

### **HHS Public Access**

Am J Obstet Gynecol. Author manuscript; available in PMC 2016 January 01.

Published in final edited form as:

Author manuscript

Am J Obstet Gynecol. 2015 January ; 212(1): 74.e1-74.e9. doi:10.1016/j.ajog.2014.09.009.

## Preventable health and cost burden of adverse birth outcomes associated with pregestational diabetes in the United States

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#### Abstract

**OBJECTIVE**—Preconception care for women with diabetes can reduce the occurrence of adverse birth outcomes. We aimed to estimate the preconception care (PCC)—preventable health and cost burden of adverse birth outcomes associated with diagnosed and undiagnosed pregestational diabetes mellitus (PGDM) in the United States.

**STUDY DESIGN**—Among women of reproductive age (15-44 years), we estimated age- and race/ethnicity-specific prevalence of diagnosed and undiagnosed diabetes. We applied age and race/ethnicity-specific pregnancy rates, estimates of the risk reduction from PCC for 3 adverse birth outcomes (preterm birth, major birth defects, and perinatal mortality), and lifetime medical and lost productivity costs for children with those outcomes. Using a probabilistic model, we estimated the reduction in adverse birth outcomes and costs associated with universal PCC compared with no PCC among women with PGDM. We did not assess maternal outcomes and associated costs.

**RESULTS**—We estimated 2.2% of US births are to women with PGDM. Among women with diagnosed diabetes, universal PCC might avert 8397 (90% prediction interval [PI], 5252-11,449) preterm deliveries, 3725 (90% PI, 3259-4126) birth defects, and 1872 (90% PI, 1239-2415) perinatal deaths annually. Associated discounted lifetime costs averted for the affected cohort of children could be as high as \$4.3 billion (90% PI, 3.4-5.1 billion) (2012 US dollars). PCC among women with undiagnosed diabetes could yield an additional \$1.2 billion (90% PI, 951 million-1.4 billion) in averted cost.

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The authors report no conflict of interest.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

No external funding was used for this study.

**CONCLUSION**—Results suggest a substantial health and cost burden associated with PGDM that could be prevented by universal PCC, which might offset the cost of providing such care.

#### Keywords

diabetes mellitus; economic analysis; pregnancy complications

Women with preexisting, or pregestational, diabetes mellitus (PGDM) have increased risk of adverse birth outcomes.<sup>1-8</sup> PGDM refers to women with type 1, type 2, or secondary diabetes before pregnancy, excluding gestational diabetes. Preconception care (PCC) for women with PGDM reduces the frequency of such outcomes, most likely by improving glycemic control before and during the critical first weeks of pregnancy.9-12 Preconception care refers to a range of interventions to improve women's health before conception and thereby improve pregnancy-related outcomes.<sup>13,14</sup> A recent US study reported significant variation in indicators within several PCC health domains, including general health status, health insurance status, tobacco, and alcohol use, and contraceptive use based on geographic location and women's age and race/ethnicity.<sup>15</sup> The American Diabetes Association recommends that PCC for women with PGDM include contraception until optimal glycemic control is achieved, appropriate diet and exercise, folic acid supplementation, discontinued use of potentially teratogenic medications, screening, and treatment for diabetic complications, screening for rubella immunity, and risk counseling.<sup>16</sup> Previous studies of a variety of small-scale PCC interventions among women with PGDM reported that PCC cost-effectively improved birth outcomes.<sup>17-22</sup>

Given PCC's proven clinical effectiveness in reducing adverse birth outcomes among women with PGDM, we aimed to estimate the preventable health and cost burden of adverse birth outcomes associated with diagnosed and undiagnosed PGDM in the United States. To our knowledge this is the first study to produce such estimates.

#### **Materials and Methods**

No single publicly available US dataset contains all information necessary to directly estimate the potential impact of identifying and treating all women with PGDM before they conceive. Such a dataset hypothetically would report long-term clinical data and associated health care payment information for women and their children, as well as laboratory results from pregnancy to identify previously undiagnosed PGDM.<sup>23</sup> Given the limitations of available data, we compiled existing information from a variety of sources as inputs for a mathematical model. All model inputs are described in detail below and reported in Table 1.

