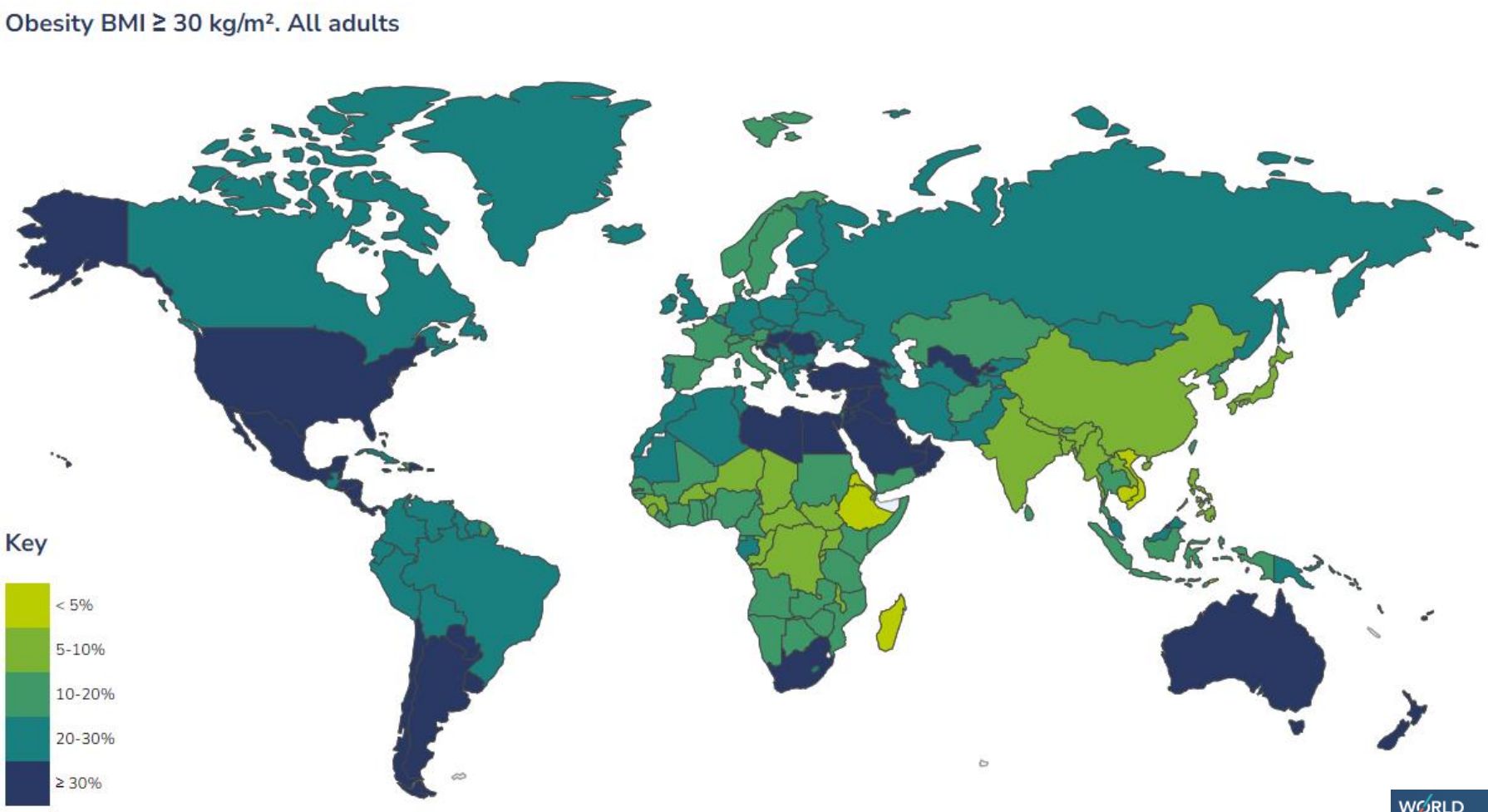
Surpoids, obésité et lipoedème

Dre Lucie FAVRE

Centre d'obésité CHUV

Lausanne, 31 octobre 2024

Estimates of prevalence of obesity in adults



The worldwide prevalence of obesity has **more than TRIPLED** between 1975 and 2022

1 billion people living with obesity

880 million adults
159 million children

WORLD OBESITY | Global Obesity Observatory

Date last updated August 23, 2024

Global Obesity Trend by Gender 2020-2035

World Obesity Atlas 2023

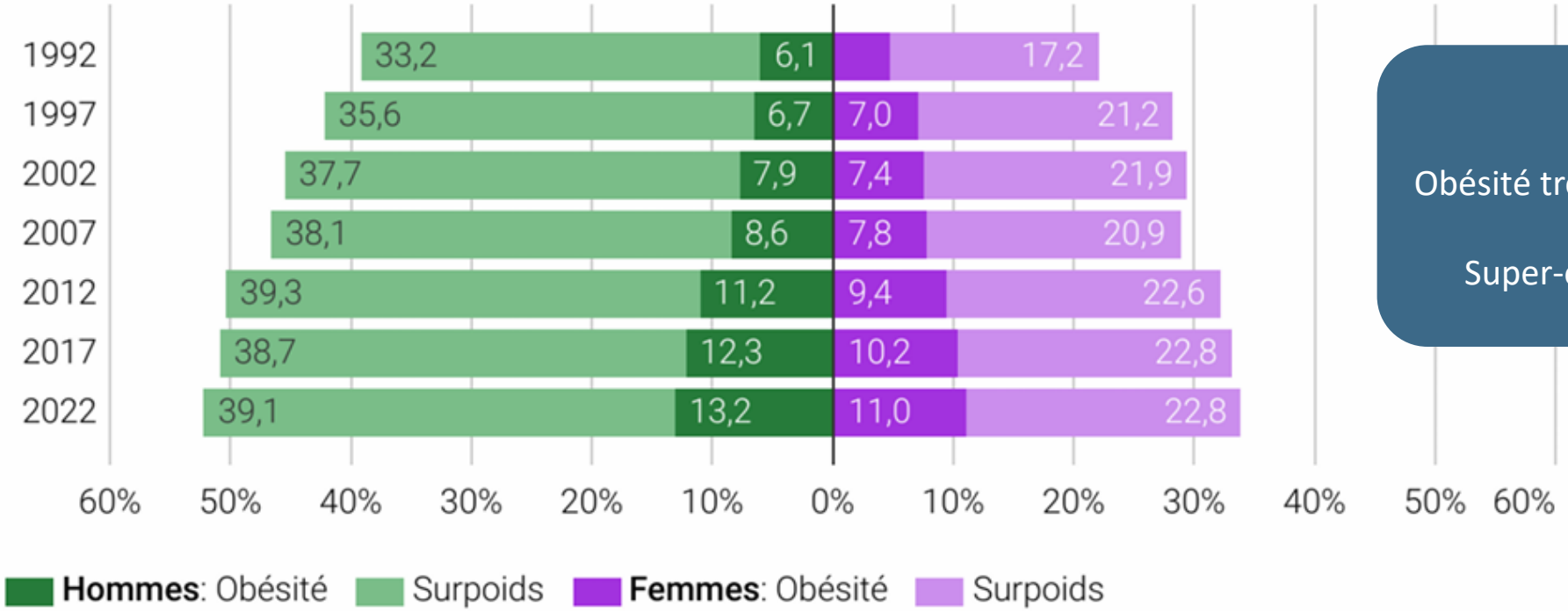
Adults (aged 20 years and over)

	Men 2020	Men 2025	Men 2030	Men 2035
Number with obesity (millions)	347	439	553	690
Proportion of all men	14%	16%	19%	23%
	Women 2020	**Women 2025**	**Women 2030**	**Women 2035**
Number with obesity (millions)	466	568	693	842
Proportion of all women	18%	21%	24%	27%

Enquête suisse sur la santé 2022

Surpoids et obésité

Population de 15 ans et plus vivant en ménage privé



?

Obésité très sévère BMI ≥ 40 kg/m²

Super-obésité BMI ≥ 50 kg/m²

Source: OFS – Enquête suisse sur la santé (ESS)

Agenda

Pathophysiologie Lipoedème

Traitement Conservateur

GLP-1 RA
GLP-1/GIP RA

Activité physique Lipoedème

Traitement chirurgical Lipoedème

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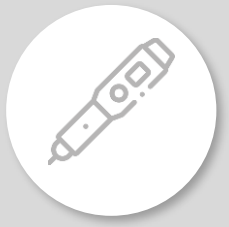
Pathophysiologie Lipoedème

Traitement Conservateur

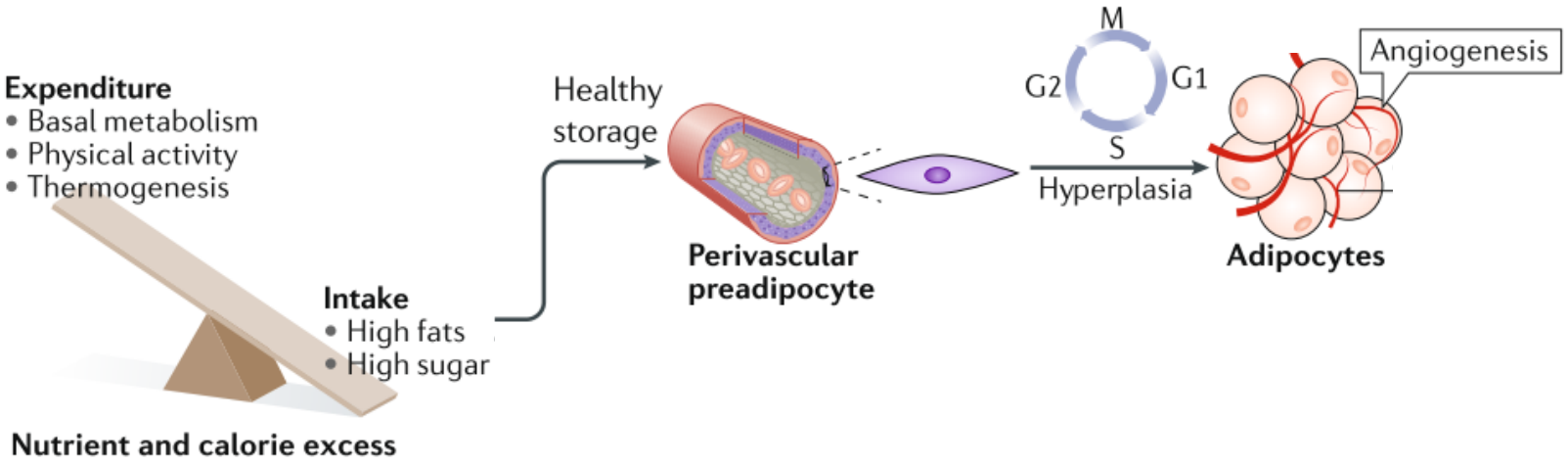


GLP-1 RA
GLP-1/GIP RA

Activité physique Lipoedème

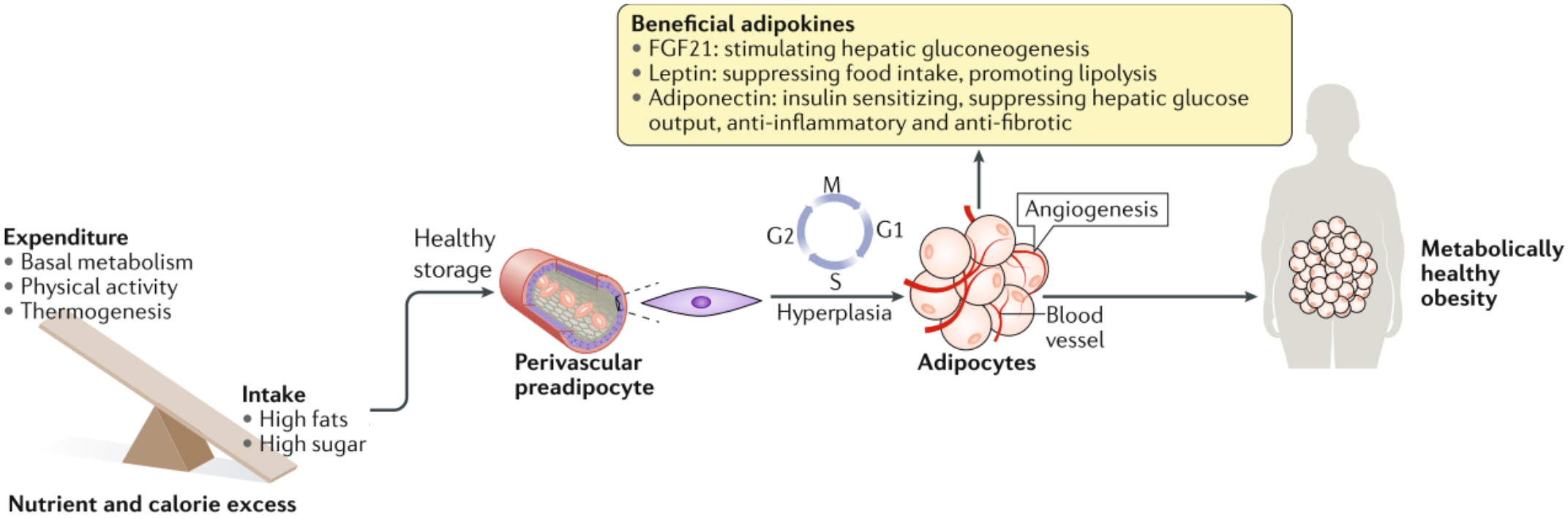
Traitement chirurgical Lipoedème

Adiposopathy or « Sick Fat »



Adapted: Ghaben AL, Scherer PE. Adipogenesis and metabolic health. Nat Rev Mol Cell Biol 2019;20:242-58.

