ΤΑΞΙΝΟΜΗΣΗ ΚΑΙ ΑΝΤΙΜΕΤΩΠΙΣΗ ΤΟΥ ΔΙΑΒΗΤΗ ΤΗΣ ΕΓΚΥΜΟΣΥΝΗΣ

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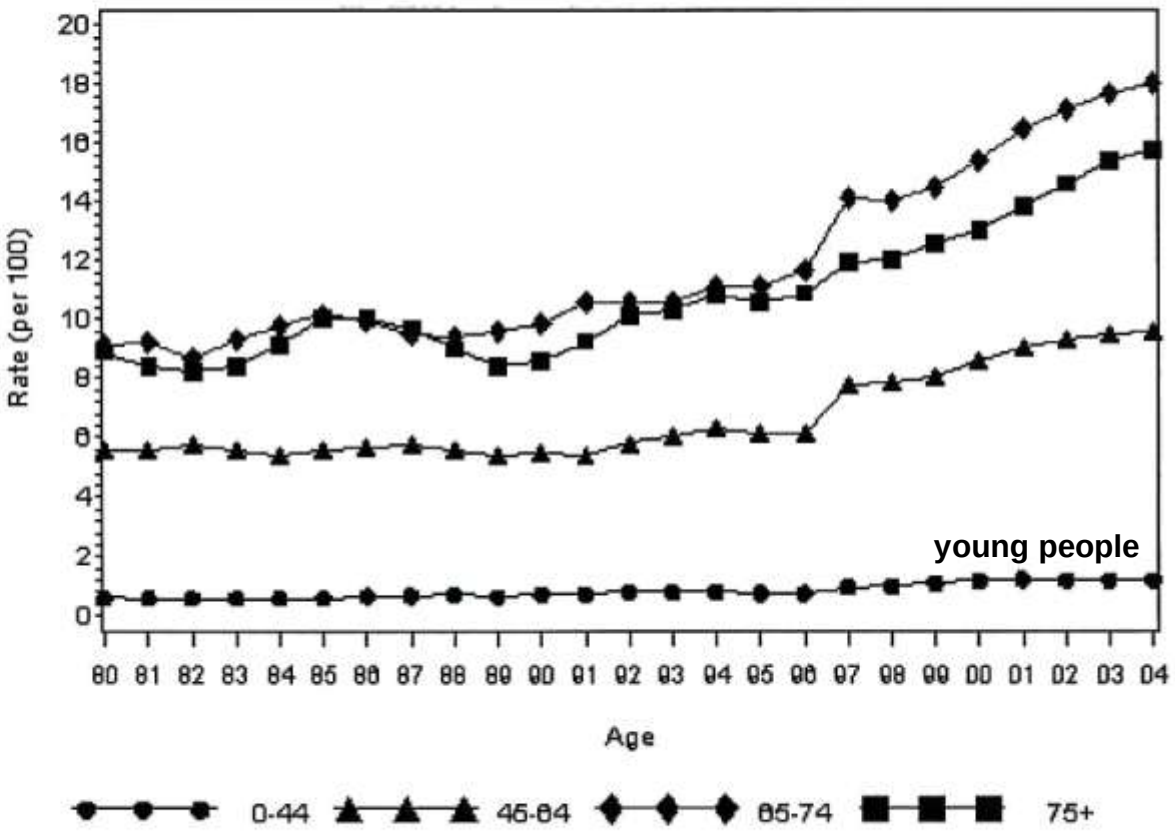
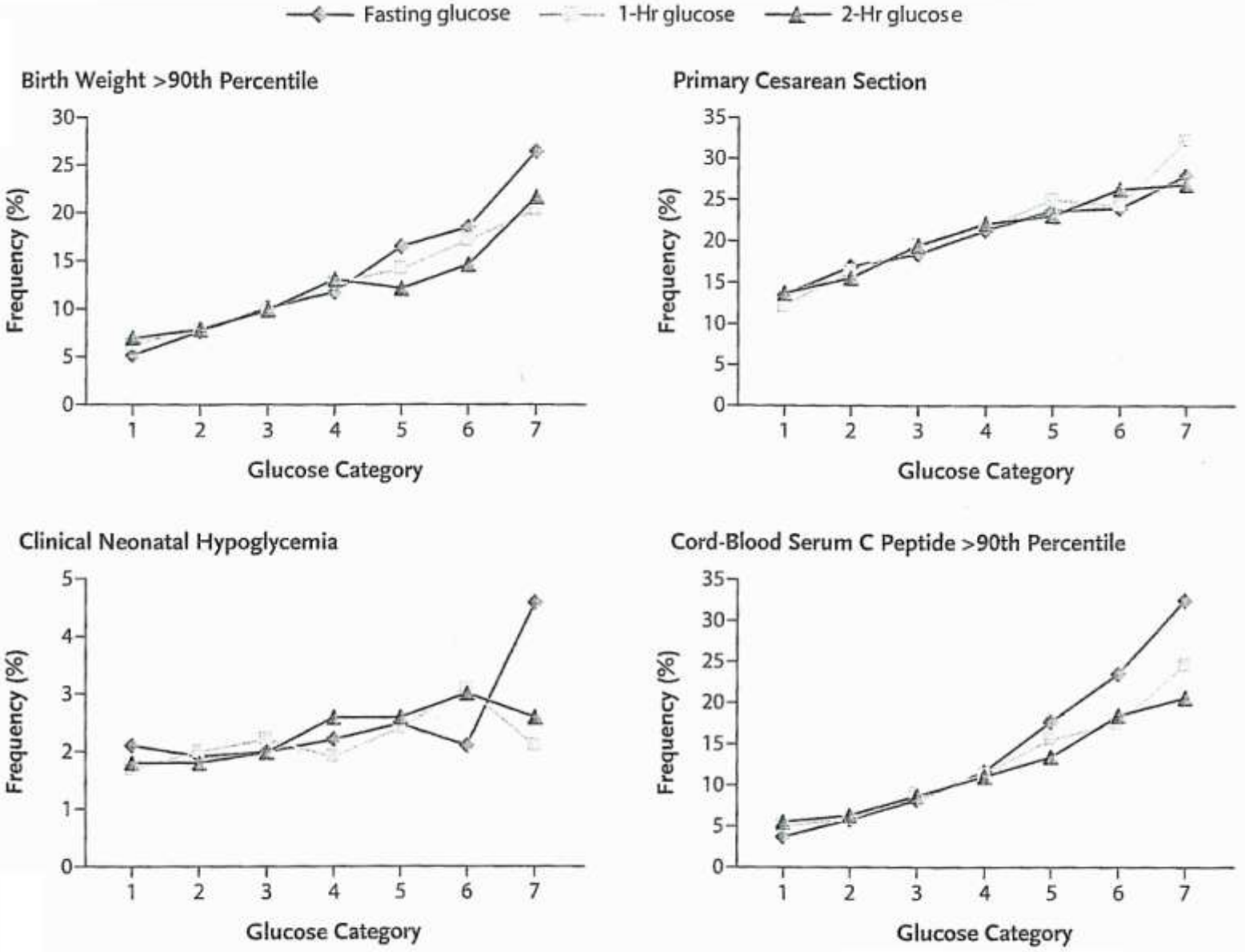
Ιθάκη 2013

