



Stand van zaken rond screenen naar zwangerschapsdiabetes: subanalyses van de BEDIP-N studie

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Endocrinologie
22-10-2022**



Overzicht

Vlaamse
consensus 2019
rond screening

Screening op
basis van
risicofactoren

Screening met
nuchtere
glycemie

Insuline
resistentie

Depressie

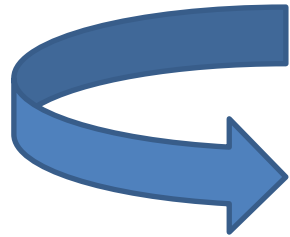
Gewichtstoename

Vetgehalte baby

Glucose
intolerantie
postpartum

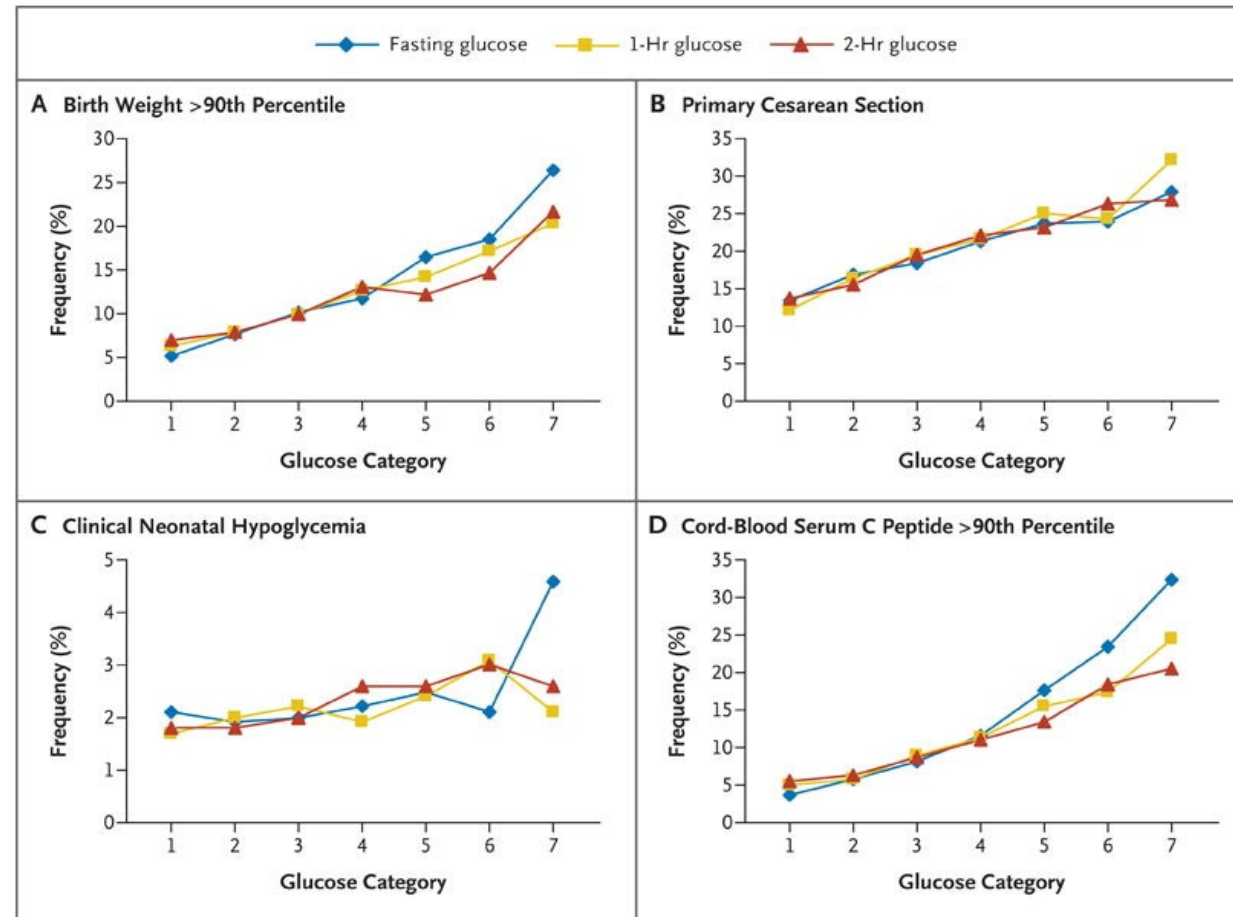
Auto-immuun
antistoffen

GDM wordt gedefinieerd als 'elke vorm van glucose intolerantie met ontstaan of eerste vaststelling tijdens de zwangerschap'

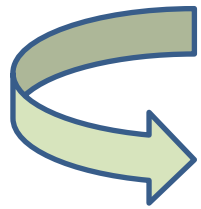


Nu pas diagnose voor GDM als een vooraf bestaande diabetes werd uitgesloten!

Frequency of Primary Outcomes across the Glucose Categories.



IADPSG: International Association of Diabetes & Pregnancy study groups (2010)



Sinds 2013 ook overgenomen door de WHO

International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnostic and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010;33:676-682.

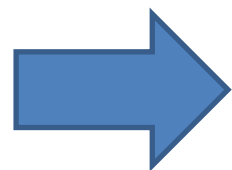
One step

Universele screening met 75g 2-u OGTT zonder glucose challenge test (GCT)