Adiposopathy or « Sick Fat »



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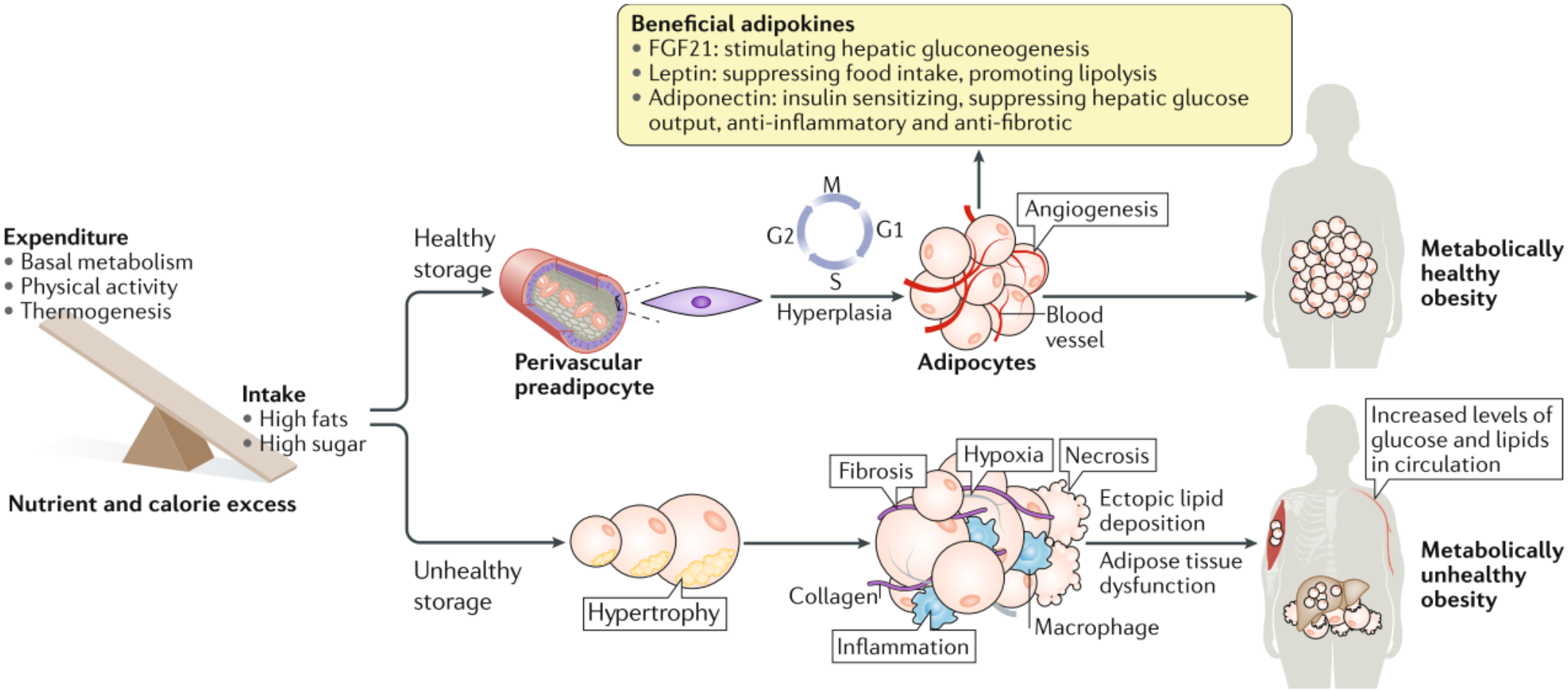
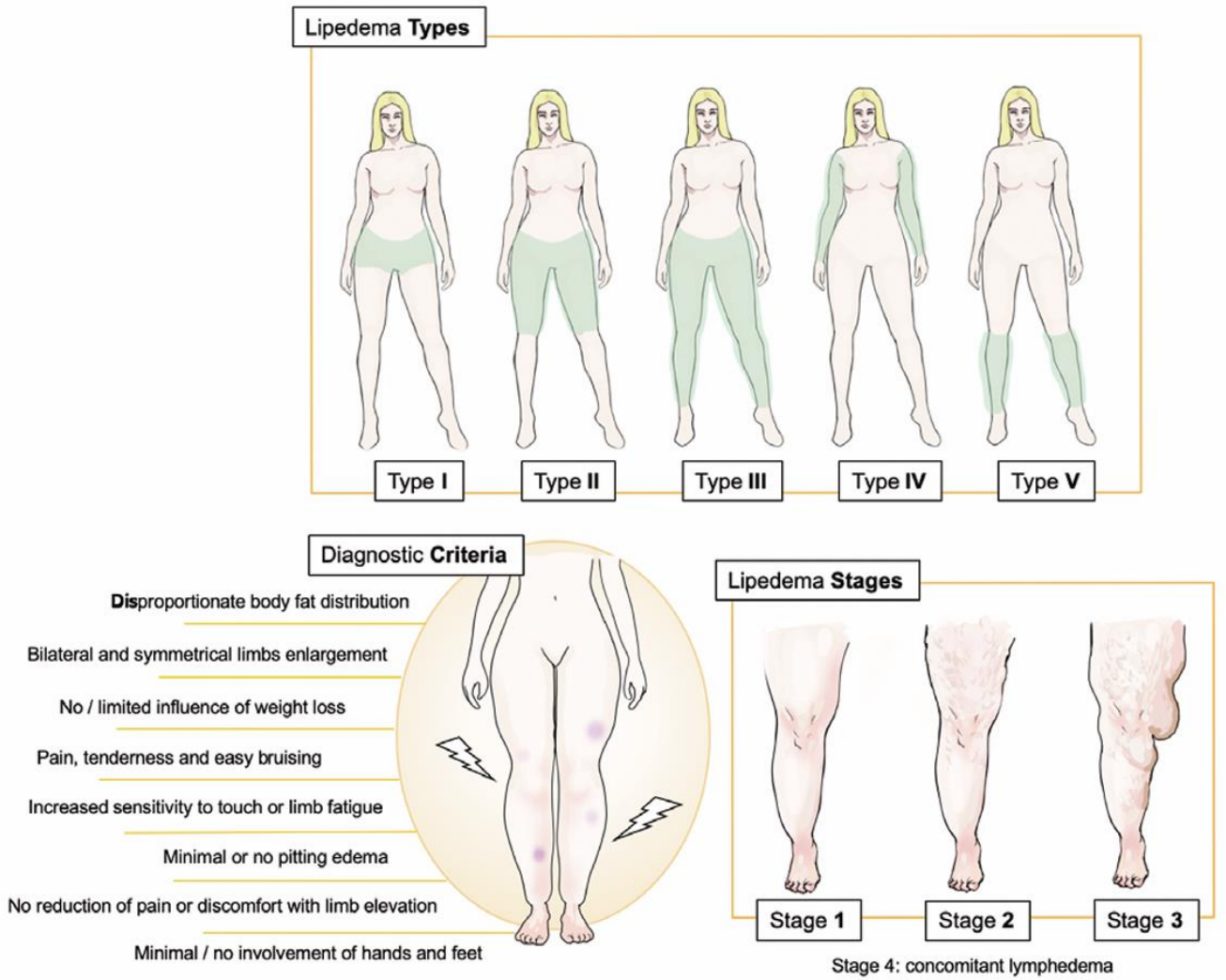


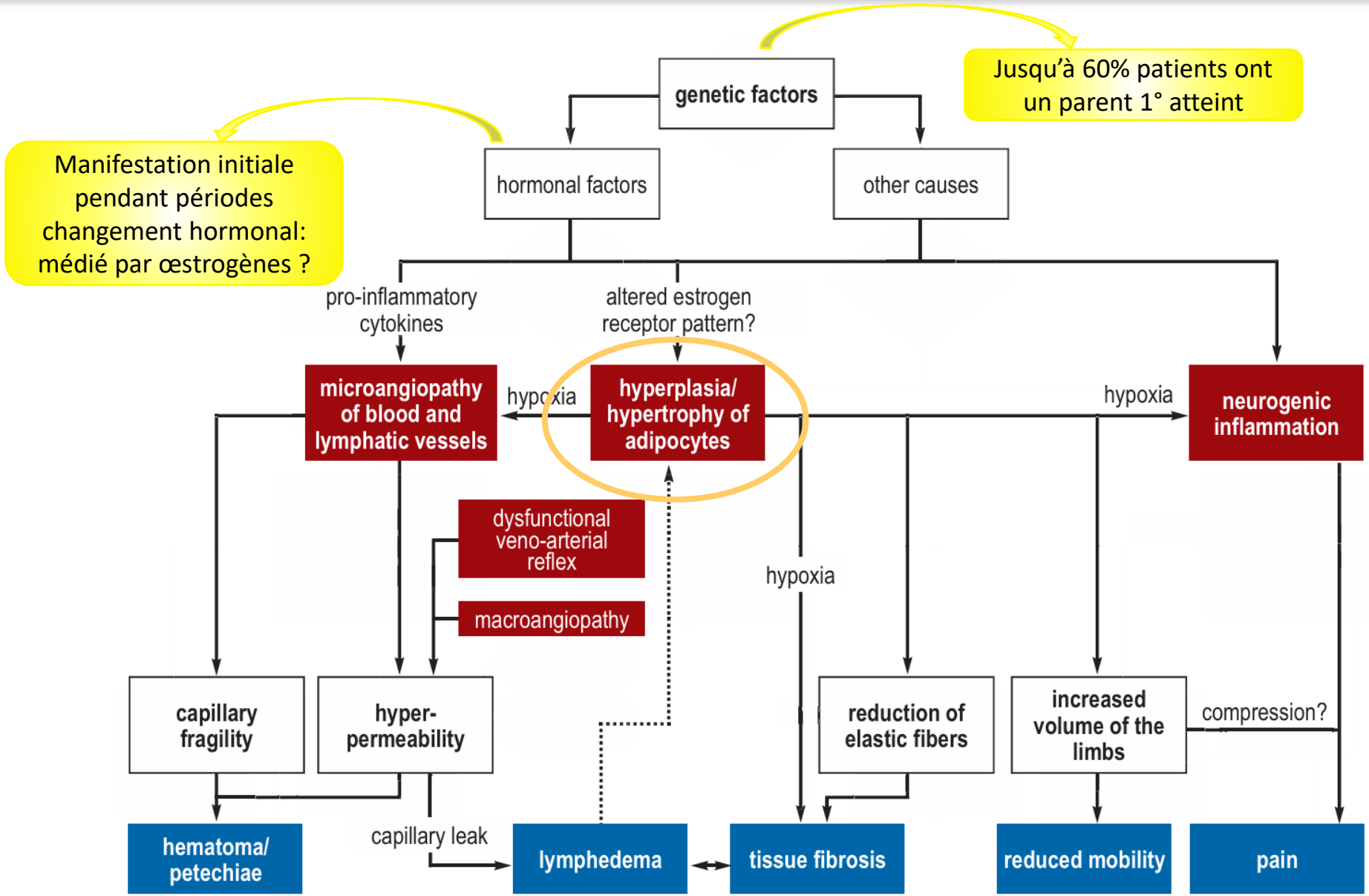
Ghaben AL, Scherer PE. Adipogenesis and metabolic health. Nat Rev Mol Cell Biol 2019;20:242-58.

Lipedema



Buso et al. Obesity Fact 2022.

