BJOG An International Journal of Obstetrics and Gynaecology

DOI: 10.1111/1471-0528.13957
www.bjog.org

An economic analysis of immediate delivery and expectant monitoring in women with hypertensive disorders of pregnancy, between 34 and 37 weeks of gestation (HYPITAT-II)

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Accepted 22 January 2016. Published Online 10 March 2016.

Objective To assess the economic consequences of immediate delivery compared with expectant monitoring in women with preterm non-severe hypertensive disorders of pregnancy.

Design A cost-effectiveness analysis alongside a randomised controlled trial (HYPITAT-II).

Setting Obstetric departments of seven academic hospitals and 44 non-academic hospitals in the Netherlands.

Population Women diagnosed with non-severe hypertensive disorders of pregnancy between $34^{0/7}$ and $37^{0/7}$ weeks of gestation, randomly allocated to either immediate delivery or expectant monitoring.

Methods A trial-based cost-effectiveness analysis was performed from a healthcare perspective until final maternal and neonatal discharge.

Main outcome measures Health outcomes were expressed as the prevalence of respiratory distress syndrome, defined as the need for supplemental oxygen for >24 hours combined with radiographic findings typical for respiratory distress syndrome. Costs were estimated from a healthcare perspective until maternal and neonatal discharge.

Results The average costs of immediate delivery (n = 352) were €10 245 versus €9563 for expectant monitoring (n = 351), with an average difference of €682 (95% confidence interval, 95% CI −€618 to €2126). This 7% difference predominantly originated from the neonatal admissions, which were €5672 in the immediate delivery arm and €3929 in the expectant monitoring arm.

Conclusion In women with mild hypertensive disorders between $34^{0/7}$ and $37^{0/7}$ weeks of gestation, immediate delivery is more

costly than expectant monitoring as a result of differences in neonatal admissions. These findings support expectant monitoring, as the clinical outcomes of the trial demonstrated that expectant monitoring reduced respiratory distress syndrome for a slightly increased risk of maternal complications.

Keywords Economic evaluation, expectant monitoring, hypertensive disorders, immediate delivery, preterm.

Tweetable abstract Expectant management in preterm hypertensive disorders is less costly compared with immediate delivery.

Linked article This article is commented on by AB Caughey. To view this mini commentary visit http://dx.doi.org/10.1111/1471-0528.14127.

Please cite this paper as: van Baaren G-J, Broekhuijsen K, van Pampus MG, Ganzevoort W, Sikkema JM, Woiski MD, Oudijk MA, Bloemenkamp KWM, Scheepers HCJ, Bremer HA, Rijnders RJP, van Loon AJ, Perquin DAM, Sporken JMJ, Papatsonis DNM, van Huizen ME, Vredevoogd CB, Brons JTJ, Kaplan M, van Kaam AH, Groen H, Porath M, van den Berg PP, Mol BWJ, Franssen MTM, Langenveld J, for the HYPITAT-II Study Group. An economic analysis of immediate delivery and expectant monitoring in women with hypertensive disorders of pregnancy, between 34 and 37 weeks of gestation (HYPITAT-II). BJOG 2016; DOI: 10.1111/1471-0528.13957.

Introduction

Approximately 10% of all pregnancies are complicated by hypertensive disorders of pregnancy, such as gestational hypertension, pre-existing hypertension, pre-eclampsia, and superimposed pre-eclampsia.[1,2] Hypertensive diseases in pregnancy are a major cause of morbidity and mortality for both mother and child. Moreover, the care for women with hypertensive disease in pregnancy imposes a substantial economic burden.[3,4]

The definitive treatment for hypertensive disorders of pregnancy is delivery of the placenta. This will stop progression, and therefore has the potential to prevent adverse pregnancy outcomes; however, immediate delivery also results in preterm or early term birth, which increases the risk of neonatal complications.[5] In addition, concerns remain that immediate delivery increases the risk of caesarean section.[6]

