

Glucosemetabolisme & Schildklierfunctie tijdens zwangerschap

Johannes Ruige

Diabetologie & Endocrinologie

VITAZ



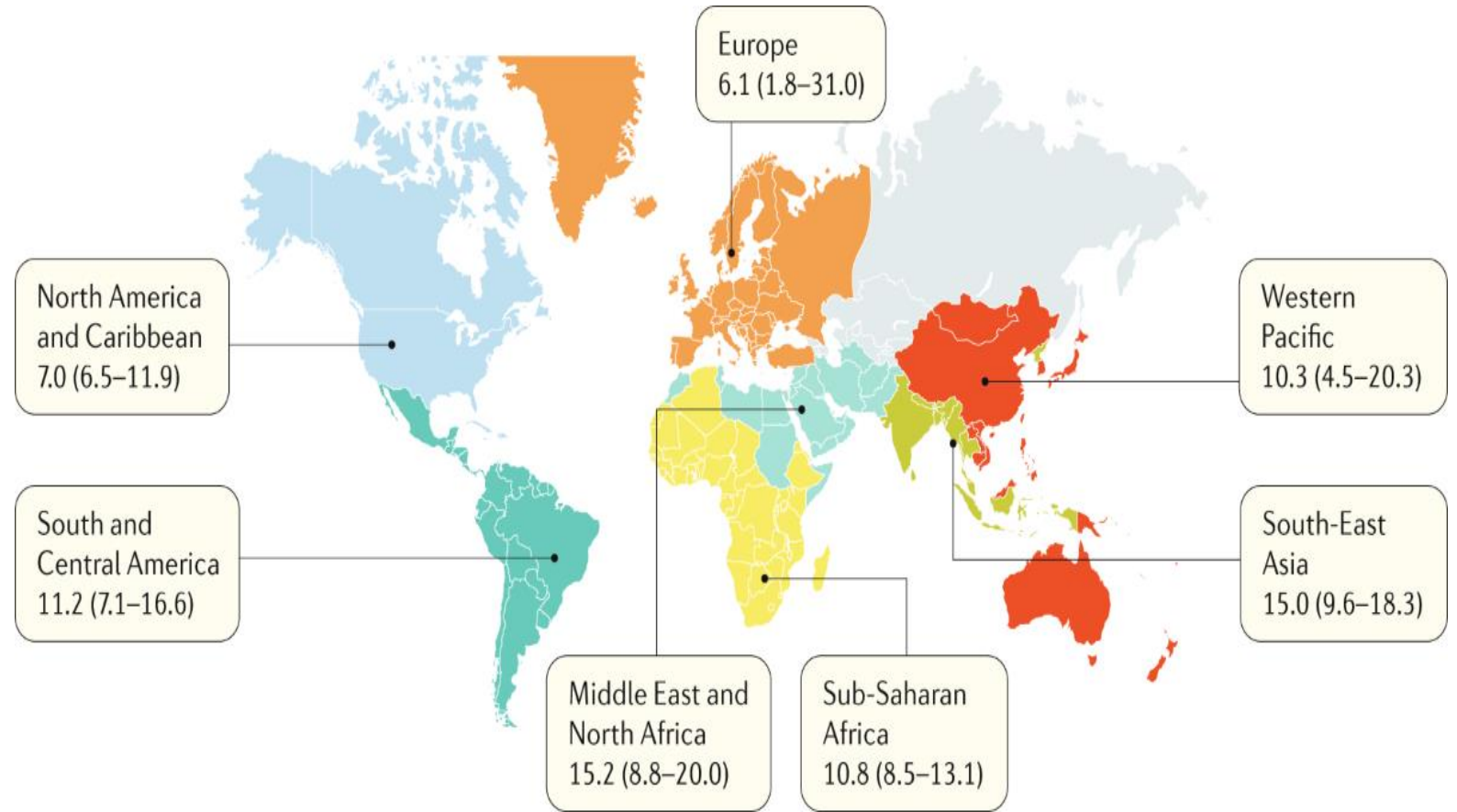
Introductie

De zogenaamde Barker-hypothese (hypothese van de foetale oorsprong van ziekten op volwassen leeftijd) stelt dat ondervoeding van de foetus tijdens kritische perioden van groei en ontwikkeling leidt tot permanente veranderingen in de structuur en fysiologie van het lichaam van de foetus, en dat deze veranderingen op hun beurt weer kunnen leiden tot coronaire hartziekten, hypertensie, hypercholesterolemie en diabetes

Introductie

- Zwangerschapsdiabetes : diabetes gediagnosticeerd tijdens zwangerschap, waarbij overte diabetes uitgesloten werd in het begin vd zwangerschap.

- Prevalentie 14%
- Neemt toe...

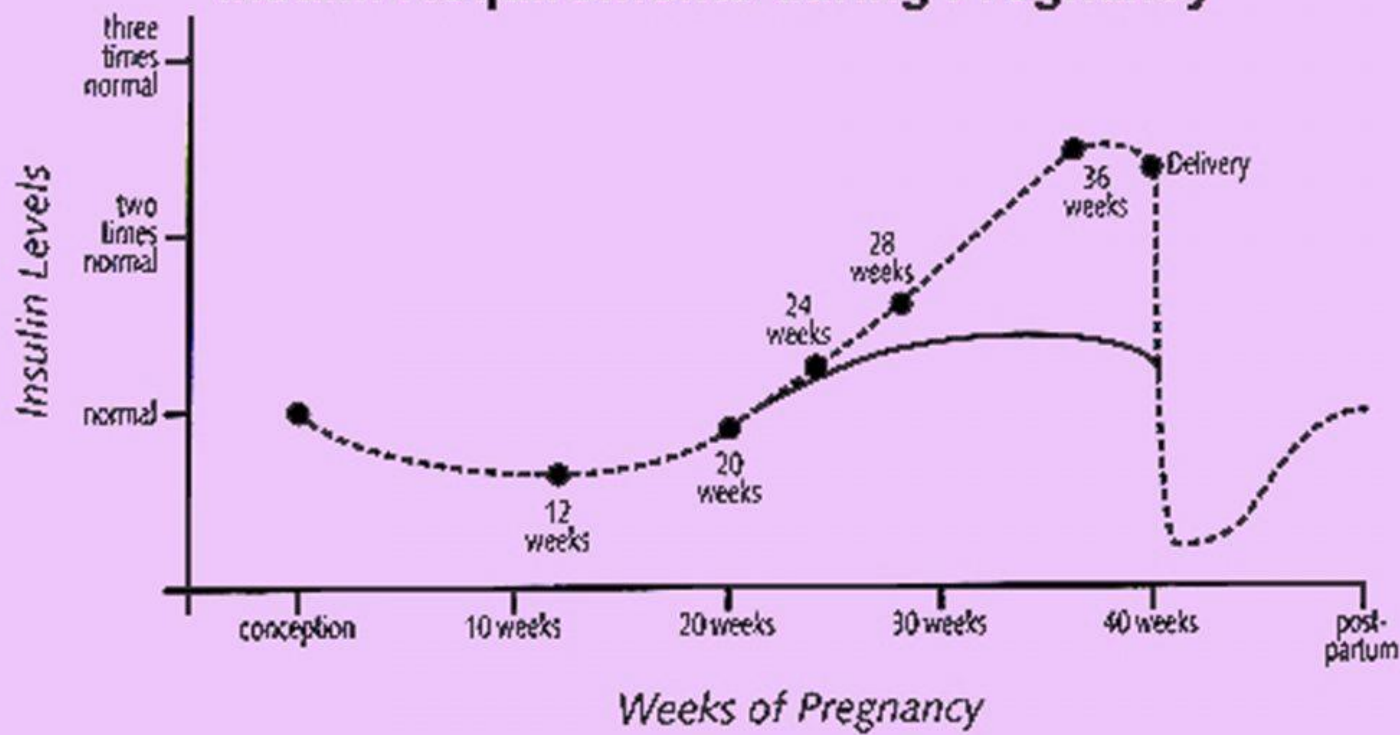


Fysiologische veranderingen

- Cardiovasculair
 - Toename bloedvolume, hartminuutvolume, hartritme
 - Verlaagde bloeddruk
- Nefrogeen
 - Toename GFR met 50%
 - Verhoogde diurese
- Hematologisch
 - Toename plasmavolume
 - Stijging rode bloedcellen
- Respiratoir
 - Toename zuurstofextractie
 - Minder longcapaciteit
- Metabole veranderingen

Healthy Baby and Beyond

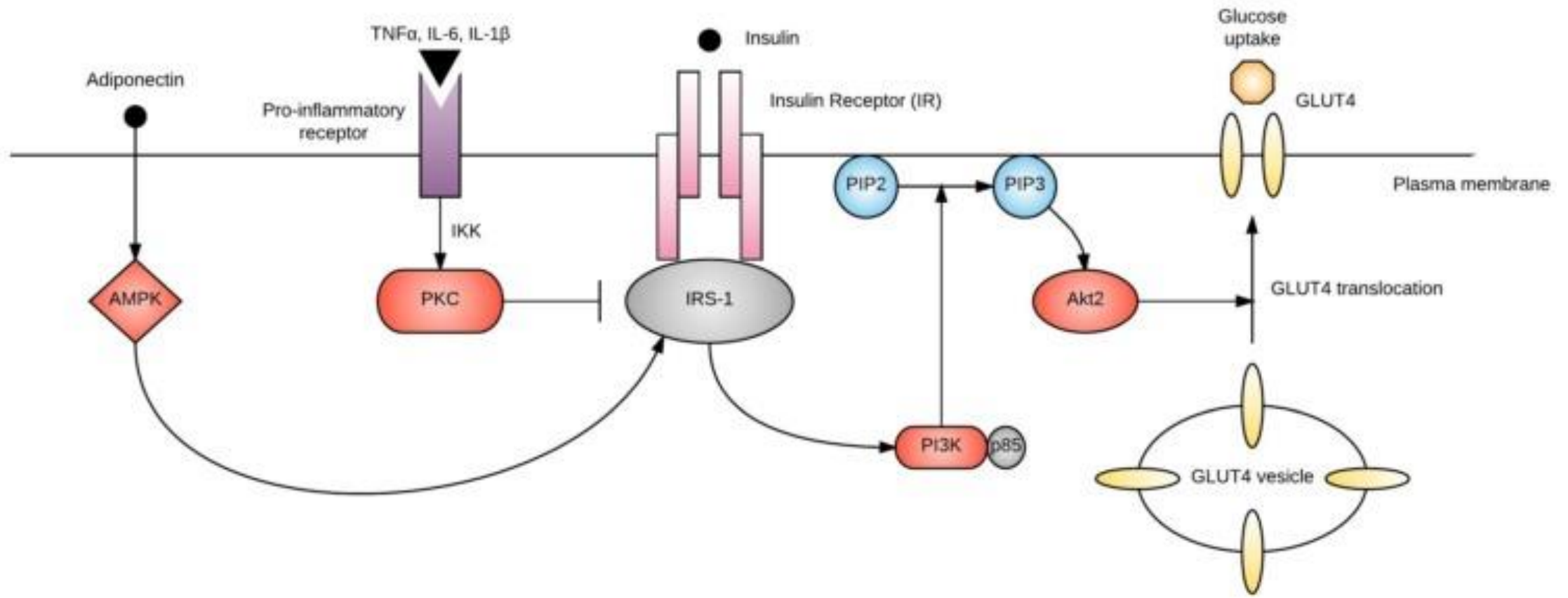
Gestational Diabetes Insulin Requirements during Pregnancy



----- = Usual insulin production during pregnancy

———— = Shortage of insulin production during pregnancy with gestational diabetes

Insulineresistentie



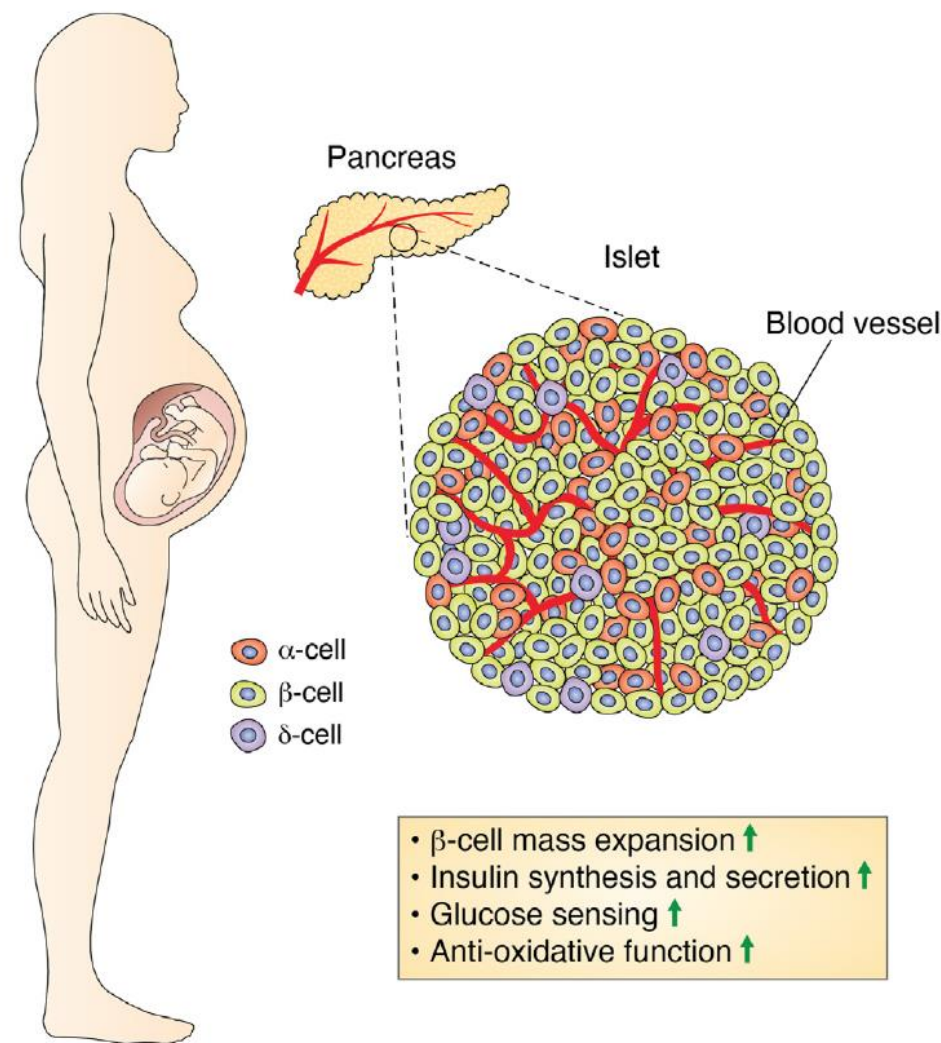


Figure 1. Gestational β -cell compensation. Pregnancy begets maternal β -cell compensation, an adaptive mechanism by which β -cells evolve to release more insulin into the blood. Gestational β -cell compensation culminates in β -cell mass expansion, increased insulin synthesis and secretion, enhanced glucose sensing, and augmented antioxidative function in maternal islets. Gestational β -cell compensation is instrumental for overcoming maternal insulin resistance to maintain normal glucose homeostasis in women during pregnancy.

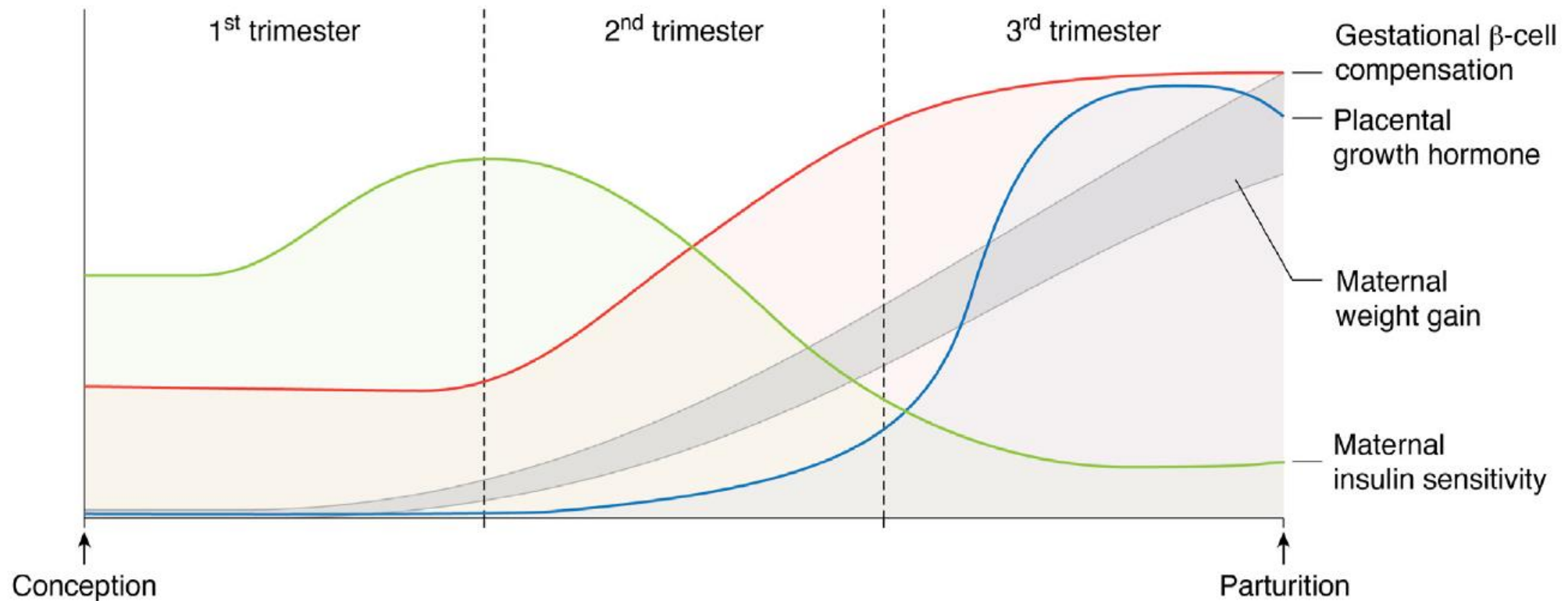


Figure 2. β -cell compensation for maternal insulin resistance during pregnancy. Pregnancy is accompanied by enhanced insulin sensitivity in the first trimester, followed by a progressive decline in maternal insulin sensitivity, resulting in overt insulin resistance in the third trimester. This effect is due to a combination of maternal weight gain and placental growth hormone, whose paracrine action contributes to insulin resistance in peripheral tissues in the mother. Gestational β -cell compensation, characterized by increased insulin secretion, initiates at the beginning of the second trimester and increases progressively to a peak level in the third trimester.

