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Short-term health and economic burden of gestational diabetes mellitus in Mexico: A modeling study

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ABSTRACT

Aim: To estimate the annual burden of gestational diabetes mellitus (GDM) in Mexico.
Methods: A model was built to conduct estimates from a healthcare system perspective, namely, the incremental costs of GDM pregnancy compared with non-GDM pregnancy from the first trimester until childbirth. The model used probabilities from the literature and surveys, and costs obtained from the Ministry of Health and national healthcare institutions. Scenario analyses were performed to estimate the GDM burden at different levels of incidence.
Results: Although a non-GDM pregnancy cost on average USD 1880.6 (low risk was USD 1043.9 and high risk was USD 1673.5), a pregnancy with GDM cost USD 2934.9. Therefore, the total additional cost was USD 1576.2 per case. Given the considerable variability of the GDM incidence in Mexico, the total burden could range from USD 86.8 to USD 827.4 million per year.
Conclusions: GDM is one of the most frequent complications of pregnancy, but research has been insufficient regarding its epidemiological and economic burden in Latin America. This paper shows that the GDM economic burden in Mexico is substantial despite only accounting for short-term medical costs. Further research to assess the GDM incidence and evaluate its long-term consequences from a broader societal perspective in Mexico is recommended.

1. Introduction

Gestational Diabetes (GDM) is "hyperglycaemia that is first recognized during pregnancy" [1]. Women who suffer from it are at greater risk of adverse pregnancy and delivery outcomes [1]. In addition, GDM is a risk factor for Type 2 diabetes (T2D) for both mother and offspring up to 25 years after delivery [2]. Worldwide, about 17% of pregnancies are affected by GDM but the incidence ranges from 1% to more than 25% according to diagnostic criteria and maternal risk factors (e.g. age, body mass index (BMI) and ethnicity) [3–7].

The Mexican health system comprises multiple subsystems targeting different groups of the population. First, the

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social security system includes multiple public institutions, namely, the Mexican Institute of Social Security (MSS) and the Institute of Security and Social Services for State Workers (ISSSTE), that provide health insurance and services for the formally employed population. Second, the Ministry of Health (MoH) covers most of the population that participates in the informal sector of the economy, and most of that population are enrolled in Seguro Popular as part of a social protection system for health. Finally, a heterogeneous private sector offers services at different levels of quality to the entire population.

In Mexico, no official national incidence of GDM is available. However, since 1988, when the first paper reporting a GDM incidence of 4% was published [8], several studies have shown an increasing trend, which was greater than 30% in 2016 [9], and large variation depending on the screening protocol and diagnostic criteria used, and the population studied (e.g., at risk or not) [10–19,9]. Although all the studies have used an Oral Glucose Tolerance Test (OGTT) to diagnose GDM in pregnant women, no consistency was observed in the use of glucose dose (75 g or 100 g), 1- or 2-step protocol (50 g glucose-load at first), and/or GDM interpretation criteria, in the majority of studies [8,10,12,15–17,20,19] relying on data from the American Diabetes Association (ADA) [21,22] and the rest on different ones [11,23–26].

These findings are not consistent with the more current evidence from two large national surveys, the Encuesta Nacional de la Dinámica Demográfica (ENADID) [27] and the Encuesta Nacional de Salud y Nutrición (ENSANUT) [28], and a cohort study, ESMaestras, [29] which stated a GDM incidence of 2.5%, 3.2%, and 1.63%, respectively. However, these estimates are based on retrospective and self-reported data (i.e. only diagnosed cases), raising concerns about their reliability and the problem of underdiagnosed rates in our population.

Whatever the real GDM incidence, every GDM case implies adverse health outcomes and additional costs. Therefore, the aim of this study was to perform the first estimate of the health and economic burden of GDM in Mexico from a healthcare system perspective by considering the period from the first trimester until and including childbirth. To achieve this aim, we calculated the incremental direct medical costs paid by the main public healthcare insurance providers for GDM pregnancy and compared that amount with a non-GDM pregnancy. To estimate the national economic burden of GDM, this difference was then applied to all Mexican women who deliver in 1 year (estimated in 2.3 million [2,339,530] given the average of babies born alive from 2006 to 2012 [30]) and are covered by the public sector through health insurance—IMSS, ISSSTE, or MoH—(74.8% of those), for a total of USD 1.7 million. Scenario analyses were performed to estimate the GDM burden at different levels of incidence if the treatment guidelines were implemented countrywide.

2. Materials and Methods

2.1. Epidemiological data

Epidemiological data was gathered from multiple sources to estimate key parameters for the cost projections. Information regarding the characteristics of the women of reproductive age at the national level and the self-report of GDM events among pregnant women during their last pregnancy were obtained and estimated using cross-sectional data from the National Health and Nutrition Survey, 2012 ["Encuesta Nacional de Salud y Nutrición," ENSANUT] and the National Dynamic Demographic Survey, 2014 ["Encuesta Nacional de Dinámica Demográfica," ENADID] by considering the complex sampling strategies and weight for each survey. We estimated the proportion of pregnant women with a low-risk and high-risk of developing GDM based on the information from ENSANUT [28] by following the criteria defined by the national GDM guidelines [31] [2]. Specific parameters related to GDM care, such as the distribution of GDM cases across different alternative treatments (diet and exercise only, metformin, or insulin) and the distribution of women on whom one-step or two-step GDM screening is performed, were obtained from a cross-sectional physician survey. The survey covered 349 healthcare practitioners from the main public health providers in four cities in Mexico (i.e., Merida, Guadalajara, Monterrey, and Mexico City); see more details in [32].

