



Influence of different diagnostic criteria on gestational diabetes mellitus incidence and medical expenditures in China

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Keywords

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ABSTRACT

Aims/Introduction: To summarize the development of the criteria for diagnosing gestational diabetes mellitus (GDM) in China, and investigate how different GDM diagnostic criteria influence the national prevalence of GDM, the national health system and the economic burden of GDM in China.

Materials and Methods: Retrospectively using data from women undergoing a 2-h, 75-g oral glucose tolerance test at 24–28 gestational weeks in the First Affiliated Hospital of Jinan University (Guangzhou, Guangdong, China) from January 2011 to December 2017, the prevalence rate of GDM and its impacts on the national health system were evaluated using different criteria (the 7th edition textbook criteria, National Diabetes Data Group 1979, World Health Organization 1985, European Association for the Study of Diabetes 1996, Japan 2002, American Diabetes Association [ADA] 2011 [International Association of the Diabetes and Pregnancy Study Groups], and National Institute for Health and Care Excellence 2015).

Results: The incidence rates of GDM based on the ADA 2011 and National Institute for Health and Care Excellence 2015 were, respectively, 22.94% ($P < 0.01$) and 21.72% ($P < 0.01$), over threefold higher than implementing the 7th edition textbook criteria ($P < 0.001$). On the contrary, the incidence rates of GDM diagnosed with the National Diabetes Data Group 1979 and World Health Organization 1985 guidelines were significantly less than the 7th edition textbook criteria ($P < 0.001$). From 2001 to 2016, the estimated national cost of treating GDM rose from ¥3.9 billion to ¥27.4 billion after implementing the ADA 2011 guidelines.

Conclusions: With the implementation of ADA 2011 (International Association of the Diabetes and Pregnancy Study Groups) guidelines, there are fewer adverse perinatal outcomes and cases of type 2 diabetes mellitus in the long term, but the medical costs increased significantly, and the cost-effectiveness of diagnostic criteria in China is still yet to be confirmed.

INTRODUCTION

Gestational diabetes mellitus (GDM) is described as temporary hyperglycemia or glucose intolerance with onset or first recognition during pregnancy that impairs perinatal outcomes. The prevalence of GDM is increasing globally, regardless of gestational age^{1,2}. Although the glucose tolerance of the GDM patients reverts to normal shortly after delivery, these individuals are still potentially susceptible to type 2 diabetes mellitus³.

Studies have shown that screening, diagnosis and intervention of GDM can significantly reduce the rate of adverse perinatal outcomes, improve criteria for the diagnosis of GDM and help increase the efficiency of medical care⁴. The Third International Workshop-Conference on Gestational Diabetes Mellitus and the American Diabetes Association (ADA) have suggested that all pregnant women should undergo screening for GDM through blood glucose testing^{5,6}.

GDM is increasingly identified in women globally, yet the adaptability of different criteria in China remains unclear.

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Diagnostic criteria on GDM can help physicians to identify individuals at risk of adverse health outcomes for better management⁷. The evolution of criteria for diagnosis continues. With the development of modern medicine, ever more factors are being considered in the development of new guidelines.

Regarding the development of screening and diagnostic guidelines to tackle GDM globally, there is as yet no uniform criterion for the diagnosis of GDM that can ensure that the benefits outweigh the risks, without the inconvenience and high expenditure⁸ (Table 1; Figure 1). Most countries have identified their own diabetes associations and establish their criteria accordingly. Furthermore, there are debates about which screening method to use, including selective (or risk factors) or universal screening, and the use of the one-step or two-step method (Figure 2).

In the history of the development of guidelines for GDM, China started relatively late (Table 2). In 1980, the first edition of the official textbook of obstetrics and gynecology in China published by the People's Medical Publishing House briefly noted a screening method to diagnose diabetes⁹. Such methods analyzed the glucose level in the urine of pregnant women, and if the result of this examination was positive, the woman's blood glucose would be examined when fasting using an oral glucose tolerance test (OGTT), where a diagnosis of diabetes could be made once the fasting value significantly exceeded 130 mg/L. This was the first time that diabetes had been included in the scope of obstetrics and gynecology in China. However, the method of diagnosing GDM was the same as that for diagnosing diabetes in internal medicine.

In 1993, Dong Zhiguang recommended a Chinese-specific criterion for the 75-g OGTT based on the OGTT results of 514

pregnant women (350 normal glucose tolerance and 164 high-risk pregnancies) at the First Affiliated Hospital of Peking University (Beijing, China) from 1989 to 1990¹⁰. The thresholds of such criteria were lower than the World Health Organization 1980 criteria, and in some respects resembled the criteria of the Japan Diabetes Society (i.e., 5.5, 10.2, 8.2 and 6.6 mmol/L for fasting, 1-, 2- and 3-h post-load values, respectively). Because of the small number of participants involved in Dong Zhiguang's study, this criterion was not implemented nationwide in China¹¹.

The subsequent guidelines for the diagnosis and treatment of GDM were jointly revised and developed by the Obstetrics and Gynecology Branch of the Chinese Medical Association and the Diabetes Collaborative Group of the Perinatal Medicine Branch of the Chinese Medical Association. This work was carried out with the intent of guiding clinical practice and promoting a universal diagnostic guideline to the entire country. In 2007, the "Guidelines for the Diagnosis and Treatment of Pregnancy with Diabetes (Draft)" was published and implemented, which recommended the National Diabetes Data Group and ADA guidelines along with the White classification (Table 3)¹².

Except for the OGTT abnormal reference values established in 1993 by Dong Zhiguang, there have been no follow-up studies pertaining to the development of domestic standards for GDM; most of the guidelines used in China are based on foreign guidelines.

Ever since the International Association of Diabetes in Pregnancy Study Group (IADPSG) criteria were established, scholars in China have been attempting to establish Chinese-specific screening criteria based on national conditions¹³.