- **Prevalence of Diagnosed Diabetes by Age, United States, 1980–2004**
- **For females,**



CDC web site
http://www.cdc.gov/diabetes/statistics/prev/national/figbyage.htm



Frequency of perinatal and maternal outcomes in relation to maternal glycemia.
N Engl J Med 2008;358:1991–2002.

Classification of diabetes mellitus

Pre-gestational diabetes

- **Type I diabetes mellitus**
  - Pancreatic islet beta cell destruction
  - Usually presents in young people <30 years old
  - Family history of other autoimmune conditions
- **Type 2 diabetes mellitus**
  - Defects of both insulin secretion and of insulin resistance
  - Usually age >30 years
  - Usually obese (80%)
  - Family history of type 2 DM
- **Other specific types**
  - Endocrine
  - Drugs and toxins (corticosteroids)
- **Gestational diabetes mellitus**
  - Any degree of glucose intolerance with onset or first recognition during pregnancy

- Among pregnant women, 2-14% ≈ 7% will develop gestational diabetes (GD)

- GD is a heterogeneous group of women and the term GD fails to specify whether the women require dietary alone or treatment with diet and insulin or oral medications and also the severity of the disease.

Negrato CA et al: Diab Metab Synd 2012;4(1):41

Complications	**(RR-95% CI)**
Infant macrosomia >4000g	1,81 (1,47-2,22)
LGA	1,53 (1,39-1,69)
Polyhydramnios	3,5 (3,3-3,8)
Perinatal mortality	1,55 (0,88-2,73)
Preeclampsia	1,69 (1,31-2,18)
Primary cesarean delivery	1,23 (1,01-1,51)

Wendland et al., Gestational diabetes and pregnancy outcomes **(in untreated women)** – a systematic **review** of the World Health Organization (WHO) and the International Association of Diabetes in Pregnancy Study Groups (IADPSG) diagnostic criteria. Pregnancy and Childbirth 2012, 12:23

Neonatal Morbidity

Outcome	No (%)
Shoulder dystocia*:	25 (14)
Clavicle fracture	4 (2)
Erb palsy	1 (1)
Neonatal hypoglycaemia:	
<2.6 mmol/l	207 (64)
<2.0 mmol/l	141 (44)
Hyperbilirubinaemia†:	82 (25)
Respiratory disorders:	47 (15)
Infant respiratory distress syndrome	17 (5)
Wet lung	22 (7)
Others	8 (2)
Hypertrophic cardiomyopathy‡	16 (5)
Apgar score <7 at five minutes	16 (5)

*% of vaginal deliveries (n=179).
†Needing treatment (phototherapy).
‡Clinical diagnosis of hypertrophic cardiomyopathy.

