EDUCATION

Healthcare expenses associated with multiple vs singleton pregnancies in the United States

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OBJECTIVE: The purpose of this study was to document cost that is associated with multiple births vs singleton births in the United States.

STUDY DESIGN: This was a retrospective cohort study that used a claims database. Women 19-45 years old with live-born infants from 2005-2010 were identified. Infant deliveries were identified by *International Classification of Diseases*, 9th Revision, Clinical Modification diagnosis codes. The cost entailed all payment made by insurers and patients. For mothers, the cost included expenses from 27 weeks before delivery to 1 month after delivery. For infants, the cost contained all expenses until their first birthday. Adjusted cost was estimated by generalized linear models after adjustment for the potential confounding variables with a gamma distribution and a log link.

RESULTS: The analysis included 437,924 eligible deliveries. Of them, 97.02% were singletons; 2.85% were twins, and 0.13% was triplets or more. Women with multiple pregnancies had higher systemic and localized comorbidities compared with women with singleton pregnancies ($P < .0001$). Twins and triplets or more were more likely to have stayed in a neonatal intensive care unit than were singletons ($P < .0001$). On average, adjusted total all-cause health care cost was $21,458 (95% confidence interval [CI], $21,302—21,614) per delivery with singletons, $104,831 (95% CI, $103,402—106,280) with twins, and $407,199 (95% CI, $384,984—430,695) with triplets or more.

CONCLUSION: Pregnancies with the delivery of twins cost approximately 5 times as much when compared with singleton pregnancies; pregnancies with delivery of triplets or more cost nearly 20 times as much.

Key words: cost, multiple pregnancy, triplets, twins

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Multiple pregnancies have been a major public health concern in the United States and the rest of the world because of the significantly high morbidity and mortality rates for both mothers and infants and increased health care cost.[1-3] The prevalence of multiple pregnancies is increasing worldwide in parallel with increased use of assisted reproductive technology (ART).[3-5] According to the Centers for Disease Control and Prevention, 3% of all infants

★ EDITORS' CHOICE ★

born in the United States were multiple deliveries in 2010; the twin birth rate was 33.1 per 1000 total births, and the rate of triplets and higher-order multiple births was 1.4 per 1000 births.[4] Accurate estimates of the relative proportions of multiple births that are attributable to ovulation induction or super ovulation and ART are difficult to determine, because ovulation induction/super ovulation cycles currently are not captured in a national registry. Nevertheless, there is consensus that most twin births result from natural conception (approximately 60%). For high-order multiple gestations, however, there is agreement that only approximately 20% result from natural conception.[6]

There is a paucity of data in the literature that documents health care expenditures associated with multiple pregnancies. Callahan et al[7] determined hospital charges and the use of ARTs in their hospital and showed that the total charges to the family in 1991 for a singleton delivery were $9845, compared with $37,947 for twins and $109,765 for triplets. Ettner et al[8] investigated factors associated with high cost of multiple pregnancies and revealed that birthweight and gestational age accounted fully for the increased use of neonatal intensive care unit (NICU) services among multiples. Bromer et al[3] modeled the financial burden of preterm birth in the United States as a consequence of ART use and estimated that total annual cost amounted to 1 billion US dollars.

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Although the cost associated with multiple pregnancies is expected to be significant, there has been no update in the literature on the economic impact of multiple pregnancies in the United States in recent years. The aim of our study was to document and compare cost that is associated with multiple pregnancies vs singleton pregnancies in the United States.

MATERIALS AND METHODS

Data source

We investigated the cost that is associated with multiple vs singleton pregnancies by analyzing the MarketScan database (Truven Health Analytics Inc, Ann Arbor, MI), which is a commercial claims and encounters database. The database contains deidentified, member-specific health data that includes clinical use, costs, and enrollment across inpatient, outpatient, and prescription drugs. The data cover >20 million individuals with employer-sponsored benefits annually, including private sector claims data from approximately 100 payers and can be linked to track detailed patient information across geographic location, types of providers, and time.

Patients and study variable measurements

The source population included all women 19-45 years old who delivered at least 1 live-born infant; the delivery types were reported (singleton, twins, triplets or more) between Jan. 1, 2005, and Sept. 30, 2010. We included only women who had continuous enrollment for at least 1 year both before and after the delivery date. Deliveries of singletons, twins, and triplets or more were identified with the use of the *International Classification of Diseases*, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes. The presence of comorbidities during pregnancy was tabulated based on ICD-9-CM diagnosis codes during the last 27 weeks of a pregnancy, which was expected to reflect the second and third trimesters of a full-term delivery. Comorbidities were categorized into systemic comorbidities and comorbidities localized to the reproductive tract.[9,10] Systemic comorbidities included hypertension, cardiovascular disease, diabetes mellitus, edema/renal disease, genitourinary infection, thyroid disease and anemia; localized comorbidities included hemorrhage (placental abruption, placenta previa, other), chorioamnionitis, amniotic sac disorders (polyhydramnios, oligohydramnios, unspecified), cervical incompetence, and structural abnormality (uterus/cervix/vagina/vulva). Current Procedure Terminology codes in the previous 42 weeks' gestation (294 days) before the delivery were used to determine whether a mother had received in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) for that pregnancy.