2.2. Estimation of costs

We estimated normative costs for diagnostic and treatment of GDM from a provider's perspective based on the most recent update of the national clinical practice guidelines (CENETEC) for the care of gestational diabetes and the care of normal pregnancy followed by the three main public health care institutions: the MSS and the Institute of Security and Social Services for State Workers (ISSSTE), targeting employees of the private and public sector, respectively and the MoH, covering individuals without official employment.

For this analysis, pre-gestational diabetes was not considered, and we estimated only the incremental cost of medical procedures recommended for GDM screening among pregnant women according to their GDM risk profile (low- or high-risk) and for GDM care according to their treatment (diet and exercise only, or[2] with metformin/insulin on top). We categorized the management of GDM care into five steps by following the national guidelines' recommendations [31]

(1) *Screening* by using either the one-step or the two-step screening method according to the GDM risk profile. Method 1 comprises an OGTT one-step with 2 h, 75 g glucose test, and 2 h. Method 2 comprises an OGTT two-step with 50 g glucose test and 1 h, followed by 100 g glucose test and 3 h. (Supplemental material Figs. 1 and 2).

[2] 1. Women considered low risk fulfill at least one of the following risk factors: belong to an ethnic group, aged under 25 years, normal BMI in pregnancy, normal birth weight, and no diabetes in first-degree relatives. Women considered high risk fulfill at least one of the following risk factors: presence of overweight/obesity, known diabetes in first-degree relatives, established diagnosis of glucose intolerance, and history of macrosomic products.

(2) *Follow-up* comprises consultations (physician and nutritionist), medicine, and laboratory fees (e.g. ultrasound, blood, and urine examinations).
(3) *Self-monitoring* comprises the screening kit (capillary glucose monitoring device, glucometer, reactive strips, and lancets) and the other facilities required to measure glucose levels for women with GDM.
(4) *Pharmacological treatment* is the costs related to nutritional supplements (iron and folic acid) and other medicine used for the care of normal pregnancy as well as the unitary cost of pharmacological treatment (metformin or insulin) of women with GDM in a proportion rates based on the aforementioned physician survey. The initial doses of metformin and insulin, recommended in the national guidelines, were based on the women's weight. The baseline average weight of a woman at a reproductive age in Mexico was 67 kg [28]. We then added to this figure the average weight gained from the onset of pregnancy to week 24, which was approximately 6 kg [33]. In cases with insulin, an additional cost was because of the time spent by health providers to train women on how to apply insulin based on the physician survey [32].
(5) *Delivery care*, either vaginal or C-section.

The input prices used in the model were calculated based on 2015 Mexican prices [34] and converted into 2017 USD dollars at an inflation rate of 9.01 and an exchange rate of MXN 1 = USD 18.16 [35]. We used the mean of prices of the three main healthcare public providers in Mexico (MoH, IMSS, ISSSTE) (see supplementary material, Table S3).

2.3. Probabilities

We estimate the economic GDM burden based on different levels of GDM incidence: 3%, 6%, 10%, and 30%. The first two figures reflected the self-reported (with medical diagnosis) proportion of women with GDM as published in the national surveys [27,28]. The 10% and 30% incidences (depending on the diagnosis criteria used) were obtained from a Mexican study performed on 803 "urban women with a singleton pregnancy, without concomitant diseases and no prior history of GDM, who underwent a 2-step screening protocol for diagnosis of GDM at admission to prenatal care" [20]. According to the physician survey implemented in Mexico [32], approximately 62.7% of physicians mentioned using one-step screening and the remaining 2-step screening protocol to test high-risk pregnant women for gestational diabetes.

To model the economic burden of GDM in Mexico, we estimated the probability for women to have gestational diabetes and to have a C-section using the ENSANUT 2012 and information from the literature [36], and to be treated with diet, insulin, or metformin in case of GDM by using information from the physician survey [32] and from different cross-sectional national health and demographic surveys [27,28]. We project four different scenarios based on different incidence levels: 3%, 6%, 10%, and 30% GDM incidence.

3. Results

3.1. Epidemiological and socioeconomic characteristics and access to health services

Table 1 shows the main epidemiological and socioeconomic characteristics of women of reproductive age [27,28]. The mean age of the women was 33.7 ± 8.3 years; approximately 85% mentioned having been pregnant; and their number of pregnant consultations was approximately 8.7 ± 4.7, which was less frequent by approximately one consultation among women that attended MoH services (8.1 ± 4.2). Most of women monitored their pregnancies with a physician (96.4%) and approximately 85% initiated antenatal care in the first trimester of pregnancy. The four most common complications during pregnancy were kidney infection, threatened abortion, high blood pressure, and anemia. Based on disaggregated information by type of provider the proportion of high sugar/-diabetes could fluctuate from 3.0% to 4.5%; however, when we disaggregated this indicator by region, this could vary from 3.0% to 6.2% (information not shown). The most common complication at birth was preeclampsia/eclampsia (20.9%), followed by threatened abortion, high blood pressure, premature birth, and vaginal bleeding.