Evers IM et al: BMJ 2004;238:915-919

According to International Association of the Diabetes and Pregnancy Study Groups (IADPSG)

1. Low Risk

- Member of an ethnic group with low incidence of GD or GD type 2
- Aged younger than 25 years
- Normal weight before pregnancy
- No history of poor obstetrical outcome
- No history of abnormal glucose metabolism

Landon MB and Gabbe SG. Obstet Gynecol. 2011;118:1379-93

2. High Risk

- History GD or prediabetes (impaired fasting glucose or impaired glucose tolerance
- Fetal malformation
- Stillbirth
- Successive abortion
- Birth weight > 4500 g

} in previous pregnancies

- Obesity
- Age >35 years old
- Vascular diseases
- Clinical symptom of diabetes (eg glucosuria)
- Strong family history of type 2 diabetes

Landon MB and Gabbe SG. Obstet Gynecol 2011;118:1379-93

Table 1 Rates of congenital anomalies for the diabetes populations studied

	No. of infants or fetuses	All major congenital anomalies		Major congenital anomalies (excluding aneuploidy)	
		n	% (95% CI)	*n*	% (95% CI)
Type 1 diabetes	221	16	7.2 (4.2–11.5)	13	5.9 (3.2–9.8)
Type 2 diabetes:					
known	317	14	4.4 (2.4–7.3)	14	4.4 (2.4–7.3)
newly recognized	237	11	4.6 (2.3–8.2)	11	4.6 (2.3–8.2)
Other GDM	1585	14	0.9 (0.5–1.5)	14	0.9 (0.5–1.5)
Total GDM	1822	25	1.4 (0.9–2.0)	25	1.4 (0.9–2.0)

Table 2 Numbers of fetuses or offspring with major congenital anomalies according tc type of diabetes and major system affected

	Type 1	Type 2 (known)	Type 2 (newly recognized)
Cardiac	6	7	3
Musculoskeletal	3	2	1
Reno-genital	2	1	2
Neurological	1	2	1
Multiple	1	2	4
Aneuploidy	3	0	0

Farrel T et al:
Diabetic Medicine 2002;19(4):323-326

A new strategy in regarding to the diagnosis of GD

First antenatal visit
(fasting blood glucose level)

≤92mg/dl

92-126mg/dl

OGTT 24-28 weeks
(75g glucose)

Gestational diabetes

>126 mg/dl

Diabetes mellitus

		(mg/dl)
1 or more values	FGL	92
	1h	180
	2h	153

Gestational diabetes

Association of Diabetes and Pregnancy Study Groups (ADPSG), 2010
(Based on the Findings from the HAPO Study)

Αντιμετώπιση διαβήτη

Effects of treatment in women with gestational diabetes mellitus: systematic review and meta-analysis

Karl Horvath, project manager EBM review center,[1] head of outpatient facility diabetes and metabolism,[2] Klaus Koch, project manager,[3] Klaus Jeitler, scientific assistant,[1] Eva Matyas, scientific assistant,[1] Ralf Bender, head of department of medical biometry,[3] Hilda Bastian, head of department of health information,[3] Stefan Lange, deputy director,[3] Andrea Siebenhofer, professor for chronic care and health services research,[4] project manager[1]

