Approach to the Patient with Obesity and Diabetes: What Every Clinician Should Know

Bartolome Burguera, MD, PhD
Professor of Medicine
Chief Medical Specialty Institute
Chairman of Endocrinology & Metabolism Department
Cleveland Clinic
Cleveland, OH
burgueb@ccf.org

CONTINUING EDUCATION COMPANY

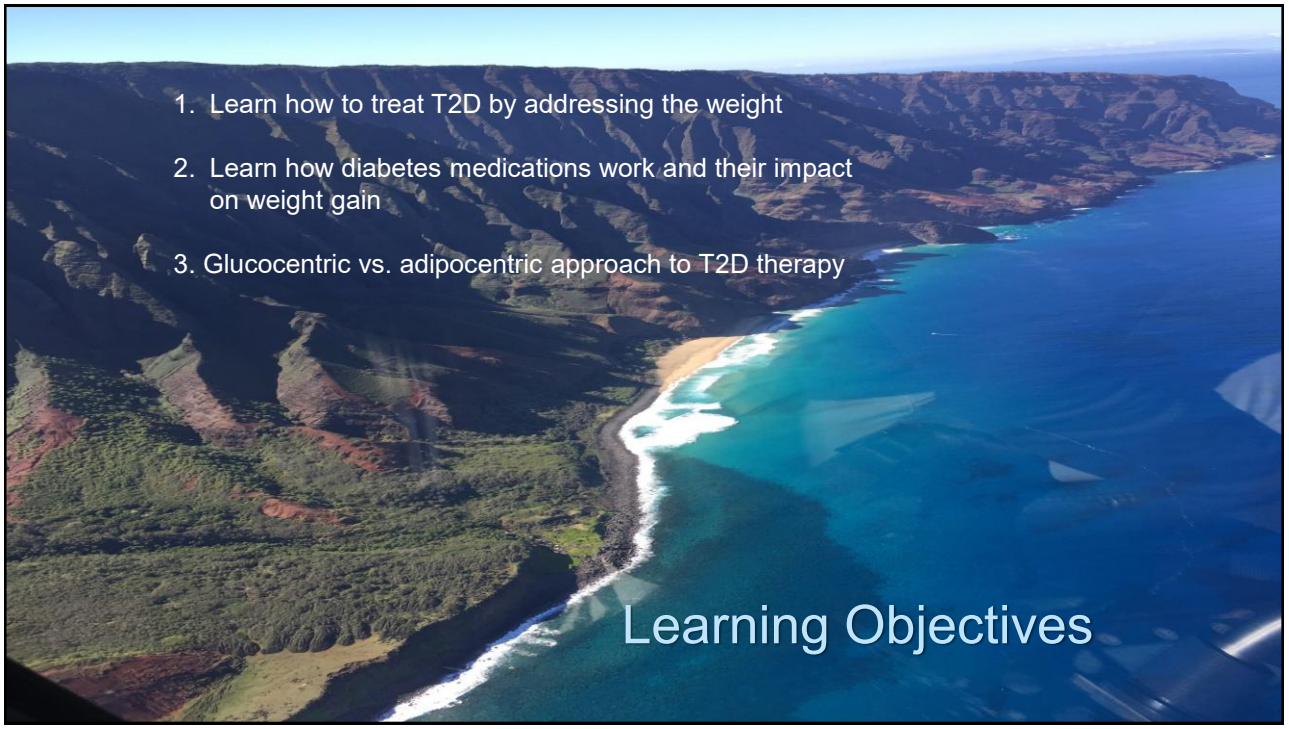
1

Disclosure

I have no financial interests or relationships to disclose.

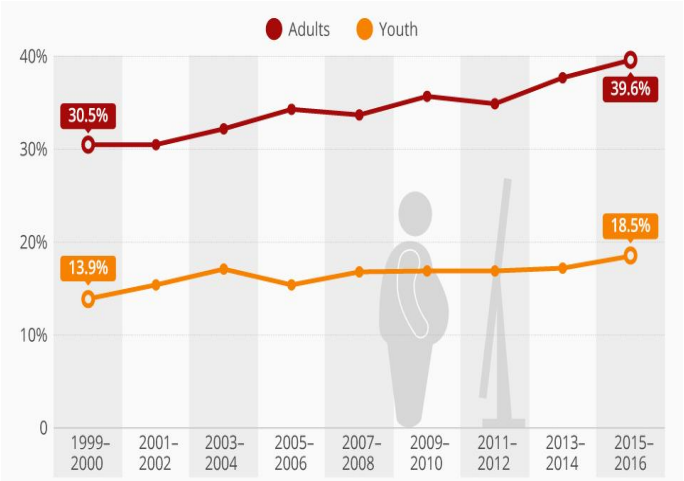
CONTINUING EDUCATION COMPANY

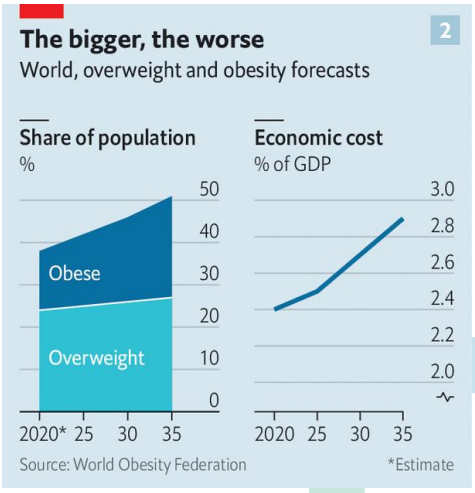
2



3

Prevalence of Obesity + Rising Costs

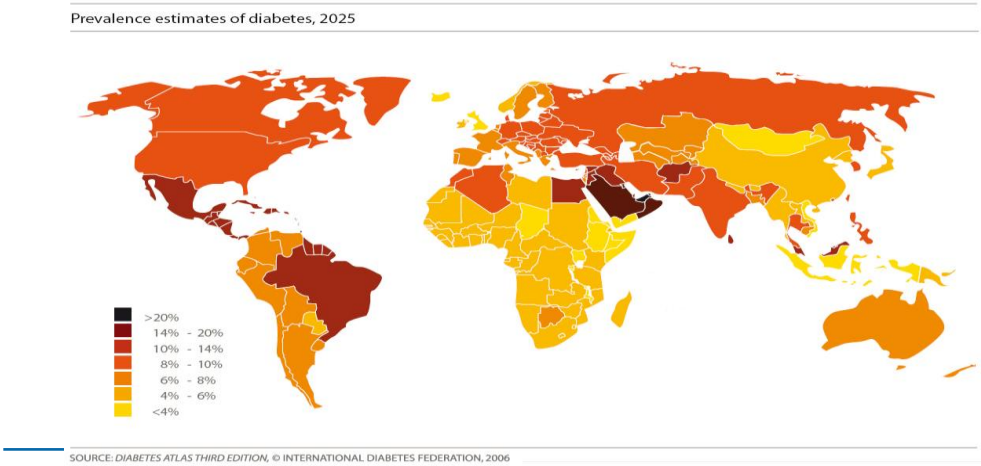




4

An Estimated 285 Million People Worldwide Are Affected by Diabetes

With a Further 7 Million People Developing Diabetes Each Year, This Number Is Expected to Hit 438 Million by 2030



