## **Original Article**

OPEN

# The Cost Implications of Less Tight Versus Tight Control of Hypertension in Pregnancy (CHIPS Trial)

Rashid J. Ahmed, Amiram Gafni, Eileen K. Hutton, Zheng Jing Hu, Eleanor Pullenayegum Peter von Dadelszen, Evelyne Rey, Susan Ross, Elizabeth Asztalos, Kellie E. Murphy, Jennifer Menzies, J. Johanna Sanchez, Wessel Ganzevoort, Michael Helewa, Shoo K. Lee, Terry Lee, Alexander G. Logan, Jean-Marie Moutquin, Joel Singer, Jim G. Thornton, Ross Welch, Laura A. Magee, for the CHIPS Trial Collaborative Group\*

Abstract—The CHIPS randomized controlled trial (Control of Hypertension in Pregnancy Study) found no difference in the primary perinatal or secondary maternal outcomes between planned "less tight" (target diastolic 100 mm Hg) and "tight" (target diastolic 85 mm Hg) blood pressure management strategies among women with chronic or gestational hypertension. This study examined which of these management strategies is more or less costly from a third-party payer perspective. A total of 981 women with singleton pregnancies and nonsevere, nonproteinuric chronic or gestational hypertension were randomized at 14 to 33 weeks to less tight or tight control. Resources used were collected from 94 centers in 15 countries and costed as if the trial took place in each of 3 Canadian provinces as a cost-sensitivity analysis. Eleven hospital ward and 24 health service costs were obtained from a similar trial and provincial government health insurance schedules of medical benefits. The mean total cost per woman—infant dyad was higher in less tight versus tight control, but the difference in mean total cost (DM) was not statistically significant in any province: Ontario (\$30191.62 versus \$24469.06; DM \$5723, 95% confidence interval, —\$296 to \$12272; P=0.0725); British Columbia (\$30593.69 versus \$24776.51; DM \$5817; 95% confidence interval, —\$385 to \$12349; P=0.0725); or Alberta (\$31510.72 versus \$25510.49; DM \$6000.23; 95% confidence interval, —\$154 to \$12781; P=0.0637). Tight control may benefit women without increasing risk to neonates (as shown in the main CHIPS trial), without additional (and possibly lower) cost to the healthcare system.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01192412.

(Hypertension. 2016;68:00-00. DOI: 10.1161/HYPERTEN\$IONAHA.116.07466.) ● Online Data Supplement

Key Words: blood pressure ■ cost analysis ■ health policy ■ hypertension ■ pregnancy ■ randomized controlled trials

Hypertension in pregnancy is common, occurring in ≤10% of all pregnancies with ≤20% of those women having preeclampsia. Treatment approaches of "less tight" and "tight" control of chronic or gestational hypertension can be found in international guidelines for management of hypertension in pregnancy.¹

To understand the effects of these contrasting approaches, we undertook an open, multicenter international randomized controlled trial. The study is described elsewhere, but briefly, 987 consenting women were enrolled between March 26, 2009 and August 2, 2012 at centers confirmed to have capacity to provide the necessary maternal and neonatal care. Eligible women

Received March 20, 2016; first decision April 19, 2016; revision accepted July 25, 2016.

From the Department of Obstetrics and Gynecology (R.J.A., E.K.H.), Department of Clinical Epidemiology and Biostatistics, Centre for Health Economics and Policy Analysis (A.G.), and Department of Mathematics and Statistics (Z.J.H.), McMaster University, Hamilton, Ontario, Canada; Biostatistics Division, Dalla Lana School of Public Health, University of Toronto, Hospital for Sick Children, Ontario, Canada (E.P.); Department of Obstetrics and Gynaecology, St. George's University of London, United Kingdom (P.v.D.); Departments of Medicine (E.R.) and Obstetrics and Gynaecology (E.R.), University of Montreal, Quebec, Canada; Department of Obstetrics and Gynaecology, University of Alberta, Edmonton, Canada (S.R.); Departments of Paediatrics (E.A.) and Obstetrics and Gynecology (E.A.), University of Toronto, Sunnybrook Health Sciences Centre, Ontario, Canada; Departments of Obstetrics and Gynaecology (K.E.M.) and Medicine (K.E.M., A.G.L.), University of Toronto, Mount Sinai Hospital, Ontario, Canada; Department of Obstetrics and Gynaecology (J.M.), Centre for Health Evaluation and Outcome Sciences, Providence Health Care Research Institute (T.L.), and School of Population and Public Health (J.S.), University of British Columbia, Vancouver, Canada; Clinical Trial Services, The Centre for Mother, Infant and Child Research, Sunnybrook Research Institute, Toronto, Ontario, Canada (J.J.S.); Department of Obstetrics and Gynecology, Academic Medical Centre, Amsterdam, The Netherlands (W.G.); Department of Obstetrics, Gynecology, and Reproductive Sciences, Women's Health, University of Manitoba, Winnipeg, Canada (M.H.); Division of Neonatology, Department of Paediatrics, University of Toronto, The Hospital for Sick Children, Ontario, Canada (S.K.L.); Department of Obstetrics and Gynaecology, University of Nottingham, Nottingham City Hospital, United Kingdom (J.G.T.); Department of Obstetrics and Gynaecology, Derriford Hospital, Plymouth, United Kingdom (R.W.); and St. George's, University of London, United Kingdom (L.A.M.).

\*A list of all Members of the CHIPS Trial Collaborative Group is given in the online-only Data Supplement.

The online-only Data Supplement is available with this article at http://hyper.ahajournals.org/lookup/suppl/doi:10.1161/HYPERTENSIONAHA. 116.07466/-/DC1.

Correspondence to Eileen K. Hutton, Department of Obstetrics and Gynecology, McMaster University, 1280 Main St. W, Room MDCL 2210, Hamilton, Ontario, Canada L8S 4K1. E-mail huttone@mcmaster.ca

© 2016 The Authors. *Hypertension* is published on behalf of the American Heart Association, Inc., by Wolters Kluwer. This is an open access article under the terms of the Creative Commons Attribution Non-Commercial-NoDervis License, which permits use, distribution, and reproduction in any medium, provided that the original work is properly cited, the use is noncommercial, and no modifications or adaptations are made.

Hypertension is available at http://hyper.ahajournals.org

were between 14 weeks 0 days and 33 weeks 6 days of gestation and had a live fetus, nonproteinuric chronic or gestational hypertension, an office diastolic blood pressure (BP) of 90 to 105 mm Hg (or 85-105 mm Hg if antihypertensive medication was being taken), and had no exclusion criteria, including a systolic BP of ≥160 mm Hg systolic or proteinuria. Women were randomized to less tight BP control (target diastolic BP of 100 mm Hg) or tight control (target diastolic BP of 85 mm Hg) until delivery, with labetalol as the drug of first choice. The primary composite outcome (pregnancy loss or high-level neonatal care for more than 48 hours) was similar between groups (adjusted odds ratio [aOR], 1.02; 95% confidence interval [CI], 0.77-1.35). The secondary outcome of serious maternal complications ≤6 weeks postpartum or until hospital discharge was not significantly different (aOR, 1.74; 95% CI, 0.79–3.84). At the prespecified 99.9% significance level for the secondary analysis of maternal outcomes adjusted for stratification factors, 40.6% of women in the less tight group experienced postrandomization severe hypertension compared with 27.5% in the tight control group (aOR, 1.80; 95% CI, 1.34–2.38). At the 95%, but not at the prespecified 99.9%, significance level, 4.3% of less tight compared with 1.6% of tight women had thrombocytopenia (platelet count <100×10°; aOR, 2.63; 95% CI, 1.15-6.05), and 4.3% compared with 1.8%, respectively, had elevated aspartate aminotransferase or alanine aminotransferase levels with symptoms (aOR, 2.33; 95% CI, 1.05–5.16), indicating a positive impact for women in the tight control group. The current analysis was planned to determine the cost to the healthcare system related to less tight compared with tight BP control of pregnancy hypertension to inform resource allocation decisions and policy.

#### Methods

Ethics approval for the trial and cost analysis was obtained from the trial coordinating center (University of British Columbia Clinical Research Ethics Board, H08-00882) and at each recruiting center. Informed consent was obtained from each woman before enrollment. The cost analysis was undertaken from the perspective of a thirdparty payer (eg, Ministry of Health) as if all the study participants had received care in each of 3 Canadian provinces (ie, Ontario, British Columbia, and Alberta) to provide a sensitivity analysis of different price structures on the robustness of cost outcomes and to enhance generalizability. The study included 3 provinces that represented 63% (21.84 million people) of Canada's population<sup>3</sup> and 62.3% of total public sector health expenditure in Canada in 2013,4 and share similar provincial government-funded healthcare systems, including funding structures for nurses and hospitals and fee-for-service or salaries for physicians. Outcomes included the difference in mean cost between tight and less tight groups of: the total cost of 24 services in each province, total cost of 11 hospital ward durations, and overall total cost of all services and ward durations in each province. All costs are presented in 2013 Canadian dollars, the year that the last recruits delivered and study data collection ended.

#### Resource Use

Using case report forms for mothers and babies, information was collected on healthcare utilization from randomization until maternal primary hospital discharge after birth and infant primary hospital discharge home. Table 1 lists the 24 services and 11 hospital ward stays that were considered to assess cost.

The total maternal hospital length of stay was available, but not by hospital ward type, which varies substantially in cost; therefore, the operating room duration and labor and delivery ward duration before and after the actual birth time were estimated for each woman using the mean ward duration by parity and delivery mode observed from a trial of women who had an external cephalic version for breech presentation.5 Women who received magnesium sulfate before or during delivery had their postnatal labor and delivery ward duration estimate increased to 24 hours after delivery for monitoring purposes according to Canadian guidelines. All women were assumed to have had a labor and delivery room duration, including those who went in to the operating room during which time their bed was held. Time in hospital after hospital admission (but before estimated labor and delivery ward admission) was ascribed to the antenatal ward, and time after estimated labor and delivery discharge to actual hospital discharge was ascribed to the postnatal ward, totaling the actual maternal hospital length of stay.

Infants admitted to high-level neonatal care did not have their actual level of care indicated, given the variability in definition of intermediate and intensive care across hospitals. For costing purposes, cases of high-level neonatal care were categorized masked to treatment allocation into level 3 or level 2 neonatal ward care. Level 3 neonatal intensive care was attributed to babies with characteristics consistent with provincial admission guidelines and billing definitions, as follows: birth at <32 weeks, birth weight <1500 g, receipt of any positive pressure ventilation (continuous positive airway pressure or endotracheal intubation), or any of ten serious neonatal morbidities (ie, patent ductus arteriosus, early-onset sepsis within the first 48 hours of life, bronchopulmonary dysplasia, retinopathy of prematurity stage >2, intraventricular hemorrhage, cystic periventricular leukomalacia, hypoxic-ischemic encephalopathy, necrotizing enterocolitis, laparotomy, or thoracotomy). All other high-level neonatal care was regarded as level 2 intermediate care. Any neonatal hospital transfer was assumed to be for the purposes of the other type of care (ie, level 3 transfer to level 2 and level 2 transfer to level 3).