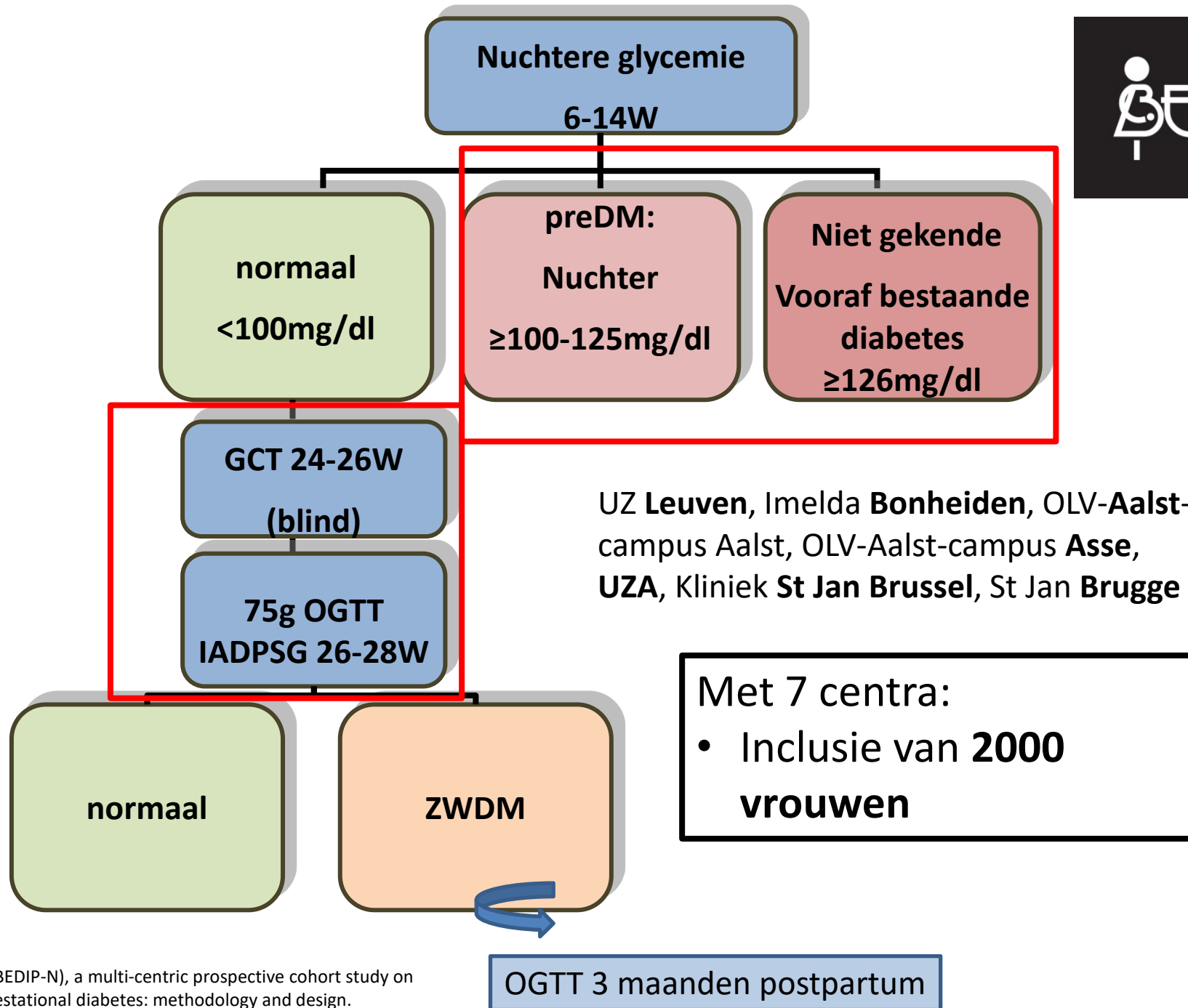
1 abnormale waarde is voldoende voor diagnose

Overview of the different diagnostic criteria for GDM.

	Carpenter & Coustan 3h-100g OGTT	IADPSG 2h-75g OGTT
fasting	≥ 95	≥ 92
1h	≥ 180	≥ 180
2h	≥ 155	≥ 153
3h	≥ 140	
Prevalence GDM	3-5%	16.1%

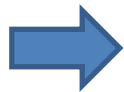
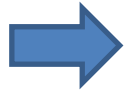


2 abnormal values (--) 1 abnormal value



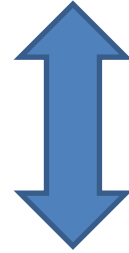
Prevalentie Zwangerschapsdiabetes

center	Number of OGTT's performed	Prevalence of GDM % (n)
Total	1841	12.5 (231)
UZ Leuven	699	16.0 (112)
Imelda Bonheiden	454	8.8 (40)
OLV Aalst	211	9.5 (20)
UZA	188	9.0 (17)
OLV Asse	133	14.3 (19)
ST Jan Brussel	107	18.7 (20)
St Jan Brugge	49	6.1 (3)