Risk factors

β -cel dysfunctie bij evolutieve insulineresistentie tijdens zwangerschap

- GDM bij vorige zwangerschap, vorige baby $\geq 4\text{kg}$
- BMI $\geq 30 \text{ kg/m}^2$
- Uitgesproken gewichtstoename 1^{ste} trimester
- PCOs
- Hoge maternale leeftijd
- Etniciteit



Summary



When adjusted for confounders, gestational diabetes mellitus was significantly associated with a range of adverse pregnancy outcomes

Study design



Systematic review and meta-analysis

Data sources

156 studies



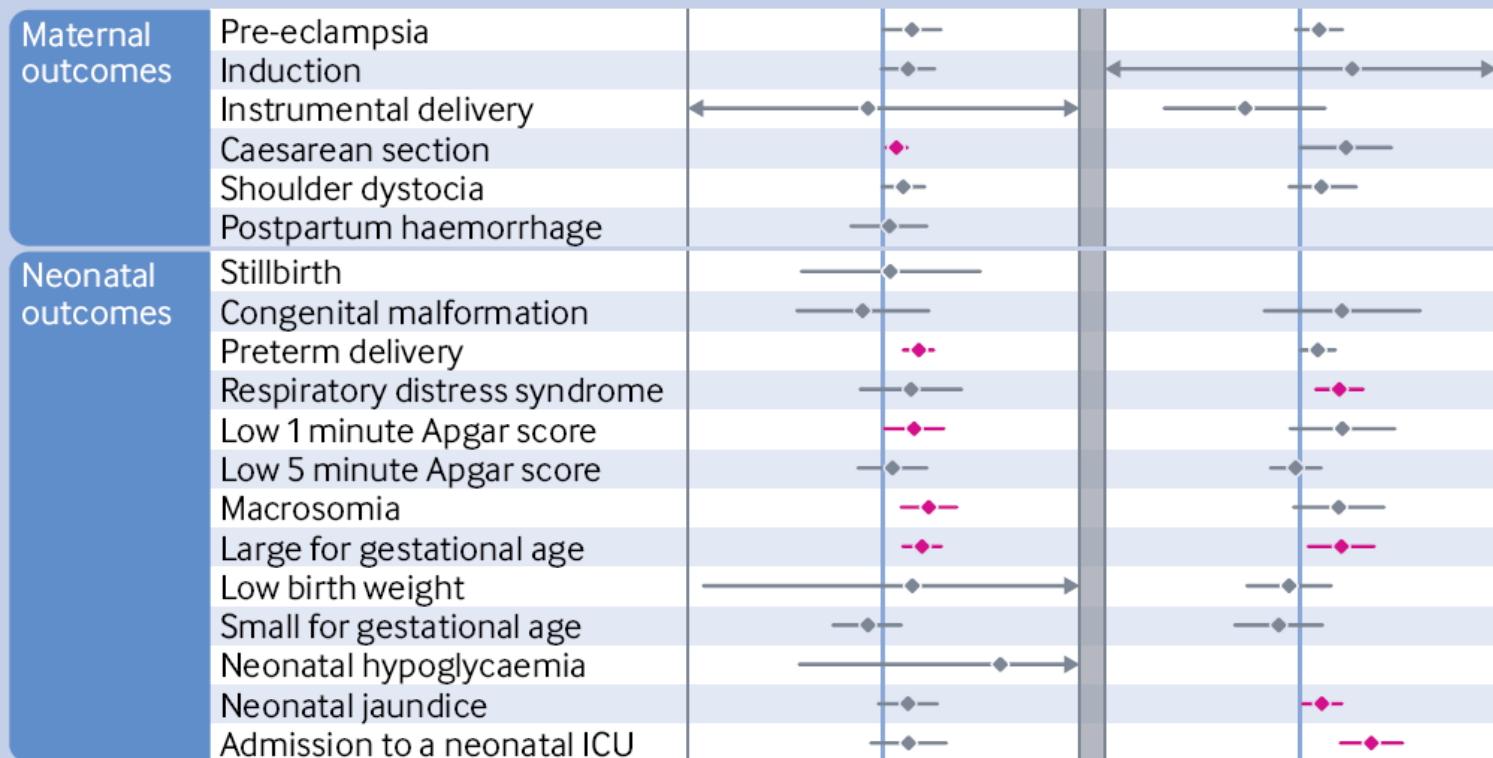
Overall risk of bias:
19% low, 13% medium, 68% high



7 506 061 pregnancies were evaluated

Results

Gestational diabetes mellitus versus normoglycaemia comparisons



Vooraf bestaande diabetes

Geboorteafwijkingen

Miskraam

Neonatale mortaliteit

Risico's van zwangerschapsdiabetes

Baby

- Macrosomie (> 4kg)
- Schouderdystocie
- Neonatol hypoglycemie ed

Moeder

- Hypertensie en preeclampsie
- Preterme arbeid
- Keizersnede

Termijn risico

- Maternal risk : diabetes, fatty liver disease, CVD ed.
- Offspring risk : obesity, neurodevelopment impairment, asthma ed.

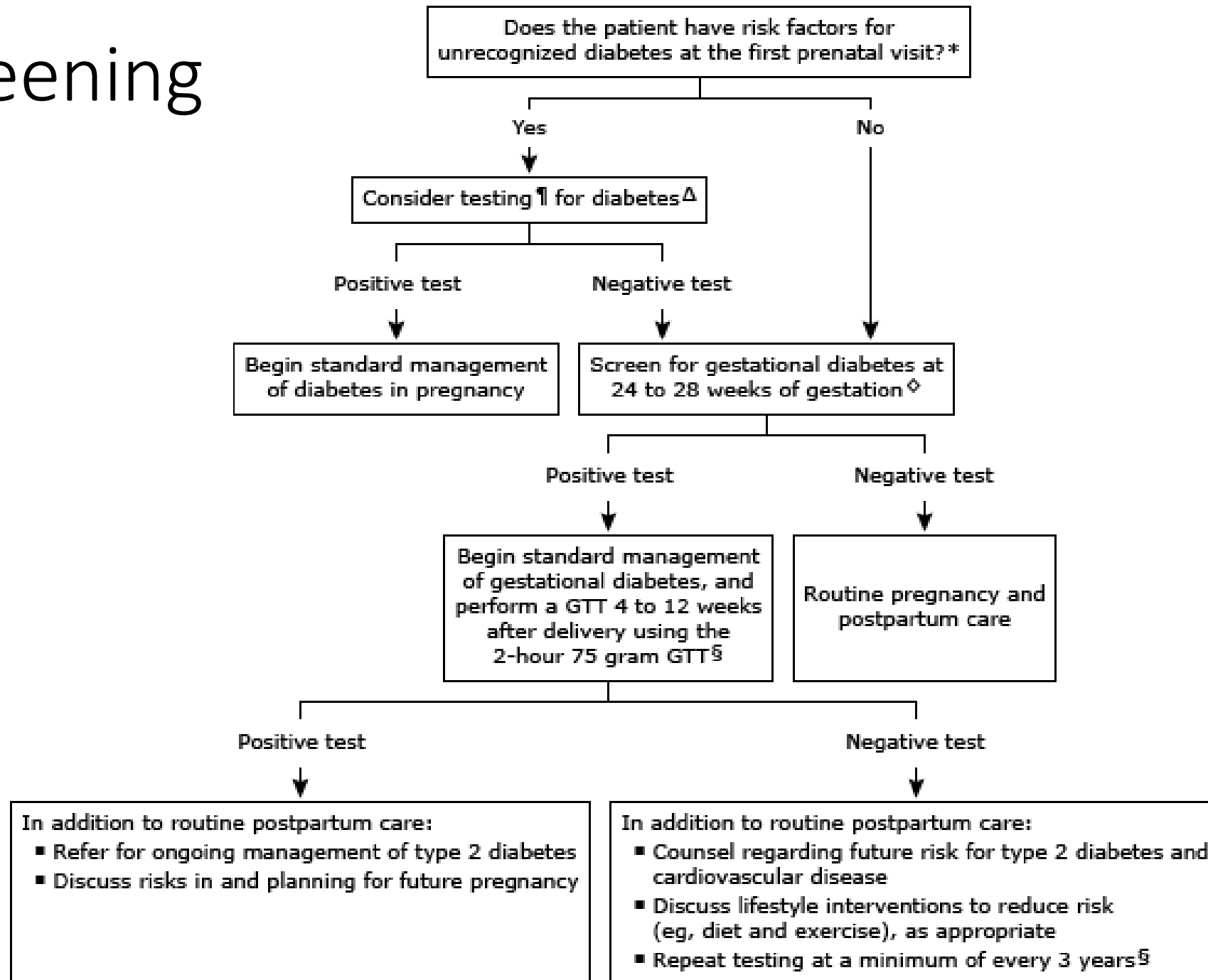
Vooraf bestaande diabetes

Geboorteafwijkingen

Miskraam

Neonatale mortaliteit

Screening



Screening



Early screening for gestational diabetes (before wk 20)?

- Modestly lower incidence adverse neonatal outcome

2 steps screening between wk 24 and 28

Screening 24 - 28 wk

Step one

1. Give 50 gram oral glucose solution without regard to time of day.
2. Measure venous plasma or serum glucose concentration at one hour after administration.
3. Glucose ≥ 135 mg/dL (7.5 mmol/L) or ≥ 140 mg/dL (7.8 mmol/L) is elevated ; tolerance test to more patients than the 140 mg/dL threshold. The lower threshold should be c

Step two

Two-hour 75-gram oral glucose tolerance test thresholds	
Fasting	92 mg/dL (5.1 mmol/L)
OR	
One hour	180 mg/dL (10 mmol/L)
OR	
Two hour	153 mg/dL (8.5 mmol/mol)

The diagnosis of gestational diabetes mellitus is made at 24 to 28 weeks of gestation when ≥ 1 plasma glucose value is at or above these thresholds.

Bariatrische chirurgie in VG

12 tot 24 mnd na ingreep voorkomen van zwangerschap

- OGTT niet bruikbaar
- Dumping
- SMBG voor en 2 uur na elke maaltijd gedurende 3-7 dg op 24-28 wk
 - Nuchter < 95 mg/dl
 - 2 uur pp < 120 mg/dl

Behandeling

SMBG voor en 2 uur na elke maaltijd wk

- Nuchter < 95 mg/dl
- 2 uur pp < 120 mg/dl

Glycemic control:

Dieet*, mediterranean-style diet**

Fysieke activiteit

Metformin***

Insuline

Preventie

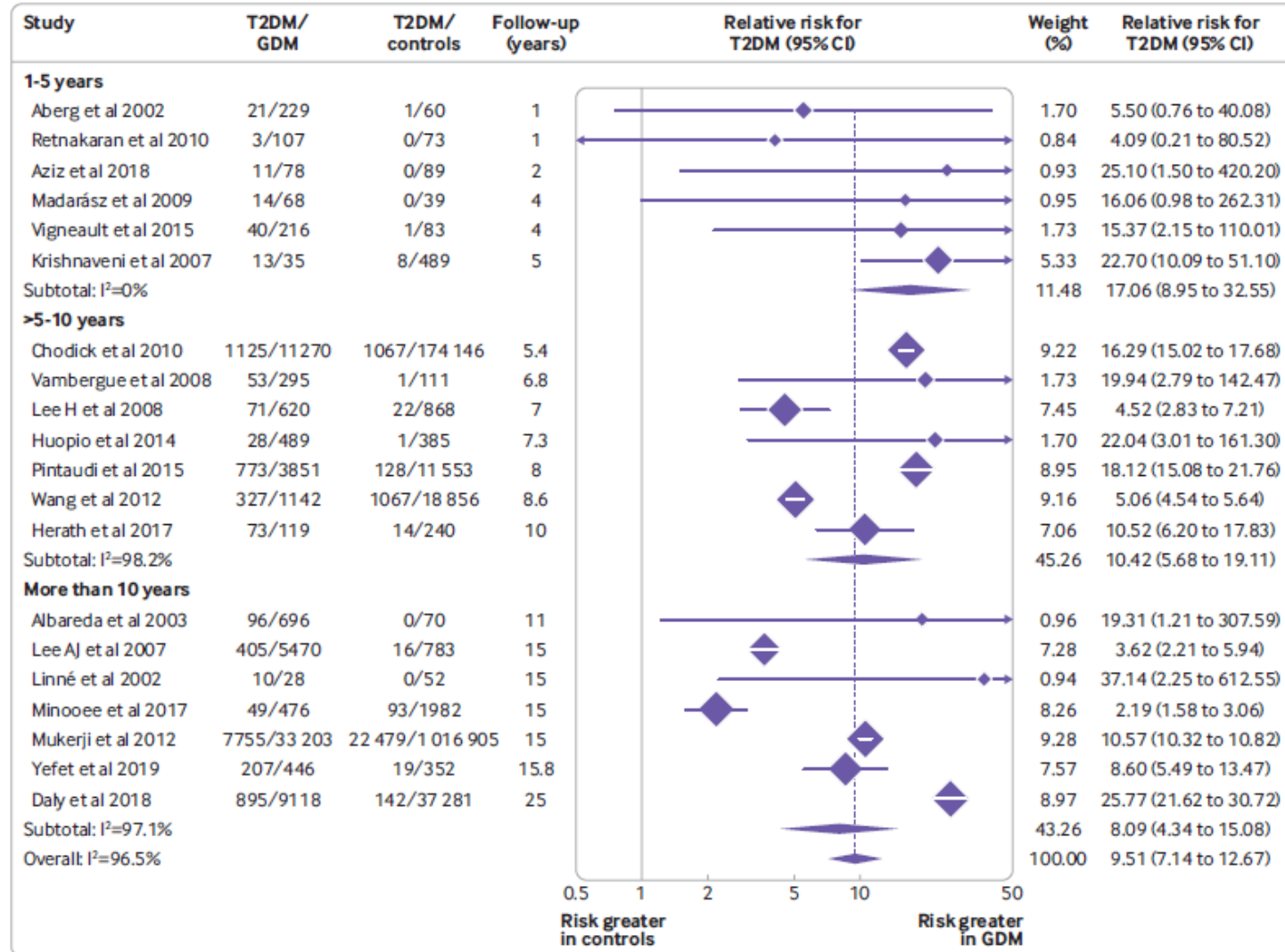


Fig 4 | Relative risk of type 2 diabetes mellitus (T2DM) in women with gestational diabetes mellitus (GDM) and controls based on study length of follow-up

Gestational Glucose Intolerance and Risk of Future Diabetes

Gestational Glucose Intolerance (GGI):

Abnormal initial gestational diabetes (GDM) screen without meeting GDM diagnostic criteria.

Question: Is GGI a risk factor for future diabetes?

Retrospective Cohort Study of 16,836 Pregnant Individuals

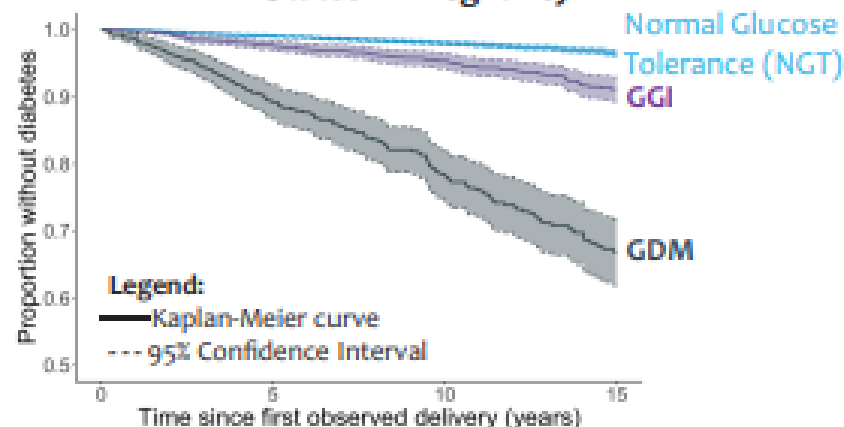


Two-step GDM Screening:

- 1) Screen: 50g glucose loading test
- 2) Diagnosis: 100g oral glucose tolerance test

Created by JGPIR
Healthcare Project

Diabetes Diagnoses Over Time According to Glucose Status in Pregnancy:



Risk of diabetes after pregnancy:

NGT 1.7 CASES PER 1000 PERSON-YEARS, REFERENCE

GGI 4.0 CASES PER 1000 PERSON-YEARS, HR 2.0 [1.5-2.6]*

GDM 23.1 CASES PER 1000 PERSON-YEARS, HR 8.3 [6.5-10.5]*

*Adjusted HR [95% confidence interval]

These findings identify gestational glucose intolerance as a risk factor for future diabetes.



Created by JGPIR
Healthcare Project

Selen et al. Diabetes Care 2022.

Samenvatting

Detectie voorafbestaande diabetes bij zwangerschap

Opvolging moeder en baby post-partum

- OGTT (kans afwijkingen groter bij early GDM) na 6 weken*
- Jaarlijks glucosemetabolisme

Preventie

- Leefstijlmaatregelen, metformin (PCOs, Asians)**

Intermezzo



VITAZ
STERK IN ZORG

Schildklierfunctie tijdens zwangerschap

- Fysiologische adaptatie
 - Toegenomen behoefte aan schildklierhormoon
 - Toename in thyroxine-binding globulin TBG -> daling ft4
 - Stimulatie TSH door hCG (human chorionic gonadotropin)
- Trimester-specifieke reference range
 - Schildklierfunctie te testen middels TSH en ft4

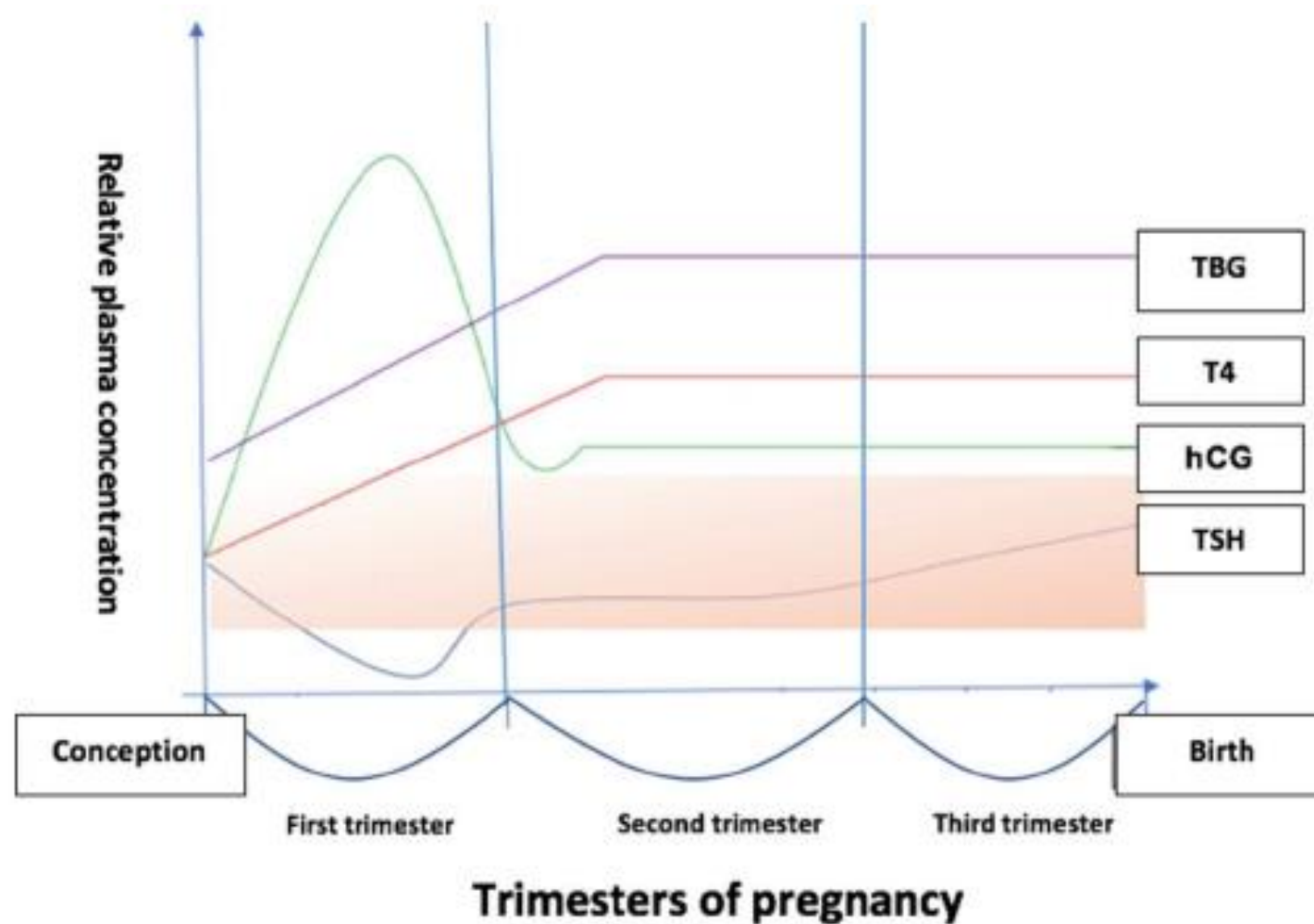


Figure 2. Changes in the plasma concentration of thyroid hormones and hCG in pregnancy. The orange surface corresponds to the normal reference range for non-pregnant women (hCG—human chorionic gonadotrophin; TBG—thyroid-binding globulin; T4—thyroxine; TSH—thyroid-stimulating hormone) [15].