Table 1 | Summary of important international diagnostic criteria for gestational diabetes mellitus[†]

| Organization | Year | Testing method | Diagnostic OGTT | Abnormal value(s) | Threshold plasma/serum sample (mmol/L) | | | | References |
|----------------------|------|----------------|-----------------|-------------------|--|------|------|-----|------------|
| | | | | | Fasting | 1 h | 2 h | 3 h | |
| O'Sullivan and Mahan | 1964 | Two-step | 100-g OGTT | 2 | 5.0 | 9.1 | 8.0 | 6.9 | 30 |
| NDDG | 1979 | Two-step | 50-g OGTT | – | – | – | – | – | 31 |
| | | | 100-g OGTT | 2 or more | 5.8 | 10.5 | 9.1 | 8.0 | |
| WHO | 1980 | Two-step | 100-g OGTT | 2 | 5.8 | 10.6 | 9.2 | 8.1 | 32 |
| CC | 1982 | Two-step | 50-g OGTT | 1 | – | 7.2 | – | – | 33 |
| | | | 100-g OGTT | 2 or more | 5.3 | 10.0 | 8.6 | 7.8 | |
| WHO | 1985 | Two-step | 75-g OGTT | 1 | 7.0 | – | 11.1 | – | 34 |
| ADA | 1988 | Two-step | 75-g OGTT | 2 or more | 5.3 | 10.0 | 8.6 | – | 35 |
| WHO | 1999 | Two-step | 75-g OGTT | 1 | 6.1 | – | 7.8 | – | 36 |
| JDS | 2002 | Two-step | 75-g OGTT | 2 or more | 5.5 | 10.0 | 8.3 | – | 37 |
| IADPSG | 2010 | One-step | 75-g OGTT | 1 | 5.1 | 10.0 | 8.5 | – | 38 |
| ADA | 2011 | One-step | 75-g OGTT | 1 | 5.1 | 10.0 | 8.5 | – | 39 |

[†]All thresholds are for venous plasma/serum sample except for the O'Sullivan and Mahan criteria, which are for venous whole blood. ADA, American Diabetes Association; CC, Carpenter-Coustan criteria; EASD, European Association for the Study of Diabetes; IADPSG, International Association of Diabetes in Pregnancy Study Group; JDS, Japanese Diabetes Society; NDDG, National Diabetes Data Group; NICE, National Institute for Health and Care Excellence; OGTT, oral glucose tolerance test; WHO, World Health Organization.

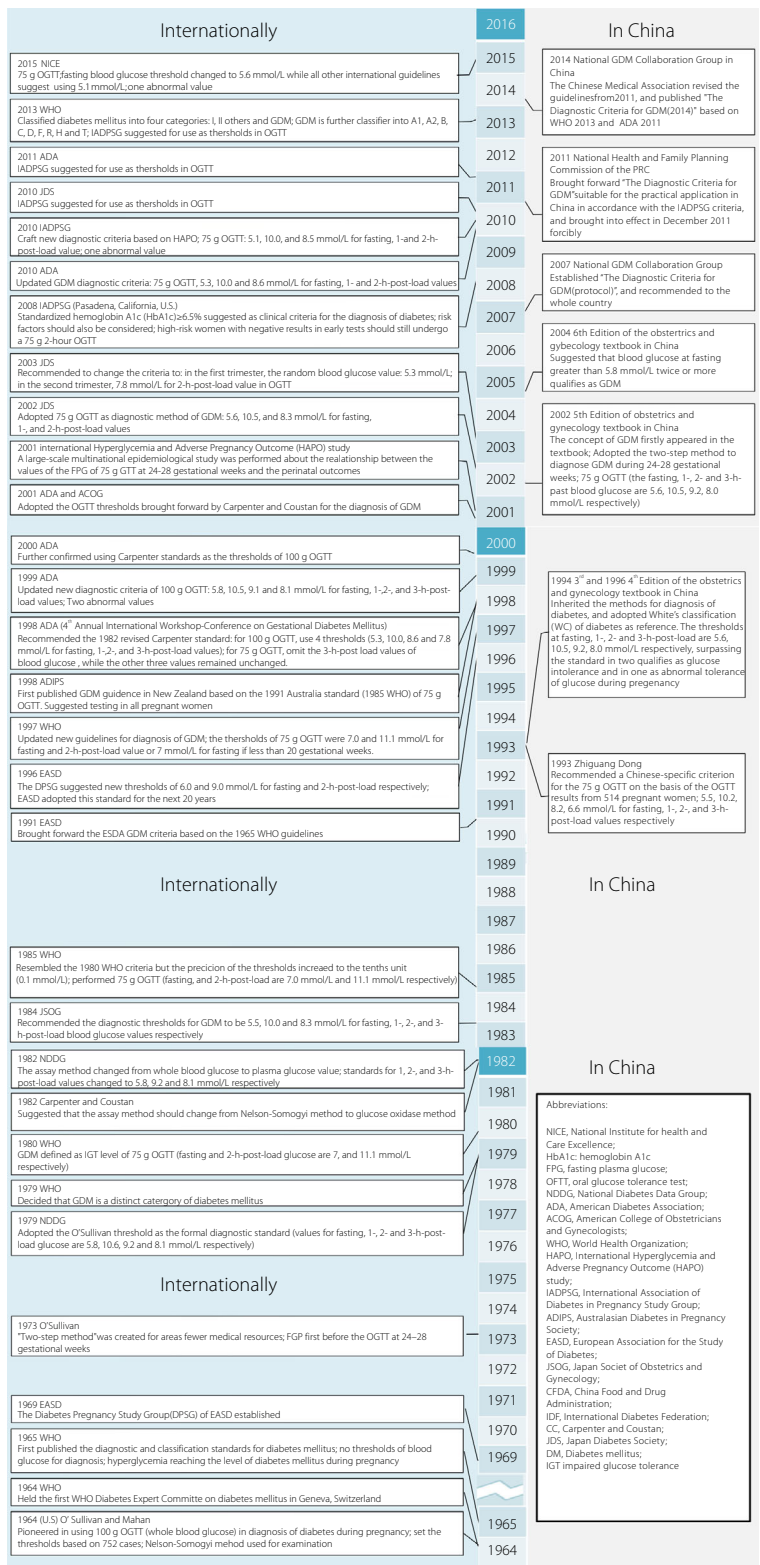


Figure 1 | The development of gestational diabetes mellitus (GDM) diagnostic criteria. The debates on whether to use universal or selective screening, and whether to use the two-step or one-step method remain controversial. Research addressing GDM in China began relatively late, but is developing rapidly.