5

Obesity Is Responsible for Many Medical Problems

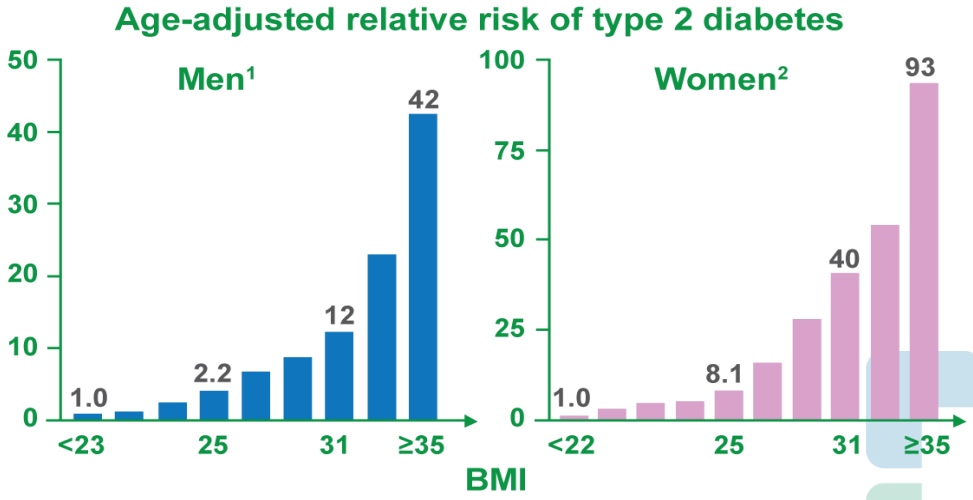
- Development of T2D (90%) and HTN (50%) of cases
- Dyslipidemia (70%)
-
- Depression (50%)
- Responsible for causing osteoarthritis in more than 25% of patients
- More than 50% of patients with sleep apnea have obesity

NCD Risk Factor Collaboration. Lancet. 2017;10113:2627-2642
WHO Technical Report Series. 894. Geneva, Switzerland, 2000
World Health Organization. Obesity and Overweight Fact Sheet

Aronow WS et al. Annals of Translational Medicine. 2017;5(17):350
Luppino FS et al. Arch Gen Psychiatry. 2010;67(3):220–229
Romero-Corral A et al. Chest. 2010;137(3):711–719

6

Obesity is the Primary Risk Factor for Type 2 Diabetes

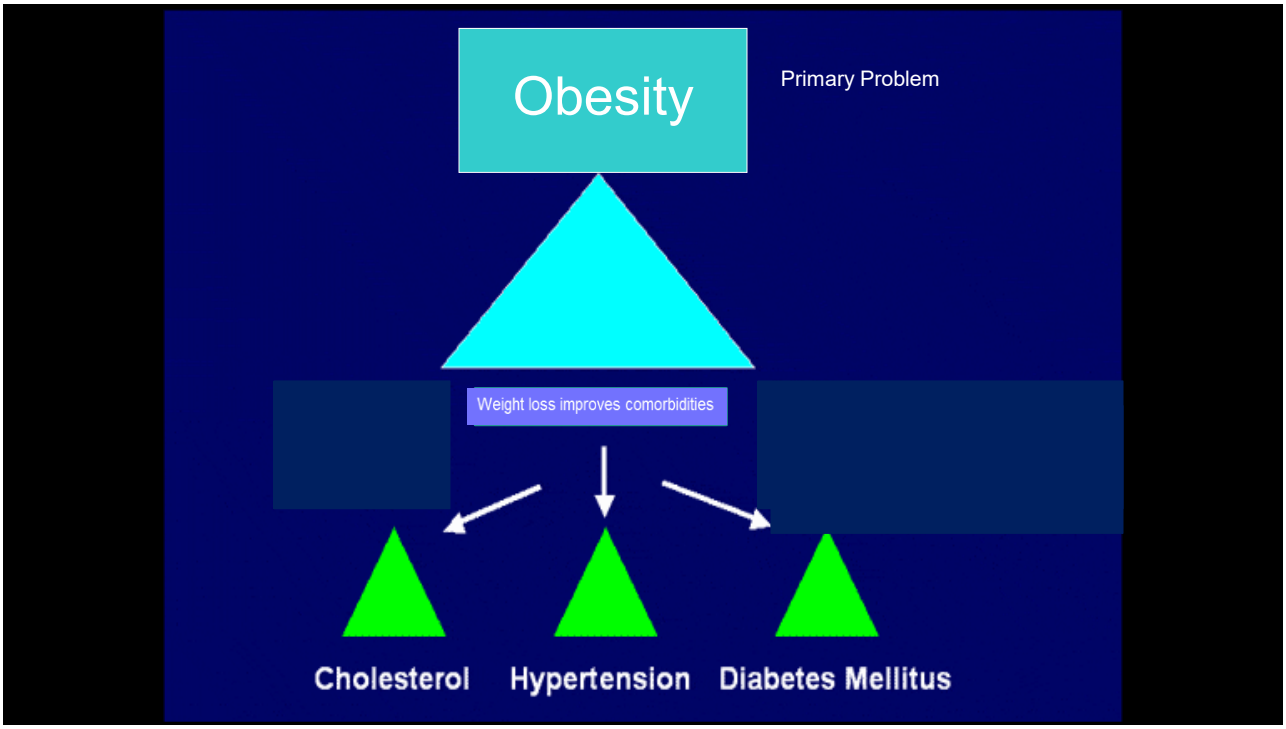


1Chan JM et al. Diabetes Care 1994;17:961-969; 2Colditz G et al. Ann Intern Med 1995;122:481-486.