Schildklierfunctie tijdens zwangerschap



- Iodine
 - Milde iodine deficiency in België*
 - No supplementation if urinary iodine concentration > 100 mcg/L
 - Iodine intake 220 mcg/d gedurende zwangerschap
 - 290 mcg/d gedurende borstvoeding
 - Suppletie effect op outcome?**

Hypothyroidie tijdens zwangerschap

- Preeclampsia and gestational hypertension.
- Placental abruption.
- Nonreassuring fetal heart rate tracing.
- Preterm delivery, including very preterm delivery (before 32 weeks).
- Low birth weight (which was likely due to preterm delivery for preeclampsia
- Increased rate of cesarean section.
- Postpartum hemorrhage.
- Perinatal morbidity and mortality.
- Neuropsychological and cognitive impairment in the child [19].

Wie screenen?

- Living in an area of moderate to severe iodine insufficiency
- Symptoms of hypothyroidism
- Family or personal history of thyroid disease
- Personal history of:
 - Thyroid peroxidase (TPO) antibodies
 - Goiter
 - Age >30 years
 - Type 1 diabetes
 - Head and neck irradiation
 - Recurrent miscarriage or preterm delivery
 - Multiple prior pregnancies (two or more)
 - Class 3 obesity (body mass index [BMI] ≥ 40 kg/m²)
 - Infertility
 - Prior thyroid surgery
 - Use of [amiodarone](#), [lithium](#), or recent administration of iodinated radiologic contrast agents

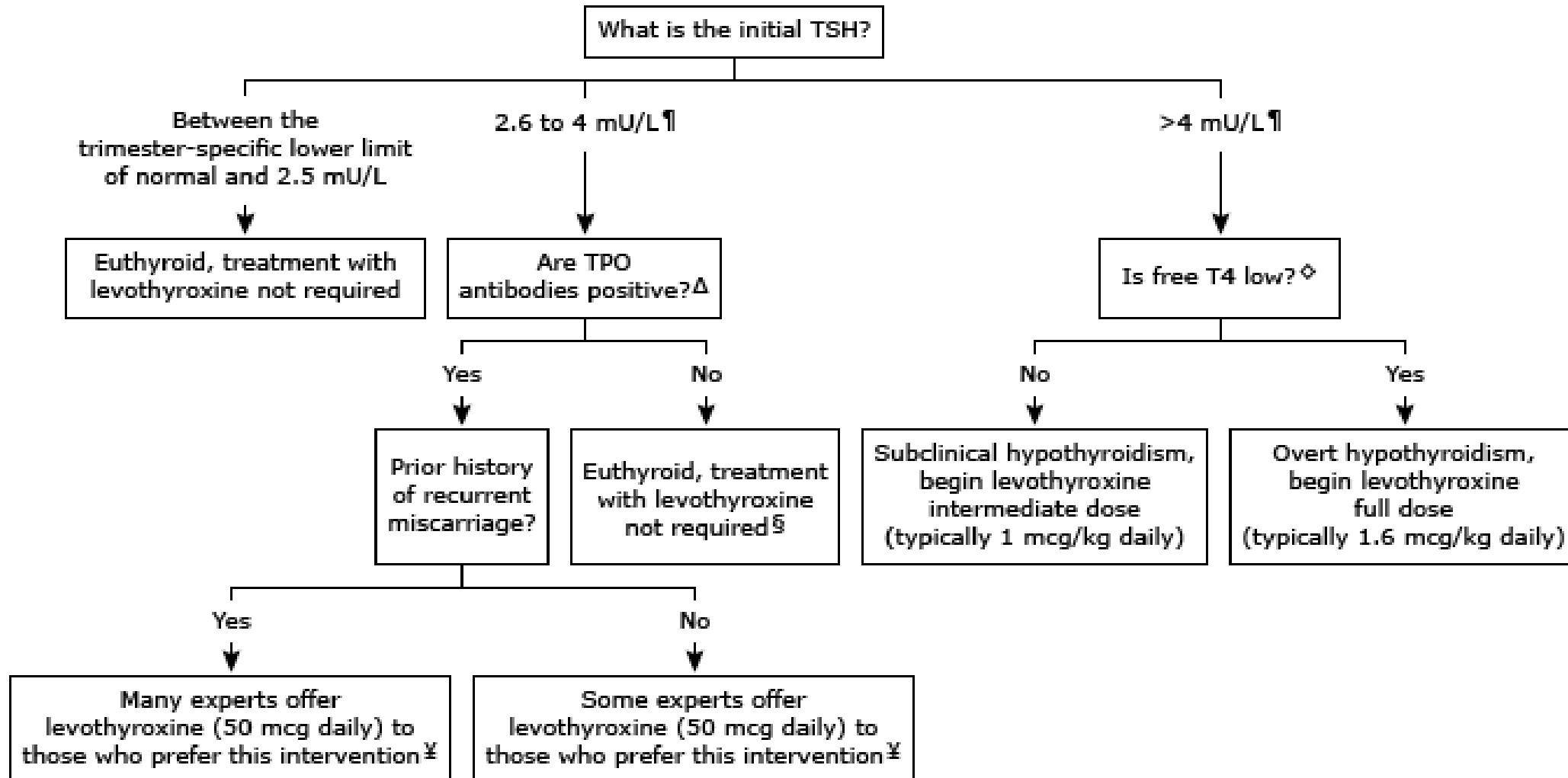
Hypothyroidie

- Increased TSH and suppressed ft4
 - Treatment (1.6 mcg/kg dg)

TPO antibodies

- Subclinical hypothyroidie wel/geen TPO antibodies
 - Increased rate of fetal loss, premature delivery
 - Treatment between wk 8 en 20 did not result in better cognitive outcome in children through 5 yrs of age*
 - Treatment may decrease pregnancy loss**
- Euthyroid women and TPO antibodies***
 - Increased rate of fetal loss, premature delivery
 - Conflicting data whether treatment is effective

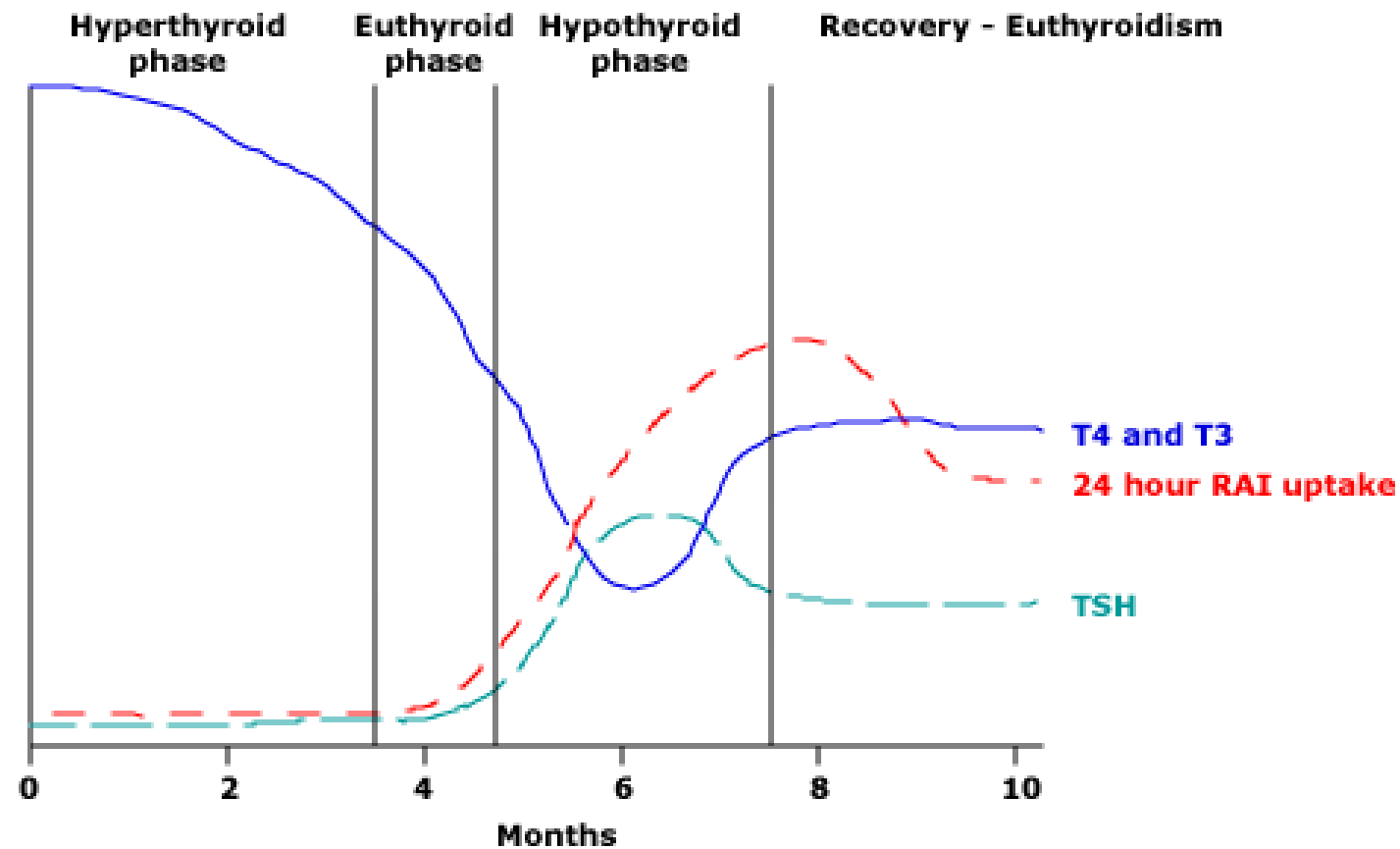
Flow chart



Hyperthyroidie

- Suppressed TSH, < 0.1 mU/L and increased ft4/ft3
- Uiteraard geen radionuclide scan!
- Treatment depends on cause
 - Graves disease, hCG mediated, etc

Postpartum thyroiditis 5 – 10%



Schildklier- & zwangerschapsdiabetes

- Subklinische hypothyroidie met TPO anti-stoffen*
 - Zwangerschapsdiabetes
 - Preeclampsia**
 - Preterm birth
- Pre-eclampic women at risk for changes in thyroid function***
- Thyroid dysfunction and gestational diabetes are interrelated****

*Lia *et al.*, Int J Gynaecol Obstet. 2019; Korevaar *et al.*, JAMA 2019; **Toloza *et al.*, Lancet Diabetes endocrinol 2022;

Hajifoghaha *et al.*, BMC Endocr Disorders 2022; *Pinto *et al.*, J Endocrinol Invest 2023

Samenvatting

Detectie hypothyroidie bij zwangerschap!

- Universal screening vs. case finding*
- Aanpassen levothyroxine bij zwangerschap (130%)

Controle schildklierfunctie na aanpassing : (4) 6 weken!