Twee-stap
screening met CC
criteria
ZWDM
prevalentie 3-5%

Prevalence GDM one-step: 12.5%



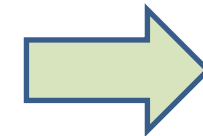
Two-step with GCT \geq 140mg/dl : 7.5%

\geq 135mg/dl : 8.3%

\geq 130mg/dl : 9.1%

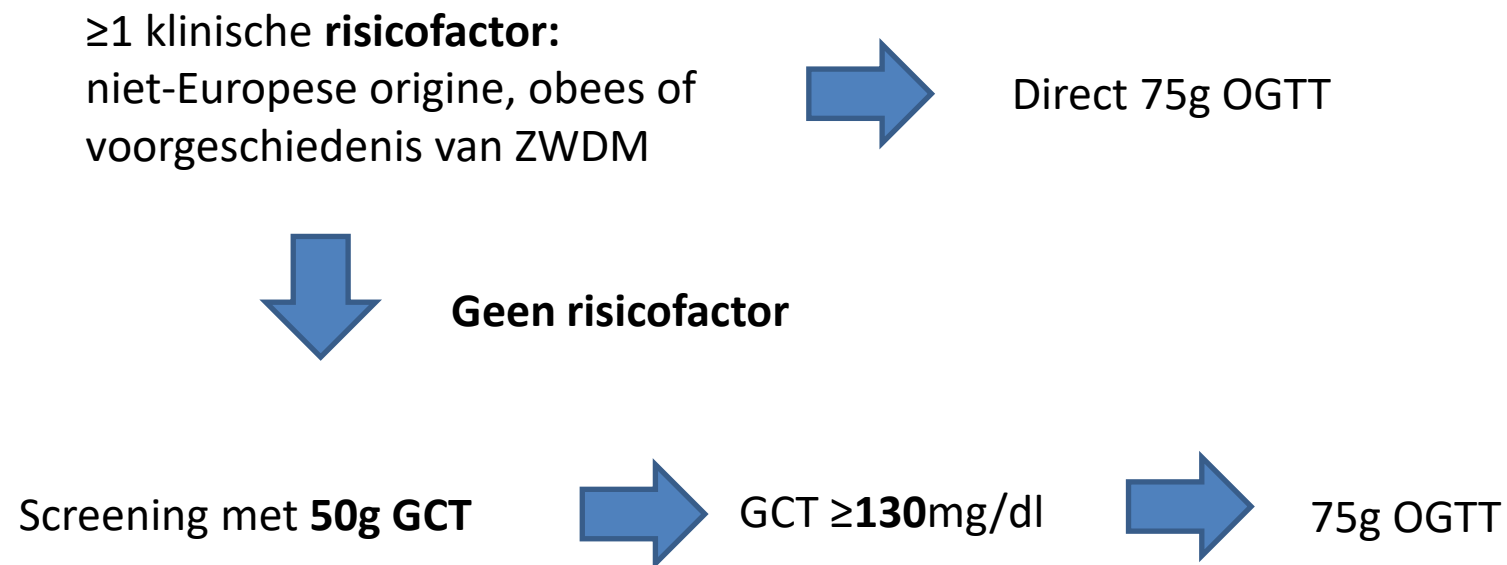
\geq 125mg/dl : 9.8%

\geq 120mg/dl : 10.3%



65% van
OGTT's
vermeden

Aangepaste twee-staps screening: combinatie van screening op basis van risicofactoren en de GCT



Prevalentie van ZWDM stijgt van 9.1% met klassieke screening met GCT naar 10.4% en bij **52% wordt OGTT vermeden**

Hoe worden de testen verdragen en wat verkiezen de deelnemers zelf?



Tolerance of GCT and OGTT

	GCT, % (n)	OGTT, % (n)
Any complaint	20.6% (377)	43.4% (784)
• Bad taste	• 27.3% (103)	• 29.6% (232)
• Nausea	• 45.1% (170)	• 55.4% (434)
• Vomiting	• 2.4% (9)	• 4.5% (35)
• Dizziness or feeling of fainting	• 38.2% (144)	• 48.5% (380)
• Abdominal pain	• 2.6% (10)	• 5.0% (39)

Preference of the participants

41.6% (750) felt it difficult to be fasting

	Preference GCT Two-step	Preference OGTT One-step	No Preference
test: GCT vs. OGTT	54.9% (987)	6.2% (112)	38.9% (700)
Screening strategy: Two-step vs. one-step	46.3% (833)	26.2% (471)	27.5% (494)



