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Length of stay and cost of birth hospitalization: effects of subfertility and ART

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Abstract

Objective: To measure delivery length of stay (LOS) and cost as proxies for infant morbidity in assisted reproductive technology (ART) and subfertile deliveries.

Study Design: Massachusetts singleton births, ≥23 weeks gestational age (GA) between 2004 and 2010 were linked with ART data, vital records, and hospital discharges. LOS and costs (2010 US Dollars) of infants born to fertile (no ART or indicators of infertility), subfertile (indicators of infertility but no ART), and ART-treated (linked to ART data) deliveries were compared. Least square means and standard errors (SE) were calculated.

Results: Of 345,756 singletons, (fertile n=332,481, subfertile n=4,987 and ART-treated n=8,288), overall LOS was 3.79±0.01, 4.32±0.05, and 4.90±0.04 days and costs were $2,980±6, $3,217±58, and $4,483 ±62, respectively. GA and birthweight predicted much of the intergroup difference.

Conclusions: Maternal fertility group was not an independent predictor of infant LOS and costs. Prematurity and birthweight were driving factors in resource utilization.

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Introduction

Healthcare costs in developed countries have risen steadily over the last five decades (1). Although the conversation is gradually shifting from the costs of care to the value (i.e. the health benefit for the dollars spent) (2), expensive technologies are often a topic of contention. Treatment with assisted reproductive technology (ART) is one example where both the patient and the payor can incur a large cost from both the procedure itself (3) and downstream associated costs related to excess morbidity and mortality of the offspring (e.g. extreme preterm birth) and the mother (3, 4). There are particular challenges in understanding the economics of infertility care and ART that are driven by the outcome being studied (e.g. early gestation heart beat vs. live birth vs. a time point later in childhood) and thus the time horizon associated with the cost accounting (5).

Analysis of the cost of ART has previously been mostly limited to the intervention plus the cost of successful pregnancy. The cost of infant outcomes has been largely driven by prematurity and low birthweight (6, 7). Other factors are known to increase the costs for singleton offspring from ART pregnancies, including the number of embryos transferred, although the increase in costs is also largely driven by prematurity (8). Twins and higher order multiples, the numbers of which are both increased as a result of ART, are both known to contribute to increased costs compared to singletons both during the birth hospitalization and first year of life (9).

Although preterm birth carries a lifelong influence on survivors (10), there is evidence that the effect of ART on health outcomes of offspring persists even after controlling for co-variates such as gestational age and birthweight; however our knowledge and data are limited on the effect of ART on costs of care for these infants is wanting (11). Furthermore, subfertility itself, in the absence of ART treatment, may be associated with additional morbidity in offspring (12). Therefore the goal of this study was to understand the overall influence of treatment with ART and of subfertility without ART treatment on the birth hospitalization length of stay (LOS) and cost of care among singletons on a population basis.

Methods:

Data Source:

The Massachusetts (MA) Outcome Study of Assisted Reproductive Technology (MOSART) is a longitudinal population cohort of all births in MA. The details of the MOSART cohort have been previously described (6, 13, 14) and are briefly reviewed here. MOSART is a database that combines the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) (15), a clinical database of treatment information on all ART cycles in MA and the Pregnancy to Early Life Longitudinal (PELL) data system (16–18), which links birth certificates to hospital discharge records for mothers and infants. PELL is a unique, longitudinal, population-based database in MA that links multiple sources of data, capturing diagnostic codes, health care utilization and associated costs using hospital related discharge data.

Patient Population

The sample for these analyses was limited to singleton births born to mothers ≥18 years of age in MA between July 1, 2004 and December 31, 2010 and it included the first delivery to each woman within the MOSART database so as not to include repeat deliveries to the same woman. The sample was limited to infants born alive at ≥23 weeks gestational age and discharged home. In order to account for inter-hospital transfers of sick neonates, we considered a "birth" hospitalization the combination of the initial birth and any inpatient hospital admission to a different hospital within one day of discharge from the original hospital (where applicable), as this would most accurately reflect the LOS and cost as related to the original birth hospitalization. This approach has been previously applied for this cohort (18). In addition, we excluded patients with a missing co-variate and/or outcome, as well as those whose LOS was implausible based on gestational age or birthweight (23–27 weeks <21 days; 28–33 weeks <7 days; ≤1,000 grams < 21 days; 1,001–1,500 grams <15 days) (Supplemental Figure 1). The plausible estimates for LOS were based on what is typically expected for babies born at the stated gestational and birthweight and how long it takes to reach physiologic maturity in order to be discharged from the hospital.