In view of the limited evidence on the choice between immediate delivery and expectant monitoring for women with gestational hypertension or mild pre-eclampsia, we subsequently performed two randomised clinical trials: HYPITAT-I and HYPITAT-II.[7,8] The HYPITAT-I trial included women who were at term, and showed that immediate delivery resulted in less adverse maternal outcomes, whereas neonatal outcomes did not deteriorate.[9] Immediate delivery was less costly, as antenatal costs were reduced.[10] The HYPITAT-II trial included women between $34^{0/7}$ and $37^{0/7}$ weeks of gestation. This study showed that in women with non-severe hypertensive disorders between 34 and 37 weeks of gestation, immediate delivery might reduce the already small risk of adverse maternal outcomes; however, it significantly increased the risk of neonatal respiratory distress syndrome (RDS). Therefore, routine immediate delivery does not seem justified on clinical grounds, and expectant monitoring until the clinical situation deteriorates can be considered.[11] In addition to these clinical outcomes, knowledge of the costs may contribute to the decision whether to deliver immediately. At present, evidence on costs and cost-effectiveness of management of women with hypertensive disorders between $34^{0/7}$ and $37^{0/7}$ weeks gestation is lacking.

Here, we report the results of the economic evaluation that we performed alongside the HYPITAT-II trial. We performed a cost-effectiveness analysis from a healthcare perspective, comparing immediate delivery with expectant monitoring in women with hypertensive disorders between $34^{0/7}$ and $37^{0/7}$ weeks of gestation.

Methods

Trial design

Full details of the HYPITAT-II trial have been reported previously.[11] The study protocol was approved by the institutional review board of the Academic Medical Centre in Amsterdam (08/244), and approved by the boards of directors of all participating centres. The trial was registered in the Netherlands Trial Register (NTR1792), and was funded by ZonMw (grant 171102012). Women diagnosed with gestational hypertension, pre-eclampsia, deteriorating pre-existing hypertension, or superimposed pre-eclampsia, and with a gestational age between $34^{0/7}$ and $37^{0/7}$ weeks were randomised to either immediate delivery or expectant monitoring. No differences were found in the baseline characteristics of the two groups.[11]

Women randomised to immediate delivery underwent induction of labour or caesarean section within 24 hours of randomisation. Women randomised to expectant monitoring were monitored according to local protocol, with delivery before 37 weeks of gestation being advised in case of severe hypertensive disorder, suspected fetal distress, or any other contraindication to the prolongation of pregnancy. If women were still pregnant at 37 weeks of gestation, delivery was planned following similar procedures to those used in the immediate-delivery group.

The primary maternal outcome measure was a composite of adverse maternal outcomes, defined as one or more of thromboembolic complications, pulmonary oedema,

HELLP syndrome (haemolysis, elevated liver enzymes and low platelet count), eclampsia, placental abruption, or maternal death. The primary neonatal outcome measure was neonatal RDS, defined as the need for supplemental oxygen for >24 hours combined with radiographic findings typical for RDS. The composite adverse maternal outcome occurred in 1.1% of 352 women allocated to immediate delivery, versus 3.1% of 351 women allocated to expectant monitoring (relative risk, RR 0.36; 95% confidence interval, 95% CI 0.12–1.1). RDS was diagnosed in 5.7 versus 1.7% of the neonates (RR 3.3, 95% CI 1.4–8.2). There were no maternal or perinatal deaths.[11]

Economic evaluation

An economic analysis was performed alongside the trial, similar to the economic evaluation of the HYPITAT-I trial. As expectant monitoring resulted in significantly fewer cases of neonatal RDS, and was found to be more effective, the economic evaluation was set up as a cost-effectiveness analysis.[12,13] All unit costs were expressed in 2011 Euros using the consumer pricing index.[14] We compared costs and effects from the moment of randomisation to final discharge of mother and child(ren). Discounting was unnecessary because all costs and effects occurred within 1 year.[12,13] We used a healthcare perspective instead of the societal perspective used in the economic evaluation of the HYPITAT-I trial. This means that we included only medical costs to examine the economic impact of both strategies. The reason for using this perspective was the poor response rate of the cost questionnaires. We intended to send the questionnaire to 200 participants, but because of logistic problems we only sent 68 questionnaires to the immediate-delivery group and 60 questionnaires to the expectant management group, and received 26 and 19 filled questionnaires, respectively.

