

Systematic Literature Review of the Costs of Pregnancy in the US

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Abstract

Background The cost of pregnancy is increasing over time despite the decline in pregnancy rates.

Objective To fully elucidate and evaluate the cost drivers of pregnancy in the US for payers, a systematic review was conducted to understand the main cost components and primary factors that contribute to the direct costs of pregnancy, pregnancy-related complications and unintended pregnancy among women of childbearing age (15–44 years).

Data Sources We performed electronic searches in the PubMed database from January 2000 to December 2012, and major women's health and pharmacoeconomics conference proceedings from 2011 to 2012.

Study Selection The systematic review is comprised of studies that reported pregnancy, pregnancy-related complications, unplanned pregnancy, and pregnancy-induced monetary costs. The review excluded narrative reports, systematic reviews, model-derived cost of pregnancy

papers, non-US-based studies, and reports based solely on expert opinions.

Study Appraisal and Synthesis Methods Two reviewers independently applied the inclusion criteria and assessed the quality of the data collected. Disagreements between reviewers were resolved by consensus or by arbitration through a third party, with reference to the original sources. We collected information on the study design and outcomes for each included study. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines in designing, performing, and reporting of the systematic review.

Results We identified 40 studies from electronic and handsearching methods. We classified studies based on the primary research topic focusing on the overall cost of pregnancy ($N = 10$), cost of pregnancy-related complications ($N = 26$), cost of unintended pregnancy ($N = 2$), cost of planned pregnancy ($N = 1$), or cost of pregnancy by facilities ($N = 1$). In the quality assessment, randomized, non-randomized, and retrospective database studies had low to moderate risk of bias. We determined primary cost drivers based on the highest cost reported in each study. The identified cost drivers were inpatient care, pregnancy delivery, multiple births, complicated cesarean sections, high-risk pregnancy, preterm birth, low birth weight, complications due to conditions such as hypertension, diabetes, anemia, and cancer, and in vitro fertilization. In 2008, the overall mean cost per hospital stay for pregnancy-related incidence ranged from \$3,306 to \$9,234 in 2012 dollars. The mean cost of pregnancy-related complications that led to preterm birth was as high as \$326,953 for an infant born at 25 weeks. It is estimated that over 50 % of live births were unintended in the US. The difference in the cost of unintended pregnancy and intended pregnancy was approximately \$536 million.

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Limitations One limitation of the systematic review was the exclusion of model-based cost studies which were excluded because of the high level of variation and heterogeneity across sources of reported cost. Another limitation of the review is that the cost of pregnancy perspective is restricted to the US.

Conclusion Preventing pregnancy-related complications and reducing unintended pregnancies may lower the overall economic burden of pregnancy on the US health care system.

Key Points for Decision Makers

- Published literature shows that complications during pregnancy are associated with increased medical resource utilization which may lead to the rising cost of pregnancy.
- Interventions to manage comorbid conditions during pregnancy may reduce the overall cost of pregnancy (e.g. insulin therapy taken before pregnancy compared with during pregnancy).
- Additional prospective studies are needed to assess potential cost savings of contraceptives for unintended pregnancies.

1 Introduction

In the US, overall pregnancy rates have declined over the past two decades. In 2008, the pregnancy rate was 105.5 pregnancies per 1,000 women aged 15–44 years—9 % below the 1990 pregnancy rate of 115.8 pregnancies per 1,000 women [1]. The declining trend is observed in teenagers and women aged 20–29 years. Conversely, the declining trend was not observed in women aged 30 years and above in which the pregnancy rate is higher than the pregnancy rate for this group in the year 2000 [1]. Also, unintended pregnancy rates have not declined significantly between 1982 and 2010 [2]. The National Survey of Family Growth reported that multiple factors contributed to the underlying differences in pregnancy rates over the past two decades. Factors include social and behavioral changes in sexual activity, marriage, divorce, and cohabitation, which affect patterns of intercourse, the social and economic context of childbearing, the introduction of contraceptive methods, and in the proportion of women using contraceptive methods [3].

Despite the decline in overall pregnancy rates in the US, pregnancy-related cost continued to rise. Approximately 25 % of hospitalizations were related to pregnancy and childbirth-related conditions [4], and mother's pregnancy and delivery was ranked as one of the top 20 most

expensive conditions treated in US hospitals in 2008 (the total national hospital bill was \$55,479 million) [5]. In the past decade, the mean pregnancy-related charge for a live birth has risen from \$7,687 in 2002 to over \$10,000 in 2010, inflated to 2012 dollars [6]. The pregnancy-related cost was \$3,018 in 2012 dollars, which reflected the actual payment made to the hospital. The 2007 Medical Expenditure Panel Survey (MEPS) estimated that pregnancy or birth-related costs were approximately 4 % of US health care expenditures [7]. Another study that analyzed 3 years of MEPS data from 2000 to 2002 reported that the total annual health care expenditures of women with female-specific conditions were estimated to be over \$100 billion, of which \$24.5 billion were pregnancy-related [8]. Kjerulff et al. [8] showed that pregnancy was a primary reason why women sought health care services; approximately 8 % of pregnant women who were uninsured were more likely to forgo prenatal care, which may lead to pregnancy-related complications. The Agency for HealthCare Research and Quality (AHRQ) reported that the total expense for live birth in 2010 was approximately \$35 billion [9].

Several factors (e.g. cesarean section, utilization of diagnostic testing, assisted conception/fertility treatments, and pregnancy-related complications) may serve as the primary contributors to the rising cost of pregnancy, but the independent effect and relative importance of each factor has not been fully evaluated. Delivery by cesarean section in the US has risen by 53 % over the past two decades [10–12]. In 2007, cesarean sections constituted approximately one-third of childbirth deliveries in the US [10–12]. The rise in cesarean sections is a potential contributor to the rising cost of pregnancy observed in the US. In addition, increases in the utilization of diagnostic tests, pregnancy-related complications, preterm births and multi-fetal pregnancies could also play a role in the rise of pregnancy-related costs.

To fully elucidate and evaluate the drivers of pregnancy-related expenditures in the US, we aimed to conduct a systematic literature review to address the research question ‘in women of childbearing age (15–44 years), what are the main cost components and primary factors that contribute to the direct costs paid by third party payers for pregnancy, pregnancy-related complications, and unintended pregnancy in the US?’ The research question focuses on evaluating the pregnancy-related cost reported in the literature that contributed to the rise in direct costs.

2 Methods

To examine the primary factors that contribute to pregnancy-related costs, we followed the guidelines provided in the Cochrane Handbook to conduct the systematic literature review [13].

2.1 Search Strategy

We performed a systematic literature review of the PubMed database from January 2000 to December 2012, and major women's health and pharmacoeconomics conference proceedings from 2011 to 2012 (American Congress of Obstetricians and Gynecologists, International Society for Pharmacoeconomics and Outcomes Research [ISPOR], Academy of Managed Care Pharmacy, Society for Maternal-Fetal Medicine, American Society for Reproductive Medicine and Women's Health Annual Congress). We searched using the following Boolean search from PubMed: “(‘Pregnancy’ [MeSH Major Topic] OR ‘Pregnancy Complications’ [MeSH Major Topic] OR ‘Pregnancy, Unplanned’ [MeSH Major Topic] OR pregnancy [Title/Abstract]) AND (Costs and Cost Analysis [MeSH Major Topic])”. In addition, handsearching was performed for additional articles from sources of grey literature, such as the Centers for Disease Control–Data and Statistics website and the Cost-Effectiveness Analysis Registry at Tufts University. Handsearching was conducted to identify studies that were not electronically indexed in PubMed, references of narrative reports, existing systematic reviews, and included studies.

2.2 Study Selection Criteria

We included studies that reported pregnancy, pregnancy-related complications, unplanned pregnancy, and monetary costs related to pregnancy in the systematic review. We excluded narrative reports, systematic reviews, non-US-based studies, and model-derived cost-of-pregnancy papers. We also excluded reports based on expert opinions.

2.3 Study Selection Process and Data Extraction

Two reviewers independently applied the inclusion criteria and assessed the quality of the data collected. Each reviewer evaluated the relevant data from the eligible studies and the information was entered electronically into an Excel data-collection form with prepared fields. If relevant data were reported only graphically, we estimated the values by physically measuring the charts with a ruler. Disagreements between reviewers were resolved by consensus or by arbitration through a third party, referring to the original sources.

We collected information on the study design and outcomes for each included study. This included the study characteristics (e.g. study objectives, data source, payer's perspective, reported cost or charge unit and cost components), comparison group, pregnancy-related complications, and the pregnancy cost or charge breakdown.