Levothyroxine op nuchtere maag, 30 minuten wachten met eten



OBESITAS

EEN ZWARE UITDAGING

Dr. Karen Decaestecker - endocrinoloog

1 op 8 = obees

Female

2022

Vrouwen

Male

2022

Mannen

Switch to Glo

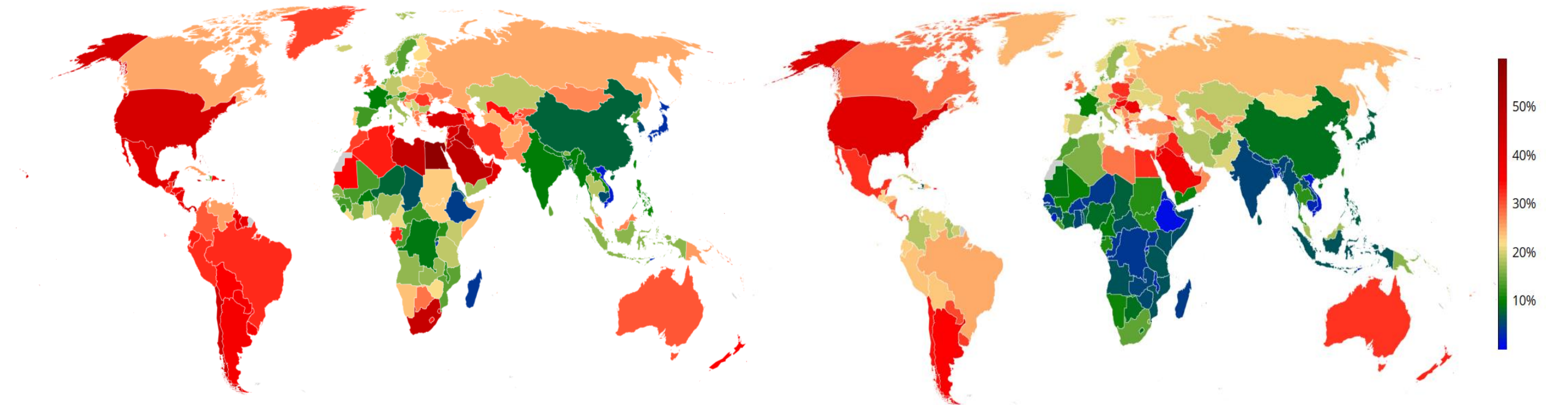
50%

40%

30%

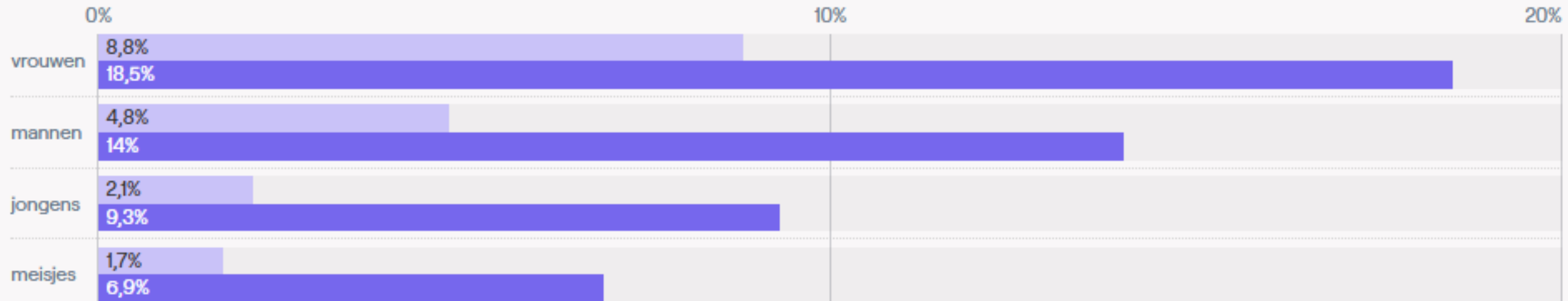
20%

10%



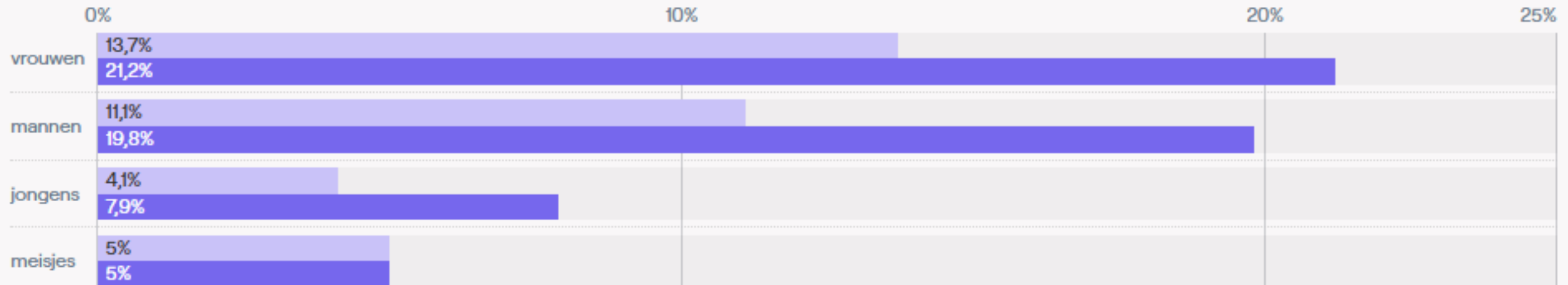
Obesitas wereldwijd

1990 2022

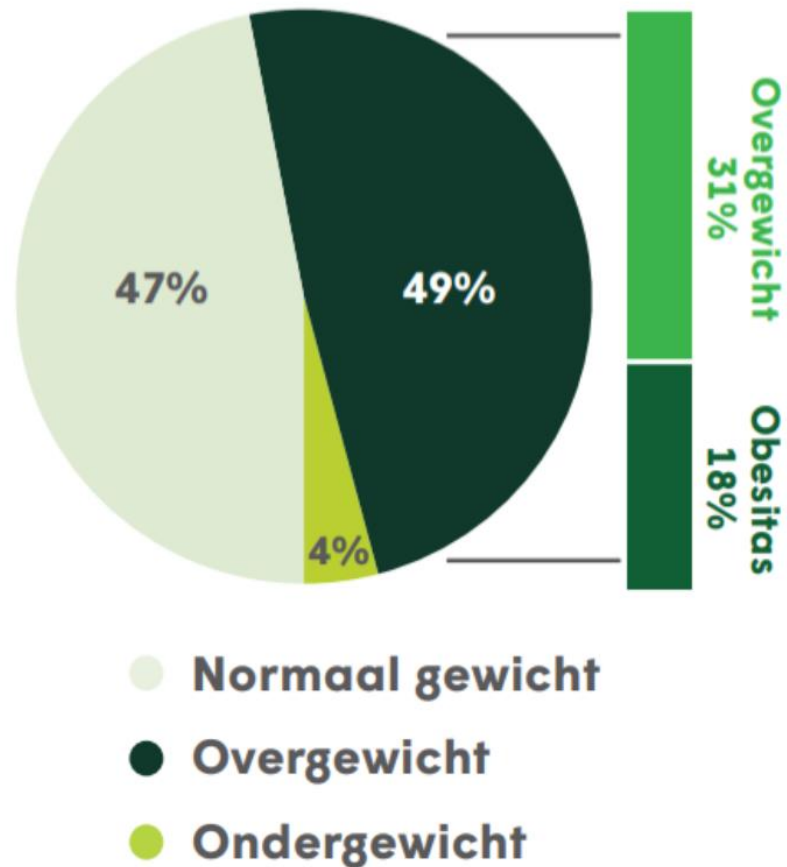


Obesitas in België

1990 2022

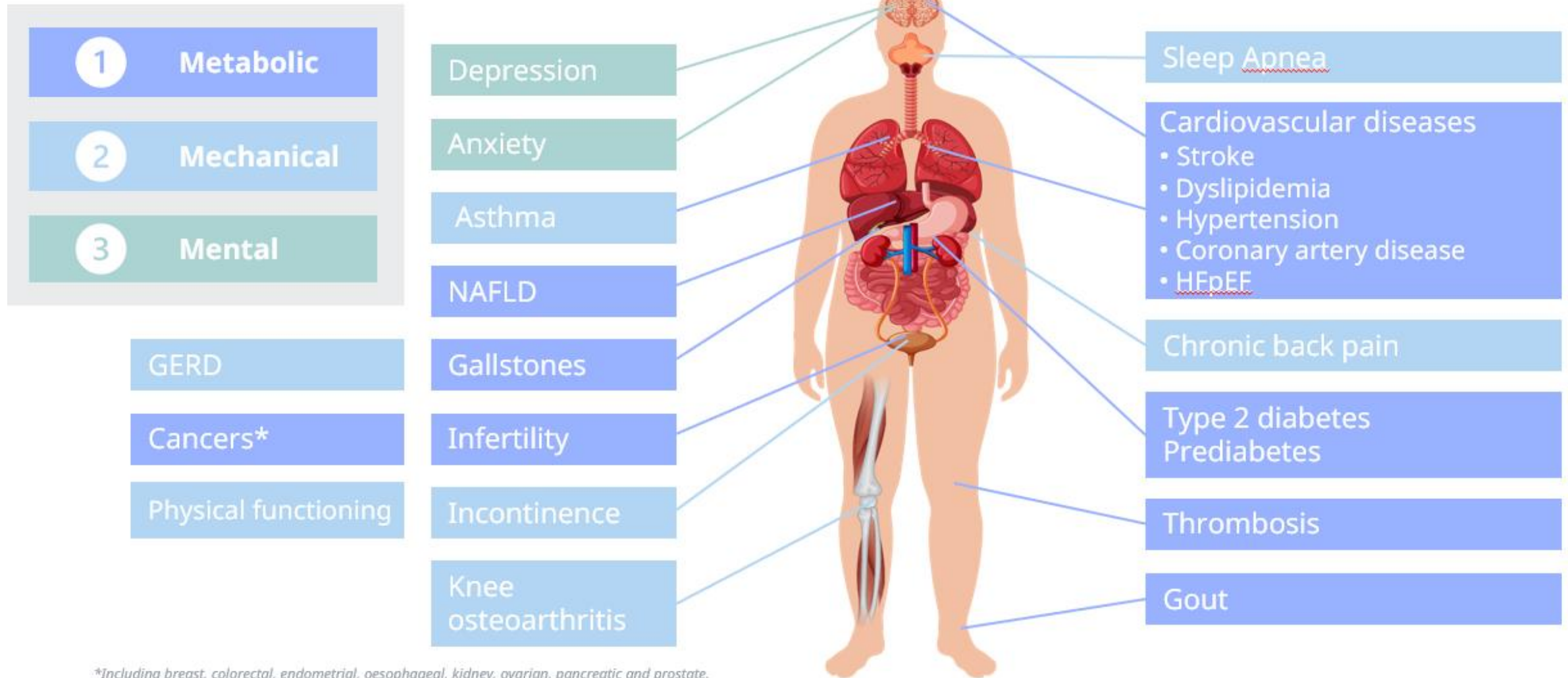


Situatie in België: 1 op 5

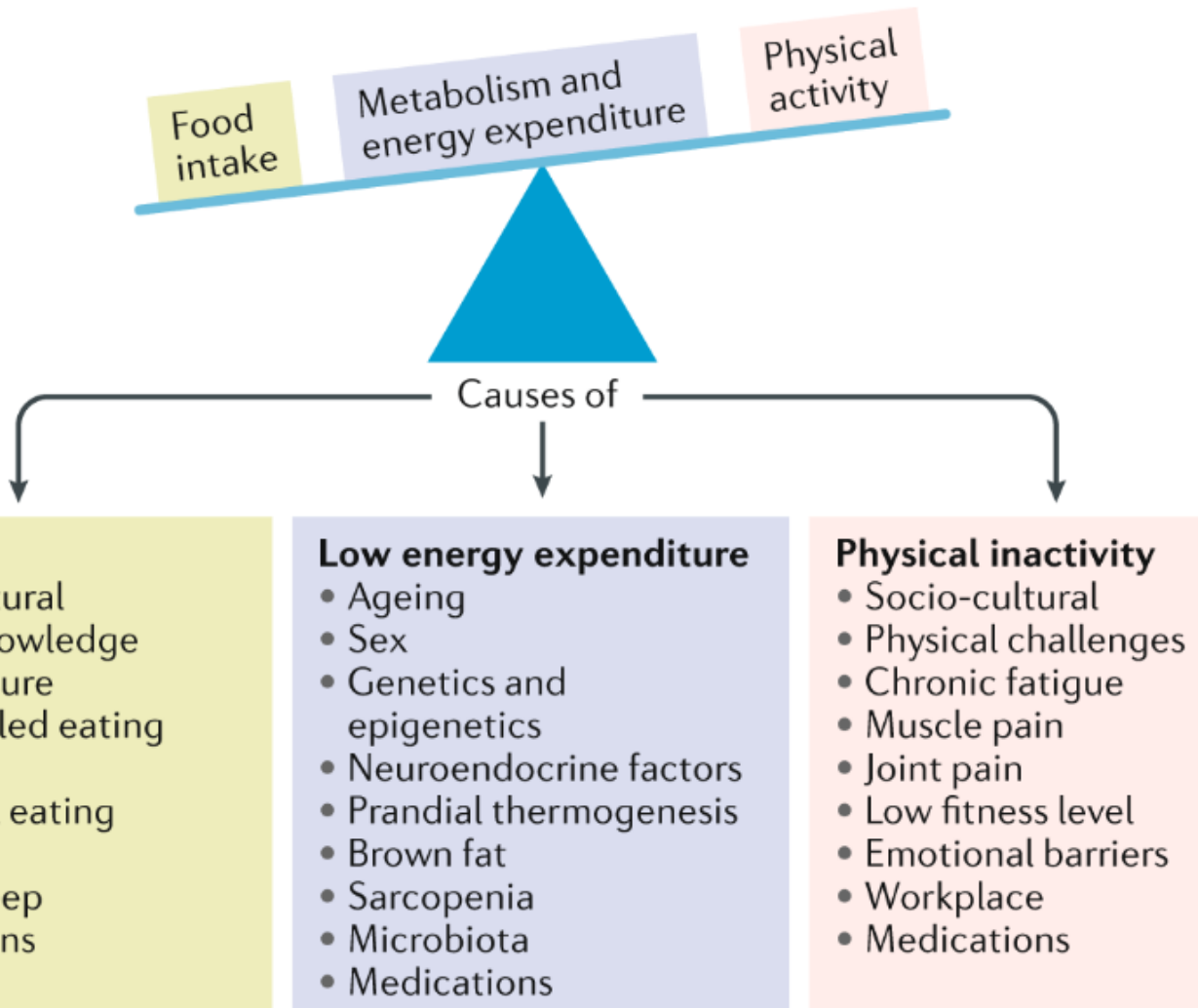


Classificatie	BMI
Normaal	18,5-24,9 kg/m ²
Overgewicht	25-29,9 kg/m ²
Obesitas klasse I	30-34,9 kg/m ²
Obesitas klasse II	35-39,9 kg/m ²
Obesitas klasse III	meer dan 40 kg/m ²

Complications



Multifactorieel



Homeostase

Empty stomach

Releases ghrelin →
increases appetite



Full stomach

Ghrelin production
stops and gut hormones
(eg, GLP-1, PPY, CCK)
are released →
suppresses appetite



Low body fat
= Low Leptin

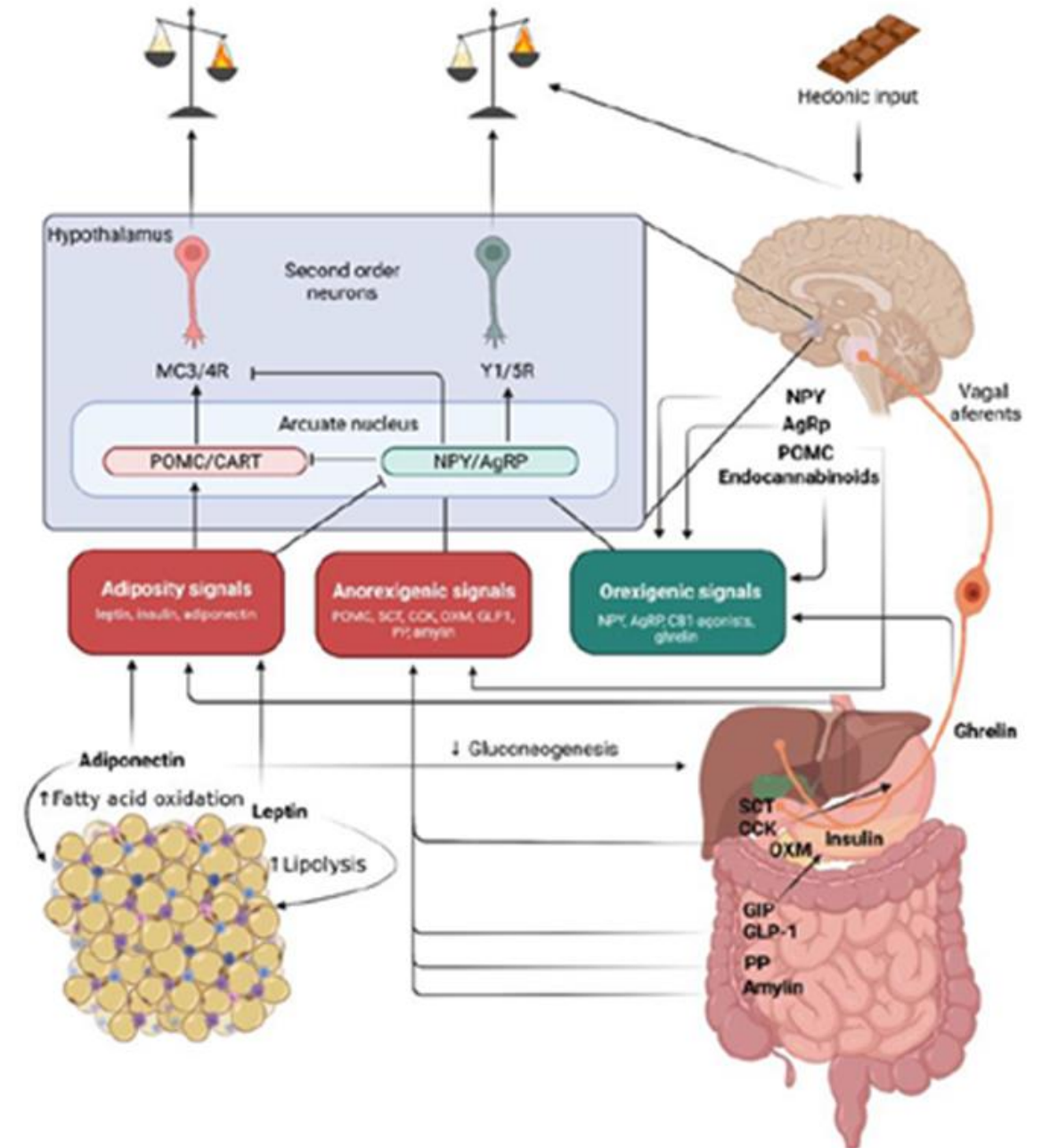


High body fat
= High Leptin



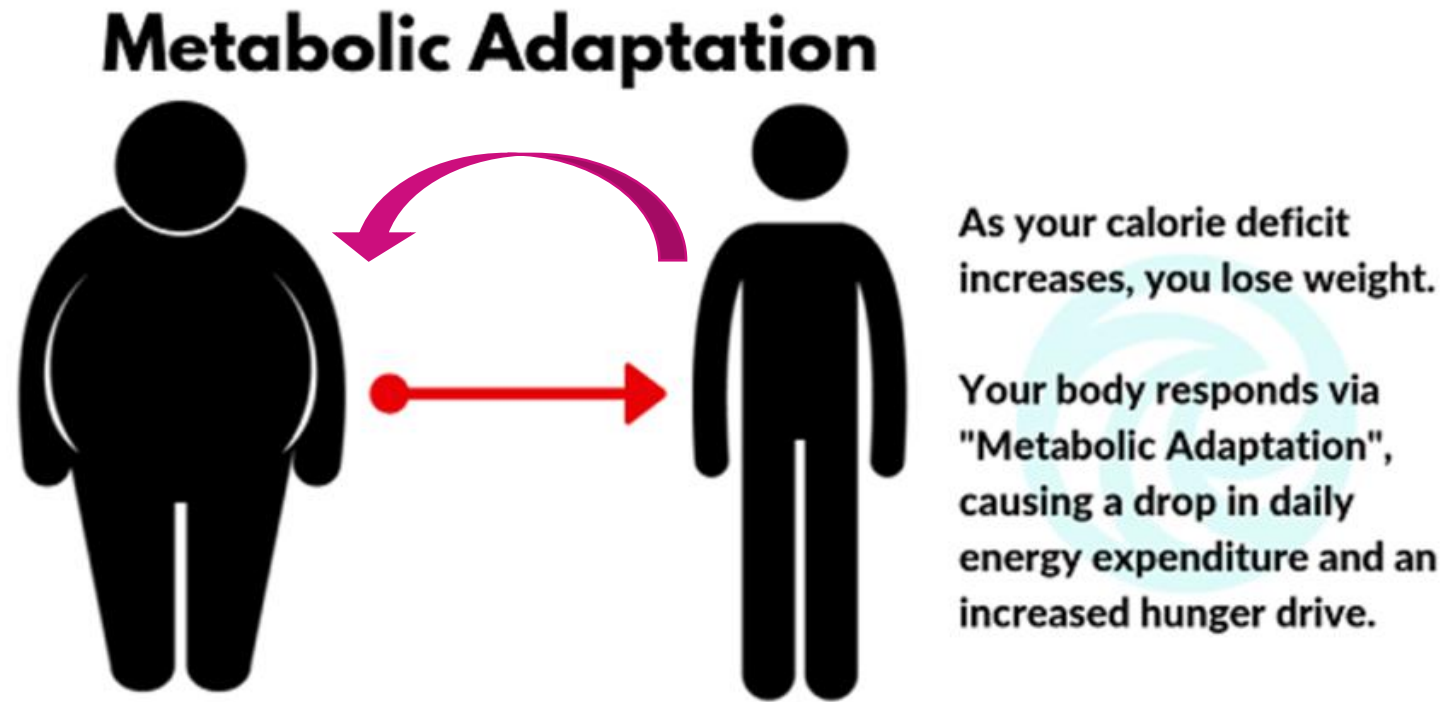
Belangrijke spelers

1. Hypothalamus
2. Hormonale input
3. Hedonisch systeem

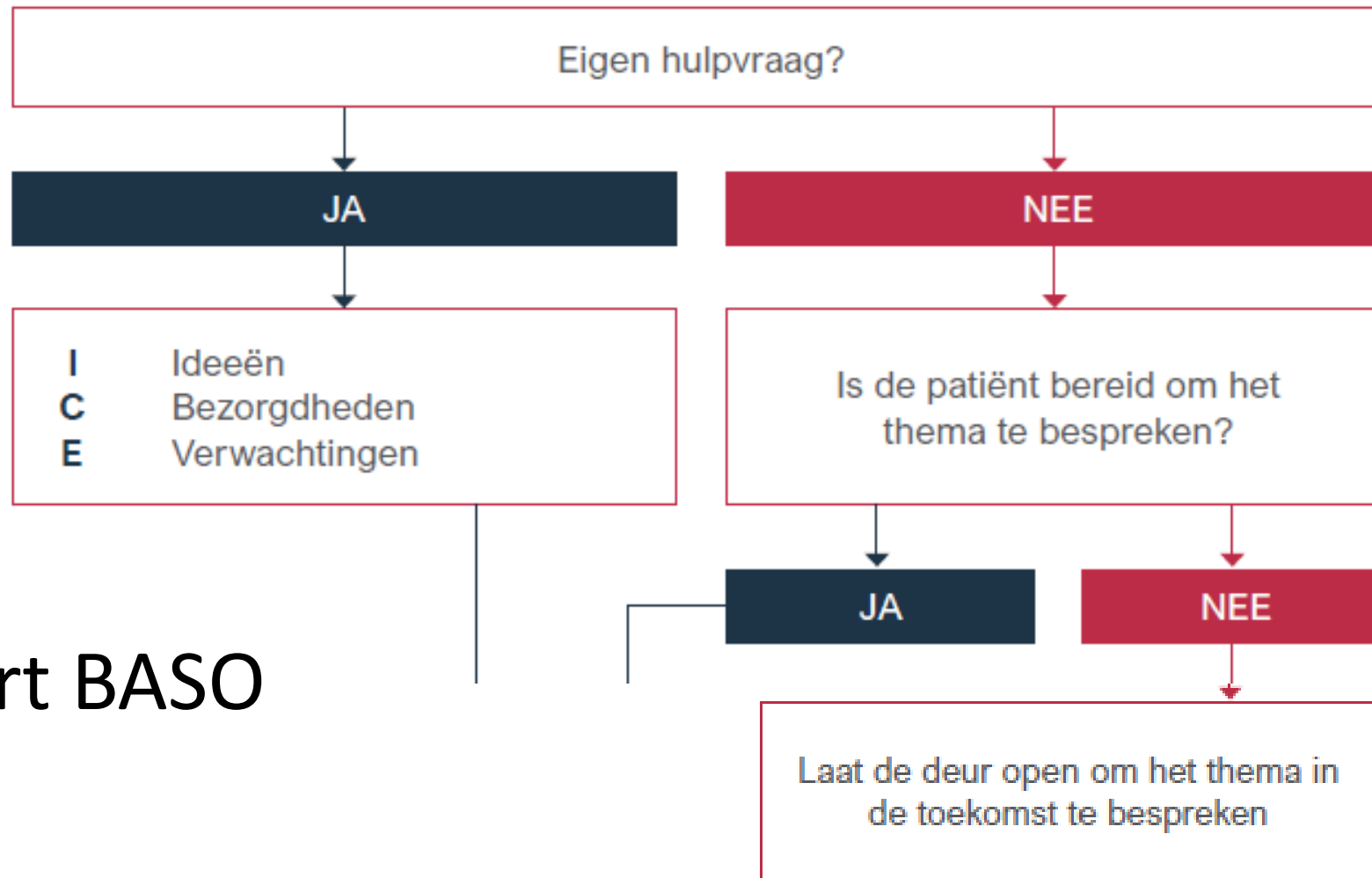


Metabole adaptatie

Het lichaam wil altijd terugkeren naar het hoogste gewicht ooit gekend



Obesitas in kaart brengen



Flowchart BASO

Anamnese

Achtergrond

- Gewichtsevolutie
- Familiale belasting
- Eerdere behandel pogingen
- Sociaal-economische situatie

Medicatie

Gewichtsverhogend? Zie tabel

Leefstijl

- Eetgedrag
- Beweging
- Slaap
- Emotieregulatie
- Roken, alcohol

Detectie psychische en somatische weerslag

- Levenskwaliteit
- Lichaamsbeleving
- Depressie-/angstklachten
- Risico eetstoornis: **SCOFF/ESP**
- Sociaal netwerk (steunfiguren)
- Slaapapnee (snurken, witnessed apnees, somnolentie, hoofdpijn)