Measuring resource use

Resource use was measured by extending the Case Record Form with specific items on healthcare use. In the Case Record Form the following resource items were collected: outpatient visits, medication, maternal laboratory tests, maternal admissions, fetal monitoring, induction method, hours in labour room and/or operating theatre, method of delivery, third-stage delivery activities, and neonatal admissions and monitoring. Maternal admissions were differentiated into three phases: the antenatal, the delivery, and the postpartum phases. For each admission, hospital stay was differentiated according to the level of care: intensive care, medium care, maternal ward, or home care, because different levels have different costs. The time in the labour room was calculated as the time from admission to the labour room to the time of birth, plus 1 hour extra for recovery care. If a caesarean section was performed a standard time in the operating theatre was used. For each neonatal admission, hospital stay was differentiated according to the level of care: intensive care, high care, medium care, medium care on maternal ward, or maternal ward, because different levels have different costs. The duration of neonatal admission was calculated as the number of days between birth and hospital discharge. For neonatal admission to the maternity ward, no extra costs were generated because it was assumed that these costs were already included in those for the mother.

Unit costs

Different methods and sources were used to estimate unit costs as valuations for documented volumes of resource use (Table 1). For maternal and neonatal admissions, third-stage delivery, and neonatal monitoring, unit-cost estimates were available from the financial departments of one participating academic hospital and one participating general hospital. For these costs we used a top-down approach, meaning that costs that were not applicable for our patients were subtracted from the overall costs. For use of the labour room and the operating theatre, unit costs were calculated per hour, using a bottom-up approach, in which all personnel, use of materials, and overheads, calculated as a m^2 price, were integrated. For some cost units (outpatient visit, specialist care, general practitioner visit, paramedical, and home care) national standardised prices were used, and for laboratory testing published tariffs were used.[15,16] Medication prices were estimated using the Dutch drug registry.[17]

Analyses

Analyses were by intention to treat. Group differences in resource use were tested using the non-parametric Mann–Whitney *U*-test, as resources generally have a skewed distribution. Resource use per woman was multiplied by unit costs, and the total costs per woman were calculated. Mean costs and median costs per woman were estimated, and the mean cost differences between study groups were calculated. Bootstrapping was used to determine 95% CIs around the difference in mean costs. Bootstrap methods are based on generating multiple replications of the statistic of interest by sampling with replacement from the original data.[12,13] These bootstrap methods were also used to create a cost-effectiveness plane and, where necessary, cost-effectiveness acceptability curves.[18]

Nine univariate sensitivity analyses were performed to explore the impact of different assumptions and alternative unit-cost estimates on the results of the costs analysis. Firstly, we examined several other ways of estimating the delivery costs using academic, general hospital, or standard Dutch unit costs (models 1, 2, and 3). Several assumptions were made in estimating labour and operating theatre costs

Table 1. Cost analysis: units of resource use, unit costs, valuation method, and volume source (2011 €)