We classified pregnancy studies into one of five groups: overall cost of pregnancy, pregnancy-related

complications, unintended pregnancy, planned pregnancy, and facility-related (i.e. baby-friendly vs. non-baby friendly institution) pregnancy costs. We inflated all cost and charge data to 2012 dollars.

2.4 Risk of Bias Assessment

We developed a quality assessment form for each type of study design based on the Cochrane Handbook report of low, unclear, and high risk of bias [13]. From studies in which participants were randomized, we assessed biases such as selection, performance, detection, attrition, and reporting using an assessment tool from the Cochrane Handbook [13]. For non-randomized studies, we adapted the Newcastle-Ottawa Scale for non-randomized studies to assess the following biases: selection, attrition, detection, and information [14]. In addition, we assessed whether the authors controlled for confounders in their analysis [14]. For retrospective claims database studies, we adapted the ISPOR checklist for retrospective database studies [15]. Of the 27 questions from this checklist, we selected questions to assess the quality of retrospective studies that used health-related retrospective databases [15]. The form can be found in the electronic supplementary material (ESM).

2.5 Data Management and Reporting

We used Endnote version X5 to store the bibliographic citations from the electronic search. For data entry and descriptive analyses, we used Microsoft Excel 2010. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [16] in designing, performing, and reporting of the systematic review.

3 Results

Figure 1 illustrates the flow diagram of the identified studies. We identified 268 articles through PubMed and handsearching of the grey literature and major conference websites. After abstract screening, we excluded 204 articles because they were either narrative report/review articles ($N = 27$), did not report information on monetary cost of pregnancy ($N = 39$), were irrelevant to the cost of pregnancy ($N = 55$), were non-US-based studies ($N = 56$), or reported model-derived cost ($N = 41$). The reasons for exclusion were not mutually exclusive (i.e. one study may have multiple reasons for exclusion). In addition, we excluded 24 articles after full-text review because they were either narrative report/review articles ($N = 3$), non-US-based studies ($N = 4$), model-derived cost of pregnancy studies ($N = 11$), or other ($N = 6$). The six articles

in the ‘other’ category included studies that reported the cost of abortion, overall health care costs, indirect costs related to health expenditure for infertility treatment, or surgical interventions specific to medical procedures.

Of the 40 studies that met the criteria for qualitative synthesis, 35 were full-text articles and 5 were abstracts from major women’s health and pharmacoeconomics conference proceedings from 2011 to 2012. We classified the studies based on the primary research topic focusing on either the overall cost of pregnancy ($N = 10$) [4, 7, 8, 17–23], cost of pregnancy-related complications ($N = 26$), cost of unintended pregnancy ($N = 2$) [24, 25], cost of planned pregnancy ($N = 1$) [26], or cost of pregnancy by facilities ($N = 1$) [27]. The cost of pregnancy-related complications category was further broken down into

studies that looked at either the cost of pre- or post-term birth ($N = 19$), comorbid conditions ($N = 5$) [28–32], or environmental exposures ($N = 2$) [33, 34]. Tables 1, 2, 3, 4, 5, 6 and 7 summarize the 40 included studies by type of pregnancy study and study design.

We examined study design and sources of cost data. Study designs included two randomized clinical trials (5 %) [35, 36], two prospective longitudinal cohort studies (5 %) [26, 37], 30 retrospective studies [of which three were longitudinal surveys (8 %) [8, 19, 29], 13 medical claims analysis (33 %) and 15 medical chart reviews (38 %)], as well as five cross-sectional surveys (13 %) [7, 25, 27, 31, 38]. The distribution of the studies by year of publication from 2000 to 2012 was relatively heterogeneous, with the majority of studies published in the years

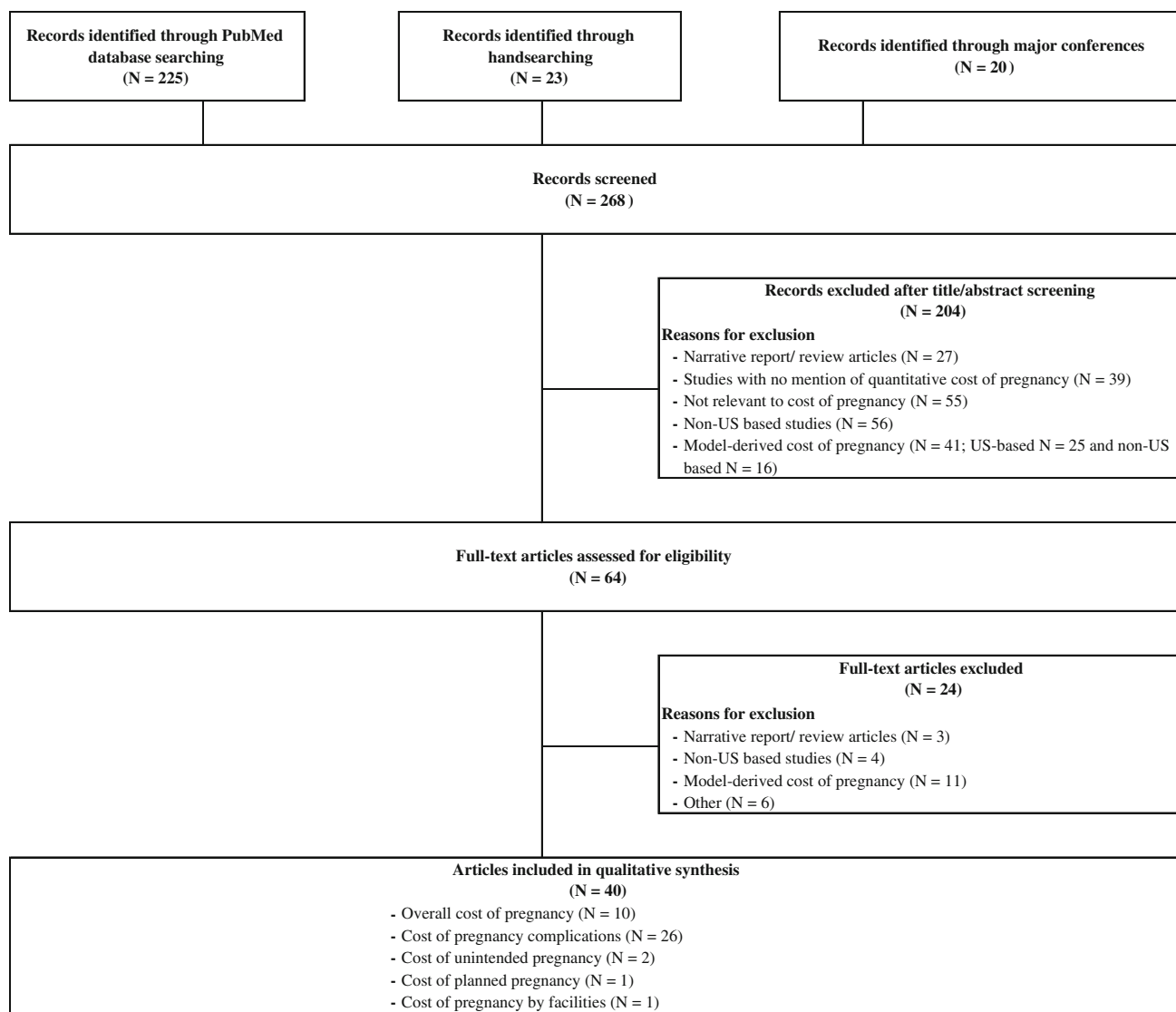


Fig. 1 Study disposition for cost of pregnancy studies (reasons for exclusion were not mutually exclusive)

Table 1 Summary of studies reporting cost of pregnancy in the US: overall pregnancy