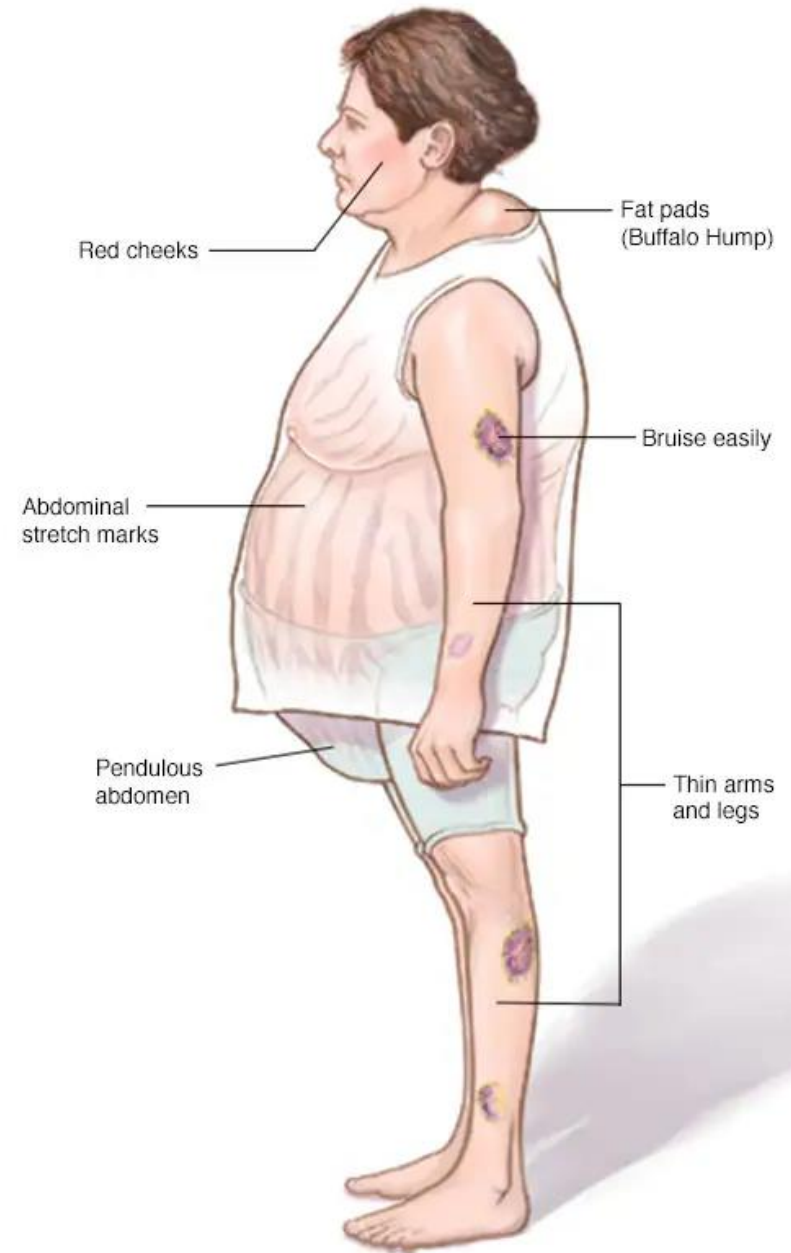
Medicatie

Categorie	Klasse	Naam	Alternatieve therapie
Antidiabetica	Insuline	Insuline	• Metformine • GLP-1-analogen: exenatide, liraglutide, dulaglutide, lixisenatide, semaglutide • Acarbose • Gliflozinen (SGLT-2 inhibitoren): canagliflozine, dapagliflozine, empagliflozine, ertugliflozine • Gliptinen (DPP4 –inhibitoren): linagliptine, sitagliptine, saxag vildagliptine • Combinatietherapie: Pioglitazon + metformine Glipizide + metformine Glibenclamide + metformine
	Glitazonen	Pioglitazon	
	Hypo-glycemiërende sulfamiden	Glimepiride Glipizide Gliclazide Glibenclamide	
	Gliniden	Repaglinide	
Antidepressiva	Tricyclische antidepressiva	Amitriptyline Imipramine Nortriptyline	• SNRI's: Duloxetine, Venlafaxine (variabel effect op gewicht) • Noradrenaline- en dopamin heropnameremmers: Bupropion • Direct werkend op de neurale transmissie: Trazodon • SSRI's: Fluvoxamine (variabel effect op gewicht), fluoxetine, sertraline
	Direct werkend op neuroreceptoren	Mirtazapine	
	MAO-inhibitoren	Fenelzine	
	SSRI's	Paroxetine Citalopram Escitalopram	
	Lithium	Lithium	

Antipsychotica		Haloperidol Clozapine Risperidone Olanzapine Quetiapine Sertindol Paliperidon Chloorpromazine	Aripiprazol (variabel effect op gewicht)
Anti-epileptica		Valproïnezuur Carbamazepine Gabapentine Pregabaline	Topiramaat Zonisamide Lamotrigine
Corticosteroiden	Orale, nasale, ... preparaten	Prednison Prednisolon Cortisone	NSAID's
Hormoon- vervangende therapie	Progestogenen*		
Antihistaminica		Difenhydramine	Voorkeur voor weinig sederende H1-antihistaminica
Bèta-blokkers		Propranolol Metoprolol Atenolol	ACE inhibitoren Angiotensine II receptor blokkers Calcium kanaal blokkers (vochtretenie) Timolol Acebutolol
Antihypertensiva	Centraal werkend	Clonidine	ACE inhibitoren Angiotensine II receptor blokkers Diuretica Prazosin

KO

- BMI (kg/m^2)
- Buikomtrek
- Huidafwijkingen



Labo

- TSH
- Screening metabole comorbiditeiten
- Bij klinische verdenking
 - Hypercortisolisme
 - Hypogonadisme
 - Androgeenbilan (PCOS)

Bloedafname

- Volledig bloedbeeld (COFO)
- Totaal-, HDL-, en LDL-cholesterol
- Triglyceriden
- Glycemie nuchter, HbA_{1c}, c-peptide
- ALT, AST, γGT en bili
- Creatinine, eGFR

Eventueel:

- Schildklierfunctie
- Vitamine D, B12
- IJzerstatus
- Urinezuur

Endocriene oorzaken

4. Hormonaal	5. Hypothalaam	6. Monogenetisch / syndromaal	
Veel voorkomend Hypothyreoidie Polycysteus ovarium syndroom (PCOS) Hypogonadisme Behoud zwangerschapskilo's Menopauze Zeldzaam Hypopituitarisme (Cyclisch) Cushing's syndroom Groeihormoon tekort	Zeldzaam Hypothalame schade na bestraling, operatie of hoofdtrauma Hypothalame tumor Craniopharyngeoom Malformatie	Zeldzaam <i>Monogenetische obesitas</i> Op jonge lft obesitas (≤ 7 jaar) Extreme eetlust Opvallend gewichtsverschil met familieleden Voorbeelden: Mutaties in genen van MC4R, POMC, leptine, leptine-receptor, PCSK1	Zeldzaam <i>Syndromale obesitas</i> Op jonge lft obesitas (≤ 15 jaar) Extreme eetlust Opvallend gewichtsverschil met familieleden Dysmorphe kenmerken of aangeboren afwijkingen Autisme Ontwikkelingsachterstand Voorbeelden: Prader-Willi, Bardet-Biedl, 16p11.2 deletie, Alström syndroom

Edmonton Obesity Staging System

INSCHATTING ERNST EN INDICATIESTELLING

EOSS stadium

Stadium 0	Stadium 1	Stadium 2	Stadium 3	Stadium 4
» geen gewichtsgelateerde risicofactoren; <u>en</u> » geen lichamelijke symptomen; <u>en</u> » geen psychologische symptomen; <u>en</u> » geen weerslag op welzijn; <u>en</u> » geen functionele beperkingen	» subklinische medische risicofactoren; <u>of</u> » milde lichamelijke symptomen die geen medische behandeling vereisen; <u>of</u> » milde gewichtsgelateerde psychologische symptomen; <u>of</u> » milde weerslag op welzijn; <u>of</u> » milde functionele beperkingen	» medische risicofactoren; <u>of</u> » gewichtsgelateerde comorbiditeit die een medische behandeling vereist; <u>of</u> » matige gewichtsgelateerde psychologische symptomen; <u>of</u> » matige weerslag op welzijn; <u>of</u> » matige functionele beperkingen	» ernstige gewichtsgelateerde comorbiditeit met orgaanschade; <u>of</u> » ernstige psychologische symptomen; <u>of</u> » ernstige weerslag op welzijn; <u>of</u> » ernstige functionele beperkingen	» zeer ernstige gewichtsgelateerde comorbiditeit in eindstadium; <u>of</u> » zeer ernstige invaliderende gewichtsgelateerde psychologische symptomen; <u>of</u> » zeer ernstige functionele beperkingen

STAGE 0

- **NO** sign of obesity-related risk factors
- **NO** physical symptoms
- **NO** psychological symptoms
- **NO** functional limitations

Case Example:

Physically active female with a BMI of 32 kg/m², no risk factors, no physical symptoms, no self-esteem issues, and no functional limitations.

Class I, Stage 0 Obesity

EOSS Score

WHO Obesity Classification

STAGE 1

- Patient has obesity-related **SUBCLINICAL** risk factors (borderline hypertension, impaired fasting glucose, elevated liver enzymes, etc.) - **OR** -
- **MILD** physical symptoms - patient currently not requiring medical treatment for comorbidities (dyspnea on moderate exertion, occasional aches/pains, fatigue, etc.) - **OR** -
- **MILD** obesity-related psychological symptoms and/or mild impairment of well-being (quality of life not impacted)

Case Example:

38 year old female with a BMI of 39.2 kg/m², borderline hypertension, mild lower back pain, and knee pain. Patient does not require any medical intervention.

Class III, Stage 1 Obesity

WHO CLASSIFICATION OF WEIGHT STATUS (BMI kg/m²)

Obese Class I	30 - 34.9
Obese Class II	35 - 39.9
Obese Class III	≥40

Stage 0 / Stage 1 Obesity

Patient **does not meet clinical criteria for admission** at this time.
Please refer to primary care for further preventative treatment options.



STAGE 2

- Patient has **ESTABLISHED** obesity-related comorbidities requiring medical intervention (HTN, Type 2 Diabetes, sleep apnea, PCOS, osteoarthritis, reflux disease) - **OR** -
- **MODERATE** obesity-related psychological symptoms (depression, eating disorders, anxiety disorder) - **OR** -
- **MODERATE** functional limitations in daily activities (quality of life is beginning to be impacted)

Case Example:

32 year old male with a BMI of 36 kg/m² who has primary hypertension and obstructive sleep apnea.

Class II, Stage 2 Obesity

STAGE 3

- Patient has **significant** obesity-related end-organ damage (myocardial infarction, heart failure, diabetic complications, incapacitating osteoarthritis) - **OR** -
- **SIGNIFICANT** obesity-related psychological symptoms (major depression, suicide ideation) - **OR** -
- **SIGNIFICANT** functional limitations (eg: unable to work or complete routine activities, reduced mobility)
- **SIGNIFICANT** impairment of well-being (quality of life is significantly impacted)

Case Example:

49 year old female with a BMI of 67 kg/m² diagnosed with sleep apnea, CV disease, GERD, and suffered from stroke. Patient's mobility is significantly limited due to osteoarthritis and gout.

Class III, Stage 3 Obesity

STAGE 4

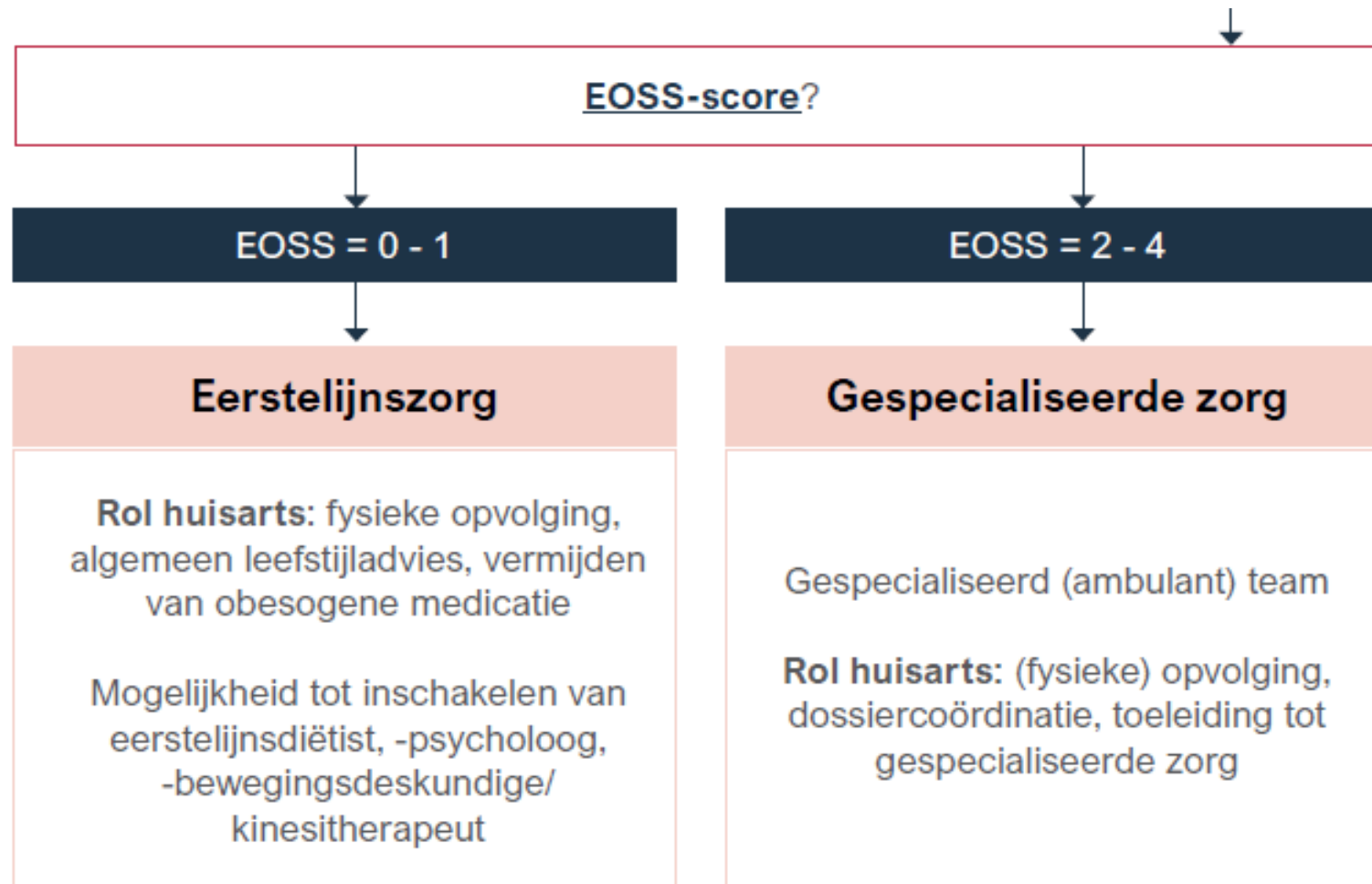
- **SEVERE** (potential end stage) from obesity-related comorbidities - **OR** -
- **SEVERELY** disabling psychological symptoms - **OR** -
- **SEVERE** functional limitations

Case Example:

45 year old female with a BMI of 54 kg/m² who is in a wheel chair because of disabling arthritis, severe hyperpnea, and anxiety disorder.

Class III, Stage 4 Obesity

Edmonton Obesity Staging System



Behandeling



Lifestyle

- Diëtiste
- Beweegtherapie
 - Beweging op verwijzing
 - Metabool programma
- Psycholoog

Metabool programma Gewicht in balans



Wij brengen u in beweging

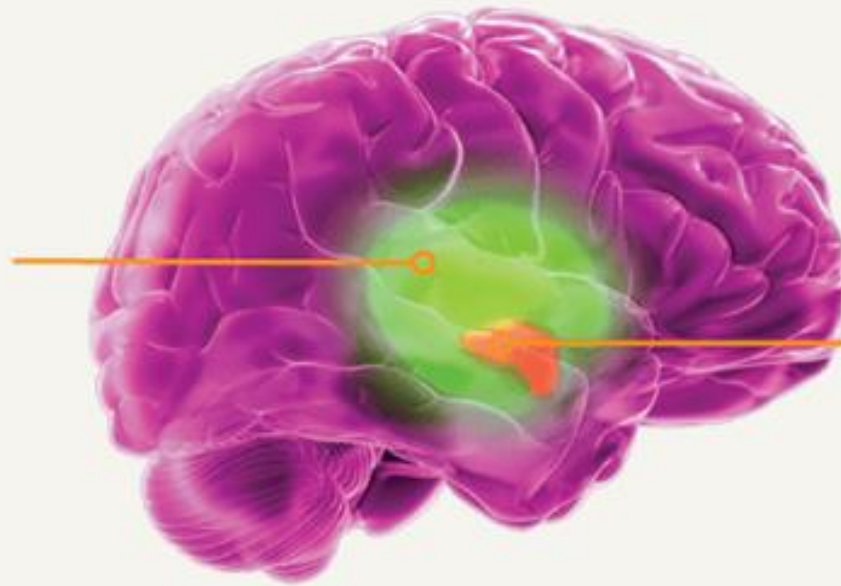
Medicamentus

- 1. Mysimba**
- 2. Saxenda**
- 3. Mounjaro**
4. Orlistat

Naltrexon/Bupropion (Mysimba)

Mesolimbic Reward System

Involved with feeling pleasure during rewarding experiences, such as eating, leading to **intense cravings**²⁻⁴



Hypothalamus

When activated, **drives the urge to eat**¹

Naltrexon/Bupropion (Mysimba)

- 4 trials
- 100kg – BMI 36kg/m²
- 3 à 5% gewichtsverlies tov placebo
- 50% drop outs
- Lange termijn data?

