Obesity is a Chronic Disease
Not Just a Lifestyle Choice

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Disclosures & Disclaimer

Honoraria
- Novo Nordisk

Speaker
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Product Advisory Board
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- Novo Nordisk South Africa does not advocate the use of their products other than described in the locally approved package insert.

- All presenters are independent healthcare practitioners and their views do not necessarily reflect those of Novo Nordisk South Africa.

- Liraglutide 3.0 mg is not approved for weight management in South Africa.
INTRODUCTION: OBESITY

AN OVERWEIGHT PATIENT WALKS INTO YOUR CONSULTING ROOMS AND YOU LOOK AT THE PATIENT AND THINK:

"Perhaps this is your fault?" (BLAME)
"Has it been due to SLOTH AND GLUTTONY?"
"IS YOUR PROBLEM DUE TO AN UNHEALTHY LIFESTYLE?"

("What am I going to do now"? (How am I going to manage?/////Frustration@@@@!!!)

The doctor feels helpless...AND THE PATIENT OFTEN FEELS GUILTY AND SELF CONSCIOUS

But is this a LIFESTYLE CHOICE or a DISEASE?
Obesity—Lifestyle choice or Disease?

- Obesity has been around for a long time
- It is a fallacy to assume that this is only a modern lifestyle condition
- It was almost certainly something that was evident thousands of years ago
- Was it a lifestyle condition then? Or is there something more fundamental to the understanding
<table>
<thead>
<tr>
<th>Date/Region</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Venus of Willendorf (25,000 BCE)</strong></td>
<td>“Fertility, an idolization of beauty or desirability, object of worship or a totem for good fortune”</td>
</tr>
<tr>
<td><strong>Early Israelites, Christians and the Talmud</strong></td>
<td>“Obesity was then stamped as shameful and undesirable”</td>
</tr>
<tr>
<td><strong>Hippocrates (460BC-370BC)</strong></td>
<td>“Obesity led to infertility, illness and early mortality”</td>
</tr>
<tr>
<td><strong>Writings in ancient Greece, India and Egypt</strong></td>
<td>“Suggested obesity as being an impediment to health”</td>
</tr>
<tr>
<td><strong>South Pacific Islands Jamaica, Kuwait and Afghanistan</strong></td>
<td>“Girls were fattened up and then presented to the chief for his admiration as an example of beauty and fertility”</td>
</tr>
<tr>
<td><strong>Early 19th and 20th Century</strong></td>
<td>“Obesity often a sign of success, sometimes an object of ridicule”</td>
</tr>
<tr>
<td><strong>Post World War II - Physicians</strong></td>
<td>“Saw obesity as a societal rather than a medical problem”</td>
</tr>
</tbody>
</table>
Obesity in Art
Definition and classification of obesity:

- Obesity is defined as abnormal or excessive fat accumulation that may impair health.

- Body mass index (BMI) provides the most convenient population-level measure of overweight and obesity currently available.

\[
\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m)}^2}
\]

Quetelet (1796-1874) “weight increases as a function of weight in kg divided by the square of the height in meters—QUETELET INDEX”

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal range</td>
<td>≥18.5 and &lt;25</td>
</tr>
<tr>
<td>Overweight</td>
<td>≥25 and &lt;30</td>
</tr>
<tr>
<td>Obesity</td>
<td>≥30</td>
</tr>
<tr>
<td>Obesity class I</td>
<td>≥30 and &lt;35</td>
</tr>
<tr>
<td>Obesity class II</td>
<td>≥35 and &lt;40</td>
</tr>
<tr>
<td>Obesity class III</td>
<td>≥40</td>
</tr>
</tbody>
</table>
Obesity is driving the type 2 diabetes pandemic

Age standardised global prevalence of obesity and diabetes

1. Adapted from NCD Risk Factor Collaboration (NCD-RisC). Lancet 2017:390;2627–42
2. Adapted from NCD Risk Factor Collaboration (NCD-RisC). Lancet 2016:387;1513–30