#### **Unit Costs for Physician Services and Wards**

Physician services were costed using the provincial government health insurance plan schedule of medical benefits applicable to 2013 for Ontario, British Columbia, and Alberta.<sup>6-8</sup> Healthcare billing experts and clinicians in each province assisted with the identification and interpretation of appropriate billing codes. All services involved a flat fee or a time-dependent fee component, usually to a maximum amount, and a time of day and day of week premium (ie, for evening, night, and weekend calls). Accordingly, the fees for some services varied for each woman in the trial and were applied individually at the record level. An average unit cost per patient was calculated to generally illustrate the unit costs applied in each province (Table S1). Hospital ward durations were costed using unit costs by ward type and delivery mode determined for an economic analysis for a similar perinatal study in 2002, the TBT (Term Breech Trial),9 that were updated to 2013 using the Canadian Consumer Price Index healthcare commodity group of 20.5%. 10 Ward unit costs were not province specific, but were derived in the TBT from reports from 4 teaching hospitals and 3 community hospitals in each of the included provinces (ie, Ontario, British Columbia, and Alberta) combined into 1 median unit cost per ward type per hour (Table S2). Further definitions and assumptions for physician services and ward durations are included in Table S3. Table S4 summarizes the methods used to derive hospital ward unit costs and their application in this study.

#### **Data Analysis**

Costing involved multiplying the actual amount of resources consumed by each participant as collected in the trial by their respective unit costs to determine the total cost of each of 24 services and each of 11 ward stays. The total cost of all 24 services, the total cost of all 11 wards, and the overall total cost of all services and wards were calculated using each province's unit costs for less tight and tight BP management groups. All results were analyzed according to the intention-to-treat approach that included 493 women in the less tight group and 488 women in the tight group, and excluded 6 women who withdrew or were lost to follow-up in CHIPS (Control of Hypertension in Pregnancy Study). The total per-participant costs for mothers and infants in each arm of the trial were not assumed

Table 1. Healthcare Resources Consumed by Study Groups in Trial

	Less Tight	Group	Tight Group		
Healthcare Resource Consumed (24 Services and 11 Hospital Ward Lengths of Stay)	n Resources	n Women/Infants	n Resources	n Women/Infants	
Outpatient assessments/visits					
1. Antenatal visit—Physician service	3683	483	3787	473	
2. Antepartum home care visit—Nursing service	545	108	529	105	
3. Obstetric day unit visit—Physician service	653	181	636	181	
4. Obstetric day unit visit—Ward care	653 visits (7836 h)	181	636 visits (7632 h)	181	
5. Emergency room visit—Physician service	403	199	387	177	
6. Emergency room visit—Ward care	403 (2015 h)	199	387 (1935 h)	177	
Antenatal hospitalizations not for delivery					
<ol><li>Antenatal hospital admission not for delivery, and daily care—Physician service</li></ol>	163	131	145	121	
8. Antenatal hospital admission not for delivery, length of stay—Ward care	450 days (10 800 h)	131	460 days (11 040 h)	121	
Diagnostic tests		'			
9. Maternal blood and urine tests—Physician laboratory service	2433	459	2306	450	
10. Nonstress tests—Physician service	1878	359	2137	355	
11. Fetal ultrasounds—Physician service	1653	458	1631	454	
12. Infant chest x-rays—Physician service	277	74	163art	54	
13. Infant head ultrasound—Physician service	166	68	Association a	62	
14. Infant head CT scan—Physician service	2	1	3	3	
15. Infant MRI—Physician service	5	4	3	3	
16. Ophthalmology examination for ROP—Physician service	97	66	84	59	
Hospital length of stay for delivery					
17. Antenatal ward	30584.76 h	480	29573.31 h	474	
18. Labor and delivery ward	6559.24 h	493	6171.56 h	488	
19. Operating room	335.86 h	258	375.38 h	290	
20. Postnatal ward	39 263.77 h	493	37 061.70 h	488	
Delivery		I			
21. Caesarean section delivery before labor—Physician service (obstetrician, assistant, and anesthetist)	159	159	163	163	
22. Caesarean section delivery during labor (CS and spontaneous or induced)—Physician service (obstetrician, assistant, and anesthetist)	72	72	87	87	
23. Spontaneous vaginal delivery—Physician service	234	234	196	196	
24. Operative vaginal delivery—Physician service	27	27	40	40	
25. Elective termination—Physician service	1	1	1	1	
26. Miscarriage—Physician service	0	0	1	1	
27. Induction—Physician service	224	224	218	218	
Neonatal care		ı			
28. NICU level 2 at delivery hospital—Physician service	765 d	84	664 d	83	
29. NICU level 3 at delivery hospital—Physician service	2531 d	72	1680 d	68	
30. NICU level 2 at transfer hospital—Physician service	580 d	19	424 d	15	
31. NICU level 3 at transfer hospital—Physician service	134 d	6	77 d	8	
Aggregated: NICU level 2 and level 3 at both delivery and transfer hospital—	96 240 h (4010 d)	156	68 280 h (2845 d)	151	
Physician service (Total high-level neonatal physician service)	55 <u>2</u> . 5 . 1 (1515 u)		22 23 11 (20 40 4)	.51	

(Continued)

Table 1. Continued

	Less Tight	Group	Tight Group		
Healthcare Resource Consumed (24 Services and 11 Hospital Ward Lengths of Stay)	n Resources	n Women/Infants	n Resources	n Women/Infants	
32. NICU level 2—Delivery hospital—ward care	724.28 d	84	626.09 d	83	
33. NICU level 3—Delivery hospital—ward care	2495.32 d	72	1651.02 d	68	
34. NICU level 2—Transfer hospital—ward care	570.44 d	19	414.39 d	15	
35. NICU level 3—Transfer hospital—ward care	131.29 d	6	72.46 d	8	
Aggregated: NICU level 2 and level 3 at both delivery and transfer hospital (Total high-level neonatal ward care)	94112.04 h (3921.34 d)	156	66 334.68 h (2763.95 d)	151	

CS indicates Caesarean section; CT, computed tomography; MRI, magnetic resonance imaging; NICU, neonatal intensive care unit; and ROP, retinopathy of prematurity.

to be normally distributed. As such, the standard errors (SEs) of the difference in the means between groups and 95% CIs of the differences in the means were estimated using bootstrap methods and *P* values were estimated using permutation in "R" statistical software version 3.2.2.<sup>11</sup> For each province, CIs and *P* values were estimated for all services, all wards, and for all services and all wards together. To demonstrate which specific services or wards were cost-drivers between less tight and tight control, we determined the absolute difference in mean cost between study groups for each service and ward, ranked the cost differences in descending order of magnitude, and for the top 5 cost-drivers where parameters were similarly estimated, we tested their significance assuming no distribution and using permutation, and found their 95% CIs using boot-strapping.

#### Results

Primary/transfer hospital ward durations were costed to a maximum of 305 days after which no women or babies remained in hospital. Women and infants in the less tight group relative to the tight group consumed less of 7 services and spent less time on 2 wards (antenatal physician visits, nonstress tests, antenatal hospitalization not for delivery ward time, Caesarean section delivery before labor, Caesarean section delivery during labor, operative vaginal deliveries, miscarriages, operating room time, and infant head CT scans), but consumed more of 16 services and spent more time on 9 wards (antepartum home care visits with a nurse, obstetric day unit visits and ward time, emergency room visits and ward time, antenatal hospital admissions not for delivery, maternal blood and urine tests, fetal ultrasounds, infant chest x-rays, infant head ultrasounds

and MRIs, ophthalmology exams for retinopathy of prematurity, longer lengths of stay in the antenatal ward, labor and delivery ward, postnatal ward, more spontaneous vaginal deliveries, inductions for labor, and more physician care and longer length of stay in level 2 and level 3 neonatal care at delivery and transfer hospitals). Both groups had the same number of elective terminations (Table 1). Although the less tight (compared with the tight) group had a similar number of overall admissions to high-level neonatal care level 2 or 3 (156 versus 151 neonates), the total length of stay of less tight group neonates was substantially longer (total of 3921.34 days versus 2763.96 days, or 41.8% more days), especially in level 3 neonatal intensive care at delivery hospitals, an important difference with associated clinical implications, regardless of cost.

The mean cost in each group represents the total cost incurred for each service or ward consumed by women in that group divided by the total number of women (493 or 488) in the study group, whether or not they incurred the service or ward (Table S5). Overall, there was no significant difference in the mean cost of all services and wards between less tight and tight control groups in each province (Table 2), with similar direction and magnitude of effect. Women in the less tight control group incurred costs that were close to \$6000 dollars more than women in the tight control, but the difference was not statistically significant.

Table S6 shows the top 5 items with the greatest difference in mean cost between the study groups. All were related to

Table 2. Analysis of Difference in Mean Costs of All Services and Wards, All Services, and All Wards by Study Group

		Less Tight Group n=493 Women/Infants		Tight Group n=488 Women/Infants		Difference Between Less			
Service and Ward Cost	Province	Mean	SE (Mean)	Mean	SE (Mean)	Tight and Tight Mean Costs*	95% Confidence Interval	SE (Difference in Means)	<i>P</i> Value
Total cost of	Ontario	\$30 191.62	\$2703.18	\$24 469.06	\$1646.23	\$5723	-\$296, \$12272	\$3184.89	0.0725
all services and wards	B.C.	\$30 593.69	\$2756.47	\$24776.51	\$1668.60	\$5817	-\$385, \$12349	\$3227.88	0.0725
and wards	Alberta	\$31 510.72	\$2821.73	\$25 510.49	\$1705.26	\$6000	-\$154, \$12781	\$3308.47	0.0637
Total cost of	Ontario	\$3323.27	\$137.19	\$3060.41	\$105.75	\$263	-\$62, \$606	\$170.74	0.1351
all services	B.C.	\$3725.34	\$187.12	\$3367.85	\$128.02	\$357	-\$80, \$826	\$230.30	0.1197
	Alberta	\$4642.37	\$255.44	\$4101.83	\$168.68	\$541	-\$42, \$1170	\$305.50	0.0784
Total cost of all wards	All Provinces	\$26 868.35	\$2573.40	\$21 408.65	\$1546.70	\$5460	<b>-</b> \$202, \$11 560	\$3015.76	0.0694

SE indicates standard error. \*Positive value favors less costly tight group.

neonatal intensive care. The top 4 cost-drivers were neonatal care ward costs at the delivering and transfer hospitals. In the less tight group, high-level neonatal intensive care ward costs represented the majority of overall costs: at 56.8% of overall cost per woman/infant dyad in Ontario, 56.1% in British Columbia, and 54.5% in Alberta. There was no statistically significant difference between the study groups in any of the top 5 cost drivers.

#### Discussion

#### **Main Findings**

There has been much debate about the best approach to the management of hypertension.<sup>2</sup> The CHIPS trial showed that tight BP control is not harmful to the baby, and consistent with literature from other clinical trials, was beneficial to the mother by decreasing the development of severe hypertension.<sup>12</sup> To our knowledge, the analysis reported here is the first to compare the cost implications of less tight versus tight BP control strategies for pregnancy hypertension. The study found that the mean cost per woman–infant dyad managed by a policy of less tight (versus tight) BP control is not significantly different with regard to overall services and hospital ward costs incurred from as early as from 14 weeks of gestation up to 305 days after delivery (ie, last neonatal primary hospital discharge date recorded), using costs obtained from Ontario, British Columbia, or Alberta, Canada.