The cost entailed all payments made by insurers and patient out-of-pocket medical expenses, including all-cause payment for inpatient and outpatient services, and prescription drugs. For mothers, the cost included medical expenses during the 27 weeks before the delivery date and up to 30 days after the delivery date. For infants, the cost contained all medical expenses up to their first birthday. Infants were linked with their mother by the family identification number. In addition, their birth year must be the same as the year of the woman's delivery date. Because we could not differentiate between siblings when a mother had >1 live-born delivery because of the database structure, costs for twins or triplets or more were summarized by each delivery. Costs were inflation-normalized to 2010 US dollars using the Consumer Price Index All Urban Consumers for medical care services in accordance with International Society for Pharmacoeconomics and Outcome Research recommendations for working with cost data.[10,9]

Women's age, plan type, and geographic region were based on the values recorded on the delivery date in the database. Plan type was reported by 4 categories: health maintenance organization, point of service, preferred provider organization, and other/unknown. Geographic region was reported as North Central, Northeast, South, West, and unknown. Institutional review board approval was not obtained because this study was an analysis of deidentified secondary data (Appendix; Supplementary Tables 1-4).

Data analysis

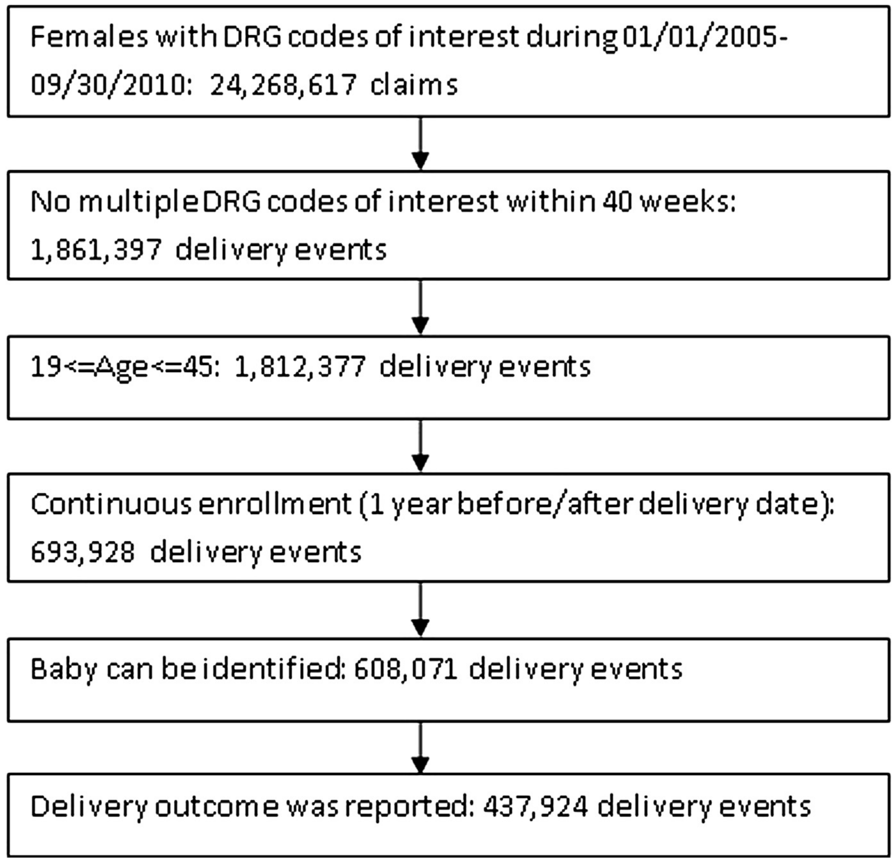
We first examined women's baseline characteristics across delivery types (singleton, twins, triplets or more). For continuous variables, including age, analysis of variance was used. For categoric variables, including year of delivery, IVF/ICSI (yes/no), plan type and region, the Chi-square test was used. Presence of each comorbidity and clinical outcomes such as death, delivery type (vaginal vs cesarean delivery), and NICU stay were compared with the use of bivariate logistic regression for twins vs singletons and triplets or more vs singletons. Continuous clinical outcomes including mothers' length of hospital stay and infants' length of NICU stay were compared with the use of nonparametric Wilcoxon-sum-rank test because of nonnormal distribution.

