept 8, 2006).
- Darmstadt GL, Bhutta ZA, Cousens S, for the Lancet Neonatal Survival Steering Team. Evidence-based, cost-effective interventions: how many newborn babies can we save? *Lancet* 2005; **365**: 977–88.
- Belizán JM, Althabe F, Barros FC, Alexander S. Rates and implications of caesarean sections in Latin America: ecological study. *BMJ* 1999; **319**: 1397–400.
- Barros FC, Victora CG, Barros AJ, et al. The challenge of reducing neonatal mortality in middle income countries: findings from three Brazilian birth cohorts in 1982, 1993, and 2004. *Lancet* 2005; **365**: 847–54.
- Belizán JM, Cafferata ML, Althabe F, Buekens P. Risks of patient choice caesarean. *Birth* 2006; **33**: 167–69.
- Althabe F, Belizán JM, Villar J, et al. Mandatory second opinion to reduce rates of unnecessary caesarean sections in Latin America: a cluster randomised controlled trial. *Lancet* 2004; **363**: 1934–40.