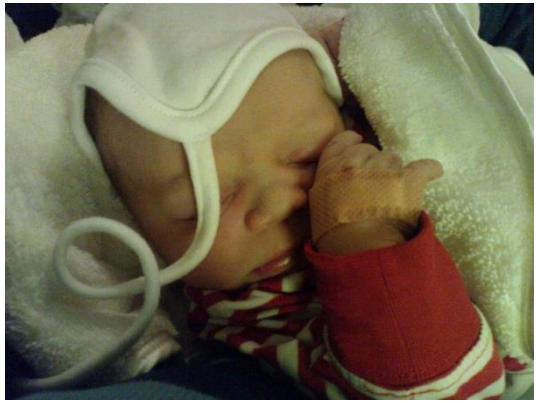

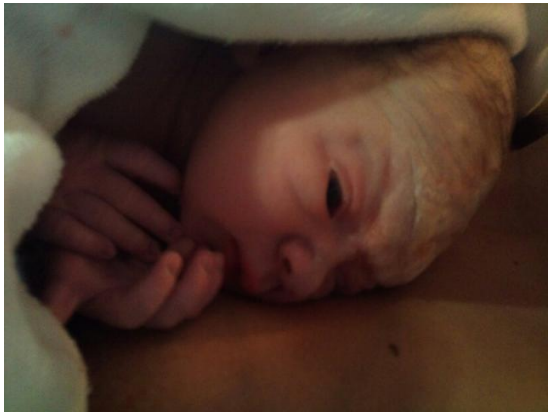

Mamma-studien

Kerstin Berntorp
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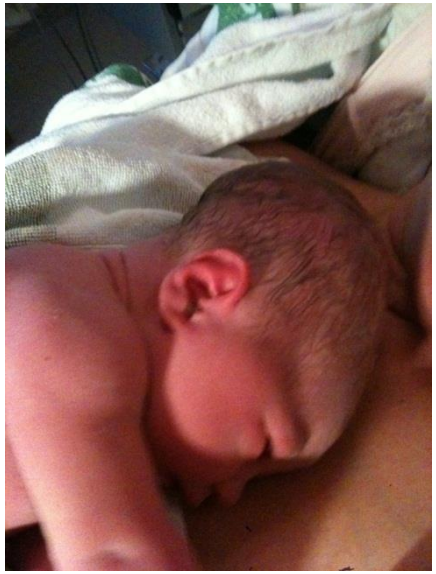


Graviditetsdiabetes (GDM) diagnostik Södra sjukvårdsregionen

- Rutinmässig 75 g OGTT i gv 28. Vid riskgraviditeter (hereditet, tidigare GDM eller stort barn, BMI >35) även i gv 12.

- Kapillärt 2-h P-glukos ≥10,0 mmol/L = graviditetsdiabetes[1]

1. EASD study group, Diabetes 1991;40 Suppl 2:8-13.

Diagnostiskt alternativ WHO 1999

- Graviditetsdiabetes definieras som den sammanslagna kategorin diabetes och IGT (impaired glucose tolerance) i den icke gravida populationen