1. Obesity
2. Diabetes

Prevalence, %
- <5
- 5–<10
- 10–<15
- 15–<20
- 20–<25
- 25–<30
- 30–<35
- ≥35
Obesity rates worldwide are increasing

**Men BMI ≥30 kg/m²**

**Women BMI ≥30 kg/m²**

South Africa has the 43rd highest average BMI in the world

## Broad causes of obesity in different socio-economic groups

<table>
<thead>
<tr>
<th>Category</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urbanization and Globalization</td>
<td>• Shift away from traditional foods</td>
</tr>
<tr>
<td>Coca-Cola epidemic</td>
<td>• South Africa is one of the largest markets for Coca Cola in the world</td>
</tr>
<tr>
<td>Socio-economic factors</td>
<td>• Obesity associated with age, level of education, ethnicity, area of residence</td>
</tr>
<tr>
<td>Cultural Factors</td>
<td>• Perceptions and beliefs about body weight</td>
</tr>
<tr>
<td>Dietary practices</td>
<td>• Take-outs, fries, fats</td>
</tr>
<tr>
<td>Physical activity</td>
<td>• More TV and computer time, less sport, office-based jobs</td>
</tr>
</tbody>
</table>
Obesity is recognised as a disease and health issue

"The World Obesity Federation *takes the position* that obesity is a chronic, relapsing, progressive disease process and emphasizes the need for immediate action for prevention and control of this global epidemic"¹

**WOF**
World Obesity Federation

"Obesity is characterized by excess body fat that can threaten or affect your health. Many organizations including Obesity Canada, now consider obesity to be a chronic disease."⁴

**OC**
Obesity Canada

"American Medical Association *recognizes* obesity and overweight as a chronic medical condition (de facto disease state) and urgent public health problem...and work towards the recognition of obesity intervention as an essential medical service..."²

**AMA**
American Medical Association

"A progressive disease, impacting severely on individuals and society alike, it is widely acknowledged that obesity is the gateway to many other disease areas..."⁵

**EASO**
European Association for the Study of Obesity

"Obesity is a chronic relapsing health risk *defined by excess body fat*"³

**FDA**
The US Food and Drug Administration

"Obesity is *recognised* as a chronic clinical condition and is considered to be the result of interactions of genetic, metabolic, environmental and behavioural factors, and is associated with increases in both morbidity and mortality"⁶

**EMA**
European Medicines Agency
Obesity meets common criteria of a disease

- An impairment of the normal functioning of some aspect of the body
- Characteristic signs or symptoms
- Harm or morbidity

AMA

- Appetite dysregulation
- Abnormal energy balance
- Endocrine dysfunction

Increased body fat
- Symptoms associated with increased body fat including:
  - Joint pain
  - Immobility
  - Sleep apnoea
  - Infertility
  - NAFLD
  - Dyslipidaemia

- Type 2 diabetes
- Cardiovascular disease
- Cancer
- Osteoporosis
- Polycystic ovary syndrome
Obesity is associated with multiple comorbidities and complications
Metabolic, mechanical and mental

- Depression
- Anxiety
- Asthma
- NAFLD
- Gallstones
- Incontinence
- Arthrosis
- Sleep apnoea
- CVD and risk factors
  - Stroke
  - Dyslipidaemia
  - Hypertension
  - Coronary artery disease
  - Congestive heart failure
  - Pulmonary embolism
- Chronic back pain
- Type 2 diabetes
- Prediabetes
- Thrombosis
- Gout
- Infertility
- NAFLD
- CVD, cardiovascular disease; NAFLD, non-alcoholic fatty liver disease
*Including breast, colorectal, endometrial, esophageal, kidney, ovarian, pancreatic and prostate

Obesity is associated with more than 195 Complications

Life expectancy decreases as BMI increases

Data are based on male subjects; n=541,452

Prospective Studies Collaboration. Lancet 2009;373:1083–96
Increasing BMI contributes to death and disability