Independent variable:

The primary predictor of outcome was the maternal fertility group, as previously described (13). The women were categorized in one of three mutually exclusive groups: (1) fertile - those without ART or other non-ART Medically Assisted Reproduction (MAR) techniques or other indicators of infertility; (2) subfertile - those without ART, but who had other indicators of infertility, including a diagnosis of infertility (i.e. ICD9 code 628.9 in maternal hospitalization records during the 5 years prior to the birth or fetal death certificate indicating use of non-ART MAR) ; and (3) ART-treated - those deliveries linked to the SART CORS online database. The definition of subfertility is closely aligned with the recent publication by the International committee for Monitoring Assisted Reproductive Technologies (19). However, the term subfertility was used instead of MAR or infertility since some patients fell into one or the other of these categories but few fell into both.

Primary Outcomes and Co-variates:

Length of Stay: We evaluated the total LOS for the birth hospitalization for survivors. Initial comparison was made for all infants from the three fertility groups and then secondarily stratified by gestational age categories (≤27 weeks, 28–33 weeks, 34–36 weeks, 37–38 weeks, ≥39 weeks) and birthweight (≤1,000 grams, 1,001–1,500 grams, 1,501–2,500grams, ≥2,501 grams). We adjusted *a priori* for a number of pre-specified variables based on previously known confounders in this cohort (13) (maternal age, race, education, payer (self-pay, private, public), pre-existing diabetes and hypertension, parity, and infant sex), as well as other factors that could affect the birth hospitalization LOS and cost (birth year, gestational age as a continuous variable, mode of delivery, (vaginal, cesarean – primary and repeat, and vaginal birth after cesarean) maternal prolonged length of stay, as well as gestational diabetes and gestational hypertension). The LOS was presented as mean number of days and standard error (SE), as well as median and interquartile range (Q1, Q3).

Cost: Cost data in US dollars were determined using the hospital charges from the PELL data system in accordance with previous publications (16–18) as described briefly here. The total costs were calculated by multiplying the charges from the discharge record by the hospital-specific cost to charge ratios. All costs were adjusted for inflation to 2010 US dollars using the General Medical and Surgical Hospitals component of Producer Price Index (Bureau of Labor Statistics). 2010 was chosen as the year of currency in order to reflect the last clinical year of patients included in the study. Professional fees are not included as part of this cost accounting method. The costs included were only for the birth hospitalization of the infant. We did not include any costs that resulted from prenatal care, prenatal testing, nor for fertility evaluations and/or treatment. The cost was presented as mean number of days and standard error (SE), as well as median and interquartile range (Q1, Q3). For multivariable modeling, we adjusted for the same co-variates as described above paragraph for LOS.

Statistical Analyses: Chi-square test ANOVA were applied for categorical and continuous variables to assess the unadjusted relationships between the co-variates and across maternal fertility groups. Initially, we determined the mean length of stay and cost by gestational age and birthweight strata. Given the non-normal distribution of the LOS and cost data, we used generalized linear model with logarithmic link function and the gamma distribution in our statistical models (both unadjusted and adjusted) to determine the least square means and standard errors for LOS and cost (20). Patients with missing data, comprising less than 1% of the eligible sample population, were excluded. SAS software version 9.3 (SAS Institute, Inc, Cary, NC) was used to perform all statistical analyses. Statistical code is available upon request. The study was approved by the Institution Review Board of the Massachusetts Department of Public Health and the Committee for the protection of Human Subjects at Dartmouth College.

