



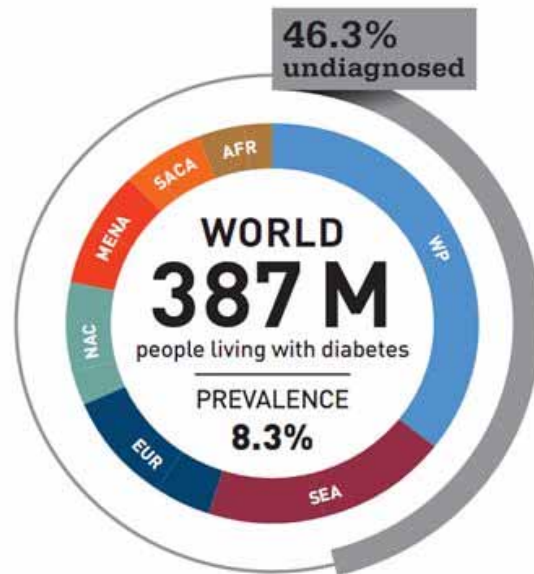
# Obesity and diabetes

Dr Yovan MAHADEB

# Diabetes Worldwide- Now and Later

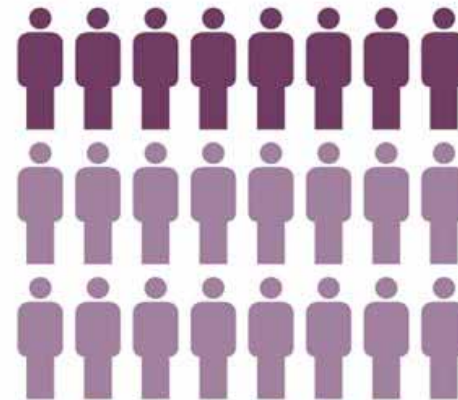
Diabetes is a huge and growing problem...

2014



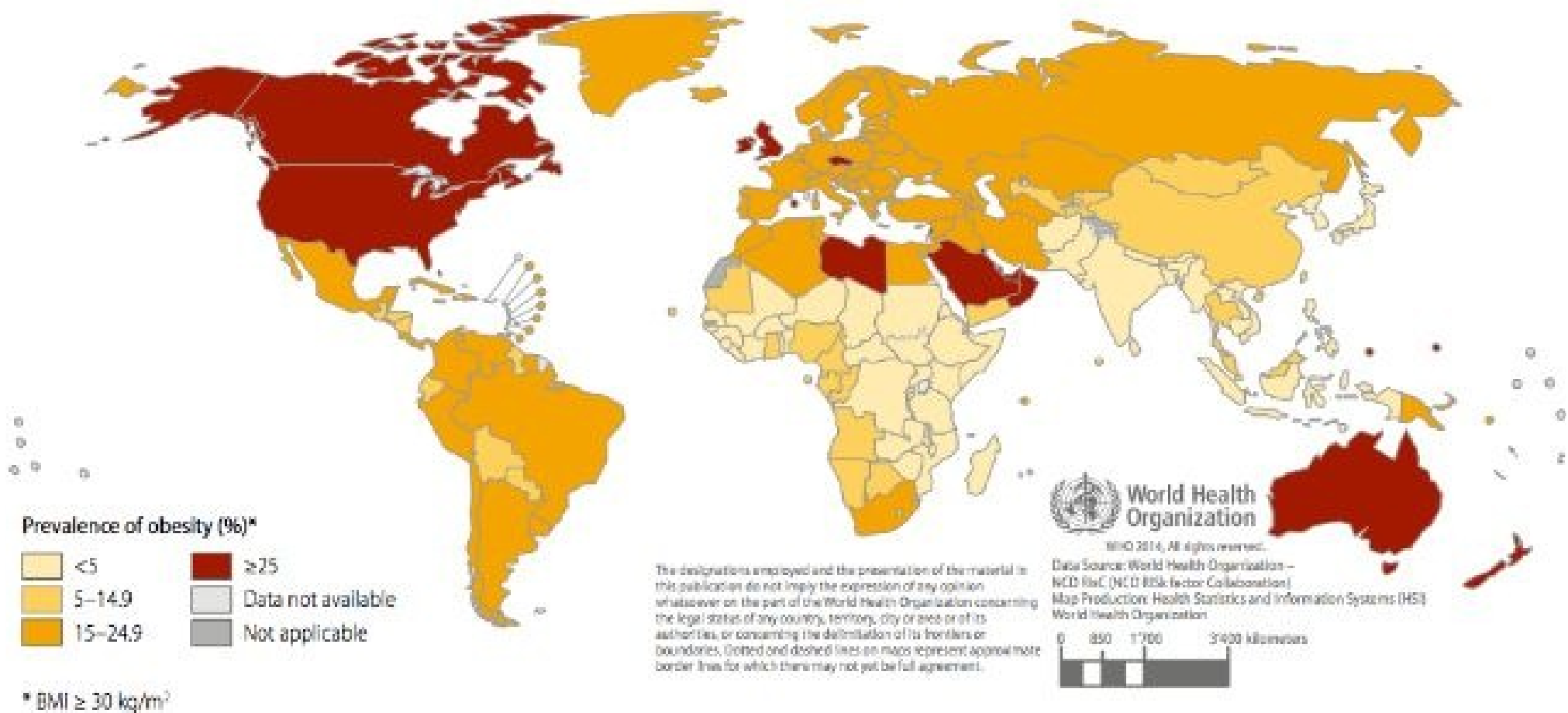
2035

**+205  
MILLION**



# Global Obesity Burden

**Fig. 7.1** Age-standardized prevalence of obesity in men aged 18 years and over (BMI  $\geq 30$  kg/m<sup>2</sup>), 2014