7

- We ignore obesity
- We focus on dealing with the consequences

8



9

Pragmatic Vision of Diabetes by an Endocrinologist Specialized in Obesity

- Obesity is responsible for the development of type 2 diabetes
- Individuals with type 2 diabetes are concerned with hypoglycemias and weight gain
- Weight loss helps remission of DT2
  - We rarely provide interdisciplinary and sustained weight loss programs
  - ADA and EASD include in their guides medications that cause weight gain and hypoglycemia
- There are new anti-diabetic medications that facilitate weight loss and do not cause hypoglycemia
- We rarely use FDA-approved medications to treat obesity
- We treat diabetes with medications that cause weight gain and perpetuate the disease

10

BARRIERS TO OBESITY Therapy:

Physicians

- - Time limitations in the clinic
- - We do not feel comfortable counseling patients with obesity
- - Lack of knowledge (and SUPPORT) about nutrition, physical activity, and weight loss meds
- - They take too much time. Complicated …
- - Bias that drug treatments are nor effective and are potentially dangerous
- New AOMs are usually not covered by insurances

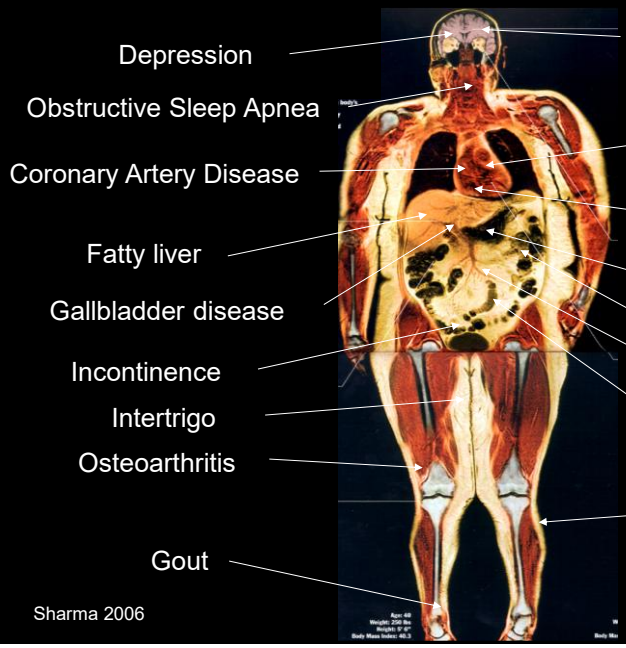
11

Pragmatic Vision of Diabetes by an Endocrinologist Specialized in Obesity

- Obesity is responsible for the development of type 2 diabetes
- Individuals with type 2 diabetes are concerned with hypoglycemias and weight gain
- Weight loss helps remission of DT2
  - We rarely provide interdisciplinary and sustained weight loss programs
  - ADA and EASD include in their guides medications that cause weight gain and hypoglycemia
- There are new anti-diabetic medications that facilitate weight loss and do not cause hypoglycemia
- We rarely use FDA-approved medications to treat obesity
- We treat diabetes with medications that cause weight gain and perpetuate the disease

12

Health Consequences of Obesity



Sharma 2006

13

There Is a Clear Correlation Between the Development of Obesity and the Appearance of

Insulin Resistance → **Pre-diabetes** → **DMT2**

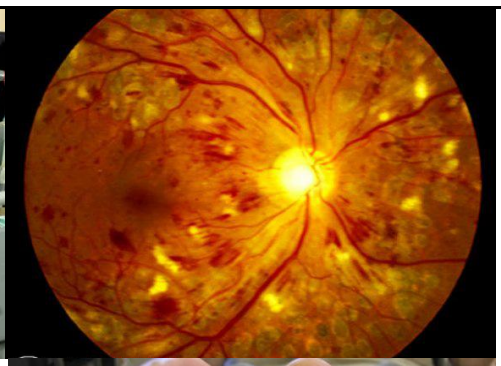
Chan J et al. *Diabetes Care* 1994;17:961.
Colditz G et al. *Ann Intern Med* 1995;122:481.

14

- In Western countries, nearly 90% of T2DM cases can be attributed to weight gain
- Two-thirds of adults diagnosed with T2D have a BMI of ≥27 kg/m^2

International Diabetes Federation, 2003.
NAASO. *Arch Intern Med* 2000;160:898–904
Ng M. et al Lancet Published online May 29, 2014

15



We treat the Complications

16

Pragmatic Vision of Diabetes by an Endocrinologist Specialized in Obesity

- Obesity is responsible for the development of type 2 diabetes
- Individuals with type 2 diabetes are concerned with hypoglycemia and weight gain
- Weight loss helps remission of DT2
  - We rarely provide interdisciplinary and sustained weight loss programs
  - ADA and EASD include in their guides medications that cause weight gain and hypoglycemia
- There are new anti-diabetic medications that facilitate weight loss and do not cause hypoglycemia
- We readily use FDA-approved medications to treat obesity
- We treat diabetes with medications that cause weight gain and perpetuate the disease

17

Patients Are Concerned About Weight Gain: Questions Posted on Diabetes Web Forums

- "I've heard that once you control blood sugar you gain weight?"
- "Is it true that insulin causes weight gain? I would have hoped to lose weight"
- "Since starting on insulin 8 months ago, I've gained 26 kg. I am so depressed. Are there other treatments I could try instead?"
- "I've tried hard to lose weight, but since starting insulin my weight has increased. I'm willing to be more strict with my diet but I worry that could cause hypoglycemia…."
- "Are there any drugs for weight loss suitable for diabetics on insulin?"

18

Key Challenges of Type 2 Diabetes

1. Diabetes is a progressive disease characterized by:

- Declining beta-cell function
- Deterioration of glycemic control
- Microvascular complications
- Increased risk of cardiovascular disease

1. As diabetes treatments are added to control glucose, physicians and patients frequently need to deal with:

- Increased risk of hypoglycemia
- Weight gain
- Complex treatment regimens
- Increased requirement for self monitoring

19

Pragmatic Vision of Diabetes by an Endocrinologist Specialized in Obesity

- Obesity is responsible for the development of type 2 diabetes
- Individuals with type 2 diabetes are concerned with hypoglycemia and weight gain
- Weight loss helps remission of DT2
  - We rarely provide interdisciplinary and sustained weight loss programs
  - ADA and EASD include in their guides medications that cause weight gain and hypoglycemia
- There are new anti-diabetic medications that facilitate weight loss and do not cause hypoglycemia
- We readily use FDA-approved medications to treat obesity
- We treat diabetes with medications that cause weight gain and perpetuate the disease

20

There Are Solid Data That Show That Weight Loss Is Associated with Improvement of:

- Insulin Resistance
- Fasting blood sugar
- HbA1c
- Sometimes remission of DT2

21

Primary Care-led Weight Management for Remission of Type 2 Diabetes (DiRECT):

At 12 Months, Almost Half of Participants Achieved Remission to a Non-diabetic State and Off Antidiabetic Drugs. Remission of Type 2 Diabetes Is a Practical Target for Primary Care