Results:

A total of 345,756 singletons, born between 2004 and 2010, at ≥23 weeks gestation, who survived to first discharge home were eligible for the analysis (332,481 fertile, 4,987 subfertile, and 8,288 ART-treated). Compared to offspring of the fertile group, infants born to women in the subfertile and ART groups were born to mothers who were older, predominantly non-Hispanic White, more likely to be college educated, have private insurance, be married, and have delivered by caesarean (Table 1). In unadjusted analyses, the infant sex distribution was similar between the two groups (51.2% male vs. 48.8% female) and those born to subfertile and ART-treated mothers were more likely to be preterm and low birthweight (Table 1).

Length of Stay

The overall unadjusted LOS for this sample was 3.79 days (SE=0.01) in the fertile group, 4.32 days (SE=0.05) in the subfertile group, and 4.90 (SE=0.04) in the ART-treated group (p <0.0001 for between subgroups and overall comparison). The unadjusted LOS was inversely related to gestational age and birthweight. There were no statistical differences between the fertile, subfertile and ART-treated groups in the younger gestational age and smaller birthweight strata, but some differences were observed for infants >37 weeks and >1,500 grams (Table 2). In the multivariable analysis, when stratified by gestational age, there was no difference in the birth hospitalization LOS for the 23–27 weeks, 28–33 weeks and 34–36 week groups, neither overall nor between the individual subgroups. However, the LOS was statistically higher in the 37–38 week strata: 4.11 days (SE=0.05) days in fertile group versus 4.16 days (SE=0.08) in the subfertile and 3.96 days (SE=0.07) in the ART-treated group with overall p-value of 0.0057 (Table 3). Similar statistical trend was noted in the ≥39 week group (Table 3).

When stratified by birthweight categories, the LOS was only statistically different in the 1,001–1,500 gram category between the three fertility subgroups: 49.95 days (SE=2.48) in the fertile group versus 61.47 (SE=5.59) in the subfertile, and 49.21 days (SE=3.23) in the ART-treated group (overall p-value=0.029) (Table 3). The remainder of birthweight strata demonstrated no statistically significant differences in the adjusted LOS across the three groups.

Costs

The overall unadjusted infant cost through first discharge home was $2,980 (SE=6) in the fertile group, $3,271 (SE=58) in the subfertile group, and $4,483 (SE=62) in the ART-treated group (p<0.0001 for between subgroup and overall comparison). Similar to LOS, the cost of the birth hospitalization was inversely related to gestational age and birthweight (Tables 4 and 5). When stratified by gestational age, the adjusted cost difference between the three groups was only different in the 37–38 week and ≥39 week categories, with a higher cost in the fertile and subfertile compared to ART-treated groups for 37–38 week strata (overall p-value <0.0001), and conversely, incrementally higher in the subfertile and ART groups compared to fertile in the ≥39 week strata (overall p-value <0.0001) (Table 5).

When stratified by birthweight, differences in adjusted cost were noted in the 1,001–1,500 gram subgroup with higher cost in the subfertile group ($83,450 SE=12,246) compared to fertile ($63,012 SE=4,995) (p=0.0343) and ART-treated ($60,608 SE=6,351) (p=0.031), as well as in the 1,501–2,500 gram and >2,500 gram populations. For the 1,501–2,500 gram strata, the adjusted cost was higher in the fertile group ($9,368 SE=491) compared to subfertile ($8,073 SE=685) (p=0.0325) and ART-treated ($8,261 SE=595) groups (p=0.018). Conversely, the 2,501 gram strata had higher costs in the ART-treated compared to fertile and subfertile groups (Table 5).