Because health care expenses may vary by maternal age, year of the delivery, health care plan, and geographic region, we used generalized linear models to adjust for these variables with a gamma distribution and a log link. This approach resolves the issue of skewed cost distribution that is common in claims data.[11] Further, it has been demonstrated that a generalized linear model can provide more robust coefficient estimates than logged ordinary least square regression, where the log transformation is often used to address skewed cost data.[12] A negative binomial distribution and a log link function were performed to test the model. All statistical analyses were performed with SAS software (version 9.2; SAS Institute, Cary, NC).

RESULTS

A total of 437,924 eligible delivery events were identified from January 1, 2005, to September 30, 2010 (Figure; Table 1). Of the eligible deliveries, 424,880 (97.02%) were singletons; 12,482 (2.85%) were twins, and 562 (0.13%) were triplets or more. The frequency of deliveries with singletons, twins; and higher-order multiples was relatively constant over the study period ($P = .0568$). On average, mothers were 31.0 ± 4.6 years old at the delivery, and women who delivered twins or higher-order multiples were approximately 2 years older than their counterparts with singletons ($P < .0001$; Table 2). IVF/ICSI was used in 1.0% of singletons, 16.9% of twins, and 24.7% of higher-order multiple births ($P < .0001$). The most common health plan enrolled was preferred provider organization (61.6%), followed by health maintenance organization (18.3%) and point of service (10.5%). Table 3 shows the presence of comorbidities by delivery multiplicity. Women with twins or higher-order multiples had significantly higher comorbidities in each systemic and localized comorbidity that was examined compared with women who delivered singletons ($P < .0001$); the most prevalent systemic comorbidities were hypertension (24.9% and 27.2%) and diabetes mellitus (19.5% and 17.3%) in contrast to singleton deliveries at 10.8% and 13.6%, respectively. The most common localized comorbidities for women with twins or higher-order multiples were cervical incompetence (10.5% and 22.2%) and hemorrhage (11.0% and 14.2%), compared with singleton deliveries at 2.0% and 8.6%, respectively. Table 4 displays the clinical outcomes by delivery multiplicity. Mothers with twins or triplets or more had a longer hospital stay for delivery and higher mortality rate compared with mothers who delivered singletons ($P < .0001$). For mothers with singletons, 22.0% of deliveries were through cesarean section in contrast to women with twins or higher-order multiples, for whom cesarean section was the dominant delivery modality (79.1% and 96.3%, respectively). Infants of twins or triplets or more were more likely to be admitted to NICU and had a higher mortality rate compared with infants of singletons (47.7% [triplets or more] vs 24.2% [twins] and 2.9% [singletons]; 2.0% [triplets or more] vs 0.5% [twins] and 0.06% [singletons]; all $P < .0001$). Similarly, among those infants who stayed in NICU, twins or triplets or more had longer stay compared with singletons (63.6 [triplets or more] vs 31.1 [twins] and 15.2 [singletons] days; all $P < .0001$).

FIGURE
Flow chart of identification of eligible delivery events



Diagnosis Related Group (*DRG*) = 370, 371, 372, 373, 374, 375 in 2005-2006 or 765, 766, 767, 768, 774, 775 in 2007-2010.

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Table 5 shows the average all-cause health care cost of infants, mothers, and overall by health plan type. All-cause health care cost is significantly different across health plan types. Point of service health plans paid much less for higher-order multiples compared with other health plan types. Table 6 displays the

TABLE 1
The number of eligible delivery events from 2005-2010

Year	Overall, n	Singletons, %	Twins, %	Higher-order multiples, %	*P* value
2005	50,513	97.00	2.87	0.17	.0568[a]
2006	54,549	96.90	2.96	0.15	
2007	84,955	97.02	2.87	0.11	
2008	97,973	97.15	2.74	0.12	
2009	88,147	97.05	2.84	0.11	
2010[b]	61,787	96.96	2.91	0.13	
Total	437,924	97.02	2.85	0.13	

[a] χ^2 test; [b] To September.