Table 2 displays the main parameters used for modeling the epidemiological and economic burden using figures from the national health and reproductive surveys and the health practitioners' survey in Mexico. Based on the criteria of national guidelines to classify women at high-risk of having GDM during pregnancy and the information from the ENSANUT 2012, we observed that almost 90% of pregnant women have a high-risk GDM pregnancy, and this result is mainly attributed to the high prevalence of overweight/obesity among women of reproductive age (70% - ENSANUT). Based on the information yielded by the practitioners' survey, more than a half the practitioners (60%) mentioned use of the one-step method to screen for GDM, and the same pattern was observed when the information was disaggregated by type of public institution. This survey demonstrated that practitioners' recommendations for treatment for women with a GDM pregnancy were as follows: approximately 40% diet and exercise only, 42% metformin, and 18% insulin [32].

3.2. Frequency of consumption and cost of healthcare resources

Table 3 displays the frequency of consumption and costs of health care according to different steps of care and the women's risk group for GDM and, in the case of having been diagnosed with GDM, treatment.

At the screening stage, high-risk non-GDM pregnancies cost as much as GDM cases, because of the 1-step or 2-step OGTT provided to all. The difference in cost with low-risk non-GDM pregnancies, in which only fasting glucose was performed, was USD 166.6.

Regarding following-up, women with GDM cost USD 1822.9 more than women without GDM because of ultrasound Doppler and non-stress tests, performed, respectively, 3 and 9 times during the pregnancy among women with GDM, not

Table 1 – Epidemiological and socioeconomic characteristics of pregnant women.

Variable	Total	Type of institution[1]		
		IMSS	ISSSTE	MoH
Characteristics of women of reproductive age				
Age, mean ± SD	33.7 ± 8.3	33.8 ± 8.2	36.8 ± 8.3	33.2 ± 8.3
Ever pregnant (yes) %	85.40	82.8	78.5	88.2
Women with a live born child in the last 5 years				
Number of prenatal consultations, mean ± SD	8.7 ± 4.7	9.6 ± 5.4	9.9 ± 3.9	8.1 ± 4.2
Medical staff that monitored pregnancy %				
Physician	96.4	97.9	97.6	95.4
Nurse	2.5	1.7	1.0	3.2
Trimester of first antenatal visit %				
First	85.6	89.2	95.1	82.5
Second	12.1	9.2	3.9	14.6
Third	2.3	1.6	1.0	2.9
Complications during pregnancy				
High blood pressure	15.2	16.5	12.5	14.6
Vaginal bleeding	10.5	12.1	9.1	9.6
Threatened abortion	19.9	21.1	19.9	19.2
Preeclampsia/eclampsia	9.1	10.1	12.5	8.2
High blood sugar/diabetes	3.4	3.8	4.5	3.0
Anemia	15.5	14.6	11.8	16.5
Urinary tract infection	36.1	37.6	34.4	35.6
Sexually transmitted infection	1.9	1.8	1.9	2.0
HIV/AIDS infection	0.5	0.4	0.1	0.5
Other diseases	2.1	2.0	1.2	2.3
Complications at birth				
Preeclampsia/eclampsia	20.9	20.1	20.1	21.6
High blood pressure	5.2	6.1	8.4	4.4
Vaginal bleeding	4.2	3.0	4.3	4.9
Abortion	1.0	0.9	0.2	1.2
Threatened abortion	5.4	5.2	6.2	5.4
Fetal malposition	3.3	4.0	5.4	5.4
Breech presentation	4.9			
Premature birth	4.6	6.0	5.0	3.7
Other disease	1.7	1.6	0.6	1.8

[1] The Mexican Institute of Social Security (IMSS), Institute of Security and Social Services for State Workers (ISSSTE), and Ministry of Health (MoH). All the data were obtained from (ENSANUT, 2012).

recommended for non-GDM pregnancies. Other follow-up interventions, such as amniotic fluid analysis (3 times) and specialized consultation in a second level of care (approximately 18 times) were also performed only among women with a GDM pregnancy, and self-monitoring of glucose levels, which varied from USD 157.2–181.1, depending on the GDM treatment. Among women with a GDM pregnancy prescribed pharmacological treatment, those requiring insulin cost USD 82 more than those requiring metformin because of the use of syringes, the need for training on how to use insulin, and the higher cost of each dose of rapid insulin (USD 0.4) and NPH insulin (USD 0.2) with respect to metformin (USD 0.03).