# WHO Europe

In the WHO/European Region



**over 50%**  
of people are  
**overweight** or **obese**

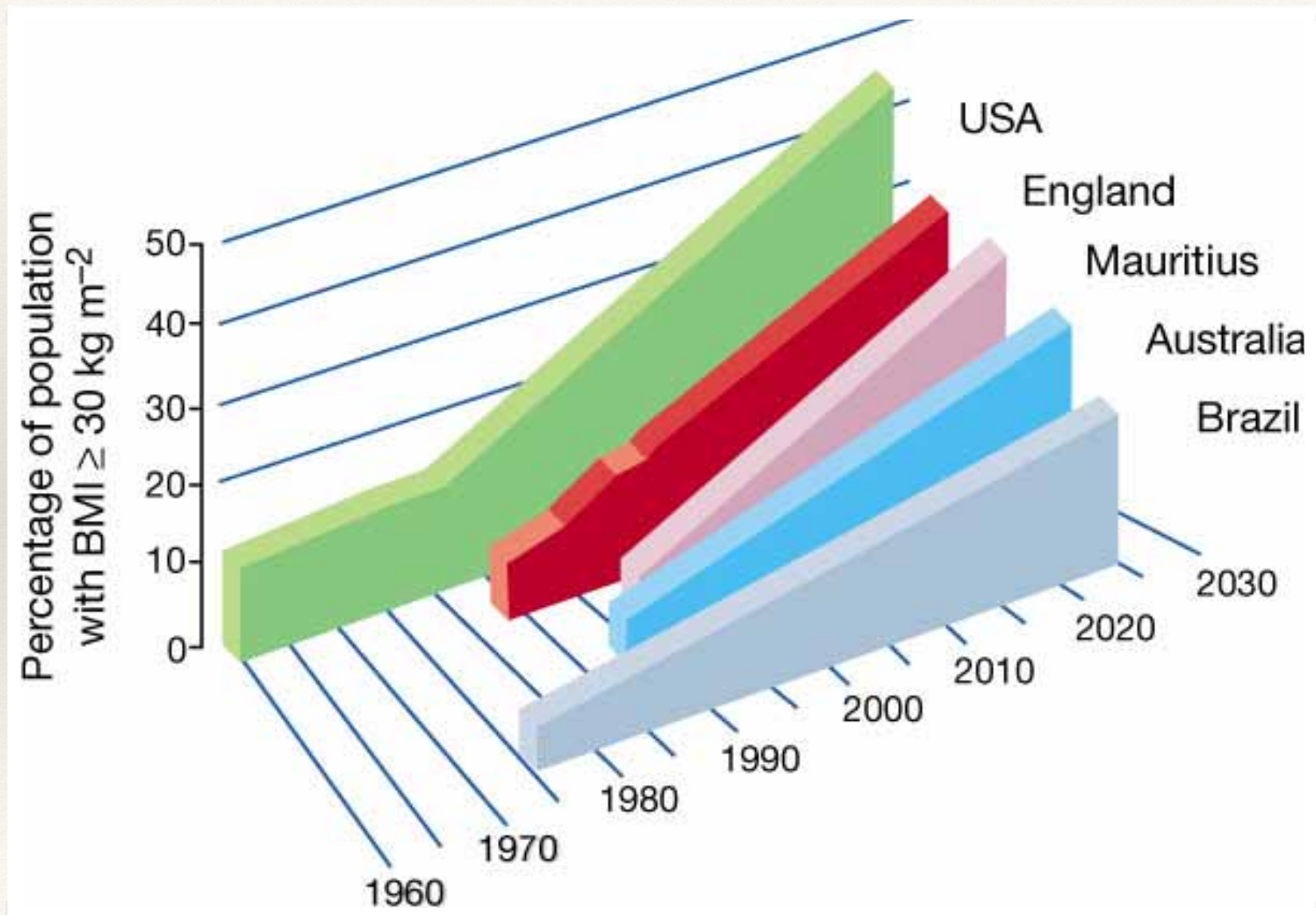


**over 20%**  
of people are  
**obese**

[www.euro.who.int/obesity](http://www.euro.who.int/obesity)

© WHO 07/2013

# Global Obesity Burden



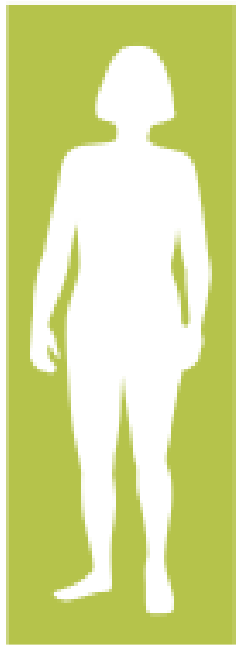
# Classification of Obesity

## BMI Classification

Classification	WHO	Asia-Pacific	Health Risk
Underweight	Under 18.5	Under 18.5	Low
Normal	18.5-24.9	18.5-22.9	Average
Overweight	25-29.9	23-24.9	Increased
Obese Class I	30-34.9	25-29.9	Moderate
Obese Class II	35-39.9 (Morbid >40)	≥30	Severe

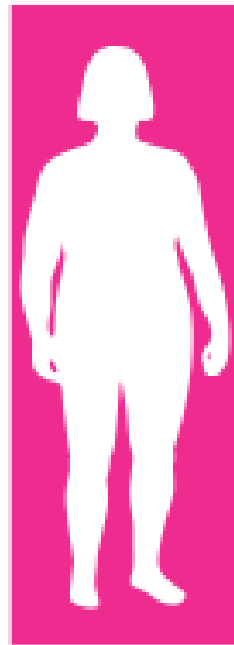
# Classification of Obesity

Normal Weight  
(BMI 19 to 24.9)



130 pounds  
BMI 22

Overweight  
(BMI 25 to 29.9)



152 pounds  
BMI 26

Obese (Class I)  
(BMI 30 to 34.9)



175 pounds  
BMI 30

Obese (Class II)  
(BMI 35 to 39.9)



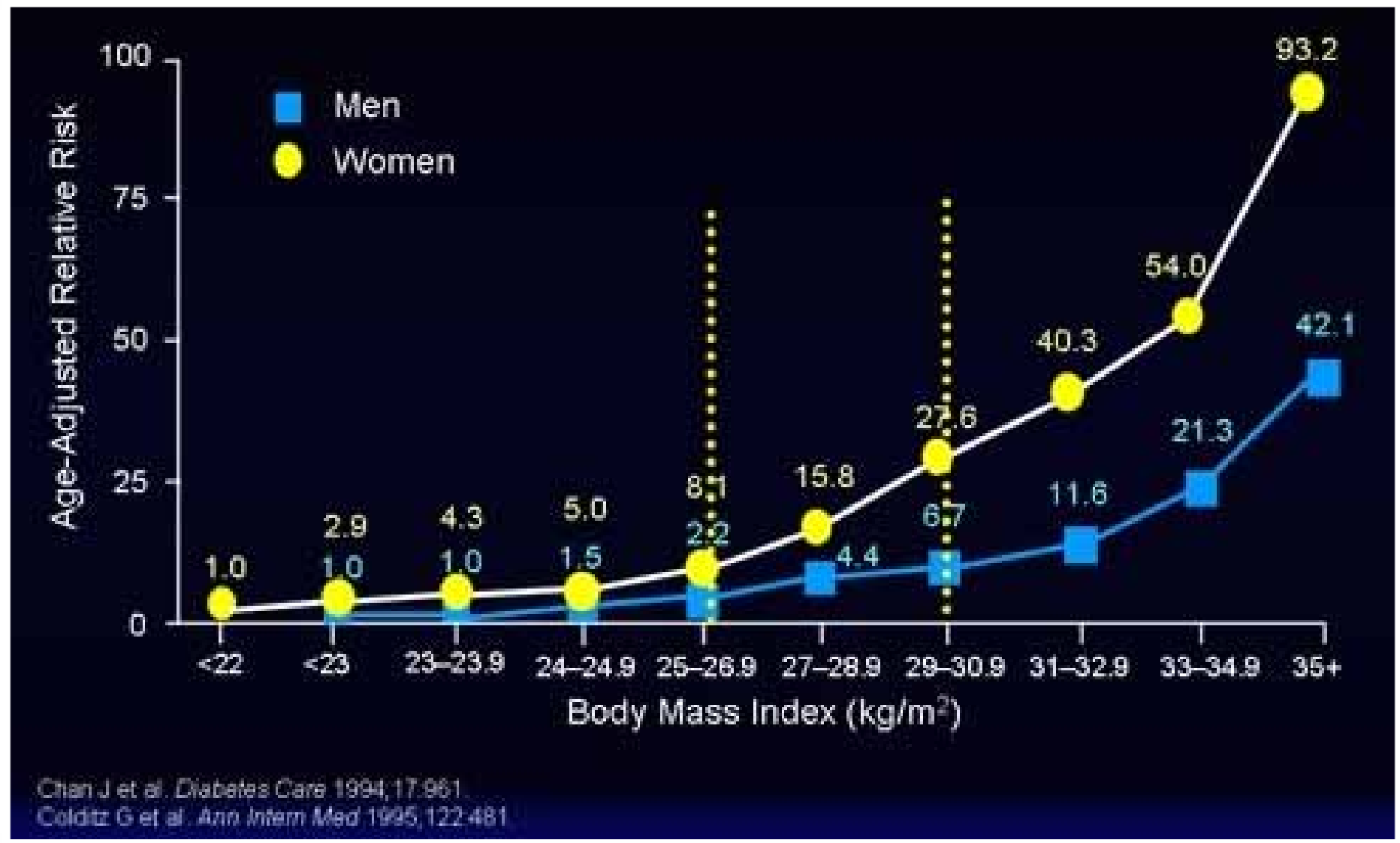
205 pounds  
BMI 35

Severely Obese  
(BMI 40+)