BMJ: 2010;340:C1395

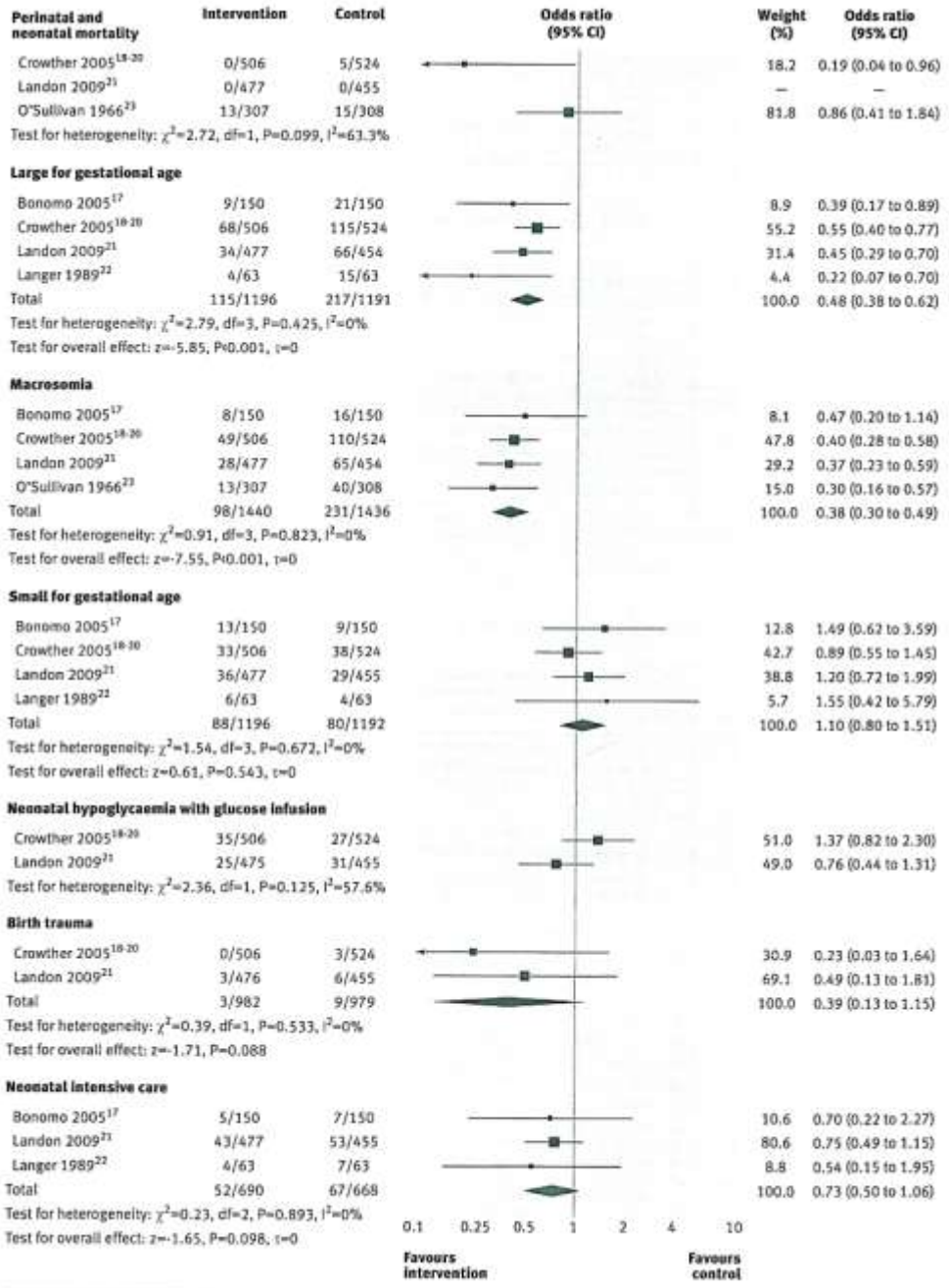


Fig 3 | Neonatal outcomes in pool A (DerSimonian and Laird random effects model, except for perinatal and neonatal morality and birth trauma, which use Peto fixed effects model)

Management of women with GDM includes

1. Treatment of the women

- The role of diet
- The role of exercise
- Blood glucose testing
- The role of insulin
- The role of antidiabetic agents

2. Antepartum fetal surveillance tests

3. Timing and mode of delivery

4. Postpartum follow-up

The role of diet

- Most of the women should receive a dietary program of 2000-2500 kcal daily
- Carbohydrate intake should be limited to 33-40% of calories
- Complex carbohydrates instead of simple carbohydrates
- Low-saturated fatty acids (SFA) (<7% calories)

Roussel MA et al: Am J Clin Nutr 2012;95:9-16

- The American Diabetes Association suggests for obese women (BMI≥30) caloric restriction of 30-33%

APA 2000;70-86

- Caloric restriction less than 1500 kcal/day is not recommended in treating of GDM

Jacqueminet S et al: Diabetes Metab 2010;;36:658-71

Crane JM, White J, Murphy P, Burrage L, Hutchens D.

The effect of gestational weight gain by body mass index on maternal and neonatal outcomes.

J Obstet Gynaecol Can. 2009 31(1):28-35.

Conclusion

The effects of gestational weight gain on pregnancy outcome depend on the woman's pre-pregnancy BMI. Pregnancy weight gains of 6.7-11.2 kg (15-25 lb) in overweight and obese women, and less than 6.7 kg (15 lb) in morbidly obese women are associated with a reduction in the risk of adverse outcome.