3.3. *Model results*

The pregnancy of a woman at low risk of glucose intolerance cost is on average USD 1043.9 and includes only the basic tests for all women. Treating a woman at high risk with a negative result on the GDM test costs on average USD 1673.5 because of the additional cost of OGTT. In the case of GDM, the cost increases consistently to USD 2934.9 per woman because of the extra tests performed during pregnancy, the higher likelihood of CS, the self-kit to monitor glycaemia, and, whenever required by the severity of the disease, the pharmacological treatment in addition to diet and exercise (metformin or insulin). The model is shown in Fig. 1.

The difference between the cost of a pregnancy with GDM (USD 2934.9) and the cost of a pregnancy without GDM (USD 1880.6) was on average USD 1043.9 for high-risk and USD 1043.9 for low-risk and equal to USD 1576.2, which, multiplied by the number of women suffering from GDM, provided the annual total burden of GDM in Mexico.

3.4. *Sensitivity analysis*

To consider the eventual differences among healthcare institutions and country regions and to check the robustness of the results, we performed deterministic and probabilistic sensitivity analyses. In the deterministic sensitivity analysis (Tornado diagram, Fig. 2), we applied ±10% variations to all the prices/unitary costs (listed in Table 3) and probabilities (reported in Table 2), except for the GDM prevalence and

Table 2 – List of parameters to estimate economic burden of GDM in Mexico.

Parameter	Indicator	Total (%)	Type of institution (%)	IMSS	ISSSTE	MoH	Source
Percentage of women in reproductive age	Women in reproductive age (14–49)/Total women	77.5	-	-	-		ENSANUT 2012
Percentage of pregnant women per year	Pregnant women per year/Total women in reproductive age	7.5	–	–	–		ENSANUT 2012
Percentage of pregnant women with GDM	Pregnant women with GDM/Total of pregnant women	3.1	–	–	–		ENSANUT 2012
Percentage of high-risk GDM pregnancies	Pregnant women at high-risk of GDM/Total of pregnant women	89.8	–	–	–		ENSANUT 2012-REGRESSION
GDM screening							
Percentage of one-step screening method	Percentage of doctors that mention using the one-step screening method	61.0*	66.6	68.2	60.2		Practitioners SURVEY 2017
Percentage of two-step screening method	Percentage of doctors that mentioned using the two-step screening method	39.0*	33.3	41.8	39.8		Practitioners SURVEY 2017
GDM treatment							
Percentage of women treated with diet and exercise	Percentage of pregnant women with GDM treated with diet and exercise according to what doctors mentioned prescribing in their consultation	40.6*	34.1	36.9	45.2		Practitioners SURVEY 2017
Percentage of women treated with metformin	Percentage of pregnant women with GDM treated with metformin according to what doctors mentioned prescribing in their consultation	41.9*	45.3	40.2	41.3		Practitioners SURVEY 2017
Percentage of women treated with insulin	Percentage of pregnant women with GDM treated with insulin according to what doctors mentioned prescribing in their consultation	17.5*	20.6	22.9	13.5		Practitioners SURVEY 2017
Type of delivery							
Percentage of women with a GDM pregnancy with normal delivery	Pregnant women with GDM-normal delivery/ pregnant women with GDM	39.5	–	–	–		ENSANUT 2012
Percentage of women with a GDM pregnancy with C-section	Pregnant women with GDM-C-section /pregnant women with GDM	60.5	–	–	–		ENSANUT 2012
Percentage of women without a GDM pregnancy with normal delivery	Pregnant women with GDM-normal delivery/ pregnant women	54.0	–	–	–		ENSANUT 2012
Percentage of women without a GDM pregnancy with C-section	Pregnant women with GDM-C-section /pregnant women	46.0	–	–	–		ENSANUT 2012

Legend:
* Weighted average.

Table 3 – Frequency of consumption and cost of healthcare resources classified by mother's risk status.