Discussion

Among this sample of singletons born between 2004 and 2010 in Massachusetts, the overall unadjusted LOS and costs were highest for the ART-treated group, followed by subfertile and then fertile group. Although the differences between the three groups were minimized when stratified by gestational age and birthweight, some statistically significant differences remained in the LOS and the cost of care during the birth hospitalization when adjusted for known confounders in offspring of mothers of the different fertility groups (fertile, subfertile, ART-treated). With the exception of the birthweight strata of 1,001 to 1,500 grams, those statistical differences were typically observed in older (≥37 weeks) and larger

(>1,501 grams) infants. The relationship in LOS and costs of those sub-populations where there were statistical differences observed did not consistently follow the hypothesized pattern where the cost of the subfertile and ART-treated offspring would be higher than those of fertile mothers. Furthermore, the relationship did not disappear despite adjustment for known co-variates of infant LOS and costs such as gestational diabetes and hypertension and mode of delivery. Regardless of the adjusted values, the unadjusted values are the actual resources spent on this patient population and are on average higher (i.e. ART-treated greater than subfertile, which is greater than fertile groups). That increase appears to result from the increased comorbidities of the mothers and complexity of the pregnancies, leading to increased risk of low birthweight, preterm birth, as well as other infant outcomes driving the costs of care (21).

Although findings are supported by the general knowledge that gestational age and birthweight are two of the largest drivers of the birth hospitalization (22), there have been reports in the literature that singletons born via ART compared with non-ART singletons are associated with a longer LOS during the birth hospitalization and larger costs related to hospitalization from birth through the first five years of life, largely driven by the birth hospitalization, even when adjusted for gestational age and birthweight (23). The different findings between our study and those by Chambers et al (23) are likely driven by their using gestational age and birthweight categories as co-variates in the model rather than stratifying the results, as was done in our work. In addition, we adjusted for pre-existing maternal diabetes and hypertension which were more prevalent in the subfertile and ART-treated groups than in the fertile group. We also adjusted for infant gender and stratified the groups into three categories (fertile, subfertile and ART), as opposed to ART vs. non-ART alone.

MOSART is a unique data source as it capitalizes on state and national data sources, as well as maternal-infant linkage and costs, and successfully links them together in order to study outcomes based on maternal infertility and fertility treatment. This population-wide approach limits the selection bias of other observational and case control studies by being inclusive of all resident births in the state of MA. Moreover, inclusion of all MA births allows for greater statistical power to find subtle differences in outcomes based on maternal fertility group that can be limited by the sample size.

Although the main findings from our analyses demonstrate some differences in LOS and costs, they do not necessarily follow the previously expected pattern of ART infants accumulating higher resources, at least in singleton deliveries. The LOS difference in the higher gestational age strata is not clinically significant, although the cost differences could be considerable given that ≥37 weeks represents the highest proportion of births. Previously published work in an Australian population where the cost of a birth admission of ART compared to non-ART population was higher, was driven by higher incidence of low birthweight and very low birthweight in that subgroup (11). Nevertheless, both the Australian population study (11) and a smaller regional US based group of patients with ART (8) included twins and higher order multiples who had incurred higher costs. Despite the large sample size, in particular in the older gestational and birthweight strata, our results do not follow the same pattern at all gestational ages. Of note, the observed differences in both the LOS and costs in the 1,001–1,500 gram birthweight strata are likely explained by the small numbers in the subfertile (n=22) and ART (n=70) groups.

Despite the comprehensive nature of MOSART, we note some limitations in our analysis. First, the generalizability of our data has to be taken in the context of MA population, where infertility treatment has had some degree of mandated insurance coverage as compared to other states, which may affect clinical practice (24). However, the advantage of using MOSART allows capturing both the racial and economic diversity within this population. Second, the cost accounting system only captures the hospital costs and not the professional fees. Although the professional fees are not insignificant in sum, they typically represent less than ten percent of the total hospital costs (25, 26) and would be unlikely to minimize the cost difference between the three groups. Furthermore, the professional fees would not affect the LOS outcome, which would be potentially more appealing for stakeholders in a different healthcare system, for example in a different non-insurance mandated state. Lastly, this dataset was limited to only singleton births. It has been previously shown that twins and higher order multiples have increased health care utilization in the first five years of life (27), and we wanted to isolate any potential findings as related to maternal fertility group in singletons, limiting the confounding of multiples despite the fact that these occur in higher numbers in the subfertile and ART-treated groups.