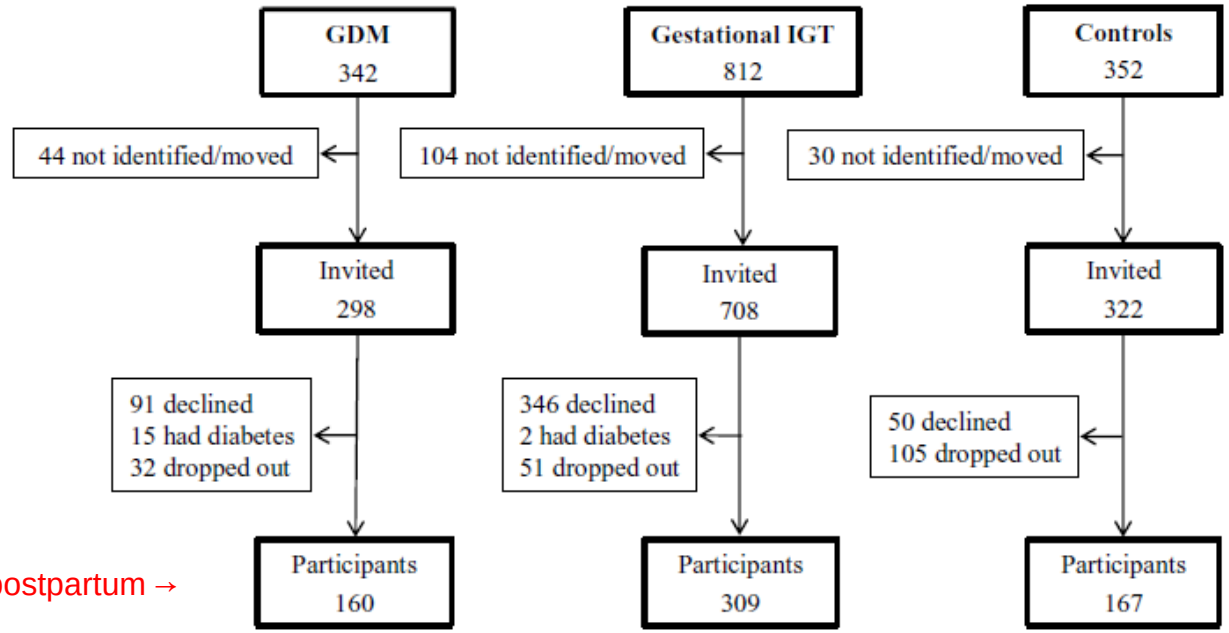
- Kapillärt 2-h P-glukos ≥8,9 mmol/L vid 75 g OGTT = graviditetsdiabetes
  - eller fP-Glukos ≥7,0 mmol/L

Graviditetsdiabetes i Skåne riskfaktorer och konsekvenser ”Mamma-studien”

Rekryteringsår 2003-2005
(Malmö, Lund/Ystad, Helsingborg = 85% täckningsgrad)

- Prospektivt under 5 år postpartum fastställa diabetesincidensen hos kvinnor med olika grad av glukostolerans under graviditet
- Parallellt kartlägga utfallet under graviditet
- Karaktärisera kvinnorna genetiskt, immunologiskt, metabolt
  - finna markörer för sjukdomsutveckling
- Studera den relativa betydelsen av insulinsekretion och insulinresistens i utvecklingen av diabetes postpartum
  - skillnader beroende på etniskt ursprung?

Mamma-studien



OGTT 1-2 år postpartum →

Figure 1. Flowchart of the study population.

Acta Obstetricia et Gynecologica Scandinavica © 2011 Nordic Federation of Societies of Obstetrics and Gynecology **90** (2011) 1252–1258

The impact of gestational diabetes mellitus on pregnancy outcome comparing different cut-off criteria for abnormal glucose tolerance

EVA ANDERBERG[1], KARIN KÄLLÉN[2] & KERSTIN BERNTORP[3]

Acta Obstetricia et Gynecologica. 2010; 89: 1532–1537

Table 2. Outcomes in mothers and infants.