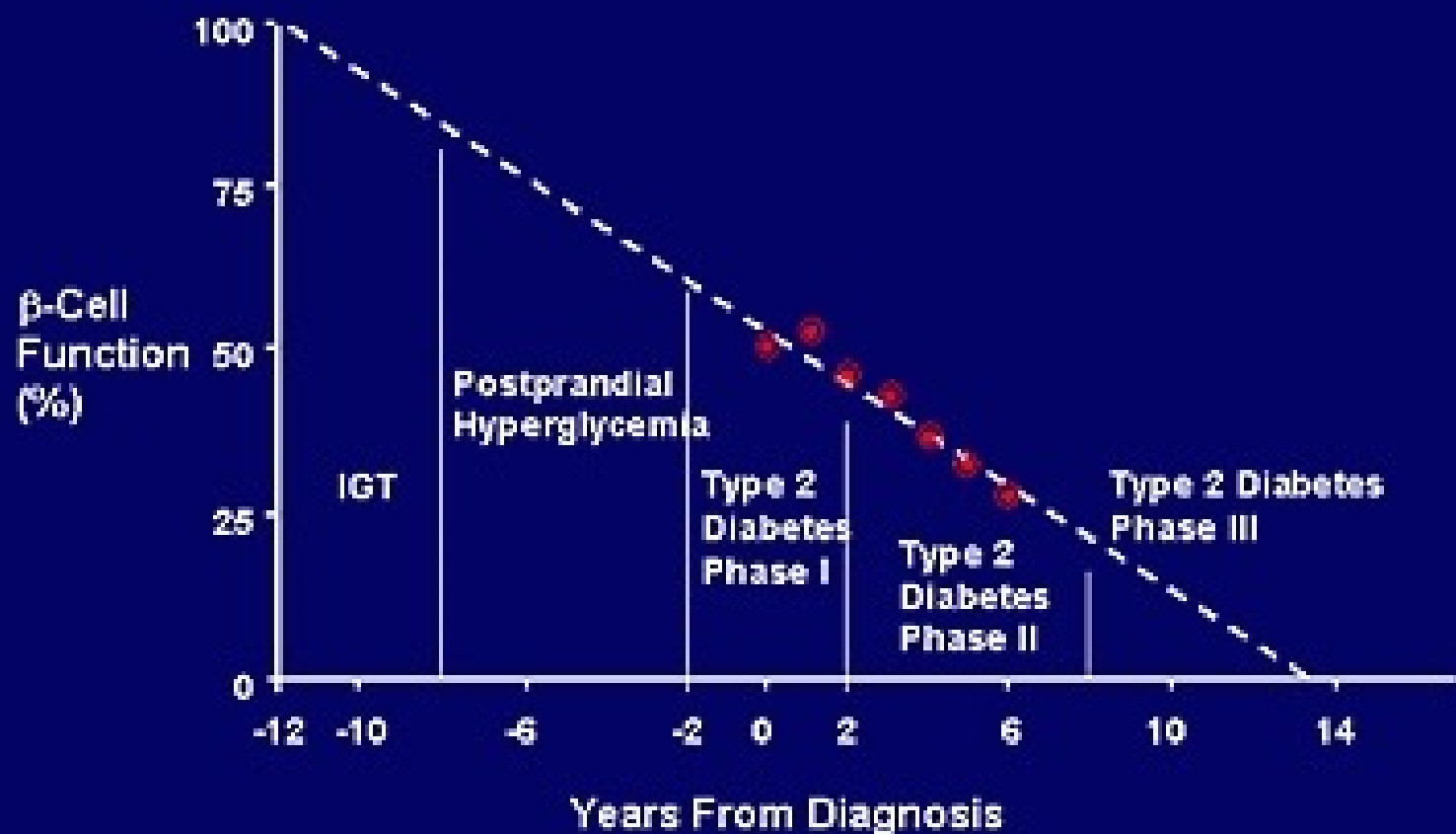
234 pounds  
BMI 40

# Relationship between BMI and T2DM



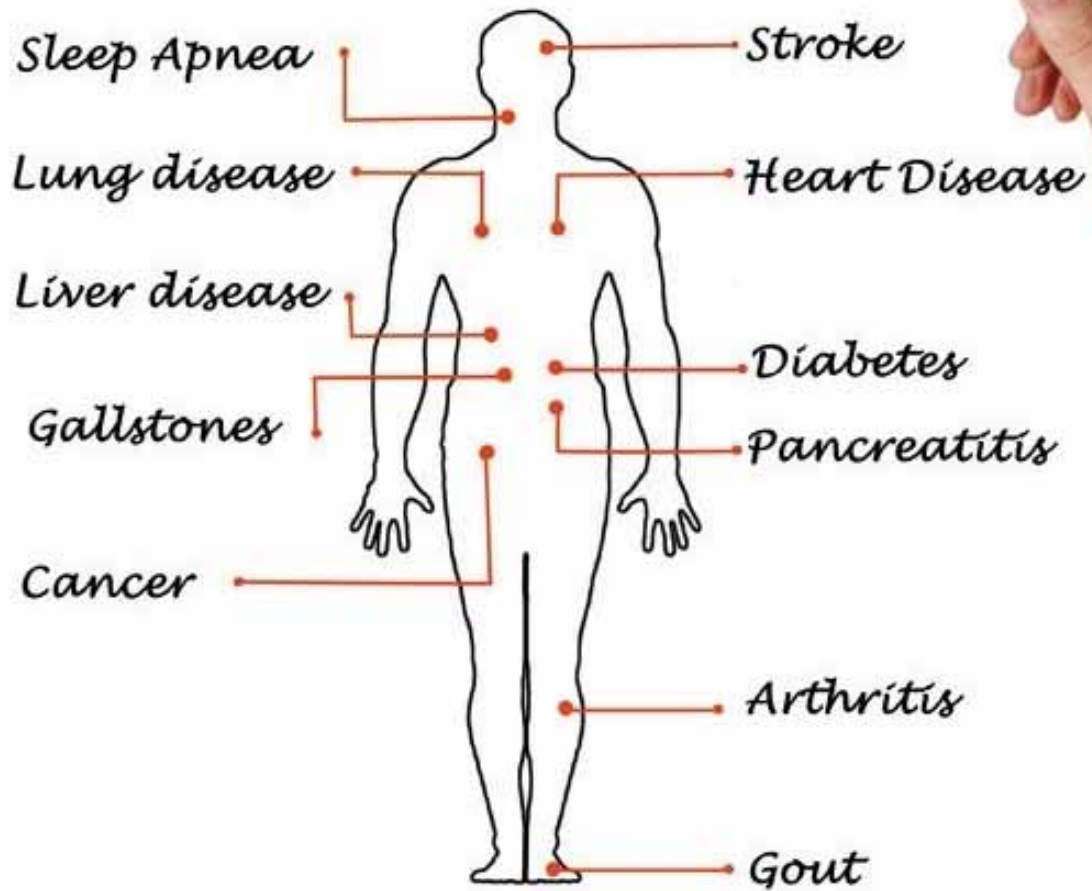


# Stages of T2DM



Lebovitz. *Diabetes Rev.* 1999;7(3):139.

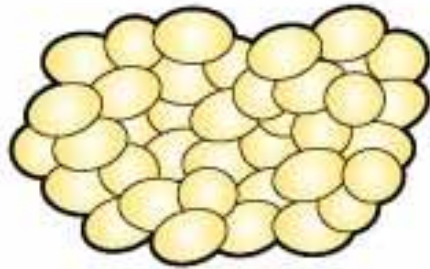
# Complications other than DM



# Pathophysiology Obesity

Genetics (polygenic diseases)  
Epigenetics (fetal/neonatal programming)  
Environment (unhealthy diet, sedentary lifestyle, and pollutants)