Model inputs included the current population size of US women of reproductive age (defined as 15-44 years<sup>24</sup>), age- and race/ethnicity-specific prevalence of diagnosed and undiagnosed diabetes, age- and race/ethnicity-specific live birth rates, the effectiveness of PCC for women with PGDM (hereafter referred to simply as PCC) in terms of reducing adverse birth outcomes, and the associated lifetime cost of those birth outcomes. The main outcome measures were the total reduction in number of adverse birth outcomes and costs achievable for a cohort of US women of reproductive age through universal PCC compared with no PCC among all women with diagnosed and undiagnosed PGDM. This analysis

examined birth outcomes and costs for affected children with a lifelong time horizon from a societal perspective, including both discounted direct (medical and other services) and indirect (lost productivity) costs. We did not assess the costs of PCC or maternal outcomes and associated costs. This study used publicly available data, did not include human subjects, and was exempt from Institutional Review Board approval.

#### Population size and birth rate

Current population estimates of women of reproductive age were obtained from the US Census.<sup>25</sup> Age- and race/ethnicity-specific live birth rates were obtained from the National Vital Statistics System.<sup>24</sup> The live birth rate among women with diabetes was assumed to be similar to the general population.<sup>26,27</sup>

#### **Diabetes prevalence**

An estimated 2.9% (95% confidence interval [CI], 2.7–3.2) of women of reproductive age (defined as 18-44 years in the source publication) have diagnosed diabetes.<sup>28</sup> This estimate is based on self-report among study participants in the nationally representative 2009 Behavioral Risk Factor Surveillance System (BRFSS). Another study estimated a 0.5% prevalence (no measure of dispersion was reported because of limited sample size) of undiagnosed diabetes among US women of reproductive age (defined as 15-44 years in the source publication) using the nationally representative 1999-2010 National Health and Nutrition Examination Survey (NHANES).<sup>29</sup> We used sex-, age-, and race/ethnicity-specific data on diagnosed diabetes from the BRFSS to estimate the number of women of reproductive age with diagnosed and undiagnosed diabetes by selected age and race/ ethnicity categories (Table 1).<sup>30</sup>

#### Impact of preconception care

A systematic review and meta-analysis of 12 observational cohort studies (n = 2502 participants) examined the health impact of PCC interventions among women with PGDM.<sup>10</sup> Interventions in original studies included a combination of some or all of the following: pharmacologic or dietary glycemic control, blood glucose monitoring, counseling or education on the risks of diabetes in pregnancy, screening and treatment of diabetic complications, and contraception until glycemic control was achieved. The metaanalysis reported the frequency of the following adverse birth outcomes among women with PGDM who did not receive PCC services: 41.4% delivered preterm (n = 155/374 women in 4 original studies), 7.3% had children with birth defects (n = 110/1512 women in 11 original studies), and 4.4% had children who died in the perinatal period (n = 28/634 women in 5 original studies). <sup>10</sup> Preterm deliveries were infants born before 37 weeks' gestation; birth defects were not defined in the metaanalysis and the contributing studies used a variety of definitions. Because of overlap among outcomes in source publications (eg, a child with birth defects could have been born preterm), the metaanalysis did not report rates of adverse birth outcomes on a per-newborn basis. We are not aware of similar US studies with which to compare these estimates. A 1996-2004 population-based UK study of women with known PGDM (n = 1258 pregnancies) reported 3.7% perinatal mortality and 9.0% of live born children had birth defects; the preterm birth rate was not reported.<sup>31</sup> However, no

information was provided on women's PCC status or glycemic control in the UK study; therefore, these results are not directly comparable.

Results of the metaanalysis indicated PCC was associated with statistically significant reductions in preterm delivery, birth defects, and perinatal mortality (Table 1). There was no significant association reported between PCC and cesarean delivery, preeclampsia, spontaneous abortion, macrosomia, neonatal hypoglycemia, respiratory distress syndrome, or newborns' small for gestational age status.<sup>10</sup> In the metaanalysis, PCC was associated with a significantly higher risk of maternal hypoglycemia, although we did not evaluate maternal outcomes in the present study.