	GDM (n = 306)			Gestational IGT (n = 744)			Controls (n = 329)
	n (%)	Crude OR	Adjusted OR (95% CI)	n (%)	Crude OR	Adjusted OR (95% CI)	n (%)
Mothers							
Preeclampsia, essential or gestational hypertension	26 (8.5)	3.0	2.7 (1.3–5.8)	46 (6.2)	2.1	2.0 (1.0–4.1)	10 (3.0)
Induction	57 (18.6)	3.4	3.1 (1.8–5.2)	86 (11.6)	1.9	1.8 (1.1–3.0)	21 (6.4)
Forceps or vacuum extraction	20 (6.5)	1.2	1.1 (0.6–2.1)	41 (5.5)	1.0	1.0 (0.6–1.8)	18 (5.5)
Cesarean section	72 (23.5)	2.3	2.1 (1.4–3.2)	114 (15.4)	1.4	1.3 (0.9–1.9)	39 (11.9)
Elective	7 (8.8)	1.6	1.4 (0.7–2.6)	45 (6.1)	1.1	1.0 (0.5–1.7)	19 (5.8)
Emergency	45 (14.7)	2.7	2.5 (1.5–4.4)	69 (9.3)	1.6	1.5 (0.9–2.6)	20 (6.1)
Infants							
Born <37 gestational weeks	27 (8.9)	3.6	3.6 (1.6–7.7)	39 (5.2)	2.0	2.0 (1.0–4.2)	9 (2.7)
Apgar score <7 at 5 minutes	8 (2.6)	8.8	9.6 (1.2–78.0)	6 (0.8)	2.7	2.8 (0.3–23.2)	1 (0.3)
Large-for-gestational age infant	26 (8.5)	2.3	2.5 (1.3–5.1)	57 (7.7)	2.0	2.1 (1.1–3.9)	13 (3.9)
Small-for-gestational age infant	6 (2.0)	1.3	1.2 (0.4–4.0)	11 (1.5)	1.0	1.0 (0.3–2.8)	5 (1.5)
Neonatal intensive care >1 day	57 (18.5)	5.2	5.2 (2.8–9.6)	62 (8.2)	2.1	2.1 (1.1–3.8)	14 (4.2)

Note: The percentage is calculated on all non-missing data for each variable within each group. OR with 95% CI for the GDM and gestational IGT groups compared to controls. Adjustment was made for maternal age and deliveries. GDM, gestational diabetes mellitus; IGT, impaired glucose tolerance; OR, odds ratio; CI, confidence interval.

Prevalence of impaired glucose tolerance and diabetes after gestational diabetes mellitus comparing different cut-off criteria for abnormal glucose tolerance during pregnancy

EVA ANDERBERG[1], MONA LANDIN-OLSSON[2], JOHAN KALÉN[3], ANDERS FRID[2], DAG URSING[2] & KERSTIN BERNTORP[2]

Diagnoskriterier	**Pat antal GDM**	**Uppföljd tid**	**DM**	**IGT**
Modifierad EASD	160	1-2 år	11%	24%
WHO 1999	469	1-2 år	6%*	23%
Kontrollgrupp	167	1-2 år	0%	10%

*4% europeiskt vs. 17% icke-europeiskt ursprung

Table 3. Univariate and multivariate logistic regression analyses of variables tested for an association with abnormal glucose tolerance postpartum.

	Univariate[a]		Multivariate[a]	
	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value
GDM or gestational IGT	3.8(2.2–6.6)	<0.001	3.3(1.8–5.9)	<0.001
Age at delivery (years)	1.1(1.0–1.1)	0.005	1.1(1.0–1.1)	0.029
Previous deliveries >3	0.9(0.6–1.4)	0.72	0.6(0.4–1.0)	0.051
BMI (kg/m^2)	1.1(1.1–1.1)	<0.001	1.1(1.0–1.1)	<0.001
First-degree relative(s) with diabetes	1.8(1.2–2.7)	0.003	1.2(0.8–1.9)	0.41
Non-European origin	3.0(2.0–4.7)	<0.001	2.4(1.5–4.0)	<0.001

[a]Adjusted for time to follow-up visit.

GDM, gestational diabetes mellitus; IGT, impaired glucose tolerance; OR, odds ratio; CI, confidence interval.

HLA-DQB1 genotypes and islet cell autoantibodies against GAD65 and IA-2 in relation to development of diabetes post partum in women with gestational diabetes mellitus

Anastasia Papadopoulou [a,b,*], *Kristian F. Lynch* [a,c], *Eva Anderberg* [d], *Mona Landin-Olsson* [e], *Ida Hansson* [a], *Carl-David Agardh* [a,b], *Åke Lernmark* [a], *Kerstin Berntorp* [b]

DIABETES RESEARCH AND CLINICAL PRACTICE 95 (2012) 260–264

Conclusions: Mothers with GDM and HLA-DQB1*0602 were less likely to develop diabetes after pregnancy, and type 1 diabetes associated high risk HLA genes did not predict type 1 diabetes post partum. Additionally, GADA were positively associated with diabetes development.