Deaths in 2015

Disability-adjusted life-years in 2015

CVD, related to a high BMI, accounted for 2.7 million deaths

34% of DALYs were the result of CVD in people with obesity

Musculoskeletal disorders
Cardiovascular diseases
Cancers
Chronic kidney disease
Diabetes mellitus

CVD, cardiovascular disease, DALYs, disability-adjusted life-years

Weight loss may improve obesity related health issues

Benefits of a 10% weight loss

1. Reduction in risk of type 2 diabetes
2. Reduction in CV mortality
3. Improvements in blood lipid profile
4. Improvements in blood pressure
5. Improvements in severity of obstructive sleep apnoea
6. Improvements in health-related quality of life

References:
Obesity is associated with significant healthcare costs

US annual medical expenditure

CI, confidence interval; US, United States

Cawley et al. Pharmacoeconomics 2015;33:707–22
Medical costs decrease with weight loss
Greater savings with higher baseline BMI

*Estimated costs are based on 2010 data for non-institutionalised US adults aged ≥18 years. Figure drawn based on data available in the reference

Adapted from Cawley et al. Pharmacoeconomics 2015;33:707–22
Endocrine and childhood causes of obesity

Hormonal imbalance or illness as a direct cause of obesity is uncommon (<5%)

• Hypothyroidism
• Cushing’s syndrome
• Hypogonadism
• Menopause: the role of FSH
• PCO? – cause or effect?
• Genetic and developmental diseases causing obesity in childhood
Neurophysiological regulation of appetite

FUNDAMENTAL TO THE CONTROL OF APPETITE
Obesity has long been misunderstood, trivialized, and stigmatized as a simple “lifestyle” issue that can be effectively be addressed by the mantra of “eat-less-move-more”.

This simplistic view of obesity disregards both the lived experience of persons with obesity as well as the vast body of scientific evidence showing that, like other chronic diseases, obesity is a rather heterogeneous condition resulting from the complex interaction of a multitude of socio-psycho-biological factors that promote excessive weight gain and ultimately impair health.

Most importantly, once established, powerful neuro-hormonal factors effectively defend our bodies against weight loss, thereby often making obesity a life-long problem, where weight regain (or relapse) is the rule.
• Obesity is associated with a prolonged imbalance between energy intake and expenditure, both of which are regulated by multiple feedback processes, each with associated internal and external factors.

• These processes constitute three hierarchical control systems – homeostatic, hedonic, and cognitive – with extensive interaction between them.
Obesity is the result of an interaction between the modern environment and our biology.

**Components of appetite**
- Hunger
- Satiation
- Satiety
- Fullness
- PFC

**External factors**
- Economic factors
- Social factors
- Cognitive

**Internal factors**
- Homeostatic
- Genetics/epigenetics
- Hedonic
- PFC, prospective food consumption

**Components of appetite**
- Wanting
- Liking
- Reward

Homeostatic regulation of appetite

**Homeostatic regulation**
- Biological systems act to maintain body weight, including regulation via peptide hormones that can induce hunger/satiety

**Gut hormone system**
- The gut, adipose tissue and pancreas produce several hormones that promote satiety or hunger
- These may influence central appetite control centres either directly via vagal afferents and the brainstem

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AP, area postrema; ARC, arcuate nucleus; AgRP, agouti-related peptide; CART, cocaine and amphetamine regulated transcript; CCK, cholecystokinin; DMN, dorsomedial hypothalamic nucleus; GLP-1, glucagon-like peptide-1; NPY, neuropeptide Y; OXM, oxyntomodulin; LHA, lateral hypothalamic area; POMC, pro-opiomelanocortin; PVN, paraventricular hypothalamic nucleus; NTS, nucleus tractus solitarius; VMN, ventromedial hypothalamic nucleus

Hedonic regulation of appetite

**Hedonic regulation**
- Reward of survival behaviours through pleasure
- Operates even in the presence of satiety signals
- Leads to food consumption beyond homeostatic need
- Link between hedonic attraction to food and obesity