Lower metabolic risk profile
More discomfort of the OGTT



Obese, history GDM

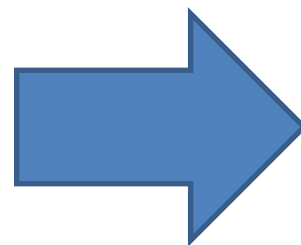
Consensusmeeting on 22-1-2019



Vlaamse
Beroepsorganisatie
van Vroedvrouwen



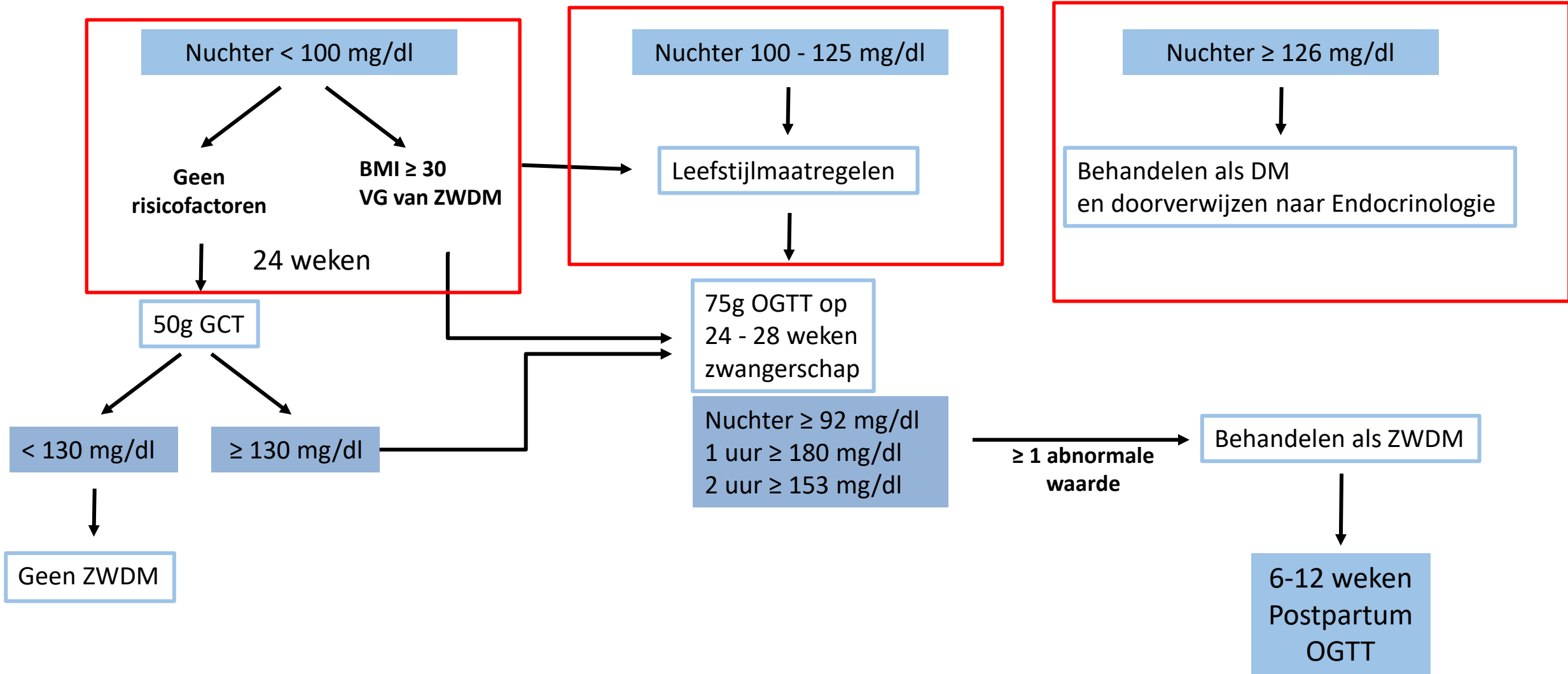
BEROEPSVERENIGING VLAAMSE DIABETESVERPLEEGKUNDIGEN



Vlaamse consensus van 2019

Vlaamse consensus 2019

Eerste prenatale contact: universele screening



Clinical Study

K Benhalima and others

Selective screening for GDM

180:6

353–363

2019

Risk factor screening for gestational diabetes mellitus based on the 2013 WHO criteria

Katrien Benhalima¹, Paul Van Crombrugge², Carolien Moyson¹, Johan Verhaeghe³, Sofie Vandeginste⁴, Hilde Verlaenen⁴, Chris Vercammen⁵, Toon Maes⁵, Els Dufraimont⁶, Christophe De Block⁷, Yves Jacquemyn⁸, Farah Mekahli⁹, Katrien De Clippel¹⁰, Annick Van Den Bruel¹¹, Anne Loccufier¹², Annouschka Laenen¹³, Caro Minschart¹, Roland Devlieger³ and Chantal Mathieu¹

EJE European Journal
of Endocrinology

CLINICAL & TRANSLATIONAL ENDOCRINOLOGY FROM AROUND THE GLOBE

The sensitivity and specificity of selective screening based on age and BMI with and without the addition of other clinical risk factors

The max. Youden index was seen for **maternal age ≥ 30** : sensitivity of 72.7% and specificity of 40.7% for **BMI at ≥ 25** : sensitivity of 48.4% and specificity of 67.5%


Risk factors	Positive rate % (n)	prevalence GDM % (n)	Number of GDM without risk factors (missing rate), % (n)	Sensitivity (95% CI), % n/N	Specificity (95% CI), % n/N
Age ≥ 30; BMI ≥ 25	69.9 (1288)	10.2 (188)	18.6 (43)	81.4 (75.8-86.2) 188/231	31.8 (29.5-34.1) 512/1612
Age ≥ 30; BMI ≥ 25; first degree with DM	69.9 (1288)	10.2 (188)	18.6 (43)	81.4 (75.8-86.2) 188/231	31.8 (29.5-34.1) 512/1612
Age ≥ 30; BMI ≥ 25; prior GDM	70.5 (1299)	10.5 (193)	16.4 (38)	83.5 (78.1-88.1) 193/231	31.4 (29.1-33.7) 506/1612
Age ≥ 30; BMI ≥ 25; first degree with DM; prior GDM	70.5 (1299)	10.5 (193)	16.4 (38)	83.5 (78.1-88.1) 193/231	31.4 (29.1-33.7) 506/1612
Age ≥ 30; BMI ≥ 25; first degree with DM; prior GDM; non- Caucasian; macrosomic baby ≥ 4.5Kg	70.5% (1300)	10.5% (193)	16.4% (38)	83.5 (78.1-88.1) 193/231	31.4 (29.1-33.7) 506/1612



ORIGINAL ARTICLE



Fasting plasma glucose level to guide the need for an OGTT to screen for gestational diabetes mellitus

Kaat Beunen¹  · Astrid Neys² · Paul Van Crombrugge³ · Carolien Moyson¹ · Johan Verhaeghe⁴ · Sofie Vandeginste⁵ · Hilde Verlaenen⁵ · Chris Vercammen⁶ · Toon Maes⁶ · Els Dufraimont⁷ · Nele Roggen⁷ · Christophe De Block⁸ · Yves Jacquemyn⁹ · Farah Mekahli¹⁰ · Katrien De Clippel¹¹ · Annick Van Den Bruel¹² · Anne Loccufier¹³ · Annouschka Laenen¹⁴ · Roland Devlieger⁴ · Chantal Mathieu¹ · Katrien Benhalima¹

FPG LEVEL WITH BEST TRADE-OFF

- A range of FPG cut-off values was evaluated: 70→91 mg/dL

Threshold FPG at the time of the OGTT	Number of OGTT needed (n)	Prevalence of GDM (n)	Number missed with GDM (n)	Sensitivity, (95% CI), n/N	NPV, (95% CI)	LR-, (95% CI)
78 mg/dL	47.8% (958)	9.3% (187)	19.0% (44)	81.0% (75.4-85.5) 187/231	97.3% (96.5- 98.0)	19.0% (14.6- 24.8)

FPG as a preliminary screening tool:

- Women with FPG <78 mg/dl: classified as normal (not OGTT needed)
- Women with FPG ≥ 92 mg/dl can be directly diagnosed as GDM
- Women with FPG between 78-91mg/dl: need an OGTT

Women with FPG <78 mg/dL had a better metabolic profile (lower BMI, less insulin resistance) and in NGT women also less fetal overgrowth.