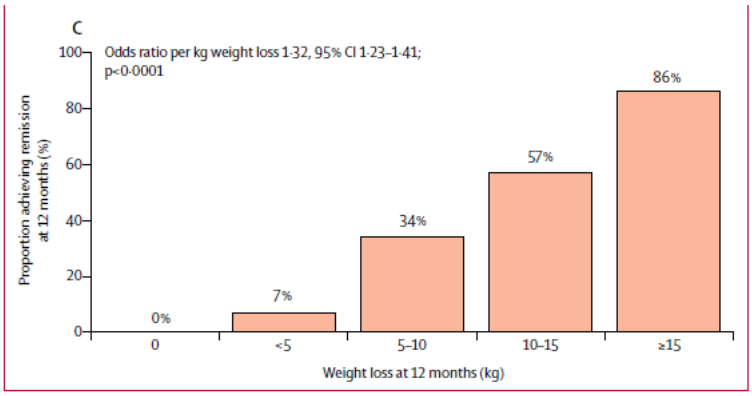


Figure 2: **Primary outcomes and remission of diabetes in relation to weight loss at 12 months**

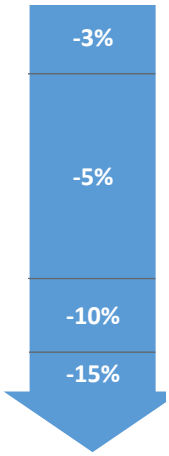
Lean ME et al. **Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial.** Lancet. 2018 Feb 10;391(10120):541-551

22

Modest Weight Loss Has Benefits, with Greater Weight Loss Associated with Greater Benefit

Measures of glycemia[1]

Triglycerides[1]



1. Wing et al. Diabetes Care 2011;34:1481-1486. ; 2. Lazo et al. Diabetes Care 2010;33:2156–2163. ; 3. Phelan et al. Urol. 2012;187:939-944.; 4. Wing et al. Diab Care 2013;36:2937-2944. ; 5. Wing et al. Journal of Sexual Medicine 2010 ; 7:156-65. ; 6. Crosby, Manual for the IWQOL-LITE Measure. ; 7. Promrat et al. Hepatology 2010;51:121–129. 18. Foster et al. Arch Intern Med 2009;169:1619–1626

23

The NEW ENGLAND JOURNAL of MEDICINE

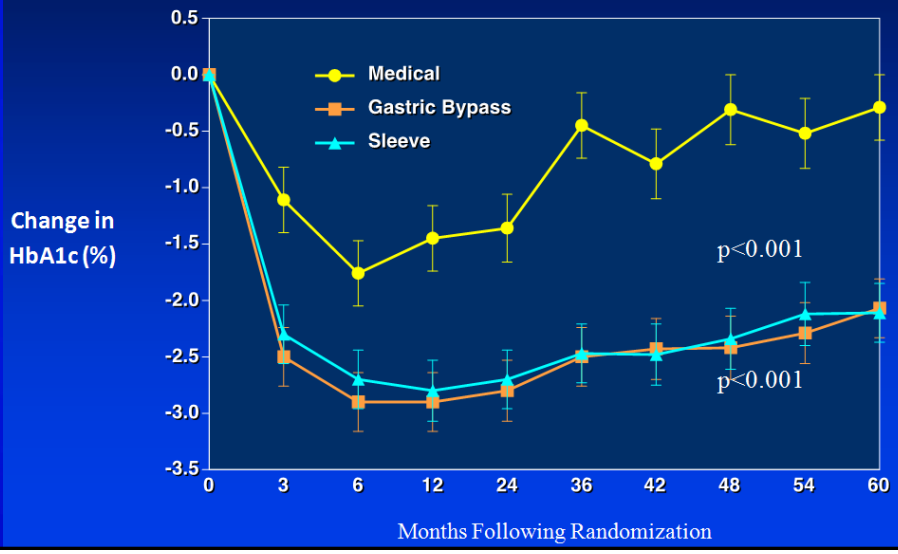
ORIGINAL ARTICLE

Bariatric Surgery versus Intensive Medical Therapy for Diabetes — 5-Year Outcomes

Philip R. Schauer, M.D., Deepak L. Bhatt, M.D., M.P.H., John P. Kirwan, Ph.D., Kathy Wolski, M.P.H., Ali Aminian, M.D., Stacy A. Brethauer, M.D., Sankar D. Navaneethan, M.D., M.P.H., Rishi P. Singh, M.D., Claire E. Pothier, M.P.H., Steven E. Nissen, M.D., and Sangeeta R. Kashyap, M.D., for the STAMPEDE Investigators*

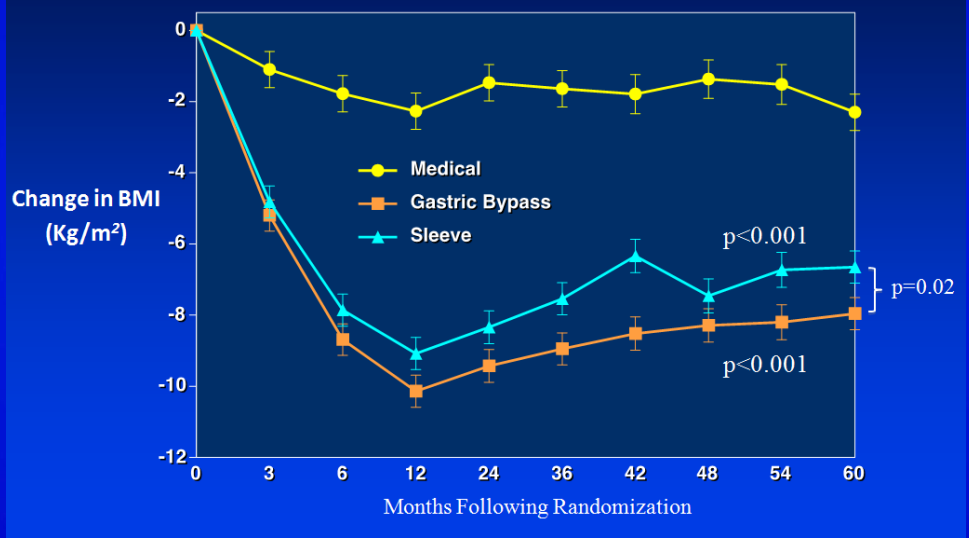
24

STAMPEDE: Change in HbA1c Over 5 Years



25

Change in BMI Over 5 years



26

Pragmatic Vision of Diabetes by an Endocrinologist Specialized in Obesity

- Obesity is responsible for the development of type 2 diabetes
- Individuals with type 2 diabetes are concerned with hypoglycemias and weight gain
- Weight loss helps remission of DT2
  - We rarely provide interdisciplinary and sustained weight loss programs
  - ADA and EASD include in their guides medications that cause weight gain and hypoglycemia
- There are new anti-diabetic medications that facilitate weight loss and do not cause hypoglycemia
- We readily use FDA-approved medications to treat obesity
- We treat diabetes with medications that cause weight gain and perpetuate the disease

27

Approach to a Patient with Obesity

28

Obesity Affects a Large Percentage of Patients Seen in Our Clinics Worldwide (5-7% with Morbid Obesity)

What Do We Usually Do?