Resource	Frequency of consumption					Price or *Unitary cost* (USD)	Total cost (USD)				
	No GDM		GDM				No GDM		GDM		
	Low-Risk pregnancy	High-Risk pregnancy	Diet & Exercise	Metformin	Insulin		Low-Risk pregnancy	High-Risk pregnancy	Diet & Exercise	Metformin	Insulin
Screening											
Fasting glucose (first trimester)	1	1	1	1	1	5.3	5.3	5.3	5.3	5.3	5.3
Fasting glucose (24–28 weeks low risk)	1	0	0	0	0	5.3	5.3	0	0	0	0
OGTT 1-step	0	1	1	1	1	31		31	31	31	31
OGTT 2-step	0	1	1	1	1	68		68	68	68	68
Total							**5.3**	**54.8**	**54.8**	**54.8**	**54.8**
Follow-up											
Blood type and RH	1	1	1	1	1	5.9	5.9	5.9	5.9	5.9	5.9
General laboratory examinations	1	1	1	1	1	39.4	39.4	39.4	39.4	39.4	39.4
Syphilis test (VRDL)	1	1	1	1	1	20	20	20	20	20	20
Glycosylated hemoglobin	1	1	3	3	3	12	12	12	36	36	36
Urine test	1	1	3	3	3	6.1	6.1	6.1	18.3	18.3	18.3
Urine culture	1	1	3	3	3	15.5	15.5	15.5	46.5	46.5	46.5
Pap smear	1	1	3	3	3	7	7	7	21	21	21
Pelvic and abdominal ultrasound plus non-stress test			5	5	5	86.5			432.5	432.5	432.5
Pelvic and abdominal ultrasound	3	3	1	1	1	59.3	177.9	177.9	59.3	59.3	59.3
Specialized consultation in a 2nd level of care			12	12	12	55.5			666	666	666
General consultation	5	5	1	1	1	28.3	141.5	141.5	28.3	28.3	28.3
Nutritional consultation	0	0	5	5	5	28.3			141.5	141.5	141.5
Total							**425.3**	**425.3**	**1514.7**	**1514.7**	**1514.7**
Self-monitoring											
Glucometer			1	1	1	42			42	42	42
Lancets			1	1	1	39			39	39	39
Self-testing kit			236	236	310	0.3			70.8	70.8	93
Total									**151.8**	**151.8**	**174**
Pharmacological treatment											
Rapid insulin (a)					98	0.4					39.2
NPH insulin (b)					98	0.2					19.6
Metformin (c)				98		0.48				47.04	
Syringes					392	0.04					15.68
Education self-application of insulin (d)					2.66	6.4					17.02
Folic acid (e)	174	174	174	174	174	0.59	102.66	102.66	102.66	102.66	102.66
Iron	270	270	270	270	270	0.07	18.9	18.9	18.9	18.9	18.9
Total							**121.56**	**121.56**	**121.56**	**168.6**	**213.1**

Delivery											
Vaginal delivery	1	1	1	1	1	435.9	435.9	435.9	435.9	435.9	435.9
C-section	1	1	1	1	1	545.9	545.9	545.9	545.9	545.9	545.9

Legend:
(a) USD 0.4 is the cost of the daily dose that is 14.6 UI/kl. According to the guidelines [CENETEC, 2016] a woman GDM take this dose for 98 days.
(b) USD 0.2 is the cost of the daily dose that is 14.6 UI/kl. According to the guidelines [CENETEC, 2016] a woman GDM take this dose for 98 days.
(c) USD 0.03 is the cost of the daily dose that is 1700 mg. According to the guidelines [CENETEC, 2016] a woman GDM take this dose for 98 days.
(d) 2.66 is the average number hours of training per nurse.
(e) Milligrams.
Assumptions:
* Pregnancy is supposed to end in week 40.
* Insulin and metformin treatments are supposed to start at week 26.
* Insulin:
– 1/3 of the total daily dose must be taken at night.
– Morning dose: 1/3 rapid and 2/3 NPH insulin.
– Evening dose: 1/2 rapid and 1/2 NPH insulin.
– 4 daily syringes throughout the whole pregnancy.

GDM treatments in case of a positive outcome (e.g., metformin), for whom were applied the specific ranges from the literature [27–29,20,32]. As expected, the probability of having GDM was the variable with the highest impact on final costs. To quantification of this variability is shown in Table 4: assuming a scenario in which the real incidence of GDM was 3.15%, the total burden would be USD 86.8 248 million year, USD 165.4 at 6% incidence, USD 275.8 at 10%, and USD 827.4 million at 30%.

In the probabilistic sensitivity analysis (Monte Carlo simulation, Fig. 3), all costs were modeled using a gamma distribution and probabilities using a beta distribution. The results were overall robust.

4. Discussion

4.1. *Main findings*

According to our review of the literature, this study is the first study to assess the economic burden of GDM in Mexico. We report that cost estimates of a GDM pregnancy range from USD 3484.7 to USD 3910.7 according to the type of treatment (diet and exercise only or the plus-pharmacological condition) and the type of delivery (vaginal or C-section), with the costs of these being at least +119.7% higher (USD 1995.2) than a pregnancy at high risk of glucose intolerance but without GDM. According to two large national surveys [27,28] and a cohort study [29], the GDM incidence in Mexico was between 3% and 6%, but there are reasons to believe these figures are underestimated. For example, data from these sources are self-reported, and the obesity rate, a well-established GDM risk factor, is higher than 70% among Mexican women [37–39]. Nevertheless, even under this conservative scenario, the estimated range of GDM burden in Mexico was USD 86.8–165.4 million a year, representing 0.3%–0.7% of the total health expenditure in 2017. Scenario analyses based on information provided by a sentinel study in Mexico [20] assuming 10% and 30% GDM incidences estimated that additional resources between USD 110.4–740.6 million per year would be required and should be invested to attend all cases of women with a GDM pregnancy. Underestimating the GDM incidence would result in underestimating costs of pregnancy health outcomes and of Type 2 diabetes mellitus, for which GDM is a well-established risk factor [2]. Thus, to develop more effective public health policy, improving the evaluation of GDM incidence in Mexico is critical.