**Hedonic control systems**
- Appetite is influenced by homeostatic (metabolic) and hedonic (pleasure, emotional) factors
- Hedonic appetite systems comprise external sensory information processing, reward processing, and cognition and executive functions
- Multiple different areas are involved including the amygdala and the cortex

AP, area postrema; ARC, arcuate nucleus; DMN, dorsomedial hypothalamic; LHA, lateral hypothalamic area; PVN, paraventricular hypothalamic nucleus; NTS, nucleus tractus solitarius; VMN, ventromedial hypothalamic nucleus

Hypothalamic regulation of appetite

- The hypothalamus integrates signals from several different systems
- Multiple hypothalamic nuclei are involved such as the ARC and PVN
- Two main opposing neuronal types:
  - AgRP/NPY neurons (hunger)
  - CART/POMC neurons (satiety)

AP, area postrema; ARC, arcuate nucleus; AgRP, agouti-related peptide; CART, cocaine and amphetamine regulated transcript; CCK, cholecystokinin; DMN, dorsomedial hypothalamic nucleus; GLP-1, glucagon-like peptide-1; NPY, neuropeptide Y; OXM, oxyntomodulin; LHA, lateral hypothalamic area; PP, pancreatic polypeptide; PYY, peptide-YY; POMC, pro-opiomelanocortin; PVN, paraventricular hypothalamic nucleus; NTs, nucleus tractus solitarius; VMN, ventromedial hypothalamic nucleus

Hypothalamic regulation of appetite

Peripheral signals modulate appetite and energy expenditure via hypothalamic neurons

Hypothalamus

Second order neurons

Arcuate nucleus

Satiety

Hunger

POMC/CART

NPY/AgRP

Leptin
Insulin

PP

GLP-1
PYY
OXM

Ghrelin

Amylin

GLP-1

Adiposity signals

Satiety signals

Hunger signals

Satiety peptide

Feeding

Gastric emptying

Metabolic rate

Hindbrain

Nucleus tractus solitarius

Area postrema

Vagal afferents

α-MSH, α-melanocyte stimulating hormone; AgRP, Agouti-related protein; CART, cocaine and amphetamine regulated transcript; GLP-1, glucagon-like peptide-1; NPY, neuropeptide Y; OXM, oxyntomodulin; POMC, pro-opiomelanocortin; PP, pancreatic polypeptide; PYY, peptide YY

Other factors contributing to the pathogenesis of obesity

• Gut biome

• Brown Fat
Other factors contributing to the pathogenesis of obesity

Genetics
Can genes explain Obesity?

• >600 loci for obesity-related traits found in the last decade, but these explain a small portion of total variance (approx. 3% of BMI)

• SNPs (single nucleotide polymorphisms) are not useful yet in predicting who will develop obesity

• Individual loci have small effects, but with sizable effects in combination
Can genes explain Obesity

• Many other loci are involved in adipocyte metabolism—sexual dimorphism

• Key benefit of gene identification is elucidation of the pathophysiology of obesity which may one day lead to new therapies

• Requires detailed knowledge of causal SNP and genes affected

• So far, only known for FTO
FTO Gene in Obesity

• So far, only known for FTO: individuals with 1 of the FTO obesity risk alleles reported increased food intake, especially high-energy foods, as well as impaired satiety.

• FTO variants mediate obesity by increasing energy output.

• People who are homozygous for the at-risk allele of r9939609 have approximately 1.7-fold increased risk of obesity and are about 3 kg heavier than average.