Author(s), year; study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost year ^a
Fitch et al., 2011 [17]; Costs of contraceptive coverage and pregnancy care	Retrospective, medical claims analysis	Examines the costs of covering pregnancy and delivery care and contraceptives for a commercial population	MedStat MarketScan Database	Commercial payer	Medical and prescription claims associated with pregnancy	2010
Gazmararian et al., 2002 [18]; Hospitalizations during pregnancy among managed care enrollees	Retrospective, medical claims analysis	Describes the prevalence of hospitalization during pregnancy and the associated costs	National managed care organization	Commercial payer	Hospitalization costs associated with pregnancy complications	1997
Thomson Healthcare, 2007 [4]; The healthcare costs of having a baby	Retrospective, medical claims analysis	Estimates the prenatal, delivery-related, and post-partum health care costs associated with having a baby among the privately insured population in the US	MarketScan Commercial Claims Database	Commercial payer	Hospitalization and postpartum costs associated with professional services fees, facility fees, laboratory fees, radiology and imaging costs, and outpatient drug costs	2004
Kjerulff et al., 2007 [8]; The cost of being a woman: a national study of health care utilization and expenditures for female-specific conditions	Retrospective, panel survey	(1) Determines the prevalence of female-specific conditions in a nationally-representative survey(2) Estimates the health care utilization and costs associated with these conditions	Medical Expenditure Panel Survey	Individual; national (Federal Government)	Out-of-pocket expenditures, total health expenditures	2002
Machlin and Rohde, 2007 [19]; Health care expenditures for uncomplicated pregnancies	Retrospective, panel survey	Estimates medical expenditures associated with uncomplicated pregnancies and in-hospital deliveries	Medical Expenditure Panel Survey	Individual; national (Federal Government); state (State Government); commercial payer	Payments to hospitals, physicians, pharmacies, and other health care providers, and include direct payments by individuals, private and public insurance plans, and other miscellaneous payment sources for services received	2004
Conway et al., 2011 [7]; Patient-centered care categorization of U.S. health care expenditures	Cross-sectional survey	Categorizes national medical expenditures into patient-centered categories	Medical Expenditure Panel Survey	National (Federal Government)	Inpatient, office-based, prescribed medicines, hospital outpatient, emergency room, home health	2007

Table 1 continued

Author(s), year; study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost year ^a
Ray and Lieu, 2003 [23]; Comparing the medical expenses of adults with Medicaid and commercial insurance in a health maintenance organization	Retrospective, medical claims analysis	Compares the costs of health care services between Medicaid and commercially-insured adults	Medicaid and Kaiser Permanente (KP) in Northern California	National (Federal Government); state (State Government); commercial payer	Hospitalization costs associated with pregnancy, childbirth, puerperium	1998
Merrill and Steiner, 2006 [21]; Hospitalizations related to childbirth, 2003	Retrospective, medical claims analysis	Examines costs related to childbirth-related hospitalizations	HCUP	Societal	Total cost per childbirth-related hospitalization	2003
Podulka et al., 2011 [22]; Hospitalizations related to childbirth, 2008	Retrospective, medical claims analysis	Examines costs related to childbirth-related hospitalizations and to research changing trends in hospital procedures for childbirth	HCUP	Societal	Total cost per childbirth-related hospitalization	2008
Main et al., 2011 [20]; Median costs and outcomes related to multiple gestations	Retrospective, medical chart review	Examines maternal and neonatal cost and length of hospital stay associated with multiple gestational pregnancies	Hospital costs	Undetermined	Neonatal and maternal hospital costs	2011
<i>HCUP Healthcare Cost and Utilization Project</i>						

^a If the article did not explicitly state the year of cost, the latest year from the data or observation period was reported. If this was not available, the year that the article was published was used

Table 2 Summary of studies reporting cost of pregnancy in the US: pregnancy complications (pre-/post-term birth)

Author, year; study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost year ^a
Adams et al., 2003 [42]; Costs of poor birth outcomes among privately insured						
Retrospective, medical claims analysis	Measures the costs of poor birth outcomes among insured mothers and infants	MedStat Claims	Commercial payer	Maternal costs included hospitalizations during the 9 months prior to delivery date, medical costs (room and board, physician, and ancillary) incurred during the delivery hospitalization. Infant costs included during the delivery hospitalization, post-delivery costs for the infant for 3 months after delivery.		1996
Kirkby et al., 2007 [46]; Clinical outcomes and cost of the moderately preterm infant						
Retrospective, medical claims analysis	Defines the morbidity and complications to care, as well as the economic impact of moderately preterm patients in the NICU	Paradigm Health claims database	Commercial payer	Hospitalization costs from birth to 2 weeks after NICU discharge, including physician fees		2004
Morrison et al., 2001 [49]; Telemedicine: cost-effective management of high-risk pregnancy						
Retrospective, medical claims analysis	Performs a cost-effectiveness analysis of telemedicine services for patients diagnosed with preterm labor	HMO cost data (paid charges)	Commercial payer	Prenatal care, antepartum hospitalization, delivery, intensive care nursery, telemedicine services, total cost per pregnancy		2001
Rolnick et al., 2000 [51]; Impact of birthweight on healthcare charges within a managed care organization						
Retrospective, medical chart review	Determines the rates of low birth weight and the associated health care utilizations and charges in a managed care organization	Hospital charge records	Commercial payer	Total discharge utilization includes inpatient and outpatient utilization. Outpatient utilization includes number of care visits, diagnoses, procedures, and health care charges. Inpatient utilization includes the number of hospitalizations, length of stay, diagnoses, procedures and hospital charges		1995
Brooten et al., 2001 [36]; A randomized trial of nurse specialist home care for women with high-risk pregnancies: outcomes and costs						
Randomized clinical trial	Examines the prenatal, maternal, and infant outcomes and costs with a nurse specialist	Hospital charges	Institutional	Prenatal hospitalization costs, maternal and infant delivery hospitalization costs, maternal and infant post-delivery rehospitalization costs		2000
Magriples et al., 2003 [40]; Delivery at 34 weeks is more costly than at 35 weeks in pregnancies with premature rupture of membranes						
Retrospective, medical chart review	Assesses the relative risks and costs of delivery with premature rupture of membranes	Newborn Special Care Unit database	Institutional	Direct medical costs associated with length of hospital stay and neonatal interventions		1999

Table 2 continued

Author, year; study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost, year ^a
Phibbs and Schmitt, 2006 [43];	Retrospective, medical chart review	Estimates of the cost and length of stay savings with respect to 1-week increases in gestational age for premature infants	Hospital charges	Institutional	Hospitalization costs by gestational age and length of stay	2003
Russell et al., 2007 [38];	Cross-sectional survey	Cost of hospitalization for preterm and low birth weight infants in the United States	Nationwide Inpatient Sample database	National (Federal Government)	Infant hospitalization (contribution of preterm/ low birth weight infant hospitalization costs toward pediatric hospital costs)	2001
Clements et al., 2007 [45];	Retrospective, medical claims analysis	Preterm birth-associated cost of early intervention services: an analysis by gestational age	Pregnancy to Early Life Longitudinal (PELL) data system	State (State Government); institutional	Early intervention program costs	2003
Gilbert et al., 2003 [39];	Retrospective, medical chart review	The cost of prematurity: quantification by gestational age and birth weight	A statewide database, consisting of linked maternal and neonatal–infant hospital discharge records that are matched to vital statistics birth records	State (State Government)	Neonatal costs, maternal costs, excess hospital costs	1996
Schmitt et al., 2006 [44];	Retrospective, medical chart	Costs of newborn care in California: a population-based study	California OSHPD	State (State Government)	Total cost for infants, total cost for mothers, total prenatal hospital costs, total maternal hospital costs	2003
Underwood et al., 2007 [47];	Retrospective, medical chart review	Examines the rates, causes, and costs of rehospitalization of premature infants	OSHPD database	State (State Government)	Cost of hospitalization for readmission	2000
Xu et al., 2009 [50];	Retrospective, medical chart review	Cost of racial disparity in preterm birth: evidence from Michigan	Linked hospital discharge and live birth certificate file, infant death records, and fetal death data for the 2003 birth cohort in the state of Michigan	State (State Government); Societal	Gestational age-specific hospitalization costs, costs associated with racial disparity in the preterm Black and White populations	2003
Cuevas et al., 2005 [52];	Retrospective, medical chart review	The cost of prematurity: hospital charges at birth and frequency of rehospitalizations and acute care visits over the first year of life	Hospital charge records	Undetermined	Initial hospitalization, rehospitalization, acute care visits	2000

