Cost-effectiveness of induction of labour versus serial antenatal monitoring in the Canadian Multicentre Postterm Pregnancy Trial

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Abstract • Résumé

Objective: To determine the cost-effectiveness of induction of labour versus serial fetal monitoring while awaiting spontaneous labour in postterm pregnancies.

Design: Cost-effectiveness and cost-minimization analyses conducted as part of a Canadian multicentre randomized clinical trial.

Setting: Twenty-two Canadian hospitals, of which 19 were teaching hospitals and 3 were community hospitals.

Patients: Women with uncomplicated pregnancies of 41 or more weeks' gestation were randomly assigned to induction of labour or serial antenatal monitoring. Of the 3418 women enrolled, no data were received on 11. Therefore, results were based on data from 1701 women in the induction arm of the study and 1706 women in the monitoring arm.

Main outcome measures: Perinatal mortality and neonatal morbidity, rates of cesarean section and health care costs. Hospital costing models were developed specifically for the study. Data on use of major resources (e.g., length of hospital stay, surgical procedures, major diagnostic tests and procedures, and medications) for all trial participants were collected and combined with data on minor tests and procedures (e.g., laboratory tests) abstracted from a detailed review of medical records of a sample of patients.

Results: Because the results of the clinical trial showed a nonsignificant difference in perinatal mortality and neonatal morbidity between the induction and monitoring arms, the authors conducted a cost-minimization rather than a cost-effectiveness analysis. The mean cost per patient with a postterm pregnancy managed through monitoring was $3132 (95% confidence interval [CI] $3090 to $3174) and per patient who underwent induction of labour was $2939 (95% CI $2898 to $2981), for a difference of $193. The significantly higher ($p < 0.0001$) mean cost per patient in the monitoring arm was due mainly to the costs of additional monitoring and the significantly higher rates of cesarean section among these patients. Estimated conservatively, the savings resulting from a universal policy of managing postterm pregnancies by induction of labour in Canada may be as high as $8 million a year.

Conclusions: A policy of managing postterm pregnancy through induction of labour not only results in more favourable outcomes than a monitoring strategy but does so at a lower cost.

Objectif : Déterminer la rentabilité de la provocation du travail par rapport à la surveillance sérielle du foetus en attendant le travail spontané dans les cas de grossesse prolongée.

Conception : Analyses de rentabilité et de minimisation des coûts effectuées dans le cadre d'un essai clinique randomisé multicentrique au Canada.

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Contexte : Vingt-deux hôpitaux canadiens, dont 19 hôpitaux d'enseignement et 3 hôpitaux communautaires.

Patientes : On a choisi au hasard des femmes qui avaient connu une grossesse sans complication de 41 semaines ou plus pour provoquer le travail ou les soumettre à une surveillance anténatale sérielle. On n'a pas reçu de données sur 11 des 3 418 femmes inscrites. Les résultats étaient donc fondés sur des données provenant de 1 701 femmes chez lesquelles on a provoqué l'accouchement et de 1 706 femmes soumises à la surveillance.

Principales mesures des résultats : Mortalité périnatale et morbidité néonatale, taux de césarienne et coûts des soins de santé. On a créé des modèles d'établissement des coûts hospitaliers spécifiquement pour l'étude. On a recueilli des données sur l'utilisation des principales ressources (p. ex., durée du séjour à l'hôpital, interventions chirurgicales, principales analyses et interventions de diagnostic, et médicaments) pour toutes les participantes et l'on a fusionné ces données à d'autres portant sur les procédures et les tests mineurs (p. ex., tests de laboratoire) tirées d'une revue détaillée des dossiers médicaux d'un échantillon de patientes.

Résultats : Comme les résultats de l'essai clinique ont fait état d'une différence non importante entre les taux de mortalité périnatale et de morbidité néonatale entre les deux groupes, les auteurs ont procédé à une analyse de minimisation des coûts plutôt qu'à une analyse de rentabilité. Le coût moyen par patiente dont la grossesse s'est prolongée et qui a été traitée par surveillance a atteint 3 132 $ (intervalle de confiance à 95 % [IC] de 3 090 $ à 3 174 $). Le coût par patiente chez laquelle on a provoqué le travail a atteint 2 939 $ (IC à 95 % de 2 898 $ à 2 981 $), ce qui représente un écart de 193 $. Le coût moyen beaucoup plus élevé ($p < 0,0001$) par patiente surveillée est attribuable principalement au coût de la surveillance supplémentaire et aux taux beaucoup plus élevés de césariennes subies par ces patientes. Une politique universelle de traitement des grossesses prolongées par provocation du travail au Canada pourrait entraîner des économies estimées de façon conservatrice à 8 millions de dollars par année.