• Diet and lifestyle changes blunt the effects of a genetic predisposition toward obesity due to the FTO risk allele, so allele carriers could be
TREATMENT
BARRIERS TO OBESITY TREATMENT: Obesity disease recognition

Results from the US ACTION study

65% of PwO recognise obesity as a disease

80% of HCPs recognise obesity as a disease

HCP: healthcare provider; PwO: people with obesity
## Gaps in obesity care

### Results from the US ACTION study

<table>
<thead>
<tr>
<th>PwO (n=3008)</th>
<th>HCPs (n=606)</th>
</tr>
</thead>
<tbody>
<tr>
<td>82% consider weight loss to be completely their own responsibility</td>
<td>Most HCPs down-prioritise weight loss discussions due to lack of time or more important matters</td>
</tr>
<tr>
<td>Only 55% have received a formal diagnosis from their HCP</td>
<td>HCPs set unrealistic weight loss targets with their patients (mean target of 19%)</td>
</tr>
<tr>
<td>Of those receiving a diagnosis, only 24% have a follow-up appointment</td>
<td>Little belief in the efficacy of weight loss medications and concerns about side-effects</td>
</tr>
</tbody>
</table>

HCP, healthcare provider; PwO, people with obesity

*Kaplan et al. Obesity (Silver Spring). 2018;26:61-69*
Current obesity treatment guidelines

Guidelines describe obesity treatment pathway

**Diagnosis of obesity**

- **BMI**
  - Staging$^+$
  - Other anthropomorphic measures$^*$

**Three-tier treatment pathway**

1. Diet and exercise
2. Pharmacotherapy
3. Surgery

**Available guidelines**

- ACC/AHA/TOS 2014$^1$
- EASO 2015$^2$
- AACE Clinical Practice 2016$^3$

**Model**

- BMI-centric
- Complication-centric

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$^*$ Other measures include waist circumference and body composition assessments. $^+$ Optional step

DIETS AND DIETING

KETO  
PALEO  
VEGETARIAN  
VEGAN

KETO vs PALEO  
WHAT'S THE DIFFERENCE?
**LIFESTYLE MODIFICATION—Diet & Exercise**

- Individual Plan
- Regular Follow-Up Visits
- Ideal diet plan
  - Smaller Plate size
  - Alcohol
  - Snacking
  - Simple Sugars
  - Low GI
Efficacy of existing weight loss interventions

- **Lifestyle intervention**
  - 3–5%

- **Very-low calorie diet**
  - 6–10%

- **IBT**
  - 4–6%

- **Pharmacotherapy**
  - 3–10%

- **Gastric band**
  - 7–23%

- **Gastric sleeve**
  - 9–38%

- **Gastric bypass**
  - 24–38%

References:
3. Tsai & Wadden. *Obesity* 2006;14:1283–1293
5. Wadden et al. *Obesity* 2018; doi:10.1002/oby.22359
### Diets (Pros and Cons)

<table>
<thead>
<tr>
<th>Diet Type</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paleo diet</td>
<td>Limits whole grains, legumes and dairy which are healthy and nutritious</td>
</tr>
<tr>
<td>Vegetarian</td>
<td>Low in certain vitamins including B12, D, and other nutrients like iron, zinc, calcium, iodine and omega-3 acids</td>
</tr>
<tr>
<td>HCG with low calorie diet in phases</td>
<td>Many side effects. May be dangerous. FDA disapproves of this diet labeling it dangerous, illegal and fraudulent</td>
</tr>
<tr>
<td>The Zone Diet</td>
<td>Limits consumption of some healthy carb sources</td>
</tr>
<tr>
<td>Intermittent fasting</td>
<td>Does not suit everyone</td>
</tr>
</tbody>
</table>
Challenges in Weight-loss

Health

Obesity research confirms long-term weight loss almost impossible

No known cure for obesity except surgically shrinking the stomach

Kelly Crowe · CBC News · Posted: Jun 04, 2014 5:00 PM ET | Last Updated: June 5, 2014

The nasty reality is that humans are efficient biological machines. "We have evolved not to lose weight," (Reuters)
The Economist April/May 2019

- Calorie counting inaccurate
- Labeling of food inaccurate
- The way different people metabolize food differs depending on many complex factors
- Not all calories are equal
- Energy absorbed is influenced by food preparation
- Chilling and reheating influences the amount of calories absorbed
Weight-Loss & Maintenance strategies
Challenges and Obstacles