Check for
updates

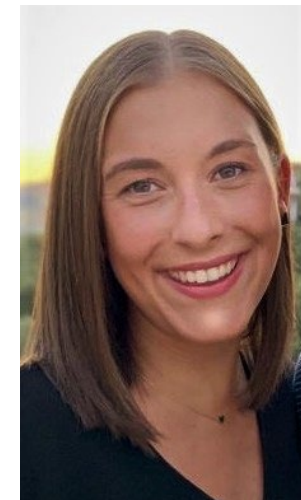
Characteristics and pregnancy outcomes across gestational diabetes mellitus subtypes based on insulin resistance

Katrien Benhalima¹ · Paul Van Crombrugge² · Carolien Moyson¹ · Johan Verhaeghe³ · Sofie Vandeginste⁴ · Hilde Verlaenen⁴ · Chris Vercammen⁵ · Toon Maes⁵ · Els Dufraimont⁶ · Christophe De Block⁷ · Yves Jacquemyn⁸ · Farah Mekahli⁹ · Katrien De Clippel¹⁰ · Annick Van Den Bruel¹¹ · Anne Loccufier¹² · Annouschka Laenen¹³ · Caro Minschart¹ · Roland Devlieger³ · Chantal Mathieu¹

	Model 1 OR (95% CI), p-value	Model 2 OR (95% CI), p-value	Model 3 OR (95% CI), p-value	Model 4 OR (95% CI), p-value	Model 5 OR (95% CI), p-value	Model 6 OR (95% CI), p-value
Labor inductions	1.74 (1.26-2.41), P<0.001	1.71 (1.19-2.45), P=0.004	1.61 (0.99-2.62), P=0.056	1.37 (0.81-2.32), P=2.334	1.56 (0.90-2.70), P=0.114	1.51 (0.98-2.32), P=0.107
Total cesarean sections	1.67 (1.18-2.37), P=0.004	1.54 (1.04-2.29), P=0.031	1.74 (0.10-3.05), P=0.052	1.68 (0.91-3.10), P=0.094	1.43 (0.75-2.71), P=0.277	1.36 (0.86-2.17), P=0.190
Emergency Cesarean sections	1.77 (1.14-2.75), P=0.010	1.72 (1.03-2.86), P=0.037	1.99 (0.88-4.50), P=0.098	1.85 (0.75-4.55), P=0.183	1.50 (0.57-3.96), P=0.415	1.57(0.86-2.90), P=0.143
Preterm delivery	1.89 (1.05-3.38), P=0.033	2.19 (1.16-4.12), P=0.015	3.04 (3.00-3.08), P<0.001	6.66 (2.10-21.16), P<0.001	3.44 (3.39-3.49), P<0.001	2.41 (1.08-5.38), P=0.031
Neonatal hypoglycaemia	4.99 (2.78-8.95), P<0.001	3.78 (1.89-7.54), P<0.001	6.60 (6.49-6.71), P<0.001	7.05 (6.93-7.17), P<0.001	8.91 (8.75-9.07), P<0.001	4.86 (2.04-11.53), P<0.001
NICU admission	1.94 (1.25-3.03), P=0.003	1.89 (1.15-3.11), P=0.012	2.40 (1.12-5.12), P=0.024	2.68 (1.18-6.07), P=0.019	2.41 (1.03-5.64), P=0.043	1.64 (0.88-3.06), P=0.116

GDM met hoge insuline resistentie

- slechter metabool profiel (sterkere graad van hyperglycemie, BMI, lipiden en BD)
- Hoger risico op zwangerschapsverwikkelingen, ook na correctie voor BMI, graad van hyperglycemie, lipiden en GWG



Clinical Research Article

Antenatal Depression and Risk of Gestational Diabetes, Adverse Pregnancy Outcomes, and Postpartum Quality of Life

Caro Minschart,¹ Kyara De Weerd, ² Astrid Elegeert,² Paul Van Crombrugge,³ Carolien Moyson,¹ Johan Verhaeghe,⁴ Sofie Vandeginste,⁵ Hilde Verlaenen,⁵ Chris Vercammen,⁶ Toon Maes,⁶ Els Dufraimont,⁷ Christophe De Block,⁸ Yves Jacquemyn,⁹ Farah Mekahli,¹⁰ Katrien De Clippel,¹¹ Annick Van Den Bruel,¹² Anne Loccufier,¹³ Annouschka Laenen,¹⁴ Roland Devlieger,⁴ Chantal Mathieu,¹ and Katrien Benhalima¹