Conclusions : Une politique qui consiste à traiter les grossesses prolongées en provoquant le travail entraîne des résultats plus favorables qu'une stratégie de surveillance et coûte en outre moins cher.

Approximately 10% of the more than 400 000 births in Canada each year occur after 41 or more weeks' gestation.[1,2] There are two competing strategies for the management of postterm pregnancies: induction of labour when the pregnancy reaches 41 to 42 weeks' gestation and waiting for spontaneous labour. The waiting strategy typically involves serial antenatal monitoring and induction of labour if there is evidence that the health of the fetus or mother is or may be affected.[3-5] Although there is strong evidence that postterm pregnancies have a higher risk of adverse maternal, fetal and neonatal outcomes than term pregnancies,[2,6,7] the effectiveness and cost-effectiveness of an induction versus a monitoring strategy has not been shown.

The Canadian Multicentre Postterm Pregnancy Trial[8] was undertaken to determine the effectiveness of these alternative management strategies. The main results of the trial showed no statistically significant differences in rates of perinatal mortality and neonatal morbidity between the patients assigned to induction and those assigned to monitoring. Although there were two fetal deaths in the monitoring arm, this difference in the mortality rate was nonsignificant given the size of the sample. The study also showed that the rate of cesarean section in the induction arm was 3.3% lower than in the monitoring arm ($p = 0.03$).

The results of this study, combined with a meta-analysis of 10 other randomized controlled trials comparing induction of labour and serial antenatal monitoring in postterm pregnancies,[9] suggest that induction of labour results in decreased rates of fetal distress and of fetal or neonatal death. A policy of induction of labour also results in lower rates of cesarean section. The implications of these findings for cost and cost-effectiveness have not been studied. We conducted a cost-effectiveness analysis with the rate of perinatal mortality and neonatal morbidity as the primary measure of effectiveness.

Methods

Eligibility, design and outcome measures

The trial was conducted in 22 Canadian hospitals, of which 19 were teaching hospitals and 3 were community hospitals. Patients were screened for eligibility and randomly assigned to one of the two management strategies.[8] The sample was stratified according to hospital, parity and duration of gestation. There were 3418 women enrolled; of these, no data were received on 11. Data were collected on 1701 women assigned to prophylactic induction of labour and 1706 assigned to serial antenatal monitoring.

Induction of labour was begun within 4 days after the women were assigned to the induction arm. Labour was induced with the use of up to three 0.5-mg doses of dinoprostone (prostaglandin E_2) gel administered intracervically, followed by amniotomy, intravenous adminis-

tration of oxytocin or both. Women assigned to the monitoring arm were asked to record daily counts of fetal kicks. They underwent nonstress tests three times per week and assessment of amniotic fluid volume by ultrasonographic examination two to three times per week.

The primary outcomes, perinatal mortality and neonatal morbidity, were measured by assigning an index score based on death and indicators of morbidity (e.g., low Apgar scores, seizures, need for ventilation, trauma and neonatal intensive care).[8] The secondary outcome measure was the rate of cesarean section.

Cost-effectiveness and cost-minimization analyses

Cost-effectiveness analysis compares the costs and outcomes of two or more alternatives, whereas cost-minimization analysis compares only the costs of alternatives; it is used when differences in outcomes are nonsignificant or deemed unimportant. The intention of our study was to conduct a cost-effectiveness analysis; however, if the difference in outcomes between the two groups was nonsignificant, we planned to conduct a cost-minimization analysis.

In our analysis we used the cost perspective of the Ontario Ministry of Health. All hospital costs, drug expenses and professional fees were included; patient expenses and time off work were excluded. We predicted that the average cost for patients in the trial would depend on the type of hospital, the method of delivery, the number of gel applications (for patients in the induction arm) and the number and type of monitoring tests conducted (nonstress tests and assessments of amniotic fluid volume for patients in the monitoring arm). These data and the length of postpartum hospital stay for each patient were obtained from the clinical-trial database.