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TABLE 2
Baseline characteristics of mothers

Characteristic	Overall	Singletons	Twins	Higher-order multiples	*P* value
Age, y[a]	31.0 ± 4.6	31.0 ± 4.6	32.8 ± 4.8	33.2 ± 4.6	< .0001[b]
Plan type, n (%)					.0043[c]
Health maintenance organization	79,960 (18.3)	77,711 (18.3)	2133 (17.1)	116 (20.6)	
Point of service	45,765 (10.5)	44,365 (10.4)	1351 (10.8)	49 (8.7)	
Preferred provider organization	269,838 (61.6)	261,770 (61.6)	7732 (62.0)	336 (59.8)	
Other/unknown	42,361 (9.7)	41,034 (9.7)	1266 (10.1)	61 (10.9)	
Region, n (%)					< .0001[c]
North Central	112,987 (25.8)	109,583 (25.8)	3237 (25.9)	167 (29.7)	
Northeast	47,864 (10.9)	46,228 (10.9)	1566 (12.6)	70 (12.5)	
South	205,816 (47.0)	199,836 (47.0)	5738 (46.0)	242 (43.1)	
West	69,789 (15.9)	67,809 (16.0)	1899 (15.2)	81 (14.4)	
Unknown	1468 (0.3)	1424 (0.3)	42 (0.3)	2 (0.4)	
In vitro fertilization, n (%)	6589 (1.5)	4342 (1.0)	2108 (16.9)	139 (24.7)	< .0001[c]

[a] Data are given as mean ± SD; [b] Analysis of variance test; [c] χ^2 test.

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mean health care expenses and their 95% CIs for infant, mother, and overall after the adjustment of maternal age, year of delivery, health plan, and geographic region. The expenses for maternal and infant care were significantly higher for known IVF/ICSI-conceived infants compared with other pregnancies for both singletons and twins. This pattern was also observed for high-order multiples; however, the difference was not statistically significant between known IVF/ICSI-conceived infants and other pregnancies. On average, for singleton deliveries, the combined all-cause health care expense from the second trimester to 30 days after the delivery for mothers and up to the first birthday for infants was $21,458 (95% confidence interval [CI], $21,302—21,614) compared with twins at $104,831 (95% CI, $103,402—106,280) and higher-order multiple births at $407,199 (95% CI, $384,984—430,695).

Comment

This study shows substantially increased health care expenses that are associated with twins and higher-order multiple births from the maternal second trimester to 30 days after the delivery for mothers and up to the first birthday for infants. On average, combined all-cause health care expenses for mothers with twins or higher-order multiple births were approximately 5 and 20 times more expensive compared with singleton delivery, respectively. The greater expenses were likely attributable to both increased systemic and localized comorbidities, nearly exclusive use of cesarean delivery and longer stay in hospitals for the deliveries in women with multiple pregnancies, and increased admission and longer stay in NICU for twins and higher-order multiple neonates. Furthermore, we also demonstrated increased mortality rates for both mothers and infants that were associated with multiple pregnancies, although the absolute rates were small.

To our knowledge, this is the first study to take into account a comprehensive assessment of the incremental cost that is associated with multiple pregnancies by estimating all-cause medical expenses from the second trimester to 30 days after the delivery for mothers and up to the first birthday for infants. This is in contrast to earlier studies that had a narrower scope by tabulating only hospital charges that were associated with neonatal deliveries or exclusive inpatient service use between birth and 5 years old.[7,13] By taking a broad approach, we have shown that medical expenses attributable to mothers and infants varied according to birth multiplicity. For singleton pregnancy, maternal expenses accounted for approximately 60% of overall cost, whereas, for twins or higher-order multiple births, expenses for infant care accounted for approximately 70% and 85% of total expenses, respectively. This is also the first study to report increased medical expenses for both mother and infant care that is associated with IVF-assisted pregnancy. The finding of greater infant care expenses in IVF-assisted pregnancy is consistent with early research, which showed that singleton pregnancies from assisted reproduction had significantly worse perinatal outcomes that included preterm delivery, lower birthweight, cesarean delivery, and admission to NICU than nonassisted singleton pregnancies, but this is less so for twin pregnancies.[13] Increased maternal medical expenses among known IVF/ICSI-conceived infants are likely attributable to more frequent use of cesarean delivery and increased monitoring of pregnancy complications as a result of