#### Lifetime cost of adverse birth outcomes

We used published estimates of the lifetime costs of preterm birth and 17 selected birth defects.<sup>32,33</sup> These estimates included separately reported medical, special education, developmental services, and lost productivity costs for affected children. Estimated costs of selected individual birth defects (eg, tetralogy of Fallot, spina bifida) were reported separately in the source publication, and estimates did not include all types of birth defects.<sup>33</sup> To estimate a general lifetime cost of birth defects, we calculated the average cost of individual defects weighted by the general population frequency of those defects reported in the source publication, which was based on California data. We estimated the lifetime cost of perinatal death as the value of lifetime lost household and labor market productivity. <sup>34</sup> The lifetime costs of preterm birth and perinatal mortality were calculated in the source publications as present values with the recommended 3% annual discount rate applied to costs in future years.<sup>35</sup> To approximate this discount rate for the birth defects estimate, we obtained the lifetime medical-only cost of birth defects discounted at 3% from the source publication's author (via personal communication, Dec. 2013), to which we applied the ratio of lifetime total costs to lifetime medical-only costs reported with a 5% discount rate in the source publication. Costs are reported as 2012 US dollars based on the Gross Domestic Product deflator and are reported separately as total, medical and other services, and lost productivity costs.<sup>36,37</sup>

#### Model

Among the US population of women of reproductive age (62.7 million<sup>25</sup>), we estimated the number with diagnosed diabetes (2.9% of the population<sup>28</sup>) and with undiagnosed diabetes (0.5% of the population without a diabetes diagnosis<sup>29</sup>) by age group and race/ ethnicity.<sup>30</sup> Among that estimated number of women with diabetes, we applied age- and race/ethnicity-specific birth rates (eg, 109.7 births per 1000 white, nonHispanic women age 25-29, 197.1 per 1000 Hispanic women age 25-29<sup>24</sup>). Among that estimated number of births to women with PGDM, we estimated the number of adverse birth outcomes in the absence of PCC (41.4% preterm deliveries, 7.3% children with birth defects, 4.4% perinatal deaths<sup>10</sup>). To estimate the PCC-preventable health burden of adverse birth outcomes associated with PGDM, we applied average rates of relative risk reduction associated with PCC for preterm birth, birth defects, and perinatal mortality estimated in the recent PCC metaanalysis.<sup>10</sup> We estimated the preventable cost burden for each outcome by multiplying the estimated number of outcomes by their associated lifetime cost estimates.<sup>32-34</sup>

We used probabilistic analysis to inform model inputs for which sufficient data were available in source publications, and we used only reported point estimates for other inputs. We included a Pert distribution for the prevalence of diagnosed diabetes among women of reproductive age based on the 95% CI that accompanied the 2.9% point estimate reported in the recent BRFSS study.<sup>28</sup> We used the same distribution to test the 95% CI for relative risk reductions associated with PCC estimated in the recent metaanalysis.<sup>10</sup> Using Latin Hypercube sampling, the number of model simulations was determined by convergence criteria. Simulations ceased when there was a 90% chance that the mean value of each simulation was within 3% of its actual value.<sup>38</sup> We reported mean estimates and 90% prediction intervals (PIs)-or, the range of outcome results that included 90% of model simulations-for all outcome measures. We separately reported results for women with diagnosed and undiagnosed PGDM. We separately reported the estimated preventable cost burden for each adverse birth outcome in terms of direct and indirect costs, as well as the sum of those costs, not taking into account the overlap across outcomes. Analysis was conducted with @RISK software for Microsoft Excel (version 6.2; Palisade Corp, Ithaca, NY).