	Unit	Unit cost	Valuation method (source)
Admission mother			
Ward*	Day	372	Top-down calculation
Medium care*	Day	565	Top-down calculation
Intensive care unit*	Day	1804	Top-down calculation
Admission child			
Maternal ward*	Day	372	Top-down calculation
Medium care*	Day	565	Top-down calculation
High care*	Day	1514	Top-down calculation
Neonatal intensive care*	Day	1568	Top-down calculation
Specialist care			
Gynaecologist	Hour	75	Dutch costing guideline[15]
Neonatologist	Hour	75	Dutch costing guideline[15]
Paediatrician	Hour	75	Dutch costing guideline[15]
Other healthcare providers			
Midwife	Hour	36	Dutch costing guideline[15]
Home care by nurses	Hour	34	Dutch costing guideline[15]
Nurse	Hour	33	Dutch costing guideline[15]
Room occupation + overhead			
Labour room*	Hour	87	Bottom-up calculation
Operating theatre*	Hour	150	Bottom-up calculation
Medication			
Antihypertensive medication**	Dose per day	8	Dutch drug registry[17]
Antibiotics**	Treatment	33	Dutch drug registry[17]
Surfactant	Treatment	1031	Dutch drug registry[17]
Delivery			
Oxytocin	Gift	1	Dutch drug registry[17]
Prostaglandin E2 gel	Unit	79	Probaat trial[21]
Foley catheter	Unit	15	Probaat trial[21]
Vaginal delivery*	Procedure	1142	Top-down calculation
Caesarean section*	Procedure	2014	Top-down calculation
Instrumental attempt*	Procedure	207	Top-down calculation
Blood transfusion	Gift	208	Dutch costing guideline[15]
Radiology			
Ultrasound	Procedure	31	Dutch health authority tariff[16]
Computed tomography scan	Procedure	192	Dutch health authority tariff[16]
X-ray	Procedure	48	Dutch health authority tariff[16]
Extra care			
Intubation	Day	107	Dutch health authority tariff[16]
Cpap	Day	34	Dutch health authority tariff[16]

*The mean of the unit cost for an academic hospital and a general hospital is presented.
**The mean of several methods/types of medication is presented.

by using a bottom-up method, such as the time spent in the labour room and/or operating theatre by obstetricians and gynaecologists (model 4). We also estimated the impact of using top-down delivery costs (model 5). Because most cost differences were expected antepartum, as a result of longer maternal hospital stays in the expectant group, we wanted to find out the impact of a lower valuation of the antepartum admissions by assuming several other monitoring strategies: admissions to medium care instead of intensive care, daycare instead of inpatient care, outpatient visits plus cardiotocograms instead of inpatient care, and home care instead of inpatient care (models 6 and 7). In our base-case analysis (model 0), we included no costs for the neonatal ward admissions because we assumed that this was covered by the maternity ward admissions. In model 8 we priced neonatal ward admissions to check their impact. Finally, we attempted to include non-medical costs (costs as result of informal care, travel, and productivity loss) and follow-up costs (model 9). We assumed that the partner provided informal care during expectant management, and that both parents could not work during hypertensive disease, and during the

admission of the mother and/or child. Maternity and paternity leave were taken into account. For the follow-up costs we used the few cost questionnaires that were returned. National standardised prices were used for travel costs, informal care, and productivity loss.

Because subgroup analyses of clinical outcomes yielded no differences, no separate cost-analyses were performed. Statistical, economic, and simulation analyses were performed using SPSS 20.0 (SPSS, Chicago, IL, USA) and Microsoft EXCEL.

Results

Resource use

For the cost analysis we used the data from all 703 randomised women. Of these women, 352 had been assigned to the immediate-delivery group and 351 had been assigned to the expectant monitoring group. Average volumes of resource use, total costs in each study group, and average costs per woman are presented in Table S1. In the immediate-delivery group the women had a shorter antenatal stay in the hospital, visited the outpatient clinic less frequently, had fewer cardiotocograms, and used less antihypertensive medication. Neonatal admissions on the medium, intensive, and high care occurred more frequently. Time in the labour room was comparable between both groups, as were the rates of caesarean section and instrumental delivery.

Costs

A summary of mean and median costs per woman is presented in Table 2. In the antepartum period costs per woman appeared to be lower in the immediate-delivery group because of shorter maternal stays (difference: −€1353). During delivery, the costs in the immediate-delivery group were higher than in the expectant monitoring group (difference: €272). This is because of longer stays in the labour room associated with the induction procedure. Postpartum, women in the immediate-delivery group generated more costs than women in the expectant monitoring group (difference: €1763), because of more and longer neonatal stays in medium, high, and intensive care units.

Overall, the average costs per woman were €10 245 (95% CI €1823–28 874) for immediate delivery and €9563 (95% CI €1522–39 305) for expectant monitoring (difference €682; 95% CI −€618 to €2126).