Although costs in each province were almost \$6000 higher for the less tight group in which infants spent more time in high-level neonatal intensive care wards, the result did not reach statistical significance and may reflect a lack of statistical power.<sup>13,14</sup>

The upper and lower limits of the 95% CI can be examined to determine whether they would exclude a minimally important (cost) difference (MID), like that used for noninferiority trials. 15,16 If the MID is either outside or included within both CI boundaries, then neither treatment strategy is significantly different in cost and the decision threshold to change policy is not reached. However, if an MID is included on one side of the 95% CI boundaries but not on the other, the decision threshold is reached for that treatment if adopted, and would be associated with cost savings per patient to at least the level of the MID: similar savings would not be experienced if the alternate treatment approach was adopted. In our study, a decision maker might determine, for example, that a difference in mean cost per patient of ±\$500 is an MID threshold above which a less tight or tight policy would be attractive to implement. Using outcomes for British Columbia in our study, the total mean cost per patient was \$30593.69 for less tight and \$24776.51 for tight groups, with a difference in mean costs of \$5817, and CI of -\$385 cost savings up to a \$12349 cost increase, for a less tight patient (Table 2). In this example, with an MID of \$500, we could exclude a cost savings with a policy of less tight control. Tight control may be substantially cheaper with a marked reduction in neonatal intensive care unit days.

#### Study Strengths and Limitations

The data come from CHIPS, a large, international, multicenter randomized trial. Resource utilization was measured prospectively and the economic analysis planned, all contributing to minimization of bias in cost assessment between groups. The analysis used mean costs from 3 Canadian provinces with different fee structures related to provincial schedules of medical benefits, especially flat rate fees, premiums for start time of day and day of week, and timedependent fees. The direction and magnitude in the difference in mean cost of overall services and wards in each of the 3 provinces were similar, all favoring tight control as less expensive. The purpose of conducting the analysis in each province was to demonstrate the independence of findings from the effect of jurisdiction and price structures, similar to a sensitivity analysis. Any specific cost differences between provinces are ultimately less important than the fact that the interventions were costed in 3 different healthcare jurisdictions with different funding and price structures, yet produced a similar magnitude and direction in results, which supports the validity of the findings. There were no major differences between provinces, which supports the generalizability in this context.

Our study is limited by the application of 2002 TBT ward unit costs scaled for health commodity inflation in Canada to 2013 trial data: true ward unit costs incurred by hospitals in each province in 2013 may be different. The TBT combined ward type unit cost data for each province, so we could not report province-specific total ward costs. TBT ward unit costs were derived for women with breech pregnancies, their infants and costs of related complications, which may underestimate these costs for hypertensive pregnancies. However, hypertension-specific care was accounted for, such as more time allocated on the labor and delivery ward to women on magnesium sulfate to capture the enhanced nursing care required. CHIPS women may have had different mean lengths of stay on the labor and delivery ward and in the operating room for Caesareans than those in the EECV2 (Early External Cephalic Version 2) trial from which costs were estimated, although these durations are not likely to be substantially different in the overall findings, and total hospital length of stay in CHIPS was preserved. Whereas CHIPS women may have received more interventions than EECV2 women, this approach is conservative and has been applied equally to both the study groups. The neonatal intensive care level 3 ward unit cost of \$107.00/h from the TBT may be higher for CHIPS neonates who may require a higher intensity of hospital care, related to nursing staff time, hospital service consumables used, and associated ward costs. The time spent in any high-level care was preserved, but we were unable to standardize a definition of levels 2 and 3 neonatal care across jurisdictions: categorization of high-level neonatal care into levels 2 and 3 care cases was performed according to an algorithm that may not have reflected the true level, intensity and cost of care received. Although every attempt was made to ensure the correct billing codes in each province were applied to the physician service resources consumed in CHIPS, actual billing practice of individual physicians vary by individual practice (such as the use of after-hours codes), time of day, and day of week that care was provided. The trial collected data from 94 centers in 15 countries, with centers selected

to have similar facilities, conditions and medical practices to fulfill the CHIPS Protocol as in Canada. However, the resources consumed in the trial may differ from that which would have been consumed in the actual Canadian context, although any potential differences cannot be easily ascertained. Nonetheless, the application of any estimates was applied to both groups equally. As for all clinical efficacy scenarios, our results apply to the 3 provinces mentioned because we used their unit prices. No subgroup analysis was done with Canadian study participants only.

The CHIPS trial, as with many randomized controlled trials, was powered for the primary study outcome and not the cost analysis, which typically requires larger sample sizes because of large variances and positively skewed distributions of cost, as observed in this analysis. It is possible that a larger sample size may have confirmed the observed trend toward a higher mean cost per woman in the less tight group, driven by the longer infant length of stay in high-level neonatal intensive care units. More than 55% of the cost of care was attributed to neonatal costs, which was the top cost-driver in each of the 3 provinces, raising the possibility that differences seen in the primary study may be real.

#### **Perspectives**

The mean cost for women/infants under a less tight treatment approach to pregnancy hypertension is not different to those under a tight control approach. However, based on our findings, there is little chance that less tight control is cheaper; and in the main CHIPS Study, less tight control was implicated in significantly more morbidity among women. Thus, a treatment approach of tight control of pregnancy hypertension may have clinical benefit for women, with no increased risk to neonates and without additional (and possibly lower) cost to the healthcare system.

#### Acknowledgments

This article is dedicated to the memory of our dear friend and colleague, Dr Andrée Gruslin. We thank all of the women who participated in the CHIPS trial (Control of Hypertension in Pregnancy Study), and members of the CHIPS Collaborative Group (online-only Data Supplement).

#### **Sources of Funding**

This economic research and corresponding randomized controlled trial (the CHIPS trial [Control of Hypertension in Pregnancy Study]) was supported by a grant (MCT 87522) from the Canadian Institutes of Health Research (CIHR) and is registered with Current Controlled Trials (ISRCTN71416914) and ClinicalTrials.gov (NCT01192412). CIHR had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

#### **Disclosures**

All authors have completed a Conflict of Interest Disclosure Questionnaire and declare that (1) none of the authors have received support from any company for the submitted work; (2) none of the authors have relationships with a company that might have an interest in the submitted work in the previous 3 years; (3) P. von Dadelszen received consulting fees and in-kind research support from Alere International related to preeclampsia and fetal growth restriction through the provision of Triage PIGF cartridges; and no

other authors have nonfinancial interests that may be relevant to the submitted work. No author had any financial or personal relationships with other people or organizations that could inappropriately influence (bias) their work on this project. P. von Dadelszen reports personal fees and other from Alere International, outside the submitted work. J. Menzies reports grants, personal fees and nonfinancial support from Canadian Institutes of Health Research (CIHR, a Canadian federal government granting agency), during the conduct of the study. M. Helewa reports grants from CIHR-Factors associated with inadequate prenatal care, grants from CIHR-Reducing inequities in access to and use of prenatal care in the Winnipeg Health Region through Health System improvement, grants from CIHR-Quality of prenatal care questionnaire development, grants from CIHR-Effect of Folic Acid supplementation in pregnancy on preeclampsia Folic Acid Clinical Trial (FACT), outside the submitted work. L.A. Magee reports grants from CIHR, during the conduct of the study; personal fees from Bill & Melinda Gates Foundation, outside the submitted work.

#### Statement on Ethics Approval and Informed **Consent From Participants**

Ethics approval for the CHIPS trial (Control of Hypertension in Pregnancy Study) and cost analysis was obtained from the trial coordinating center (University of British Columbia Clinical Research Ethics Board, H08-00882) and at each of the recruiting centers. Informed consent was obtained from each woman participating in the trial before enrollment.

#### References

- 1. Gillon TE, Pels A, von Dadelszen P, MacDonell K, Magee LA. Hypertensive disorders of pregnancy: a systematic review of international clinical practice guidelines. PLoS One. 2014;9:e113715. doi: 10.1371/ journal.pone.0113715.
- 2. Magee LA, von Dadelszen P, Rey E, et al. Less-tight versus tight control of hypertension in pregnancy. N Engl J Med. 2015;372:407–417. doi: 10.1056/NEJMoa1404595.
- Statistics Canada. Population by year, by province and territory, CANSIM, table 051-0001. Ottawa, Canada. 2013. http://www.statcan. gc.ca/tables-tableaux/sum-som/l01/cst01/demo02a-eng.htm. Accessed October 5, 2015.
- 4. Canadian Institute for Health Information (CIHI). National Health Expenditure Trends, 1975 to 2013, Spending and Health Workforce. Ottawa, Canada. 2014. https://secure.cihi.ca/estore/productSeries. htm?pc=PCC52. Accessed October 5, 2015.
- 5. Ahmed RJ, Gafni A, Hutton EK; Early ECV2 Trial Collaborative Group. The Cost Implications in Ontario, Alberta, and British Columbia of Early Versus Delayed External Cephalic Version in the Early External Cephalic Version 2 (EECV2) Trial. J Obstet Gynaecol Can. 2016;38:235-245.e3. doi: 10.1016/j.jogc.2015.12.019.
- 6. Ministry of Health and Long Term Care, Government of Ontario. Schedule of Benefits - Physician Services Under the Health Insurance Act, Revised October 1, 2013. 2013. Toronto, Ontario, Canada.
- 7. Ministry of Health, Government of British Columbia. Medical Services Commission Payment Schedule, Revised November 1, 2013. 2013. Vancouver, British Columbia, Canada.
- 8. Alberta Health, Government of Alberta. Schedule of Medical Benefits, Health Professional Fees, Medical Benefits Price List, Alberta Health Care Insurance Plan, Revised April 1, 2012 (applicable to 2013 services). 2012. Edmonton, Alberta, Canada.
- 9. Palencia R, Gafni A, Hannah ME, et al; Term Breech Trial Collaborative Group. The costs of planned cesarean versus planned vaginal birth in the Term Breech Trial. CMAJ. 2006;174:1109-1113. doi: 10.1503/ cmaj.050796.
- 10. Statistics Canada. CANSIM table 326-0021 Consumer Price Index (CPI), Canada, 2013 basket, annual, Commodities and commodity groups=Health care. http://www5.statcan.gc.ca/cansim/a26?lang=eng& retrLang=eng&id=3260021&paSer=&pattern=&stByVal=1&p1=1&p2 =37&tabMode=dataTable&csid=. Accessed May 15, 2012.
- 11. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria. 2015. http://www.R-project.org/. Accessed September 1, 2015.

- Abalos E, Duley L, Steyn DW. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. *Cochrane Database Syst Rev.* 2014;2:CD002252.
- Briggs A. Economic evaluation and clinical trials: size matters. BMJ. 2000;321:1362–1363.
- Gafni A, Walter SD, Birch S, Sendi P. An opportunity cost approach to sample size calculation in cost-effectiveness analysis. *Health Econ*. 2008;17:99–107. doi: 10.1002/hec.1244.
- Treadwell J, Uhl S, Tipton K, Singh S, Santaguida L, Sun X, Berkman N, Viswanathan M, Coleman C, Shamliyan T, Wang S, Ramakrishnan R, Adam Elshaug A. Assessing Equivalence and Non-InferiorityAssessing Equivalence and Noninferiority Rockville (MD): Agency for Healthcare Research and Quality (US); 2012 Jun. Report No.: 12-EHC045-EF.
- Lesaffre E. Superiority, equivalence, and non-inferiority trials. Bull NYU Hosp Jt Dis. 2008;66:150–154.

