病例-对照研究案例分析

Gestational diabetes and the risk of late stillbirth: a case–control study from England, UK

研究案例目录

- 研究背景
- 研究目的
- 研究设计
- 研究方法
- 研究结果
- 结论

研究背景

1.英国的死产患病率高于欧洲平均水平，怀孕28周后几乎每300名孕妇中就有1名受到影响。妊娠期糖尿病会增加4到6倍的死产风险。

2.在英国，2015年NICE指南建议选择性筛查妊娠期糖尿病，推荐的妊娠期糖尿病诊断标准是空腹血糖≥5.6 mmol/l或口服葡萄糖耐量试验2小时血糖≥7.8 mmol/l。这与世界卫生组织的建议(≥5.1和≥8.5 mmol/l)不同。

3.迄今为止，还没有评估NICE建议的阈值的影响，也没有评估英国的筛查做法对孕晚期死产的影响。

研究目的：

探讨“高危”妊娠期糖尿病(GDM)与接受GDM血糖筛查，以及提高空腹血糖 (FPG)与临床诊断GDM对孕晚期死产风险的联合和单独影响。

研究设计：

病例对照研究

研究设计：

研究对象：来自英国的41个产科医院，纳入2014-2016年283名单胎妊娠＞28周死产孕妇（病例组）和729例妊娠活产孕妇（对照组）。

主要结局变量：GDM和空腹血糖水平。

研究设计：

研究因素：妊娠期糖尿病的“高危状态”是主要暴露因素，接受妊娠期糖尿病筛查是主要的调节因素。空腹血糖升高(作为有害暴露)和接受专门护理(作为缓解因素）。

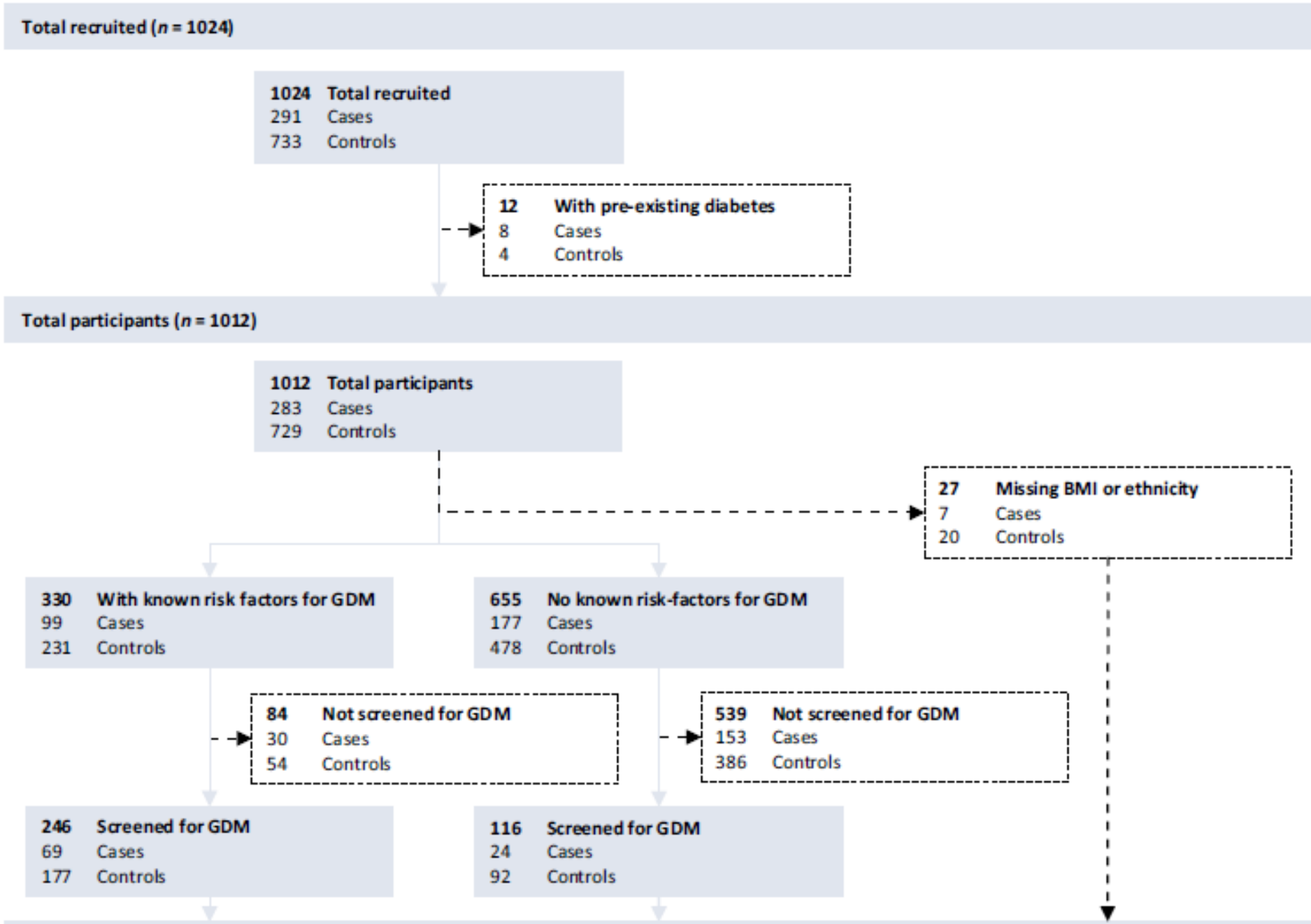
“高危”定义：包括南亚或黑加勒比海种族，体重指数≥30 kg/m2，曾患妊娠期糖尿病或分娩过巨大儿(出生体重≥4.5kg)。