4.2. *Comparison with other studies*

Despite GDM being one of the most common pregnancy complications worldwide [40], few studies have investigated its economic burden [41–44]. The first study is a modeling study from the United States (US) that estimated that the cost of a GDM pregnancy was double the cost of a pregnancy without GDM (USD 7803 difference), and the total GDM economic burden in 2014 was USD 1.8 billion. In this case, this figure is likely to be higher, because the GDM incidence used (5.5%) might be underestimated because the US has not adopted the internationally accepted the criteria of the International

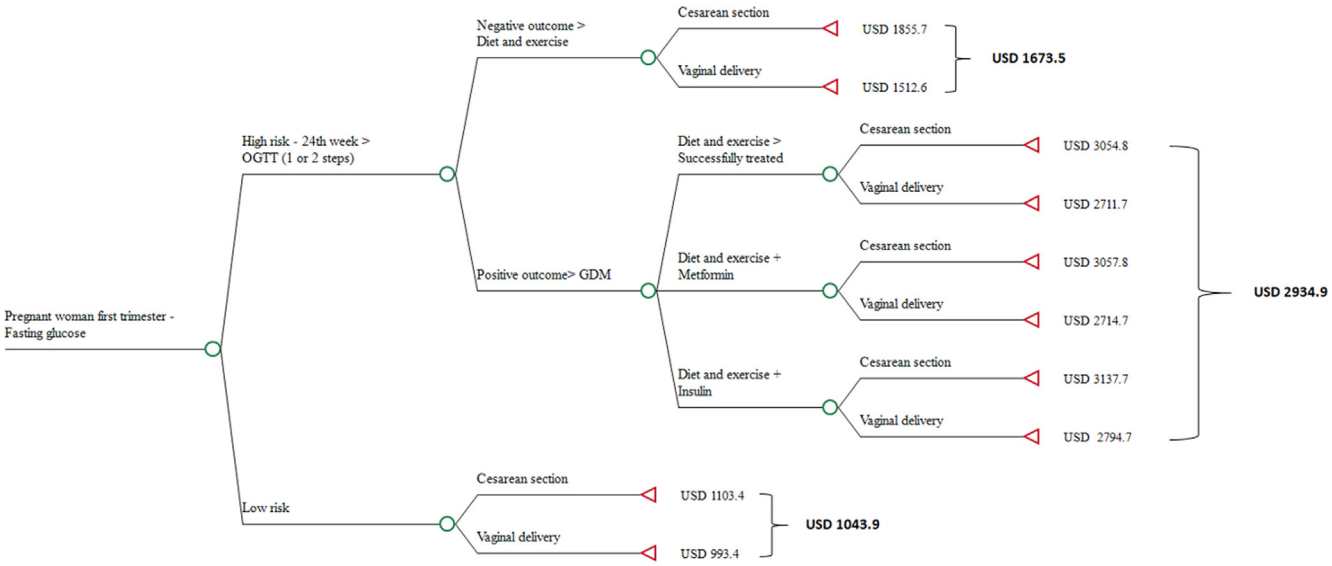

Fig. 1 – Screening and treatment path for GDM according to the guidelines. According to the national guidelines [CENETEC, 2016], all pregnant women take a fasting glucose test in the first trimester of pregnancy and, depending on the outcome, are classified as "high" or "low risk." At week 24, women at "low risk" take another fasting glucose test and women at "high risk" take an OGTT to check for GDM. If suffering from GDM, the women are treated with diet and exercise. For women at "high risk" without GDM, and in severe cases, metformin or insulin is added. All branches end with a delivery—vaginal or C-section. Circles indicate chance events, triangles indicate terminal nodes, and the symbol "#" indicates that the probability is complementary to the probability in the parallel branch (they must sum to one). The numbers in USD at the end of the branches represent the cost of that branch.