METHODS

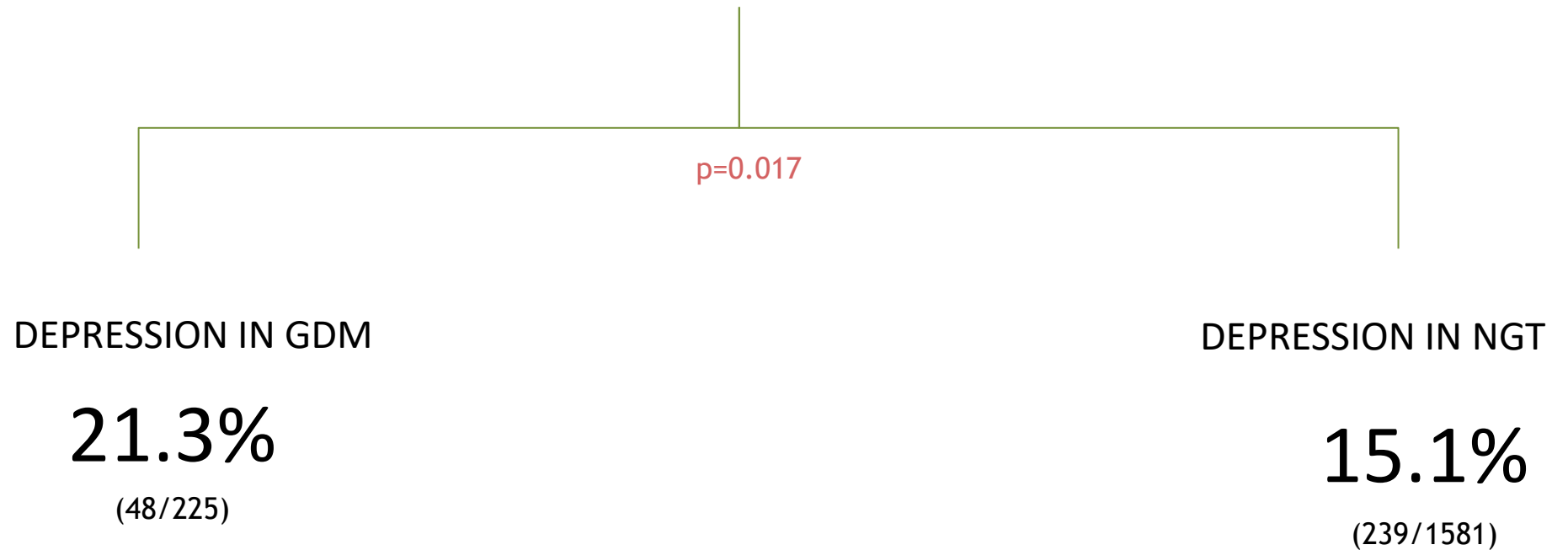
QUESTIONNAIRES

before diagnosis of GDM
was communicated



	VISIT 1	VISIT 2B: OGTT	VISIT 3: postpartum
questionnaire on general habits & socio-economic factors.	x		
questionnaire on lifestyle	x	x	x
IPAQ questionnaire on physical activity		x	x
CES-D questionnaire on depression		x	x
questionnaire on breastfeeding			x
questionnaire on general health			x

DEPRESSION IN WOMEN WITH GDM VERSUS NGT



RESULTS

1. GDM WITH VS. WITHOUT DEPRESSION - GENERAL & PREGNANCY CHARACTERISTICS

GDM SUBGROUP	depression N= 48 (21.3%)	no depression N= 177 (78.7%)	p - value
age (years)	31.4 ± 5.5	32.3 ± 4.40	0.205
% ethnic minority background	29.2 (14)	15.4 (27)	0.003
% higher degree diploma	63.7 (28)	73.1 (125)	0.315
% smoking before pregnancy	37.5 (18)	35.4 (62)	0.791
% smoking during pregnancy	12.5 (6)	4.0 (7)	0.025
BMI at first prenatal visit (Kg/m ²)	27.9 ± 5.3	26.3 ± 5.3	0.048
% overweight at first prenatal visit	31.2 (15)	29.5 (52)	0.167
% obese at first prenatal visit	31.2 (15)	22.1 (39)	0.167
HOMA-IR at 24 weeks	21.3 (15.5-29.9)	16.7 (11.2-26.2)	0.055
% IPAQ category 'low'	25.5 (12)	18.0 (31)	0.361
diet score on lifestyle questionnaire	1.0 (-2.0-3.0)	2.0 (0.0-4.0)	0.027

RESULTS

1. GDM WITH VS. WITHOUT DEPRESSION - POSTPARTUM OUTCOMES

GDM SUBGROUP	depression N= 48 (21.3%)	no depression N= 177 (78.7%)	p - value
% present at OGTT	68.7 (33)	87.6 (155)	0.002
% glucose intolerance	18.2 (6)	18.7 (29)	0.944
% breastfeeding	85.3 (29)	82.1 (124)	0.658
% IPAQ category 'low'	6.9 (2)	12.3 (18)	0.304
% clinical depression (≥ 16 on CES-D)	37.1 (13)	12.4 (19)	<.001
SF-36 scores:			
physical functioning	80.0 (65.0-95.0)	90.0 (80.0-100.0)	0.002
role physical	75.0 (56.2-100.0)	87.5 (68.7-100.0)	0.083
role emotional	83.3 (50.0-100.0)	100.0 (75.0-100.0)	0.038
energy	50.0 (43.7-68.7)	64.6 (56.2-75.0)	<.001
emotional well-being	70.0 (60.0-75.0)	70.0 (65.0-75.0)	0.017
social functioning	87.5 (62.5-100.0)	100.0 (75.0-100.0)	0.003
pain	80.0 (67.5-100.0)	90.0 (77.5-100.0)	0.039
general health	65.0 (45.0-80.0)	75.0 (65.0-85.0)	0.007
health transition	50.0 (25.0-75.0)	50.0 (50.0-50.0)	0.369

Gewichtstoename in de zwangerschap bij zwangerschapsdiabetes

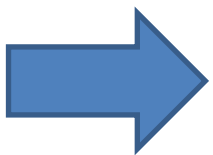


	BMI Kg/m²	Gewicht in Kg
Ondergewicht	< 18,5	12,5 - 18
Normaal gewicht	18,5 - 24,9	11,5 - 16
Overgewicht	25 - 29,9	7 -11,5
Obees	> 30	5-9

Low gestational weight gain in women with gestational diabetes is safe with better metabolic profile postpartum



- **52.4%** van GDM: **GWG lager dan de aanbevelingen** en 16% excessieve GWG
- **Groep met lage GWG:**
 - geen verhoogd risico op te kleine baby's of vroeggeboorte
 - Beter metabool profiel postpartum (minder vaak overgewicht/obesitas en minder vaak gewichtsretentie)
- **Groep met excessieve GWG:**
 - Hoger risico op neonatale hypoglycemia
 - Postpartum vaker overgewicht/obesitas, hogere BD, insuline resistentie, minder vaak borstvoeding en vaker meer gewichtsretentie



Striktere richtlijnen rond GWG bij GDM aangewezen?



Predictors of neonatal adiposity and associations by fetal sex in women with gestational diabetes mellitus and normal glucose-tolerant women

Katrien Benhalima¹ · Anaïs De Landtsheer¹ · Paul Van Crombrugge² · Carolien Moyson¹ · Johan Verhaeghe³ · Hilde Verlaenen⁴ · Chris Vercammen⁵ · Toon Maes⁵ · Els Dufraimont⁶ · Christophe De Block⁷ · Yves Jacquemyn⁸ · Annouschka Laenen⁹ · Roland Devlieger³ · Caro Minschart¹ · Chantal Mathieu¹