TABLE 3
Presence of maternal comorbidities by multiplicity

Variable	Pregnancy, % Overall (n = 437,924)	Singleton (n = 424,880)	Twins (n = 12,482)	Higher-order multiples (n = 562)	Odds ratio (95% CI)[a] Twins vs singleton	Higher-order multiples vs singleton
Systemic comorbidity						
Hypertension	11.2	10.8	24.9	27.2	2.8 (2.6–2.9)	3.1 (2.6–3.7)
Cardiovascular disease	1	1	1.3	2	1.4 (1.2–1.6)	2.1 (1.1–3.8)
Diabetes mellitus	13.8	13.6	19.5	17.3	1.5 (1.5–1.6)	1.3 (1.1–1.7)
Edema/renal disease	2.1	2.1	3.2	3.6	1.6 (1.4–1.8)	1.8 (1.1–2.8)
Genitourinary infection	4.4	4.4	6	7.5	1.4 (1.3–1.5)	1.8 (1.3–2.4)
Thyroid disease	2.7	2.7	4	6.2	1.5 (1.4–1.7)	2.4 (1.7–3.4)
Anemia	4.8	4.7	8.4	9.3	1.9 (1.8–2.0)	2.1 (1.6–2.8)
Localized comorbidity						
Hemorrhage	8.7	8.6	11	14.2	1.3 (1.2–1.4)	1.7 (1.4–2.2)
Chorioamnionitis	1.5	1.5	2.1	2.9	1.4 (1.3–1.6)	1.9 (1.2–3.2)
Amniotic sac disorder	6.2	6.1	9.3	8.7	1.6 (1.5–1.7)	1.5 (1.1–2.0)
Cervical incompetence	2.2	2	10.5	22.2	5.9 (5.5–6.3)	14.4 (11.8–17.5)
Structural abnormality	4.7	4.5	9.3	14.8	2.2 (2.0–2.3)	3.7 (2.9–4.6)

CI, confidence interval.

[a] Bivariate logistic regression: probability values are all < .0001.

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the presence of comorbidities. Presence of certain risk factors, which have been implicated as cause of infertility in some women (eg, smoking and obesity) may also contribute to the increased maternal medical care expenses.[14,15]

The incremental medical expenses that are associated with multiple births in our study were higher than the early study in terms of both absolute amount and relative percentage when compared with singleton delivery. Ettner et al[8] found that

TABLE 4
Maternal and infant clinical outcomes by multiplicity

Clinical outcome	Pregnancy Singleton (n = 424,880)	Twins (n = 12,482)	Higher-order multiples (n = 562)	Odds ratio (95% CI)/*P* value[a] Twins vs singleton	Higher-order multiples vs singleton
Maternal					
Death, %	0.007	0.024	0.18	3.5 (1.1–11.6)	26.1 (3.6–192.0)
Cesarean delivery, %	22.0	79.1	96.3	13.5 (12.9–14.1)	91.6 (59.2–141.6)
Length of hospital stay, d[b]	3.3 ± 1.8	6.2 ± 8.5	13.4 ± 17.7	< .0001[c]	< .0001[c]
Infant					
Death, %	0.06	0.5	2	8.5 (6.4–11.1)	33.2 (18.1–61.1)
Intensive care admission, %	2.9	24.2	47.7	10.9 (10.4–11.4)	31.1 (26.3–36.7)
Length of intensive care unit stay, d[b]	15.2 ± 22.6	31.1 ± 37.4	63.6 ± 57.5	< .0001[c]	< .0001[c]

CI, confidence interval.

[a] Bivariate logistic regression: probability values are all < .0001; [b] Data are given as mean ± SD; [c] Nonparametric Wilcoxon-sum-rank test.

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TABLE 5
Average all-cause health care cost by health plan type[a]

Health plan type	Pregnancy[a] Singleton	Twins	Higher-order multiples	*P* value[b]
Infant				< .0001
Health maintenance organization	\$8463 ± \$50,505 (\$3497)	\$73,099 ± \$223,573 (\$13,910)	\$329,053 ± \$802,375 (\$95,412)	
Point of service	\$8770 ± \$46,618 (\$3975)	\$71,424 ± \$164,356 (\$17,380)	\$169,802 ± \$202,595 (\$97,856)	
Preferred provider organization	\$8343 ± \$41,617 (\$3731)	\$76,382 ± \$205,039 (\$15,678)	\$369,721 ± \$606,736 (\$162,833)	
Other + unknown	\$9166 ± \$54,877 (\$3874)	\$84,100 ± \$216,943 (\$16,446)	\$388,833 ± \$487,869 (\$235,697)	
Mother				< .0001
Health maintenance organization	\$13,011 ± \$11,774 (\$10,943)	\$31,865 ± \$44,300 (\$21,945)	\$51,743 ± \$84,760 (\$32,651)	
Point of service	\$12,899 ± \$8908 (\$11,113)	\$30,035 ± \$39,540 (\$22,724)	\$48,463 ± \$76,562 (\$32,290)	
Preferred provider organization	\$13,040 ± \$9462 (\$11,208)	\$30,392 ± \$32,984 (\$22,670)	\$64,599 ± \$146,299 (\$37,727)	
Other + unknown	\$13,249 ± \$9451 (\$11,395)	\$29,868 ± \$28,941 (\$23,195)	\$69,169 ± \$91,399 (\$39,693)	
Infant and mother				< .0001
Health maintenance organization	\$21,473 ± \$53,181 (\$15,249)	\$104,964 ± \$234,183 (\$41,182)	\$380,795 ± \$808,040 (\$169,679)	
Point of service	\$21,669 ± \$48,318 (\$15,867)	\$101,459 ± \$186,402 (\$46,387)	\$218,264 ± \$214,078 (\$146,600)	
Preferred provider organization	\$21,383 ± \$43,595 (\$15,688)	\$106,774 ± \$212,813 (\$44,494)	\$434,320 ± \$648,774 (\$216,003)	
Other + unknown	\$22,415 ± \$56,416 (\$15,965)	\$113,968 ± \$224,818 (\$44,148)	\$458,002 ± \$510,117 (\$301,716)	

[a] Data are given as mean ± SD (median); [b] Two-way analysis of variance test.