#### **Novelty and Significance**

#### What Is New?

This study presents a cost analysis of less tight versus tight blood pressure management strategies for women with chronic or gestational hypertension in a large, multicenter randomized controlled trial.

#### What Is Relevant?

- The CHIPS trial (Control of Hypertension in Pregnancy Study) found no difference in pregnancy loss or high-level neonatal care >48 hours when comparing a less tight (target 100 mm Hg) and tight (target 85 mm Hg) approach to blood pressure management during pregnancy. However, women in the CHIPS study experienced significantly less morbidity with a tight approach.
- No significant difference was found in mean total cost of all services and wards per woman-infant dyad between less tight versus tight strategies.

#### Summary

Tight blood pressure control in pregnancy may benefit women without increasing risk to neonates (as shown in the main CHIPS trial), without additional (and possibly lower) cost to the healthcare system.









## The Cost Implications of Less Tight Versus Tight Control of Hypertension in Pregnancy (CHIPS Trial)

Rashid J. Ahmed, Amiram Gafni, Eileen K. Hutton, Zheng Jing Hu, Eleanor Pullenayegum, Peter von Dadelszen, Evelyne Rey, Susan Ross, Elizabeth Asztalos, Kellie E. Murphy, Jennifer Menzies, J. Johanna Sanchez, Wessel Ganzevoort, Michael Helewa, Shoo K. Lee, Terry Lee, Alexander G. Logan, Jean-Marie Moutquin, Joel Singer, Jim G. Thornton, Ross Welch, Laura A. Magee and for the CHIPS Trial Collaborative Group

Hypertension. published online August 22, 2016;
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2016 American Heart Association, Inc. All rights reserved.

Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://hyper.ahajournals.org/content/early/2016/08/22/HYPERTENSIONAHA.116.07466 Free via Open Access

Data Supplement (unedited) at:

http://hyper.ahajournals.org/content/suppl/2016/08/22/HYPERTENSIONAHA.116.07466.DC1.html

**Permissions:** Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Hypertension* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

**Reprints:** Information about reprints can be found online at: http://www.lww.com/reprints

**Subscriptions:** Information about subscribing to *Hypertension* is online at: http://hyper.ahajournals.org//subscriptions/

## THE COST IMPLICATIONS OF 'LESS TIGHT' VERSUS 'TIGHT' CONTROL OF HYPERTENSION IN PREGNANCY (CHIPS TRIAL)

Rashid J Ahmed, Amiram Gafni, Eileen K Hutton, Zheng Jing Hu, Eleanor Pullenayegum, Peter von Dadelszen, Evelyne Rey, Susan Ross, Elizabeth Asztalos, Kellie E Murphy, Jennifer Menzies, J. Johanna Sanchez, Wessel Ganzevoort, Michael Helewa, Shoo K Lee, Terry Lee, Alexander G Logan, Jean-Marie Moutquin, Joel Singer, Jim G Thornton, Ross Welch, Laura A Magee, for the CHIPS Trial Collaborative Group.

#### **Online Supplements**

This appendix has been provided by the authors to give readers additional information about their work.

- CHIPS Collaborative Group
- S1. Average or general unit cost of 24 services per woman/infant by province and study group
- S2. Unit cost per hour for 11 hospital wards
- S3. Definitions and Assumptions for Physician Services and Ward Durations
- S4. Methods used to derive hospital ward unit costs in the Term Breech Trial and their application in the CHIPS trial
- S5. Mean costs of healthcare resources by province and study group
- S6. Analysis of top five cost drivers

#### **CHIPS Collaborative Group**

Steering Committee: Laura A. Magee (Chair), Elizabeth Asztalos, Amiram Gafni, Andrée Gruslin, Michael Helewa, Eileen Hutton, Shoo Lee, Alexander Logan, Jennifer Menzies, Jean-Marie Moutquin, Kellie Murphy, Evelyne Rey, Sue Ross, Johanna Sanchez, Joel Singer, Peter von Dadelszen, Evelyne Rey, Susan Ross, Elizabeth Asztalos, Kellie E. Murphy, Jennifer Menzies, Johanna Sanchez, Andrée Gruslin, Wessel Ganzevoort, Michael Helewa, Shoo K. Lee, Terry Lee, Alexander G. Logan, Jean Marie Moutquin, Joel Singer, Jim G. Thornton, Ross Welch.

**Working Group:** Laura A. Magee (Chair), Elizabeth Asztalos, Peter von Dadelszen, Trinh Hoac, Joanne Kirton, Jennifer Menzies, Sue Ross, Johanna Sanchez, Katherine Trigiani, Ainy Zahid.

**Adjudication Committee:** Laura A. Magee (Chair), Elizabeth Asztalos, Kellie Murphy, Evelyne Rey, Peter von Dadelszen

**Data Safety Monitoring Board:** Michael B. Bracken (Chair), Patricia Crowley, Lelia Duley, Richard Ehrenkranz, Kevin Thorpe

Data Programmers and Analysts: Sunny Chan, Michael Shi, Shelley Yu

**Collaborators:** The number of women recruited in each country and center is specified in brackets.

#### ARGENTINA (36):

Hospital LC Lagomaggiore, Mendoza (16): Raquel de Lourdes Martin, Maria Florencia Bassi, Mirta Clara Caruso, Valeria Lagunas, Fernando Vera

Hospital Avellaneda, Tucuman (10): Maria Mohedano de Duhalde, Alicia Beatriz Roque, Patricia Roldan, Esteban Marcos Duhalde, Viviana Dip

Hospital JR Vidal, Corrientes (8): Jesus Daniel Aguirre, Elba Mirta Alicia Morales, Griselda Itati Abreo, Teresa De Sagastizabal, Carolina Gomez, Nadia Rizzi

Hospital JM Cullen, Santa Fe (2): Carlos Arias, Ricardo Antonio Bruno AUSTRALIA (85):

Ipswich Hospital, Ipswich (36): Kassam Mahomed, Alison Drew, Ann Green, Jane Hoare Women's and Children's Hospital, Adelaide (18): Bill Hague, Suzette Coat, Caroline Crowther, Peter Muller, Sophie Trenowden

King Edward Memorial Hospital, Subiaco (17): Barry Walters, Claire Parker, Dorothy Graham, Craig Pennell, Eileen Sung

Campbelltown Hospital, Penrith South (8): Angela Makris, Gaksoo Lee, Charlene Thornton, Annemarie Hennessy

Liverpool Hospital, Penrith South (5): Angela Makris, Gaksoo Lee, Charlene Thornton, Annemarie Hennessy

St John of God Hospital, Subiaco (1): Louise Farrell, Claire Parker, Eileen Sung, Barry Walters BRAZIL (19):

Maternidade de Vila Nova Cachoeirinha, Sao Paulo (7): Nelson Sass, Henri Korkes, Dayana Couto Ferreira

Hospital Universitario Antonio Pedro, Niteroi (6): Renato Augusto Moreira de Sa, Monique Schmidt Marques Abreu

Maternidade Escola da UFRJ, Rio de Janeiro (4): Rita Guerios Bornia, Nancy Ribeiro da Silva, Fernanda Freitas Oliveira Cardoso

Hospital Sao Lucas - PUCRS, Porto Alegre (2): Caio Coelho Marques, Jorge Hornos, Ricardo Leal Davdt, Letícia Germany Paula, Pedro Luis Zanella CANADA (233):

British Columbia Women's Hospital and Health Centre, Vancouver (32): Laura A. Magee, Peter von Dadelszen, Gabrielle Inglis, Ruth Dillon, Ashley Docherty, Anna Hutfield

Jim Pattison Outpatient Care and Surgery Centre, Surrey (26): Keith Still, Sayrin Lalji, Tamara Van Tent, Chris Hotz, Tracy Messmer

St Michael's Hospital, Toronto (22): Joel G. Ray, Howard Berger, Leanne De Souza, Andrea Lausman, Tatiana Freire-Lizama, Kate Besel

Foothills Medical Centre, Calgary (21): Paul Gibson, Greta Ellsworth, Leslie Miller, T. Lee-Ann Hawkins

Sunnybrook Health Sciences Centre, Toronto (19): Michelle Hladunewich, Anna Rogowsky, Dini Hui, Virginia Collins

IWK Health Centre, Halifax (19): Isabelle Delisle, Cora Fanning

Royal Alexandra Hospital, Edmonton (16): Nestor Demianczuk, Rshmi Khurana, Winnie Sia, Catherine Marnoch, Carmen Young, Cheryl Lux

CHU Sainte-Justine, Montreal (15): Evelyne Rey, Sophie Perreault, Valerie Tremblay

CHUS Fleurimont, Sherbrooke (13): Jean-Marie Moutquin, Sophie Desindes, Anne-Marie Côté, Veronique Dagenais

Ottawa Hospital Civic Division, Ottawa (13): Andrée Gruslin, Heather Clark, Elaine O'Shea, Ruth Rennicks White

Mount Sinai Hospital, Toronto (8): Shital Gandhi, Mary-Jean Martin, Cheryl Brush, Gareth Seaward

Royal University Hospital, Saskatoon (6): Jill Newstead-Angel, Judy Brandt, Jocelyne Martel, Kristine Mytopher, Elise Buschau

Ottawa Hospital General Division, Ottawa (5): Andrée Gruslin, Erin Keely, Patti Waddell, Ruth Rennicks White, Svetlana Shachkina, Alan Karovitch

St Paul's Hospital, Vancouver (5): Robert Anderson, Nicole Koenig, Theresa Yong

Toronto East General Hospital, Toronto (5): Marie Vasiliou, Peri Johnson, Beth Allan

London Health Sciences Centre, London (4): Renato Natale, Laura Kennedy

Royal Victoria Hospital, Montreal (2): Lucie Opatrny, Lorraine Lavigne

Regina General Hospital, Regina (1): George Carson, Sheila Kelly

Women's Health Centre, St John's (1): Joan Crane, Donna Hutchens CHILE (57):

Hospital Dr Sotero del Rio, Puente Alto (45): Juan Pedro Kusanovic, Christian Figueroa, Karla Silva Neculman, Juan Andres Ortiz, Paula Vargas

Hospital Base Osorno, Osorno (12): Pedro Ferrand, Jorge Carrillo

COLOMBIA (36):

Corporacion Comfenalco Valle - Universidad Libre (20), Clinica Versalles (11), Clinica Materno Infantil Farallones (5), Cali: Rodrigo Cifuentes Borrero, Dahiana Marcela Gallo, Luisa Fernanda Moreno

ESTONIA (19):

Tartu University Hospital - Women's Clinic, Tartu (19): Fred Kirss, Kristiina Rull, Anne Kirss HUNGARY (5):

University of Debrecen, Debrecen (5): Tamas Major, Andrea Fodor, Tunde Bartha ISRAEL (12):