Table – Key results^{12,13,19-22}

Outcome (56 weeks unless stated)	Trial	Naltrexone/bupropion vs. placebo (difference, p-value)	
		Full analysis set	Intention-to-treat population
Change in bodyweight from baseline	COR- Diabetes	5.0% vs. 1.8% (3.2%, p<0.001)	3.7% vs. 1.7% (2.0%, p<0.001)
	COR-I	6.1% vs. 1.3% (4.8%, p<0.008)	5.4% vs. 1.3% (4.1%, p<0.001)
	COR-BMOD	9.3% vs. 5.1% (4.2%, p<0.001)	8.1% vs. 4.9% (3.2%, p<0.001)
	COR-II (28 weeks)	6.5% vs. 1.9% (4.6%, p<0.001)	5.7% vs. 1.9% (3.8%, p<0.001)
		Full analysis set	All randomised participants

Naltrexon/Bupropion (Mysimba)

Heeft de patiënt:	Nee	Ja
Ongereguleerde hypertensie?	☐	☐
Aandoening met toevallen, voorgeschiedenis van toevallen of bekende CZS-tumor?	☐	☐
Huidige of vroegere diagnose van boulimie of anorexia nervosa?	☐	☐
Momenteel afhankelijk van chronische opioïden of opiaatagonisten?	☐	☐
Lopende behandeling bij acute onthouding van alcohol, benzodiazepine of opiaat?	☐	☐
Huidige behandeling met bupropion of naltrexon?	☐	☐
Voorgeschiedenis van bipolaire stoornis?	☐	☐
Behandeling met een MAO-remmer in de afgelopen 14 dagen?	☐	☐
Ernstige leverfunctiestoornis of eindstadium nierfalen?	☐	☐

Contra-indicaties
SCHRIJF MYSIMBA
NIET VOOR
als u een van deze
vakjes heeft
aangevinkt

	Week 1	Week 2	Week 3	Week 4 and Beyond
 AM: Take with breakfast	 1 tablet	 1 tablet	 2 tablets	 2 tablets
 PM: Take before dinner		 1 tablet	 1 tablet	 2 tablets

GLP-1 analogen

- Liraglutide (Saxenda®)
- Semaglutide (Wegovy®, Ozempic®, Rybelsus®)

	Semaglutide	Liraglutide	Dulaglutide	Lixisenatide	Exenatide	Tirzepatide*
Obesity 	 s.c. injection 2.4 mg Once weekly 	 s.c. injection 3.0 mg Once daily	Not approved	Not approved	Not approved	 s.c. injection 5, 7.5, 10, 12.5, 15 mg Once weekly
T2D 	 s.c. injection 0.5, 1.0, 2.0 mg Once weekly  Oral tablet 7, 14 mg Once daily	 s.c. injection 1.2, 1.8 mg Once daily	 s.c. injection 0.75, 1.5, 3.0, 4.5 mg Once weekly	 s.c. injection 20 µg Once daily	 s.c. injection 5, 10 µg Twice daily (IR)  s.c. injection 2 mg Once weekly (ER)	 s.c. injection 5, 7.5, 10, 12.5, 15 mg Once weekly

Liraglutide

SCALE studie

Inclusion criteria

- ≥ 18 years
- Stable BW
- BMI ≥ 30 kg/m² or ≥ 27 kg/m² + comorbidities

3731 participants

Without
prediabetes

Liraglutide 3.0 mg (n=959)

Placebo (n=487)

With
prediabetes¹

Liraglutide 3.0 mg (n=1528)

Placebo (n=757)

Lifestyle intervention: -500 kcal/day diet + 150 min/week physical activity



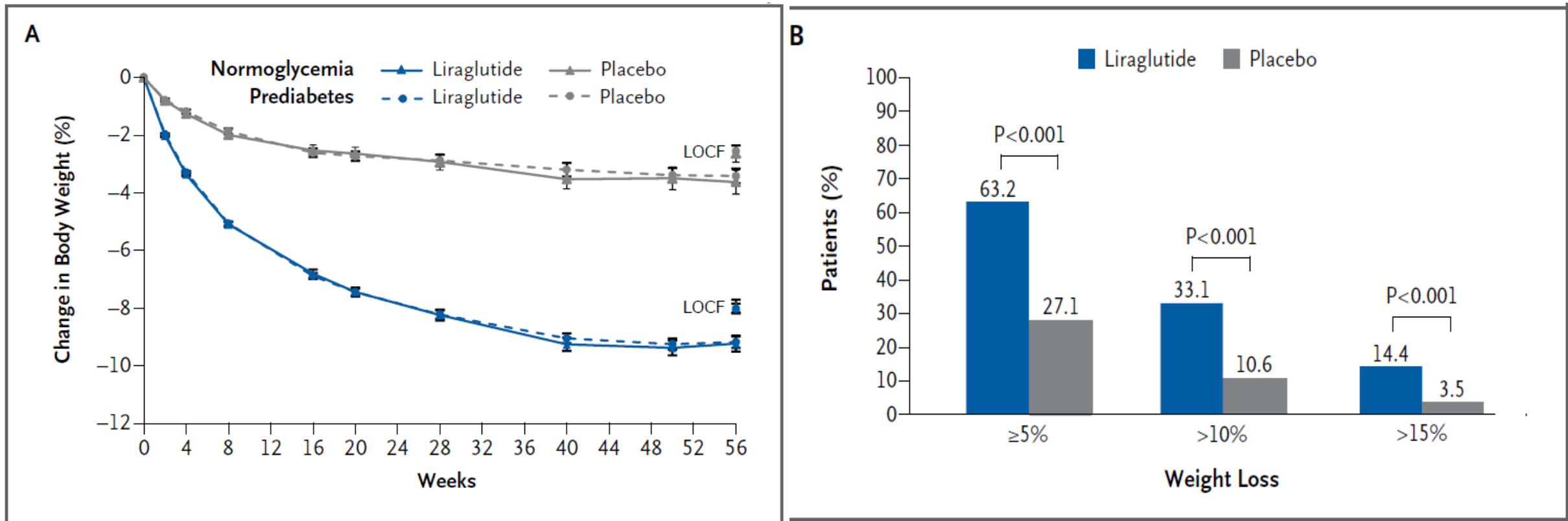
Trial information

- June 2011 to March 2013
- Randomised controlled double-blind study
- 191 sites in 27 countries
- Duration: 56 weeks (with prediabetes), 68 weeks (without prediabetes)

Liraglutide

Mean baseline BMI: 38.3kg/m²

Mean baseline weight: 106.2 kg



Semaglutide

Oral semaglutide (14mg - OD)

- Rybelsus®
- PIONEER trial program
- Indicated for uncontrolled T2DM
- **Not** indicated for weight loss
- Subject to reimbursement criteria



Available in Belgium

SC semaglutide (1mg - OW)

- Ozempic®
- SUSTAIN trial program
- Indicated for uncontrolled T2DM
- **Not** indicated for weight loss
- Subject to reimbursement criteria



SC Semaglutide (2.4mg - OW)

- Wegovy®
- STEP/SELECT trial program
- Indicated for weight loss
- **Not** EMA approved for HFpEF treatment
- **Not** EMA approved for reducing CV risk
- **Not** available in Belgium



Semaglutide 2,4mg

Mean body
weight

105.4 kg

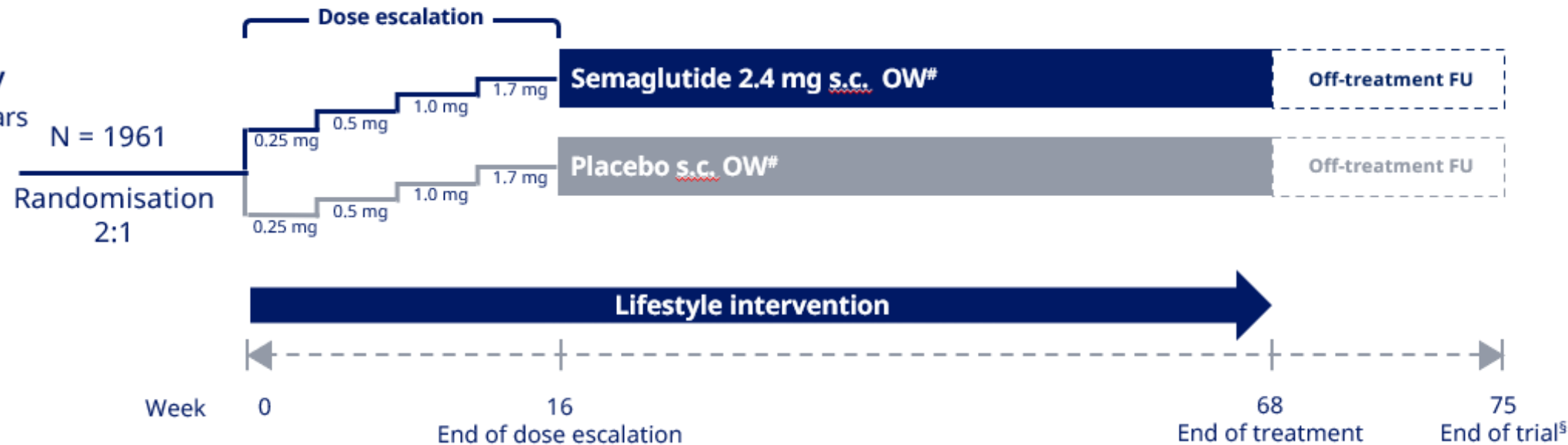
Mean BMI

37.8 kg/m²

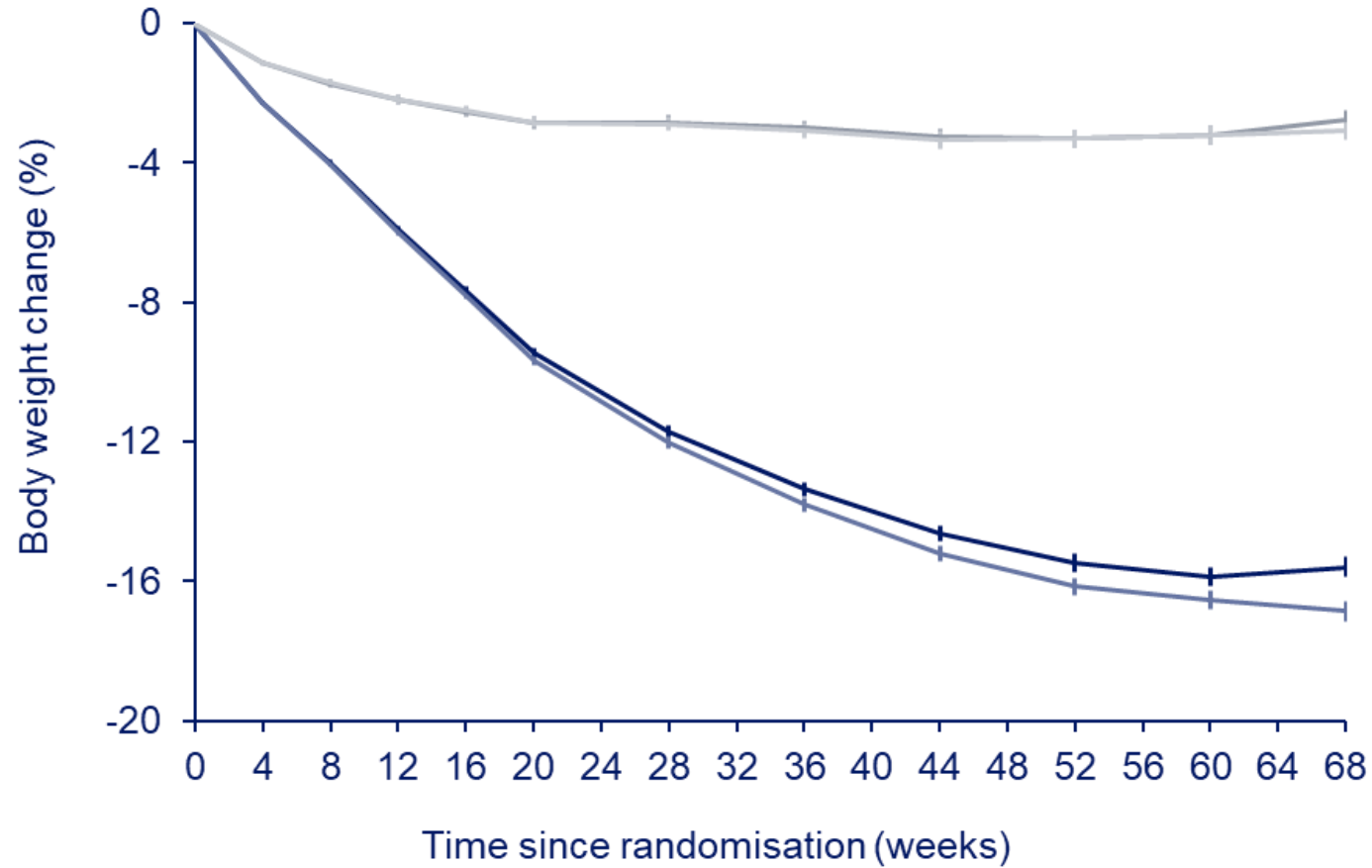
STEP 1: Randomised, double-blind, multicentre, placebo-controlled trial

1961 participants with overweight or obesity

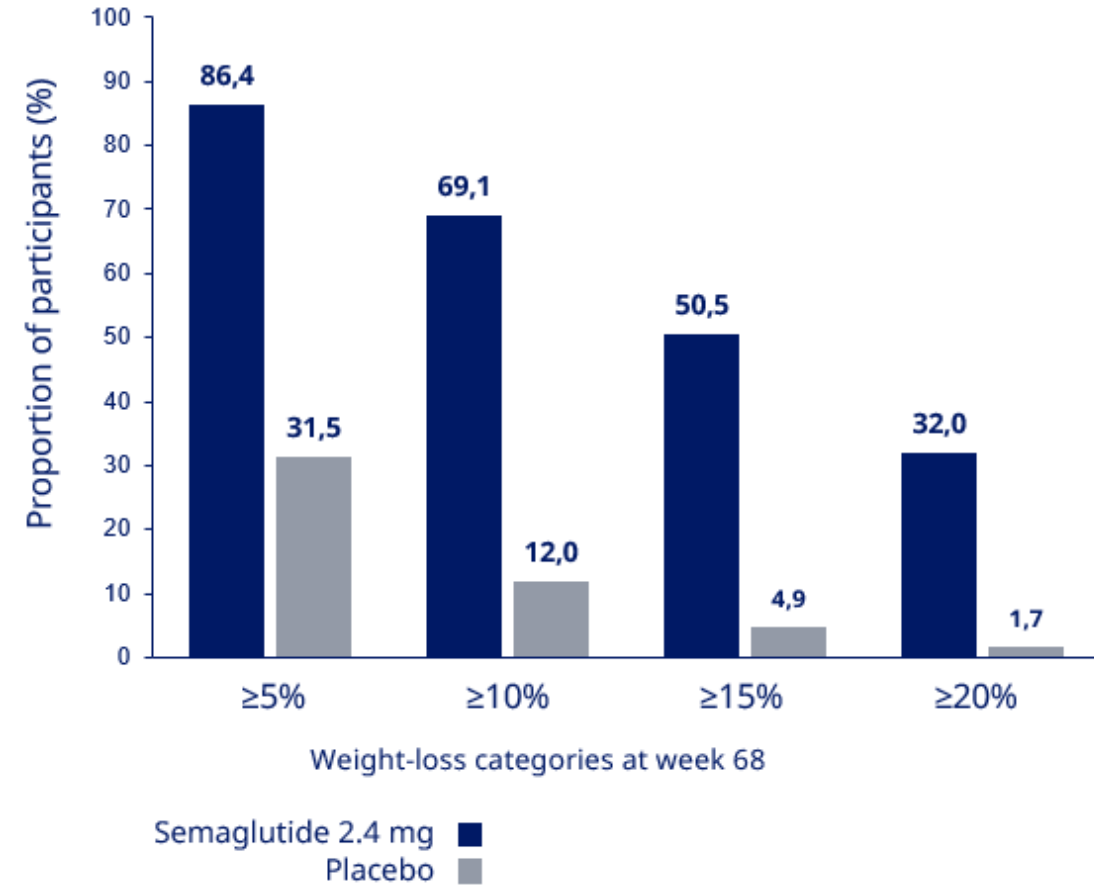
- Male or female ≥ 18 years
- BMI: ≥ 30 kg/m² or ≥ 27 kg/m² and ≥ 1 comorbidity
- Stable body weight ≥ 90 days
- HbA_{1c} < 6.5%