研究方法：

采用因果中介分析方法探讨：

（Ⅰ）“高危”妊娠期糖尿病与妊娠期糖尿病筛查对孕晚期死产风险的单独作用和联合影响。

(Ⅱ)提高空腹血糖（≥5.6mmol/L)与临床诊断妊娠期糖尿病对孕晚期死产风险的单独作用和联合影响。


Total recruited (n = 1024)
1024 Total recruited
291 Cases
733 Controls
12 With pre-existing diabetes
8 Cases
4 Controls
Total participants (n = 1012)
1012 Total participants
283 Cases
729 Controls
27 Missing BMI or ethnicity
7 Cases
20 Controls
330 With known risk factors for GDM
99 Cases
231 Controls
655 No known risk-factors for GDM
177 Cases
478 Controls
84 Not screened for GDM
30 Cases
54 Controls
539 Not screened for GDM
153 Cases
386 Controls
246 Screened for GDM
69 Cases
177 Controls
116 Screened for GDM
24 Cases
92 Controls

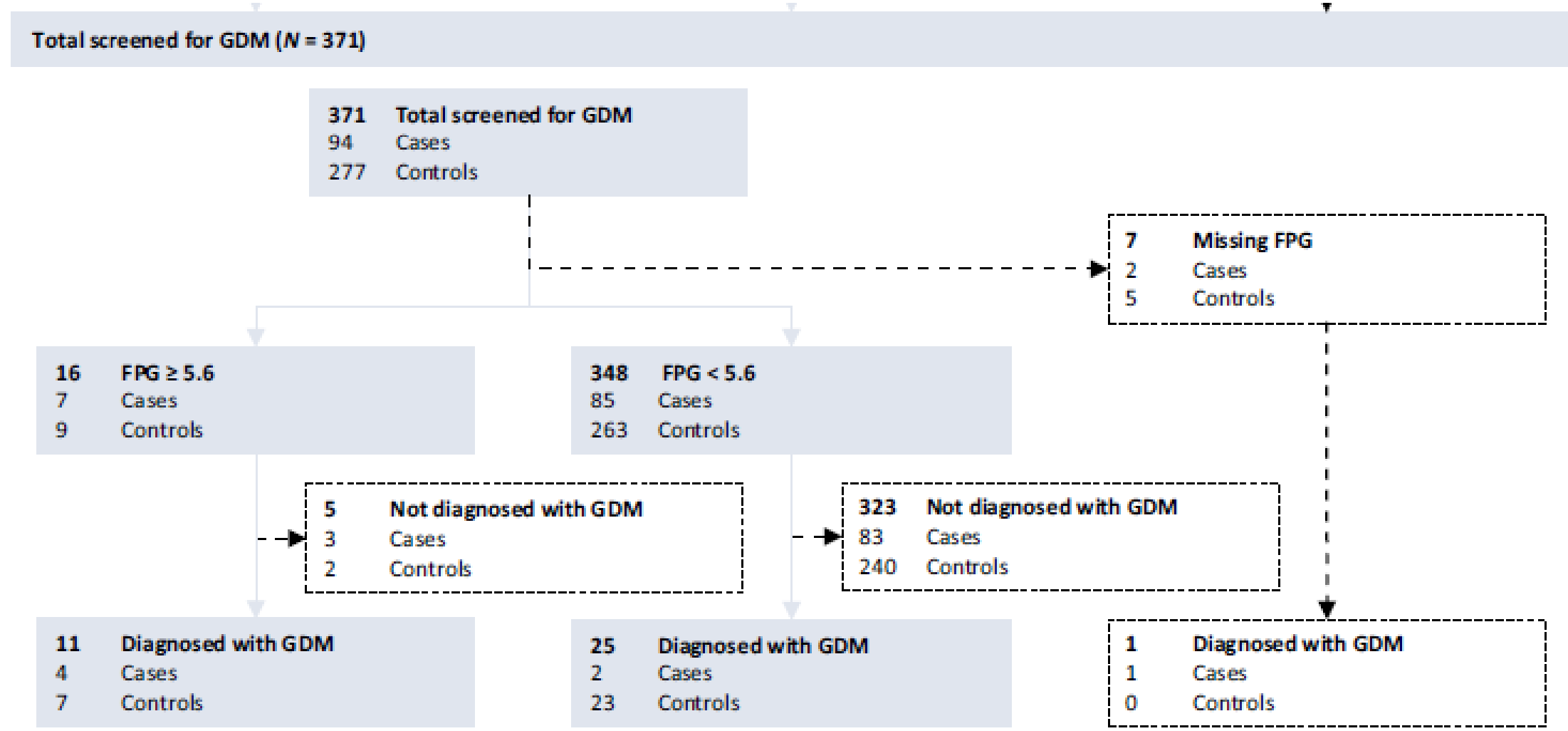


Figure 1. Derivation of the study and analytic sample(s).

研究结果：

1、妊娠期糖尿病（GDM）高危但未查筛血糖的孕妇比非GDM高危孕妇的晚期死产的风险高44%，而GDM高危但筛查血糖的孕妇该风险并不增加；

2、空腹血糖（FPG）升高但临床上未被诊断为GDM的孕妇晚期死产的风险是正常FPG孕妇的4倍；

3、FPG升高且临床诊断为GDM的孕妇上述风险没有增高。

Table 2. Estimated effects of 'at risk' of GDM* and screening for GDM on risk of late stillbirth

Effect estimated	Exposure regimen	Reference regimen	aOR** (95% CI)	*E*-value (lower CI)
Total effect	'At risk' of GDM + screened for GDM	Not 'at risk' + + not screened	0.98 (0.70–1.36)	
Natural effect	'At risk' of GDM + 'natural' chance of screening	Not 'at risk' + + not screened	1.17 (0.87–1.57)	
Controlled direct effect	'At risk' of GDM + not screened for GDM	Not 'at risk' + + not screened	1.44 (1.01–2.06)	2.24 (1.11)
Total indirect effect	'At risk' of GDM + screened for GDM	'At risk' of GDM + + not screened	0.68 (0.47–0.97)	2.30 (1.21)