In conclusion, maternal fertility, subfertility or ART treatment were not independent predictors of infant LOS or costs during the birth hospitalization after adjustment for other potential confounders and stratified by GA and BW in singleton pregnancies in this patient population. Prematurity and birthweight remain the predominant inverse correlates of LOS and cost, and are thus two of the most heavily weighted factors for birth hospitalization resource utilization in a newborn. Despite that adjustment, since ART and subfertility are associated with increased prematurity and low birthweight, the actual costs of care will remain higher in these groups. Furthermore, the effects of maternal fertility group on resource utilization and downstream costs in the offspring may require a longer time horizon to understand the complete economic impact of fertility group as hinted by previous work demonstrating higher odds of early intervention enrollment in ART-treated and subfertile groups compared to the fertile group (28). Future work will be needed to assess the associated healthcare costs of the offspring born to mothers of different fertility groups beyond infancy and into later childhood.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ART	assisted reproductive technology
LOS	Length of Stay
MOSART	Massachusetts Outcome Study of Assisted Reproductive Technology
PELL	Pregnancy to Early Life Longitudinal
SART CORS	Society for Assisted Reproductive Technology Clinic Outcome Reporting System

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Table 1:

Maternal and Infant Characteristics

Demographic Characteristic		Total	Fertile	Subfertile	ART
Total N		**345756**	**332481**	**4987**	**8288**
Percent		**%**	**%**	**%**	**%**
Age *	18–29	48.2	49.7	13.7	8.8
	30–34	30.2	30.2	33.5	32.1
	35–37	12.4	11.9	24.8	24.2
	38–40	6.5	6	17.6	19.6
	41–42	1.8	1.6	6.6	8.5
	43+	0.9	0.7	3.8	6.7
Race/Ethnicity *	Hispanic	14	14.4	5.1	3.6
	Non-Hispanic White	66.7	66	82.5	84.1
	Non-Hispanic Black	8.8	9	3.8	3.2
	Non-Hispanic Asian	8.2	8.2	7.4	7.9
	Other Non-Hispanic	2.3	2.3	1.2	1.1
Education *	< HS/HS graduate	36.2	37.2	12.8	10
	Some college	22.2	22.4	17.8	16.1
	College graduate	41.6	40.4	69.4	73.9
Insurance at delivery [1]*	Private	58.8	57.4	90.2	95.4
	Public	40.4	41.8	9	3.4
	Self-pay	0.8	0.8	0.8	1.2
Non-gestational diabetes *	No	98.8	98.8	98.1	97.9
	Yes	1.2	1.2	1.9	2.1
Chronic hypertension *	No	98.2	98.3	97.1	96.8
	Yes	1.8	1.7	2.9	3.2
Parity *	1	57.4	56.9	58.8	74.9
	2	26.7	26.8	28.2	19.5
	3+	16	16.3	13	5.6
Method of Delivery *	Vaginal	66.9	67.4	55.5	53.5
	VBAC	1.5	1.5	1.9	0.8
	Primary CS	21.8	21.4	29.2	37.1
	Repeated CS	9.8	9.7	13.4	8.6
Year of birth *	2004	10.2	10.3	14.3	5.2
	2005	19.7	19.7	22	17.7
	2006	17.7	17.7	19.6	17
	2007	15.3	15.3	13.5	16.2
	2008	13.5	13.5	11.2	14
	2009	12.2	12.2	10	13.9
	2010	11.3	11.2	9.4	16

Demographic Characteristic		Total	Fertile	Subfertile	ART
Infant Characteristics					
Infant Sex^	Male	51.2	51.2	51	51.4
	Female	48.8	48.8	49	48.6
Gestational Age (weeks) *	Overall[2]	39.01 (1.76)	39.02 (1.74)	38.80 (1.89)	38.67 (2.10)
	23–27 weeks	0.2	0.2	0.3	0.5
	28–33 weeks	1.2	1.2	1.7	2.4
	34–36 weeks	4.8	4.8	6.1	7.5
	37–38 weeks	21	20.8	24.9	23.7
	≥39 weeks	72.7	73	66.9	66
Birthweight (grams) *	Overall[2]	3352 (543)	3354 (541)	3360 (572)	3305 (591)
	≤1,000 grams	0.3	0.3	0.4	0.5
	1,001–1,500 grams	0.4	0.4	0.4	0.8
	1,501–2,500 grams	4.8	4.7	5.7	6.3
	≥2,501 grams	94.5	94.6	93.5	92.3