1. Den för typ 1 diabetes skyddande HLA-genotypen var negativt associerat med såväl GDM som diabetesutveckling postpartum.
2. Förekomsten av högrisk HLA-genotyp var inte ökad vid GDM och predikterade inte diabetesutveckling postpartum.
3. Förekomst av GAD-ak (5% GDM) var positivt associerat med diabetesutveckling.

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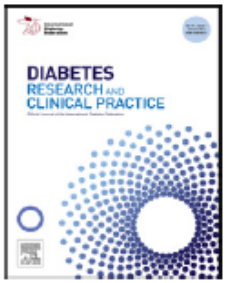
Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

2012;97:394-7

International Diabetes Federation



Genetic prediction of postpartum diabetes in women with gestational diabetes mellitus

M. Ekelund [a,1,*], N. Shaat [b,1], P. Almgren [c], E. Anderberg [d], M. Landin-Olsson [a], V. Lyssenko [c], L. Groop [c], K. Berntorp [b]

Aims: To examine whether genetic variants that predispose individuals to type 2 diabetes (T2D) could predict the development of diabetes after gestational diabetes mellitus (GDM).
Methods: 13 SNPs (*FTO* rs8050136, *CDKAL1* rs7754840 and rs7756992, *CDKN2A/2B* rs10811661, *HHEX* rs1111875, *IGF2BP2* rs1470579 and rs4402960, *SLC30A8* rs13266634, *TCF7L2* rs7903146, *PPARG* rs1801282, *GCK* rs1799884, *HNF1A* rs1169288, and *KCNJ11* rs5219) were genotyped in 793 women with GDM after a median follow-up of 57 months.

Conclusions: The *TCF7L2* rs7903146 and *FTO* rs8050136 polymorphisms, and particularly a weighted risk score of T2D risk alleles, predict diabetes after GDM. Further studies in other populations are needed to confirm our results.

Den relativa betydelsen av insulinsekretion och insulinresistens i utvecklingen av diabetes postpartum

Table 1. Descriptive data and results from OGTT for Controls and women after GDM, grouped according to glucose tolerance at follow-up.

	Controls	Women after GDM								
	(*n*=150)	NGT (n=334)	*p*	*p*‡	IGT (*n*=105)	*p*	*p*‡	Diabetes (*n*=31)	*p*	*p*‡
Age (years)	32 (31-33)	34 (33-34)	0.11		35 (34-36)	0.002		36 (32-39)	0.010	
BMI (kg/m^2)	24.1 (23.1-25.2)	23.6 (23-24)	0.11		25.4 (24.5-26.9)	0.036		31.7 (28.8-35.4)	$2*10^{-6}$	
Non-European ethnicity	11 (7.5)	49 (15)	0.025		29 (28)	$2*10^{-5}$		14 (52)	$2*10^{-8}$	
First grade diabetes heredity	26 (18)	101 (32)	0.001		42 (42)	$5*10^{-5}$		13 (48)	0.004	
Deliveries >3	4 (2.8)	17 (5.2)	0.33		14 (13)	0.003		4 (14)	0.027	
Time to follow-up (days)	430 (414-451)	462 (442-484)	0.30		512 (481-551)	$1*10^{-4}$		525 (403-628)	0.10	
HOMA-IR†	1.3 (1.2-1.5)	1.4 (1.3-1.6)	0.65	0.83	1.6 (1.3-1.8)	0.15	0.74	3.2 (2.3-4.4)	$2*10^{-5}$	0.009
Available samples	109 (73)	238 (71)	0.83		72 (69)	0.49		25 (81)	0.50	
I/G30†	16.8 (14.4-19.7)	13.8 (12.6-15.0)	0.026	0.021	11.4 (9.9-13.2)	0.002	0.001	7.3 (5.5-9.9)	0.012	0.003
Available samples	93 (62)	224 (67)	0.30		69 (66)	0.60		21 (68)	0.68	
(I/G30)/HOMA-IR†	12.8 (10.8-15.2)	9.6 (8.7-10.6)	0.008	0.006	7.8 (6.5-9.4)	$3*10^{-4}$	0.002	2.5 (1.8-3.6)	$2*10^{-8}$	$9*10^{-6}$
Available samples	91 (61)	220 (66)	0.31		65 (62)	0.90		21 (68)	0.54	