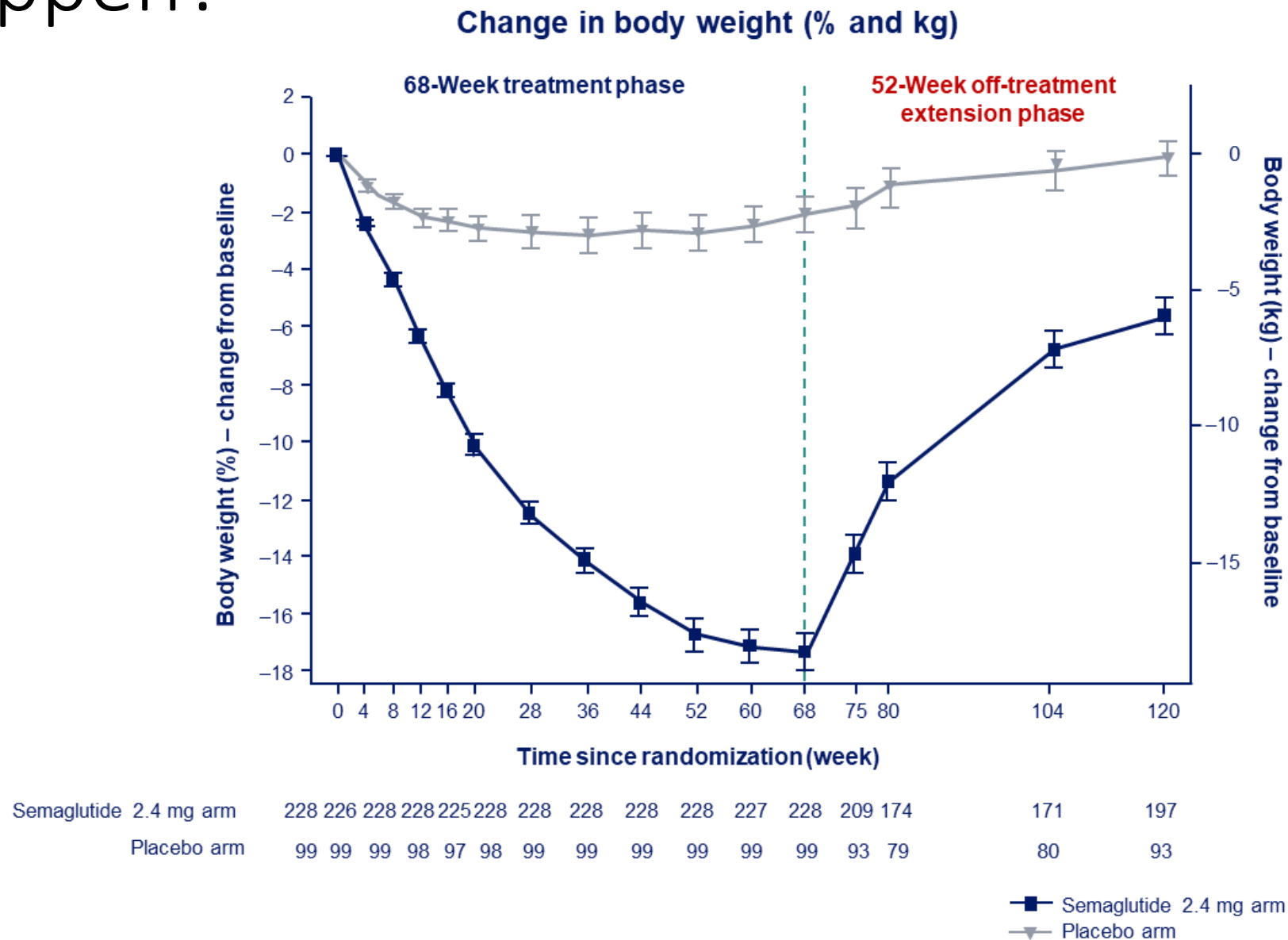
Semaglutide 2,4mg



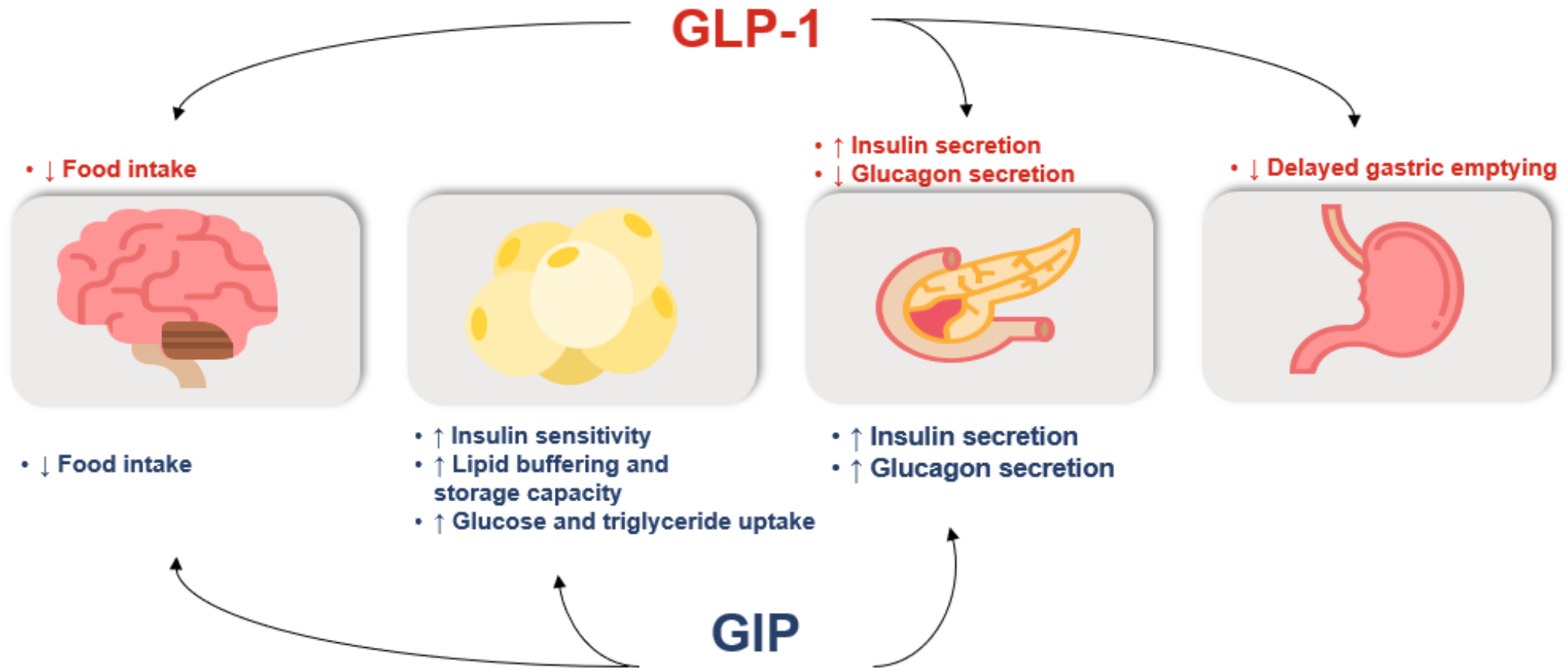
In-trial



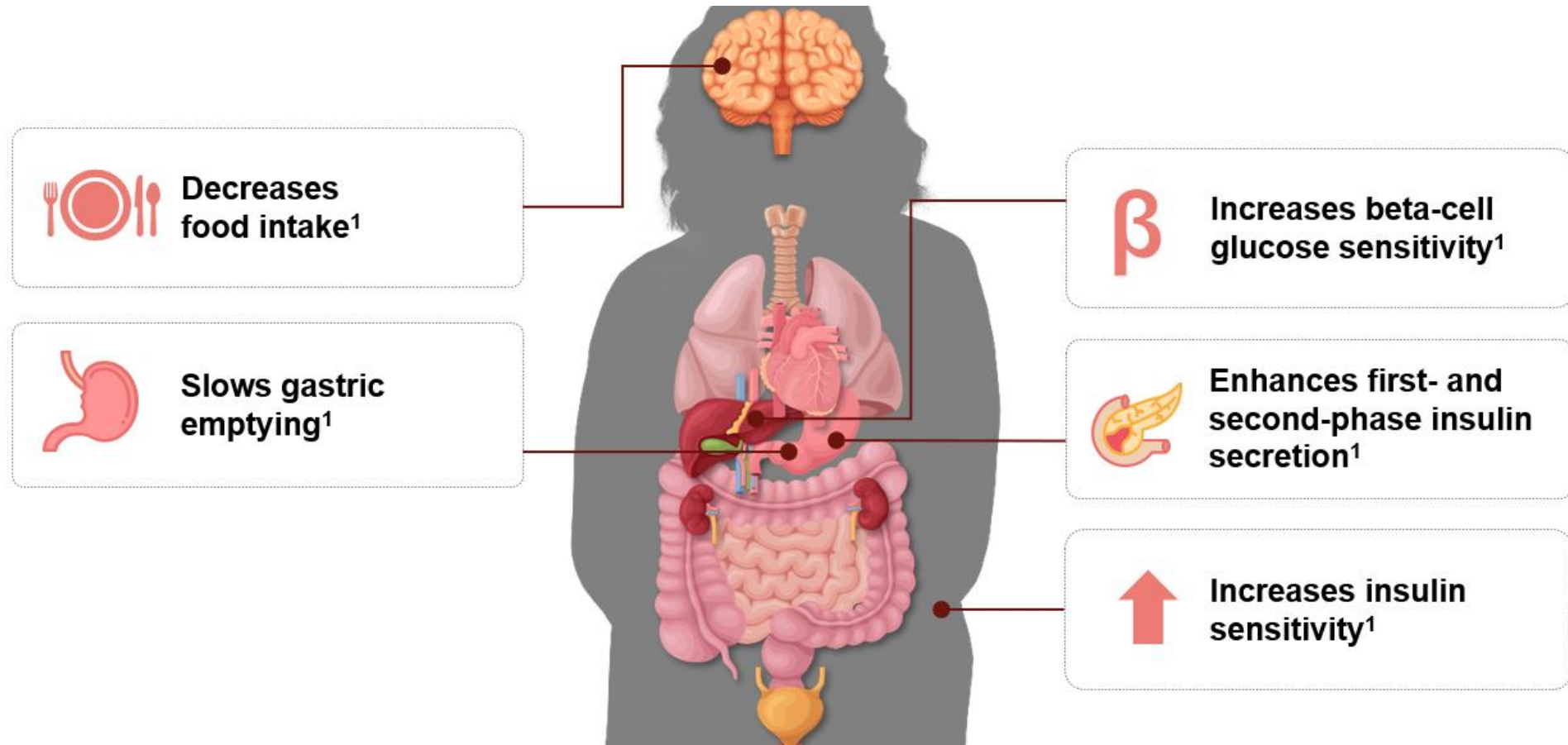
Wat na stoppen?



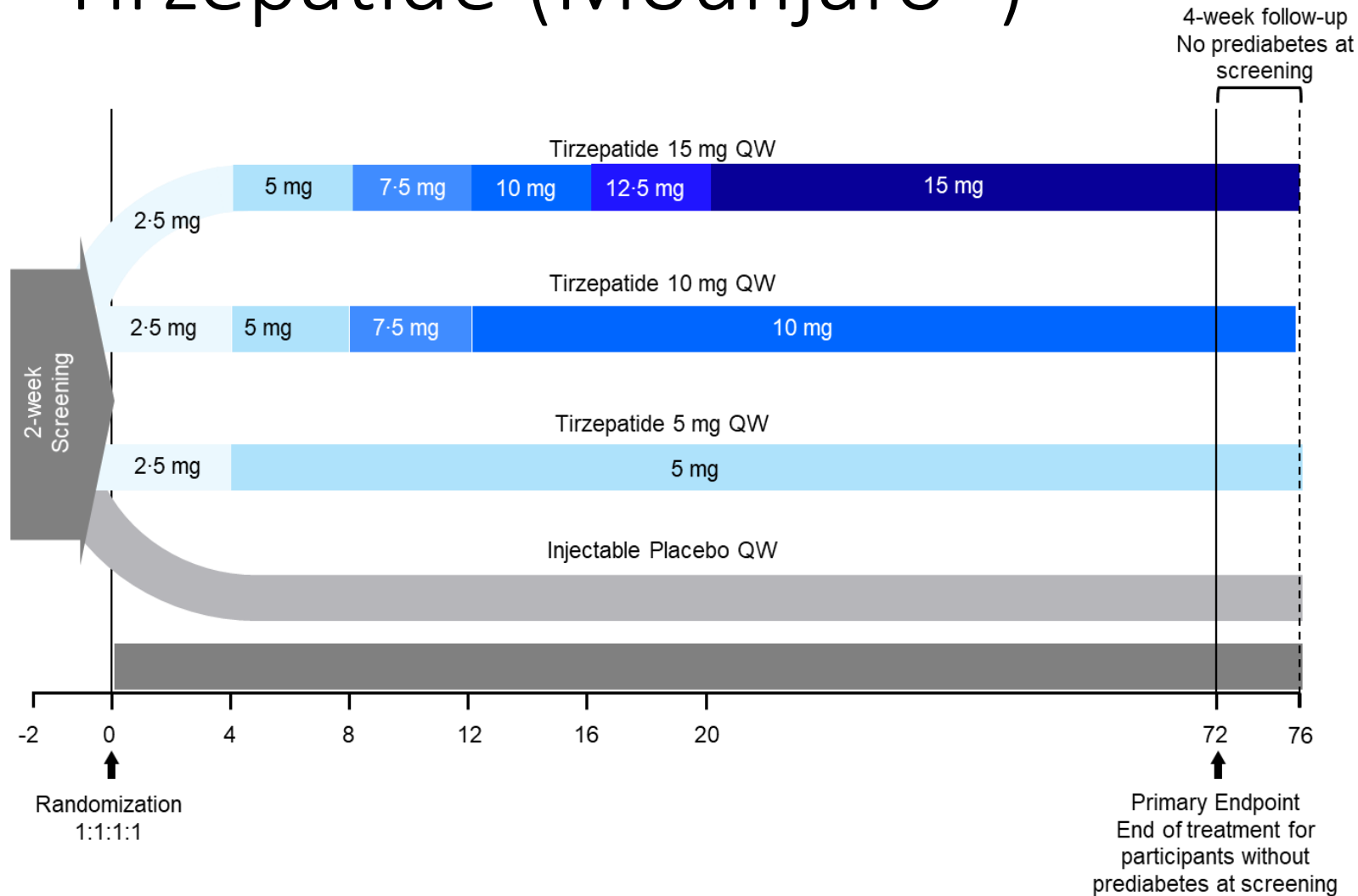
GLP-1/GIP analog



GLP-1/GIP analog



Tirzepatide (Mounjaro®)

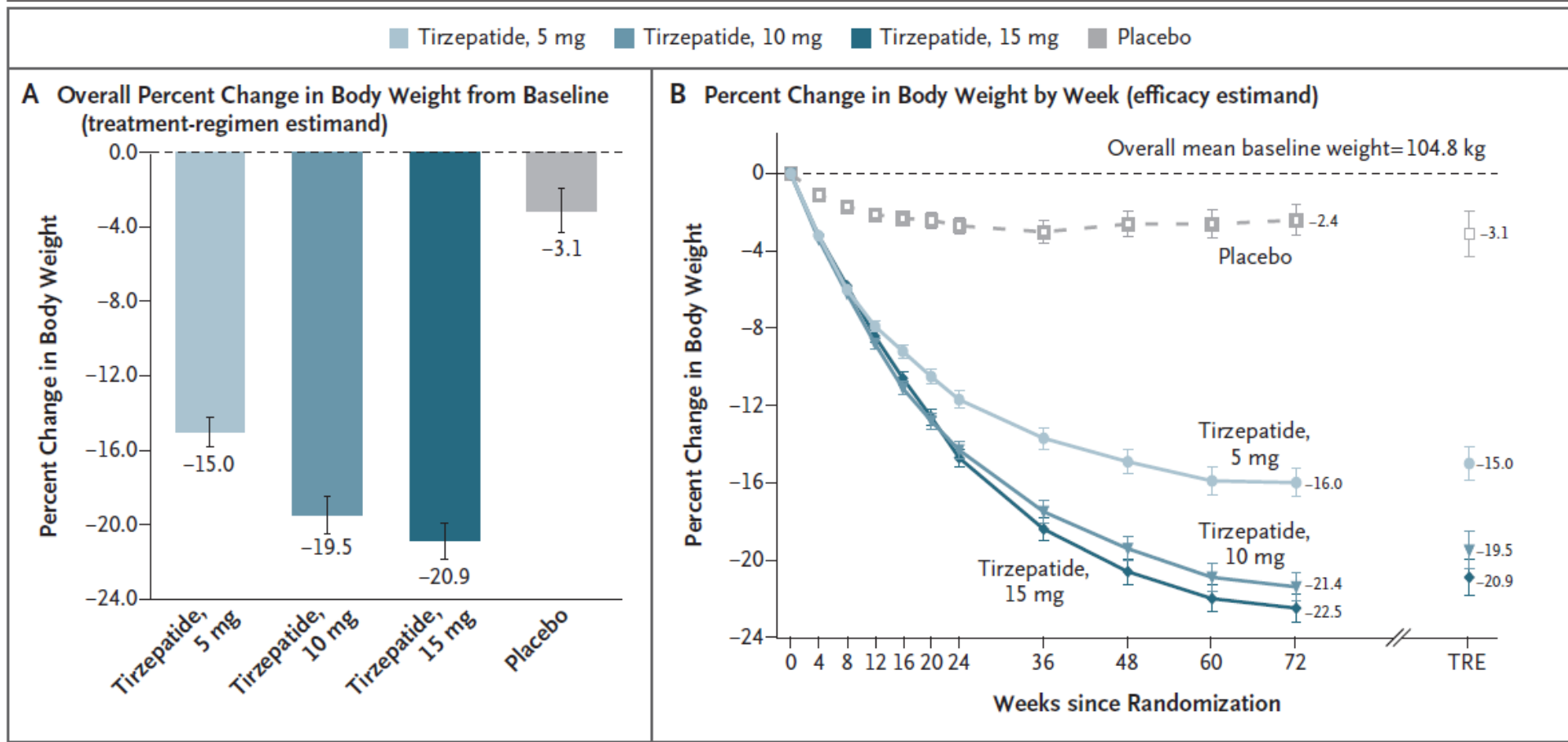


SURMOUNT TRIAL

Inclusiecriteria

- ≥ 18 jaar
- BMI $\geq 30 \text{ kg/m}^2$ of $\geq 27 \text{ kg/m}^2$ en ≥ 1 comorbiditeit (AHT, dyslip, OSAS, CV lijden)
- ≥ 1 dieetpoging

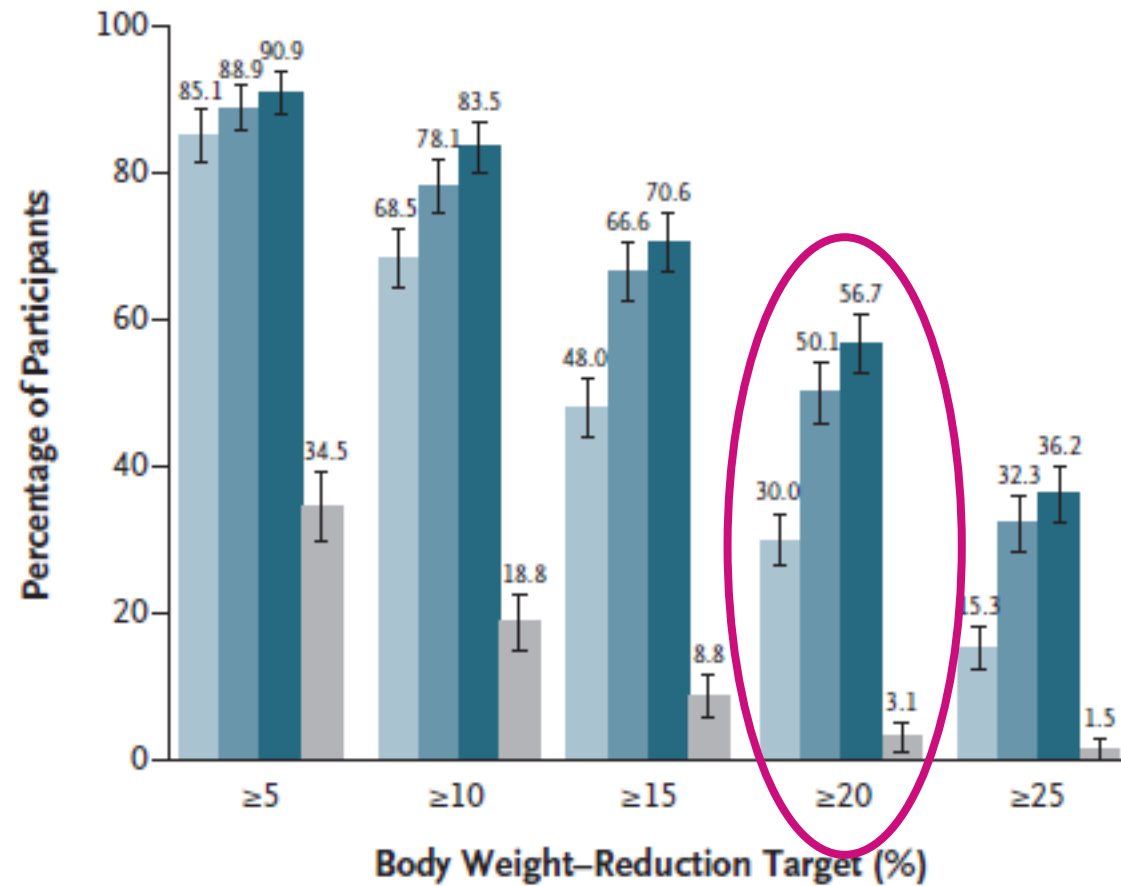
Tirzepatide



Body weight (kg)	104.8 ± 22.1
BMI (kg/m ²)	38.0 ± 6.8

Tirzepatide

C Participants Who Met Weight-Reduction Targets
(treatment-regimen estimand)



Tirzepatide

	Tirzepatide 5 mg (N=630)	Tirzepatide 10 mg (N=636)	Tirzepatide 15 mg (N=630)	Placebo (N=643)
Adverse events leading to discontinuation of study drug n (%)	27 (4.3)	45 (7.1)	39 (6.2)	17 (2.6)
Nausea n (%)	6 (1.0)	7 (1.1)	12 (1.9)	2 (0.3)
Diarrhea n (%)	2 (0.3)	5 (0.8)	3 (0.5)	0
Abdominal pain n (%)	0	2 (0.3)	3 (0.5)	0
Vomiting n (%)	0	4 (0.6)	0	0
Discontinuation of study drug due to gastrointestinal events (%)	1.9	4.4	4.1	0.5

	Tirzepatide 5 mg (N=630)	Tirzepatide 10 mg (N=636)	Tirzepatide 15 mg (N=630)	Placebo (N=643)
Adverse events of special interest n (%)				
Pancreatitis (adjudication-confirmed)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)
Severe or Serious Gastrointestinal Events	11 (1.7)	20 (3.1)	21 (3.3)	7 (1.1)
Gallbladder disease*	5 (0.8)	11 (1.7)	6 (1.0)	5 (0.8)