Hillel Yaffe Medical Center, Hadera (6): Mordechai Hallak, Nardin Aslih, Saja Anabousi-Murra, Ester Pri-Or

Ma'ayney Hayeshua Medical Center, Bnei Brak (3): Linda Harel, Sima Siev

Nazareth Hospital (EMMS), Nazareth (3): Marwan Hakim, Christina Simona Khoury, Najla Hamati

JORDAN (13):

Islamic Hospital, Amman (13): Mazen El-Zibdeh, Lama Yousef

NEW ZEALAND (17):

Christchurch Women's Hospital, Christchurch (16): Ruth Hughes, Di Leishman, Barbra Pullar Waitemata Health-North Shore Hospital, Auckland (1): Matthew Farrant POLAND (21):

Medical University of Gdansk, Gdansk (9): Malgorzata Swiatkowska-Freund, Krzysztof Preis, Anette Aleksandra Traczyk-Los, Anna Partyka, Joanna Preis-Orlikowska, Mariusz Lukaszuk Polish Mothers Memorial Hospital, Lodz (9): Grzegorz Krasomski, Michael Krekora, Anna Kedzierska-Markowicz, Katarzyna Zych-Krekora

University School of Medical Sciences, Poznan (3): Grzegorz H. Breborowicz, Anna Dera-Szymanowska

THE NETHERLANDS (96):

Academic Medical Center, Amsterdam (28): Wessel Ganzevoort, Jannet Bakker, Joost Akkermans, Anouk Pels

OLVG, Amsterdam (13): Eline van den Akker, Sabine Logtenberg

UMCU, Utrecht (10): Steven Koenen, Maartje de Reus, David Borman, Martijn A. Oudijk

VU Medical Center, Amsterdam (9): Annemiek Bolte, Viki Verfaille, Bart Graaf

Maxima Medical Centre, Veldhoven (8): Martina Porath, Corine Verhoeven, Ben Willem Mol UMCG, Groningen (6): Maureen T.M. Franssen, Lida Ulkeman, Ineke Hamming, Jose H.M. Keurentjes, Ina van der Wal

Isala Klinieken Zwolle, Zwolle (5): S.W.A. Nij Bijvank, A.A. Lutjes

Tergooiziekenhuizen, Hilversum (5): Henricus Visser, Jannet Bakker

MUMC Maastricht, Maastricht (4): Hubertina Catharina Johanna Scheepers

St Antonius Ziekenhuis, Nieuwegein (3): Erik van Beek, David Borman, Coby van Dam, Kathy van den Berg-Swart

Kennemer Gasthuis Haarlem, Haarlem (2): Paula Pernet, Birgit van der Goes

Diakonessen Ziekenhuis, Utrecht (1): Nico Schuitemaker

Flevo ziekenhuis, Almere (1): Gunilla Kleiverda, Marcel van Alphen, Ageeth Rosman Jeroen Bosch Hospital, 's-Hertogenbosch (1): Ingrid Gaugler-Senden, Marieke Linders UNITED KINGDOM (268):

Guy's & St Thomas' Hospital, London (38): Catherine Nelson-Piercy, Annette Briley, May Ching Soh, Kate Harding, Hayley Tarft

New Cross Hospital, Wolverhampton (31): David Churchill, Katherine Cheshire, Julia Icke, Mausumi Ghosh

Nottingham City Hospital, Nottingham (30): James Thornton, Yvonne Toomassi, Karen Barker, Joanne Fisher, Nicky Grace, Amanda Green, Joanne Gower, Anna Molnar, Shobhana Parameshwaran, Andrew Simm

Queen's Medical Centre, Nottingham (22): James Thornton, George Bugg, Yvette Davis, Ruta Desphande, Yvette Gunn, Mohammed Houda, Anna Molnar, Nia Jones

Royal Victoria Infirmary, Newcastle upon Tyne (22): Jason Waugh, Carly Allan, Gareth Waring Liverpool Women's Hospital, Liverpool (16): Steve A. Walkinshaw , Angela Pascall, Mark

Clement-Jones, Michelle Dower, Gillian Houghton, Heather Longworth, Tej Purewal

Bradford Royal Infirmary, Bradford (13): Derek Tuffnell, Diane Farrar, Jennifer Syson, Gillian Butterfield, Vicky Jones, Rebecca Palethorpe, Tracey Germaine

Leicester Royal Infirmary, Leicester (12): Marwan Habiba, Debbie Lee

Wexham Park Hospital, Slough (12): Olufemi Eniola, Lynne Blake, Jane Khan

City Hospitals Sunderland NHS Foundation Trust, Sunderland (10): Helen M. Cameron, Kim Hinshaw, Amanda Bargh, Eileen Walton

South Warwickshire NHS Trust, Warwick (9): Olanrewaju Sorinola, Anna Guy, Zoe D'Souza, Rhiannon Gabriel, Jo Williams

Derriford Hospital, Plymouth (8): Ross Welch, Heidi Hollands

York Hospital, York (8): Olujimi Jibodu, Sara Collier, Pauline Tottie, Claire Oxby, James Dwyer

Singleton Hospital, Swansea (7): Franz Majoko, Helen Goldring, Sharon Jones

Chesterfield Royal Hospital, Chesterfield (6): Janet Cresswell, Louise Underwood, Mary Kelly-Baxter, Rebecca Robinson

Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield (6): Dilly Anumba, Anne Chamberlain, Clare Pye

St Mary's Hospital, Manchester (6): Clare Tower, Sue Woods, Lisa Horrocks, Fiona Prichard, Lynsey Moorhead, Sarah Lee, Louise Stephens, Cara Taylor, Suzanne Thomas, Melissa Whitworth, Jenny Myers

Birmingham Women's Hospital, Birmingham (5): Ellen Knox, Katie Freitas, Mark Kilby, Amanda Cotterill

Lancashire Teaching Hospitals NHS Foundation Trust, Lancashire (3): Khalil Abdo, Katrina Rigby, Julie Butler, Fiona Crosfill, Sean Hughes, Sanjeev Prashar, Fatimah Soydemir

The Royal Derby Hospital, Derby (3): Janet Ashworth, Lorraine Mycock, Jill Smith

Basildon & Thurrock University Hospital, Basildon (1): Amaju Ikomi, Kerry Goodsell, Jean Byrne, Maxwell Masuku, Alice Pilcher

USA (70):

Cooper University Hospital, Camden (13): Meena Khandelwal, Gunda Simpkins, Michelle Iavicoli, Yon Sook Kim, Richard Fischer, Robin Perry

Medical University of South Carolina, Charleston (11): Eugene Y. Chang, Tamara D. Saunders, Betty W. Oswald, Kristin D. Zaks

Beth Israel Deaconess, Boston (8): Sarosh Rana, Dawn McCullough

Yale-New Haven Hospital, New Haven (8): Anna Sfakianaki, Cheryl Danton, Erin Kustan, Luisa Coraluzzi

Norton Hospital Downtown (7), Norton Suburban Hospital (2), Louisville: Helen How, Christina Waldon

East Carolina University, Greenville (6): Jeffrey Livingston, Sherry Jackson, Lisa Greene Meriter Hospital, Madison (6): Dinesh Shah

Oregon Health & Science University, Portland (5): Jorge E. Tolosa, Monica Rincon, Leonardo Pereira, Amy E. Lawrence, Janice E. Snyder University of North Carolina, Chapel Hill (4): D. Michael Armstrong, Teresa Blue, Austin Hester, Kathryn Salisbury

S1. Average or general unit cost of 24 services per woman/infant by province and study group

Service	Province	'Less tight' Group		'Tight' Group	
		Average	SD	Average	SD
Assessments/Visits					
1. Antenatal visit - Physician service	Ontario	\$256.97	\$150.88	\$269.81	\$159.48
	B.C.	\$229.90	\$134.98	\$241.39	\$142.68
	Alberta	\$268.87	\$157.86	\$282.30	\$166.87
2. Antepartum home care visit - Nursing service	Ontario	\$583.81	\$467.70	\$582.86	\$470.74
	B.C.	\$691.04	\$553.61	\$689.92	\$557.20
	Alberta	\$700.58	\$561.25	\$699.44	\$564.89
3. Obstetrical Day Unit visit - Physician service	Ontario	\$269.50	\$232.06	\$262.48	\$207.97
	B.C.	\$166.75	\$143.59	\$162.41	\$128.68
	Alberta	\$181.29	\$156.11	\$176.57	\$139.90
4. Emergency room visit - Physician service	Ontario	\$75.33	\$80.05	\$81.34	\$77.75
	B.C.	\$143.22	\$152.18	\$154.63	\$147.81
	Alberta	\$193.56	\$205.68	\$208.98	\$199.77
Antenatal Hospitalization Not For Delivery					
5. Antenatal hospital admission not for delivery and daily visits	Ontario	\$167.33	\$113.91	\$176.45	\$131.34
- Physician service	B.C.	\$168.19	\$114.77	\$177.43	\$132.32
·	Alberta	\$164.06	\$118.14	\$174.68	\$135.97
Diagnostic Tests					
6. Maternal blood and urine tests - Physician laboratory service	Ontario	\$235.18	\$188.97	\$226.33	\$172.56
·	B.C.	\$272.80	\$218.34	\$262.52	\$199.20
	Alberta	\$556.43	\$467.84	\$535.78	\$430.75
7. Non-stress tests - Physician service	Ontario	\$50.48	\$58.01	\$58.09	\$71.60
•	B.C.	\$81.61	\$93.78	\$93.91	\$115.74
	Alberta	\$72.14	\$82.90	\$83.01	\$102.31
8. Fetal ultrasounds - Physician service	Ontario	\$295.77	\$219.52	\$294.41	\$210.46
•	B.C.	\$381.13	\$282.87	\$379.37	\$271.19
	Alberta	\$586.47	\$498.01	\$583.37	\$477.46