Table 2 continued

Author, year; study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost year ^a
Fonseca et al., 2003 [41];	Retrospective, medical chart review	Postdates pregnancy in an indigent population: the financial burden	Hospital billing data (Lyndon Baines Johnson General Hospital)	Undetermined	Cost of antenatal testing for postdates and ultrasounds	2002
Grobman et al., 2004 [35];	Randomized clinical trial	Does fetal fibronectin use in the diagnosis of preterm labor affect physician behavior and health care costs? A randomized trial	Medical records, hospital billing data, and patient interviews	Undetermined	Maternal inpatient and outpatient costs (number of hospital admissions, length of stay, hours on labor and delivery, number of tocolytic treatments); indirect costs (lost income from time off work and need to hire additional home assistance)	2003
Jones et al., 2002 [37];	Prospective longitudinal cohort	Is 34 weeks an acceptable goal for a complicated singleton pregnancy?	Hospital charges/medical records from across stored in central database (Matria Healthcare, Marietta, GA, USA)	Undetermined	Nursery costs, including regular nursery, NICU with no RDS, and NICU with RDS	2002
Nicholson et al., 2011 [48];	Retrospective, medical chart review	The active management of risk in pregnancy at term (AMOR-IPAT) cost-effectiveness study	Hospital charges	Undetermined	Maternal care, infant care, combined mother/infant care	2011
Unal et al., 2012 [53];	Retrospective, medical chart review	Planned evening labor induction: the cost of convenience	Hospital database	Undetermined	Total hospital costs	2012

AMOR-IPAT Active Management of Risk in Pregnancy at Term, HMO health maintenance organization, LOS length of stay, NICU neonatal intensive care unit, OSHPD Office of Statewide Health Planning and Development, RDS respiratory distress syndrome

^a If the article did not explicitly state the year of cost, the latest year from the data or observation period was reported. If this was not available, the year that the article was published was used

Table 3 Summary of studies reporting cost of pregnancy in the US: pregnancy complications (comorbidities)

Author, year; study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost year ^a
Rein et al., 2000 [32]; Direct medical cost of pelvic inflammatory disease and its sequelae: decreasing, but still substantial						
	Retrospective, medical claims	Estimates the direct medical and lifetime costs associated with pelvic inflammatory disease	MedStat claims data	Commercial payer	Outpatient and inpatient costs, inpatient pharmacy costs, the cost of intravenous and directly observed medications	1998
Chinthammit and Skrepnek, 2012 [29]; Cancer during pregnancy: clinical and economic characteristics associated with inpatient cases in the United States						
	Retrospective, panel survey	Assesses clinical characteristics and national charges for maternal hospitalizations and complications associated with cancers during pregnancy	Agency for Healthcare Research and Quality HCUP Nationwide Inpatient Sample data	National (Federal Government)	Maternal hospital charges	2009
James et al., 2008 [31]; An assessment of medical resource utilization and hospitalization cost associated with a diagnosis of anemia in women with obstetrical bleeding in the United States						
	Cross-sectional survey	Estimates the hospital costs and utilization associated with anemia in hospitalized women with obstetrical bleeding	HCUP Nationwide Inpatient Sample hospital charges	Societal	Average hospitalization cost for patients with and without anemia	2003
Barton et al., 2006 [28]; Cost-savings analysis of an outpatient management program for women with pregnancy-related hypertensive conditions						
	Retrospective, medical chart review	Evaluates the cost savings of outpatient management for women with pregnancy-related hypertensive conditions	Hospital charges/medical records from across stored in central database (Matria Healthcare, Marietta, GA, USA)	Undetermined	Cost of outpatient disease management; treatment for various pregnancy-related hypertensive conditions	2003
Gabbe et al., 2000 [30]; Benefits, risks, costs, and patient satisfaction associated with insulin pump therapy for the pregnancy complicated by type 1 diabetes mellitus						
	Retrospective, medical chart review	Evaluates the benefits, risks, and costs associated with insulin pump therapy for type 1 diabetes mellitus	Medical records	Undetermined	Total maternal and infant inpatient and outpatient costs	1999

HCUP Healthcare Cost and Utilization Project

^a If the article did not explicitly state the year of cost, the latest year from the data or observation period was reported. If this was not available, the year that the article was published was used

2003 ($N = 5$, 13 %) [23, 39–42], 2006 ($N = 4$, 10 %) [21, 28, 43, 44], 2007 ($N = 7$, 18 %) [4, 8, 19, 38, 45–47] and 2011 ($N = 9$, 23 %) [7, 17, 20, 22, 24–27, 48].

Data for the cost of pregnancy came from multiple sources. Nineteen studies (48 %) incorporated hospital billing data that comprised individual hospital data or cost information from the AHRQ and Healthcare Utilization Project (AHRQ HCUP). Eight studies (20 %) [18, 23–25, 27, 33, 34, 49] used cost data from managed care programs from health maintenance organizations such as Kaiser Permanente or state/federal programs such as Medicaid or

Medicare. Five studies (13 %) [39, 44, 45, 47, 50] used cost data from linked state registries, five studies (13 %) [4, 17, 32, 42, 46] used data from medical claims databases, including MarketScan, MedStat, or Paradigm Health, and three (8 %) [7, 8, 19] used data from national surveys.

The distribution of payers' perspectives across studies was heterogeneous as there were several studies reporting multiple perspectives. Three studies were from a federal government perspective (8 %) [7, 29, 38], three from a state government perspective (8 %) [39, 44, 47], nine from a commercial payer perspective (23 %) [4, 17, 18, 32, 33,

Table 4 Summary of studies reporting cost of pregnancy in the US: Pregnancy complications (environmental exposures)

Author, year; study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost year ^a
Goler et al., 2012 [33]; Early start: a cost-beneficial perinatal substance abuse program	Retrospective, medical chart review	Conducts a cost-benefit analysis of a prenatal intervention program for substance abuse during pregnancy	Kaiser Permanente in Northern California	Commercial payer	Cost of delivery, delivery care (up to 1 year), maternal outpatient costs (mental health, gynecology, primary care), ER, pharmacy	2009
Thorsen and Khalil, 2004 [34]; Cost savings associated with smoking cessation for low-income pregnant women	Retrospective, medical claims	Compares medical costs associated with women who do and do not smoke during pregnancy	Medicaid data from the Division of Health Care Financing within the Wisconsin Department of Health and Family Services	National (Federal Government); state (State Government)	Medical costs of mother's maternity admissions, inpatient neonatal care, and infant's medical costs for the first 6 months	2002

ER emergency room

^a If the article did not explicitly state the year of cost, the latest year from the data or observation period was reported. If this was not available, the year that the article was published was used

Table 5 Summary of studies reporting cost of pregnancy in the US: unintended pregnancy

Author, year; study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost year ^a
Monea and Thomas, 2011 [24]; Unintended pregnancy and taxpayer spending	Retrospective, medical claims analysis	Estimates public costs of spending related to unintended pregnancy at a national level	Data from the National Governors Association on the number of births financed by Medicaid in 2001; data from the Census Bureau's Medicaid Undercount Project; 2002 National Survey of Family Growth	National (Federal Government); state (State Government)	Total cost of unintended pregnancy vs. abortion or fetal loss	2008
Sonfield et al., 2011 [25]; The public costs of births resulting from unintended pregnancies: national and state-level estimates	Cross-sectional survey	Estimates the public costs of unintended pregnancies associated with maternal and infant care at the national and state level	Pregnancy Risk Assessment Monitoring System, Medicaid, and Children's Health Insurance Program data	National (Federal Government); state (State Government)	Prenatal care, labor and delivery, post-partum care, and 1 year of care for infant	2006

^a If the article did not explicitly state the year of cost, the latest year from the data or observation period was reported. If this was not available, the year that the article was published was used

42, 46, 49, 51], three from an institutional perspective (8 %) [36, 40, 43], three from the societal perspective (8 %) [21, 22, 31], and the perspectives for ten studies were undetermined (25 %) [20, 26, 28, 30, 35, 37, 41, 48, 52, 53]. Nine studies (23 %) [8, 19, 23–25, 27, 34, 45, 50] looked at multiple payers' perspectives. For instance, four studies [24, 25, 27, 34] observed both the national and state perspectives, while Clements et al. [45] and Xu et al. [50] looked at the state and institutional level, and the state and

societal level, respectively. Machlin and Rohde [19] included federal, state, commercial and individual perspectives.

We determined the primary cost drivers based on the highest cost reported in each study. The identified cost drivers were inpatient care, pregnancy delivery, multiple births, complicated cesarean section, high-risk pregnancy, preterm birth, low birth weight, complications due to conditions such as hypertension, diabetes, anemia, and cancer, and in vitro fertilization.