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the cost for twins and higher-order multiple birth was approximately 4 and 9 times greater comparing singleton deliveries in 1991. This may be because our broader scope measures medical expenses by including both maternal prenatal care and health care services for infants until their first birthday. We did not include health care expenses beyond the first full year for infants because, although multiple births were associated with increased hospital costs in the first 5 years of life, the cost differences are concentrated in the first year of life.[16]

Over the past 30 years, the birth rate of twins has increased by 76%, and the birth rate of triplets or higher-order birth rate has almost quadrupled from 37.0-137.6 per 100,000 infants delivered in 2010.[4] Much of such an increase is the consequence of greater use of ARTs, which first were used successfully in the United States in 1981, to overcome the problem of infertility. In 2009, a total of 60,190 infants were born as a result of use of ARTs. Although infants conceived with ART accounted for 1.4 % of US births, 47% of those infants were born as multiple-birth infants, compared with only 3% of infants among the general birth population.[1] In evaluating economic impact of multiple-gestation pregnancies and the contribution of ARTs to their incidence, Callahan et al[7] documented that ARTs were used in 2% of singletons, 35% of twins, and 77% of higher-order multiple-gestation pregnancies in their hospital. Although significantly higher use of ARTs in mothers with multiple pregnancy births was also observed in our study, the use of ARTs was underestimated in our study because reimbursement of ARTs was limited or not covered at all in many health plans in the United States.

The findings of our study have broad health care policy implications. For women who undergo IVF treatment for infertility, the risk of multiple pregnancies nearly entirely is due to multiple embryos transfer. Nationally, the average number of embryos transferred varied from 2.1 among women who were <35 years old to 2.5 among women who were 35-40 years old, and 3.0 among women who were >40 years old in 2009. In women with the best pregnancy prospects (eg, <35 years old), elective single embryo transfer was used in only 7.4% of all IVF procedures that were performed.[17] In the United States, most IVF treatment is funded out of pocket by patients, which on average amounts to 25% of annual family income per treatment cycle.[18] There is an enormous economic incentive for patients to pay for the fewest cycles. The idea of 2 babies

TABLE 6
Adjusted all-cause health care cost by multiplicity

Variable	Pregnancy[a] Singleton	Twins	Higher-order multiples
Infant			
In vitro fertilization or intracytoplasmic sperm injection	$11,358 ($10,959—11,772)	$81,757 ($77,785—85,932)	$376,622 ($311,947—454,704)
Others	$8300 ($8199—8402)	$72,995 ($71,214—74,821)	$334,942 ($300,516—373,313)
All infants	$8327 ($8226—8430)	$74,369 ($72,673—76,106)	$344,822 ($313,787—378,927)
Mother			
In vitro fertilization or intracytoplasmic sperm injection	$15,542 ($15,322—15,765)	$33,729 ($33,066—34,405)	$61,541 ($57,090—66,339)
Others	$13,084 ($13,020—13,148)	$29,335 ($29,047—29,625)	$59,711 ($57,185—62,349)
All mothers	$13,102 ($13,039—13,167)	$30,043 ($29,767—30,320)	$60,089 ($57,871—62,391)
Infant and mother			
In vitro fertilization or intracytoplasmic sperm injection	$26,922 ($26,354—27,501)	$115,238 ($111,875—118,702)	$434,668 ($388,595—486,204)
Others	$21,412 ($21,257—21,569)	$102,865 ($101,364—104,388)	$398,763 ($373,854—425,331)
All infants and mothers	$21,458 ($21,302—21,614)	$104,831 ($103,402—106,280)	$407,199 ($384,984—430,695)

[a] Data are given as mean (95% confidence interval).