Service	Province	'Less tight	' Group	'Tight' Group		
		Average	SD	Average	SD	
9. Chest X-rays - Physician service	Ontario	\$79.73	\$143.30	\$64.29	\$88.69	
	B.C.	\$125.89	\$226.25	\$101.51	\$140.04	
	Alberta	\$105.15	\$188.98	\$84.79	\$116.97	
10. Infant head ultrasound - Physician service	Ontario	\$187.60	\$147.49	\$146.26	\$103.86	
	B.C.	\$246.49	\$193.77	\$192.17	\$136.46	
	Alberta	\$370.79	\$291.50	\$289.08	\$205.28	
11. Infant head CT scan - Physician service	Ontario	\$86.50	-	\$43.25	\$0.00	
	B.C.	\$88.62	-	\$44.31	\$0.00	
	Alberta	\$131.34	-	\$65.67	\$0.00	
12. Infant MRI - Physician service	Ontario	\$183.44	\$73.38	\$146.75	\$0.00	
	B.C.	\$221.25	\$88.50	\$177.00	\$0.00	
	Alberta	\$239.39	\$95.76	\$191.51	\$0.00	
13. Ophthalmology exam - Physician service	Ontario	\$176.36	\$136.77	\$170.85	\$128.40	
	B.C.	\$134.49	\$104.30	\$130.29	\$97.92	
	Alberta	\$173.85	\$134.82	\$168.41	\$126.57	
Delivery						
14. Caesarean section delivery before labor - Physician service	Ontario	\$1,178.62	\$271.81	\$1,207.93	\$271.62	
(obstetrician, assistant, anesthetist)	B.C.	\$1,008.42	\$228.32	\$1,024.20	\$230.04	
(obstetreran, assistant, anestnetist)	Alberta	\$1,106.27	\$114.99	\$1,115.89	\$114.82	
15. Caesarean section delivery during labor (spontaneous or	Ontario	\$1,339.50	\$271.12	\$1,297.69	\$283.63	
induced) - Physician service (obstetrician, assistant, anesthetist)	B.C.	\$1,237.66	\$258.34	\$1,240.92	\$265.52	
induced) Triy stellar service (obstetrelar, assistant, anesthetist)	Alberta	\$1,364.05	141.40	\$1,339.62	\$139.37	
16. Spontaneous vaginal delivery - Physician service	Ontario	\$724.07	\$144.35	\$716.88	\$143.06	
10. Spontaneous vaginar denvery 1 nysieran service	B.C.	\$610.11	\$33.77	\$609.38	\$33.47	
	Alberta	\$495.03	\$46.71	\$490.15	\$45.31	
17. Operative vaginal delivery - Physician service	Ontario	\$808.36	\$131.20	\$783.32	\$156.24	
	B.C.	\$807.41	\$32.16	\$809.74	\$31.27	
	Alberta	\$645.03	\$41.70	\$641.42	\$46.42	
18. Elective termination - Physician service	Ontario	\$804.81	-	\$804.81	_	
<b>y</b>	B.C.	\$899.08	_	\$899.08	_	
	Alberta	\$941.73	_	\$941.73	-	

Service	Province	'Less tigh	ıt' Group	'Tight' Group		
		Average	SD	Average	SD	
19. Miscarriage - Physician service	Ontario	-	-	\$1,107.76	-	
	B.C.	-	-	\$665.22	-	
	Alberta	-	-	\$747.12	-	
20. Induction - Physician service	Ontario	\$126.35	\$0.00	\$126.35	\$0.00	
	B.C.	\$258.82	\$12.91	\$259.56	\$16.22	
	Alberta	\$240.42	\$0.00	\$240.42	\$0.00	
Neonatal care						
21. NICU level 2 at delivery hospital - Physician service	Ontario	\$1,241.21	\$1,171.83	\$1,105.25	\$811.62	
, 1	B.C.	\$1,637.17	\$1,274.50	\$1,511.21	\$918.67	
	Alberta	\$2,118.32	\$2,219.60	\$1,860.80	\$1,537.32	
22. NICU level 3 at delivery hospital - Physician service	Ontario	\$5,203.49	\$4,404.27	\$4,020.72	\$2,824.94	
	B.C.	\$6,822.58	\$7,039.61	\$5,054.63	\$3,636.66	
	Alberta	\$8,176.54	\$9,955.46	\$5,746.59	\$4,966.99	
23. NICU level 2 at transfer hospital - Physician service	Ontario	\$3,748.63	\$2,014.64	\$3,471.15	\$2,414.18	
	B.C.	\$4,105.00	\$1,998.83	\$3,812.37	\$2,414.62	
	Alberta	\$7,100.42	\$3,816.00	\$6,574.83	\$4,572.80	
24. NICU level 3 at transfer hospital - Physician service	Ontario	\$3,086.13	\$3,887.51	\$1,722.39	\$662.27	
	B.C.	\$4,262.47	\$5,660.83	\$2,249.82	\$727.10	
	Alberta	\$5,194.73	\$7,905.21	\$2,238.77	\$860.82	
Aggregate: NICU level 2 and level 3 at both delivery and transfer	Ontario	\$3,645.21	\$4,013.55	\$2,854.24	\$2,812.76	
hospital - Physician service (Total "high level" neonatal	B.C.	\$4,694.35	\$5,793.23	\$3,604.83	\$3,444.36	
physician service)	Alberta	\$5,979.01	\$8,091.79	\$4,382.43	\$4,743.68	

SD (standard deviation)

NICU (neonatal intensive care unit)

Note: Average unit costs were calculated using the total cost divided by the number of women or infants that actually incurred that service to illustrate a general form of unit cost; whereas actual fees varied for each study participant depending on the number of services received for each woman/infant, the duration of the service or the time of day and week fee premiums applicable according to each province's Schedule of Medical Benefits.

### **S2.** Unit cost per hour for 11 hospital wards

Hospital Ward	Delivery Mode	Unit Cost Per Hour <sup>8,9</sup> CAN\$2013
Antenatal ward (pre-labor Caesarean delivery unit cost used for emergency	Pre-labor Caesarean delivery	\$31.86
room ward; all other modes unit cost used for: obstetrical day unit, antenatal hospital admission not for delivery, and antenatal ward for delivery)	All other modes	\$30.98
Labor and delivery ward	Caesarean delivery	\$281.17
	Vaginal delivery	\$213.49
Operating room	All modes	\$989.75
Postnatal ward	Caesarean delivery	\$31.86
	Vaginal delivery	\$30.98
Intermediate nursery care unit level 2 at delivery or transfer hospital	All modes	\$55.14
Neonatal intensive care unit level 3 at delivery or transfer hospital	All modes	\$107.00

#### **S3.** Definitions and Assumptions for Physician Services and Ward Durations

In general, no fee premiums were applied for special physician visits (e.g. no sacrifice of office hours or travel to attend to a case) or special patient fee modifiers (e.g. high maternal BMI, preterm delivery). No initial complex patient bonus or initial assessment fee was applied to antenatal physician visits (minor) as the first visit occurred prior to randomization. Antepartum home care visits assumed one hour total return travel and one hour home visit by one senior obstetrical nurse with commensurate wages, benefits, pension, travel premium, responsibility premium and car depreciation fee where applicable according to provincial or hospital collective agreements. Obstetrical day unit physician visits assumed one physician high risk prenatal visit/complex obstetrical patient (20 minute) with no interventions, procedures, delivery or hospital admission, time of day or week premiums, travel or sacrifice of office hours during regular office hours; cost of any physician interpretation of non-stress test was included under NST cost. Each obstetrical day unit visit ward cost assumed 12 hours at pre-labor Caesarean section antenatal ward unit cost per hour that included nursing and hospital overhead costs. Emergency room visits were assumed to be during weekdays 9am-5pm with an emergency family physician on fee-for-service basis (not salaried, no sessional fees) for a moderate complexity case that included comprehensive visit, detailed history, prolonged observation, continuous therapy and multiple reassessments, and no premiums for time of day, day of week or holiday, travel, calls, first/additional person(s) seen, special visits, consultations, major intervention/invasive procedures, investigative ultrasounds, transfers, re-assessment, admission or follow-up while waiting in emergency room for further evaluation, bed or transfer. Emergency room visit ward cost assumed pre-labor Caesarean section antenatal ward unit cost and 5 hours length of stay for each visit. Antenatal hospital admission not for delivery physician cost included physician fee for hospital admission assessment on first day admitted for each hospitalization, plus physician fee for hospital visit on each subsequent day while in hospital, plus discharge assessment fee which is same as hospital visit fee; any admissions prior to randomization and any admissions missing either admission and/or discharge dates were excluded; assumed hospital admission during weekday regular hours (no premium), no callback or sacrifice of office hours premiums; admission not via emergency room. Antenatal hospital admission not for delivery excluded any length of stay prior to randomization and any stay missing admission and/or discharge date and assumed antenatal ward unit cost for deliveries other than pre-labor Caesarean section; assumed 0000h admission and 2359h discharge times where 1 day equal to 24 hours; inpatients recruited in hospital were included, but not their length of stay before randomization. Only the total number and not type of blood/urine tests was collected per patient. Laboratory costs assumed all blood/urine tests were recorded were on an outpatient basis. If woman was <=21 weeks gestational age at randomization, then first blood/urine test included: specimen collection fee, Triple Marker Screening (TMS: alphafetoprotein AFP, human chorionic gonadotropin hCG and unconjugated estriol uE3), Glucose Challenge Test for gestational diabetes (GCT) and complete blood count (CBC). If gestational age >21 weeks and <=24 weeks at randomization, then first blood/urine test included: specimen collection fee, GCT and CBC (no TMS, since before randomization); any remaining blood/urine tests were assumed to be for pre-eclamptic toxemia (PET) panel: specimen collection fee, CBC, urea/BUN, creatinine, AST, ALT, LDH, bilirubin, uric acid, and mean cost of 4 different common proteinuria tests: urinary dipstick for creatinine or proteins, protein:creatinine ratio, 24 hour urine collection for creatinine or proteins and albumin:creatinine ratio; no laboratory ward

cost was included. Non-stress test included physician interpretation; any ward cost was considered elsewhere, e.g. in ODU, ER, hospitalization not for delivery, antenatal ward for delivery, etc. Fetal ultrasound physician cost assumed private out-of-hospital clinic associated with hospital, no ward cost, and included physician interpretation fee and technician fee if applicable, with physician on-site to supervise ultrasound technician and interpret ultrasound; all ultrasounds were complete and not partial; first ultrasound was assumed for pregnancy and subsequent ultrasound(s) for high risk assessment. Infant chest x-ray and infant head ultrasound unit costs included physician interpretation and technician fees where applicable and assumed inhospital ward cost was already included in level 2 or level 3 neonatal care ward cost. Infant head CT scan and infant head MRI unit costs included physician interpretation fee, and assumed technician fee and in-hospital ward cost already included in level 2 or level 3 neonatal care ward cost. Retinopathy of prematurity unit costs included physician consultation/assessment fees and assumed ward fee already included in level 2 or level 3 neonatal care unit or postnatal ward. CHIPS total actual maternal hospital length of stay from admission to maternal hospital discharge home was divided in antenatal, labor and delivery, operating room and postnatal ward durations, based on EECV2 trial mean length of stay (excluding breech births) in the labor and delivery ward and operating room for Caesarean section, by parity and delivery mode, where remaining time between actual hospital admission and calculated labor and delivery ward admission time was assigned as antenatal ward length of stay, and remaining time from calculated labor and delivery ward discharge to actual hospital discharge was assigned as postnatal ward length of stay for each study participant. Operating room time was embedded within labor and delivery ward duration where the bed was kept. The sum of all estimated ward lengths of stay was equal to the total actual CHIPS hospital length of stay for each patient. Some patients were randomized as inpatients whose length of stay prior to labor and delivery was included in the antenatal ward duration. Inpatients may contribute more antenatal ward time per patient than expected for a typical delivery, and was assumed to be balanced between study groups due to randomization. Women who received magnesium sulfate anytime before or during delivery had an additional 24 hours for monitoring added to their existing labor and delivery unit ward duration and 24 hours reduced from their postpartum ward duration. Caesarean section before labor or during labor (CS and spontaneous or induced) physician fee assumed one obstetrician, one surgical assistant and one anesthetist with time of day and week premiums for operating room modelled around actual birth time and operating room duration modelled based on EECV2 trial mean ward duration by delivery mode and parity. No procedural fee modifiers (i.e. patient complexity fee) were used. The majority of service provided was assumed to be within initial start time of day and week period, where all physicians worked on one case only, with no sacrifice of office hours, no travel premiums; uncomplicated patient and fetus, Ontario (or equivalent) ASA level 1 (uncomplicated patient for anesthesia); anesthetist cost is the same regardless of approach (epidural, spinal or general anesthesia); no surgeon or anesthetist presurgery patient assessment time cost; no post-operative anesthetic monitoring fee or postoperative pain management cost (monitoring); anesthetist time was assumed to be only during operating room; no surgeon follow-up visit. Spontaneous vaginal and operative vaginal delivery physician fees assumed one obstetrician only, cephalic presentation, no second assistant obstetrician, no anesthetist and no episiotomy or repair of tear; for operative delivery, assumed mid-cavity extraction, vacuum or forceps. Elective terminations of pregnancy were assumed to involve dilatation and evacuation, miscarriages were assumed to involve dilation and curettage, and both procedures assumed one obstetrician and one anesthetist for 30 minutes operating room