- Regular exercise and healthy lifestyle is recommended for GD women

Avery MD, et al: Obstet Gynecol 1997;89:10-15

- Self blood glucose monitoring is essential for GDM women (four times per day glucose testing is recommended: fasting glucose determination followed by three postprandial tests)

Crowther CA et al: N Engl J Med 2005;352:2477-86

Landon MB et al: N Engl J Med 2009;361:1339-48

- Some authors prefer 1 hour postprandial assessment of glucose levels and others 2-hour postprandial assessment

Metzger BE et al: Diabetes Care 2007;30 (suppl. 2): S 251-60

Target Plasma Glucose Levels in Pregnancy

Time	mg/dL
Before breakfast	60–90
Before lunch, supper, bedtime snack	60–105
2 h after meals	At or below 120
2 AM to 6 AM	Above 60

Longer O et al: Am J Obstet Gynecol 1994;170:1036-46

The role of insulin

a) Insulin is the medication for women who fail to achieve satisfactory glucose control

b) those whose the fetuses present to have abdominal circumference (greater than the 75th percentile)

Kjos SL et al: Diabetes Care 2001;24:1904-10

The role of antidiabetic agents

Metformin versus Insulin for the Treatment of Gestational Diabetes

Janet A. Rowan, M.B., Ch.B., William M. Hague, M.D., Wanzhen Gao, Ph.D., Malcolm R. Battin, M.B., Ch.B., and M. Peter Moore, M.B., Ch.B., for the MiG Trial Investigators*

N Engl J Med 2008;358:2003-15

Secondary Outcomes and Additional Measurements.*

Variable	Metformin Group (N=363)	Insulin Group (N=370)	P Value
Neonatal			
Gestational age at birth — wk	38.3±1.4	38.5±1.3	0.02
Birth weight — g	3372±572	3413±569	0.33
Birth-weight percentile	54.6±30.1	54.3±31	0.91
Birth weight <10th percentile — no. (%)	26 (7.2)	36 (9.7)	0.21
Birth weight >90th percentile — no. (%)	70 (19.3)	69 (18.6)	0.83
Head circumference — cm	34.8±1.6	34.9±1.6	0.24
Crown–heel length — cm	50.3±2.8	50.3±2.4	0.87
Crown–rump length — cm†	33.4±2.7	33.6±2.6	0.46
Chest circumference — cm‡	33.9±2.3	34.1±2.5	0.33
Abdominal circumference — cm§	32.8±2.7	32.8±2.8	0.91
Mid-upper-arm circumference — cm§	11.2±1.3	11.1±1.4	0.51
Triceps skin-fold thickness — mm¶	5.2±1.6	5.1±1.2	0.30
Subscapular skin-fold thickness — mm‖	5.2±1.5	5.2±1.3	0.60
Ponderal index**	2.6±0.3	2.7±0.3	0.28
Umbilical-cord serum insulin concentration — pmol/liter††			0.18
Median	50.0	40.4	
Interquartile range	26.3–81.7	20.3–71.4	
Maternal‡‡			
Glycemic control from randomization until delivery			
Capillary glucose level after an overnight fast — mg/dl	93.6±10.8	91.8±12.6	0.24
2-Hr postprandial capillary glucose level — mg/dl	111.6±10.8	115.2±16.2	0.003
Glycemic control at 1 week after randomization			
Capillary glucose level after an overnight fast — mg/dl	100.8±16.2	99.0±18.0	0.31
Postprandial capillary glucose level — mg/dl	117.0±16.2	120.6±18.0	0.006
Glycemic control during the last 2 wk before delivery			
Capillary glucose level after an overnight fast — mg/dl	90.0±10.8	88.2±12.6	0.16
2-Hr postprandial capillary glucose — mg/dl	109.8±12.6	111.6±18.0	0.19
Glycated hemoglobin at wk 36–37 — %§§	5.6±0.5	5.7±0.6	0.25
Plasma glucose level at wk 36–37 after an overnight fast — mg/dl¶¶	81.0±10.8	79.2±12.6	0.10
Capillary glucose level 12 hr before delivery — mg/dl‖‖	97.2±10.8	95.4±16.2	0.35
Hypertensive complications — no. (%)***			
Gestational hypertension	14 (3.9)	23 (6.2)	0.14
Preeclampsia	20 (5.5)	26 (7.0)	0.40
Results of 75-g oral glucose-tolerance test at 6 to 8 wk post partum†††			
Fasting plasma glucose level — mg/dl	91.8±14.4	91.8±16.2	0.34
2-Hr postprandial plasma glucose level — mg/dl	115.2±43.2	115.2±41.4	0.87
Diabetes — no./total no. (%)	23/270 (8.5)	15/282 (5.3)	0.14
Impaired glucose level after an overnight fast — no./total no. (%)‡‡‡	13/270 (4.8)	13/282 (4.6)	0.91
Impaired glucose tolerance — no./total no. (%)§§§	30/270 (11.1)	41/282 (14.5)	0.23
Body-mass index	31.6±7.6	31.8±7.5	0.74

Brown *N Engl J Med, 2008*

Niromanesh S, Alavi A, Sharbaf FR, Amjadi N, Moosavi S, Akbari S.