Table 2. Comparison of costs between immediate delivery and expectant monitoring (2011 €)

	Delivery				Expectant monitoring				Diff
	Mean Cost	Median Cost	IQR		Mean Cost	Median Cost	IQR		(D−EM)
Maternal admission	505	309	0	618	1511	1010	0	2459	−1006
Cardiotocography and ultrasound	114	94	62	125	262	250	125	374	−149
Outpatient visits	8	0	0	0	73	0	0	66	−65
Laboratory tests	3	2	2	3	5	5	3	7	−3
Medication*	273	39	38	46	402	44	39	136	−129
Total antepartum phase	**901**				**2254**				**−1353**
Admission because of labour*	1778	1122	511	2344	1483	966	501	2092	295
Induction material*	40	14	14	76	35	14	0	76	5
Medication during labour*	68	3	0	173	70	3	0	173	−2
Other monitoring and interventions*	154	125	125	125	176	125	125	125	−22
Instrumental delivery	23	0	0	0	23	0	0	0	0
Caesarean delivery	46	0	0	150	49	0	0	150	−3
Total delivery phase	**2108**				**1,836**				**272**
Maternal admission	1469	1347	927	1853	1487	1235	927	1853	−18
Neonatal admission	5672	2693	0	6200	3929	1010	0	4040	1743
Extra care*	49	0	0	0	29	0	0	0	20
Transfers (mother + child)	45	0	0	0	27	0	0	0	17
Total postpartum	**7235**				**5473**				**1763**
Total costs	**10 245**				**9563**				**682**
						95% confidence interval**		**−618**	2126

*Costs are a summation of several types of medication, treatments or monitoring techniques.
**Non-parametric confidence interval based on 1000 bootstrap replications.
IQR, interquartile range.

Cost-effectiveness

For the cost-effectiveness analyses we considered RDS as an undesirable outcome. The cost-effectiveness plane (Figure 1) demonstrates that, with high certainty, immediate delivery is not a cost-effective strategy compared with expectant monitoring in pregnant women with mild hypertensive disorders (gestational hypertension or mild pre-eclampsia). Eighty-five per cent of all bootstrap estimates were in the upper left quadrant, meaning that immediate delivery was more costly and less effective (more RDS). Thus, expectant monitoring is the dominant strategy, irrespective of the willingness-to-pay/accept threshold. The remaining bootstrap estimates were in the lower left quadrant, meaning that immediate delivery was less effective, but also less costly. If one was willing to accept extra cases of RDS to save money, immediate delivery might be cost-effective according to these estimates. Figure S1 shows the probability of immediate delivery being cost-effective when the willingness-to-accept threshold is increased. This probability increased only marginally to 15%, as it was only affected by bootstrap estimates in the lower left quadrant.

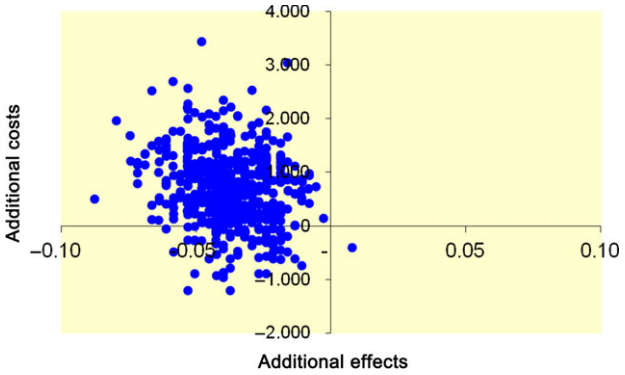

Figure 1. Cost-effectiveness plane. Each point in the cost-effectiveness plane represents the additional costs and health gain of immediate delivery compared with expectant management (multiple samples from original data set).

Sensitivity analyses

In Table 3 the results of the sensitivity analyses are shown. Immediate delivery was more costly than expectant monitoring in all sensitivity analyses, except for the model including non-medical and follow-up costs (model 9). In this analysis immediate delivery was less costly (−€714 (95% CI −€2126 to €802) because the cost of informal care and productivity loss were higher in the expectant monitoring group (Table S2). When admissions were valued by using academic unit prices or Dutch standard prices the mean costs in both groups increased, but the costs increased more in the immediate-delivery group. When antepartum admissions were replaced by outpatient visits and cardiotocograms or home care, mean costs decreased in both groups, but the costs decreased less in the immediate-delivery group (increasing the difference between the two groups). Top-down calculation of delivery costs and incorporating costs of neonatal ward admission resulted in a decrease in the difference in costs. All other assumptions did not yield major changes in cost and cost differences.