time. Induction assumed only one oxytocin-type induction during day time on a weekday, and only one hour of oxytocin infusion billable to physician, although infusion may have been longer. Assessment of a normal newborn was included in the physician delivery fee. Neonatologist consultation fees for admission to a level 2 neonatal intermediate care unit or level 3 neonatal intensive care unit were included in the first day level 2 or level 3 physician fee per diem. Level 2 neonatal intermediate care ward included monitoring (invasive or non-invasive), oxygen administration and intravenous therapy or parenteral alimentation but without ventilatory support. Level 3 neonatal intensive care ward included full life support, full intensive monitoring (either invasive or non-invasive), artificial ventilation, parenteral alimentation (all modalities) if necessary, and all procedures. Ontario and British Columbia fee schedules considered neonatologist per diems for level 2 and level 3 neonatal care. An Alberta neonatologist per diem was derived from the "Neonatal Intensive Care Unit (NICU) Calgary Clinical Alternative Relationship Plan (ARP)" [Government of Alberta Ministerial Order M.O. 124/2103, dated March 28, 2013, amending M.O. 124/2013] contract for neonatologists serving 102 NICU level 2 and level 3 beds at: Foothills Medical Centre NICU (levels 2 and 3, total 39 beds), Peter Lougheed Centre (NICU levels 2 and 3, total 30 beds) and Rockyview General Hospital (NICU levels 2 and 3, total 33 beds) out of a total of 251 NICU levels 2 and 3 beds in Alberta overall (87 NICU level 3 beds and 164 NICU level 2 beds with an overall occupancy rate of 90% in 2013, according to personal communication with Jeremy Anthony, Manager, Program Design and Delivery, Workforce Design Branch, Alberta Health on February 19, 2015), towards calculating a per diem based on 41% of neonatal care beds in Alberta. The 2013 ARP stipulates a maximum annual compensation of \$7,799,237.32 (total NICU neonatologist budget) from April 1, 2013 to March 31, 2014 for a maximum of 15.55 Full Time Equivalent neonatologists (\$501,558.67 annual payment rate per FTE) serving a total of 102 NICU level 2 and level 3 beds at these 3 hospitals. Assuming 102 NICU beds for 365.25 days/year for maximum 37,255.5 bed days/year at 90% occupancy, the estimated total number of actual NICU beds is 33,529.95 bed days/year. The Alberta NICU level 2 and level 3 neonatologist per diem was calculated by dividing the total NICU neonatologist budget of \$7,799,237.32 by the total number of NICU bed days of 33,529.95 days/year for a per diem of \$232.60 per neonate per day for either level 2 or level 3 neonatal care. Length of stay in a level 2 or level 3 neonatal care ward was calculated to the hour for ward costs, and was rounded up to the nearest integer day for neonatologist per diem.

**S4.** Methods used to derive hospital ward unit costs in the Term Breech Trial and their application in the CHIPS trial

The CHIPS trial study used hospital ward unit costs as determined for 2002 in the Term Breech Trial (TBT) and adjusted to 2013 using the Canadian Consumer Price Index (CPI) health care commodity group. In summary: [9] TBT ward unit costs were calculated using financial and statistical reports on ICD codes and case mix groups provided by 4 teaching hospitals and 3 community hospitals in each of Ontario, British Columbia and Alberta. A group of women and infants similar to those in the TBT was selected in each of the 7 hospitals for whom all direct and indirect (i.e. overhead) costs were provided related to their length of hospital stay, the duration of stay in each hospital ward and the costs of different services allocated to these wards. The total unit cost per hour for each hospital ward was determined by adding the per-hour costs of all of the services that occurred in that ward. The median unit cost between the high and low unit cost estimates across the 7 hospitals was used. TBT ward unit costs were scaled from 2002 by 20.5% to 2013 Canadian dollars, the year when recruitment ended in the CHIPS trial, using the Canadian Consumer Price Index (CPI) for health care commodities. In the CHIPS trial, 2013 adjusted TBT antenatal ward unit cost for vaginal delivery was applied to: obstetrical day unit, antenatal hospital stay not for delivery ward and antenatal ward for vaginal delivery; the slightly higher TBT antenatal ward unit cost for pre-labor Caesarean delivery was applied to emergency room ward to reflect a greater intensity of care. The TBT labor and delivery ward and postnatal ward unit costs were applied accordingly in the CHIPS trial by Caesarean or vaginal delivery modes. The TBT operating room, intermediate nursery care unit and neonatal intensive care unit ward unit costs were applied accordingly in the CHIPS trial. Only "high level" neonatal care was collected in the CHIPS trial. For the purpose of physician and ward costing, CHIPS neonates in "high level" neonatal care were categorized into NICU level 2 or level 3 care using an algorithm based on severity of illness: Level 3 NICU=Gestational age (GA) <32 weeks or any Positive Pressure Ventilation (PPV; within first 72 hours of life beyond the initial resuscitation period via Endotracheal Intubation, EI, or Continuous Positive Airway Pressure, CPAP) or birthweight<1500g or any of 10 serious morbidities (cases may overlap with previous criteria: patent ductus arteriosus, early-onset sepsis within first 48hr of life, bronchopulmonary dysplasia, retinopathy of prematurity stage >2, intraventricular hemorrhage, cystic periventricular leukomalacia, hypoxic-ischemic encephalopathy, necrotizing enterocolitis, laparotomies or thoracotomies). All other "high level" care cases were considered in level 2. It was assumed that hospital transfer was necessary either for the purpose of greater or lesser care and no other purpose (e.g. family convenience); if care began in level 3 care, transfer was to level 2, and if care began in level 2, transfer was to level 3, i.e. level 3 neonates were "stepped down" and level 2 neonates needed higher intensity care following initial care are were "stepped up". These criteria use a maximum of the case report form data for its intended purpose and are the most sensitive set of criteria as they include cases that would be most appropriate in level 3 care. GA<32 weeks is congruent with Ontario and B.C. level 3 admission guidelines. Any PPV (that uses CPAP or EI) discriminates between level 3 and level 2 medical benefits in Ontario and B.C. BW<1500g cases are most often sent to level 3 and also agree with both Ontario and B.C. provincial guidelines. The 10 serious morbidities are cases severe enough for level 3 admission. Costing included costs up to the time of discharge for mother and for baby following birth. This excluded the costs of any maternal or neonatal re-admission, but the data to inform costs beyond discharge are very limited, and introduce considerable room for error. The timeframe included is

a commonly used timeframe and is justified. Physician hours are rounded up to the nearest whole

day for per diem fees; ward hours remain as actual for costing.							

**S5.** Mean costs of healthcare resources by province and study group

Service or Ward	Province	'Less tight N=493wome	-	'Tight' Group N=488 women/infants		Difference Between 'Less	Rank of Cost Driver <sup>2</sup>		
						tight' and			
		Mean	SD	Mean	SD	'Tight' Mean Costs <sup>1</sup>	Ontario	B.C.	Alberta
Outpatient Assessments/Visits									
1. Antenatal visit - Physician cost	Ontario	\$251.76	\$153.67	\$261.52	\$163.78	-\$9.76	18		
	B.C.	\$225.24	\$137.49	\$233.97	\$146.53	-\$8.73		21	
	Alberta	\$263.41	\$160.79	\$273.63	\$171.37	-\$10.22			20
2. Antepartum home care visits	Ontario	\$127.89	\$325.58	\$125.41	\$323.74	\$2.48	26		
<ul> <li>Nursing visit cost</li> </ul>	B.C.	\$151.38	\$385.38	\$148.45	\$383.20	\$2.93		25	
	Alberta	\$153.47	\$390.70	\$150.49	\$388.49	\$2.98			25
3. Obstetrical Day Unit visit	Ontario	\$98.94	\$191.34	\$97.35	\$179.15	\$1.59	28		
- Physician cost	B.C.	\$61.22	\$118.39	\$60.24	\$110.85	\$0.98		31	
	Alberta	\$66.56	\$128.71	\$65.49	\$120.51	\$1.07			31
4. Obstetrical Day Unit visit	All	\$492.41	\$952.25	\$484.51	\$891.59	\$7.90	20	22	21
- Ward cost	provinces								
5. Emergency room visit	Ontario	\$30.41	\$62.83	\$29.50	\$60.97	\$0.91	30		
- Physician cost	B.C.	\$57.81	\$119.45	\$56.08	\$115.90	\$1.73		27	
	Alberta	\$78.13	\$161.44	\$75.80	\$156.65	\$2.33			27
6. Emergency room visit	All	\$130.22	\$269.06	\$126.33	\$261.08	\$3.89	24	24	24
- Ward cost	provinces								
Antenatal Hospitalizations Not									
For Delivery									
7. Antenatal hospital admission	Ontario	\$44.46	\$94.36	\$43.75	\$100.34	\$0.71	32		
not for delivery and daily care	B.C.	\$44.69	\$94.93	\$43.99	\$100.98	\$0.70		33	
- Physician cost	Alberta	\$43.59	\$94.60	\$43.31	\$101.28	\$0.28			33
8. Antenatal hospital admissions	All	\$678.67	\$1,641.90	\$700.86	\$1,790.57	-\$22.19	15	13	16
not for delivery - length of stay - Ward cost	provinces		,		•	·			