Pathophysiology Lipedema

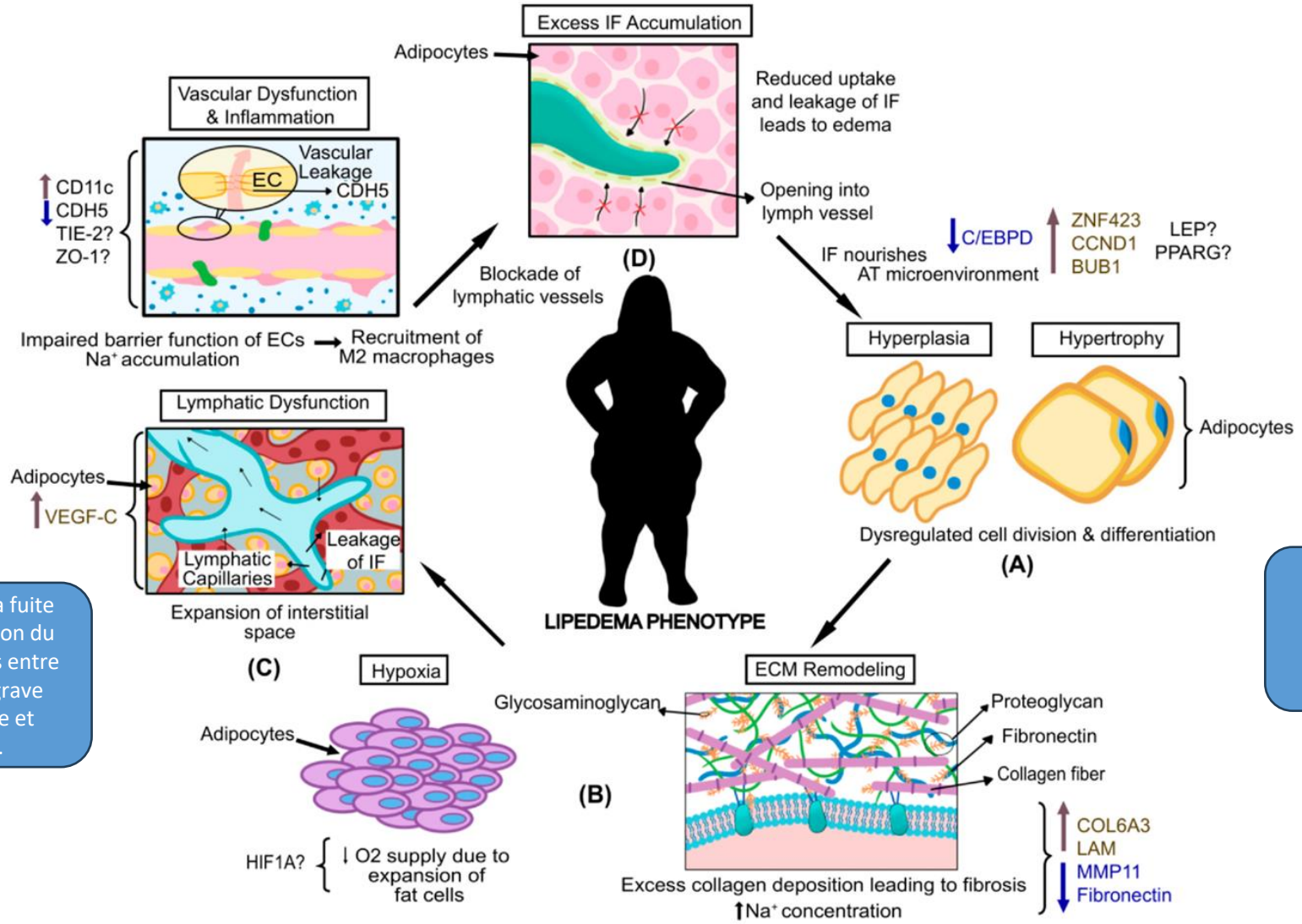


Kruppa et al. Dtsch Artzebl Int 2020.

Pathophysiology Lipedema

La capacité des capillaires lymphatiques à absorber le liquide interstitiel est diminuée, ce qui entraîne une fuite du FI, favorise le dysfonctionnement lymphatique et l'expansion de l'espace interstitiel.

La perméabilité endothéliale et la fuite paracellulaire augmentent en raison du relâchement des jonctions serrées entre les cellules endothéliales ➔ aggrave encore la dégradation vasculaire et provoque une inflammation.



La croissance excessive des adipocytes entraîne une réduction de l'apport en oxygène et un remodelage de la matrice extracellulaire (MEC)

Poojari et al. Biomedicines 2022

Health Implications of Lipedema

Health Implications of Lipedema: Analysis of Patient Questionnaires and Population-Based Matched Controls

Sally Kempa

Life **2024**, *14*, 295. https://doi.org/10.3390/life14030295

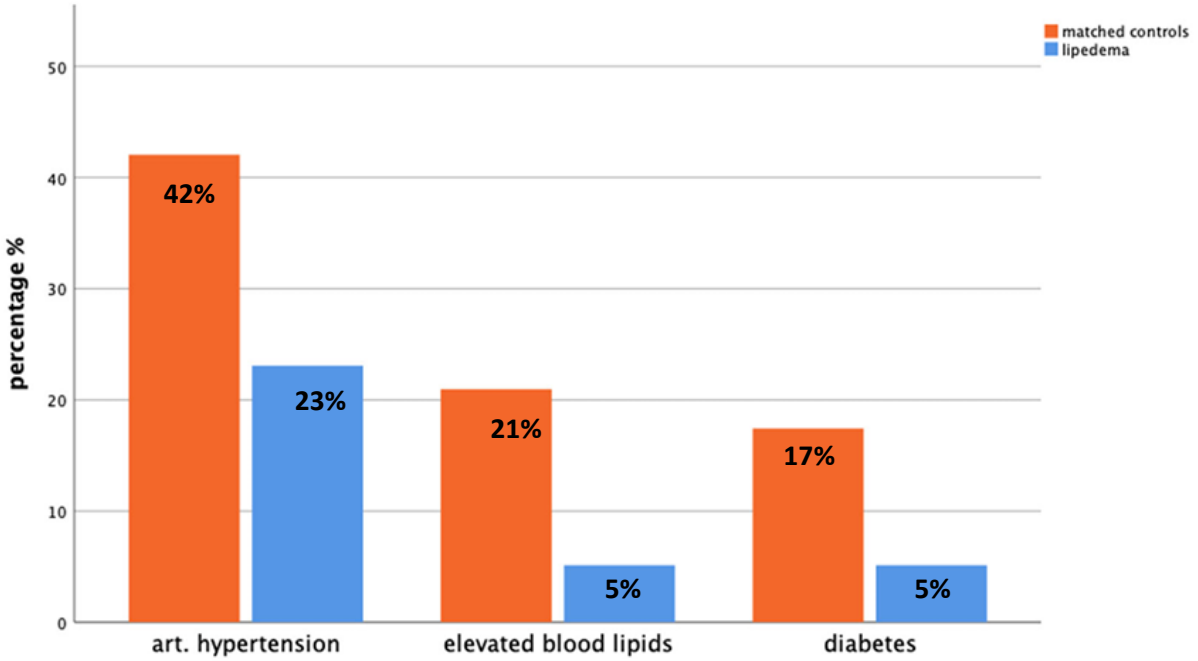
Patient population

39 patients BMI with
- Lipedema stage 1-3
- Female
- 46 yo
- BMI 35 kg/m²

Matching 1:5

Control population

- Age
- Sex
- BMI



Nature distincte lipoedème et de l'obésité

Kempa. Life. 2024

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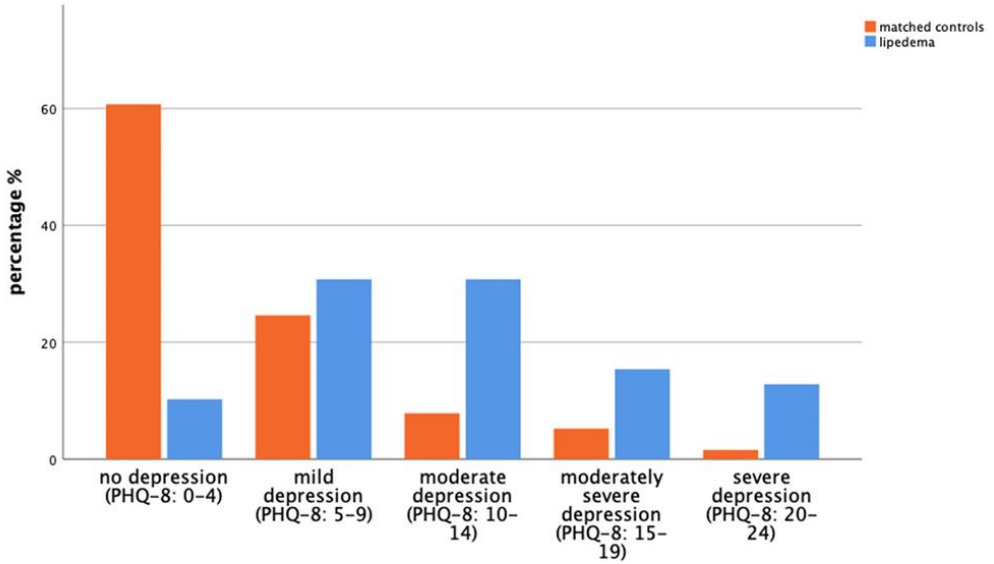

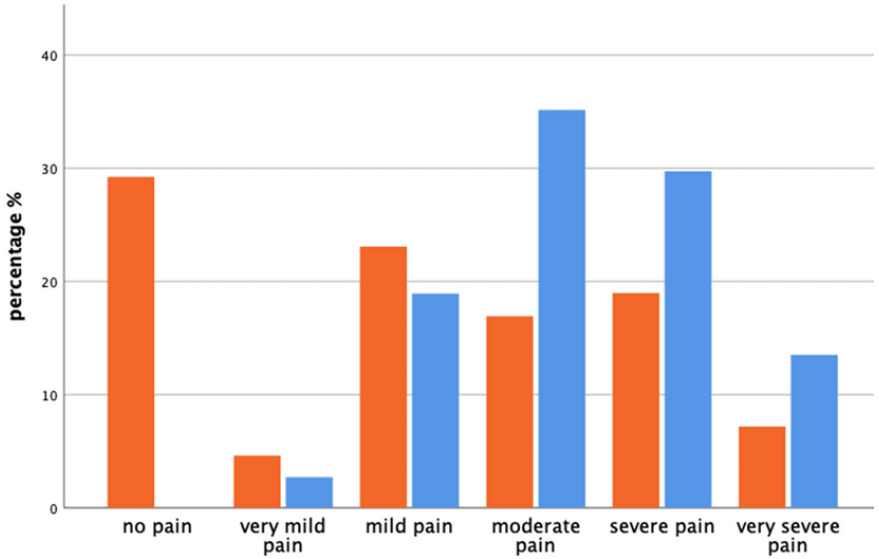

Kempa. Life. 2024

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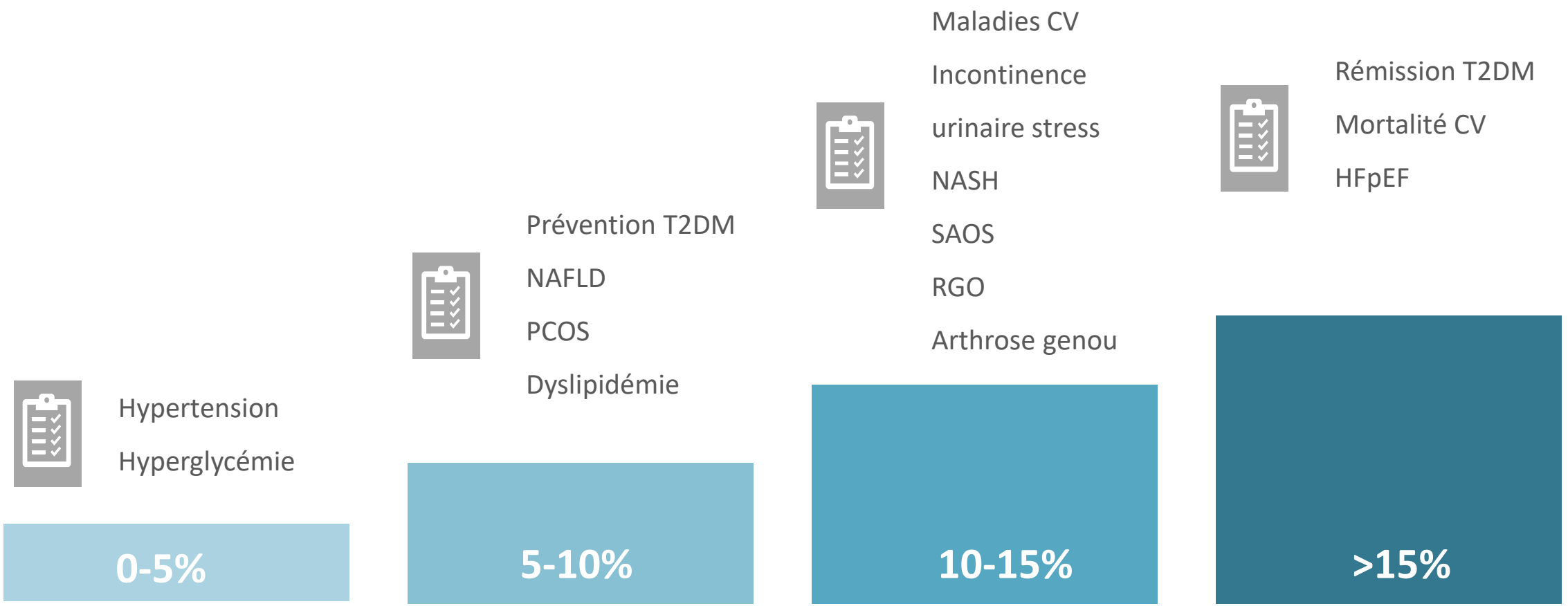
Objectif de perte pondérale