Discussion

Main findings

This study assessed the economic consequences of immediate delivery or a strategy of expectant monitoring in pregnant women with gestational hypertension, pre-eclampsia, deteriorating pre-existing hypertension, or superimposed pre-eclampsia between $34^{0/7}$ and $37^{0/7}$ weeks of gestation, from a healthcare perspective. In addition to the original

Table 3. Sensitivity analyses results (2011 €)

Model		Immediate delivery	Expectant monitoring	Difference	95% confidence interval	
0	Base case	10 245	9563	682	−744	1857
1	Value admissions by using academic unit prices only	13 123	12 030	1093	−401	2690
2	Value admissions by using general unit prices only	9460	8794	666	−642	2220
3	Value admissions by using Dutch standard prices	16 676	14 874	1802	−160	4042
4	Higher labour ward (€172) and operating (€301) theatre costs	12 061	11 079	983	−418	2601
5	Top-down calculation of delivery costs	9748	9379	369	−943	2013
6	Replace antepartum admissions by outpatient visits and cardiotocograms	9895	8626	1269	−92	2643
7	Replace antepartum admissions by home care	9846	8486	1360	−92	2743
8	Value all neonatal ward admission	10 600	10 157	443	−998	1704
9	Including non-medical costs and follow-up costs	11 365	12 079	−714	−2126	802

trial that showed that immediate delivery significantly increased the risk of neonatal RDS with a limited reduction of adverse maternal outcomes, the current analyses showed that the mean costs per woman generated by immediate delivery were €682 (95% CI −€618 to €2126) higher than those for expectant monitoring. The difference in costs predominantly originated in the postpartum period, because of more and longer neonatal hospital stays. Bootstrap analyses showed a very low probability that immediate delivery is cost-effective. Sensitivity analyses demonstrated that when antepartum care is situated in an outpatient or home-care setting, expectant monitoring might be even more cost saving.

Strengths and limitations

The prospective design of the trial, the large number and diversity of participating hospitals, and the well-organised structure of randomisation and data collection within the Dutch Obstetric Consortium are likely to extend both the internal and external validity of our results.

Because of the low incidence of adverse maternal outcomes and insignificant difference between both groups, we focused on the neonatal outcomes; however, adverse maternal outcomes occurred in four women (1.1%) allocated to immediate delivery, as compared with 11 women (3.1%) allocated to expectant monitoring (RR 0.36, 95% CI 0.12–1.1). This difference cannot be completely denied. A common solution to deal with results from multiple outcomes/dimensions is to use an aggregate health metric such as the quality-adjusted life year (QALY).[12] This was problematic in the current analyses for the following reasons. First, the impact of a composite of adverse maternal outcomes on quality of life is controversial, as raters from different groups or countries may value them differently. Second, we would have had to combine QALYs from mothers and newborns because the nature of the intervention influences both, but there is little evidence on how this can be achieved. Finally, a QALY-based analysis should probably incorporate a long-term (lifetime) perspective. At present, reliable estimates of long-term outcomes – clinical as well as quality of life – are not available for studies evaluating perinatal interventions.[19]

A second limitation concerns the short time horizon. We were unable to estimate the impact of both strategies for a longer time horizon than the duration of the trial. This also precluded the incorporation of indirect costs that may be relevant in the longer term. Despite the short time horizon of the trial, we can speculate on the long-term impact on costs. Because less RDS and neonatal admissions occurred in the expectant monitoring group, resource use and costs are probably lower in the (near) future. In contrast, Mangham et al. analysed costs after a preterm birth surviving up to 18 years of age. They found that the largest contribution to the economic implications of preterm birth are hospital inpatient costs directly after birth, which are responsible for 92% of the incremental costs per preterm survivor.[20]