Measurements of skinfold thickness



2. Schouderblad

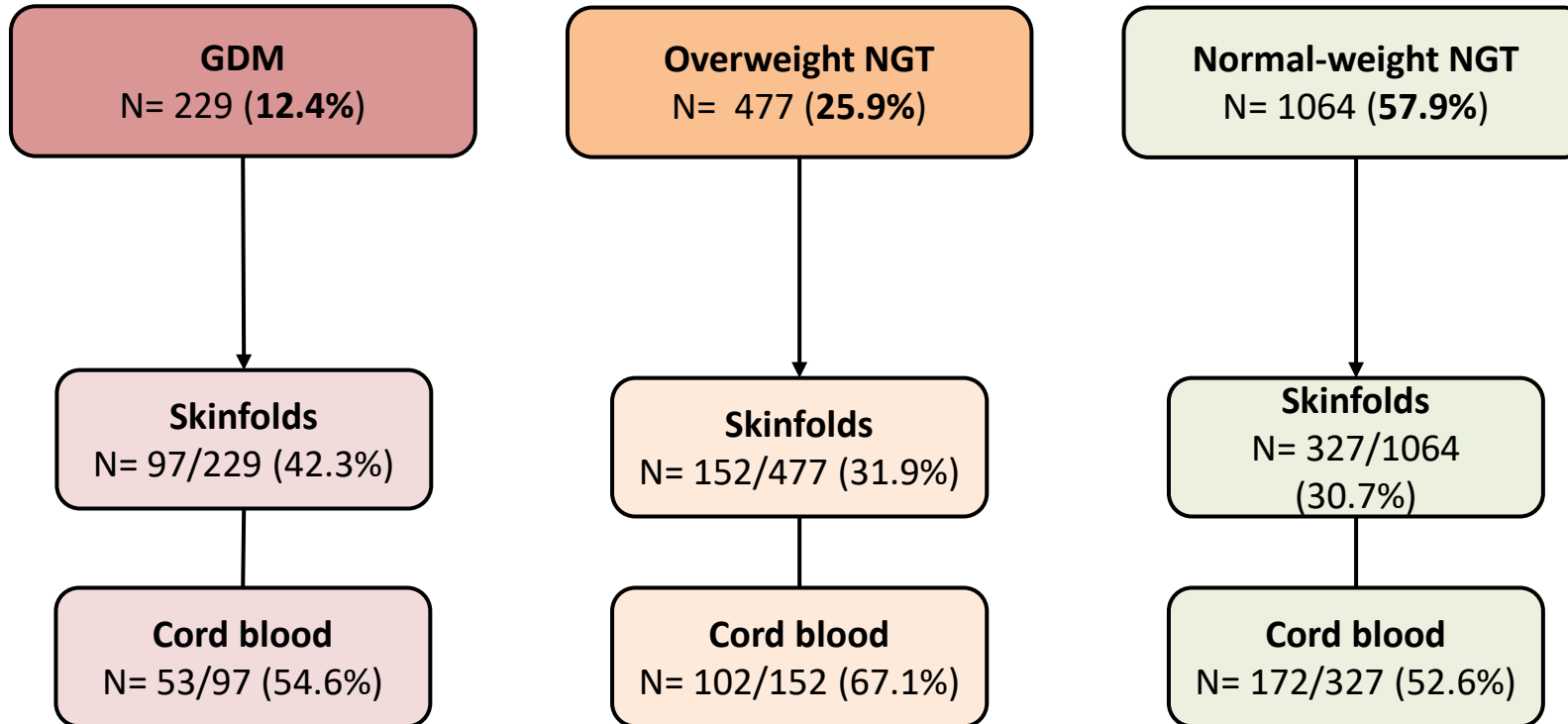
3. Flank



1. Bovenarm



1838 women received universal screening for GDM between 24-28 weeks



	GDM	NGT overweight	NGT normal-weight	p-value	p-value	p-value
	N = 97	N =152	N =327			
	Group 1	Group 2	Group 3	1 vs. 2	1 vs. 3	2 vs. 3
Neonatal outcomes						
Gestational age at delivery (weeks)	39.1 ± 1.2	39.4 ± 1.2	39.3 ± 1.3	0.048	0.085	0.599
% excessive weight gain	13.6 (11)	55.3 (73)	19.4 (54)	<.001	0.229	<.001
Birth weight (g)	3408.7 ± 424.7	3549.6 ± 430.6	3349.3 ± 411.5	0.001	0.419	<.001
Length (cm)	50.4 ± 1.8	51.1 ± 2.1	50.4 ± 2.2	0.005	0.789	0.001
Head circumference (cm)	34.6 ± 1.4	34.9 ± 1.4	34.4 ± 1.4	0.212	0.245	0.003
% Macrosomia >4Kg	8.2 (8)	12.5 (19)	5.8 (19)	0.293	0.388	0.012
LGA	16.5 (16)	17.1 (26)	8.6 (28)	0.900	0.024	0.006
Ponderal index (cm³)	6769.9 ± 693.2	6934.7 ± 691.5	6631.6 ± 674.6	0.014	0.165	<.001
Sum of skinfolds (mm)	13.9 ± 2.9	14.3 ± 2.6	13.2 ± 2.6	0.191	0.067	<.001
% Skinfolds >90th percentile	12.4 (12)	11.8 (18)	7.6 (25)	0.900	0.148	0.135
Neonatal Fat mass (g)	1333.0 ± 166.8	1386.0 ± 168.6	1307.3 ± 160.9	0.002	0.356	<.001
% >90th percentile neonatal fat mass	9.6 (9)	15.2 (23)	7.1 (23)	0.201	0.422	0.005
Cord blood						
Cord blood leptin (µg/l)	11.5 (6.4-18.2)	12.0 (8.3-20.0)	10.1 (5.0-18.0)	0.331	0.747	0.075
Cord blood C-peptide (nmol/l)	0.4 (0.3-0.5)	0.4 (0.1-1.3)	0.3 (0.3-0.4)	0.979	0.174	0.051
Cord blood HDL (mmol/l)	0.7 (0.7-1.0)	0.7 (0.6-0.9)	0.7 (0.6-0.9)	0.399	0.349	0.994
Cord blood TG (mmol/l)	0.4 (0.3-0.5)	0.3 (0.2-0.5)	0.4 (0.3-0.5)	0.266	0.963	0.080