Table 6 Summary of studies reporting cost of pregnancy in the US: planned pregnancy

Author, year; study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost year ^a
Katz et al., 2011 [26]; Costs of infertility treatment: results from an 18-month prospective cohort study	Prospective longitudinal cohort	Examines the costs and resource utilization by women presenting infertility evaluation	Medical records and interviews	Undetermined	Maternal infertility treatment costs, medication and lab tests, and maternal and neonatal hospitalization costs, cost of successful pregnancy	2006

^a If the article did not explicitly state the year of cost, the latest year from the data or observation period was reported. If this was not available, the year that the article was published was used

Table 7 Summary of studies reporting cost of pregnancy in the US: pregnancy by facilities

Author, year; Study title	Study type	Study description	Data source	Perspective	Type of reported cost data	Reported cost year ^a
DelliFraine et al., 2011 [27]; Cost comparison of baby friendly and non-baby friendly hospitals in the United States	Cross-sectional survey	Compares the institutional costs associated with baby-friendly and non-baby friendly hospitals	Centers for Medicare and Medicaid cost reports and American Hospital Association annual survey database	National (Federal Government); state (State Government)	Nursery labor and delivery expenses	2007

^a If the article did not explicitly state the year of cost, the latest year from the data or observation period was reported. If this was not available, the year that the article was published was used

3.1 Overall Cost of Pregnancy

Among the ten studies that reported overall cost of pregnancy, high variability in how cost was reported was observed across all studies. For example, cost data for Merrill and Steiner [21] and Podulka et al. [22] came from the same source, the Nationwide Inpatient Sample sponsored by AHRQ, but comparisons could not be made because the metric for reporting cost was different. Merrill and Steiner reported cost as mean hospital charges per delivery (ranging from \$8,680 to \$22,400 per delivery), while Podulka et al. converted the hospital charges to cost and presented cost as a mean cost per hospital stay (ranging from \$3,306 to \$9,234 per stay). Conway et al. [7] reported that 69 % of overall cost, estimated at \$46 billion in 2007, is due to inpatient care. In Gazmararian et al. [18], among the reasons for hospitalization and the associated costs for pregnant women, preterm labor made up approximately 19 % of overall hospitalization charges, estimated at \$50 million. They also reported the cost associated with pregnancy loss and found that ectopic pregnancy contributed to almost 50 % of the

hospitalization charges for pregnancy loss, estimated at \$9 million. A medical claims analysis study examined the costs of pregnancy and delivery and prescription contraceptives, including oral contraceptives and intrauterine devices [17]. The cost of pregnancy/delivery per member per month was \$15.62 for pregnancy and delivery care, \$1.82 for oral contraceptives, and \$0.32 for intrauterine devices [17]. Table 8 provides a summary of the overall cost of pregnancy.

3.2 Pregnancy-Related Complications

Studies that examined the cost of pregnancy-related complications were categorized as the cost of pre- or post-term birth, comorbid conditions, or environmental exposures. Table 9 provides additional information on the cost or charge breakdown for maternal or neonatal care. Nineteen studies that compared the costs of pre- or post-term birth stratified costs by gestational age or birth weight. For example, Phibbs and Schmitt [43] linked California vital records data with hospital discharge data to examine premature infants between 24 and 37 weeks of gestation. They

Table 8 Summary of overall cost of pregnancy

Author, year	Comparison group	Reported cost/charge unit	Cost/charge breakdown	2012 USD
Conway et al., 2011 [7]	Pregnancy/birth	Total expenditure in 2007 in billions	Maternal	46
Fitch et al., 2011 [17]	Pregnancy and delivery	Pregnancy/delivery per member per month	Maternal	15.6
	Oral contraceptives			1.8
	Intrauterine devices			0.3
Gazmararian et al., 2002 [18]	Live birth outcome	Mean hospital charges	Maternal	13,622
	Pregnancy loss outcome		Maternal	19,173
Kjerulff et al., 2007 [8]	Pregnancy-related expenditures	Mean expenditure	Maternal	6,454
Machlin and Rohde, 2007 [19]	All pregnant women	Mean expenditure in 2004	Maternal	10,136
	Private insurance in the month of delivery and in the 8 months prior	Mean expenditure in 2005		11,210
	Medicaid in the month of delivery and in the 8 months prior	Mean expenditure in 2006		8,764
Main et al., 2011 ^a [20]	Singleton	Cost range	Neonatal	1,086–2,784
	Twins			2,071–23,576
	Triplets			20,443–142,238
	Quads			55,246–184,650
	Singleton		Maternal	5,328–11,901
	Twins			9,353–18,576
	Triplets			12,810–39,152
	Quads			13,734–112,392
Merrill and Steiner, 2006 [21]	All types of delivery	Mean charges	Maternal	11,620
	Vaginal delivery without complication			8,680
	Vaginal delivery with complication			11,480
	Vaginal delivery with sterilization and/or D&C			14,560
	Vaginal delivery with operating room procedures except sterilization and/or D&C			22,400
	C-section without complication			16,100
	C-section with complication			21,700
Podulka et al., 2011 [22]	All types of delivery	Mean cost per stay	Maternal	4,332
	Vaginal delivery without complication			3,306
	Vaginal delivery with complication			4,332
	Vaginal delivery with sterilization and/or D&C			5,700
	Vaginal delivery with operating room procedures except sterilization and/or D&C			9,234
	C-section without complication			5,358
	C-section with complication			7,410
Ray and Lieu, 2003 [23]	Medicaid	Mean hospital-related costs per member, per year	Maternal	663

Table 8 continued

Author, year	Comparison group	Reported cost/charge unit	Cost/charge breakdown	2012 USD
Thomson Healthcare, 2007 [4]				
	Overall delivery	Mean expenditures	Maternal	11,795
	Vaginal delivery			10,368
	Cesarean delivery			14,684

C-section cesarean section, *D&C* dilation and curettage

^a The authors only reported a range of cost values

reported the neonatal cost per birth by gestational ages between 24 and 37 weeks, with costs ranging as high as \$326,953 at 25 weeks to \$2,838 by 37 weeks. Clements et al. [45] linked Massachusetts birth certificate, death certificate, and birth-related hospital discharge data from 1998 to 2003 births for both mothers and infants who participated in a preterm prevention program, and compared the cost of pregnancy categorized by preterm (gestational age of 24–31 weeks), moderately preterm (gestational age of 32–36 weeks) and on-term (gestational age of 37–42 weeks). The neonatal cost per live birth was reported to be \$7,550 for preterm infants, \$2,209 for moderately preterm infants and \$1,015 for on-term infants. Several studies that reported the cost of pregnancy by gestational age have shown an exponential decline in the cost of pregnancy with respect to an increase in gestational age [39, 43, 44, 52].

Studies such as those by Rolnick et al. [51], which identified patients using medical records from two hospitals, and Schmitt et al. [44], which linked California vital statistics with maternal and newborn hospital discharge records to examine the association between premature delivery and birth weight, reported costs by birth weight. Normal birth weight infants had an estimated total health care charge of approximately 50 % (\$5,488) less than moderately low birth weight infants (gestational age of 32–36 weeks) after 1-year post-discharge from the hospital [51]. Schmitt et al. [44] reported mean cost per low birth weight infants to be in the range of \$12,582 to \$309,123 for neonatal care with birth weight from 2000 grams to less than 500 grams. Some studies, such as that by Nicholson et al. [48], which identified patients from hospital records, compared the cost of labor induction methods with usual care. They reported a total neonatal and maternal mean cost of \$17,184 for the Active Management of Risk in Pregnancy at Term (AMOR-IPAT) program and mean cost of \$17,901 for usual care.

Five studies provided the cost of pregnancy-related complications related to comorbid conditions. Barton et al. [28] compared the cost of an intervention program for pregnancy-related hypertension and reported the maternal cost to be \$6,843 for women who participated in the

program and \$14,458 for those who did not. Chinthammit et al. [29] reported that the maternal cost of pregnancy was \$34,503 among patients with cancer. Gabbe et al. [30] conducted a medical chart review and cross-sectional survey of diabetic mothers after delivery and compared the cost of insulin pump therapy related to complications of type 1 diabetes among women who initiated insulin pump therapy during pregnancy, women who used multiple insulin injections, and women who used insulin pump therapy before pregnancy. They reported that the combined maternal and neonatal cost was \$54,677 for mean gestational age at delivery of approximately 36 weeks for type 1 diabetic mothers who initiated insulin pump therapy during pregnancy. Additional comparison of costs for different mean gestational ages and breakdown of costs by maternal or neonatal care across the three groups of diabetic mothers can be found in Table 10. James et al. [31] used the Nationwide Inpatient Sample and reported the cost for mothers diagnosed with anemia to be \$7,487 compared with \$5,002 for mothers without anemia. Rein et al. [32] used the National Hospital Discharge Survey and reported \$3,524 as the mean unit cost of ectopic pregnancy related to pelvic inflammatory disease; inpatient and outpatient costs were presented as \$11,734 and \$2,059, respectively.