- Try to rule out a secondary cause of obesity.
- We encourage our patients to improve their dietary habits & more PA
  - We usually refer them for a consult with our dietitians.
  - We ask them to be more physically active, (without usually providing any specific exercise plan).
  - Rarely we prescribe weight loss medications.
- If they have severe obesity?
  - we may refer them for bariatric surgery.
- Finally we tell them to come back in 3-6 months
  - Short follow-up visit
  - Hopefully with nutrition or nursing team

Subconsciously: how can I get rid of this patient?

29

Pragmatic Vision of Diabetes by an Endocrinologist Specialized in Obesity

- Obesity is responsible for the development of type 2 diabetes
- Individuals with type 2 diabetes are concerned with hypoglycemias and weight gain
- Weight loss helps remission of DT2
  - We rarely provide interdisciplinary and sustained weight loss programs
  - ADA and EASD include in their guides medications that cause weight gain and hypoglycemia
- There are new anti-diabetic medications that facilitate weight loss and do not cause hypoglycemia
- We readily use FDA-approved medications to treat obesity
- We treat diabetes with medications that cause weight gain and perpetuate the disease

30

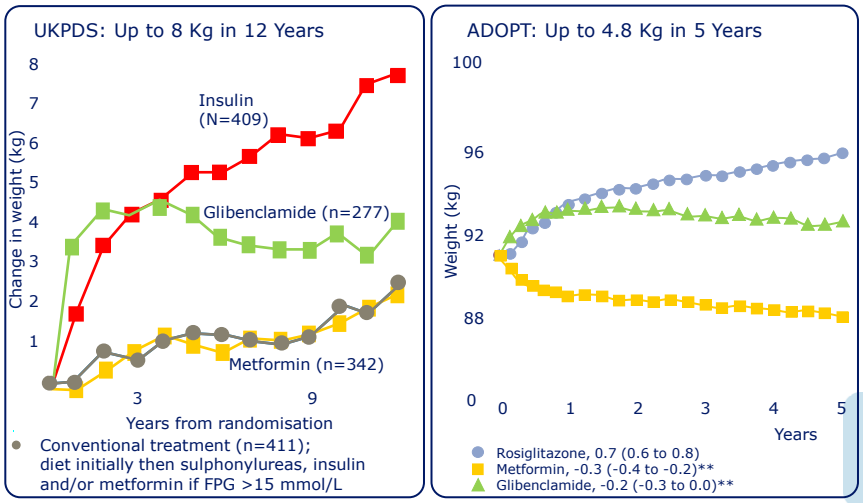
Drugs to Treat Diabetes and Weight Gain

WEIGHT GAIN ASSOCIATED WITH USE	ALTERNATIVES (WEIGHT REDUCING IN PARENTHESES)*
Insulin (weight gain differs with type and regimen used) Sulfonylureas Thiazolidinediones Mitiglinide	(Metformin) (Acarbose) (Miglitol) (Pramlintide) (Exenatide) (Liraglutide) (sGLT-2 inh) Semaglutide Tirzepatide

Apovian CM, Aronne LJ, Bessesen DH et al. Pharmacologic Management of obesity: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2015 doi:10.1210/jc.2014-3415