Vers une plus grande perte de poids et une amélioration globale de la santé

Cefalu. Diab Care 2015
Lean et al. Lancet 2018
Sundström et al. Circulation 2017

Régime alimentaire et Lipoedème

Research Article

The Benefits of Low-Carbohydrate, High-Fat (LCHF) Diet on Body Composition, Leg Volume, and Pain in Women with Lipedema

Małgorzata Jeziorek

Journal of Obesity
Volume 2023, Article ID 5826630

Patient population

28 patients
- Lipedema stage 1-3
- Female
- 39 yo
- BMI 34 kg/m^2

7 months

12.9 % weight loss

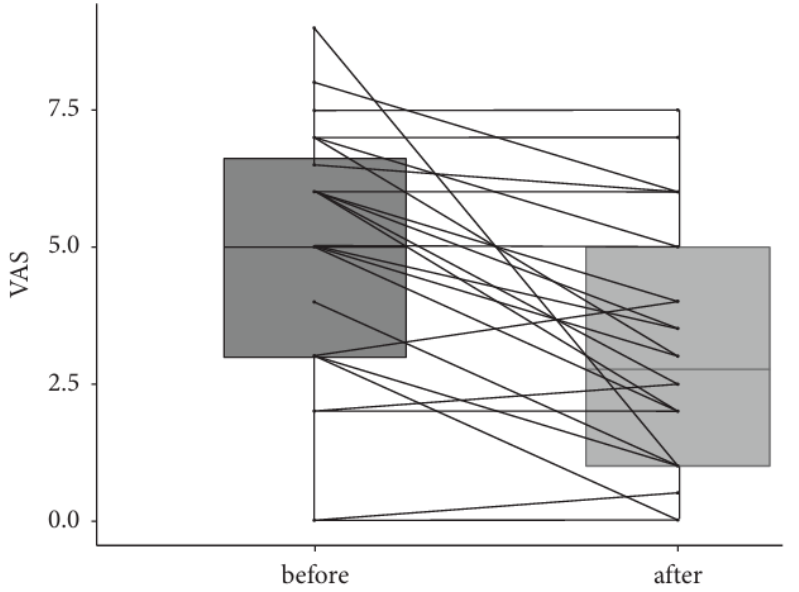


FIGURE 4: Change in pain level of each participant before and after dietary intervention in the lipedema group.

In conclusion, this study contributes valuable insights into the potential benefits of an LCHF diet for reducing weight, body fat mass, and leg volume and managing pain in women with lipedema.

Jeziorek. J Obesity. 2023

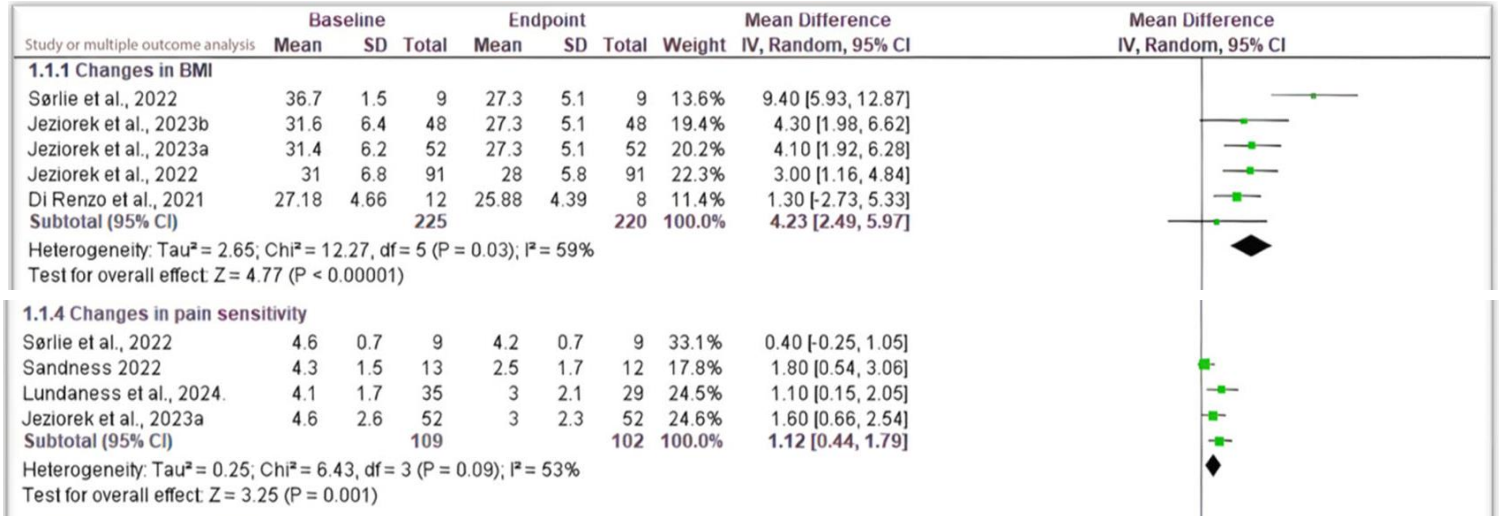
Régime alimentaire et Lipoedème

Systematic Review

The Efficacy of Ketogenic Diets (Low Carbohydrate; High Fat) as a Potential Nutritional Intervention for Lipedema: A Systematic Review and Meta-Analysis

Alexandre Campos Moraes Amato

Nutrients **2024**, *16*,



Study or multiple outcome analysis	Baseline Mean	Baseline SD	Baseline Total	Endpoint Mean	Endpoint SD	Endpoint Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Changes in BMI								
Sørlie et al., 2022	36.7	1.5	9	27.3	5.1	9	13.6%	9.40 [5.93, 12.87]
Jeziorek et al., 2023b	31.6	6.4	48	27.3	5.1	48	19.4%	4.30 [1.98, 6.62]
Jeziorek et al., 2023a	31.4	6.2	52	27.3	5.1	52	20.2%	4.10 [1.92, 6.28]
Jeziorek et al., 2022	31	6.8	91	28	5.8	91	22.3%	3.00 [1.16, 4.84]
Di Renzo et al., 2021	27.18	4.66	12	25.88	4.39	8	11.4%	1.30 [-2.73, 5.33]
Subtotal (95% CI)			**225**			**220**	**100.0%**	**4.23 [2.49, 5.97]**
Heterogeneity: Tau² = 2.65; Chi² = 12.27, df = 5 (P = 0.03); I² = 59%								
Test for overall effect: Z = 4.77 (P < 0.00001)								
1.1.4 Changes in pain sensitivity								
Sørlie et al., 2022	4.6	0.7	9	4.2	0.7	9	33.1%	0.40 [-0.25, 1.05]
Sandness 2022	4.3	1.5	13	2.5	1.7	12	17.8%	1.80 [0.54, 3.06]
Lundaness et al., 2024.	4.1	1.7	35	3	2.1	29	24.5%	1.10 [0.15, 2.05]
Jeziorek et al., 2023a	4.6	2.6	52	3	2.3	52	24.6%	1.60 [0.66, 2.54]
Subtotal (95% CI)			**109**			**102**	**100.0%**	**1.12 [0.44, 1.79]**
Heterogeneity: Tau² = 0.25; Chi² = 6.43, df = 3 (P = 0.09); I² = 53%								
Test for overall effect: Z = 3.25 (P = 0.001)								

Patient population

329

- Lipedema
- Female

5. Conclusions

The aim of this systematic review and meta-analysis was to highlight the potential therapeutic benefits of an LCHF ketogenic diet in treating and managing lipedema. Our findings suggest that the LCHF ketogenic diet can significantly reduce body weight, BMI, pain, and other anthropometric measurements, improving overall quality of life for lipedema patients.

Mean study duration: 15.8 weeks !!??

Amato. Nutrients 2024

Intensive lifestyle intervention DiRECT Trial Scotland

Lean et al. Lancet 2018;391:541-51

298 patients, T2DM dg depuis 6 ans max, sans tt insuline

149 groupe intervention / 149 groupe contrôle

Intervention:

- diet : 12 semaines substituts repas COMPLET (825-850 kcal/j)

Co-primary outcomes:

- Diminution pondérale ≥ 15 kg
- Rémission T2DM :HbA1c < 6.5 % sans ttt depuis 2 mois

	Intervention group (n=149)	Control group (n=149)
Sex		
Female	66 (44%)	56 (38%)
Male	83 (56%)	93 (62%)
White ethnicity	146 (98%)	147 (99%)
Age (years)	52·9 (7·6)	55·9 (7·3)
Weight (kg)	101·0 (16·7)	98·8 (16·1)
Body-mass index (kg/m²)	35·1 (4·5)	34·2 (4·3)
Waist (cm)	107·5 (8·4)	106·5 (8·9)
Systolic blood pressure (mm Hg)	132·7 (17·5)	137·2 (16·0)
Diastolic blood pressure (mm Hg)	84·6 (10·2)	85·5 (8·8)
Time since diabetes diagnosis (years)		
Mean (SD)	3·0 (1·7)	3·0 (1·8)
Median (range)	3·1 (0·0–6·0)	2·6 (0·2–6·0)
HbA_{1c}		
%	7·7 (1·25)	7·5 (1·05)
mmol/mol	60 (13·7)	58 (11·5)
Fasting glucose (mmol/L)	9·22 (3·29)	8·82 (2·54)
Prescribed oral antidiabetic medication	111 (74·5)	115 (77·2)
Number of oral antidiabetic medications		
0	38 (26%)	34 (23%)
1	65 (44%)	79 (53%)
≥2	46 (31%)	36 (24%)