Data are median (95% CI) or n (%). Differences in medians were tested by Mann-Whitney U-test and in frequency by Fisher's Exact test.
†Log-transformed in main analysis. Values are geometric means (95% CI). Differences tested by analysis of variance adjusting for age, non-European ethnicity, first grade diabetes heredity, number of deliveries, time from delivery to follow up. ‡Also adjusting for BMI.
All comparisons performed vs. controls.
GDM, gestational diabetes mellitus; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test

Skillnader beroende på etniskt ursprung?

Table 2. Results of main analysis from OGTT for women after GDM, grouped according to ethnicity.

	European (n=362)	Non-European (n=94)	*p*	*p*‡	Arab (n=41)	*p*	*p*‡	Asian (n=43)	*p*	*p*‡
Age (years)	34 (33-34)	35 (33-36)	0.23		35 (31-38)	0.40		35 (32-37)	0.54	
BMI (kg/m2)	23.8 (23.0-24.0)	25.7 (24.5-27.7)	$9*10^{-5}$		28.0 (25.7-32.2)	$2*10^{-7}$		24.2 (23.4-25.5)	0.39	
Time to follow-up (days)	462 (442-483)	538 (504-563)	$9*10^{-5}$		545 (504-685)	$5*10^{-5}$		506 (460-568)	0.11	
HOMA-IR†	1.5 (1.3-1.6)	2.0 (1.7-2.3)	0.001	0.033	2.1 (1.6-2.7)	0.004	0.65	1.9 (1.5-2.3)	0.046	0.016
Available samples	255 (70)	69 (73)	0.61		28 (68)	0.86		32 (74)	0.72	
I/G30†	12.6 (11.6-13.7)	12.7 (10.8-15.1)	0.79	0.91	14.0 (10.8-18.1)	0.32	0.61	12.7 (9.7-16.5)	0.91	0.90
Available samples	240 (66)	63 (67)	1.0		27 (66)	1.0		29 (67)	1.0	
(I/G30)/HOMA-IR†	8.8 (7.9-9.7)	6.8 (5.5-8.4)	0.027	0.26	7.3 (5.3-10.0)	0.24	0.58	6.9 (5.1-9.4)	0.14	0.10
Available samples	235 (65)	60 (64)	0.9		25 (61)	0.61		29 (67)	0.87	

Data are median (95% CI) or n (%). Differences in medians were tested by Mann-Whitney U-test and in frequency by Fishers Exact test. †Log-transformed in main analysis. Values are geometric means (95% CI). Differences tested by analysis of variance adjusting for age and time from delivery to follow-up. ‡Also adjusting for BMI.
All comparisons performed vs. Europeans. In the Non-European group, subgroups of Arab and Asian women are included.
GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test

Skillnader inom den utom-europeiska gruppen?

Table 3. Logistic regression analyses of variables tested for associations with diabetes after GDM.

	Univariate		Multivariate					
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Age (years)	1.1 (1.0-1.2)	0.057	1.0 (0.9-1.1)	0.58	1.1 (0.9-1.2)	0.27	1.0 (0.9-1.1)	0.89
BMI (kg/m2)	1.2 (1.1-1.2)	$1*10^{-7}$	1.1 (1.1-1.2)	$5*10^{-5}$	1.1 (1.0-1.2)	0.003	1.1 (1.0-1.2)	0.003
Deliveries >3	2.6 (0.8-8.4)	0.11	1.3 (0.3-5.6)	0.68	1.7 (0.3-9.2)	0.55	1.7 (0.3-10.4)	0.59
First grade diabetes heredity	1.9 (0.9-4.2)	0.11	0.9 (0.3-2.5)	0.87	0.9 (0.3-2.8)	0.85	1.3 (0.4-4.2)	0.62
Non-European ethnicity	6.5 (2.9-14.5)	$6*10^{-6}$	5.1 (1.9-14.0)	0.001				
Arab ethnicity	7.9 (2.7-23.1)	$2*10^{-4}$			3.1 (0.8-12.3)	0.11		
Asian ethnicity	5.2 (1.8-15.0)	0.003					5.7 (1.5-21.5)	0.010