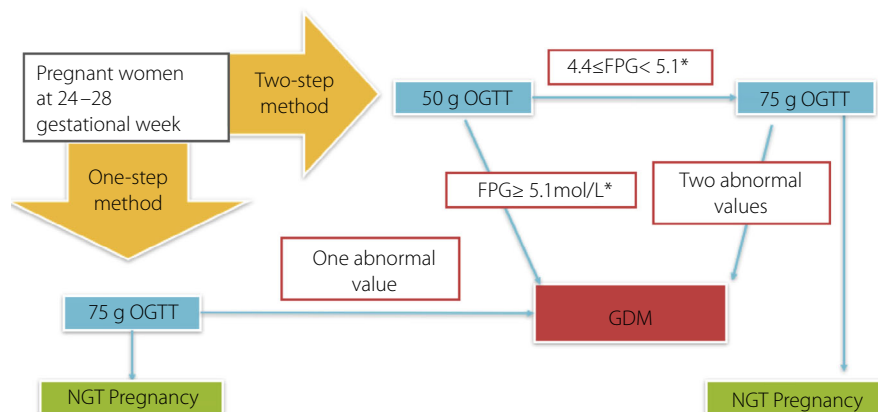


Figure 2 | The one-step and two-step methods of gestational diabetes mellitus screening. *The 7th edition of the obstetrics and gynecology textbook published by the People's Medical Publishing House. FPG, fasting plasma glucose; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test.

In 2011, the National Health and Family Planning Commission officially issued obstetrics and gynecology industry standards related to the diagnosis of GDM. These standards, in agreement with international guidelines and taking into consideration current research outcomes carried out by several universities in China, were called the “Guidelines for Diagnosis and Treatment of GDM (Draft)” and were based on ADA 2011 (IADPSG) criteria. These documents recommended testing the fasting plasma glucose of pregnant women at their first prenatal examination to screen out the possibility of diabetes. Thus, early management can be implemented to improve maternal and neonatal prognosis, and perinatal outcomes.

In 2014, the Chinese Obstetrics and Gynecology Division revised these documents based on the Diagnostic Criteria and Classification of Hyperglycemia First Detected in Pregnancy issued by the World Health Organization in 2013. These new standards were known as the “Guidelines for Diagnosis and Treatment of Gestational Diabetes Mellitus (2014)”^{13,14}. The guidelines also include evidence-based medical studies related to the treatment of GDM.

With various lifestyles, climates and economic conditions, China is a huge country with important internal differences, which is reflected in the controversies surrounding GDM diagnostic methods. Most of the studies regarding GDM diagnostic methods have been based on Western countries. Therefore, it is necessary to provide insights into the current conditions of GDM diagnosis in China, so that researchers can determine appropriate and agreed-upon criteria to better treat GDM.

Since 2011, China has adopted the ADA 2011 (IADPSG) guidelines with the intent of remaining consistent with international standards. Nevertheless, many research studies have found that although implementing ADA 2011 (IADPSG) guidelines yields better perinatal outcomes, doing so also greatly increases the number of women with GDM who receive a

clinical intervention^{15–17}. Although the adverse health outcomes decrease with more inclusive criteria, such acts can significantly add to the economic burdens of public medical resources and patients if the compatibility and feasibility regarding the status quo are not fully considered.

Some experts in China advocated the implementation of the ADA 2011 (IADPSG) criteria as soon as they were published, believing that these would have helped researchers and doctors to better understand the prevalence of GDM in different regions, and ensure that the country's standards were aligned with international ones¹⁵.

It is necessary to implement such international criteria, but the urgency of doing so is coupled with the necessity of evaluating them from the perspective of medical economics, such as from the societal, public health, healthcare system, healthcare payers' and patients' perspectives. Therefore, here we aim to provide a health economics perspective of the adaptability of the present GDM guidelines in China by investigating the influences of different criteria on the national prevalence rate of GDM in China. We also summarize the evolution of GDM guidelines in China, and evaluate the national prevalence rate and economic burdens associated with GDM diagnoses and management in China.

METHODS

A retrospective study was carried out to evaluate all women with a singleton pregnancy to have received the 2-h, 75-g OGTT at 24–28 gestational weeks in the antenatal clinic of the First Affiliated Hospital of Jinan University (Guangzhou, Guangdong, China) from January 2011 through December 2017. We analyzed the incidence rate of GDM according to different clinical guidelines, including the 7th edition of the obstetrics and gynecology textbook published by the People's Medical Publishing House guidelines, World Health Organization 1985, European Association for the Study of Diabetes 1996, Japan

Table 2 | Summary of Chinese diagnostic criteria for gestational diabetes mellitus

| Guidelines | Year | Testing method | Diagnostic method | Abnormal value (s) | Threshold (≥) mmol/L (plasma/serum sample) | | | | References |
|--|------|----------------|-----------------------|--------------------|--|-----|-----|-----|------------|
| | | | | | Fasting | 1 h | 2 h | 3 h | |
| 1st–2nd edition textbook [†] | 1980 | Two-step | Urine glucose + OGTT | – | – | – | – | 25 | |
| Dong Zhiguang | 1993 | Two-step | 50-g OGTT + 75-g OGTT | 2 | 10.2 | 8.2 | 6.6 | 10 | |
| 4th edition textbook | 1996 | Two-step | 50-g OGTT + 75-g OGTT | 2 | 10.5 | 9.2 | 8.0 | 26 | |
| 5th edition textbook | 2002 | Two-step | 50-g OGTT + 75-g OGTT | 2 | 10.5 | 9.2 | 8.0 | 27 | |
| 6th edition textbook | 2004 | Two-step | 50-g OGTT + 75-g OGTT | 2 | 10.3 | 8.6 | 6.7 | 28 | |
| 7th edition textbook | 2008 | Two-step | 50-g OGTT + 75-g OGTT | 2 | 10.3 | 8.6 | 6.7 | 29 | |
| Current Chinese guidelines (ADA 2011) [‡] | 2011 | One-step | 75-g OGTT | 1 | 10.0 | 8.5 | – | 39 | |

[†]The textbook of obstetrics and gynecology in China published by People's Medical Publishing House, [‡] ADA, American Diabetes Association. OGTT, oral glucose tolerance test.