• Most successful dieters have 3% more protein, 5% more fat and 8% less carbohydrate
• No sugar
• Exercise
• Persistence
• Patience
• Encouragement

• Difference managing a person with a BMI of <30 and >30
• While lifestyle modification is essential in both situations the chances for successful weight loss to target (whatever that is) will decrease as the BMI increases
• Why is this SOOOO difficult?
REASONS WHY DIETS FAIL

Failed Diet

- Neuronal Signalling
- Chemical
- Body weight set-point
- Hormonal
- Adherence
- Environment

Physiological responses to weight loss favour weight regain\(^1\), \(^2\)

\[\text{Hunger} \quad \text{Desire to eat}\]

Gut

- GLP-1
- CCK
- PYY
- Ghrelin

Adipose tissue

- Leptin

\[\text{Energy intake} \quad \text{Energy expenditure}\]

CCK, cholecystokinin; GLP-1, glucagon-like peptide-1; PYY, peptide YY

Weight management interventions are often followed by weight rebound.
Hunger increases in response to weight loss

- 50 individuals with overweight/obesity lost weight on a 10-week VLCD
- Appetite was measured using VAS scores at 0, 10 and 62 weeks


* p<0.001, § p=0.008, † p=0.09 vs mean at baseline (week 0)
A long-term approach to obesity management is required for maintaining weight loss.
## Pharmacological options for weight management

<table>
<thead>
<tr>
<th>Pharmacological Options</th>
<th>Mode of Action</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>✓</td>
<td>Energy wastage</td>
</tr>
<tr>
<td>Phentermine*</td>
<td>X</td>
<td>Appetite suppression</td>
</tr>
<tr>
<td>Phentermine/topiramate</td>
<td>X</td>
<td>Appetite suppression</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>X</td>
<td>Appetite suppression</td>
</tr>
<tr>
<td>Naltrexone/bupropion</td>
<td>✓</td>
<td>Appetite suppression</td>
</tr>
<tr>
<td>Liraglutide 3.0 mg</td>
<td>✓</td>
<td>Appetite suppression</td>
</tr>
<tr>
<td>Sibutramine</td>
<td>X</td>
<td>Appetite suppression</td>
</tr>
</tbody>
</table>


Naltrexone/bupropion 3.0 mg is not approved for weight management in South Africa.
## Pharmacological options for weight management

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</tr>
<tr>
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<td>✗  ✔️</td>
<td>Appetite suppression, Adjunct to diet and physical activity for chronic weight management in</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a) obesity BMI ≥30 kg/m²</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b) overweight BMI ≥27 kg/m² with comorbidity</td>
</tr>
<tr>
<td>Naltrexone/bupropion</td>
<td>✔️  ✔️</td>
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</tr>
</tbody>
</table>


Liraglutide 3.0 mg is not approved for weight management in South Africa.
Many new pharmacological options in development

Trials are in progress

Watch this space.................................
**What is GLP-1?**

- GLP-1 is a peptide comprised of 31 amino acids
- Member of incretin family
- Secreted predominantly from L-cells in the gut, but also the brain (nucleus tractus solitarius)

Human endogenous GLP-1

Enzymatic degradation by DPP-4

$t_{1/2}$=1.5–2 min

GLP-1 is a peptide comprised of 31 amino acids, a member of the incretin family. It is secreted primarily from L-cells in the gut, but also from the brain (nucleus tractus solitarius). Enzymatic degradation by DPP-4 results in a half-life ($t_{1/2}$) of 1.5–2 minutes. GLP-1, glucagon-like peptide-1; DPP-4, dipeptidyl peptidase-4; human endogenous GLP-1.
GLP-1 is released in response to food intake