- Adipokines (eg, leptin and adiponectin)
- Pro-inflammatory cytokines
- NEFA



- Excess visceral (ectopic) fat
- Adiposopathy



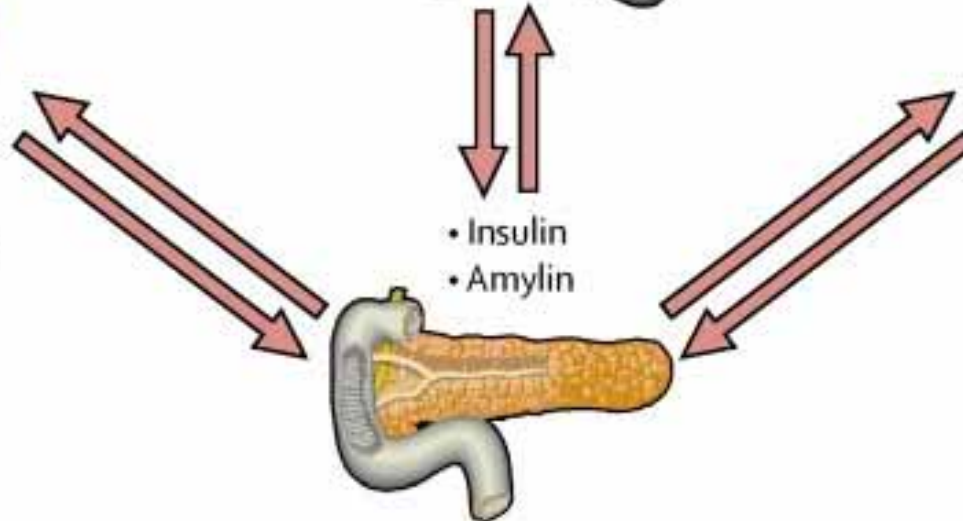
- Ghrelin
- GLP-1
- GIP
- Cholecystokinin
- Oxyntomodulin



- Microbiota changes
- Gut barrier dysfunction

- Insulin
- Amylin

- $\beta$ -cell burden, dysfunction, or apoptosis



# Pathophysiology Obesity

## Gut microbiota and obesity/type 2 diabetes mellitus

ARTICLE

doi:10.1038/nature11450

### A metagenome-wide association study of gut microbiota in type 2 diabetes

Qin, Nature 2012

Junjie Qin<sup>1\*</sup>, Yingrui Li<sup>1\*</sup>, Zhiming Cai<sup>2\*</sup>, Shenghui Li<sup>1\*</sup>, Jianfeng Zhu<sup>1\*</sup>, Fan Zhang<sup>1\*</sup>, Suisha Liang<sup>1</sup>, Wenwei Zhang<sup>1</sup>, Yuanlin Guan<sup>1</sup>, Dongqian Shen<sup>1</sup>, Yangqing Peng<sup>1</sup>, Dongya Zhang<sup>1</sup>, Zhuye Jie<sup>1</sup>, Wenxian Wu<sup>1</sup>, Youwen Qin<sup>1</sup>, Wenbin Xue<sup>1</sup>, Junhua Li<sup>1</sup>, Lingchuan Han<sup>3</sup>, Donghui Lu<sup>3</sup>, Peixian Wu<sup>3</sup>, Yali Dai<sup>3</sup>, Xiaojuan Sun<sup>2</sup>, Zesong Li<sup>2</sup>, Aifa Tang<sup>2</sup>, Shilong Zhong<sup>2</sup>, Xiaoping Li<sup>2</sup>, Weineng Chen<sup>1</sup>, Ran Xu<sup>1</sup>, Mingbang Wang<sup>1</sup>, Qiang Feng<sup>1</sup>, Meihua Gong<sup>1</sup>, Jing Yu<sup>1</sup>, Yanyan Zhang<sup>1</sup>, Ming Zhang<sup>1</sup>, Torben Hansen<sup>7</sup>, Gaston Sanchez<sup>8</sup>, Jeroen Raes<sup>7,9</sup>, Gwen Falony<sup>7,9</sup>, Shujiro Okuda<sup>7,9</sup>, Mathieu Almeida<sup>9</sup>, Emmanuelle LeChatelier<sup>9</sup>, Pierre Renault<sup>9</sup>, Nicolas Pons<sup>9</sup>, Jean-Michel Batto<sup>9</sup>, Zhaoxi Zhang<sup>1</sup>, Hua Chen<sup>1</sup>, Ruifu Yang<sup>1,10</sup>, Weimou Zheng<sup>1</sup>, Songgang Li<sup>1</sup>, Huanming Yang<sup>1</sup>, Jian Wang<sup>1</sup>, S. Dusko Ehrlich<sup>1</sup>, Rasmus Nielsen<sup>9</sup>, Oluf Pedersen<sup>9,11,12</sup>, Karsten Kristiansen<sup>1,13</sup> & Jun Wang<sup>1,3,13</sup>

i:10.1038/nature12506

### Richness of human gut microbiome correlates with metabolic markers

Le Chatelier, Nature 2013

Emmanuelle Le Chatelier<sup>1\*</sup>, Trine Nielsen<sup>2\*</sup>, Junjie Qin<sup>3\*</sup>, Edi Prifti<sup>1\*</sup>, Falk Hildebrand<sup>4,5</sup>, Gwen Falony<sup>4,5</sup>, Mathieu Almeida<sup>1</sup>, Manimozhiyan Arumugam<sup>2,3,5</sup>, Jean-Michel Batto<sup>3</sup>, Sean Kennedy<sup>1</sup>, Pierre Leonard<sup>1</sup>, Junhua Li<sup>1,7</sup>, Kristoffer Burgdorf<sup>2</sup>, Niels Grarup<sup>7</sup>, Torben Jørgensen<sup>8,9,10</sup>, Ivan Brandtslund<sup>11,12</sup>, Henrik Bjørn Nielsen<sup>13</sup>, Agnieszka S. Juncker<sup>13</sup>, Marcelo Bertalan<sup>13</sup>, Florence Levenez<sup>2</sup>, Nicolas Pons<sup>1</sup>, Simon Rasmussen<sup>13</sup>, Shinichi Sunagawa<sup>6</sup>, Julien Tap<sup>1,6</sup>, Sebastian Tims<sup>14</sup>, Erwin G. Zoetendal<sup>14</sup>, Søren Brunak<sup>13</sup>, Karine Clément<sup>15,16,17</sup>, Joël Doré<sup>1,18</sup>, Michiel Kleerebezem<sup>14</sup>, Karsten Kristiansen<sup>19</sup>, Pierre Renault<sup>18</sup>, Thomas Sicheritz-Ponten<sup>13</sup>, Willem M. de Vos<sup>14,20</sup>, Jean-Daniel Zucker<sup>15,16,21</sup>, Jeroen Raes<sup>4,5</sup>, Torben Hansen<sup>2,22</sup>, MetaHIT consortium†, Peer Bork<sup>6</sup>, Jun Wang<sup>1,19,23,24,25</sup>, S. Dusko Ehrlich<sup>1</sup> & Oluf Pedersen<sup>2,26,27,28</sup>

