

# Premature rupture of membranes at term: a medical and economic rationale for active management

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## Résumé

DANS CE NUMÉRO (PAGE 1519), le Dr Amiram Gafni et ses collègues démontrent que l'induction immédiate du travail par l'oxytocine coûte beaucoup moins cher que l'induction à la prostaglandine ou le traitement expectant chez les femmes enceintes à terme dont la poche des eaux s'est rompue prématurément. Même s'ils reconnaissent que leur analyse comporte certaines limites, ils ne mentionnent pas 3 facteurs possibles de confusion : les économies qu'on pourrait réaliser en utilisant le misoprostol au lieu de la prostaglandine E<sub>2</sub>, l'impact économique des soins hospitaliers par rapport aux soins externes et l'importance des décès périnataux chez les femmes traitées de façon expectante. Même si le Dr Gafni et ses collègues affirment que sur le plan clinique, il n'y a pas de bon ou de mauvais choix en ce qui concerne le traitement actif par rapport au traitement expectant, l'auteur de l'éditorial conclut que les données financières et cliniques présentent un argument convaincant en faveur du traitement actif.

Premature rupture of the membranes complicates 5% to 10% of all pregnancies. Approximately 60% of cases occur among women at term, whose clinical management can be surprisingly complicated.<sup>1</sup> The specific dilemma is how best to treat patients whose cervixes have not ripened. The 2 basic approaches to management are immediate induction of labour and expectant management. The principal adverse outcomes of immediate induction are failed induction (and hence a need for cesarean delivery) and increased risk of maternal and neonatal infection secondary to protracted labour. The potential adverse effects of expectant management are increased risk of infection resulting from the prolonged rupture of the membranes, umbilical cord prolapse or compression, and abruptio placentae. Expectant management may also lead to increased costs, especially when patients are observed in hospital, as is the practice in the US.<sup>2</sup>

In their original article describing the largest prospective, randomized trial of management strategies for premature rupture of the membranes at term, the TERMPROM (Term Prelabor Rupture of the Membranes) Study Group<sup>3</sup> provided valuable insight into the clinical advantages and disadvantages of active versus expectant management. In this issue (page 1519), Dr. Amiram Gafni and colleagues from the TERMPROM group give an equally thoughtful assessment of the economic impact of the different management strategies. They demonstrate that immediate induction of labour with oxytocin costs significantly less than either immediate induction with prostaglandin E<sub>2</sub> gel or expectant management followed by oxytocin induction (if needed) after 4 days. This difference in cost applied to the 3 countries considered in the economic analysis: Canada, the UK and Australia. The absolute cost difference was modest, ranging from Can\$46 to Can\$114, £63 to £113 and A\$30 to A\$49 respectively. The calculated difference in cost between induction with prostaglandin and expectant management followed by induction with prostaglandin was not statistically significant.

Gafni and colleagues acknowledge the limitations of their analysis. They were able to assess direct costs only and could not accurately evaluate indirect costs such as time off work. Because the calculation of costs at all 72 institutions in the multi-centre study would have been prohibitively expensive, they selected 12 teaching and community hospitals from the 3 countries with the largest study recruitment.



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They also acknowledge the wide variation in costs between medical centres and countries, an effect compounded by the range of fees collected by different types of obstetric attendants.

At least 3 other important confounders were not considered explicitly by the authors in their analysis. First, the prostaglandin E<sub>2</sub> preparations used in their study are significantly more expensive than misoprostol, the prostaglandin E<sub>1</sub> preparation currently gaining favour in the US.<sup>4</sup> The 2-mg application of prostaglandin E<sub>2</sub> used in the TERMPROM study cost approximately Can\$50. The equivalent dose of misoprostol (25 to 50 µg) costs less than Can\$1.50. The use of the latter may make induction with prostaglandin more attractive economically, especially in view of the agent's efficacy in patients whose cervixes are unripe.<sup>4</sup>

Second, women randomly assigned to expectant management were further assigned to inpatient or outpatient care. The criteria for this second randomization were not specified, and the assessment of clinical outcomes was not stratified according to the site of expectant management. Outpatient management of premature rupture of the membranes at term is not accepted practice in the US. If all patients managed expectantly had been admitted to hospital, the cost of their treatment would certainly have been greater than that reported by Gafni and colleagues.

Finally, the authors do not consider the economic consequences of the 4 perinatal deaths that occurred in the expectant management groups. Although the observed difference in perinatal mortality was not statistically significant, the authors appropriately acknowledge that a much larger study would be necessary to conclude with reasonable certainty that expectant management is as safe for the neonate as active management.

Despite the authors' statement that "clinically, there is no right or wrong choice," the present economic assessment, combined with the investigators' original clinical observations, makes a compelling case for immediate induction of labour in women with premature rupture of the membranes at term. Women managed in this manner had a lower rate of infection than those managed expectantly for 4 days and then induced with oxytocin.<sup>3</sup> This finding is consistent with at least 3 other published investigations<sup>5-7</sup> and a recent meta-analysis.<sup>8</sup> The infants of these patients were less likely to receive antibiotics for suspected sepsis and less likely to be admitted to a special care nursery than those in the expectant management group. When admission to a special care nursery was required, infants in the induction group had a shorter mean duration of stay. The 4 perinatal deaths all occurred in the expectant management group, and 2 of the mothers whose infants died had been treated as outpatients. Although the mothers in the TERMPROM study were not asked about their preference for treatment until after delivery, those managed by

immediate induction were significantly less likely to have negative reactions than those treated expectantly.

Finally, immediate induction of labour with oxytocin was associated with a modest yet significant reduction in cost (Can\$46 to Can\$114 per patient). Small cost savings for the individual patient can translate into major cost savings for an entire health care system. If we assume, with Gafni and colleagues, that 8% of the approximate 3.6 million term births in the US are complicated by premature rupture of the membranes, and if we use the Canadian cost savings as a basis for comparison, a savings of US\$8.6 to US\$21.9 million would be realized if patients were managed by immediate induction rather than observation. As noted earlier, the cost of induction with prostaglandin would also be reduced if misoprostol were used instead.

I agree with Gafni and colleagues' contention that patients should be allowed to choose between equally effective options. In this situation, however, medical and economic evidence favours active management. Patients who oppose intervention can be treated expectantly, but they probably should be managed in hospital until the safety of outpatient management has been confirmed in controlled, prospective trials. In addition, labour should not be induced after an arbitrary period; rather, patients should be allowed to enter labour spontaneously. *Delayed induction*, as described in this and other studies,<sup>3,5-7</sup> combines the potential disadvantages of induction and of expectant management, increasing the risk of maternal and possibly neonatal infection and the duration and expense of hospital care without effecting a beneficial decrease in the rate of cesarean delivery. I suspect that, when presented with this objective medical and economic assessment, most thoughtful patients would choose active management.

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