[1] Public is a composite of Free care and Public

[2] Mean and Standard Deviation

* Denotes statistical significance at P<0.0001 (for characteristics with more than two strata, the test for significance is across the entire characteristic and not for each strata;

^ p=0.96

VBAC = Vaginal Birth After Cesarean; CS = Cesarean Section

Table 2:

Unadjusted Length of Stay (Days) Stratified by Gestational Age and Birthweight

		TOTAL	FERTILE (F)	SUBFERTILE (S)	ART (A)	P-value S vs F	P-value A vs F	P-value A vs S	Overall P-value
		N=345,756	**N= 332,481**	**N = 4,987**	**N = 8,288**				
Overall	Mean (SE) median (IQR)	3.83 (0.01) 2 (2, 4)	3.79 (0.01) 2 (2, 4)	4.32 (0.05) 3 (2, 4)	4.90 (0.04) 3 (2, 4)	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Gestational Age									
23–27 wks	N (kids) Mean (SE) median (IQR)	792 98.60 (1.24) 95 (76, 115)	739 98.40 (1.23) 94 (76, 115)	15 101.67 (8.94) 98 (83, 116)	38 101.32 (5.60) 100 (89, 122)	0.71	0.61	0.97	0.82
28–33 wks	N (kids) Mean (SE) median (IQR)	4210 36.62 (0.37) 31 (20, 47)	3925 36.53 (0.34) 31 (20, 47)	87 36.24 (2.26) 28 (19, 46)	198 38.76 (1.60) 34 (21, 49)	0.90	0.16	0.37	0.36
34–36 wks	N (kids) Mean (SE) median (IQR)	16760 7.26 (0.08) 4 (2, 9)	15836 7.25 (0.05) 4 (2, 9)	305 6.78 (0.33) 4 (3, 8)	619 7.68 (0.26) 5 (3, 10)	0.18	0.1	**0.037**	0.097
37–38 wks	N (kids) Mean (SE) median (IQR)	72491 3.28 (0.02) 2 (2, 4)	69285 3.27 (0.01) 2 (2, 4)	1242 3.47 (0.06) 3 (2, 4)	1964 3.41 (0.05) 3 (2, 4)	**0.0004**	**0.0025**	0.37	**<0.0001**
≥39 wks	N (kids) Mean (SE) median (IQR)	251503 2.91 (0.01) 2 (2, 4)	242696 2.90 (0.00) 2 (2, 4)	3338 3.13 (0.03) 3 (2, 4)	5469 3.22 (0.02) 3 (2, 4)	**<0.0001**	**<0.0001**	**0.012**	**<0.0001**
Birthweight									
≤1000 g	N (kids) Mean (SE) median (IQR)	919 94.87 (1.18) 91 (71, 112)	860 94.41 (1.16) 90 (70, 112)	18 99.00 (8.40) 96 (83, 106)	41 102.68 (5.77) 101 (89, 122)	0.58	0.14	0.72	0.29
1001–1500 g	N (kids) Mean (SE) median (IQR)	1458 50.56 (0.67) 46 (34, 61)	1366 50.44 (0.60) 46 (34, 61)	22 52.45 (4.89) 47 (28, 76)	70 52.27 (2.73) 49 (37, 64)	0.68	0.51	0.97	0.74
1501–2500 g	N (kids) Mean (SE) median (IQR)	16579 10.54 (0.11) 5 (2, 14)	15770 10.44 (0.08) 5 (2, 14)	285 12.05 (0.70) 6 (4, 17)	524 12.80 (0.55) 7 (4, 17)	**0.014**	**<.0001**	0.40	**<.0001**
≥2501 g	N (kids) Mean (SE) median (IQR)	326800 3.02 (0.01) 2 (2, 4)	314485 3.01 (0.00) 2 (2, 4)	4662 3.25 (0.03) 3 (2, 4)	7653 3.40 (0.02) 3 (2, 4)	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**