LETTER

Karlsson, Nature 2013

### Gut metagenome in European women with impaired and diabetic glucose control

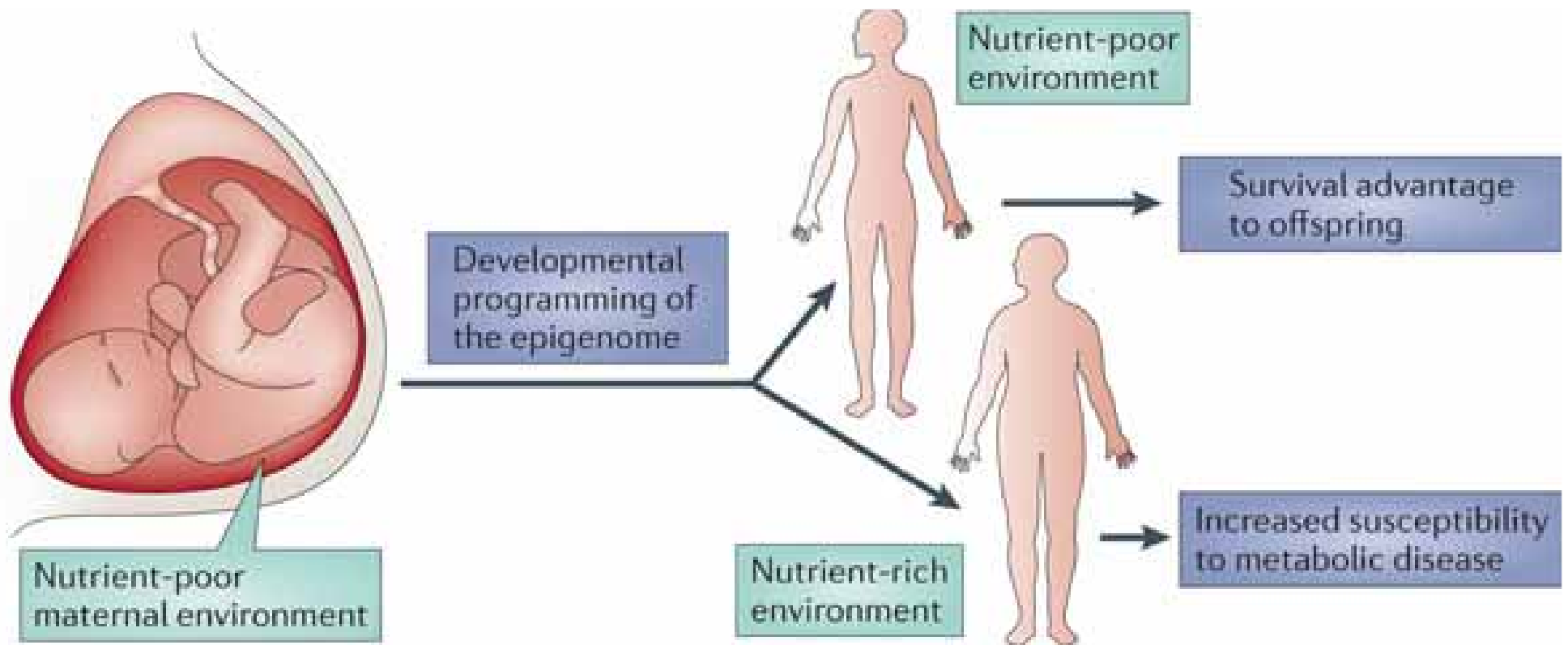
Fredrik H. Karlsson<sup>1\*</sup>, Valentina Tremaroli<sup>2\*</sup>, Intawat Nookaew<sup>1</sup>, Göran Bergström<sup>2</sup>, Carl Johan Behre<sup>3</sup>, Jens Nielsen<sup>1</sup> & Fredrik Bäckhed<sup>2,3</sup>

### Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice

Ridaura, Science 2013

Vanessa K. Ridaura, Jeremiah J. Faith, Federico E. Rey, Jiye Cheng, Alexis E. Duncan, And L. Kau, Nicholas W. Griffin, Vincent Lombard, Bernard Henrissat, James R. Bain, Michael Muehlbauer, Olga Ilkayeva, Clay F. Semenkovich, Katsuhiko Funai, David K. Hayashi, Bar J. Lyle, Margaret C. Martini, Luke K. Ursell, Jose C. Clemente, William Van Treuren, Willia Walters, Rob Knight, Christopher B. Newgard, Andrew C. Heath, Jeffrey I. Gordon\*

# Pathophysiology Obesity

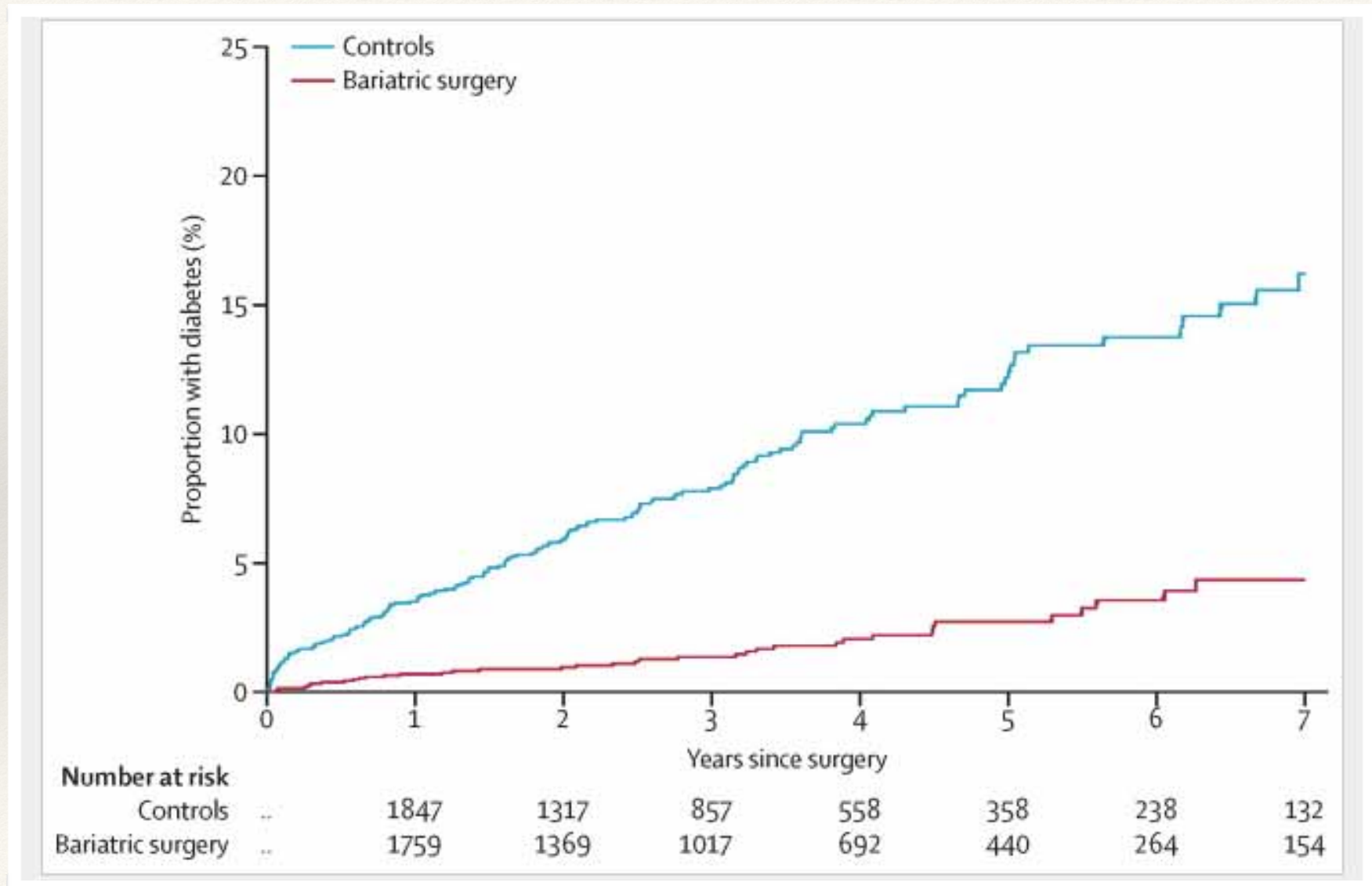


# Overview of Surgery, DM/Pre-DM and obesity

## Effects of bariatric surgery at the different stages of the clinical course of type 2 diabetes

Stage of type 2 diabetes	Effects of bariatric surgery
Prediabetes	Well documented, highly significant reduction of new cases of type 2 diabetes ( <a href="#">5,6</a> )
Recently onset type 2 diabetes	Well documented high potential for diabetes remission ( <a href="#">7-10</a> ); documented reduction in the incidence of macro- and micro-vascular complications ( <a href="#">11,12</a> )
Type 2 diabetes with initial macro- and micro-vascular complications	Possible regression of macro- and micro-vascular complication suggested in some study ( <a href="#">13,14</a> )
Type 2 diabetes with established end-stage macro- or micro-vascular complications	No regression and in some cases progression of micro-vascular complications (diabetic nephropathy and retinopathy) ( <a href="#">14,15</a> ); no gain in survival ( <a href="#">16</a> )

# Bariatric surgery as a preventive treatment for DM



# Remission rates after Bariatric Surgery

**Table 2.** Two- and 10-year diabetes incidence and remission\* rates from the Swedish Obese Subjects Study [7]

	<b>Surgical</b>	<b>Control</b>
2-year incident	1%	8%
10-year incident	8%	24%
2-year remission	72%	21%
10-year remission	36%	13%

\* Remission based on fasting plasma glucose < 7.0 mmol/l and not on hypoglycaemic therapy [7].