Natural indirect effect	'At risk' of GDM + 'natural' chance of screening	'At risk' of GDM + + not screened	0.81 (0.67–0.98)	

*Known risk factors for GDM (indicated by NICE for blood glucose screening) comprise South Asian or Black Caribbean ethnicity, body mass index ≥30 kg/m^2, and previous pregnancy affected by gestational diabetes or macrosomic birth (birthweight >4.5 kg).
**Models included the exposure ('at risk' of GDM) and mediator (screened for GDM) only, as all partial confounding variables were also partial mediators.

Table 3. Estimated effects of FPG concentration and clinical diagnosis of GDM on risk of late stillbirth

Effect estimated	Exposure regimen	Reference regimen	aOR* (95% CI)	*E*-value (lower CI)
Total effect	≥5.6 mmol/l** + diagnosed with GDM	<5.6 mmol/l + not diagnosed	1.10 (0.31–3.91)	
Natural effect	≥5.6 mmol/l** + 'natural' chance of diagnosis	<5.6 mmol/l + not diagnosed	1.97 (0.61–6.32)	
Controlled direct effect	≥5.6 mmol/l** + not diagnosed with GDM	<5.6 mmol/l + not diagnosed	4.22 (1.04–17.02)	7.91 (1.24)
Total indirect effect	≥5.6 mmol/l** + diagnosed with GDM	≥5.6 mmol/l** + not diagnosed	0.26 (0.07–0.93)	7.15 (1.36)
Natural indirect effect	≥5.6 mmol/l** + 'natural' chance of diagnosis	≥5.6 mmol/l** + not diagnosed	0.47 (0.23–0.96)	

*Models included the exposure (binary FPG concentration), mediator (clinical diagnosis of GDM), and all observed variables in the minimum sufficient adjustment set (maternal ethnicity, socio-economic circumstances, family history of GDM, height, weight, age, parity, previous histories of GDM and macrosomia, and smoking).
**NICE criteria for diagnosis of GDM.