Two studies reported the cost of environmental exposures related to pregnancy (Table 11). Goler et al. [33] compared the costs of an intervention program (Early Start) among women who screened positive for substance abuse with women who did not participate in the intervention program. The maternal and neonatal costs ranged from \$9,110 to \$11,956 across the comparators. Thorsen and Khalil [34] compared the cost of pregnancy for women who smoked and women who did not smoke during pregnancy (\$8,828 vs. \$6,980 in total costs, respectively).

3.3 Unintended Pregnancy

Table 12 provides the costs of unintended pregnancy reported in two studies. Monea and Thomas [24] focused on unintended pregnancies resulting in births, fetal losses, and abortions, as identified through Medicaid and Children's Health Insurance Program databases. The mean

Table 9 Summary of pregnancy-related complications (pre- or post-term birth) cost

Author, year	Comparison group	Reported cost/charge unit	Cost/charge breakdown	2012 USD
Adams et al., 2003 [42]	Normal delivery	Mean delivery cost	Maternal	12,070
			Neonatal	5,453
	Complicated cesarean		Maternal	25,140
			Neonatal	33,666
	Uncomplicated cesarean		Maternal	19,081
			Neonatal	11,794
Brooten et al., 2001 [36]	Prenatal and postpartum care, with half receiving home visits by nurse specialists	Mean hospitalization charges	Maternal	15,670
			Neonatal	6,820
			Prenatal hospitalization	9,879
			Maternal delivery	16,534
			Neonatal delivery	26,744
	Prenatal care only		Maternal post-delivery rehospitalization	897
			Infant post-delivery rehospitalization	383
			Prenatal hospitalization	16,212
			Maternal delivery	18,048
			Neonatal delivery	46,701
Clements et al., 2007 [45]	32–36 weeks	Mean cost per live birth	Neonatal	2,209
	37–42 weeks			1,015
Cuevas et al., 2005 [52]	<26 weeks	Mean hospital charge	Neonatal	Not reported
	26–28 weeks			381,201
	29–32 weeks			88,709
	33–36 weeks			16,792
	≥37 weeks			7,613
Fonseca et al., 2003 [41]	Bi-weekly fetal testing	Total financial burden within study population	Maternal	365,571
	Routine ultrasound and induction			1,308,680
Gilbert et al., 2003 [39]	25 weeks	Mean total hospital cost, in thousands	Neonatal	369
	26 weeks			267
	27 weeks			218
	28 weeks			157
	29 weeks			114
	30 weeks			84
	31 weeks			54
	32 weeks			34
	33 weeks			20
	34 weeks			13
	35 weeks			8
	36 weeks			5
	37 weeks			3
	38 weeks			2

Table 9 continued

Author, year	Comparison group	Reported cost/charge unit	Cost/charge breakdown	2012 USD
	25 weeks	Mean total hospital cost, in thousands	Maternal	14
	26 weeks			14
	27 weeks			15
	28 weeks			17
	29 weeks			13
	30 weeks			13
	31 weeks			11
	32 weeks			9
	33 weeks			8
	34 weeks			7
	35 weeks			6
	36 weeks			6
	37 weeks			5
	38 weeks			5
Grobman et al., 2004 [35]	Fetal fibronectin results available	Total log mean cost	Total	11
			Hospital	10
			Non-hospital	9
	Fetal fibronectin results not available	Total log mean cost	Total	11
			Hospital	10
			Non-hospital	10
Jones et al., 2002 [37]	Regular nursery at 34 weeks	Mean per live birth	Neonatal	3,698
	NICU (no RDS) at 34 weeks			21,950
	NICU (with RDS) at 34 weeks			45,199
	Regular nursery at 35 weeks			2,195
	NICU (no RDS) at 35 weeks			18,374
	NICU (with RDS) at 35 weeks			35,577
	Regular nursery at 36 weeks			2,084
	NICU (no RDS) at 36 weeks			16,985
	NICU (with RDS) at 36 weeks			34,965
Kirkby et al., 2007 [46]	32 weeks	Mean per live birth	Neonatal	58,514
	33 weeks			42,257
	34 weeks			30,251
Magriples et al., 2003 [40]	34 weeks	Mean cost	Total cost	11,100
			Maternal	4,522
			Neonatal	6,575
	35 weeks	Mean cost	Total cost	6,788
			Maternal	3,370
			Neonatal	3,416

Table 9 continued

Author, year	Comparison group	Reported cost/charge unit	Cost/charge breakdown	2012 USD
Morrison et al., 2001 [49]				
	Women with preterm labor who did not receive telemedicine services	Mean cost per pregnancy	Prenatal care	2,105
			Antepartum hospitalization	3,552
			Delivery	2,794
			Intensive care nursery	24,508
			Telemedicine services	0
			Total cost	32,960
	Women with preterm labor who received telemedicine services		Prenatal care	2,006
			Antepartum hospitalization	1,239
			Delivery	2,315
			Intensive care nursery	1,163
			Telemedicine services	4,259
			Total cost	10,982
Nicholson et al., 2011 [48]				
	Usual care	Mean cost per case	Total	18,617
			Maternal	13,384
			Neonatal	5,228
	AMOR-IPAT		Total	17,871
			Maternal	12,904
			Neonatal	4,967
Phibbs and Schmitt, 2006 [43]				
	24 weeks	Mean cost per birth	Neonatal	311,588
	25 weeks			326,953
	26 weeks			290,692
	27 weeks			249,312
	28 weeks			204,569
	29 weeks			162,121
	30 weeks			130,035
	31 weeks			95,824
	32 weeks			64,564
	33 weeks			42,203
	34 weeks			14,749
	35 weeks			8,410
	36 weeks			4,822
	37 weeks			2,838
Unal et al., 2012 [53]				
	Morning (6–10 am) labor induction	Mean cost per case	Maternal	4,106
	Evening (5–10 pm) labor induction			6,399
Rolnick et al., 2000 [51]				
	Moderately low birth weight	Total mean healthcare charge 1-year post-discharge	Neonatal	11,163
	Normal birth weight			5,488
Russell et al., 2007 [38]				
	Preterm/ low birth weight infants	Mean per birth	Medicaid	24,016
			Private/commercial	22,800
			Uninsured/self-pay	13,224
			Other	27,208
	Uncomplicated newborns		Medicaid	912
			Private/commercial	1,003
			Uninsured/ self-pay	988
			Other	806

Table 9 continued

Author, year	Comparison group	Reported cost/charge unit	Cost/charge breakdown	2012 USD	
Schmitt et al., 2006 [44]					
	<500 grams	Mean cost per case	Neonatal	178,899	
	500–749 grams			309,123	
	750–999 grams			271,366	
	1,000–1,249 grams			166,342	
	1250–1499 grams			97,719	
	All <1,500 grams			190,722	
	1,500–1,749 grams			62,989	
	1,750–1,999 grams			38,563	
	2,000–2,499 grams			12,582	
	All <2,500 grams			47,558	
	>2,500 grams			2,306	
	All birth weights			4,994	
	<500 grams		Prenatal	11,869	
	500–749 grams			8,519	
	750–999 grams			6,756	
	1,000–1,249 grams			8,383	
	1,250–1,499 grams			9,561	
	All <1,500 grams			8,497	
	1,500–1,749 grams			9,971	
	1,750–1,999 grams			9,068	
	2,000–2,499 grams			7,864	
	All <2,500 grams			8,365	
	>2,500 grams			5,508	
	All birth weights			5,970	
	<500 grams		Maternal hospital	14,787	
	500–749 grams			15,449	
	750–999 grams			16,841	
	1,000–1,249 grams			17,083	
	1,250–1,499 grams			17,977	
	All <1,500 grams			16,997	
	1,500–1,749 grams			15,492	
	1,750–1,999 grams			13,215	
	2,000–2,499 grams			8,522	
	All <2,500 grams			10,948	
	>2,500 grams			4,729	
	All birth weights			5,097	
Underwood et al., 2007 [47]					
	<25 weeks	Mean total cost in millions	Neonatal cost of readmission	29	
	25 weeks			19	
	26 weeks			18	
	27 weeks			30	
	28 weeks			23	
	29 weeks			25	
	30 weeks			31	
	31 weeks			43	
	32 weeks			48	
	33 weeks			72	
	34 weeks			102	
	35 weeks			148	

Table 9 continued

Author, year	Comparison group	Reported cost/charge unit	Cost/charge breakdown	2012 USD
Xu et al., 2009 [50]	20 weeks	Mean cost per live birth	Maternal and neonatal	15,956
	21 weeks			28,087
	22 weeks			86,248
	23 weeks			215,195
	24 weeks			537,176
	25 weeks			526,694
	26 weeks			769,452
	27 weeks			606,581
	28 weeks			535,170
	29 weeks			474,219
	30 weeks			394,919
	31 weeks			368,020
	32 weeks			329,948
	33 weeks			315,173
	34 weeks			286,702
	35 weeks			260,170
	36 weeks			214,107
	≥37 weeks			117,171

AMOR-IPAT Active Management of Risk in Pregnancy at Term, NA not available, NICU neonatal intensive care unit, RDS respiratory distress syndrome

costs per live birth, abortion, and fetal loss were \$6,395, \$111, and \$268, respectively. Sonfield et al. [25] examined the proportion of births that resulted from unintended pregnancies for 2006 derived from the Pregnancy Risk Assessment Monitoring System, a population-based surveillance project of the Centers for Disease Control and Prevention, and reported the cost for intended live births and unintended live births. Combined maternal and neonatal costs of care were \$13,166 million for intended live births and \$13,702 million for unintended live births [25].