Intensive lifestyle intervention DiRECT Trial Scotland

Lean et al. Lancet 2018;391:541-51

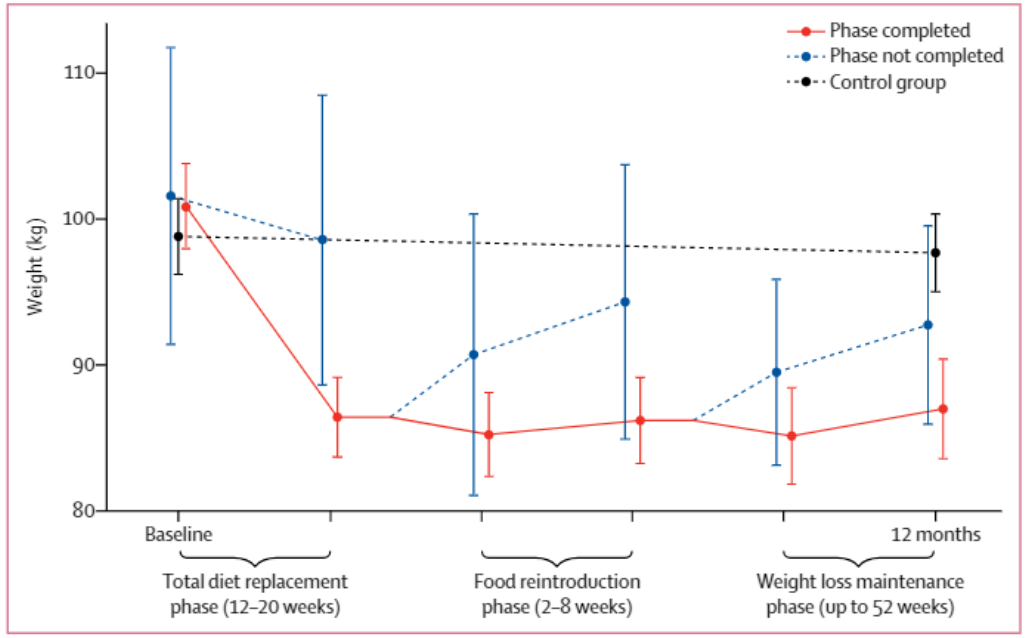
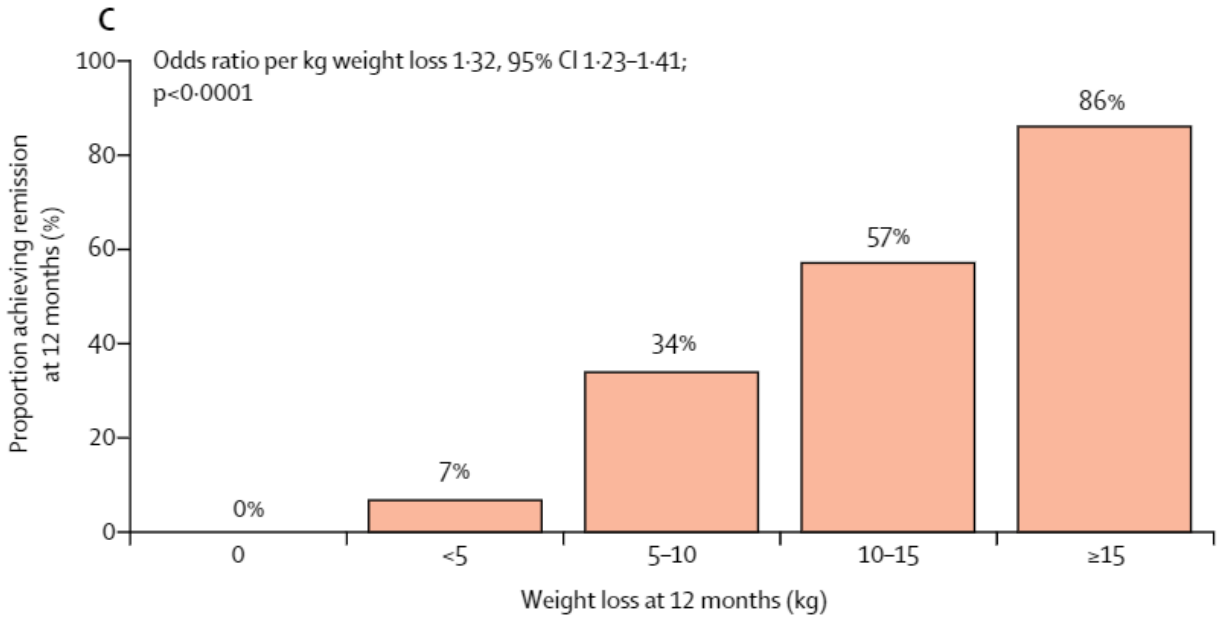


Figure 3: **Change in weight of participants who remained in the trial and those who dropped out during each phase of the intervention**
Error bars represent 95% CIs.

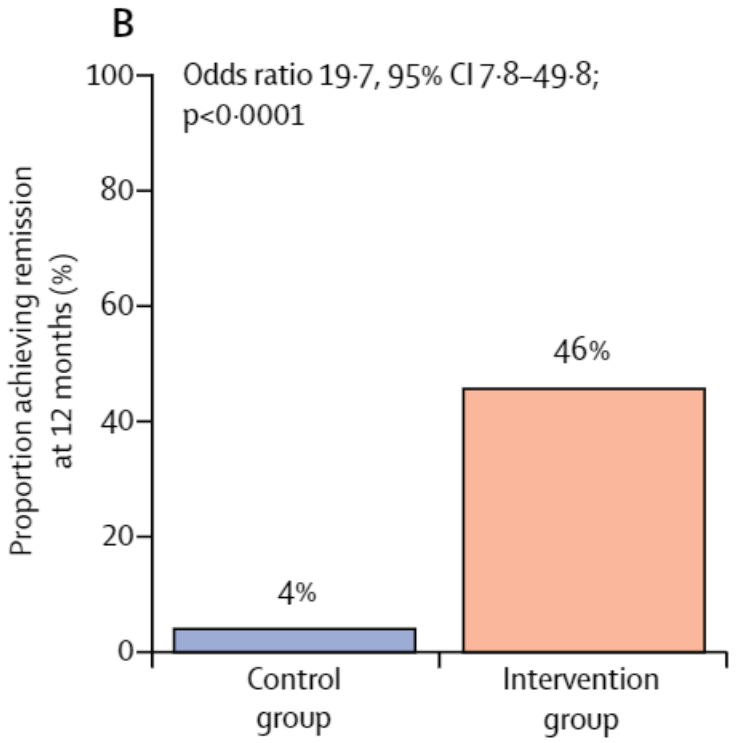


Intensive lifestyle intervention DiRECT Trial Scotland

Lean et al. Lancet 2018;391:541-51

Intervention lifestyle **intensive**

- Perte pondérale significative à 12 mois
- Rémission T2DM 46% participants
- « La rémission du diabète de type 2 est un objectif pratique pour les soins primaires»



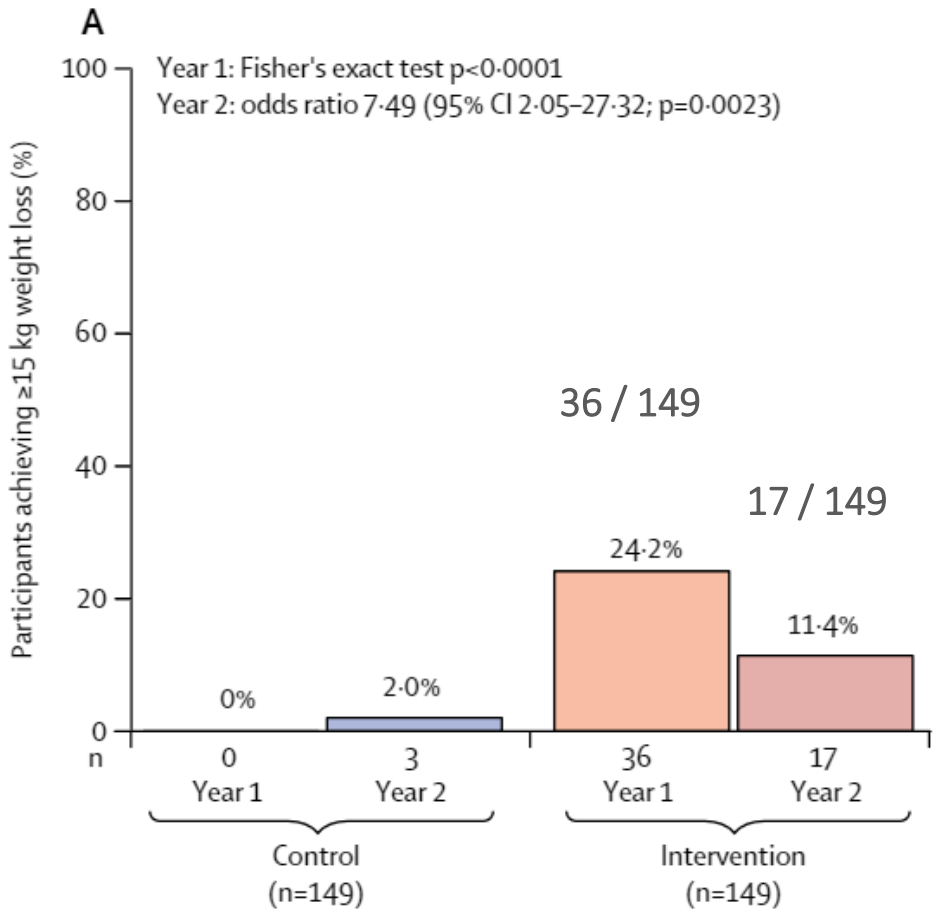
Diabetes remission ➔ HbA1c < 6.5% sans ttt depuis 2 mois

Intensive lifestyle intervention DiRECT Trial DURABILITY ?

Lean et al. Lancet Diabetes Endocrinol 2019;7(5):344-355

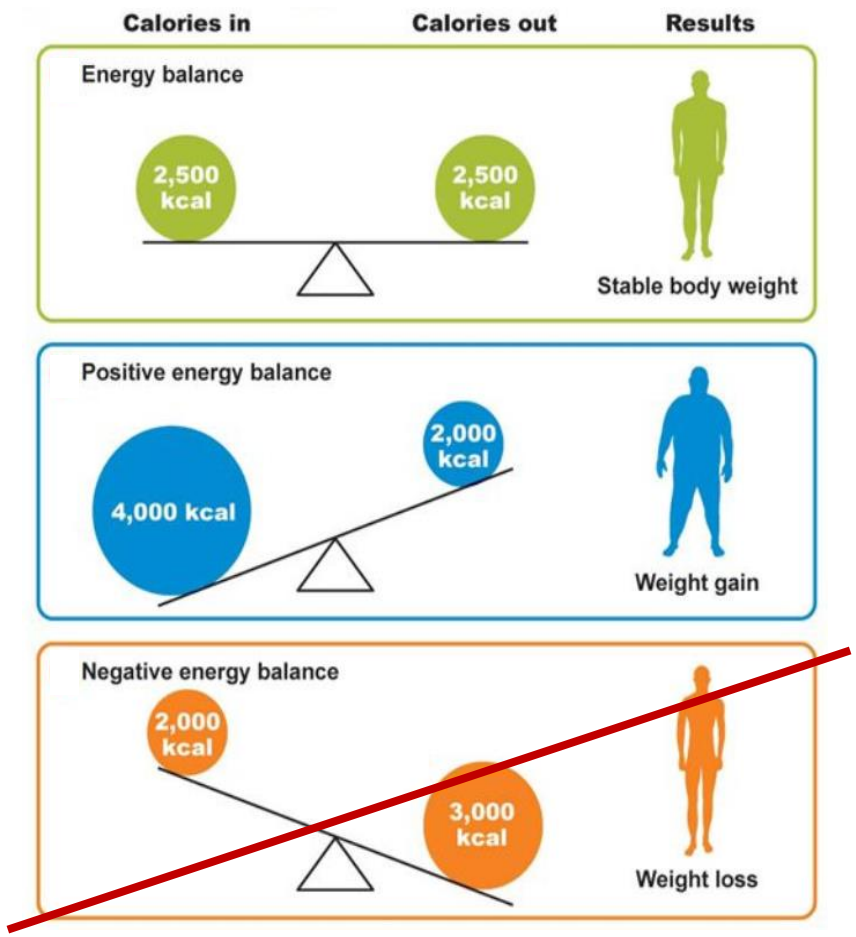
Maintenance phase

- 30 mn/month ; dietician / practice nurse
- > 2 kg weight regain ➔ «rescue plan» = 2-4 wks partial meal replacement
- > 4 kg weight regain ➔ «rescue plan» = 4 wks total diet replacement ± orlistat