# Remission Prediction Score

Prediction factor		Score
Age (years)	If age <40, enter 0 →	2
	If age 40–49, enter 1 →	
	If age 50–59, enter 2 →	
	If age 60+, enter 3 →	
HbA1c (%)	If HbA1c <6.5, enter 0 →	4
	If HbA1c 6.5–6.9, enter 2 →	
	If HbA1c 7.0–8.9, enter 4 →	
	If HbA1c >9, enter 6 →	
Diabetes medication	If not sulfonylureas or ISA*, enter 0 →	3
	If sulfonylureas or ISA*, enter 3 →	
Insulin treatment	If not on insulin, enter 0 →	10
	If on insulin, enter 10 →	
<b>DiaRem score (sum) →</b>		<b>19</b>

DiaRem score	Probability of remission
0–2	88%–99%
3–7	64%–88%
8–12	23%–49%
13–17	11%–33%
18–22	2%–16%

\*Insulin sensitizing agent other than metformin

# Indications for bariatric surgery

**BMI  $\geq$  40 kg/m<sup>2</sup>**

In any case, providing surgery risk acceptable (well established)

**BMI  $\geq$  35 kg/m<sup>2</sup>**

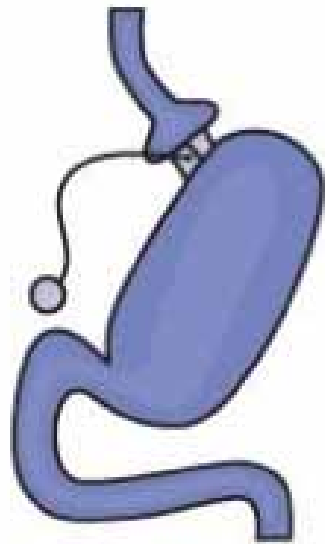
If there are  $\geq$  1 obesity-related morbidities (well established)

- Type 2 diabetes, hypertension, dyslipidemia, CV disease
- Sleep apnea, obesity-hypoventilation, Pickwick's syndrome
- Fatty liver disease
- Idiopathic intracranial hypertension (*pseudotumor cerebri*)
- Gastro-esophageic reflux
- Asthma
- Lower extremities venous insufficiency
- Severe urinary incontinence
- Disabling osteoarthritis

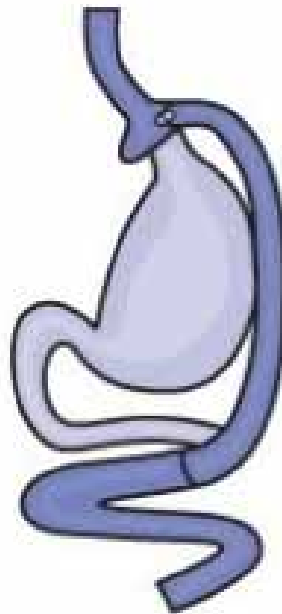
**BMI between 30 and 34,9 kg/m<sup>2</sup>**

If type 2 diabetes or metabolic syndrome ("metabolic surgery")  
(Under scrutiny; less established indication)

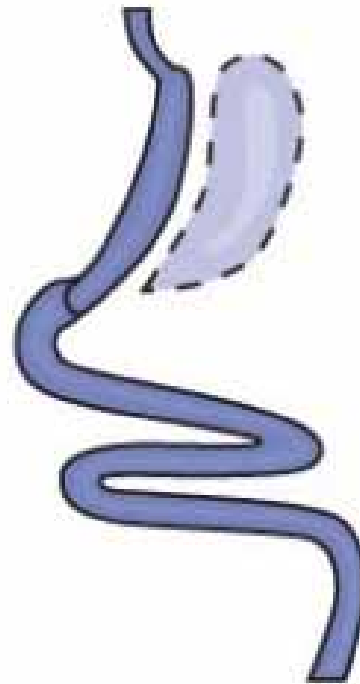
# Bariatric surgery options



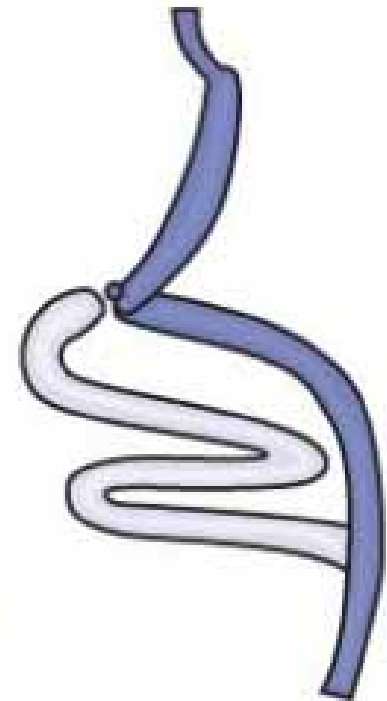
Adjustable  
Gastric Band  
(AGB)



Roux-en-Y  
Gastric Bypass  
(RYGB)



Vertical Sleeve  
Gastrectomy  
(VSG)



Biliopancreatic  
Diversion With a  
Duodenal Switch  
(BPD-DS)

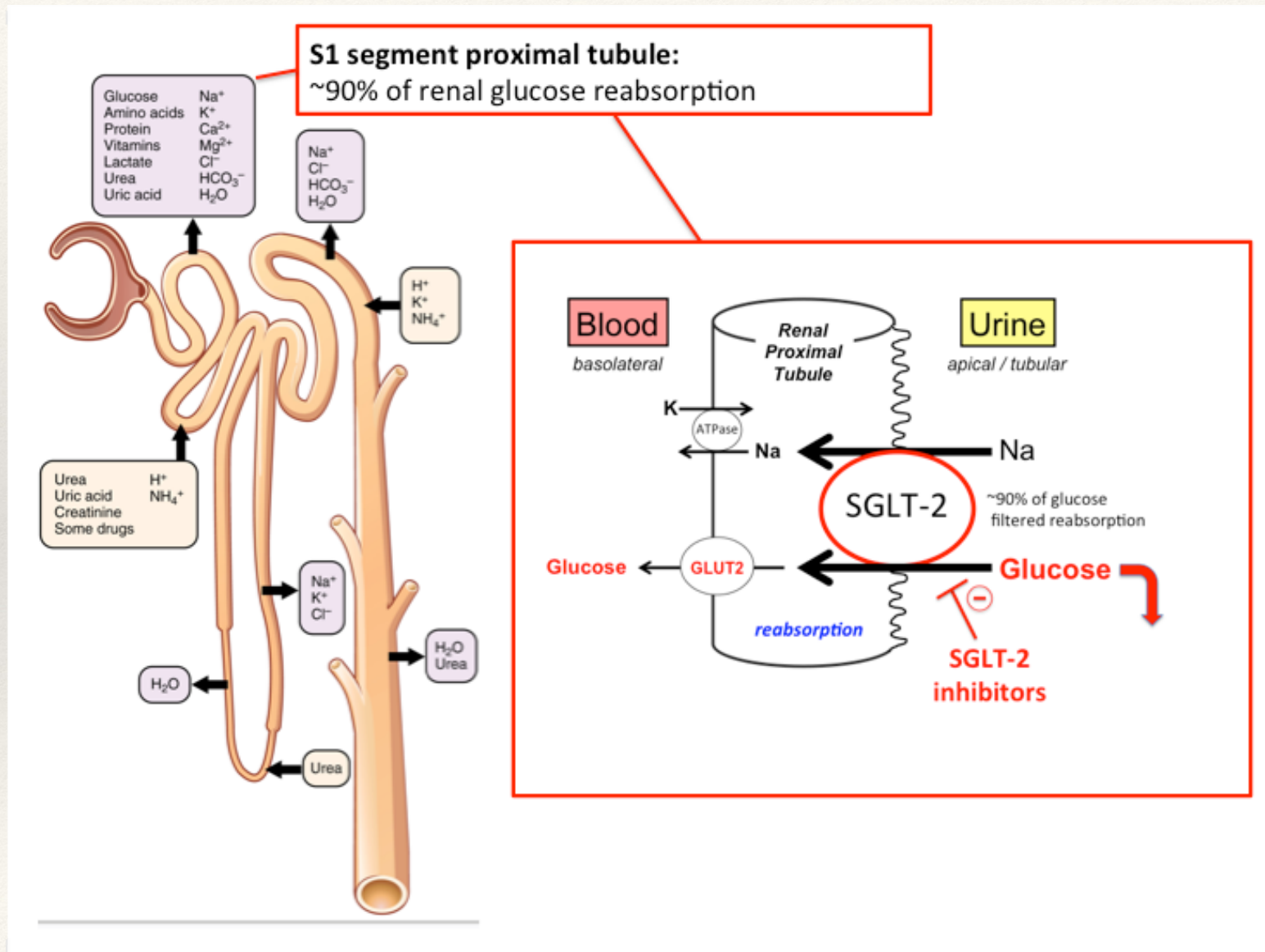
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# Available Medical Treatment