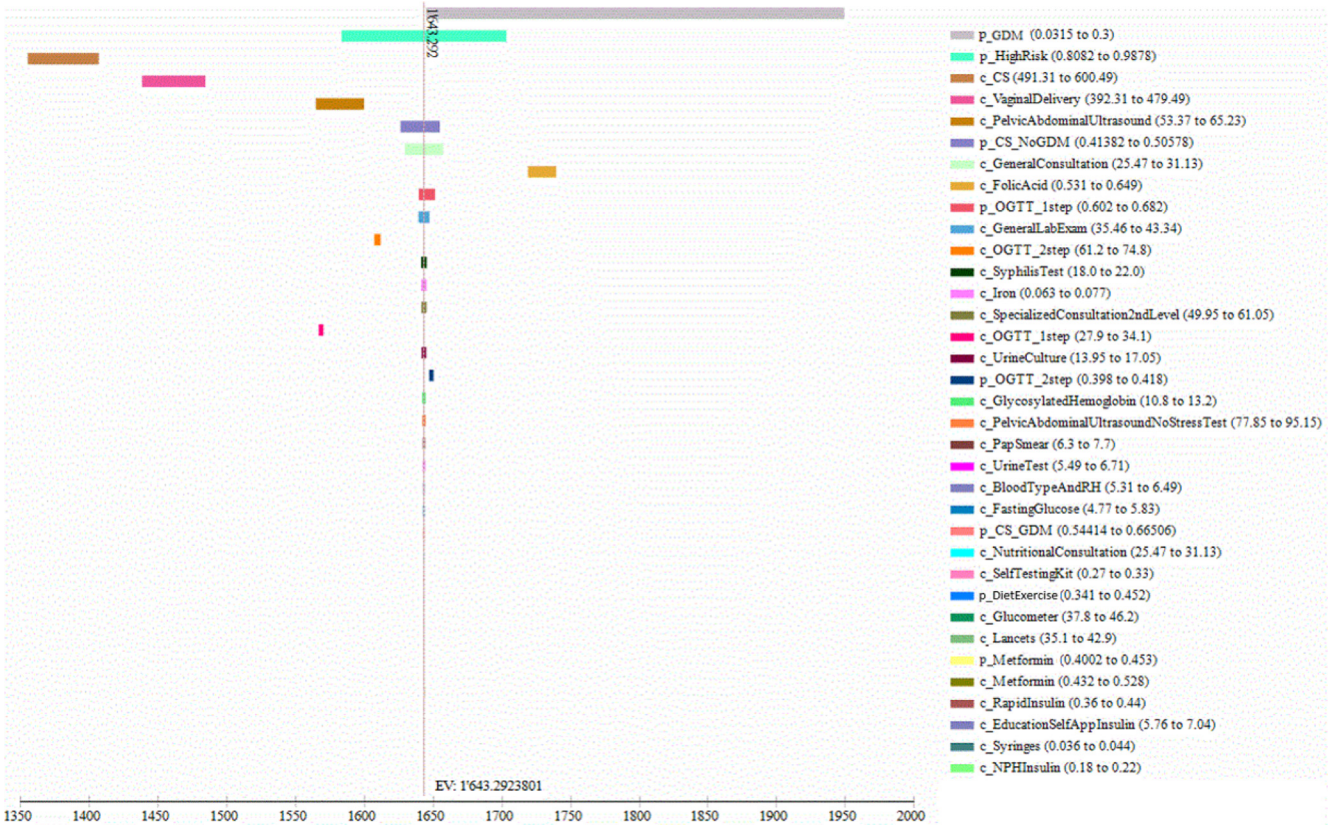

Fig. 2 – Sensitivity analysis: Tornado diagram. Bars represent the relative importance of the variables on the expected value (EV): the larger the bar, the higher the impact of that parameter on the model results.

Table 4 – Burden of GDM at different levels of GDM incidence.

Prevalence GDM (%)	Source	Number of women suffering from GDM (n)	Total GDM burden per year (USD)
3.15	ENADID 2009; Gutierrez, 2012; Maestras 2008–2011	55 124	86 886 458
6	ENADID 2009; Gutierrez, 2012; Maestras 2008–2011	104 998	165 498 015
10	Reyes, 2012 (ADA criteria)	174 997	275 830 026
30	Reyes, 2012 (IADSPG criteria)	524 991	827 490 077

Different prevalence of GDM were considered (column 1); for each of those, we calculated the number of women suffering from GDM (column 3) as prevalence × total number of women included in the study (1.7 million). This figure was then multiplied by the difference in cost between a pregnancy with GDM and a pregnancy without GDM (USD 1576.2), to obtain the yearly burden of GDM associated with that prevalence (column 4), for example, the first line: [(3.15/100) * 1 700 000] * 1576.2 = 86 886 458 USD, yearly burden of GDM at a 3.15% GDM prevalence.