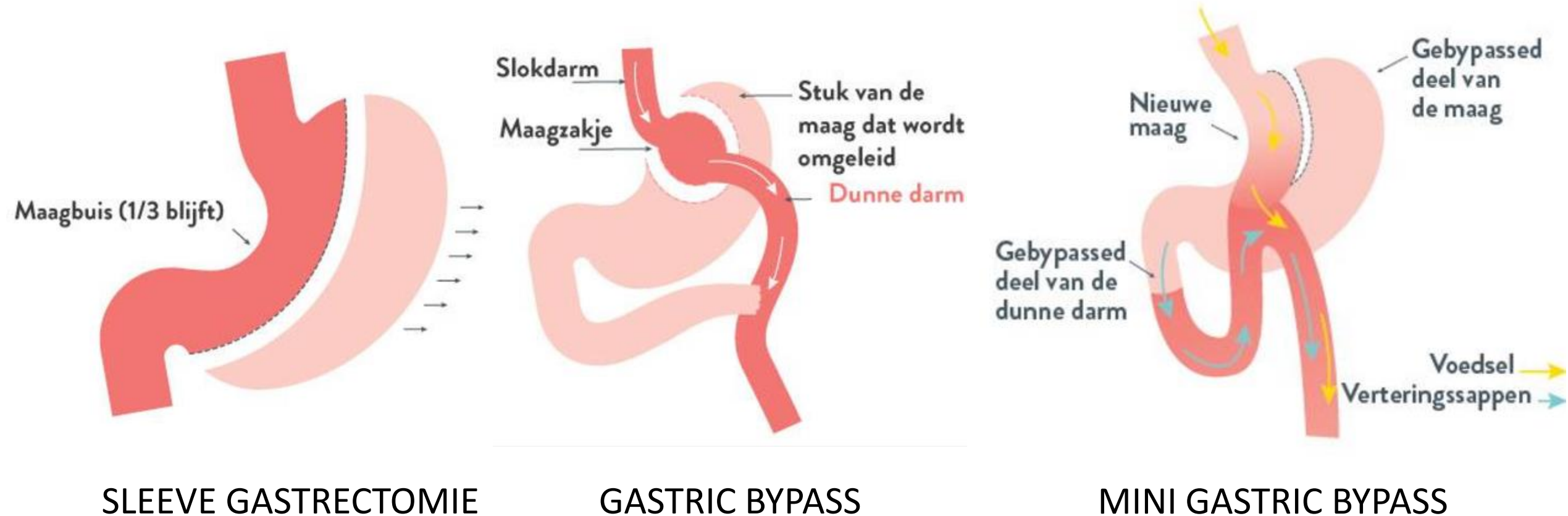
Samengevat

	Orlistat	Mysimba	Saxenda 3mg	Tirzepatide 5mg
Gewichtsverlies	<5%	+/- 5%	8%	15% (à 21%)
Werking	↓ GI vetresorptie	↓ appetijt	↓ appetijt ↑ insulinesecretie ↑ maaglediging	Idem + ↑ insulinesens
Bijwerkingen	Steatorroe	AHT, angst, insomnie, droge mond, hoofdpijn, GI	GI	GI
Kostprijs	€66/m	€105/m	€245/m	€233/m
Keuze		Binge eating, craving Rookstop	Metabool sy	Metabool sy
CI	Malabsorptie	Ongecontr AHT / psychisch lijden	Pancreatitis? MTC / MEN2	Pancreatitis? MTC / MEN2

Informeer je patiënt

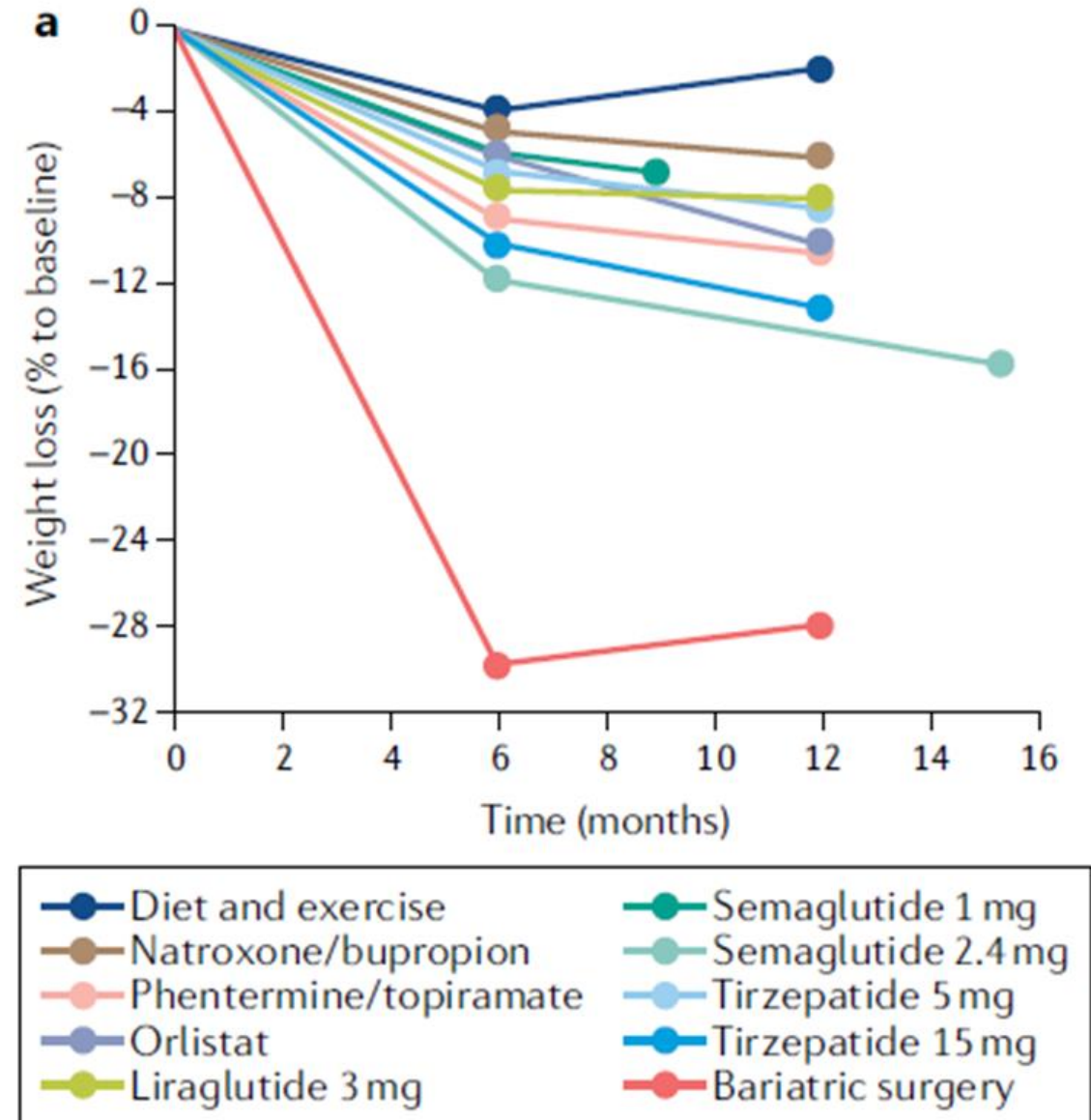
- Niet iedereen is responder
- Bijwerkingen
- Verlies vetmassa, maar ook verlies van lean mass
- Prijs (géén terugbetaling)
- Stockbreuk
- Gewichtstoename na stoppen

Bariatrische heelkunde

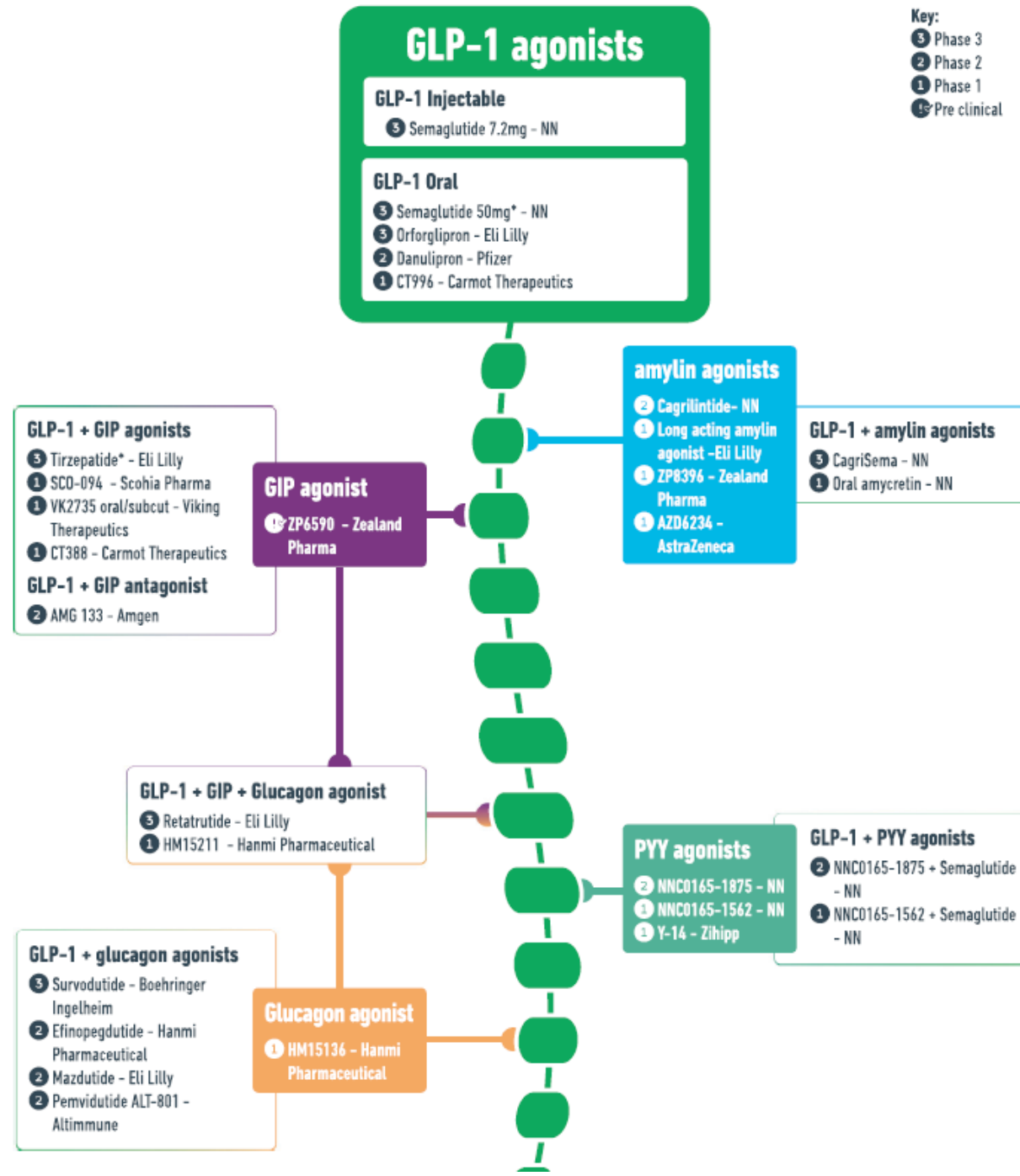


Farmacotherapie of bariatrie?

- “Double digit” weight loss
- **5-10% gewichtsverlies:**
significant effect op HbA1c,
bloeddruk, lipiden
- **>10-15% gewichtsverlies:**
remissie co-morbiditeiten
- Beste cijfers: bariatrische
heelkunde



Toekomst?



Bedankt voor Uw aandacht

Interessante websites

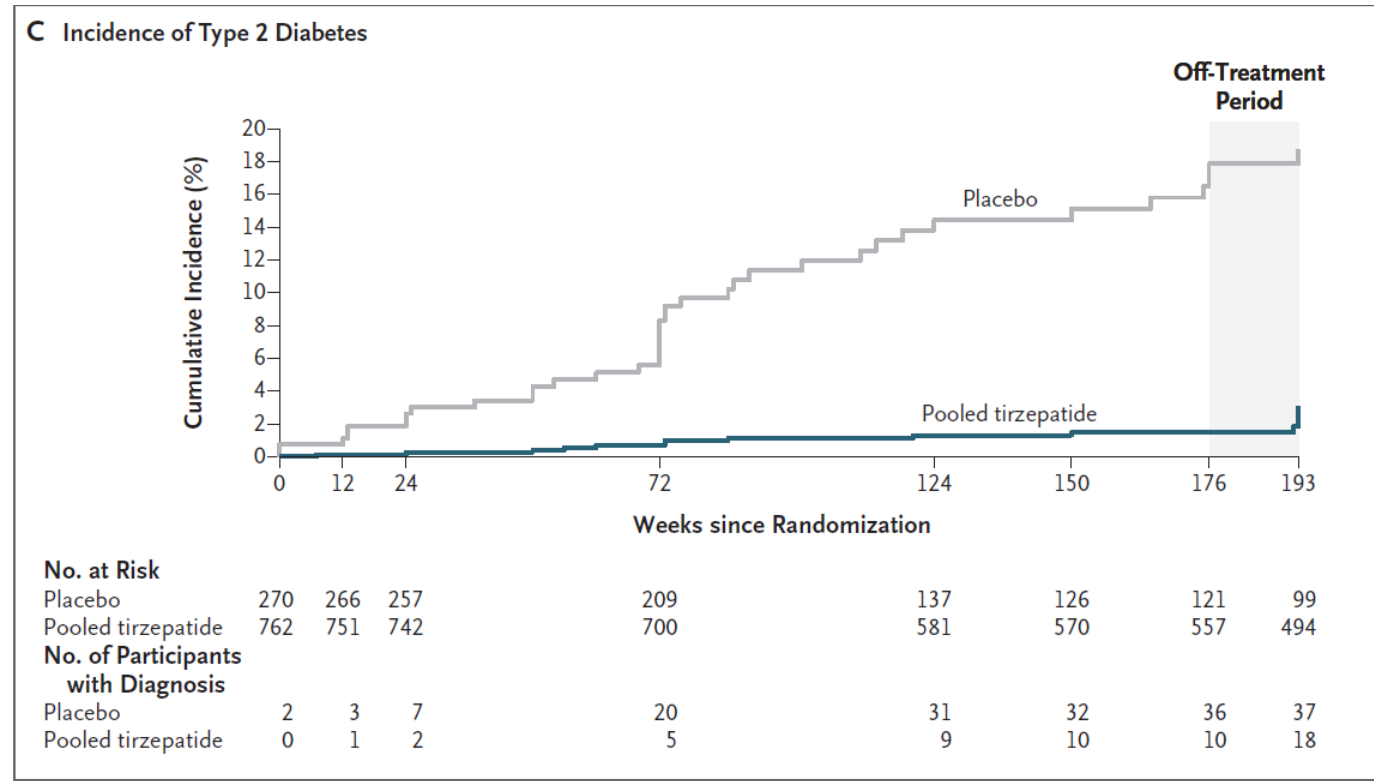
- BASO : <https://belgium.easo.org/nl/>
- Eetexpert : <https://eetexpert.be/>
- Beweging op verwijzing :
<https://www.gezondleven.be/projecten/bewegen-op-verwijzing>

Reserve slides

EOSS-stadium			
0	Eerste lijn		
1			
2		Ambulante gespecialiseerde zorg	
3			Obesitaskliniek
4			

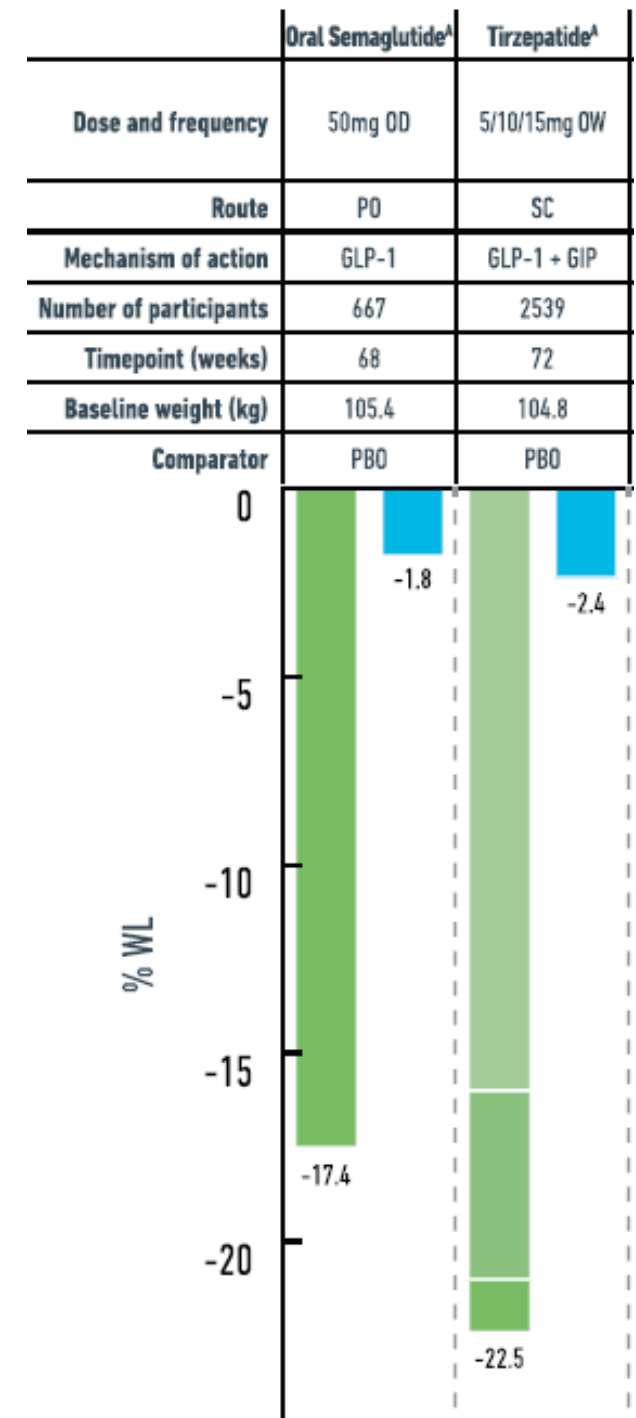
Figuur 4. Koppeling van EOSS-stadia aan eerstelijns-, en gespecialiseerde zorg.

Na 3 jaar Tirzepatide gebruik



Semaglutide PO

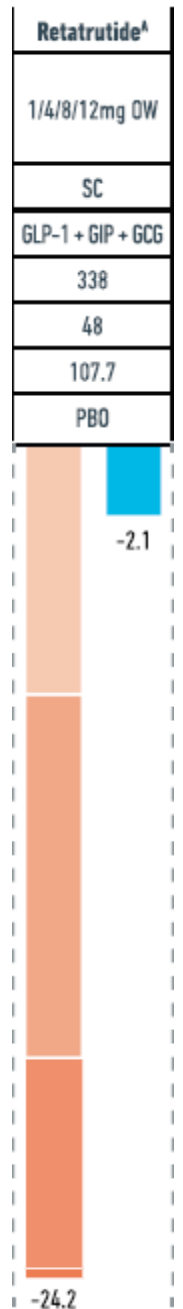
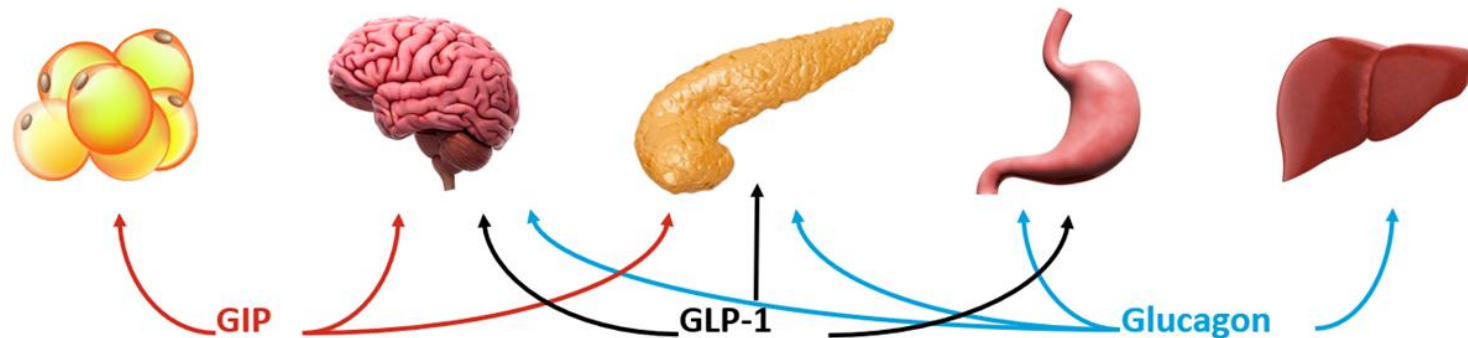
- 50mg/dag
- 17,4% gewichtsverlies
- Krachtiger dan Semaglutide SC 2,4mg
- Uptake?



GLP-1-GIP-Glucagon agonist

Retatrutide

- SC injectie
- 24,2 % gewichtsverlies
- Afname leversteatose



Pathofysiologie
= complex