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- Orlistat
- Topiramate
- Lorcaserin
- GLP-1 Receptor Agonists
- SGLT-2 Inhibitors

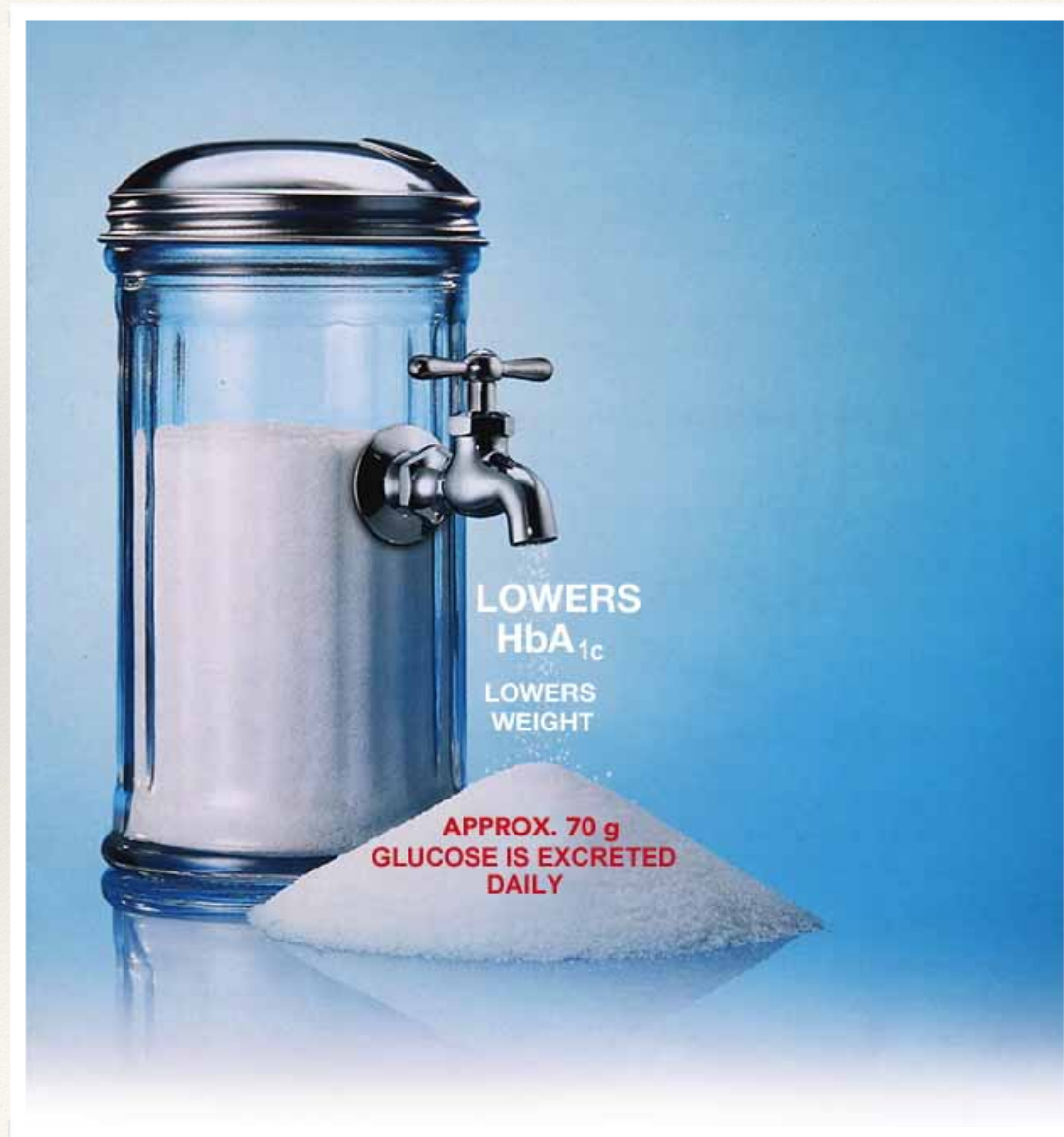
# SGLT2 Inhibitors and weight loss



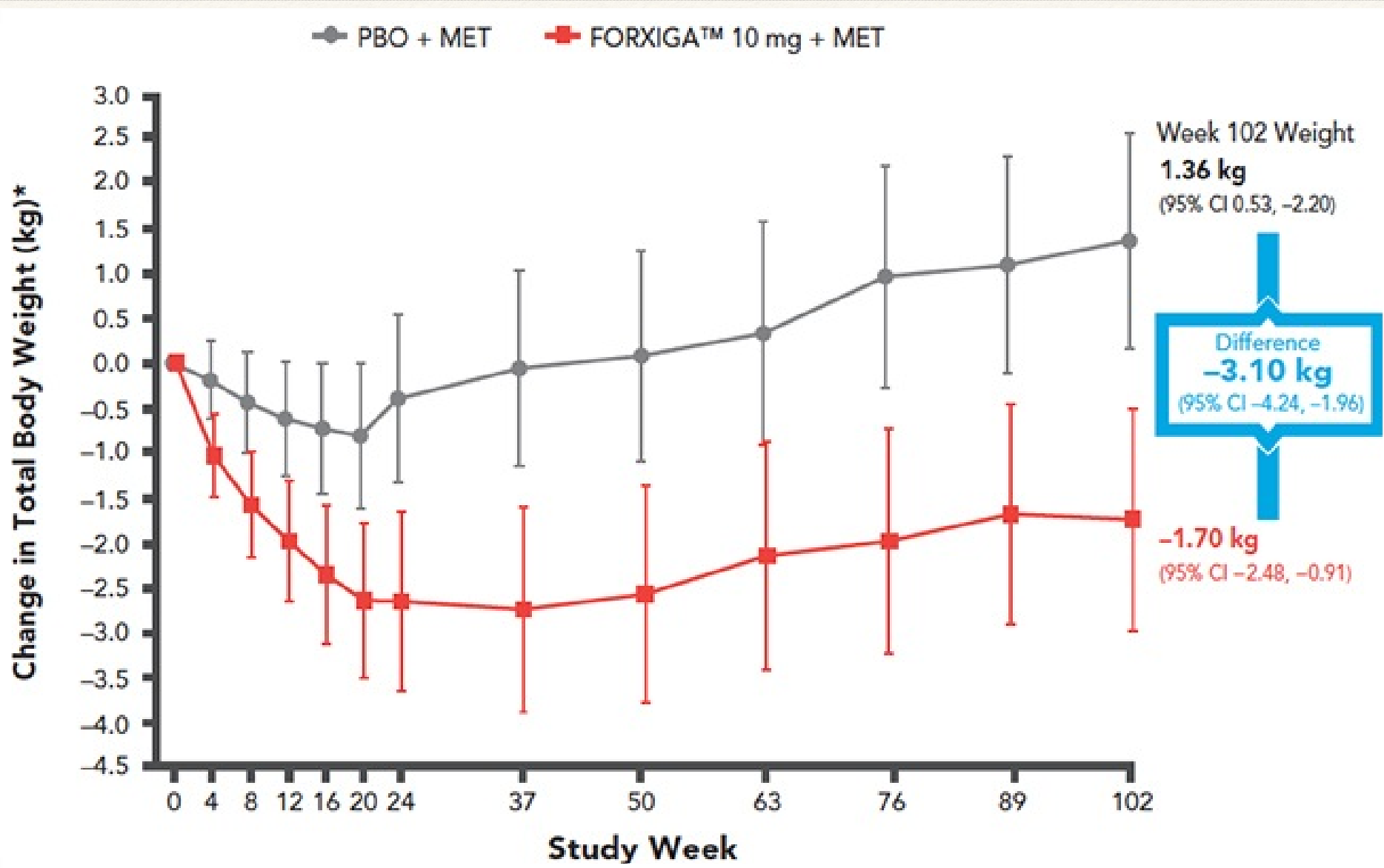
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# SGLT2 Inhibitors and weight loss