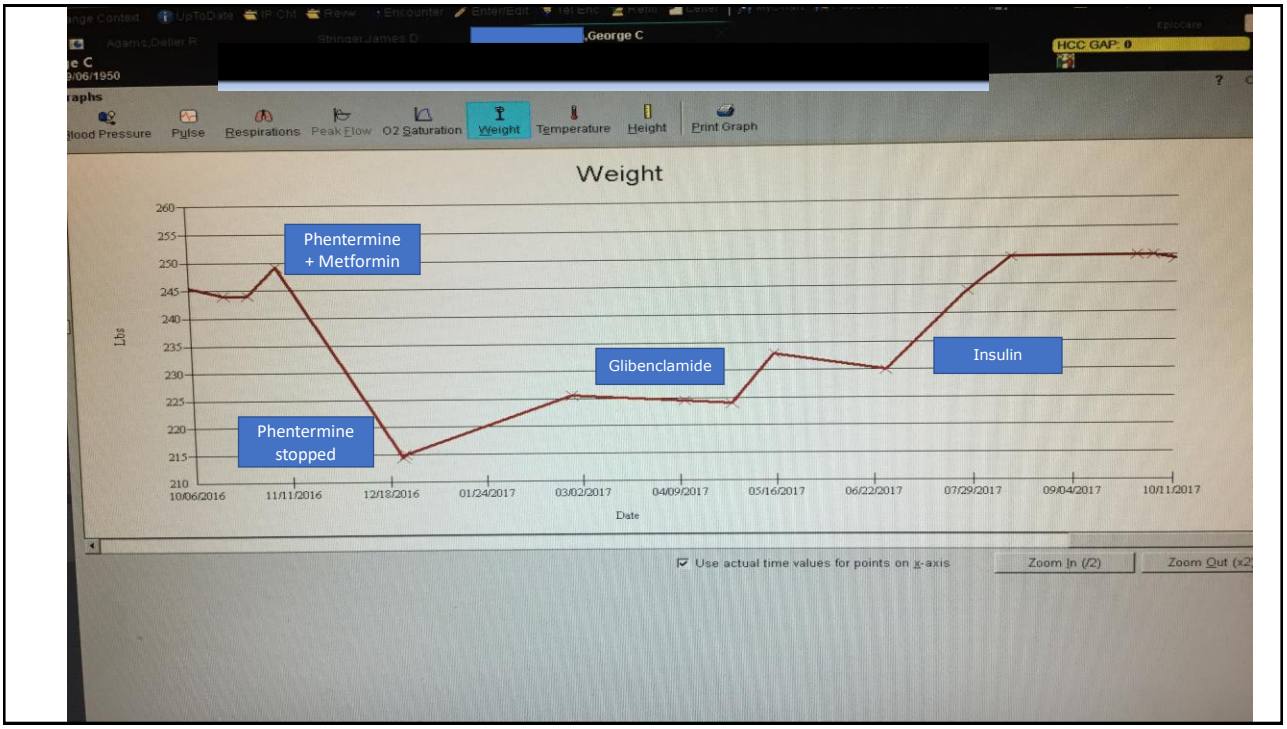
31

Most Therapies Result in Weight Gain Over Time

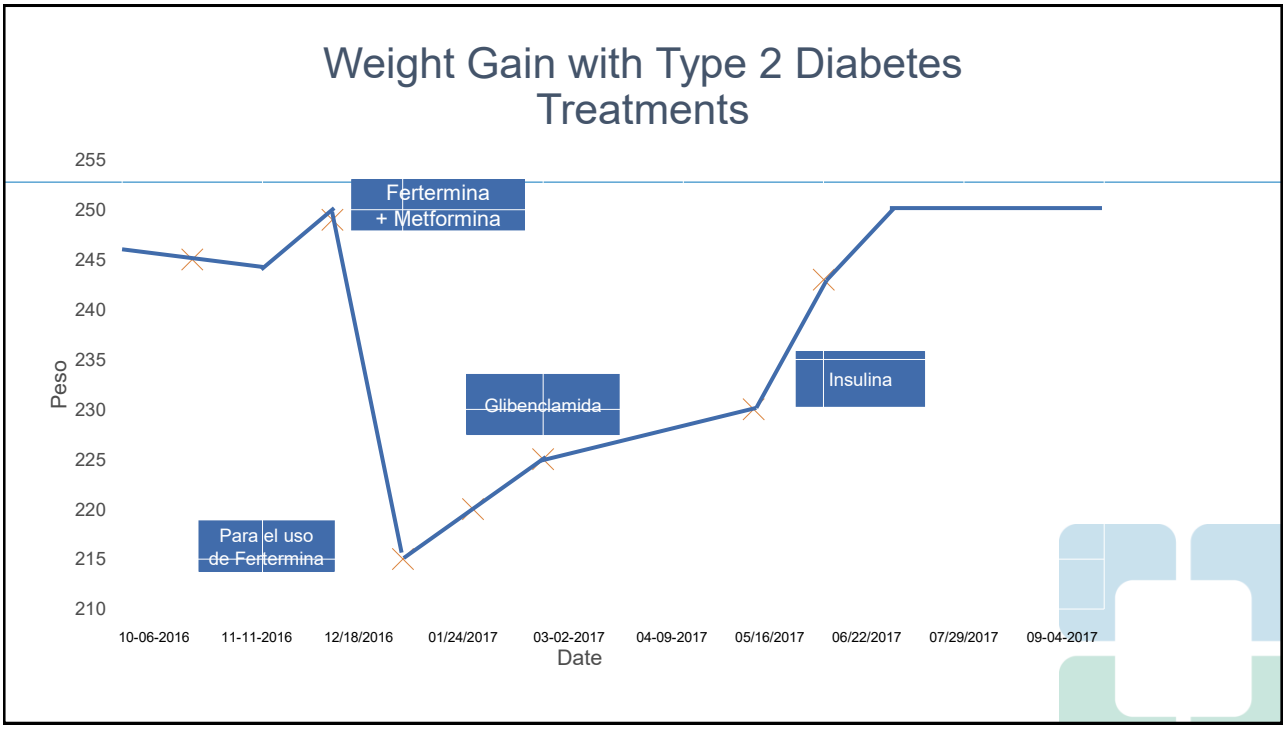


UKPDS 34. *Lancet* 1998:352:854–65. n=at baseline; Kahn *et al* (ADOPT). *NEJM* 2006;355(23):2427–43

32

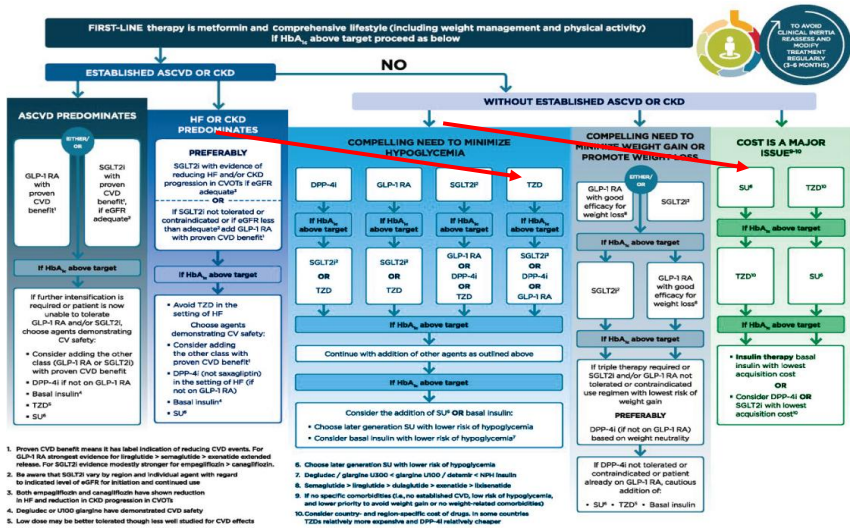

Weight
Blood Pressure
Pulse
Respirations
Peak Flow
O2 Saturation
Weight
Temperature
Height
Print Graph
Phentermine + Metformin
Phentermine stopped
Glibenclamide
Insulin
Lbs
Date
Use actual time values for points on x-axis
Zoom In (/2)
Zoom Out (x2)

33


Weight Gain with Type 2 Diabetes Treatments
Peso
Fertermina + Metformina
Para el uso de Fertermina
Glibenclamida
Insulina
10-06-2016
11-11-2016
12/18/2016
01/24/2017
03-02-2017
04-09-2017
05/16/2017
06/22/2017
07/29/2017
09-04-2017
Date

34

EASD-ADA Consensus Guidelines on Managing Hyperglycemia in Type 2 Diabetes



American Diabetes Association Dia Care 2019;42:S90-S102

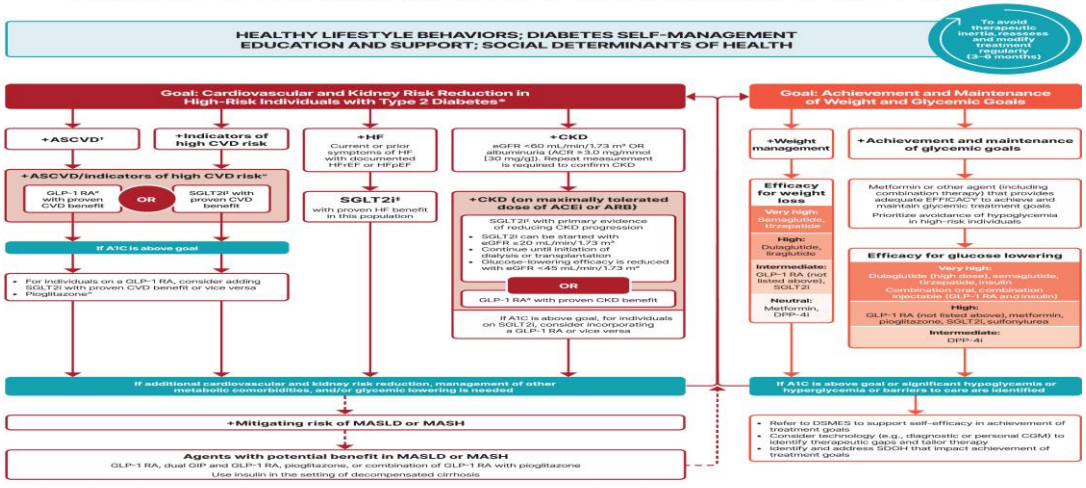
35

American Diabetes Association.

Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2025

Diabetes Care. 2024;48(supplement_1):s181-S206. Doi:10.2337/Dc25-S009

Use of Glucose-Lowering Medications in the Management of Type 2 Diabetes



* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be made irrespective of background use of metformin or A1C.

† ASCVD: Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, and arterial revascularization procedure) and variably included conditions such as transient ischemic attack, unstable angina, amputation, and symptomatic or asymptomatic coronary artery disease. Indicators of high risk: While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria).

= A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high-risk CVD. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details.

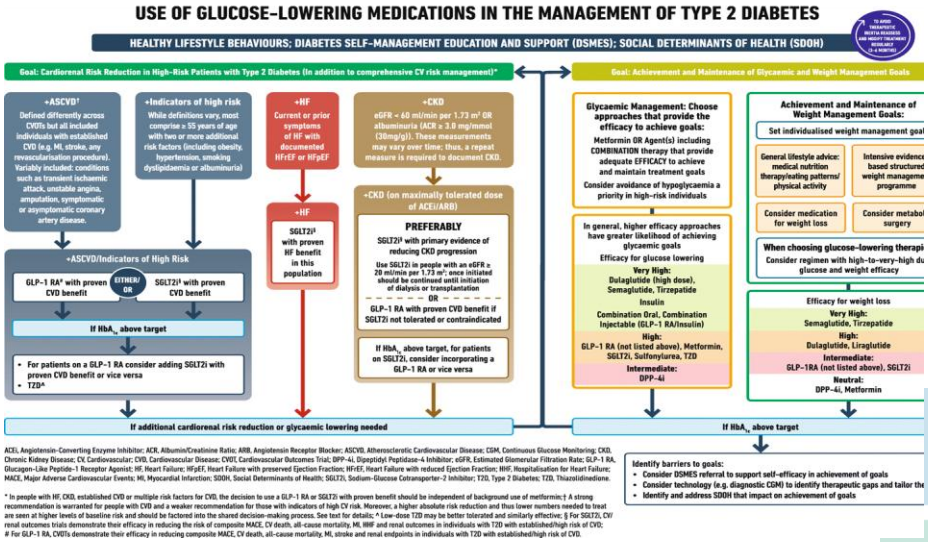
For GLP-1 RAs, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and kidney end points in individuals with T2D with established or high risk of CVD. One kidney outcome trial demonstrated benefit in reducing persistent eGFR reduction and CV death for a GLP-1 RA in individuals with CKD and T2D.

‡ For SGLT2is, CV and kidney outcomes trials demonstrate their efficacy in reducing the risks of composite MACE, CV death, all-cause mortality, MI, HHF, and kidney outcomes in individuals with T2D and established or high risk of CVD.

^ Low-dose pioglitazone may be better tolerated and similarly effective as higher doses.

36

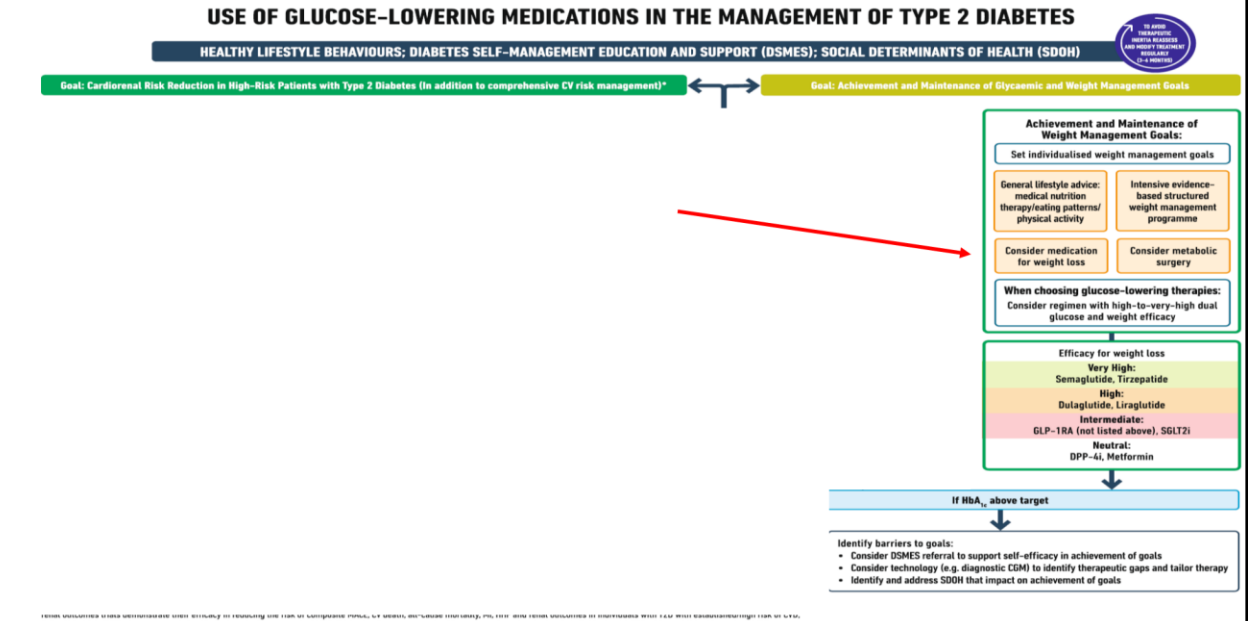
Management of hyperglycaemia in type 2 diabetes, 2022.
A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)



ACEi, Angiotensin-Converting Enzyme Inhibitor; ACR, Albumin/Creatinine Ratio; ARB, Angiotensin Receptor Blocker; ASCVD, Atherosclerotic Cardiovascular Disease; CGM, Continuous Glucose Monitoring; CKD, Chronic Kidney Disease; CV, Cardiovascular; CVD, Cardiovascular Disease; CVOT, Cardiovascular Outcomes Trial; DPP-4i, Dipeptidyl Peptidase-4 Inhibitor; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; HFpEF, Heart Failure with preserved Ejection Fraction; HFrEF, Heart Failure with reduced Ejection Fraction; HHF, Hospitalisation for Heart Failure; MACE, Major Adverse Cardiovascular Events; MI, Myocardial Infarction; SDOH, Social Determinants of Health; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes; TZD, Thiazolidinedione.

* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/ renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD.

37



For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD.