2002, ADA 2011 (IADPSG) and National Institute for Health and Care Excellence 2015. The study was approved by the ethics committee of Jinan University.

Participants

A total of 12,324 women with a singleton pregnancy were included with informed consent. The exclusion criteria were the following: multiple gestations, OGTT carried out before 12 weeks, an abnormal glucose screen without a subsequent glucose tolerance test, delivery in another hospital and major fetal malformation.

For patients with more than one pregnancy in the study period who satisfied the inclusion criteria, only the first pregnancy was included.

Data source

The clinical data of the OGTT were obtained from the outpatient clinic of the First Affiliated Hospital of Jinan University from January 2011 through December 2017. The total number of deliveries and the prenatal examination rate in the whole of China were obtained from the 2017 China Health and Family Planning Statistics Yearbook. Expenditures related to the treatment of gestational diabetes were obtained from literature data.

Statistical analysis

Microsoft Excel 2016 (Microsoft Corporation, One Microsoft Way, Redmond, WA, USA) and Stata 14.0 (StataCorp LLC, College Station, TX, USA) were used to calculate the prevalence rate and the economic costs.

The number of national GDM cases was the number of deliveries in the year multiplied by the prenatal examination rate (%), multiplied by the incidence of GDM in the year.

The national cost of treating gestational diabetes (¥) was the number of national GDM cases multiplied by the cost of treatment for each GDM case.

RESULTS

Influence of the different GDM guidelines on the prevalence of GDM

Using the ADA 2011 (IADPSG) guidelines, the incidence rate of GDM in 12,324 pregnant women was 22.94% ($P < 0.001$), nearly fourfold the rate according to the 7th edition of the Chinese obstetrics and gynecology textbook published by the People's Medical Publishing House criteria (the 7th edition textbook criteria; Table 4; Figure 3).

Influence of different GDM guidelines on the total number of GDM cases in China

According to the childbirth statistics and the prenatal examination rate in the 2017 Health and Family Planning Statistics Yearbook, we estimated the incidence rate of GDM from 2001 to 2016 using different GDM diagnostic criteria. Using 2016 as an example, if we used the 7th edition textbook guidelines, the number of women with GDM was approximately 1 million.

Table 3 | Priscilla White classification of gestational diabetes mellitus

| Class | Age at onset | Duration | Criteria (symptoms) |
|--|--------------|-------------|--|
| Diabetes that begins during pregnancy | | | |
| A1 | Any | Any | GDM; dietary treated |
| A2 | Any | Any | GDM; insulin treated |
| Diabetes with onset before the pregnancy | | | |
| B | ≥20 years | <10 years | None |
| C | 10–19 years | 10–19 years | None |
| D | <10 years | >20 years | Background retinopathy |
| F | Any | Any | Diabetic nephropathy |
| H | Any | Any | Coronary disease, ischemic heart disease |
| R | Any | Any | Proliferative retinopathy |
| RF | Any | Any | Retinopathy and nephropathy |
| T | Any | Any | Renal transplant |

White's classification was developed in 1949 based on a cohort of type 1 diabetes patients with the aim of estimating the risk of adverse perinatal outcomes. GDM, gestational diabetes mellitus

However, if we applied the ADA 2011 (IADPSG) guidelines, that number ballooned to >4 million (Table 5; Figure 4).

Estimated national medical expenditures related to GDM treatment using the different GDM guidelines

Based on Table 5, we statistically estimated the total number of cases of GDM in China (Table 6). Using the data obtained, we calculated the medical expenditures regarding the treatment of GDM nationally on the basis that each GDM patient averagely spent ¥6677.37 more on treatment and management of GDM than her non-GDM counterpart in 2015¹⁸. Of this ¥6677.37, ¥4421.49, ¥1340.94 and ¥914.94 were for GDM diagnosis and treatment, intervention of maternal complications and neonatal complications, respectively.

Rate of missed diagnosis using different combinations of OGTT

Using different combinations of the criteria for OGTT based on the ADA 2011 (IADPSG) guidelines, we estimated the rate

of missed diagnosis in accordance to the OGTT data we collected from the First Affiliated Hospital of Jinan University from January 2011 through December 2017 (Table 7).

DISCUSSION

Different GDM diagnostic criteria significantly influence the incidence of GDM and medical expenditures. We found that applying the ADA 2011 (IADPSG) guidelines increased the incidence rate of GDM by nearly four-fold compared with the previous guidelines (i.e., the 7th edition textbook guidelines).

If we applied the incidence rate obtained from the First Affiliated Hospital of Jinan University to the national level, we found that in 2016, there were 3 million more GDM patients diagnosed by the ADA 2011 (IADPSG) criteria than those diagnosed by the 7th edition textbook criteria. We noted a robust increase in the number of births in 2016, which might be due to the complete opening up of the two-child policy in China (Table 5).

An increase in the prevalence of GDM increases medical costs, due to, for example, additional blood glucose testing, as

Table 4 | Influence of different gestational diabetes mellitus guidelines on the prevalence of gestational diabetes mellitus in Chinese women

| Guidelines | Cases (people) | GDM (cases) | Prevalence of GDM (%) | Compared with the 7th edition textbook criteria <i>P</i> -value [†] |
|---------------------------------------|----------------|-------------|-----------------------|--|
| The 7th edition textbook [†] | 12,324 | 750 | 6.08 | – |
| WHO 1985 | 12,324 | 140 | 1.13 | / |
| EASD 1996 | 12,324 | 1,072 | 8.70 | <0.001 |
| Japan 2002 | 12,324 | 995 | 8.07 | <0.001 |
| ADA 2011 | 12,324 | 2,828 | 22.94 | <0.001 |
| NICE 2015 | 12,324 | 2,083 | 21.72 | <0.001 |

Based on American Diabetes Association (ADA) 2011 guidelines, the prevalence of gestational diabetes mellitus (GDM) was 22.94%, over threefold higher than the prevalence based on implementing the 7th edition textbook criteria ($P < 0.001$). [†]The 7th edition textbook: the GDM guidelines promoted in the 7th edition of the Chinese obstetrics and gynecology textbook published by the People's Medical Publishing House. EASD, European Association for the Study of Diabetes; NICE, National Institute for Health and Care Excellence; WHO, World Health Organization.

well as the management and treatment of GDM. Therefore, the expenditures of GDM patients themselves and society as a whole will also rise concomitantly. Also, with the focus on precision medicine, internationally, whether the screening of GDM

should be risk factor-related (selective screening) or universal (universal screening) remains a controversy, as its cost-effectiveness or adaptability in developing countries remains unclear¹⁹.