#### Results

Our approach estimated 2.2% of current US births occur to women with diagnosed and undiagnosed PGDM combined (Table 2). Among women with diagnosed diabetes who give birth (n = 69,357 births), universal PCC compared with no PCC might avert 8397 (90% PI, 5252-11,449) preterm deliveries, 3725 (90% PI, 3259-4126) birth defects, and 1872 (90% PI, 1239-2415) perinatal deaths annually (Table 2). Among women with undiagnosed diabetes who give birth (n = 18,723 births), PCC might avert an additional 2267 (90% PI, 1380-3072) preterm deliveries, 1106 (90% PI, 883-1102) birth defects, and 505 (90% PI, 336-653) perinatal deaths annually.

The estimated PCC-preventable discounted lifetime costs among children of women with diagnosed PGDM were \$502 million (90% PI, 314-684 million) for preterm births, \$1.5 billion (90% PI, 1.3-1.7 billion) for birth defects, and \$2.3 billion (90% PI, 1.5-3.0 billion) for perinatal deaths, for a combined total of \$4.3 billion (90% PI, 3.4-5.1 billion), not taking into account potential double-counting of newborns with more than 1 measured outcome (Table 2). The total cost included \$767 million (90% PI, 2.7-4.3 billion), or 18%, in direct medical and other costs and \$3.6 billion (90% PI, 2.7-4.3 billion), or 82%, in lost productivity costs (Table 2). Likewise, the total PCC-preventable cost among women with undiagnosed PGDM was \$1.2 billion (90% PI, 951 million-1.4 billion); \$207 million (18%) in direct medical and other costs, and \$963 million (82%) in lost productivity costs (Table 2).

#### Comment

We estimated thousands of adverse birth outcomes might be prevented each year among US women with PGDM through universal PCC at an estimated lifetime societal cost savings of up to \$5.5 billion. This study estimated the potential impact of PCC services with proven effectiveness. Our estimates drew on population-based age- and race/ethnicity-specific

PGDM prevalence data and birth rates as well as results from a metaanalysis of PCC studies. Our model included probabilistic elements to test a range of possible values of diagnosed diabetes prevalence and PCC effectiveness. We separately reported results for women with diagnosed and undiagnosed PGDM, and we differentiated between direct medical as well as other service costs and lost productivity costs. With improved availability of populationbased electronic health data, it might be possible to use large-scale, comprehensive health care and payment data to directly estimate the health and cost impact of PCC.

Our estimate of the proportion of US births to women with PGDM heavily influenced our final estimates of preventable health and cost burden. Our estimate that 2.2% of US births are to women with PGDM lies between 2 previous population-based estimates.<sup>27,40</sup> One study of births (n = 209,287) among women enrolled in a single large managed care organization in California from 1999-2005 estimated 1.8% of births-adjusted for women's age and race/ethnicity—were to women with diagnosed PGDM in 2005, a significant increase from 0.8% among the population in 1999.<sup>40</sup> Another study estimated 3.9% of US births in 2013-adjusted for women's age, but not race/ethnicity-were to women with diagnosed and undiagnosed PGDM. That study's estimate was derived from a global systematic review of population-based studies of hyperglycemia first detected in pregnancy, applying new World Health Organization criteria to distinguish preexisting diabetes and gestational diabetes.<sup>23,27</sup> The most recent published US birth certificate data suggests 0.7% of births in 2008 were to women with PGDM, based on 27 states reporting 2.7 million births, or 65% of births that year.<sup>41</sup> However, birth information among states contributing to that estimate was not generalizable to the country as a whole because of demographic differences in terms of race/ethnicity, maternal age, marital status, and infant characteristics.<sup>41</sup> Moreover, reporting of mothers' preexisting diabetes on birth certificates is known to be incomplete.42,43

It is important to note that a substantial fraction of the total PCC-preventable burden of adverse birth outcomes among women with diagnosed diabetes is likely already realized through PCC. Some evidence suggests that up to one-half of American women with diagnosed PGDM may receive preconception counselling and achieve glycemic control before pregnancy.<sup>44,45</sup> A 1996-2010 regional study from the UK suggested PCC attendance among women with PGDM (n = 2293 pregnancies) was around 40% and that compliance with key PCC goals such as folate consumption and adequate glycemic control because of pregnancy was even lower (37% and 28%, respectively).<sup>46</sup>