Metformin compared with insulin in the management of gestational diabetes mellitus: a randomized clinical trial.

Diabetes Res Clin Pract. 2012;98(3):422-9.

Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Women Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Conclusion:

Metformin is an effective and safe alternative treatment to insulin for women with GDM. This study does not show significant risk of maternal or neonatal adverse outcome with the use of metformin.

- However, 46% of women receiving metformin require insulin or are switched to insulin therapy in order to achieve glycemic control

Landon MB, Goble SG. Obstet Gynecol, 2011

- A sonogram with measurement of growth-rump distance should be performed early in pregnancy to confirm gestational dating
- First trimester nuchal translucency screening should be offered
- Sonogram should be performed at 16-20 weeks of gestation for fetal anomalies
- Sonograms should de done at 4 weeks intervals and (the 38^{th} week of gestation) for monitoring of fetal growth and measure AF volume

Antepartum fetal surveillance tests

- **Group at low risk for antepartum and intrapartum death**
  - Women who are well controlled with diet only
  - Women with no complications

- **Group at high risk for antepartum and intrapartum death**
  - Women with complications (hypertension, macrosomia, prior stillbirth, hydramnios)
  - Women who require insulin or oral agents

NST or BP trice-weekly at 32-34 weeks of gestation

Landon MB and Gable SG, Diabetes, 34:50-4, 1985
Landon MB, Gable SG. Obstet Gynecol 2011;118:1379-93

Timing and node of delivery

ADA (American Diabetes Association)	AGOG (American College of Ob/Gyn)	NICE (National Institute for Health and Clinical Excellence in the U.K.)
Delivery during the 38th week is recommended unless obstetric considerations dictate otherwise. Prolongation of gestation past 38 weeks increases the risk of fetal macrosomia without reducing cesarean rates.	The timing of delivery in GDM remains relatively open. If estimated fetal weight is 4,500 g or more, cesarean delivery may be considered.	Induce/elective cesarean after 38 weeks if normally grown fetus; glucose monitoring hourly target 4–7 mmol/l if higher intravenous dextrose/insulin

Simmods D et al: Diabetes Care 2010;33:34-37

Postpartum follow-up

The risk of developing Diabetes type 2

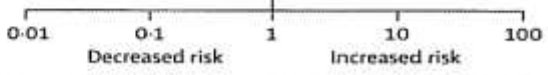
Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis

Leanne Bellamy, Juan-Pablo Casas, Aroon D Hingorani, David Williams

Lancet 2009;373:1773-79

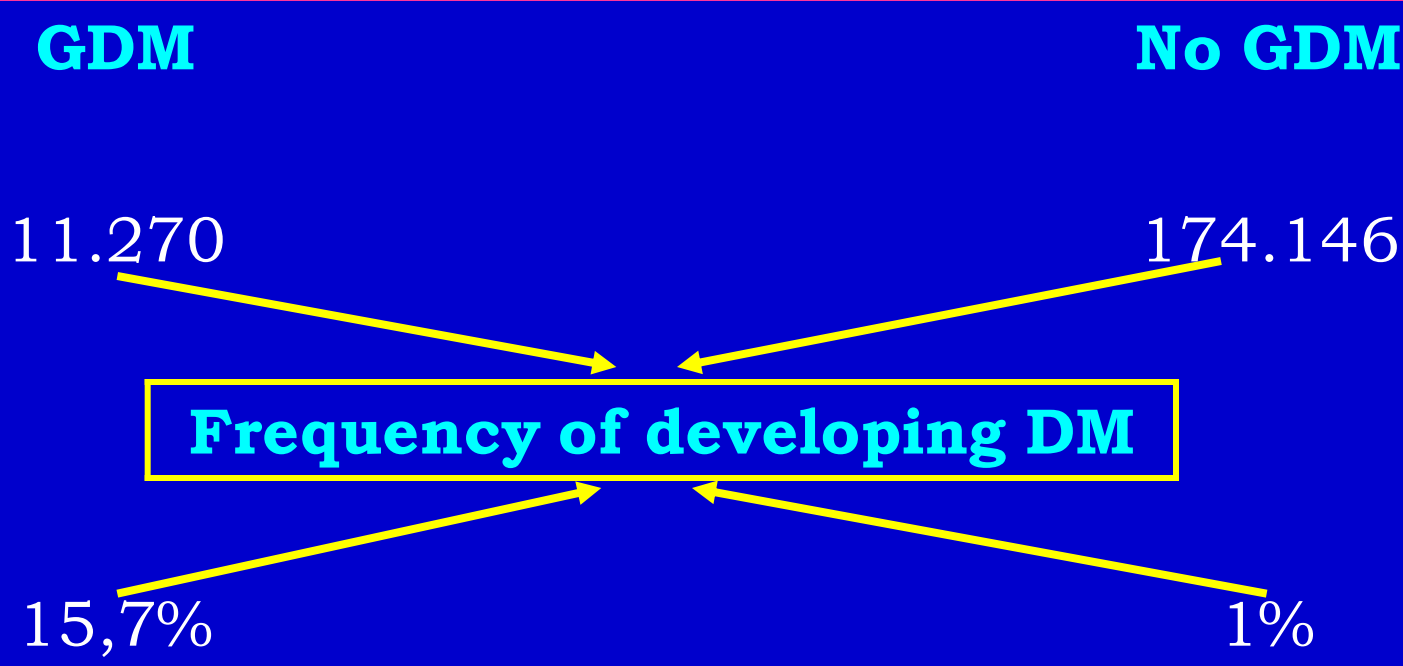
	Country	T2DM/GDM	T2DM/no GDM	Relative risk (95% CI)
Feig et al,[18] 1995–2002	Canada	2874/21823	6628/637341	12·66 (12·15–13·19)
Lee H et al,[15] 1995–97	Korea	71/620	22/868	4·52 (2·83–7·21)
Madarasz et al,[21] 1995	Hungary	21/68	0/39	24·93 (1·55–400·64)
Gunderson et al,[22] 1985–206	USA	43/166	150/2242	3·87 (2·87–5·22)
Vambergue et al,[23] 1992	France	53/295	1/111	19·94 (2·79–142·47)
Lee A et al,[24] 1971–2003	Australia	405/5470	16/783	3·62 (2·21–5·93)
Ferraz et al[17]*	Brazil	6/70	7/108	1·32 (0·46–3·78)
Krishnaveni et al,[25] 1997–98	India	13/35	8/489	22·70 (10·09–51·08)
Morimitsu et al,[26] 1999–2001	Brazil	7/23	0/11	7·50 (0·47–120·11)
Järvelä et al,[5] 1984–94	Finland	23/435	0/435	47·00 (2·86–771·65)
Albareda et al,[27] 1966–93	Spain	44/696	0/70	9·07 (0·56–146·25)
Åberg et al,[28] 1991–99	Sweden	21/229	1/61	5·59 (0·77–40·66)
Linné et al,[16] 1964–65	Sweden	10/28	0/52	38·38 (2·33–631·74)
Bian et al,[29] 1964–65	China	15/45	1/39	13·00 (1·80–93·93)
Ko et al,[30] 1988–95	China	105/801	7/431	8·07 (3·79–17·19)
Osei et al,[31] 1990–91	USA	10/15	0/35	47·25 (2·95–757·28)
Damm et al,[32] 1978–85	Denmark	33/241	0/57	16·06 (1·00–258·06)
Benjamin et al,[33] 1961–88	New Mexico	14/47	3/47	4·67 (1·43–15·21)
O'Sullivan,[34] 1954–60 and 1962–70	USA	224/615	18/328	6·64 (4·19–10·52)
Persson et al,[35] 1961–84	Sweden	5/145	0/41	3·16 (0·18–55·76)
Total		**3997/31867**	**6862/643588**	**7·43 (4·79–11·51)**

Test for heterogeneity: τ^2=0·50, χ^2=126·67, df=19 (p<0·0001), I^2=85·0% (95%CI 78–90)
Test for overall effect: Z=9·39 (p<0·0001)