After the implementation of the ADA 2011 (IADPSG) guidelines, a retrospective study of 14,593 pregnant women with GDM who visited the First Affiliated Hospital of Peking University showed that, compared with the National Diabetes Data Group criteria, the morbidity of GDM according to the ADA 2011 (IADPSG) criteria increased to 14.7%. If patients diagnosed with these criteria do not receive treatment, the occurrence of perinatal complications will also increase¹⁶. According to the previous criteria (the 7th edition textbook criteria), the prevalence of GDM was 8.9% and, Zhu *et al.*¹⁷ showed that the prevalence of GDM was 18.9% in Beijing after the implementation of the ADA 2011 (IADPSG) diagnostic criteria in 2015. In theory, the blood glucose level of most pregnant women with GDM can be controlled solely with dietetic treatment. Therefore, from the viewpoint of treatment, the adoption of the ADA 2011 (IADPSG) criteria in China is reasonable.

China is a vast country. In 2016, Jing *et al.*²⁰ found that the incidence of GDM in China followed specific geographic patterns. First, the diagnostic rate of GDM varied from high to low in the northeast, coastal, river coast and northwest portions of the country, respectively. The eastern and southern parts of China, which are characterized by relatively better economic development, have a much higher rate of GDM. This finding is consistent with the previous conclusion that economic condition, lifestyle and even climate relate to the prevalence of

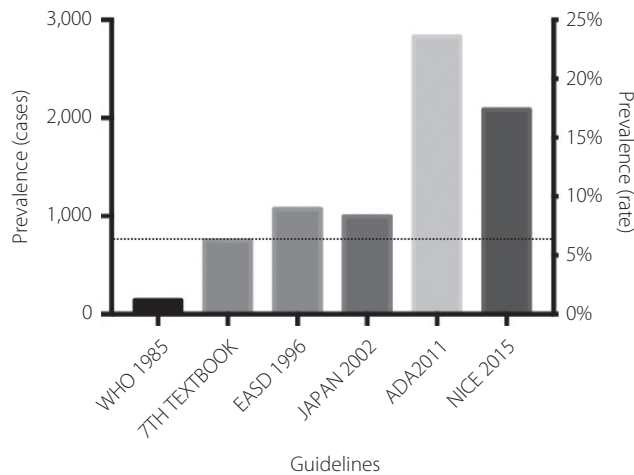


Figure 3 | The influence of different gestational diabetes mellitus (GDM) guidelines on the prevalence of GDM in Chinese women. Implementing the American Diabetes Association (ADA) 2011 (International Association of Diabetes in Pregnancy Study Group) guidelines resulted in a nearly fourfold increase in the incidence of GDM. EASD, European Association for the Study of Diabetes; NICE, National Institute for Health and Care Excellence; WHO, World Health Organization.

Table 5 | Estimated number cases of gestational diabetes mellitus in China using different gestational diabetes mellitus diagnostic criteria

| Year | No. of births [†] (millions) | Antenatal care coverage rate [†] (%) | Estimated cases of GDM in China (thousands) | | | | | |
|------|--|--|---|--------------|---------------|-------------------------|-------------|--------------|
| | | | WHO 1985 | EASD 1996 | Japan 2002 | 7th edition textbook | ADA 2011 | NICE 2015 |
| 2001 | 10.7 | 90.3 | 110.1 | 840.6 | 779.7 | 587.5 | 2,216.5 | 2,098.6 |
| 2002 | 10.6 | 90.1 | 108.9 | 830.9 | 770.7 | 580.7 | 2,190.9 | 2,074.4 |
| 2003 | 10.2 | 88.9 | 103.4 | 788.9 | 731.8 | 551.3 | 2,080.2 | 1,969.5 |
| 2004 | 10.9 | 89.7 | 111.5 | 850.6 | 789.0 | 594.5 | 2,242.9 | 2,123.6 |
| 2005 | 11.4 | 89.8 | 116.7 | 890.6 | 826.1 | 622.4 | 2,348.4 | 2,223.5 |
| 2006 | 11.8 | 89.7 | 120.7 | 920.9 | 854.2 | 643.5 | 2,428.1 | 2,299.0 |
| 2007 | 12.5 | 90.9 | 129.5 | 988.5 | 917.0 | 690.8 | 2,606.6 | 2,467.9 |
| 2008 | 13.3 | 91.0 | 138.0 | 1,053.0 | 976.7 | 735.9 | 2,776.4 | 2,628.8 |
| 2009 | 13.8 | 92.2 | 145.0 | 1,107.0 | 1,026.8 | 773.6 | 2,918.8 | 2,763.6 |
| 2010 | 14.2 | 94.1 | 152.3 | 1,162.5 | 1,078.3 | 812.4 | 3,065.3 | 2,902.3 |
| 2011 | 14.5 | 93.7 | 154.9 | 1,182.0 | 1,096.4 | 826.1 | 3,116.7 | 2,951.0 |
| 2012 | 15.4 | 94.8 | 166.4 | 1,270.1 | 1,178.2 | 887.6 | 3,349.1 | 3,170.9 |
| 2013 | 15.1 | 95.7 | 164.7 | 1,257.2 | 1,166.2 | 878.6 | 3,315.0 | 3,138.7 |
| 2014 | 14.2 | 96.2 | 155.7 | 1,188.5 | 1,102.4 | 830.6 | 3,133.7 | 2,967.0 |
| 2015 | 14.50 | 96.5 | 159.5 | 1,217.3 | 1,129.2 | 850.7 | 3,209.9 | 3,039.2 |
| 2016 | 18.50 | 96.6 | 203.7 | 1,554.8 | 1,442.2 | 1,086.6 | 4,099.6 | 3,881.6 |

From 2001 to 2016, the prevalence of gestational diabetes mellitus (GDM) increased from 587.5 thousand women to 4,099.6 thousand. [†]Data source of the childbirth volume and prenatal examination rate: the 2017 Health and Family Planning Statistics Yearbook. ADA, American Diabetes Association; EASD, European Association for the Study of Diabetes; NICE, National Institute for Health and Care Excellence; WHO, World Health Organization.