Much of the preventable burden among women with PGDM remains among those who do not receive PCC and among those with undiagnosed diabetes. However, women with undiagnosed diabetes may have less severe hyperglycemia and therefore have a lower risk of adverse birth outcomes, in which case our estimates may overstate the preventable health and cost burden among that group. Our estimates of preventable adverse birth outcomes among women with undiagnosed diabetes are speculative, inferred from PCC impact estimates among women with diagnosed diabetes. To prevent adverse birth outcomes among women with undiagnosed diabetes, diagnosis in the preconception period is needed; the first step would be screening women of reproductive age to identify those with undiagnosed

diabetes. In a future study, it would be relevant to investigate targeted biochemical screening for PGDM among high-risk women.

This study had a number of limitations. First, we examined only live births—excluding examination of the health and cost outcomes associated with spontaneous and therapeutic abortions—and we assumed women with PGDM have approximately general population fertility.<sup>26,27</sup> Data from a 1965-2004 population-based study in Sweden suggested women with type 1 diabetes had only 80% of the number of births predicted based on general population fertility, although the birth rate among such women increased to be statistically indistinguishable from that of the general population beginning in the 1980s.<sup>26</sup> Some US evidence suggests clinicians provide contraceptive and preconception counseling less frequently to women with diabetes than women without any chronic medical conditions, which could suggest a higher birth rate among women with PGDM than without.<sup>47-49</sup>

A second limitation is that estimates of PCC effectiveness from the recent metaanalysis might have been biased because of the age of contributing studies (published 1986-2006), as well as differences in patient characteristics such as age and smoking status among women who received PCC compared with those who did not in the original observational cohort studies.<sup>10</sup> In particular, the metaanalysis estimate of preterm birth among women with PGDM without PCC, 41%, is primarily attributable to 1 contributing study. Moreover, the studies that contributed to the meta-analysis did not systematically control for antepartum care, which means the benefits of PCC from those studies could be overstated through confounding with other types of obstetric care. Some of the studies on which the metaanalysis was based are over 20 years old. The reduction in adverse birth outcomes associated with PCC may now be more modest because of better diabetes care, for example, better A1C control, and improved awareness of this issue in the population with diagnosed PGDM. Additional studies of the impact of PCC are needed. Areas for further investigation include the impact of PCC on preterm birth by gestational age and the impact on early fetal death.

Third, the present study consisted of a single cross-sectional analysis of all women of reproductive age. We lacked estimates of the annual incidence of diabetes in this cohort, which could have allowed us to incorporate factors such as passing time and changing cohort composition. Fourth, the lifetime cost of birth defects was based on older data from 1 state, although it was the most recent available comprehensive estimate.<sup>33</sup> A related limitation is that we used a general estimate of the lifetime cost of birth defects, which might not reflect the average cost of birth defects that occur most frequently among women with PGDM.<sup>50</sup>

A fifth limitation is that our analysis focused only on birth outcomes and did not include mothers' health outcomes and associated costs. The cost of diabetes treatment and management can be substantial, although there is evidence that undiagnosed diabetes also incurs a substantial cost in terms of both medical care and lost productivity.<sup>51-53</sup> One small study of women with type 1 diabetes found that PCC was associated with significantly fewer hospitalizations during pregnancy and shorter inpatient stays as well as shorter length of stay after delivery.<sup>22</sup> Only one-half as many women who received PCC were hospitalized, 40%

vs. 80%, primarily for control of diabetes complications. The implication of these findings is that our estimates of the preventable burden among women with PGDM are understated because they do not take into account the preventable burden of excess hospital care among pregnant and postpartum women with PGDM. Additional studies of the impact of PCC on maternal outcomes are desirable.