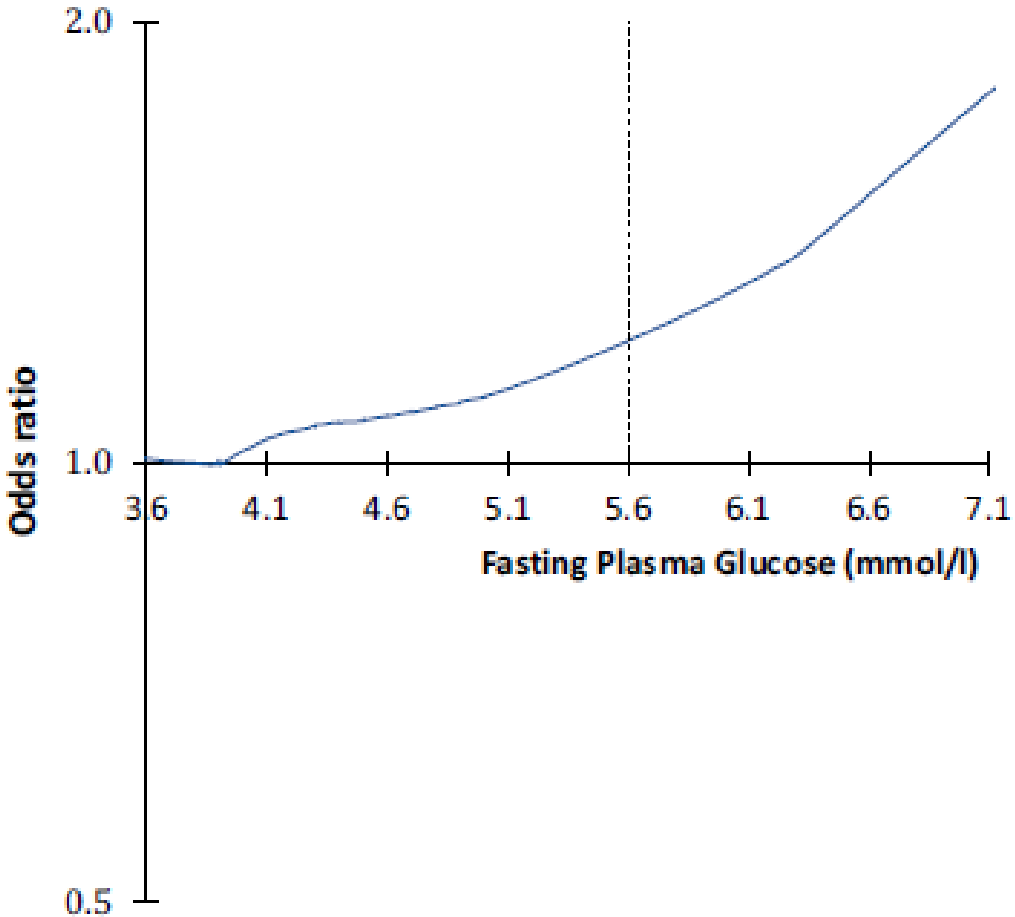


Figure 2. Unconditional odds ratio for late stillbirth across typical values of FPG, relative to women with FPG < 4.1 mmol/l. Dotted line indicates current FPG threshold recommended by NICE.[3]

Table 4. Estimated odds ratio for late stillbirth for different levels of FPG – with and without diagnosis and treatment for GDM – relative to (undiagnosed) women with FPG < 4.1 mmol/l

FPG (mmol/l)	No diagnosis and treatment aOR* (95% CI)	Diagnosed and treated aOR* (95% CI)
4.1	1.15 (1.01–1.30)	
4.6	1.46 (1.01–2.10)	
5.1	1.87 (1.02–3.42)	
5.6	2.39 (1.03–5.55)	0.61 (0.21–1.72)
6.1	3.05 (1.03–9.02)	0.78 (0.26–2.34)
6.6	3.89 (1.03–14.65)	1.00 (0.30–3.33)
7.1	4.97 (1.04–23.80)	1.27 (0.33–4.90)
7.6	6.34 (1.04–38.67)	1.62 (0.35–7.40)

*Models included the exposure (continuous FPG concentration), mediator (clinical diagnosis of GDM), and all observed variables in the minimum sufficient adjustment set (maternal ethnicity, socio-economic circumstances, family history of GDM, height, weight, age, parity, previous histories of GDM and macrosomia, and smoking).

研究结论：

◆血糖筛查和及时准确的临床诊断可能会降低GDM高危和/或FPG升高孕妇妊娠晚期死产的风险。

◆不诊断GDM会使FPG升高的妇女暴露于可避免的妊娠晚期死产风险。