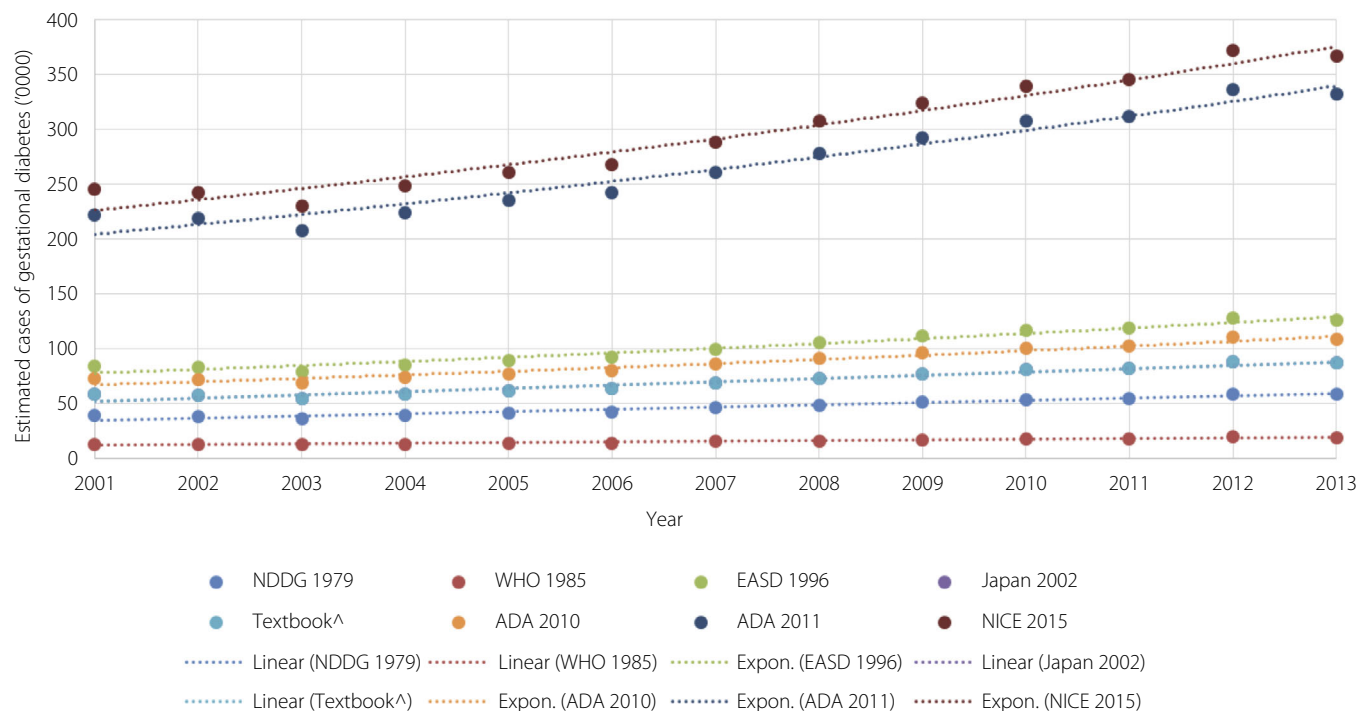


Figure 4 | Estimated gestational diabetes mellitus cases using different criteria. Red line: World Health Organization (WHO) 1985; blue line: National Diabetes Data Group (NDDG) 1979; emerald line: textbook; orange line: American Diabetes Association (ADA) 2010; green line: European Association for the Study of Diabetes (EASD) 1996; indigo blue line: ADA 2011 (International Association of Diabetes in Pregnancy Study Group); purple line: Japan 2002; brown line: National Institute for Health and Care Excellence (NICE) 2015

Table 6 | Estimated national expenditure on gestational diabetes mellitus treatment

| Year | No. of births (millions) | Antenatal care coverage rate (%) | Estimated national expenditure (billions) [†] | | | | | |
|-------|--------------------------|----------------------------------|--|-----------|------------|----------------------|----------|-----------|
| | | | WHO 1985 | EASD 1996 | Japan 2002 | 7th edition textbook | ADA 2011 | NICE 2015 |
| 2001 | 10.7 | 90.3 | 0.7 | 5.6 | 5.2 | 3.9 | 14.8 | 14.0 |
| 2002 | 10.6 | 90.1 | 0.7 | 5.5 | 5.1 | 3.9 | 14.6 | 13.9 |
| 2003 | 10.2 | 88.9 | 0.7 | 5.3 | 4.9 | 3.7 | 13.9 | 13.2 |
| 2004 | 10.9 | 89.7 | 0.7 | 5.7 | 5.3 | 4.0 | 15.0 | 14.2 |
| 2005 | 11.4 | 89.8 | 0.8 | 5.9 | 5.5 | 4.2 | 15.7 | 14.8 |
| 2006 | 11.8 | 89.7 | 0.8 | 6.1 | 5.7 | 4.3 | 16.2 | 15.4 |
| 2007 | 12.5 | 90.9 | 0.9 | 6.6 | 6.1 | 4.6 | 17.4 | 16.5 |
| 2008 | 13.3 | 91 | 0.9 | 7.0 | 6.5 | 4.9 | 18.5 | 17.6 |
| 2009 | 13.8 | 92.2 | 1.0 | 7.4 | 6.9 | 5.2 | 19.5 | 18.5 |
| 2010 | 14.2 | 94.1 | 1.0 | 7.8 | 7.2 | 5.4 | 20.5 | 19.4 |
| 2011 | 14.5 | 93.7 | 1.0 | 7.9 | 7.3 | 5.5 | 20.8 | 19.7 |
| 2012 | 15.4 | 95 | 1.1 | 8.5 | 7.9 | 5.9 | 22.4 | 21.2 |
| 2013 | 15.1 | 95.6 | 1.1 | 8.4 | 7.8 | 5.9 | 22.1 | 21.0 |
| 2014 | 14.2 | 96.2 | 1.0 | 7.9 | 7.4 | 5.5 | 20.9 | 19.8 |
| 2015 | 14.5 | 96.5 | 1.1 | 8.1 | 7.5 | 5.7 | 21.4 | 20.3 |
| 2016 | 18.5 | 96.6 | 1.4 | 10.4 | 9.6 | 7.3 | 27.4 | 25.9 |
| Total | | | 15.0 | 114.2 | 105.9 | 79.8 | 301.1 | 285.1 |