On the other hand, our estimate of PCC-preventable cost burden could be a high-end estimate for 2 reasons. First, data on the frequency of adverse birth outcomes in the source publications did not explicitly report per-newborn outcomes; therefore, costs for children with multiple outcomes (eg, a child born preterm and with birth defects) were potentially double counted. Because a large number of perinatal deaths are associated with preterm birth and/or birth defects, the degree of double-counting of costs in our model is likely substantial. Second, input data on the lifetime costs of adverse birth outcomes were not mutually exclusive. For example, the lifetime cost of birth defect estimates in the source publication included the costs of both perinatal mortality and preterm birth among infants with birth defects. Similarly, the estimated lifetime cost of preterm births included the costs of infant mortality and some birth defects for infants born preterm. To address these issues, we reported estimated preventable costs separately by birth outcome. If one takes the estimated averted cost of just 1 outcome, such as birth defects (Table 2), there is still a substantial preventable health and cost burden associated with PGDM.

Delivery models for PCC services are highly varied;<sup>54</sup> thus, it is difficult to calculate a valid point estimate for the cost of potential PCC interventions. Because a cost-effectiveness analysis of PCC would require robust PCC cost estimates, in this study we focused on calculating the potential health and cost benefits of PCC services as a first step toward an economic evaluation of PCC for women with PGDM. Further study of the cost and associated benefits of PCC for participating women, as well as women's compliance with PCC, is needed.

The preconception period is critical for preventing adverse birth outcomes in women with PGDM. By some estimates nearly half of US pregnancies, including pregnancies among women with PGDM, are unplanned.<sup>15,55,56</sup> Targeted blood glucose testing among women of reproductive age during existing physician office visits to identify women with undiagnosed diabetes might incur a nominal cost per woman.<sup>57</sup> Once women's PGDM status is known, information on both women's pregnancy intent and existing birth control methods might assist clinicians to cost-effectively triage women to PCC services ranging from counselling on the risk of conception when glucose levels are elevated as part of an existing physician visit, to more intensive regimens such as glucose monitoring and pharmacologic control.

Because our aim was to quantify the total preventable burden of PGDM, our estimates implicitly assume full PCC participation once PGDM is identified. Not all women identified with PGDM accept glucose screening or PCC or, once begun, fully adhere to recommended interventions. Further, access to reproductive services is not equally distributed across the US female population of reproductive age; it is possible that lack of insurance coverage might disproportionately affect women with both unintended pregnancies and undiagnosed

Our results suggest the PCC-preventable health and cost burden of adverse birth outcomes associated with PGDM is substantial. The cost of interventions to identify and provide PCC to women of reproductive age with diabetes could be compared with our results to assess how clinical and public health activities might cost-effectively address this preventable burden.

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**TABLE 1** 

		Distribution	of estimate by	y age and race	/ethnicity	
Parameter	Estimate	White, NH	Black, NH	Other, NH	Hispanic	Details and source
Women age 15-44 y, n	62,744,930					2012 estimate, US Census $(2013)^{25}$
Diabetes prevalence, %						
Diagnosed	2.9 (2.7–3.2) <sup>b</sup>					2009 estimate, crude prevalence for women age 18-44 years, Hayes et al (2011) <sup>28</sup>
Undiagnosed	0.5					1999-2010 estimate, crude prevalence for women age 15-44 years, Razzaghi et al (2013) <sup>29</sup>
Diabetes cases, % of total	1.00					Calculated as the survey-weighted number
18-24 y <sup>a</sup>		3.0%	2.3%	0.6%	1.6%	of women reporting a diabetes diagnosis by age and race/ethnicity divided by the total number of women renorting a diabetes diagnosis BRFSS
25-29 y		5.7%	2.6%	0.4%	2.2%	(2009) <sup>30</sup>
30-34 y		9.4%	3.0%	1.8%	4.5%	
35-39 y		10.1%	4.7%	2.4%	6.9%	
40-44 y		19.7%	7.2%	2.8%	9.2%	
Annual births, n	3,952,841					$2011$ estimate, Martin et al $(2013)^{39}$
Births, rate per 1000 women	68.1					2008 estimate, Ventura et al (2012) <sup>24</sup>
15-19 y		26.7	60.4	17.3	111.5	
20-24 y		82.8	131.5	54.8	229.5	
25-29 y		109.7	108.8	93.9	197.1	
30-34 y		100.8	75.3	102.2	149.2	
35-39 y		45.2	36.3	54.4	87.2	
40-44 y		9.6	9.3	14.7	23.9	
Births affected by adverse birth out	tcomes among women	with untreated I	PGDM, % <sup>c</sup>			
Preterm delivery	41.4	I	I	I	I	Wahabi et al (2010) <sup>10</sup>
Birth defects	7.3	I	I	Ι	I	
Perinatal mortality	4.4	I	I	Ι	I	
PCC effectiveness, risk reduction <sup>d</sup>						