Data on the use of major resources were collected as part of the clinical trial; however, for budgetary reasons, minor tests and procedures were not recorded on the case-report forms. In order to capture all of the costs involved, we conducted a retrospective review of the medical charts of a sample of patients to obtain information on these minor tests (e.g., laboratory tests) and procedures. The sample included patients who delivered in a teaching hospital and those who delivered in a community hospital as well as those who had each method of delivery (spontaneous vaginal, vaginal with the use of forceps and cesarean section). A total of 67 charts from the teaching hospital and 62 charts from the community hospital were reviewed. In both hospitals, charts reviewed involved 20 spontaneous vaginal deliveries, 20 vaginal deliveries with the aid of forceps and cesarean sections in the remaining cases (27 at the teaching hospital and 22 at the community hospital).

Costing of hospital services involves two components: resource use (quantities) and cost per unit. Since unit costs for most hospitals in Canada are unavailable, the standard approach to estimating hospital costs is to use unit-cost estimates from one or more representative hospital and data on resource use from all trial participants.[10] Since the clinical study included both teaching and community hospitals, and since practice patterns and unit costs can differ substantially between teaching and community hospitals, one teaching hospital and one community hospital were selected on the basis of their share of patient enrolment in the clinical trial and their geographic proximity to the study team. The teaching hospital selected was Women's College Hospital, Toronto, and the community hospital was North York General Hospital, Willowdale, Ont.

To estimate unit costs, we designed costing models for these hospitals consistent with Canadian management-information-systems guidelines[11] for allocating expenses within hospital departments and to patients. The costing method used in both models was a "simultaneous, fully allocated" approach. This involved first allocating hospital overhead expenses (e.g., depreciation on equipment and buildings) and direct department expenses to hospital departments. Next, the expenses of departments that provide services to other departments but not directly to patients (i.e., hospital-support departments), were allocated among each other with the use of simultaneous linear equations and then to departments that provide services directly to, or on behalf of, patients (e.g., laboratories, operating rooms and wards). In the final step, these "simultaneous, fully allocated" expenses for patient service and care departments were allocated to patients on the basis of service use or department resources (e.g., the number of days the patient spent on various wards, the number of minutes in the operating room or the weighted time units for laboratory and radiology services). Expenses for each patient service and care department were then added to calculate the total cost of each hospital stay. Fees for professional visits, consultations, interpretation of results and diagnostic and surgical procedures were calculated by combining the clinical-trial data with the Ontario provincial schedule of benefits for medical services.[12]

Total use of resources per patient in the induction and monitoring arms was calculated by combining data on resource use from all trial participants with those on minor tests and procedures from the sample of patients from two hospitals. From these data, hospital costs and professional fees were calculated and compared with the use of Statistical Package for the Social Sciences, version 5 for Windows (SPSS Inc., Chicago). Hospital costs include ward, operating-room, drug and laboratory costs. Professional fees include those for consultations, visits,

deliveries, interpretation of results and diagnostic and therapeutic procedures. All costs were calculated and expressed in 1992 Canadian dollars.

In addition to comparing the costs of the two strategies, we calculated the potential cost savings to the Canadian health care system resulting from the universal adoption of one management policy over the other. In calculating these savings, we adjusted our results to take into account the overrepresentation of deliveries in teaching hospitals and to nulliparous women in our sample by applying the proportions of such deliveries in Canada as a whole to our cost findings. Of all deliveries in our study, 85% were in teaching hospitals, whereas approximately 32% of deliveries in Canada as a whole are performed in such hospitals.[13] Similarly, 68% of the deliveries in our study were to nulliparous women, whereas 44% of those in Canada as a whole are to nulliparous women.[14] We also assumed that approximately 10% of the 400 000 deliveries in Canada each year involve postterm pregnancies.

Results

Because the results of the clinical trial showed a nonsignificant difference in perinatal mortality and neonatal morbidity between the induction and monitoring arms,[8] we conducted a cost-minimization rather than a cost-effectiveness analysis. As shown in Table 1, most of the difference in hospital and physician resource use between the induction and monitoring arms resulted from the serial monitoring tests and the higher rate of cesarean section in the monitoring arm. Although no difference was found in the average number of minor tests and procedures, these data were based on only a sample of patients, not all trial participants.