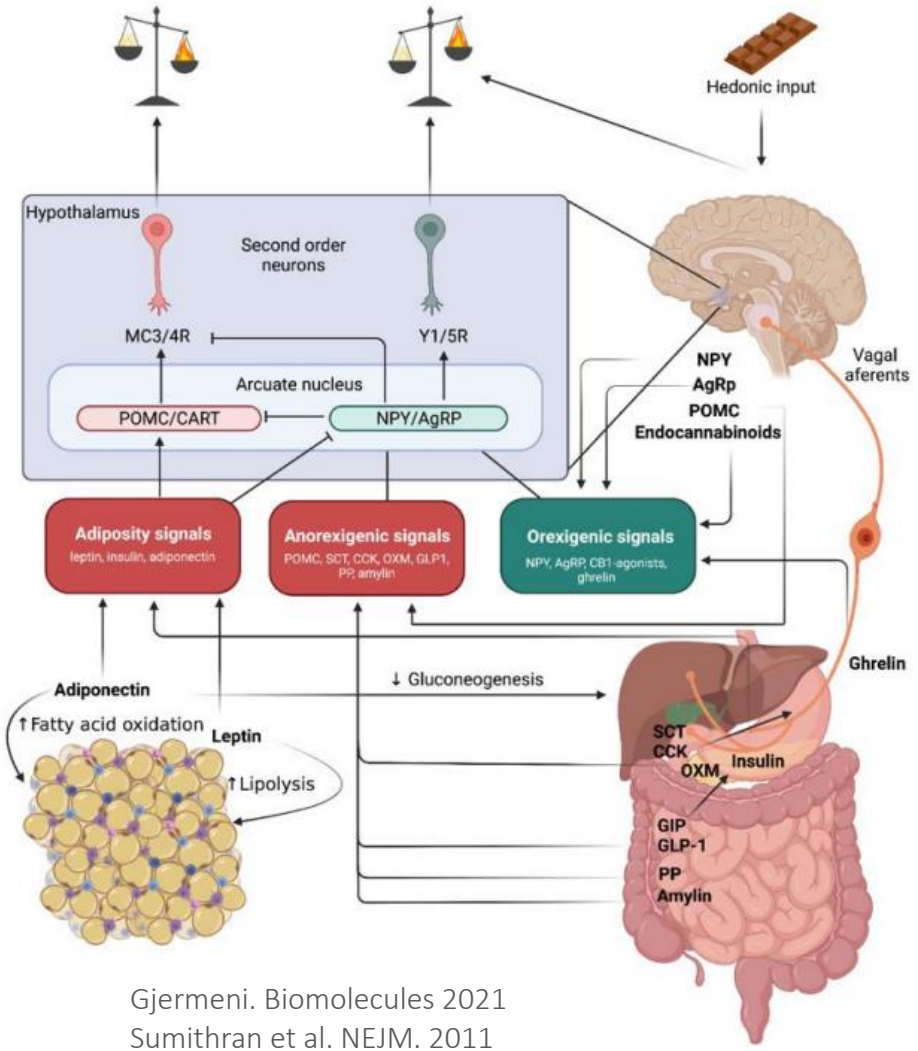


Powerful compensatory biological mechanisms

Physical Logic



Human Physiology: weight loss response



Gjermeni. Biomolecules 2021
Sumithran et al. NEJM. 2011
Rosenbaum et al. Am J Clin Nutr 2008
Fothergill et al. Obes 2016

Lipoedème vs Obésité

TABLE 2 Differential diagnosis of lipedema

	Lipedema	Lymphedema	Obesity
Increase in fat	+++	(+/+++)	+++
Disproportion	+++	+	(+)
Edema	+/+++	+/+++	(+)
Tenderness to pressure	+++	–	–
Easy bruising	+++	–	–

+ to +++, present; (+), possible; +/+++, variable severity; –, not present.

Buso et al. Obesity 2019.

1. **Lipoedème touche essentiellement les femmes**
2. **Nb patientes avec lipoedème ont obésité**
3. **Lors d'une perte pondérale chez patientes avec lipoedème ➔ très faible impact sur zones touchées par lipoedème**

Amato. Nutrients 2024

Agenda

Pathophysiologie
HTA-Obésité

Traitement
Conservateur

GLP-1 RA
GLP-1/GIP RA

Activité physique
Lipoedème

Traitement
chirurgical
Lipoedème

Liraglutide and Semaglutide: GLP-1 receptor agonist

Glucagon-like Peptide-1 Receptor Agonism

↓ Body weight

Central Nervous System
- ↑ Satiety
- ↓ Food Intake
- ↑ Nausea

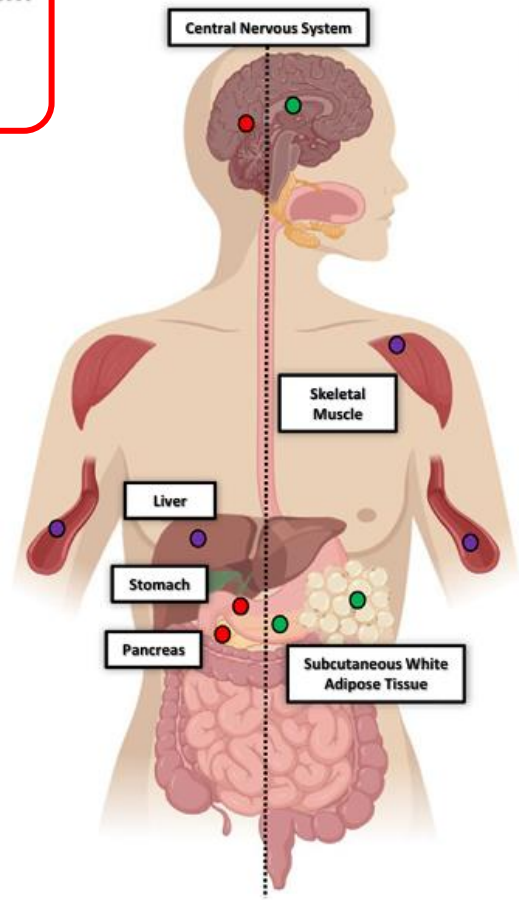
Pancreas
- ↑ Insulin
- ↓ Glucagon

Stomach
- ↓ Gastric Emptying

Systemic
- ↓ Hyperglycemia

Indirect action

Liver
- ↑ Insulin Sensitivity
- ↓ Hepatic Glucose Production
- ↓ Ectopic Lipid Accumulation



Adapted from: Samms et al. . Trends in Endocrinology & Metabolism. 2020 (31)

Tirzepatide: dual GLP-1 / GIP receptor agonist

Glucagon-like Peptide-1 Receptor Agonism

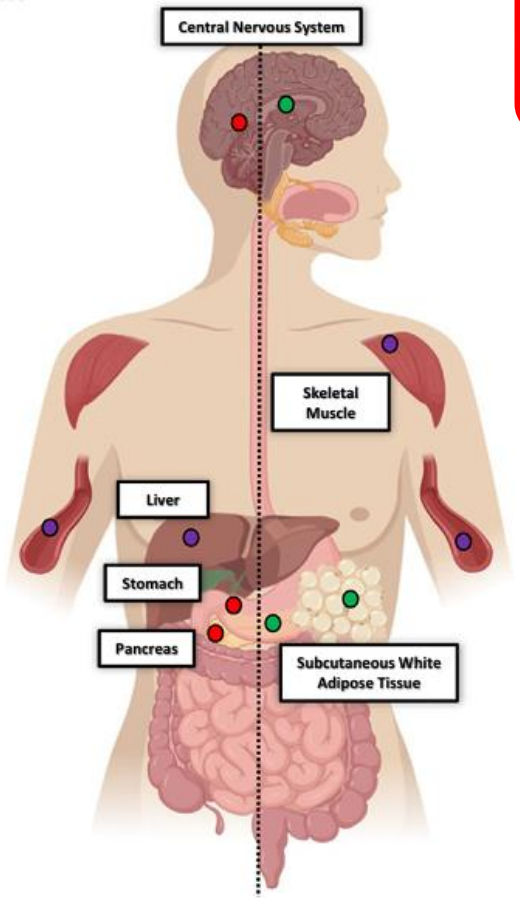
Central Nervous System
- ↑ Satiety
- ↓ Food Intake
- ↑ Nausea
- ↓ Body Weight

Pancreas
- ↑ Insulin
- ↓ Glucagon

Stomach
- ↓ Gastric Emptying

Systemic
- ↓ Hyperglycemia

Liver
- ↑ Insulin Sensitivity
- ↓ Hepatic Glucose Production
- ↓ Ectopic Lipid Accumulation



Glucose-dependent Insulinotropic Polypeptide Receptor Agonism
Glucagon-like Peptide 1 Receptor Agonism
Indirect Action

Glucose-dependent Insulinotropic Polypeptide Receptor Agonism

Central Nervous System
- ↓ Food Intake
- ↓ Nausea
- ↓ Body Weight

Pancreas
- ↑ Insulin
- ↑ Glucagon

Subcutaneous White Adipose Tissue
- ↑ Insulin Sensitivity
- ↑ Lipid Buffering Capacity
- ↑ Blood Flow
- ↑ Storage Capacity
- ↓ Proinflammatory Immune Cell Infiltration

Systemic
- ↓ Hyperglycemia
- ↓ Dietary Triglyceride

GIP drive weight loss:
1. **Directly** targeting receptor in CNS to inhibit caloric intake
2. **Indirectly** by reducing drug-induced nausea to expand GLP-1 RA efficacy

Samms et al. . Trends in Endocrinology & Metabolism. 2020 (31)

Approved Treatments for Obesity in Switzerland

GLP-1 RA

- **liraglutide 3 mg/d Saxenda®**
- **semaglutide 2.4 mg/wk Wegovy®**

Dual GLP-1 /GIP RA

- **tirzepatide 15 mg/wk Mounjaro®**

Patient population

Patients BMI ≥ 30 kg/m²
or
BMI ≥ 27 kg/m² +
related complications
Key exclusion: T2DM

N= ~ 2000

Randomization

- **Active Treatment**
- Placebo injectable 1x /wk

56 to 72 weeks

Individual counseling sessions
-500 kcal/j
Physical activity ≥ 150 mn/wk

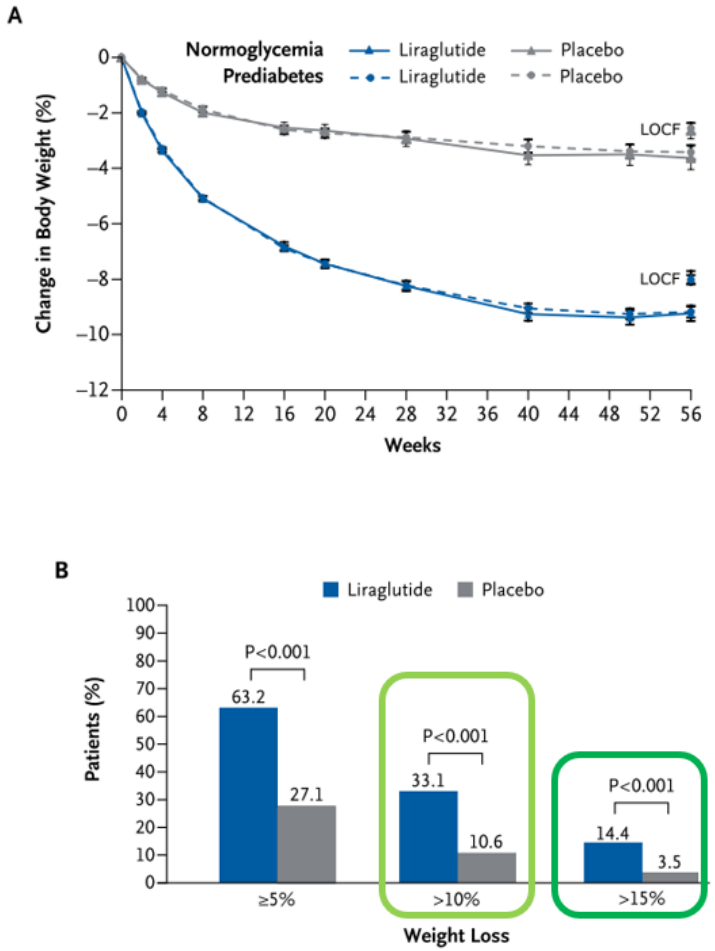
Primary endpoints

- % change in bodyweight
- 5% weight reduction

Approved Treatments for Obesity in Switzerland

liraglutide 3 mg/d
Saxenda®

Pi-Sunyer. NEJM. 2015 (373)