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for the price of 1 appears to be an attractive proposition. Even after being educated on the complications that can arise with a multiple pregnancy, as many as 85% of childless women in fertility clinics wanted twins.[19] The third-party payers' decision for not covering ARTs is, unfortunately, a short-sighted benefit coverage policy because the savings from limiting ARTs are offset and, perhaps exceeded by the cost of multiple pregnancies. Given that multiple birth is an undesirable outcome because of the health risks that are involved and the vastly higher medical and social costs compared with singletons, a strategy of government funding of ART with a concomitant transfer of fewer embryos has been adopted in many European countries. In countries in which ART is funded, there has been a corresponding reduction in the rate of multiple births by at least 50%.[20,21] In addressing the epidemic of multiple births that resulted from ARTs, the government of Quebec has adopted a new IVF reimbursement policy with restrictions of the number of embryos transferred since July 2010. The preliminary results from this program show a frequency of twin gestation of only 3.8% compared with 32% multiple birth rates across Canada before the program was implemented.[5]

Several limitations of this study are worth noting. First, the classification of singletons, twins, or higher-order multiples was based on ICD-9-CM diagnosis codes. Coding inaccuracies may lead to misclassification of the delivery outcome. Second, we acknowledge that the use of IVF/ICSI is underestimated because those procedures entirely self-financed by patients would be missing from this electronic claims database. However, the Truven Health MarketScan database is composed primarily of large employers in the United States, which tend to have more generous health benefit coverage than smaller employers or organizations. Despite the lack of complete documentation of IVF/ICSI use, we still found that medical care expenses that are associated with known IVF/ICSI-conceived infants were significantly higher than pregnancies that were achieved through other means for singletons and twins, respectively. Furthermore, the absence of complete IVF/ICSI use data does not invalidate the results of our study, because our primary objective was to document incremental medical expenses that were attributable to multiple pregnancies rather than net cost explainable by the use of IVF/ICSI. Third, the incremental medical expenses that are associated with multiple births were estimated per delivery, not per child delivered. Nevertheless, the higher cost that is attributable to multiple gestation pregnancies remains when the cost is estimated per child delivered; the cost per baby delivered for twins or triplets can be estimated at approximately $52,416 and $135,733 per infant, respectively, compared with singleton births at $21,458. Fourth, we did not include all maternal costs because we captured the information only 27 weeks before delivery and excluded costs that were incurred before this (eg, cost associated with IVF/ICSI). Fifth, the costs that are associated with stillborn infants were not considered; however, they would likely represent an additional cost to the delivery of twins or higher-order multiples. Finally, the study was limited to managed care enrollees; thus, the results may not be generalized to the entire US population or to individuals covered by other federal insurance programs (eg, Medicaid, Veterans Affairs).

In conclusion, multiple births are associated with significantly higher morbidity and mortality rates for mothers and infants. Furthermore, they have significant health care expenses impact for payers; pregnancies with the delivery of twins and triplets or more cost approximately 5 and 20 times more than singletons, respectively. Strategies that aim at minimizing multiple embryos transfer should be considered to reduce the burden that is associated with multiple pregnancies. ■

REFERENCES

1. Adashi EY, Barri PN, Berkowitz R, et al. Infertility therapy-associated multiple pregnancies (births): an ongoing epidemic. Reprod Biomed Online 2003;7:515-42.

2. Blondel B, Kogan MD, Alexander GR, et al. The impact of the increasing number of multiple births on the rates of preterm birth and low birthweight: an international study. Am J Public Health 2002;92:1323-30.

3. Bromer JG, Ata B, Seli M, et al. Preterm deliveries that result from multiple pregnancies associated with assisted reproductive technologies in the USA: a cost analysis. Curr Opin Obstet Gynecol 2011;23:168-73.

4. Martin JA, Hamilton BE, Ventura SJ, et al. Births: final data for 2010. Natl Vital Stat Rep 2012;61:1-72.

5. Janvier AB, Spelke B, Barrington KJ. The epidemic of multiple gestations and neonatal intensive care unit use: the cost of irresponsibility. J Pediatr 2011;159:409-13.

6. Practice Committee of American Society for Reproductive Medicine. Multiple gestation associated with infertility therapy: an American Society for Reproductive Medicine Practice Committee opinion. Fertil Steril 2012;97:825-34.

7. Callahan TL, Hall JE, Ettner SL, et al. The economic impact of multiple-gestation pregnancies and the contribution of assisted-reproduction techniques to their incidence. N Engl J Med 1994;331:244-9.

8. Ettner SL, Christiansen CL, Callahan TL, Hall JE. How low birthweight and gestational age contribute to increased inpatient costs for multiple births. Inquiry 1997;34:325-39.

9. Auger N, Nhi Le TU, Park AL, Luo ZC. Association between maternal comorbidity and preterm birth by severity and clinical subtype: retrospective cohort study. BMC Pregnancy Childbirth 2011;11:67.

10. Mullins CD, Seal B, Seoane-Vazquez E, et al. Good research practices for measuring drug costs in cost-effectiveness analyses: Medicare, Medicaid and other US government payers perspectives: the ISPOR Drug Cost Task Force report: part IV. Value Health 2010;13:18-24.