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		Distribution	of estimate by	y age and race	/ethnicity	
Parameter	Estimate	White, NH	Black, NH	Other, NH	Hispanic	Details and source
Preterm delivery	0.70 (0.55–0.90) <sup>b</sup>	Ι	Ι	I	I	Wahabi et al (2010) <sup>10</sup>
Birth defects	0.25 (0.15–0.42) <sup>b</sup>	Ι	I	I	I	
Perinatal mortality	0.35 (0.15–0.82) <sup>b</sup>	I	Ι	I	I	
Unit costs, USD $2012^{36}$ (% of total	cost)					
Preterm delivery <sup>e</sup>	\$59,750	Ι	I	I	I	Institute of Medicine $(2012)^{32}$
$ullet$ Medical and other services $^f$	\$46,762 (78.3)					
<ul> <li>Lost productivity</li> </ul>	\$12,988 (21.7)					
Birth defects (lifetime) $^{\mathcal{R}}$	\$411,723	Ι	I	I	I	Waitzman et al (1994) <sup>33</sup>
$ullet$ Medical and other services $^f$	\$100,395 (24.4)					
<ul> <li>Lost productivity</li> </ul>	\$311,328 (75.6)					
Perinatal mortality (lifetime) $h$	\$1,227,372	Ι	Ι	I	I	Grosse et al (2009) <sup>34</sup>
<ul> <li>Medical and other services</li> </ul>	\$0 (0.0)					
<ul> <li>Lost productivity</li> </ul>	\$1,227,372 (100.0)					
BRFSS, Behavioral Risk Factor Surve	illance System; NH, no	onHispanic; <i>PC</i>	C, preconcept	ion care; <i>PGD</i>	M, pregestati	onal diabetes mellitus; USD, US dollars.
Peterson. Preventable burden of adve	rse birth outcomes ass	ociated with P0	GDM. Am J Ol	bstet Gynecol	2014.	
<sup>a</sup> Number of women with diagnosed d	liabetes assumed to be	evenly divided	among ages 1:	5-19 y and 20-	24 y	

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 $b_{\rm Dett}$  distributions for model simulations assigned point estimate (95% confidence interval) as reported in the table, from source publications

<sup>C</sup>Not mutually exclusive (ie, a child born with birth defects might also have been born preterm and suffered perinatal mortality)

 $^d$ Risk ratios from PCC metaanalysis<sup>10</sup>

<sup>e</sup>Lifetime cost of preterm birth included medical care (including attributable labor and delivery services), early intervention, special education, and lost productivity (for newborn) costs attributable to preterm birth, discounted at 3% in source publication<sup>32</sup>

<sup>1</sup>Includes early intervention and special education services (preterm birth estimate) and medical, developmental, special education, and long-term care services (birth defects estimate)

<sup>8</sup>Lifetime cost of birth defects included medical care, developmental services, and special education costs attributable to birth defects, with an approximated 3% discount rate based on 3% discounted

medical costs (from source publication author) multiplied by the proportion of non-medical costs to medical costs reported with a 5% discount rate in the source publication.<sup>33</sup> Overall birth defects estimate represents the average cost of 17 selected birth defects, weighted by the prevalence of those defects reported in the source publication for the analysis year

h. The cost of perinatal mortality was assessed as the estimated lifetime cost of lost household and labor market productivity for age 0 (reported in an appendix from the source publication). 34 Author Manuscript

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Estimated annual preventable US health and cost burden of adverse birth outcomes associated with pregestational diabetes