Furthermore, we were unable to perform an economic evaluation from a societal perspective as planned in the protocol. Despite the effort to collect questionnaires about the societal costs, the response rate was too low for meaningful analysis. We attempted to estimate the impact of societal costs in a sensitivity analysis, which should be interpreted with caution. It showed that societal costs were higher in the expectant monitoring group during the episode of the hypertensive disorder. Several assumptions were made that probably resulted in an overestimation of the informal care costs and productivity loss: i.e. that the partners provided informal care during expectant management. Furthermore, the few returned questionnaires were used to estimate follow-up costs. We expected the follow-up costs to be lower in the expectant monitoring group, as fewer children suffered from RDS; however the results from the questionnaires showed that the costs were higher. Because of the low response rate we believe that selection bias may have occurred.

As in every economic evaluation, the analyses are based on cost estimates that may vary; however, the estimates we used were retrieved from frequently used sources in the Netherlands. In addition, we performed extensive sensitivity analyses in which we vary cost estimates to investigate their impact on the results. Our conclusions did not change.

Interpretation

To our knowledge this is the first economic evaluation that prospectively compared immediate delivery with expectant monitoring in women with hypertensive disorders between $34^{0/7}$ and $37^{0/7}$ weeks of gestation. A similar economic evaluation has been performed in women with hypertensive disorders at term (HYPITAT-I).[10] In contrast with the HYPITAT-II trial, immediate delivery was found to be the best strategy in the HYPITAT-I trial, as it resulted in lower antenatal costs and fewer adverse maternal outcomes, compared with expectant management. Adverse neonatal outcomes and postpartum costs were comparable between both strategies. Caesarean section rates were not influenced by either strategy in both studies. Results of the HYPITAT-I and HYPITAT-II studies, including the costs, suggest that the preferable strategy changes between 34 and 41 weeks of gestation, probably around 37 weeks of gestation. Secondary conditions, like the severity of the hypertensive disorder, and/or the presence of proteinuria, may influence the clinician's decision.

Conclusion

According to the clinical results of the HYPITAT-II study, expectant monitoring until the clinical situation deteriorates

seems preferable over routine delivery of all women with hypertensive disorders of pregnancy between $34^{0/7}$ and $37^{0/7}$ weeks of gestation. The results as described in this economic evaluation indicate that this strategy is also associated with lower average costs per woman.

Disclosure of interests

None declared. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship

BWJM, JL, and MTMF designed the trial. BWJM, JL KB, and GJB coordinated the trial. GJB, KB, MGP, WG, JMS, MDW, MAO, KWMB, HCJS, HAB, RJPR, AJL, DAMP, JMJS, DNMP, MEH, CBV, JTJB, MK, AHK, HG, MP, PPB, BWJM, MTMF, and JL participated in the collection of the data. GJB analysed the data and wrote the first draft of the article. GJB, KB, MGP, WG, JMS, MDW, MAO, KWMB, HCJS, HAB, RJPR, AJL, DAMP, JMJS, DNMP, MEH, CBV, JTJB, MK, AHK, HG, MP, PPB, BWJM, MTMF, and JL critically revised the first draft and approved the final version of the article.

Details of ethics approval

The study protocol was approved by the institutional review board of the Academic Medical Centre in Amsterdam (08/244), and was also approved by the boards of directors of all participating centres. The trial was registered in the Netherlands Trial Register (NTR1792).

Funding

Funded by the Dutch government, ZonMw (grant 171102012).

Acknowledgements

The authors would like to thank all of the women who participated in the trial. We would like to thank all members of the Dutch Obstetric Consortium (www.studies-obsgyn.nl).

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Cost-acceptability curve: probability of immediate delivery to be cost-effective compared with expectant management in preventing neonatal respiratory distress syndrome.

Table S1. Comparison of resource uses and costs between immediate delivery and expectant monitoring.

Table S2. Comparison of resource uses and costs between immediate delivery and expectant monitoring, including non-medical and follow-up costs. ■

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