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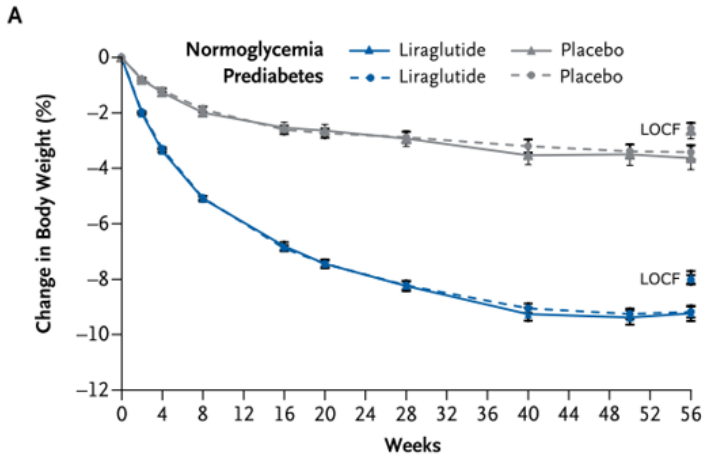
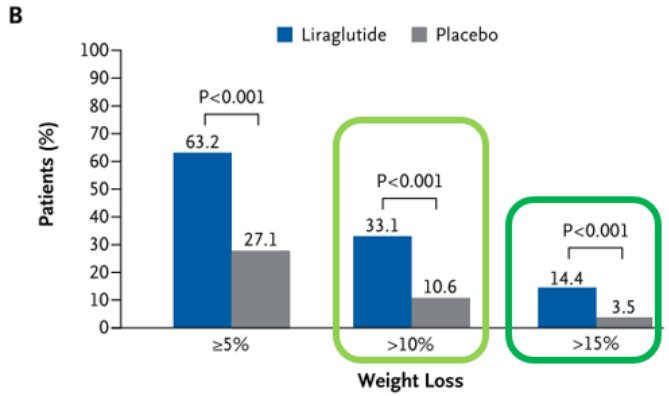
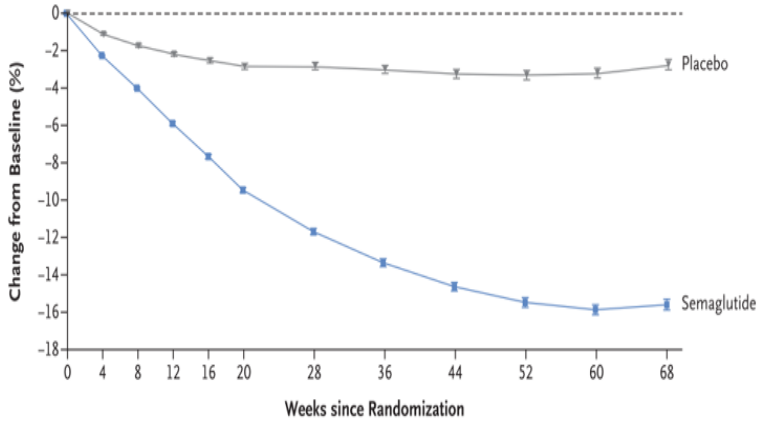
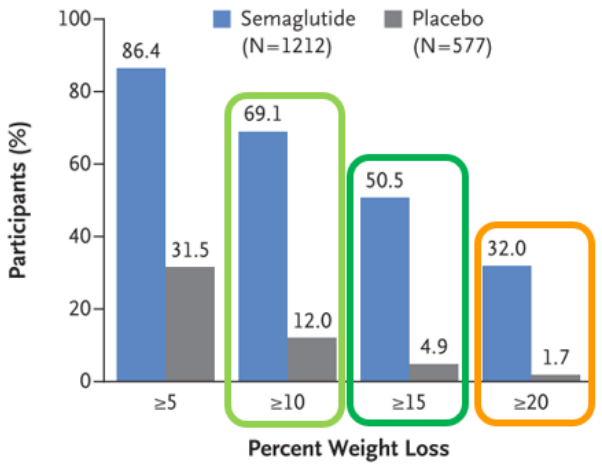




semaglutide 2.4 mg/wk
Wegovy®

Wilding. NEJM. 2021 (384)





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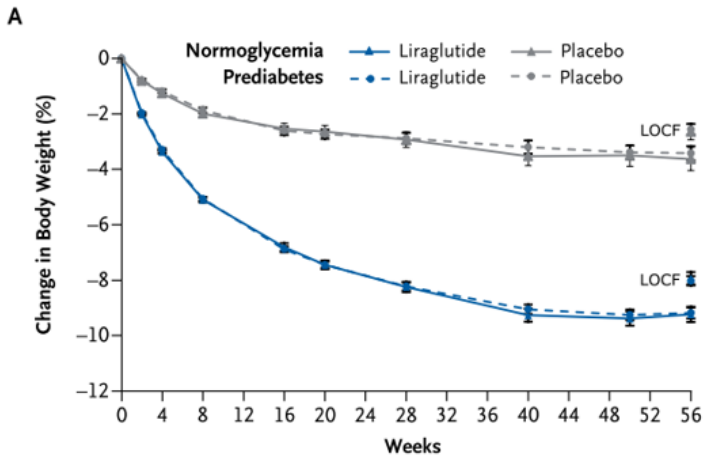
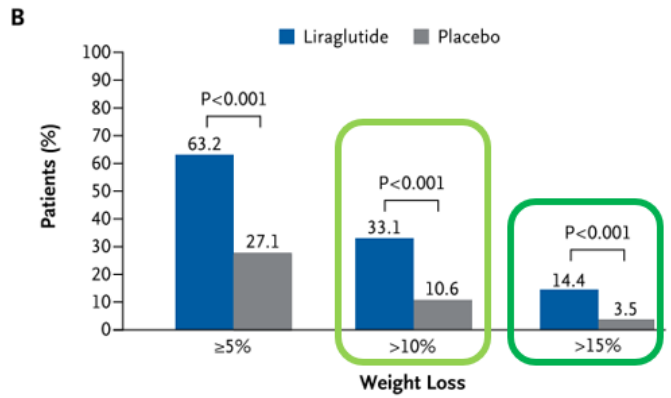
liraglutide 3 mg/d Saxenda®

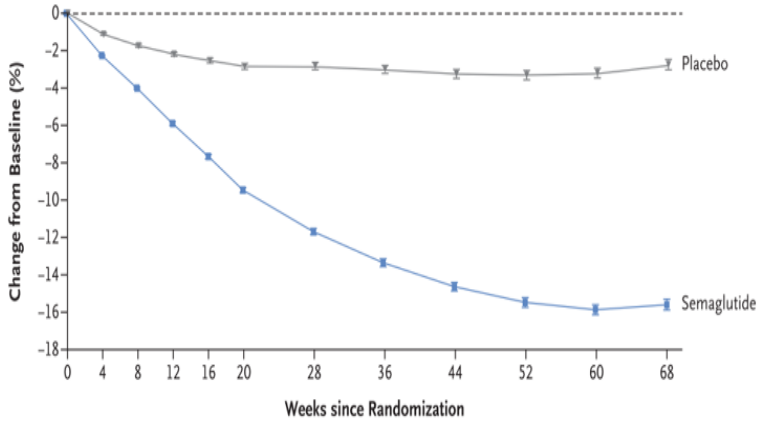
Pi-Sunyer. NEJM. 2015 (373)

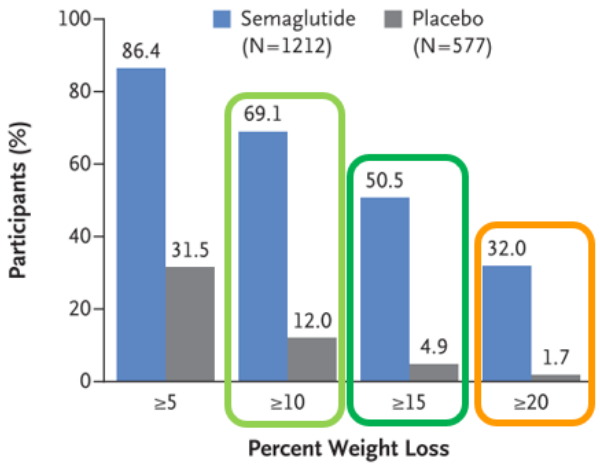




semaglutide 2.4 mg/wk Wegovy®

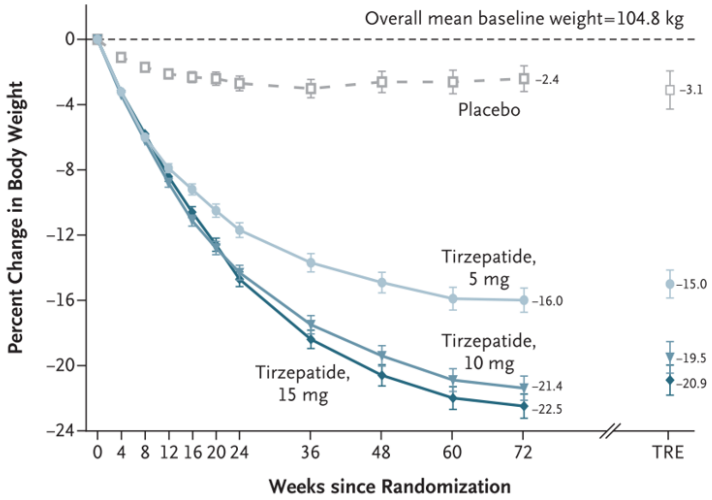
Wilding. NEJM. 2021 (384)

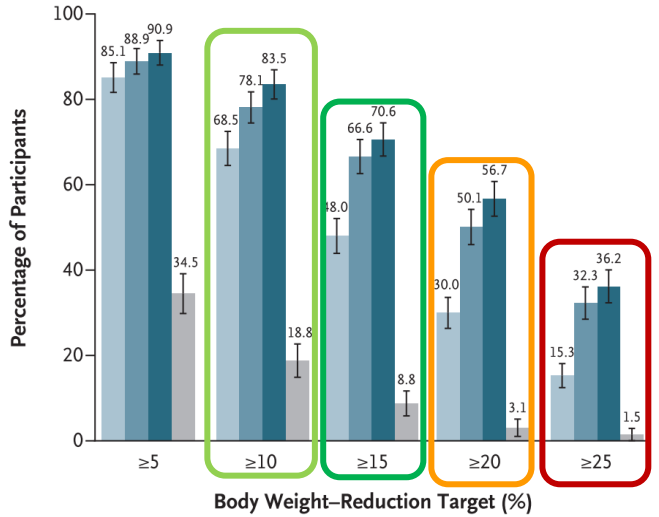




tirzepatide 15 mg/wk Mounjaro®

Jastreboff. NEJM. 2022 (387)





Approved Treatments for Obesity in Switzerland

liraglutide 3 mg/d
Saxenda®

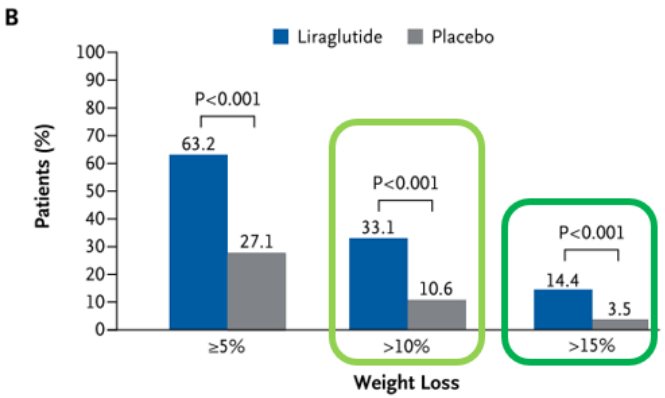
- Approved
- Reimbursed
- Not available
- Max CHF 183/month

semaglutide 2.4 mg/wk
Wegovy®

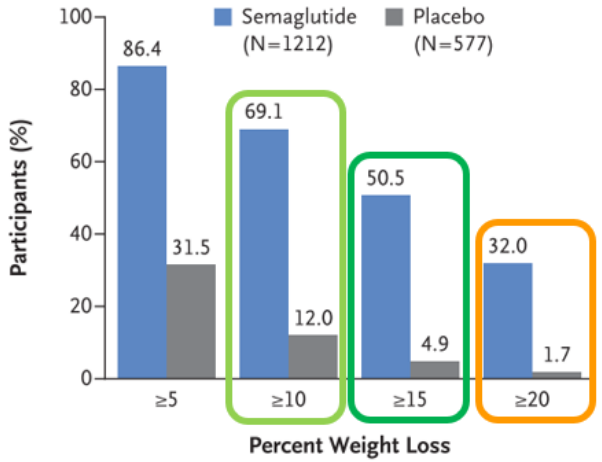
- Approved
- Reimbursed
- Available
- Max CHF 179/month

tirzepatide 15 mg/wk
Mounjaro®

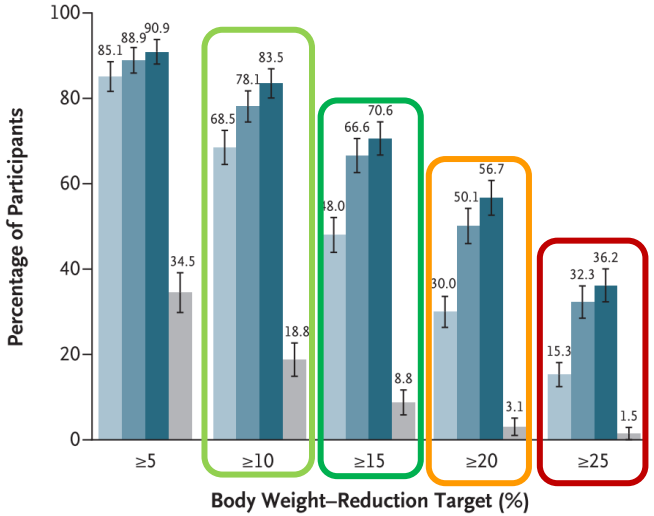
- Approved
- Not Reimbursed
- Available
- CHF 389/month