Mean length of stay (days) and Standard Error (SE) represent the unadjusted model using gamma distribution; IQR (Interquartile Range)

Table 3:

Adjusted Length of Stay (Days) Stratified by Gestational Age and Birthweight

	FERTILE (F)	SUBFERTILE (S)	ART (A)	P-value S vs F	P-value A vs F	P-value A vs S	Overall P-value
Overall	4.19 (0.03)	4.20 (0.04)	4.17 (0.03)	0.69	0.46	0.42	0.69
Gestational Age							
23–27 wks	97.38 (5.31)	99.64 (9.79)	96.14 (6.94)	0.78	0.81	0.70	0.93
28–33 wks	36.72 (1.16)	38.07 (2.07)	38.08 (1.66)	0.45	0.26	0.99	0.42
34–36 wks	7.38 (0.23)	7.04 (0.36)	7.38 (0.31)	0.27	0.98	0.36	0.54
37–38 wks	4.11 (0.05)	4.16 (0.08)	3.96 (0.07)	0.35	**0.0023**	**0.0067**	**0.0057**
≥39 wks	3.82 (0.03)	3.88 (0.04)	3.88 (0.04)	**0.018**	**0.0048**	0.93	**0.0015**
Birthweight							
≤1000 g	94.53 (4.78)	99.80 (9.07)	95.89 (6.58)	0.49	0.79	0.66	0.77
1001–1500 g	49.95 (2.48)	61.47 (5.59)	49.21 (3.23)	**0.011**	0.75	**0.015**	**0.029**
1501–2500 g	8.78 (0.30)	8.60 (0.48)	8.25 (0.38)	0.65	0.072	0.45	0.19
≥2501 g	3.93 (0.02)	3.95 (0.04)	3.97 (0.03)	0.43	0.082	0.63	0.17

Least Square Mean (Standard Error) using Gamma Distribution, adjusted for maternal age, race, education, payer (self pay, private, public), pre-existing diabetes and hypertension, parity, gender, gestational age (continuous), birth year, method of delivery, mother's prolonged stay, gestational diabetes and hypertension.

Table 4:

Unadjusted Cost (US Dollars) Stratified by Gestational Age and Birthweight

		TOTAL	FERTILE (F)	SUBFERTILE (S)	ART (A)	P-value S vs F	P-value A vs F	P-value A vs S	Overall P-value
		N=345,756	**N= 332,481**	**N = 4,987**	**N = 8,288**				
Overall	Mean (SE) median (IQR)	3,021 (27) 1,011 (676, 1599)	2,980 (6) 1,005 (671, 1589)	3,271 (58) 1,051 (703, 1675)	4,483 (62) 1,252 (834, 1973)	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
Gestational Age									
23–27 wks	N (kids) Mean (SE) median (IQR)	792 186,789 (4140) 158,857 (107179, 237725)	739 187,987 (3791) 159,225 (107581, 238337)	15 157,306 (22267) 138,217 (100437, 226065)	38 175,141 (15576) 145,565 (95207, 222134)	0.21	0.44	0.52	0.37
28–33 wks	N (kids) Mean (SE) median (IQR)	4210 49,855(801) 33,445 (18822, 62101)	3925 49,778 (653) 33,398 (18822, 61802)	87 42,990 (3789) 29,239 (18186, 52743)	198 54,404 (3178) 34,858 (19719, 72518)	0.1	0.14	**0.026**	0.082
34–36 wks	N (kids) Mean (SE) median (IQR)	16760 7,559 (165) 2,027 (986, 7776)	15836 7,540 (77) 2,000 (975, 7730)	305 6,396 (469) 2,269 (1121, 6712)	619 8,610 (443) 2,453 (1284, 9151)	**0.026**	**0.012**	**0.0009**	**0.003**
37–38 wks	N (kids) Mean (SE) median (IQR)	72491 2,036 (35) 984 (659, 1543)	69285 2,038 (8) 977 (655, 1534)	1242 2,078 (61) 1,029 (689, 1560)	1964 1,932 (45) 1,223 (797, 1811)	0.52	**0.025**	0.054	0.066
≥39 wks	N (kids) Mean (SE) median (IQR)	251503 1,639 (16) 977 (664, 1503)	242696 1,632 (3) 972 (661, 1496)	3338 1,702 (27) 996 (679, 1539)	5469 1,938 (24) 1,178 (807, 1755)	**0.0076**	**<0.0001**	**<0.0001**	**<0.0001**
Birthweight									
≤1000 g	N (kids) Mean (SE) median (IQR)	919 178,605 (3799) 148,682 (100769, 226913)	860 179,030 (3516) 148,734 (101607, 227824)	18 148,398 (20147) 127,062 (89687, 202262)	41 182,955 (16458) 169,998 (110765, 222134)	0.17	0.81	0.20	0.40
1001–1500 g	N (kids) Mean (SE) median (IQR)	1458 72,615 (1576) 57,268 (35781, 91955)	1366 72,361 (1320) 56,827 (35855, 91948)	22 74,065 (10648) 55,428 (39791, 86220)	70 77,123 (6216) 63,514 (31985, 95168)	0.87	0.44	0.81	0.73
1501–2500 g	N (kids) Mean (SE) median (IQR)	16579 11,930 (209) 2,688 (1078, 13196)	15770 11,804 (127) 2,625 (1069, 12991)	285 12,495 (1002) 4,278 (1317, 16474)	524 15,412 (912) 5,507 (1391, 17872)	0.48	**<0.0001**	**0.035**	**<0.0001**
≥2501 g	N (kids) Mean (SE) median (IQR)	326800 1,764 (15) 983 (664, 1522)	314485 1,755 (3) 977 (660, 1514)	4662 1,812 (25) 1,021 (684, 1568)	7653 2,114 (23) 1,204 (815, 1825)	**0.022**	**<0.0001**	**<0.0001**	**<0.0001**

Mean length of stay (days) and Standard Error (SE) represent the unadjusted model using gamma distribution; IQR (Inter Quartile Range)

Table 5:

Adjusted Cost (US Dollars) Stratified by Gestational Age and Birthweight

	FERTILE (F)	**SUBFERTILE (S)**	**ART (A)**	**P-value S vs F**	**P-value A vs F**	**P-value A vs S**	**Overall P-value**
Overall	2,917 (34)	2,928 (51)	2,953 (45)	0.79	0.24	0.59	0.48
Gestational Age							
23–27 wks	162,581 (13648)	141,621 (21417)	140,848 (15686)	0.28	0.089	0.97	0.16
28–33 wks	49,230 (2351)	46,223 (3834)	50,245 (3322)	0.38	0.68	0.32	0.61
34–36 wks	7,795 (386)	7,240 (586)	7,897 (531)	0.27	0.79	0.28	0.52
37–38 wks	3,120 (75)	3,140 (113)	2,702 (87)	0.82	**<.0001**	**<.0001**	**<.0001**
≥39 wks	2,488 (35)	2,562 (52)	2,689 (48)	**0.045**	**<.0001**	**0.0088**	**<.0001**
Birthweight							
≤1000 g	156,002 (12551)	135,681 (19619)	143,502 (15570)	0.26	0.33	0.70	0.38
1001–1500 g	63,012 (4995)	83,450 (12246)	60,607 (6351)	**0.034**	0.61	**0.031**	0.072
1501–2500 g	9,367 (491)	8,073 (686)	8,261 (595)	**0.033**	**0.018**	0.79	**0.0099**
≥2501 g	2,622 (31)	2,622 (45)	2,734 (42)	0.99	**<.0001**	**0.01**	**0.0002**

Least Square Mean (Standard Error) using Gamma Distribution, adjusted for maternal age, race, education, payer (self pay, private, public), pre-existing diabetes and hypertension, parity, gender,gestational age (continuous), birth year, method of delivery, mother's prolonged stay, gestational diabetes and hypertension.