The unit-cost estimates for the teaching and community hospitals, calculated from the models developed specifically for this study, are presented in Table 2. Table 3 gives the average costs for each management strategy by major cost category. It shows that 94% of the $193 difference in average cost per patient between the monitoring and induction arms was due to differences in hospital costs, including those for inpatient and outpatient services. Almost all (99%) of the difference in hospital costs was accounted for solely by the number and cost of the tests required in the monitoring arm.

On the basis of these cost differences, we calculated the minimum potential cost savings, excluding patient expenses, resulting from a universal policy of managing postterm deliveries through induction of labour. As noted earlier, we adjusted the results to take into account the overrepresentation of teaching hospitals and deliveries to nulliparous women and we assumed that approxi-

Table 2: Estimated unit costs of selected hospital services in a teaching hospital (Women's College Hospital, Toronto) and a community hospital (North York General Hospital, Willowdale, Ont.)

Hospital service	Estimated unit cost, 1992 $	
	Teaching hospital	Community hospital
Antenatal care, per diem	452.93	355.96
Labour and delivery, per hour	41.45	37.89
Operating room, per hour	440.12	389.99
Complete blood count	6.25	3.45
Urinalysis	4.75	3.96
Analysis of blood gases	6.00	5.28
Nonstress test	10.50	10.50
Assessment of amniotic fluid volume	120.84	110.77

Table 1: Use of resources by patients enrolled in the Canadian Multicentre Postterm Pregnancy Trial

Variable	Study arm		Difference between arms
	Monitoring	Induction	
Resources used*			
Nonstress tests	2.1	NA‡	2.1
Assessments of amniotic fluid volume	1.6	NA	1.6
Minor tests and procedures (estimate based on a sample of patients)	5.0	5.0	0
Consultations and follow-up visits (estimate based on a sample of patients)	5.9	5.9	0
Length of stay†	4.0	3.9	0.1
Rate of cesarean section, %	24.5	21.2	3.3

*Mean no. per patient
†Mean no. of days per patient
‡NA = not applicable.

mately 10% of the 400 000 deliveries in Canada each year occur after 41 or more weeks' gestation. After these adjustments were made, the potential cost saving of a universal induction-management policy was calculated at $8 million per year.

Discussion

Although we observed a significant difference in mean cost per patient between strategies, there are several reasons to suspect that the cost difference in favour of the induction strategy would be even larger if a wider cost perspective was used. Our analysis did not include the cost and quality of life for patients. Patient expenses would be higher with the monitoring strategy than with the induction strategy because of increased monitoring, travel costs, inconvenience and possibly time off work. Higher patient expenses and lower quality of life would also result from the significantly higher rate of cesarean section among patients managed through monitoring. These issues highlight the importance of including and measuring patient preferences in future studies.

The results of the Canadian Multicentre Postterm Pregnancy Trial[8] and of the meta-analysis discussed earlier,[9] combined with the significant difference in cost between the two strategies, unambiguously support the induction strategy as a "win–win" alternative in the management of postterm pregnancies. That is, an induction-management policy produces better outcomes at a lower cost. These findings also support recent recommendations that induction of labour should be offered to women with pregnancies of 41 or more weeks.[15] Research is needed to determine the most effective methods of induction (e.g., medication, nipple stimulation, stripping or sweeping of the membranes or mechanical methods).

There are two principal limitations of the cost findings in our study. First, costs for minor tests and procedures were estimated on the basis of a sample of patients. These data were not collected as part of the main trial because of the exorbitant cost involved. However, since minor tests and procedures account for only a fraction of the total cost of hospital care for a patient, it is unlikely that more detailed collection of data on the costs of these tests would substantially affect the results. Second, unit-cost estimates were obtained from only two centres, one teaching and one community hospital. Again, the reason for this approach was the exorbitant cost of setting up detailed costing models for all 22 hospitals participating in the study. Since the mix of patients in teaching and community hospitals was the same in both arms of the study, it is unlikely that more detailed costing data from all of the hospitals would have made a difference in the results.