From 2001 to 2016, the estimated national cost of treating gestational diabetes mellitus cases rose from ¥3.8 billion to ¥22.4 billion after implementing the new American Diabetes Association (ADA) 2011 guidelines. [†]Calculation based on an estimation of ¥6677.37 for the treatment of each gestational diabetes mellitus patient. EASD, European Association for the Study of Diabetes; NICE, National Institute for Health and Care Excellence; WHO, World Health Organization.

Table 7 | Screening for gestational diabetes mellitus according to different combinations of American Diabetes Association 2011 oral glucose tolerance test screening criteria

| Screening | No. pregnant women | GDM | Prevalence of GDM (%) | Rate of missed diagnosis (%) | P-value |
|---|--------------------|--------|-----------------------|------------------------------|---------|
| ADA 2011 criteria | | | | | |
| Any abnormal items | 12,324 | 2,828 | 22.94 | – | – |
| Only fasting blood glucose abnormal | 12,324 | 1,081 | 8.77 | 61.76 | <0.001 |
| Only 1-h load blood glucose abnormal | 12,324 | 1,514 | 12.28 | 46.45 | <0.001 |
| Only 2-h load blood glucose abnormal | 12,324 | 1,582 | 12.84 | 44.04 | <0.001 |
| Fasting or 1-h load blood glucose abnormal | 12,324 | 2,172 | 17.62 | 23.17 | <0.001 |
| 1- or 2-h load blood glucose abnormal | 12,324 | 2,267 | 18.40 | 19.81 | <0.001 |
| Fasting or 2-h-load blood glucose abnormal | 12,324 | 2,294 | 18.61 | 18.86 | <0.001 |
| Fasting and 1-h load blood glucose abnormal | 12,324 | 423 | 3.43 | 85.04 | <0.001 |
| 1- and 2-h load blood glucose abnormal | 12,324 | 829 | 6.73 | 70.68 | <0.001 |
| Fasting and 2-h load blood glucose abnormal | 12,324 | 369 | 2.99 | 86.95 | <0.001 |
| Two or more items abnormal | 12,324 | 1082.5 | 8.78 | 61.71 | <0.001 |
| All three items abnormal | 12,324 | 272 | 2.21 | 90.38 | <0.001 |

If fasting and 2-h load blood glucose values or fasting and 1-h load blood glucose values are used for screening, the rate of missed diagnoses can be limited to approximately 19%. ADA, American Diabetes Association; GDM, gestational diabetes mellitus.

GDM. Second, for every additional year of age of the mother, there is a 0.8% increase in the diagnostic rate of GDM. Life-style, economic situation, weather and public medical resources vary from place to place; the incidence of GDM also varies from place to place²¹. Some remote areas lack adequate resources and conditions for complete prenatal examination, in-depth diagnosis, and proper management of GDM²². Due to the limitations of education and the transportation conditions in rural remote and mountainous areas, some pregnant women do not go to the hospital for examination at the beginning of the pregnancy, and more than half of the pregnant women will not go to the hospital until gestational week 8 of pregnancy^{22,23}. According to the National Bureau of Statistics, the health expenditures invested in different regions of China differ, and the input of funds and the per capita gross domestic product of the region are not positively correlated. For example, Guangdong province has a rather high per capita gross domestic product (approximately ¥58,000), but the regional health expenditure is just ¥450 per person, far lower than regions with a low per capita gross domestic product, such as Tibet and Qinghai. This situation shows that the distribution of medical resources in China is uneven; there is no unified health policy or funding. Therefore, in terms of the development of national medical guidelines, it is necessary to consider the applicability of the national promotion and region-related health policies.

Regarding the solutions to GDM screening in less-developed areas, some scholars have suggested that a lower-cost fasting blood glucose screening method at the 24–28th gestational week can reduce the number of pregnant women having to undergo the 75-g OGTT by a factor of two, which would certainly be more cost-effective¹⁵. However, we estimated the rate of missed diagnoses based on the OGTT data collected from the First Affiliated Hospital of Jinan University using different

combinations of OGTT criteria based on the ADA 2011 (IADPSG) guidelines (Table 7). If we only examined fasting blood glucose, we found that 8.77% of pregnant women did not need to undergo the full-version 2-h, 75-g OGTT to be diagnosed as normal glucose tolerance or GDM. However, >90% of pregnant women still needed to undergo the OGTT; if not, the rate of missed diagnoses would reach 61.7%. Nevertheless, if practitioners use fasting and 2-h load blood glucose values or fasting and 1-h load blood glucose values for screening, the rate of missed diagnoses can be limited to approximately 19%. Therefore, for areas characterized by poor economics, the GDM screening can be carried out using such methods.

It is true that some pioneering experts in China have suggested that the country cannot give up on applying the ADA 2011 (IADPSG) guidelines for fear of their side-effects^{12,24}. The debate between using selective or universal screening of GDM is still ongoing, and so far, it seems infeasible to apply the 75-g OGTT to all pregnant women between the 24 and 28th gestational weeks in China. Here, we need to highlight that, with more inclusive criteria, the perinatal outcomes improve and the chances of GDM women developing type 2 diabetes decrease. However, to determine a proper balance between medical treatment and economic burdens while maximizing use of limited resources, it is important to consider the medical situation of the whole country and the patients themselves. The present study was not intended to overturn the medical policy, but simply to provide a general outlook for improving the GDM diagnosis situation in China and other countries facing the same situation.

Evolution of the diagnostic method of GDM in China is still ongoing, and is based on both the international trend of the establishment of the screening method and the specific situation in China. Nevertheless, there is currently little research related to the adaptability of the ADA 2011 (IADPSG) diagnostic

method in China, and it is still uncertain whether it is appropriate to use such a universal method nationally in China or whether other appropriate guidelines for GDM should be implemented. Furthermore, adopting this method is associated with unknown changes in medical expenditures. Therefore, there remains much opportunity to improve the GDM diagnosis criteria in China, as well as in the rest of the world.