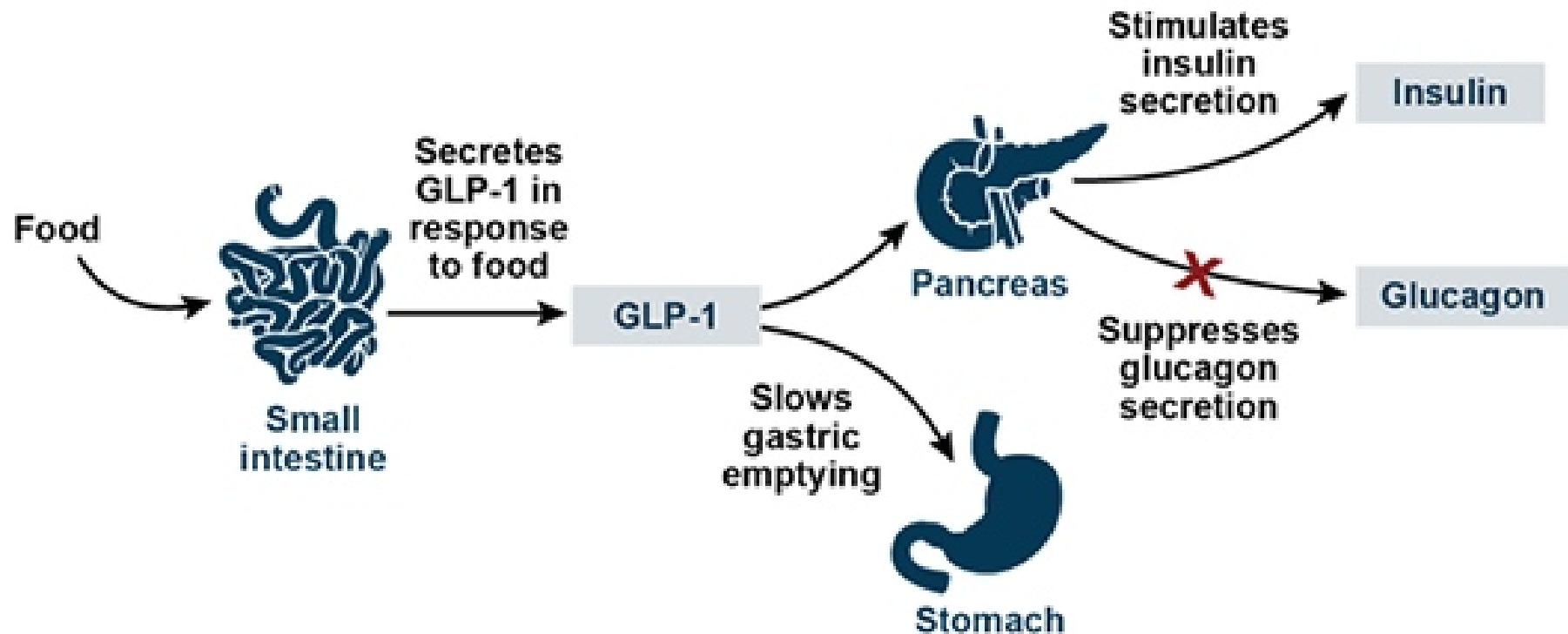
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# SGLT2 Inhibitors and weight loss

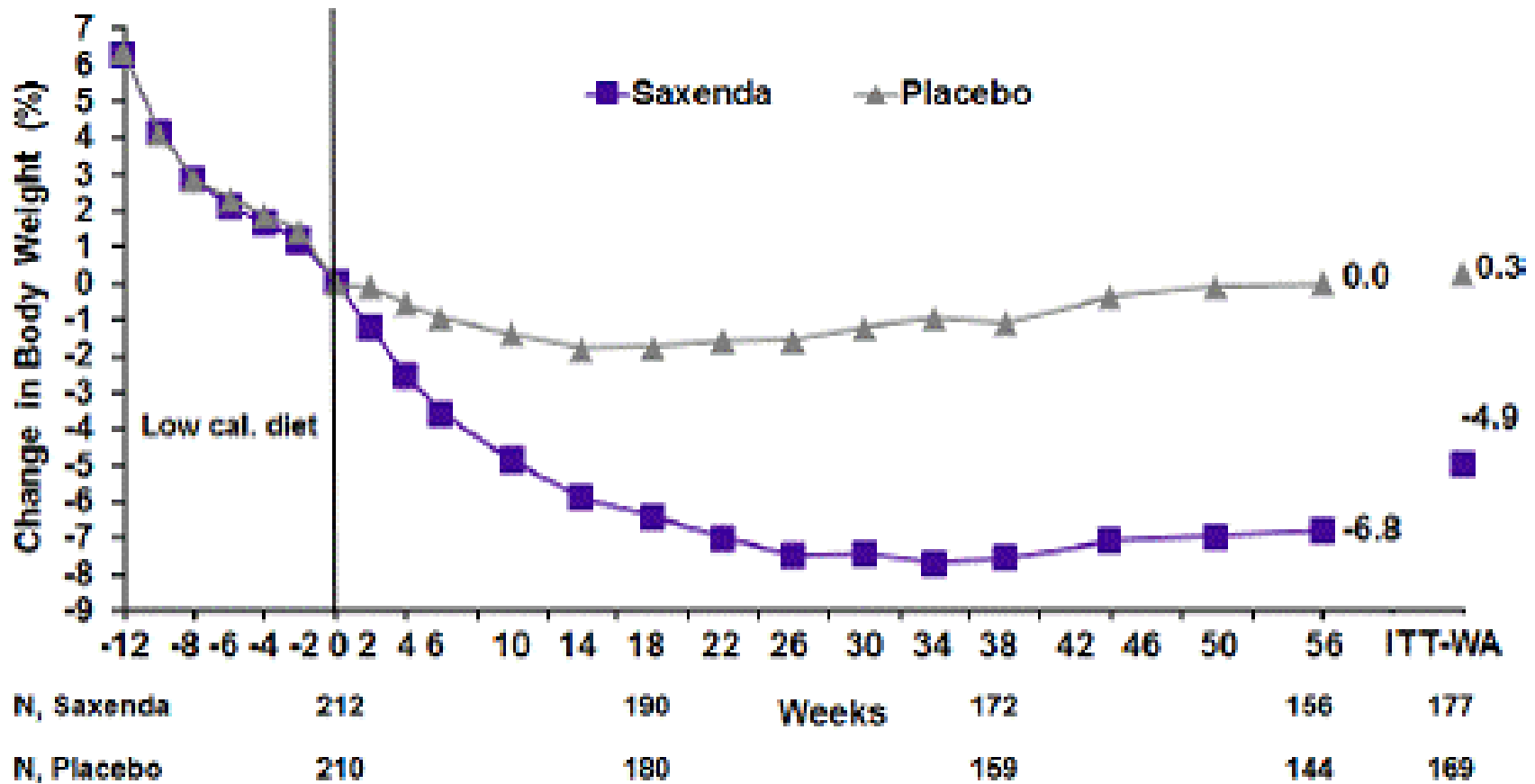


# GLP-1 Receptor Agonists





# Liraglutide licensed for weight loss



Observed values for patients on study drug completing each scheduled visit, and ITT with weighted average (ITT-WA)

Thank you