GDM groep: werd behandeld

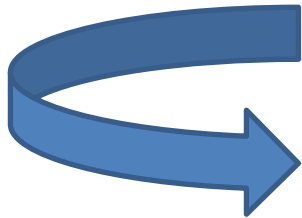
Minder excessieve gewichtstoename in de zwangerschap

Gelijkaardig % vetgehalte baby in vergelijking met groep zonder GDM en normaal gewicht

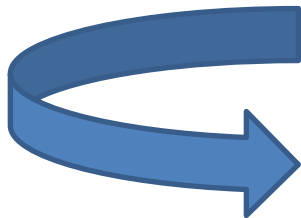
Zwangeren met overgewicht zonder GDM

- Geen behandeling gekregen
- Vaker te veel gewichtstoename in de zwangerschap
- Overgewicht/obesitas belangrijke onafhankelijke risicofactor voor risico te zware baby and verhoogd vet%

GDM: increased risks on the long term



**30-50% will develop diabetes within 10 years after the index pregnancy
Risk 7x higher compared to women without GDM**



Also increased risk for cardiovascular complications at a younger age






Journal of
Clinical Medicine



Article

Prediction of Glucose Intolerance in Early Postpartum in Women with Gestational Diabetes Mellitus Based on the 2013 WHO Criteria

Katrien Benhalima ^{1,*} , Paul Van Crombrugge ², Carolien Moyson ¹, Johan Verhaeghe ³, Sofie Vandeginste ⁴, Hilde Verlaenen ⁴, Chris Vercammen ⁵, Toon Maes ⁵, Els Dufraimont ⁶, Christophe De Block ⁷, Yves Jacquemyn ⁸, Farah Mekahli ⁹, Katrien De Clippel ¹⁰, Annick Van Den Bruel ¹¹, Anne Loccufier ¹², Annouschka Laenen ¹³, Caro Minschart ¹ , Roland Devlieger ³  and Chantal Mathieu ¹

% glucose intolerance postpartum in the BEDIP study

83.1% attended the postpartum OGTT:

None with Diabetes

18.7% (35) prediabetes:

➤ IFG: 37.1% (13)

➤ IGT: 54.3% (19)

➤ IFG + IGT: 8.6% (3)

OGTT is still needed in early postpartum
Fasting glycaemia and/or HbA1c not
sensitive enough

Plasma glycated CD59 predicts postpartum glucose intolerance after gestational diabetes

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EJE European Journal
of Endocrinology

CLINICAL & TRANSLATIONAL ENDOCRINOLOGY FROM AROUND THE GLOBE

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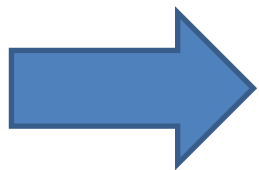
SPECIALTY SECTION
This article was submitted to
Clinical Diabetes,
a section of the journal
Frontiers in Endocrinology

Type 1 diabetes-related autoimmune antibodies in women with gestational diabetes mellitus and the long-term risk for glucose intolerance

Kaat Beunen ^{1*}, Lies Vercauter ², Paul Van Crombrugge ³, Carolien Moyson ¹, Johan Verhaeghe ⁴, Sofie Vandeginste ⁵, Hilde Verlaenen ⁵, Chris Vercammen ⁶, Toon Maes ⁶, Els Dufraimont ⁷, Nele Roggen ⁷, Christophe De Block ⁸, Yves Jacquemyn ⁹, Farah Mekahli ¹⁰, Katrien De Clippel ¹¹, Annick Van Den Bruel ¹², Anne Loccufier ¹³, Annouschka Laenen ¹⁴, Roland Devlieger ⁴, Chantal Mathieu ¹ and Katrien Benhalima ¹



- 8% antistoffen in de zwangerschap
- Vaak borderline gestegen, negatief postpartum
- Indien duidelijk gestegen, wel vaak stijging postpartum
- Enkel twee vrouwen met glucose intolerantie (waarvan 1 met T1D) en nog antistoffen na 4,6 jaar postpartum



Geen systematische screening naar antistoffen bij GDM in de zwangerschap aangewezen

Anderere studies



Melindaproject.be



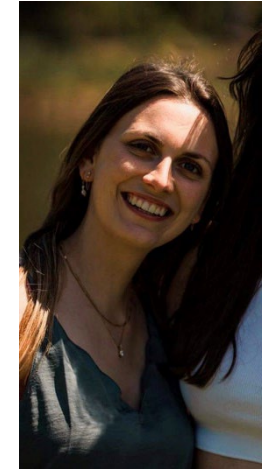
MELINDA

Mobile-based lifestyle intervention to promote a healthy lifestyle in women with recent GDM

UZ Leuven, UZA, Kortrijk, OLV Aalst, Klina, GZA, Bonheiden

Mobile-based lifestyle intervention in women with glucose intolerance after gestational diabetes mellitus (MELINDA), a multicenter randomized controlled trial: methodology and design. Caro Minschart, Toon Maes, Christophe De Block, Inge Van Pottelbergh, Nele Myngheer, Pascal Abrams, Wouter Vinck, Liesbeth Leuridan, Chantal Mathieu, Jaak Billen, Christophe Matthys, Bab Weyns, Annouschka Laenen, Annick Bogaerts, Katrien Benhalima. J Clin Med. 2020 Aug 13;9(8):E2635. doi: 10.3390/jcm9082635

SERENA study: Semaglutide for the treatment of glucose intolerance in women with prior gestational diabetes: a double blind RCT





2014-2018



Start 2021

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Take home message

- Vlaamse consensus: aangepast twee-staps screeningsstrategie met GCT ≥ 130 mg/dl
- GDM met hoge insuline resistentie: hoog risico groep
- Depressie zeer frequent, impact op zwangerschap en postpartum
- Bij GDM, GWG lager dan aanbevolen veilig en beter metabool profiel postpartum
- Overgewicht zonder GDM: hoog risico voor neonatale adipositas
- OGTT nodig vroeg postpartum, alternatieve biomarkers
- Geen systematische screening naar antistoffen nodig bij GDM



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