We summarized studies that looked at planned pregnancy and, in particular, in vitro treatment and differences in facility-related characteristics. Description and cost information can be found in the ESM (Tables SI–SII).

3.4 Quality Assessment of Included Studies

We grouped studies into three categories for quality assessment. We classified two studies as randomized controlled trials, 25 studies as non-randomized studies, and 13 studies as retrospective database studies. Tables 13, 14 and 15 provide the quality assessment for each study.

Among the two randomized controlled trials (Table 13), there was a moderate to low risk of bias overall. Minimal levels of selection, attrition, and reporting biases were present across the two studies. The presence of performance and detection biases was high because blinding of

participants and personnel were not reported. Brooten et al. [36] had a high risk of performance bias and an unclear risk of detection bias. Grobman et al. [35] had high risk of both performance and detection biases.

Non-randomized studies included prospective and retrospective studies and cross-sectional surveys (Table 14). Overall, the studies described the study eligibility criteria, identified the study population as similar to the target population, had ascertainment of the exposures without the participant's knowledge about the outcomes, and applied methods to control for confounders. Five studies [39, 40, 43, 51, 53] excluded participants from the analysis of the outcome without pre-specification. Differential selection bias was observed in one study [7] in which a difference in the proportion of participants excluded was found for two groups of participants. Two studies [8, 43] did not report how missing data were addressed. Three studies [37, 43, 47] used different protocols for assessing patients during follow-up, which may have introduced detection bias. Approximately 50 % of the non-randomized studies were found to be susceptible to misclassification due to the method of ascertaining the exposure or outcome, which could lead to information bias.

Among the 13 retrospective database studies (Table 15), we observed low to moderate risk of bias for detailed descriptions on the rationale for data source, a priori database analysis plans, descriptions of sample selection,

Table 10 Summary of pregnancy-related complication (comorbid conditions) costs

Author, year	Comorbid condition	Comparison group	Reported cost/charge unit	Cost/charge breakdown	2012 USD
Barton et al., 2006 [28]	Hypertension	Women with pregnancy-related hypertensive conditions who participated in the program	Mean antepartum charges per patient	Maternal	6,843
		Women with pregnancy-related hypertensive conditions who did not participate in the program			14,458
Chinthammit and Skrepnek, 2012 [29]	Cancer	Hodgkin’s disease and other lymphomas, breast cancer, leukemia, genitourinary cancers, and thyroid/endocrine cancers	National cost per case	Maternal	34,503
Gabbe et al., 2000 [30]	Diabetes	Women who started insulin pump therapy during pregnancy	Mean total cost of care	Maternal and neonatal	54,677
				Maternal	42,586
				Neonatal	12,091
		Women who used multiple insulin injections		Maternal and neonatal	46,704
				Maternal	35,853
				Neonatal	10,851
		Women who had already used the insulin pump before pregnancy		Maternal and neonatal	48,938
				Maternal	29,903
				neonatal	19,035
James et al., 2008 [31]	Anemia	Patients with a diagnosis of anemia	Average total hospitalization cost	Maternal	7,487
		Patients without a diagnosis of anemia			5,002
Rein et al., 2000 [32]	Pelvic inflammatory disease and ectopic pregnancy	Privately insured pregnant women with ectopic pregnancy	Mean unit cost of ectopic pregnancy related to PID	Maternal	3,524
				Maternal inpatient	11,734
				Maternal outpatient	2,059

PID pelvic inflammatory disease

eligibility of participants for the time period in which measurement was assessed, a temporal relationship observed between exposure and outcome, establishment of a link between the natural progression of the disease and the time period of analysis, and methods to control for confounders were applied. Five studies [23, 32, 34, 42, 45] did not take into account differences in coding and reporting across studies. Only three studies [34, 45, 49] had a comparator group and described the identification and characteristics of the comparator in detail. Thorsen and Khalil [34] did not report information on censoring participants during the course of the analysis and did not mention the criteria for establishing the temporal relationship between the identification of a participant with a

condition and the outcome of interests. It was often unclear whether the data could differentiate and identify the occurrence of the interventions and outcomes in three studies [32, 42, 45]; thus, the presence of detection bias was plausible.

4 Discussion

Overall, we found a high level of heterogeneity among the included studies due to variability in study design, duration of study period, sources of cost data, reporting of cost, absence of a comparator group, and the types of outcomes reported across studies. Study design played a key role in

Table 11 Summary of pregnancy-related complication (environmental exposure) costs

Author, year	Comparison group	Reported cost/charge unit	2012 USD ^a
Goler et al., 2012 ^b [33]			
	Women who were screened positive (by questionnaire with or without positive urine toxicology), assessed, and diagnosed as chemically-dependent, substance abusing, or at-risk for alcohol or substance use by an Early Start specialist and had at least one follow-up Early Start appointment	Median costs of utilization of maternal health services per patient	10,373
	'Screened-assessed' included women who were screened positive (by questionnaire with or without positive urine toxicology), assessed, and diagnosed as chemically-dependent, substance abusing, or at-risk for alcohol or substance use by an Early Start specialist but had no Early Start follow-up appointments		10,153
	'Screened-positive-only' included women identified as substance abusers based on a positive urine toxicology (with or without positive screening questionnaires) but were never assessed or followed-up by Early Start		11,956
	'Controls' included women with no evidence of substance abuse during pregnancy and were defined as having a negative screening questionnaire and a negative screening urine toxicology test		9,110
Thorsen and Khalil, 2004 ^b [34]			
	Women who smoked during pregnancy	Total amount paid ^c	8,828
	Women who did not smoke during pregnancy		6,980

^a Costs are defined as combined maternal and neonatal costs

^b Thorsen and Khalil [34] defined infant's medical costs for the first 6 months of life; Goler et al. [33] defined costs through the first year of life

^c Sum of costs was calculated

Table 12 Summary of unintended pregnancy costs

Author, year	Comparison group	Reported cost/charge unit	Cost/charge breakdown	2012 USD
Monea and Thomas, 2011 [24]				
	Live births	Mean cost per incident in millions ^a	Maternal	6,395
	Abortion			111
	Fetal loss			268
Sonfield et al., 2011 [25]				
	Intended live births	In millions in 2006, unadjusted	All, maternal and neonatal	13,166
			Federal, maternal and neonatal	7,598
			State, maternal and neonatal	5,568
	Unintended live births		All, maternal and neonatal	13,702
			Federal, maternal and neonatal	8,023
			State, maternal and neonatal	5,679
			Per woman (15–44 years of age)	221

^a An incident is defined as a live birth, an abortion or a fetal loss

the source of cost data. For retrospective claims analyses, costs were reported from the perspective of the commercial payer. For retrospective chart reviews linked to registries, estimated costs came from hospital billing data and, in many instances, the cost perspective was not reported. Study design also determined the duration of the study period. In retrospective claims studies, a longer duration of study period was observed compared with prospective studies. The metric for reporting costs varied among individual patient costs, combined maternal and neonatal costs

of care, total cost of care, and cost of care broken down to additional subcategories. Differences in the metrics for reporting cost made it challenging to summarize or standardize costs across studies. Furthermore, there was no comparator group for some studies and the types of outcomes observed, and the associated costs related to the outcomes differed across studies. Therefore, direct comparisons of cost across studies could not be assessed. Reporting of a cost driver is limited to the costs reported within each study.