Two cautions are warranted in generalizing the results of our study to Canada as a whole. First, deliveries in teaching hospitals were overrepresented in the trial (85% of deliveries in our trial in comparison with 32% of those in Canada[13]). Second, deliveries to nulliparous women were overrepresented (68% of deliveries in our trial in comparison with 44% of those in Canada[14]). These factors may influence outcomes and cost. In our analysis, adjustments were made to the cost findings to reflect the overrepresentation of teaching hospitals and nulliparous women.

There are two main areas in which additional research could assist in providing more precise cost estimates. First, there are several reasons to suspect that the cost difference we observed between the monitoring and the induction strategies was conservative and would have been larger if a wider cost perspective, including patient expenses and quality of life, had been used. Second, the big uncertainty in calculating the potential savings resulting from a universal induction-management policy is the percentage of postterm pregnancies currently managed through monitoring. In this study, we assumed that approximately 10% of the 400 000 deliveries in Canada each year occur after 41 or more weeks' gestation. The potential savings from a universal induction-management policy could be estimated more precisely if the percentage of pregnancies of 41 or more weeks' gestation were known.

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Table 3: Calculated mean costs for care of patients enrolled in the Canadian Multicentre Postterm Pregnancy Trial

	Mean cost per patient, 1992 $			
	Study arm		Difference between study arms	
Cost category	Monitoring	Induction	(95% confidence interval)	*p* value
Hospital costs	2684	2502	182 (129–234)	< 0.0001
Professional fees	448	437	11 (1– 21)	0.025
Total	3132	2939	193 (133–252)	< 0.0001

References

1. Beischer NA, Evans JH, Townsend L: Studies in prolonged pregnancy. I. The incidence of prolonged pregnancy. *Am J Obstet Gynecol* 1969; 103: 476–482
2. McClure Browne JC: Postmaturity. *Am J Obstet Gynecol* 1963; 85: 573–582
3. Crowley P, O'Herlihy C, Boylan P: The value of ultrasound measurement of amniotic fluid volume in the measurement of prolonged pregnancies. *Br J Obstet Gynaecol* 1984; 91: 444–448
4. Shime J, Gare DJ, Andrews J et al: Prolonged pregnancy: surveillance of the fetus and the neonate and the course of labor and delivery. *Am J Obstet Gynecol* 1984; 148: 547–552
5. Johnson JM, Harman CR, Lange IR et al: Biophysical profile scoring in the management of the postterm pregnancy: an analysis of 307 patients. *Am J Obstet Gynecol* 1986; 154: 269–273
6. Bakketeig L, Bergsjo P: Post-term pregnancy: magnitude of the problem. In Chalmers I, Enkin M, Keirse MJNC (eds): *Effective Care in Pregnancy and Childbirth*, Oxford University Press, Oxford, England, 1989: 765–775
7. Crowley P: Post-term pregnancy: induction or surveillance? In Chalmers I, Enkin M, Keirse MJNC (eds): *Effective Care in Pregnancy and Childbirth*, Oxford University Press, Oxford, England, 1989: 776–791
8. Hannah ME, Hannah WJ, Hellmann J et al and the Canadian Multicenter Post-term Pregnancy Trial Group: Induction of labor as compared with serial antenatal monitoring in post-term pregnancy. *N Engl J Med* 1992; 326: 1587–1592
9. Hannah ME: Postterm pregnancy: should all women have labor induced? A review of the literature. [review] *Fetal Matern Rev* 1993; 5: 3–17
10. Drummond MF, Stoddart GL, Torrance GW: *Methods for the Economic Evaluation of Health Care Programmes*, Oxford University Press, London, England, 1987
11. *Guidelines for Management Information Systems in Canadian Health Care Facilities*, MIS Group, Toronto, 1993
12. Ontario Ministry of Health: *OHIP Schedule of Benefits*, Publications Ontario, Toronto, 1993
13. *Diagnostic and Therapeutic Services*. Vol 3 of *Health Reports: Hospital Annual Statistics* [cat no 82-003S20], Statistics Canada, Ottawa, 1992
14. *Health Reports: Births* [cat no 82-003S14], Statistics Canada, Ottawa, 1992
15. Hannah M: Management of post-term pregnancy. [SOGC committee opinion] *J Soc Obstet Gynecol Can* 1994; Apr: 1581–1586

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June 9–10, 1995: Something's in the Air — a Conference on Air Quality and Lung Health

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Sept. 21–23, 1995: Canadian Fertility and Andrology Society Annual Meeting

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