All variables were adjusted for time from delivery to follow-up. European ethnicity was used as reference.
Multivariate analyses were performed separately for each ethnic group.
CI, confidence interval; GDM, gestational diabetes mellitus; OR, odds ratio

Scandinavian Journal of Clinical & Laboratory Investigation, 2011; Early Online, 1–6

ORIGINAL ARTICLE

Evaluation of the relationship between capillary and venous plasma glucose concentrations obtained by the HemoCue Glucose 201+ system during an oral glucose tolerance test

CLAES IGNELL[1] & KERSTIN BERNTORP[2]

Table I. Capillary and venous plasma glucose concentrations during the oral glucose tolerance tests.

Time interval (min)	0	30	120
n	53	55	52
Capillary[a]	6.0 (0.7)	10.5 (1.7)	9.2 (1.9)
Venous[a]	5.8 (0.7)	8.7 (1.6)	7.7 (2.0)
Capillary-venous difference[a]	0.2 (0.3)	1.8 (1.0)	1.5 (0.7)
P	<0.001	<0.001	<0.001

[a]Plasma glucose concentration (mmol/L). Data shows mean (SD). Differences between means were tested by Student's paired *t*-test.

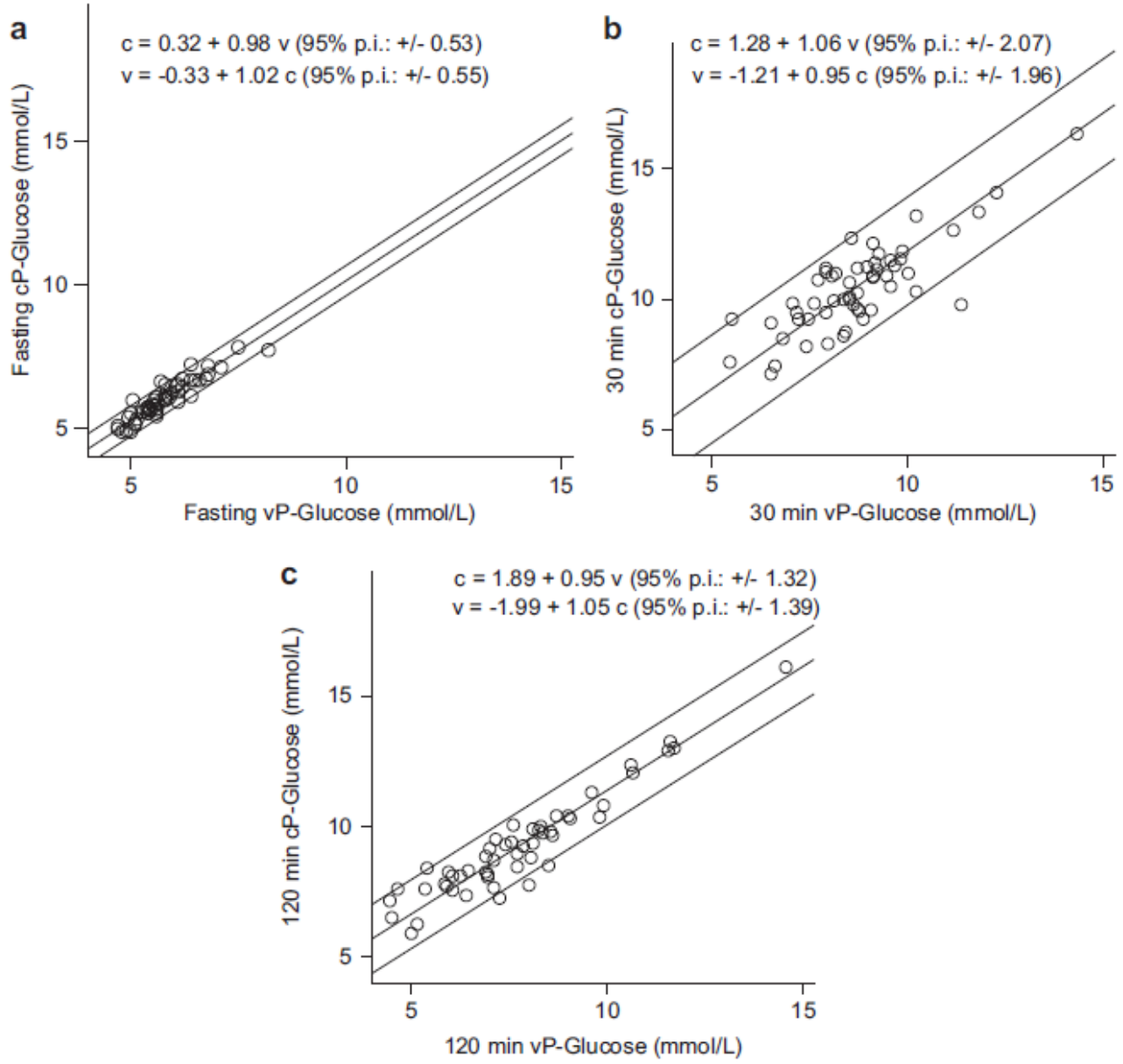


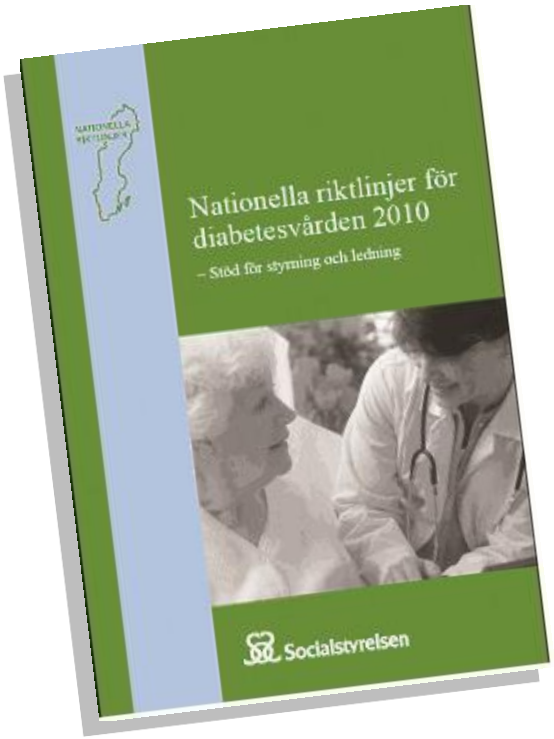
Figure 1. Scatter plots of Capillary (c) and venous (v) plasma glucose concentrations during the oral glucose tolerance test; panel (a) fasting ($n = 53$), panel (b) 30 min ($n = 55$), panel (c) 120 min ($n = 52$). Equations for the conversions are given. Conversion lines and 95% prediction intervals (p.i.) are drawn.

Konvertering av cut off gränser baserat på HAPO

Diabetes Care 2010;33:676-82.

	mmol/l	Kumulativ risk %	kP-Glukos mmol/l *enligt algoritm C. Ignell & K. Berntorp*
vP-Glukos 0 h	5,1	8,3	5,3
vP-Glukos 1 h	10,0	14	11,9
vP-Glukos 2 h	8,5	16,1	10,0

Graviditetsdiabetes – prevention av typ 2 diabetes



Rekommendation

Hälso- och sjukvården bör

Efter genomgången graviditetsdiabetes ge allmän rådgivning om livsstilsbehandling och systematiskt följa upp vikt, blodglukos och riskfaktorer för hjärt-kärlsjukdom (*prioritet 3*)