11. Wedderburn RWM. Quasi-likelihood functions, generalized linear models, and the Gauss-Newton method. Biometrika 1974;61:439-47.

12. Manning WG, Mullahy J. Estimating log models: to transform or not to transform? J Health Econ 2001;20:461-94.

13. Helmerhorst FM, Perquin DA, Donker D, Keirse MJ. Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies. BMJ 2004;328:261-4.

14. Augood C, Duckitt K, Templeton AA. Smoking and female infertility: a systematic review and meta-analysis. Hum Reprod 1998;13:1532-9.

15. Practice Committee of the American Society for Reproductive Medicine. Obesity and reproduction: an educational bulletin. Fertil Steril 2008;90:S21-9.

16. Henderson J, Hockley C, Petrou S, Goldacre M, Davidson L. Economic implications of multiple births: inpatient hospital costs in the first 5 years of life. Arch Dis Child Fetal Neonatal Ed 2004;89:F542-5.

17. Centers for Disease Control and Prevention. Assisted reproductive technology surveillance: United States, 2009. MMWR Surveill Summ 2012;61:1-23.

18. Collins JA. An international survey of the health economics of IVF and ICSI. Hum Reprod Update 2002;8:265-77.

19. Pinborg A, Loft A, Schmidt L, Andersen AN. Attitudes of IVF/ICSI-twin mothers towards twins and single embryo transfer. Hum Reprod 2003;18:621-7.

20. Gerris JMR. Single embryo transfer and IVF/ICSI outcome: a balanced appraisal. Hum Reprod Update 2005;11:105-21.

21. Bissonnette F, Cohen J, Collins J, et al. Incidence and complications of multiple gestation in Canada: proceedings of an expert meeting. RBM Online 2007;14:773-90.

APPENDIX

SUPPLEMENTARY TABLE 1
The Diagnosis Related Group codes that were used to identify births

Study years	Codes
2005-2006	370, 371, 372, 373, 374, 375
2007-2010	765, 766, 767, 768, 774, 775

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SUPPLEMENTARY TABLE 2
The *International Classification of Diseases*, 9th Revision, Clinical Modification codes that were used to identify multiple births

Pregnancy	Codes
Singleton	650 or V27.0
Twins	651.0 or V27.2
Triplets or more	651.1, 651.2, 651.8, or V27.5

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SUPPLEMENTARY TABLE 3

The *International Classification of Diseases*, 9th Revision, Clinical Modification codes that were used to identify comorbidities

Comorbidity	Codes
Systemic comorbidity	
Hypertension	642
Cardiovascular disease	648.5, 648.6
Diabetes mellitus	648.0, 648.8
Edema/renal disease	646.1, 646.2
Genitourinary infection	646.6
Thyroid disease	648.1
Anemia	648.2
Other	643, 646.3, 646.4, 646.7-646.9, 647, 648.3, 648.4, 648.7, 648.9
Localized comorbidity	
Hemorrhage	641.0, 641.1, 641.2, 641.3, 641.8, 641.9
Chorioamnionitis	658.4
Amniotic sac	657, 658.0, 658.8, 658.9
Cervical incompetence	654.5
Structural abnormality (uterus/cervix/vagina/vulva)	654.0, 654.1, 654.3, 654.4, 654.6-654.9

Reference.[3]

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SUPPLEMENTARY TABLE 4

The Current Procedure Terminology codes that were used to identify in vitro fertilization

Code	Description
58970	Follicle puncture for oocyte retrieval, any method
58974	Embryo transfer, intrauterine
58976	Gamete, zygote, or embryo intrafallopian transfer, any method
76948	Echo guide ova aspiration
89250	Culture of oocyte(s)/embryo(s), $<$4 days
89251	Culture of oocyte(s)/embryo(s), $<$4 days; with coculture of oocyte(s)/embryos
89253	Assisted embryo hatching, microtechniques (any method)
89254	Oocyte identification from follicular fluid
89255	Preparation of embryo for transfer (any method)
89257	Sperm identification from aspiration (other than seminal fluid)
89258	Cryopreservation; embryo(s)
89259	Cryopreservation; sperm
89260	Sperm isolation; simple prep (eg, sperm wash and swim-up) for insemination or diagnosis with semen analysis
89261	Sperm isolation; complex prep (eg, Percoll gradient, albumin gradient) for insemination or diagnosis with semen analysis
89264	Sperm identification from testis tissue, fresh or cryopreserved
89268	Insemination of oocytes
89272	Extended culture of oocyte(s)/embryo(s), 4-7 days
89280	Assisted oocyte fertilization, microtechnique; $\leq$10 oocytes
89281	Assisted oocyte fertilization, microtechnique; $\geq$10 oocytes

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