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DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

- American Diabetes Association. Summary of revisions to the 2011 clinical practice recommendations. *Diabetes Care* 2011; 34: S3.
- Metzger BE, Coustan DR. Summary and recommendations of the fourth international workshop-conference on gestational diabetes mellitus. The Organizing Committee. *Diabetes Care* 1998; 21: B161.
- Bellamy L, Casas J-P, Hingorani AD, et al. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet* 2009; 373: 1773–1779.
- Gasim T. Gestational diabetes mellitus: maternal and perinatal outcomes in 220 Saudi women. *Oman Med J* 2012; 27: 140.
- American Diabetes Association. Position statement. Gestational diabetes mellitus. *Diabetes Care* 2003; 26: S103–S105.
- Metzger BE. Summary and recommendations of the third international workshop-conference on gestational diabetes mellitus. *Diabetes* 1991; 40(Supplement 2): 197–201.
- Houshmand A, Jensen DM, Mathiesen ER, et al. Evolution of diagnostic criteria for gestational diabetes mellitus. *Acta Obstet Gynecol Scand* 2013; 92: 739–745.
- Committee UNS. Criteria for Appraising the Viability, Effectiveness and Appropriateness of a Screening Programme, 2003.
- Cao Y. Chinese Obstetric and Gynecology, 1st edn. Peking: People's Medical Publishing House, 2004.
- Dong Z, Xiao W. The research on the oral glucose tolerance test during the late trimester. *Chin J Obstet Gynecol* 1993; 3: 136–138.
- Wei Y, Huixia Y. The evolution of the diagnostic criteria for gestational diabetes mellitus. *Chinese Journal of Practical Gynecology and Obstetrics*. 2013; 4: 295–298.
- Yang H. Obstetrics and Gynecology Branch of Chinese Medical Association. Recommended guidelines for clinical diagnosis and treatment of pregnancy with diabetes (draft). *Chinese Journal of Perinatal Medicine*. 2007; 23: 475–477.
- Yang H, Xu X, Wang Z et al. Obstetrics and Gynecology Branch of Chinese Medical Association. Guidelines for the diagnosis and treatment of pregnancy complicated with diabetes (2014). *Chinese Journal of Obstetrics and Gynecology* 2014; 8: 489–498.
- World Health Organization. Diagnostic Criteria and Classification of Hyperglycaemia first Detected in Pregnancy, 2013.
- Yang H. Current status and countermeasures of diagnosis and treatment of gestational diabetes in China. *Chin J Pract Gynecol Obstet* 2013; 4: 241–243.
- Wei Y, Yang H. Comparison of the diagnostic criteria for gestational diabetes mellitus in China. *Chin J Obstet Gynecol* 2011; 46: 578–581.
- Zhu W, Yang H, Wei Y, et al. Comparing the diagnostic criteria for gestational diabetes mellitus of World Health Organization 2013 with 1999 in Chinese population. *Chin Med J* 2015; 128: 125.
- Xu T, Dainelli L, Yu K, et al. The short-term health and economic burden of gestational diabetes mellitus in China: a modelling study. *BMJ Open* 2017; 7: e018893.
- Mialhe G, Kayem G, Girard G, et al. Selective rather than universal screening for gestational diabetes mellitus? *Eur J Obstet Gynecol Reprod Biol* 2015; 191: 95–100.
- Jing Z, Ying-hua X. Age distribution and regional distribution characteristics of 3367 cases of patients with gestational diabetes mellitus. *China Modern Med* 2016; 23: 156–159.
- National Health and Family Planning Commission. China's Health and Family Planning Statistical Yearbook 2017. Peking Union Medical College Press Beijing, 2017.
- Ma X. Treatment and fetal detection of gestational diabetes in rural and remote mountainous areas. *The world's latest medical information abstracts* 2016; 16: 26–27.
- Wang H, Zhang W. Determinants of Gestational Diabetes Mellitus among Rural Women of Childbearing Age. *Chin Mater Child Health Res* 2017; 28: 59–63.
- Song G, Yang H. Discussion on diagnostic criteria of gestational diabetes. *Chin J Perinat Med* 2017; 20: 9.
- Kezhong Z. Obstetrics and Gynaecology, 2 edn. Peking, China: People's Medical Publishing House, 1981.
- Le J. Obstetrics and Gynaecology, 4th edn. Peking, China: People's Medical Publishing House, 1996.
- Le J. Obstetrics and Gynaecology, 5th edn. Peking, China: People's Medical Publishing House, 2002.
- Le J. Obstetrics and Gynaecology, 6th edn. People's medical publishing house, Peking, 2004.
- Le J. Obstetrics and Gynaecology, 7th edn. Peking, China: People's Health Publishing House, 2008.
- O'Sullivan JB, Mahan CM. Criteria for the Oral Glucose Tolerance Test in Pregnancy. *Diabetes* 1964; 13: 278–285.

31. Group NDD. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 1979; 28: 1039–1057.
32. Listed N. WHO Expert Committee on Diabetes Mellitus: second report. *World Health Organization Technical Report* 1980; 646: 1.
33. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. *Am J Obstet Gynecol.* 1982; 144: 768–773.
34. Cunningham F, Leveno K, Bloom S, et al. Overview of obstetrics. *Williams obstetrics* 23rd ed New York: McGraw-Hill. 2010.
35. Association AD. Diagnosis and classification of diabetes mellitus. *Diabetes care* 2004; 27(suppl 1): S5–S10.
36. Alberti KGMM, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO Consultation. *Diabet Med* 1998; 15: 539–553.
37. Kawamori R. Diabetes trends in Japan. *Diabetes/metabolism Research & Reviews* 2002; 18(S3): S9–S13.
38. Hivert M, Pettitt D, Nolan C, et al. IADPSG Collaborative Research Workshop Wednesday 7 th April 2010 Pasadena California.
39. Association AD. Diagnosis and classification of diabetes mellitus. *Diabetes care* 2014; 37(Supplement 1): S81–S90.