Outcome	Diagnosed PGDM	Undiagnosed PGDM	Total
Births to women with PGDM, n (% of total births) <sup><math>a</math></sup>	69,357 (1.8)	18,723 (0.5)	88,081 (2.2)
Health outcomes, n (90% PI) $^b$			
Preterm deliveries	8397 (5252–11,449)	2267(1380–3072)	10,664 (6610–14,527)
Birth defects	3725 (3259–4126)	1006 (883–1102)	4731 (4158-5215)
Perinatal mortality	1872 (1239–2415)	505 (336–653)	2377(1586–3090)
Costs, USD 2012 (90% PI)			
Preterm deliveries	\$501,703,904 (313,785,577–684,076,491)	\$135,473,915 (82,442,051–183,528,026)	\$637,177,820(394,974,563–868,009,686)
• Medical and other services <sup>c</sup>	\$392,647,563 (245,577,404–535,377,471)	\$106,025,690 (64,521,464–143,634,186)	\$498,673,253 (309,118,184–679,328,754)
<ul> <li>Lost productivity</li> </ul>	109,056,341 (68,208,173–148,699,021)	229,448,225 (17,920,587–39,893,839)	\$138,504,566 (85,856,379–188,680,932)
Birth defects	\$1,533,587,532 (1,341,975,970–1,698,795,150)	\$414,118,465 (363,744,098–453,596,957)	\$1,947,705,997 (1,711,989,755–2,147,080,326)
• Medical and $\frac{1}{c}$	\$373,952,105 (327,229,277–414,236,559)	\$100,979,219 (88,695,864–110,605,709)	\$474,931,325 (417,453,950–523,547,037)
other services			
<ul> <li>Lost productivity</li> </ul>	\$1,159,635,427 (1,014,746,693–1,284,558,591)	313,139,246 (275,048,234–342,991,247)	1,472,774,672 (1,294,535,805–1,623,533,289)
Perinatal mortality	\$2,297,401,879 (1,520,397,400–2,963,922,475)	620,375,541 (412,304,510–801,716,482)	22,917,777,420 (1,946,698,633–3,793,161,251)
Medical and     other services	80	\$0	80
<ul> <li>Lost productivity</li> </ul>	\$2,297,401,879 (1,520,397,400–2,963,922,475)	620,375,541 (412,304,510–801,716,482)	22,917,777,420 (1,946,698,633–3,793,161,251)
Total	\$4,332,693,315 (3,433,535,264–5,084,229,581)	1,169,967,922 (950,579,806–1,364,940,585)	\$5,502,661,237 (4,402,017,112–6,449,170,166)
Medical and     other services	\$766,599,668 (610,886,323–927,731,787)	\$207,004,910 (163,235,877–247,895,257)	\$973,604,578 (768,193,443–1,176,403,784)
<ul> <li>Lost productivity</li> </ul>	\$3,566,093,647 (2,737,605,347–4,250,007,368)	\$962,963,012 (745,247,121–1,151,210,044)	44,529,056,659 $(3,477,538,487-5,411,362,584)$
Data are estimates from a simulat	tion model with narameters snecified in Table 1 Ber	imates refer to the difference in the number of ad-	Perse hirth outcomes and costs associated with preco

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nception care for all women with pregestational diabetes compared with no preconception care. A 90% PI indicates that 90% of model simulations fell within the reported range. Costs separately modeled for total and component parts, therefore the component cost estimates do not sum precisely to total cost estimates.

PGDM, pregestational diabetes mellitus; PI, prediction interval; USD, US dollars.

Peterson. Preventable burden of adverse birth outcomes associated with PGDM. Am J Obstet Gynecol 2014.

 $^{a}$ Based on 3,952,841 total births;<sup>39</sup>

 $^{b}$ Not mutually exclusive (ie, a child born with birth defects might also have been born preterm and suffered perinatal mortality)

<sup>c</sup> Includes early intervention and special education services (preterm birth estimate) and medical, developmental, special education, and long-term care services (birth defects estimate).

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