Pi-Sunyer. NEJM. 2015 (373)



Wilding. NEJM. 2021 (384)



Jastreboff. NEJM. 2022 (387)

Traitement approuvé et remboursés en Suisse : semaglutide

Semaglutide 2.4 mg/semaine: remboursé par LAMal dès 01.03.2024

Contrôle efficacité — 4 mois

Contrôle efficacité — 10 mois

Contrôle efficacité — Tous les 6 mois — 3 ans max

Demande au médecin conseil par médecin spécialiste FMH endocrinologie-diabétologie ou par médecin d'un centre d'obésité reconnu, qui atteste que :

1. Les conditions de prise en charge sont respectées
2. Le patient suit un régime alimentaire avec déficit de 500 kcal/j
3. Le patient bénéficie de conseils diabétiques
4. Le patient pratique une activité physique renforcée
5. Le patient n'a pas bénéficié d'une chirurgie bariatrique dans le passé
6. Le patient diabétique n'a jamais reçu de traitement par GLP-1RA

28 ≤ IMC < 35 kg/m²
en présence d'au moins une comorbidité parmi :
- Prédiabète ou diabète
- Hypertension artérielle
- Dyslipidémie

- Perte **≥ 5 %** poids départ — Fin remboursement
- Perte **≥ 10 %** poids départ — Fin remboursement
- Maintien objectif **≥ 10 %** Durée max 3 ans — Fin remboursement

IMC ≥ 35 kg/m²

- Perte **≥ 7 %** poids départ — Fin remboursement
- Perte **≥ 12 %** poids départ — Fin remboursement
- Maintien objectif **≥ 12 %** Durée max 3 ans — Fin remboursement

Le remboursement est suspendu en cas IMC < 25 kg/m²
Le traitement pourra être repris si reprise pondérale avec IMC ≥ 25 kg/m²

Une seule tentative. En cas d'échec, pas de possibilité d'envisager un nouveau remboursement

- Lipoedème n'est pas critère reconnu pour bénéficier ttt
- Pas de données cliniques sur impact nouveaux ttt sur lipoedème

Agenda

Pathophysiologie Lipoedème

Traitement Conservateur

GLP-1 RA
GLP-1/GIP RA

Activité physique Lipoedème

Traitement chirurgical Lipoedème

Physical Activity and Lipedema

The Role of Physical Exercise as a Therapeutic Tool to Improve Lipedema: A Consensus Statement from the Italian Society of Motor and Sports Sciences (*Società Italiana di Scienze Motorie e Sportive, SISMeS*) and the Italian Society of Phlebology (*Società Italiana di Flebologia, SIF*)

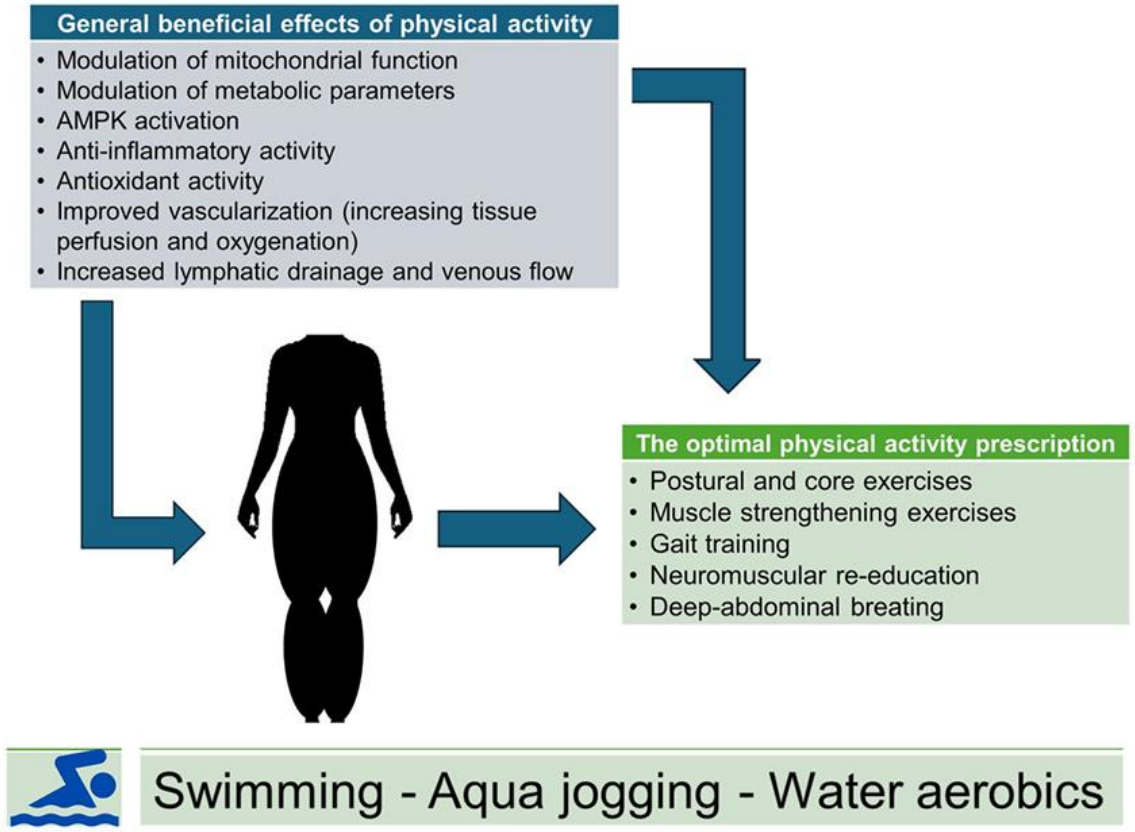
Giuseppe Annunziata

Current Obesity Reports

Published online: 03 July 2024

Main goal lipedema treatments:
- **To manage pain**
- **To reduce functional limitations**

- Entraînement endurance ++ ➔ modulation mitochondries TA
- AP ➔ diminution inflammation et lipolyse
- Augmentation drainage lymphatique et flux veineux



Annuziata. Cur Obes Reports 2024

Agenda

Pathophysiologie Lipoedème

Traitement Conservateur

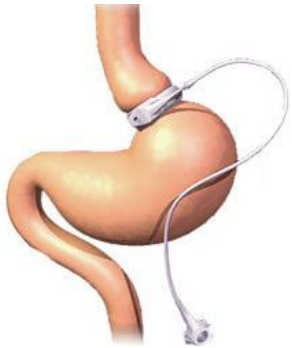
GLP-1 RA
GLP-1/GIP RA

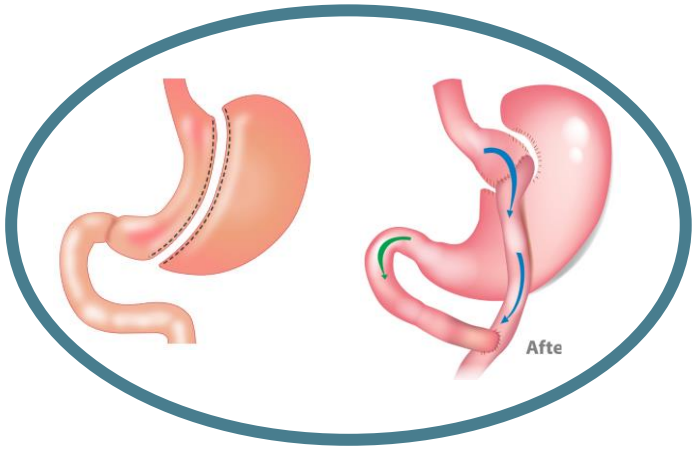
Activité physique Lipoedème

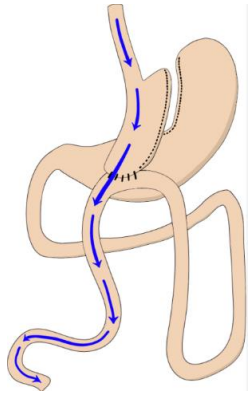
Traitement chirurgical Lipoedème

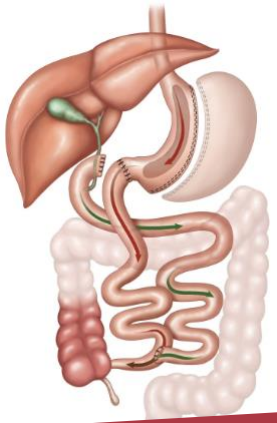
Bariatric and Metabolic Surgery

- **Restrictive**
  - Gastric Banding
  - Sleeve Gastrectomy
- **Restrictive and Malabsorptive**
  - Roux-en-Y Gastric Bypass RYGB
- **Malabsorptive and Restrictive**
  - One anastomosis gastric bypass OAGB
  - Bilio-pancreatic diversion with duodenal switch









NUTRITIONAL DEFICIENCIES

Lipedema and Bariatric Surgery

Case Report

Lipoedema in patients after bariatric surgery: report of two cases and review of literature

clinical obesity

S. Pouwels **Clinical** Obesity **8**, 147–150, April 2018

Before surgery
35 yo
BMI 57 kg/m2
Circumference:
- **Upper legs. 78-83 cm**
- **Calves: 54-55 cm**

Sleeve gastrectomy

Reduction 68 kg
BMI 34 kg/m2
Circumference:
- **Upper legs. 82-82 cm**
- **Calves: 54-55 cm**

Lipedema and Bariatric Surgery

Persistent lipedema pain in patients after bariatric surgery: a case series of 13 patients

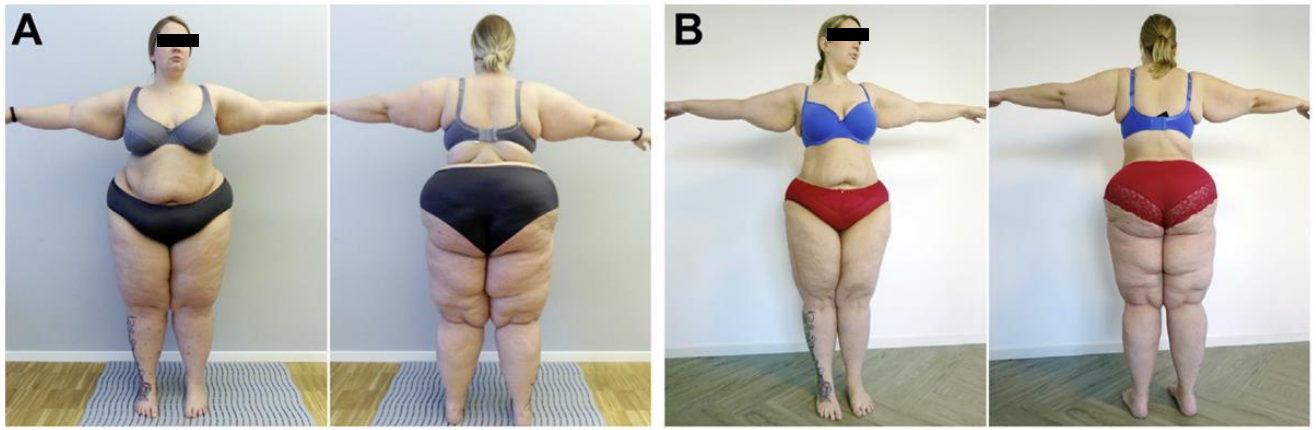
Surgery for Obesity and Related Diseases 18 (2022) 628–633

Manuel E. Cornely

13 patients with lipedema
BMI 50 kg/m2

2 years: BMI 32 kg/m2

Before surgery:
BMI 56 kg/m^2



8 months:
BMI 39 kg/m^2

20 months: BMI
28 kg/m^2
Persistent pain

Conclusions

Bariatric surgery, used in the treatment of obesity, does not cure lipedema, and as our study shows, even large weight reductions of more than 80% excess weight do not reduce lipedema pain. Following a correct diagnosis, depending on the patient's weight, a treatment sequence focusing on lipedema or obesity first should be chosen.

Conclusions

- Lipoedème: affection particulièrement complexe et multifactorielle
- Diagnostic attentif
- Traitement par une approche multidisciplinaire
- Souvent associé à l'obésité qui aggrave probablement la maladie
- Modifications lifestyle: pierre angulaire de la prise en charge
  - Ne pas attendre une perte pondérale significative
- **Traitements médicamenteux :** nouvelles options de prise en charge
  - Prescriptions limitées par accès médecin spécialiste
  - Remboursement limité dans le temps !
- **Chirurgie métabolique:**
  - Traitement de l'obésité mais pas du lipoedème
  - Les patients doivent être attentivement informés

Dre Lucie FAVRE

Centre d’obésité CHUV

lucie.favre@chuv.ch