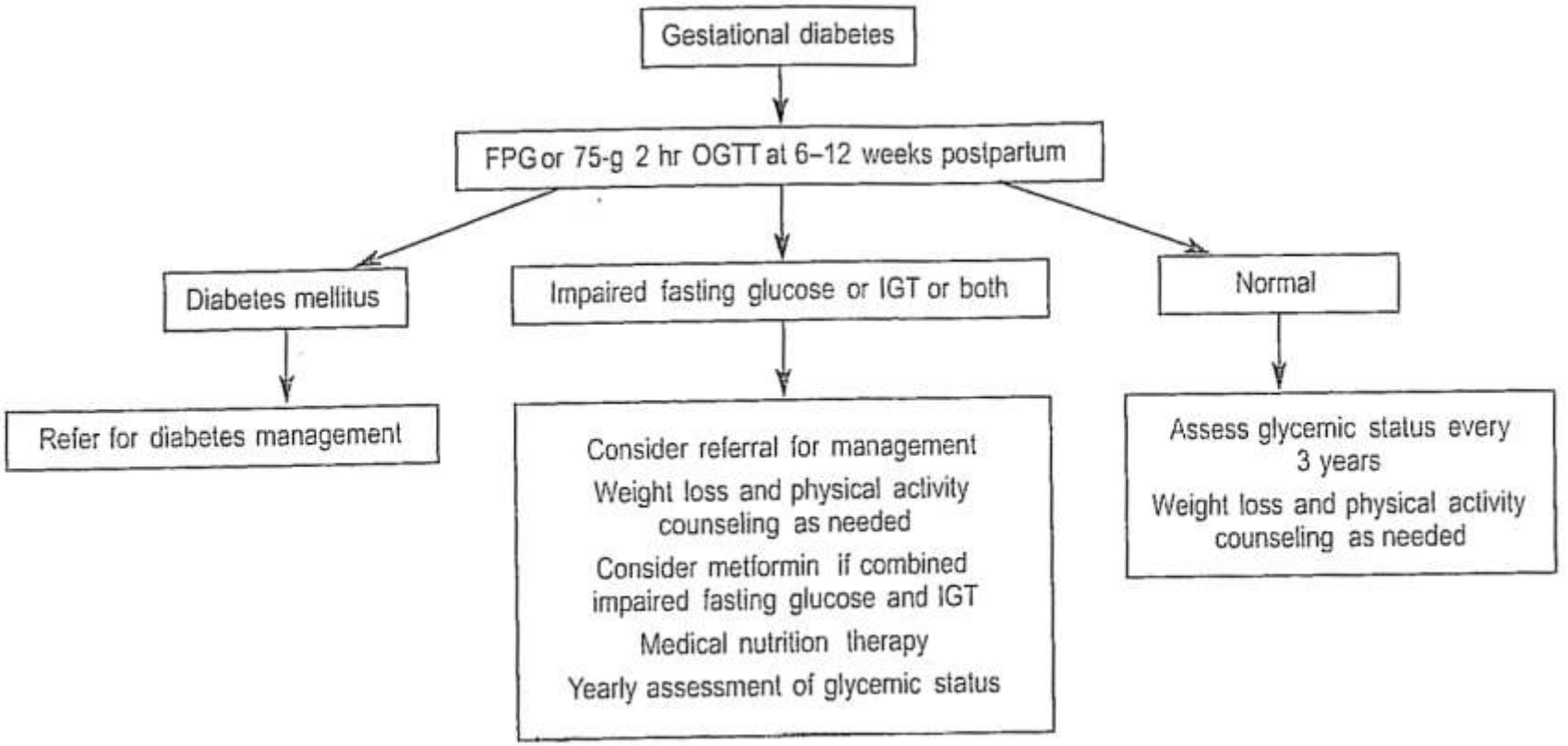


Risk of type 2 diabetes mellitus (T2DM) after gestational diabetes mellitus (GDM)
x-axis is log scale. Each solid square represents a relative risk. Horizontal lines indicate 95% CIs. df=degrees of freedom. *Dates not available.

Follow-up of up to 10 years



Chodick G et al: Diabet Med 27:779-85, 2010



Ob Gynecol 2009;113:1419-21

OBSTETRICS

Gestational diabetes: risk of recurrence in subsequent pregnancies

Darios Getahun, MD, MPH; Michael J. Fassett, MD; Steven J. Jacobsen, MD, PhD

OBJECTIVE: We sought to examine the recurrence risk of gestational diabetes mellitus (GDM) in a subsequent pregnancy and determine whether recurrence risk is modified by race/ethnicity.

STUDY DESIGN: We used the Kaiser Permanente Southern California longitudinally linked records (1991-2008) to study women with first 2 (n = 65,132) and first 3 (n = 13,096) singleton pregnancies. Adjusted odds ratios (ORs) were used to estimate the magnitude of recurrence.

RESULTS: Risks of GDM in the second pregnancy among women with and without previous GDM were 41.3% and 4.2%, respectively (OR, 13.2; 95% confidence interval, 12.0–14.6). The recurrence risk of GDM in the third pregnancy was stronger when women had GDM in both prior pregnancies (OR, 25.9; 95% confidence interval, 17.4–38.4). Hispanics and Asian/Pacific Islanders have higher risks of recurrence.

CONCLUSION: A pregnancy complicated by GDM is at increased risk for subsequent GDM. The magnitude of risk increases with the number of prior episodes of GDM. These recurrence risks also showed heterogeneity by race-ethnicity.

Key words: gestational diabetes, race/ethnicity, recurrence, subsequent pregnancy

Cite this article as: Getahun D, Fassett MJ, Jacobsen SJ. Gestational diabetes: risk of recurrence in subsequent pregnancies. Am J Obstet Gynecol 2010;203:467.e1-6.

Ευχαριστώ πολύ!