<sup>–</sup> Online Supplements - July 13, 2016 –

16

Service or Ward	Province	'Less tight' N=493wome		'Tight' Group N=488 women/infants		Difference Between 'Less	Rank of Cost l		Priver <sup>2</sup>
		Mean	SD	Mean	SD	tight' and 'Tight' Mean Costs¹	Ontario	B.C.	Alberta
Maternal, Fetal, and Infant									
Diagnostic Tests									
9. Maternal blood and urine tests	Ontario	\$218.96	\$191.83	208.71	176.46	\$10.25	17		
<ul> <li>Physician laboratory cost</li> </ul>	B.C.	\$253.98	\$221.73	242.07	203.82	\$11.91		18	
	Alberta	\$518.05	\$472.94	494.06	437.86	\$23.99			15
10. Non-stress tests	Ontario	\$36.76	\$54.35	\$42.26	\$66.31	-\$5.50	22		
- Physician cost	B.C.	\$59.43	\$87.87	\$68.31	\$107.19	-\$8.88		20	
	Alberta	\$52.53	\$77.67	\$60.39	\$94.75	-\$7.86			22
11. Fetal ultrasounds	Ontario	\$274.77	\$224.81	\$273.89	\$216.40	\$0.88	31		
- Physician cost	B.C.	\$354.07	\$289.69	\$352.94	\$278.85	\$1.13		30	
	Alberta	\$544.83	\$503.10	\$542.73	\$483.90	\$2.10			28
12. Chest X-rays - Physician cost	Ontario	\$11.97	\$62.12	\$7.11	\$35.55	\$4.86	23		
	B.C.	\$18.90	\$98.09	\$11.23	\$56.13	\$7.67		23	
	Alberta	\$15.78	\$81.93	\$9.38	\$46.88	\$6.40			23
13. Infant head ultrasound	Ontario	\$25.88	\$84.59	\$18.58	\$61.06	\$7.30	21		
- Physician cost	B.C.	\$34.00	\$111.14	\$24.41	\$80.23	\$9.59		19	
·	Alberta	\$51.14	\$167.19	\$36.73	\$120.69	\$14.41			19
14. Infant head CT scan	Ontario	\$0.18	\$3.90	\$0.27	\$3.38	-\$0.09	34		
- Physician cost	B.C.	\$0.18	\$3.99	\$0.27	\$3.47	-\$0.09		34	
·	Alberta	\$0.27	\$5.92	\$0.40	\$5.14	-\$0.13			34
15. Infant MRI - Physician cost	Ontario	\$1.49	\$17.44	\$0.90	\$11.48	\$0.59	33		
•	B.C.	\$1.80	\$21.04	\$1.09	\$13.85	\$0.71		32	
	Alberta	\$1.94	\$22.76	\$1.18	\$14.98	\$0.76			32
16. Ophthalmology exam	Ontario	\$23.61	\$78.01	\$20.66	\$71.22	\$2.95	25		
- Physician cost	B.C.	\$18.01	\$59.49	\$15.75	\$54.31	\$2.26		26	
•	Alberta	\$23.27	\$76.90	\$20.36	\$70.20	\$2.91			26

Service or Ward	Province	'Less tight N=493wome	-	'Tight' Group N=488 women/infants		Difference Between 'Less	Rank o	of Cost I	Oriver <sup>2</sup>
						tight' and			
		Mean	SD	Mean	SD	'Tight' Mean Costs <sup>1</sup>	Ontario	B.C.	Alberta
Hospital Length of Stay For Delivery									
17. Antenatal ward cost	All provinces	\$1,947.60	\$3,409.93	\$1,897.82	\$3,767.42	\$49.78	10	9	10
18. Labor and delivery ward cost	All provinces	\$3,279.45	\$2,438.95	\$3,152.22	\$2,339.13	\$127.23	6	6	6
19. Operating room ward cost	All provinces	\$674.27	\$651.04	\$761.34	\$639.13	-\$87.07	8	8	8
20. Postnatal ward cost	All provinces	\$2,508.48	\$1,952.02	\$2,394.59	\$1,468.31	\$113.89	7	7	7
Delivery									
21. Caesarean section before	Ontario	\$380.12	\$572.60	\$403.47	\$591.42	-\$23.35	14		
labor - Physician cost	B.C.	\$325.23	\$489.27	\$342.10	\$501.43	-\$16.87		16	
	Alberta	\$356.79	\$521.73	\$372.73	\$530.99	-\$15.94			18
22. Caesarean section during	Ontario	\$195.63	\$484.60	\$231.35	\$511.28	-\$35.72	12	10	
labor - Physician cost	B.C.	\$180.75	\$448.40	\$221.23	\$488.36	-\$40.48		12	10
22	Alberta	\$199.21	\$485.19	\$238.83	\$516.59	-\$39.62	0		12
23. Spontaneous vaginal	Ontario B.C.	\$343.68 \$289.59	\$375.32 \$305.86	\$287.93 \$244.75	\$363.26 \$299.79	\$55.75 \$44.84	9	10	
- Physician cost	Alberta	\$289.39 \$234.96	\$303.80 \$249.53	\$244.73 \$196.86	\$299.79	\$38.10		10	13
24. Operative vaginal	Ontario	\$234.90 \$44.27	\$2 <del>4</del> 9.55 \$186.56	\$190.80	\$242.23	-\$19.94	16		13
- Physician cost	B.C.	\$44.22	\$184.04	\$66.37	\$222.53	-\$17.54	10	14	
i nysician cost	Alberta	\$35.33	\$147.22	\$52.58	\$176.62	-\$17.25		14	17
25. Elective termination	Ontario	\$1.63	\$36.25	\$1.65	\$36.43	-\$0.02	35		17
- Physician cost	B.C.	\$1.82	\$40.49	\$1.84	\$40.70	-\$0.02	23	35	
<b>,</b>	Alberta	\$1.91	\$42.41	\$1.93	\$42.63	-\$0.02			35

Service or Ward	Province	'Less tight' Group N=493women/infants						Difference Between 'Less tight' and	Rank of Cost Driver <sup>2</sup>		
		Mean	SD	Mean	SD	'Tight' Mean Costs <sup>1</sup>	Ontario	B.C.	Alberta		
26. Miscarriage - Physician cost	Ontario	\$0.00	\$0.00	\$2.27	\$50.15	-\$2.27	27				
	B.C.	\$0.00	\$0.00	\$1.36	\$30.11	-\$1.36		29	20		
27. Induction - Physician cost	Alberta Ontario	\$0.00 \$57.41	\$0.00 \$62.98	\$1.53 \$56.44	\$33.82 \$62.88	-\$1.53 \$0.97	29		30		
27. muucuon - Physician cost	B.C.	\$117.60	\$129.29	\$115.95	\$129.63	\$1.65	29	28			
	Alberta	\$109.24	\$119.83	\$107.40	\$119.65	\$1.84			29		
Neonatal care											
28. NICU level 2 at delivery	Ontario	\$211.48	\$670.72	\$187.98	\$532.64	\$23.50	13				
hospital - Physician cost	B.C.	\$278.95	\$808.50	\$257.03	\$682.00	\$21.92		15			
	Alberta	\$360.93	\$1,211.08	\$316.49	\$942.18	\$44.44			11		
29. NICU level 3 at delivery	Ontario	\$759.94	\$2,486.55	\$560.26	\$1,743.75	\$199.68	5				
hospital - Physician cost	B.C.	\$996.40	\$3,601.17	\$704.33	\$2,211.30	\$292.07		4			
	Alberta	\$1,194.14	\$4,759.99	\$800.75	\$2,713.43	\$393.39			3		
30. NICU level 2 at transfer	Ontario	\$144.47	\$818.69	\$106.70	\$726.12	\$37.77	11				
Hospital - Physician cost	B.C.	\$158.20	\$878.55	\$117.18	\$775.57	\$41.02		11			
	Alberta	\$273.65	\$1,550.70	\$202.10	\$1,375.38	\$71.55			9		
31. NICU level 3 at transfer	Ontario	\$37.56	\$518.00	\$28.24	\$232.89	\$9.32	19				
hospital - Physician cost	B.C.	\$51.88	\$737.92	\$36.88	\$298.97	\$15.00		17			
	Alberta	\$63.22	\$979.88	\$36.70	\$302.71	\$26.52			14		
Aggregated: NICU level 2 and 3	Ontario	\$1,153.46	\$2,820.43	\$883.18	\$2,044.80	\$270.28	-	-	-		
at both delivery and transfer	B.C.	\$1,485.43	\$3,917.85	\$1,115.43	\$2,537.04	\$370.00	-	-	-		
hospital - Physician cost (Total "high level" service cost)	Alberta	\$1,891.94	\$5,326.93	\$1,356.04	\$3,323.14	\$535.90	-	-	-		
32. NICU level 2 - Delivery hospital - Ward cost	All provinces	\$1,944.18	\$6,749.05	\$1,697.83	\$5,194.38	\$246.35	4	5	5		
33. NICU level 3 - Delivery hospital - Ward cost	All provinces	\$12,997.94	\$52,274.70	\$8,688.14	\$29,682.07	\$4,309.80	1	1	1		

Service or Ward	Province	'Less tight' Group N=493women/infants		'Tight' Group N=488 women/infants		Difference Between 'Less tight' and	Rank of Cost Driver <sup>2</sup>		
		Mean	SD	Mean	SD	'Tight' Mean Costs <sup>1</sup>	Ontario	B.C.	Alberta
34. NICU level 2 - Transfer hospital - Ward cost	All provinces	\$1,531.24	\$8,714.01	\$1,123.73	\$7,714.98	\$407.51	2	2	2
35. NICU level 3 – Transfer hospital - Ward cost	All provinces	\$683.88	\$10,736.19	\$381.29	\$3,162.56	\$302.59	3	3	4
Aggregated: NICU level 2 and 3 at both delivery and transfer hospital- Ward cost (Total "high level" ward cost)	All provinces	\$17,157.25	\$54,956.36	\$11,890.99	\$32,045.34	\$5,266.26	-	-	-

Notes: The mean cost here represents the total cost incurred for each service or ward divided by the total number of women in each study group (493 or 488), whether or not they incurred the service or ward (intention-to-treat principle), yielding a mean cost per study group.

- 1. The difference between mean costs per group determines which group is more costly: a positive value favors the less costly 'tight' study group.
- 2. The absolute difference between 'less tight' and 'tight' group mean costs was ranked from 1=highest to 35=lowest cost difference, to determine which costs contribute the most difference between study groups, where 1=highest cost driver.

**S6.** Analysis of top five cost drivers

Service or Ward Cost	Province		'Less tight' Group N=493 women/infants		'Tight' Group N=488 women/infants		95% Confidence	SE(Diffe rence in	P- Value	Rank of Cost Driver		
		Mean	SE(Mean)	Mean	SE(Mean)	'Less tight' and 'Tight' Mean Costs <sup>1</sup>	Interval	Means)		Ontario	B.C.	Alberta
33. NICU level 3 - Delivery hospital - Ward cost	All	\$12,997.94	\$2,354.33	\$8,688.14	\$1343.64	\$4,310	-\$804, \$9,987	\$2,741	0.112	1	1	1
34. NICU level 2 - Transfer hospital - Ward cost	All	\$1,531.24	\$392.46	\$1,123.73	\$349.24	\$408	-\$624, \$1,436	\$520	0.446	2	2	2
35. NICU level 3 - Transfer hospital - Ward cost	All	\$683.88	\$483.53	\$381.29	\$143.16	\$303	-\$439, \$1,450	\$501	0.824	3	3	4
32. NICU level 2 - Delivery hospital - Ward cost	All	\$1,944.18	\$303.96	\$1,697.83	\$235.14	\$246	-\$510, \$1,017	\$388	0.525	4	5	5
29. NICU level 3 - Delivery hospital	Ontario B.C. Alberta	\$759.94 \$996.40	\$111.99 \$162.19	\$560.26 \$704.33	\$78.94 \$100.10	\$200 \$292	-\$65, \$466 -\$64, \$687	\$135 \$193	0.142 0.134	5	4	
- Physician cost	32 ***	\$1,194.14	\$214.38	\$800.75	\$122.83	\$393	-\$73, \$898	\$248	0.111			3

Notes:

1. Positive value favors less costly 'tight' group