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Plasma GLP-1 concentration (pmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>13</td>
<td>30</td>
</tr>
<tr>
<td>19</td>
<td>20</td>
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<tr>
<td>22</td>
<td>15</td>
</tr>
<tr>
<td>24</td>
<td>10</td>
</tr>
</tbody>
</table>

Adapted from: Orskov et al. Scand J Gastroenterol 1996;31:665–70
GLP-1 secretion and receptor expression

GLP-1 is secreted by:
- Neurons in hindbrain
- L-cells of the gut

GLP-1R is expressed in:
- Brain
- Lung
- Heart (AV node)
- Pancreas
- Kidney
- GI tract

AV, atrioventricular; GI, gastrointestinal; GLP-1R, glucagon-like peptide-1 receptor

GLP-1 increases satiety and reduces hunger

In normal weight subjects

- Infusion increased plasma GLP-1 from 10 pmol/L to 60–90 pmol/L


GLP-1 increases satiety and reduces hunger in normal weight subjects

- Infusion increased plasma GLP-1 from 10 pmol/L to 60–90 pmol/L

*At an ad libitum lunch during GLP-1 or saline infusion in 19 healthy normal-weight male subjects. Data are mean ± SEM. GLP-1, glucagon-like peptide-1; SEM, standard error of mean

Liraglutide 3.0 mg is not approved for weight management in South Africa
Liraglutide 3.0 mg influences all dimensions of appetite

5 weeks treatment including 0.6 mg weekly dose escalation. Ratings are AUC_{15-300 min/285 min} reported as FAS LS-means.

*Statistical significance \( p \leq 0.01 \) vs. placebo. Data for overall includes 100 minus scores for hunger and PFC.

AUC, area under-the-curve; FAS, full analysis set; LS, least squares; PFC, prospective food consumption.


Liraglutide 3.0 mg is not approved for weight management in South Africa.
Liraglutide increases satiety and reduces hunger

Via neurons in the arcuate nucleus

AgRP, Agouti-related peptide; CART, cocaine- and amphetamine-regulated transcript; NPY, neuropeptide Y; POMC, pro-opiomelanocortin
Persistence with obesity pharmacotherapy is low

Persistence rate (%)

Follow up months

Persistence rate at 6 months
- Liraglutide 3.0 mg: 41.8%
- Phentermine/topiramate: 27.3%*
- Naltrexone/bupropion: 18.1%*
- Lorcaserin: 15.9%*

*P<0.0001

Persistence rate at 12 months
- Liraglutide 3.0 mg: 33.0%
- Phentermine/topiramate: 16.8%*
- Naltrexone/bupropion: 12.7%*
- Lorcaserin: 10.3%*

*P<0.0001


Kaplan–Meier plot
How to manage the very obese?

• Bariatric surgery: indications and outcomes

• Bariatric surgery is currently the most efficacious long-term treatment option, with the degree of weight loss depending on the type of surgical procedure performed

• However, due to the complexity and cost of this intervention, it is typically only used in individuals with a BMI $\geq 40$ kg/m$^2$ or a $\geq 35$ kg/m$^2$ with comorbidities, and is therefore only available to a limited number of individuals.
Bariatric surgery is associated with sustained weight loss over 20 years

Mean weight loss from baseline:
- Control: ~1% (control)
- Banding: ~18% (mean, surgical interventions)

Data are mean ± 95% confidence interval

Sjöström L et al. JAMA 2012;307:56–65
SUMMARY: OBESITY

• There are complex multifactorial interactions between
  • external environment
  • genetic,
  • metabolic and neurophysiological factors

• “adiposity-based chronic disease or ABCD” is a better term than obesity to more accurately represent the condition as a disease and focusing on the distribution and abnormal function of adipose tissue and not only on the BMI”–AACE 2017

• 10% Body Mass weight loss = improved outcomes
Summary

• Treatment is difficult—higher dose GLP-1 analogues might be an answer

• Bariatric surgery is still the most effective way to treat severe obesity

• Cost considerations for surgery is still a problem
Thank You
Thank You