Table 13 Quality assessment for randomized clinical trials

Author, year	Random sequence generation (selection bias)			Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
	Low risk of bias ^a	Unclear risk of bias ^a	High risk of bias ^a					
Brooten, 2001 [36]	+	?	-	+	-	?	+	+
Grobman, 2004 [35]	+	?	-	+	-	-	+	+

^a Each quality assessment category was coded according to the level of information available or addressed by the authors. Green indicates low risk of bias (i.e. plausible bias unlikely to seriously alter the results); yellow indicates unclear risk of bias (i.e. plausible bias that raises some doubt about the results); red indicates high risk of bias (i.e. plausible bias that seriously weakens confidence in the results)

Among studies that looked at pregnancy-related complications, we observed an increase in medical resource utilization compared with no medical complications during pregnancy. Merrill and Steiner [21] and Podulka et al. [22] examined vaginal delivery and cesarean sections with and without complications, respectively. The reported costs in the groups without complication were lower than in the groups with complication by approximately 25 %. Studies that examined preterm labor and low birth weight observed that the cost of pregnancy in the preterm labor and low birth weight groups was approximately ten times higher than in the normal gestational age group of 37 weeks. Another study that compared anemic mothers with non-anemic mothers reported a higher average total hospitalization cost among anemic mothers than non-anemic mothers. Although direct comparisons of pregnancy-related complications could not be made across the included studies, the within-study comparisons provided evidence that complications during pregnancy were correlated with increased medical resource utilization.

Cost of pregnancy-related complications and cesarean section are two factors that contribute to the overall cost of pregnancy in the US. Another factor is unintended pregnancy, which could place an additional cost burden on the US health care system, as illustrated by Sonfield et al. [25]. In light of the limited number of prospective studies examining unintended pregnancy, an economic model examining the burden of unintended pregnancy in the US developed by Trussell et al. [54] further support the findings of Sonfield et al. [25]. This model estimates the direct costs of unintended pregnancy among women who had poor contraceptive adherence. Overall, the model reported that the annual cost of unintended pregnancy was \$4.6 billion [54]. Of this, 53 % of the cost could be attributed to women who had poor contraceptive adherence [54]. Under the assumption that a small percentage of women under the age of 30 years switched from oral contraception to long-acting reversible contraception, the authors estimated a reduction in cost of \$288 million per year [54]. The limitation of the economic model is that the cost was driven by expected probabilities that were not substantiated by real-world cost data relating to unintended pregnancy.

The limited number of studies that reported on this topic may also be due to the challenge of designing a prospective study that assesses intended and unintended births and contraceptive use simultaneously. A further limitation of the review is the exclusion of model-based cost studies which may provide additional studies on cost. We excluded model-based cost studies because the sources of cost were heterogeneous. Another limitation is the restriction of the cost of pregnancy perspective to the US. In settings where population growth is an issue, family planning and contraceptive methods are widely promoted. Research on the

Table 14 Quality assessment for non-randomized studies

Author, year	Eligibility criteria explicitly described (selection bias)			Selection of eligible population from the target population (selection bias)	Exclusion of participants from analysis of the outcome (selection bias)	Proportion of excluded participants were similar between exposed and unexposed groups (selection bias)	Accounting for missing data (attrition bias)	Ascertainment of exposure without participant's knowledge (detection bias)	Ascertainment of exposure using the same measurement tool for all participants (detection bias)	Methods for ascertainment of exposure and outcome was susceptible to misclassification (information bias)	Controlled for confounders
	Low risk of bias ^a	Unclear risk of bias ^a	High risk of bias ^a								
Conway, 2011 [7]	+	?			+	-	+	+	+	-	+
Kjerulff, 2007 [8]	+	+		+	+	?	-	+	?	?	+
Machlin, 2007 [19]	+	+		+	?	+	?	+	+	+	+
Main, 2011 [20]	?	+		+	?	?	?	+	?	?	?
Cuevas, 2005 [52]	+	+		+	+	+	?	+	+	+	+
Fonseca, 2003 [41]	+	+		+	+	?	+	+	+	-	+
Gilbert, 2003 [39]	+	+		+	-	+	+	+	?	-	+
Jones, 2002 [37]	+	+		+	+	+	?	+	-	-	+
Magriples, 2003 [40]	+	+		+	-	+	+	+	+	?	+
Nicholson, 2011 [48]	?	+		+	+	?	+	?	?	?	?
Phibbs, 2006 [43]	+	+		+	-	?	-	+	-	-	+
Ramsey 2012 [53]	?	+		?	-	?	+	+	?	?	?
Rohnick, 2000 [51]	+	+		+	-	+	+	+	?	-	?
Russell, 2007 [38]	+	+		+	+	+	+	+	?	-	+
Schmitt, 2006 [44]	+	+		+	+	+	+	+	+	-	+
Underwood, 2007 [47]	+	+		+	?	+	+	+	-	-	+
Xu, 2009 [50]	+	?		?	?	+	?	+	?	?	+
Barton, 2006 [28]	+	+		+	+	+	+	+	?	?	+
Chinthamit, 2012 [29]	+	+		+	+	+	?	+	+	?	?
Gabbe, 2000 [30]	+	+		+	+	+	+	?	?	?	+
James, 2008 [31]	+	+		+	?	?	?	+	+	?	+
Goler, 2012 [33]	+	+		+	?	+	?	+	?	?	+
Sonfield, 2011 [25]	+	+		+	?	+	+	+	+	-	+
Katz, 2011 [26]	+	+		+	?	+	+	+	+	+	+
DelliFraine, 2011 [27]	+	+		+	+	?	+	?	+	?	+

^a Each quality assessment category was coded according to the level of information available or addressed by the authors. Green indicates low risk of bias (i.e. plausible bias unlikely to seriously alter the results); yellow indicates unclear risk of bias (i.e. plausible bias that raises some doubt about the results); red indicates high risk of bias (i.e. plausible bias that seriously weakens confidence in the results)

Table 15 Quality assessment for retrospective database studies

		Low risk of bias ^a			Unclear risk of bias ^a			High risk of bias ^a				
Author, year	Rationale for using data source was described (database bias)	Differences in coding and linkages described (selection bias)	A priori specifications of analysis plan (data dredging bias)	Specification of a comparator group (selection bias)	Eligibility criteria explicitly described (selection bias)	Participants eligible during the measurement period (assessment bias)	Description of censoring criteria for censoring bias)	Exposure and outcome definitions are clearly defined (temporal bias)	Sequential relationship exist between exposure and outcome (analytical bias)	Identification of the occurrence of intervention and outcome (detection bias)	Identification of link between the disease and time period for analysis (detection bias)	Controlled for confounders
Fitch 2011 [17]	+	+	+	n/a	+	?	?	+	+	?	?	?
Gazmararian, 2002 [18]	+	+	+	n/a	+	+	?	+	+	+	+	+
Merrill, 2006 [21]	+	+	?	n/a	+	+	?	+	+	+	+	+
Podulka, 2011 [22]	+	+	?	n/a	+	+	?	+	+	+	+	+
Ray, 2003 [23]	?	-	+	n/a	+	+	?	+	+	+	+	+
Thomson Healthcare, 2007 [4]	+	+	+	n/a	+	+	?	+	+	+	+	+
Adams, 2003 [42]	?	-	+	n/a	+	+	?	+	+	-	+	+
Clements, 2007 [45]	+	-	+	+	+	+	?	+	+	-	+	+
Kirkby, 2007 [46]	+	+	+	n/a	+	+	?	+	+	?	+	+
Morrison, 2001 [49]	+	?	+	+	+	+	?	+	+	?	+	+
Rein, 2000 [32]	?	-	+	n/a	+	+	?	+	+	-	?	+
Thorsen, 2004 [34]	?	-	+	+	+	?	-	-	+	?	+	+
Monca, 2011 [24]	+	?	+	n/a	+	+	?	?	?	?	+	?

^a Each quality assessment category was coded according to the level of information available or addressed by the authors. Green indicates low risk of bias (i.e. plausible bias unlikely to seriously alter the results); yellow indicates unclear risk of bias (i.e. plausible bias that raises some doubt about the results); red indicates high risk of bias (i.e. plausible bias that seriously weakens confidence in the results)

costs of intended and unintended pregnancy in these settings is warranted.

Preconception and continuous care and treatment of pregnant women at risk for complications is needed to reduce the cost of care for complication-related events. Additional findings from one study showed that diabetic mothers treated with an insulin pump before pregnancy had a lower mean total cost of care than women who started insulin pump therapy during pregnancy.

5 Conclusion

Overall, the available evidence suggests that preventing pregnancy-related complications and reducing unintended pregnancies may lower the overall economic burden of pregnancy on the US health care system.

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