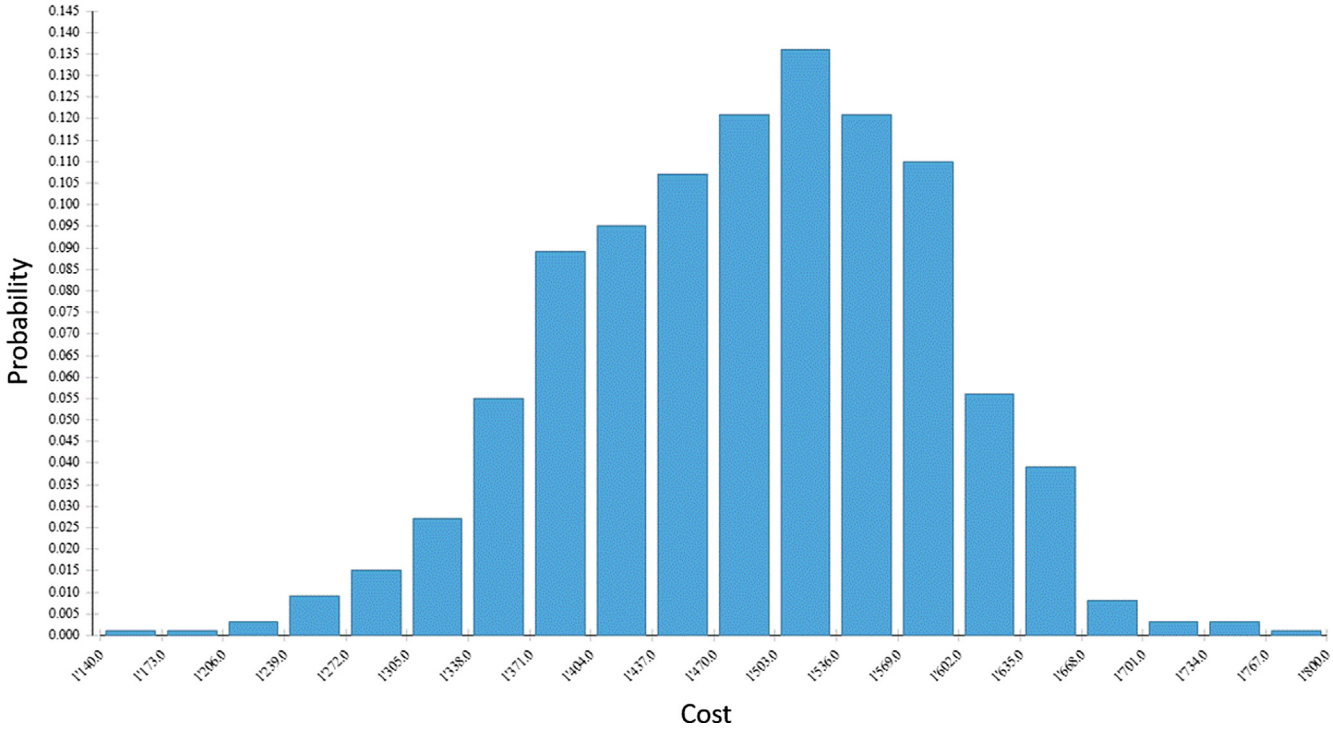

Fig. 3 – Sensitivity analysis: Monte Carlo simulation. Monte Carlo probability distribution (1000 iterations) of the expected cost per case. The most likely value (the highest bar in the histogram) corresponds to the base case result.

Association of Diabetes and Pregnancy Study Groups (IADSPG) [45]. The second study is a modeling study from China that considered only the last gestational trimester [42] and estimated that the difference in cost between a GDM pregnancy and a pregnancy without GDM was USD 1008 (CNY 6677.37, +95%) and a total burden of GDM in 2015 of USD 2.92 billion (CNY 19.36 billion). The latter used a GDM incidence rate of 17.5% (based on the IADSPG criteria).

Three additional studies from Europe—one from Finland [43], from 2007 to 2009, one from Ireland [46], from 2007 to 2010, and one from Italy [44] that estimated the GDM burden in 2014—have reported GDM incidences between 10% and 12% and differences in cost between a GDM pregnancy and a pregnancy without GDM of USD 1439 (EUR 1289, +25%) for Finland, and of USD 965 (EUR 817) for Ireland (+133%) and Italy (+29%); of these, only Italy reported the total burden, which was USD 52.79 million (EUR 44.8 million). Each of these studies, including our study, were based on local healthcare systems' specific costs, demography, and characteristics and used different methodologies. Despite the differences, all the studies, including our study, highlight the considerable economic burden and cost differences between a GDM pregnancy and a pregnancy without GDM, which range from 20% to 130%.

4.3. *Strengths and limitations*

The first strength of this study was the conservative and simple approach adopted because of data availability. Only the main healthcare costs due to GDM, such as the self-monitoring kit and the pharmacological treatments, were included, ignoring other possible expenses on supplies (e.g.,

nutritional supplements) and healthcare costs related to the care of adverse health outcomes (e.g., pre-eclampsia and shoulder dystocia [40,47]) associated with GDM because no Mexican studies have reported this data. A second strength was the use of representative data and of recent publications, indicating the actual GDM incidence in Mexico in line with international studies.

This study presents some limitations. First, we rely on heterogeneous sources for probabilities and costs, such as the literature, surveys, and national tariff lists. Second, the absence of infant health outcomes in the analyses, that is, in the data used, was because we could not identify the babies born to women suffering from GDM. Third, the probably unrealistic assumption that all women were compliant with the treatment prescribed (diet and exercise only or the plus-pharmacological condition). However, in this case, we can assume that non-compliant behavior would lead to even higher costs because the adverse health outcomes due to a non-treated GDM would be higher [48]. Fourth, and similar to the third, we assumed that 15% of women with a GDM pregnancy were undiagnosed because they had no healthcare insurance coverage, which would not generate direct GDM treatment costs for the healthcare system but most probably generate indirect costs as a result of the unknown adverse health outcomes in the short and long terms [48–50]. Finally, although differences in costs among the main healthcare insurances operating in Mexico were considered, differences between urban and rural areas were not, this assuming, not necessarily correctly, equal medical facility across the country.

4.4. *Conclusions*

Although GDM is one of the most frequent complications during pregnancy, in Latin America, there has been an insufficient amount of research performed on the epidemiological and economic burden associated with it. Under a scenario in which GDM in Mexico is underdiagnosed, and therefore not treated, additional economic resources are urgently required to help pregnant women suffering from GDM avoid the associated adverse health outcomes and economic consequences. Targeted preventive approaches in an effort to reduce the related total costs are strongly encouraged.

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Declaration of Competing Interest

The authors declare no conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.05.014.

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