Fig. 3 Use of glucose-lowering medications in the management of type 2 diabetes

38

Pragmatic Vision of Diabetes by an Endocrinologist Specialized in Obesity

- Obesity is responsible for the development of type 2 diabetes
- Individuals with type 2 diabetes are concerned with hypoglycemias and weight gain
- Weight loss helps remission of DT2
  - We rarely provide interdisciplinary and sustained weight loss programs
  - ADA and EASD include in their guides medications that cause weight gain and hypoglycemia
- There are new anti-diabetic medications that facilitate weight loss and do not cause hypoglycemia
- We readily use FDA-approved medications to treat obesity
- We treat diabetes with medications that cause weight gain and perpetuate the disease

39

Weight Control

- Agents that cause weight loss, such as GLP-1 analogues or SGLT-2 inhibitors would provide the best outcomes
- Weight gain is associated with sulfonylureas, thiazolidinediones, and insulin
- Metformin and DPP-IV inhibitors are weight neutral

Cleveland Clinic

40

GLP-1 Receptor Agonist Therapies

- Benefits
  - Weight loss
  - Low (no) risk of hypoglycemia
  - Improved glycemic control
  - Reduction in systolic BP
  - Reduce CV risk (liraglutide and semaglutide)

- Side Effects/Adverse Reactions/Warnings
  - Nausea, vomiting, diarrhea, injection site reactions
  - Acute pancreatitis
  - Thyroid C-cell tumors, including medullary thyroid carcinoma (MTC)

Cleveland Clinic

41

SGLT2 Inhibitors

- Benefits
  - Weight loss
  - Low (no) risk of hypoglycemia
  - Improved Glycemic control
  - Reduction in systolic BP (~ 5 mmHg)
  - CV Risk Reduction (Empagliflozin, Canagliflozin)
  - Reduction in CV Death Risk (Empagliflozin)

- Risks/Negatives
  - Slight increase in LDL cholesterol
  - Hypotension
    - Intravascular volume contraction
  - UTIs, genital mycotic infections
  - Increase risk of DKA
  - Bone loss and increase in fracture risk (Canagliflozin)
  - Amputations (Canagliflozin)

Cleveland Clinic

42

Pragmatic Vision of Diabetes by an Endocrinologist Specialized in Obesity

- Obesity is responsible for the development of type 2 diabetes
- Individuals with type 2 diabetes are concerned with hypoglycemias and weight gain
- Weight loss helps remission of DT2
  - We rarely provide interdisciplinary and sustained weight loss programs
  - ADA and EASD include in their guides medications that cause weight gain and hypoglycemia
- There are new anti-diabetic medications that facilitate weight loss and do not cause hypoglycemia
- We rarely use FDA-approved medications to treat obesity
- We treat diabetes with medications that cause weight gain and perpetuate the disease

43

- There are FDA-approved anti-obesity, which achieves between 5-10% weight loss
- In many cases, this weight loss is sufficient to improve fasting blood glucose and HbA1c

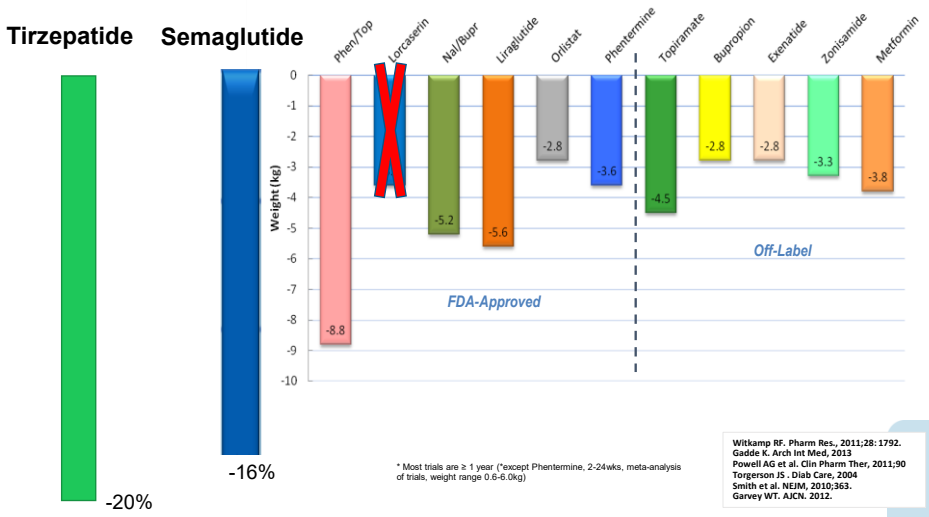
44

Anti-Obesity Medications Approved by the FDA for Weight Loss:

- Orlistat (Xenical)
- Phentermine (Adipex-P, Lomaira)
- Phentermine and topiramate (Qsymia)
- Bupropion and naltrexone (Contrave)
- Liraglutide (Saxenda)

Burguera B et al. Anti-obesity Drugs in the Management of Type 2 Diabetes: A Shift in Thinking? *Cleveland Clinic Journal of Medicine.* 2017;84:S39-S46

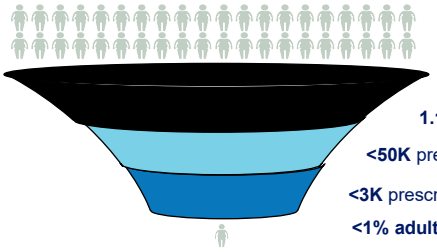
45



46

Healthcare Professionals (HCPs) Do Not Proactively Treat Obesity

Critical Mass HCPs Not Engaging



Approximately **80 million adults** with obesity[1]

1.1M licensed HCPs in the US[2]

<50K prescribers writing **≥1** branded script/month[3]

<3K prescribers writing **10+** branded scripts/month[3]

<1% adults being treated with Obesity Medication or Surgery

1. CDC 2014 (adult defined as > 20yrs). American Heart Association. Statistical Fact Sheet 2013 Update: Overweight and Obesity. 2. >815k Physicians - http://www.ama-assn.org/ama/pub/about-ama/physician-data-resources.page? ; >205k NPs - https://www.aanp.org/all-about-nps/np-fact-sheet ; >100k PAs - https://www.aapa.org/WorkArea/DownloadAsset.aspx?id=2233 3. IMS Xponent Dec-15

47

Received: 13 February 2025 | Revised: 1 May 2025 | Accepted: 2 May 2025
DOI: 10.1002/oby.24331

ORIGINAL ARTICLE
Clinical Trials and Investigations

Obesity The Obesity Society WILEY

Changes in weight and glycemic control following obesity treatment with semaglutide or tirzepatide by discontinuation status

Hamlet Gasoyan[1,2] | W. Scott Butsch[3,4] | Rebecca Schulte[5] | Nicholas J. Casacchia[1] | Phuc Le[1,2] | Christopher B. Boyer[5] | Marcio L. Griebeler[2,6] | Bartolome Burguera[2,6] | Michael B. Rothberg[1,2]

Weight loss after 1 year with semaglutide or tirzepatide:

11.9% Patients who continued the drug

6.8% Adults discontinuing the drug between 3 months and 1 year

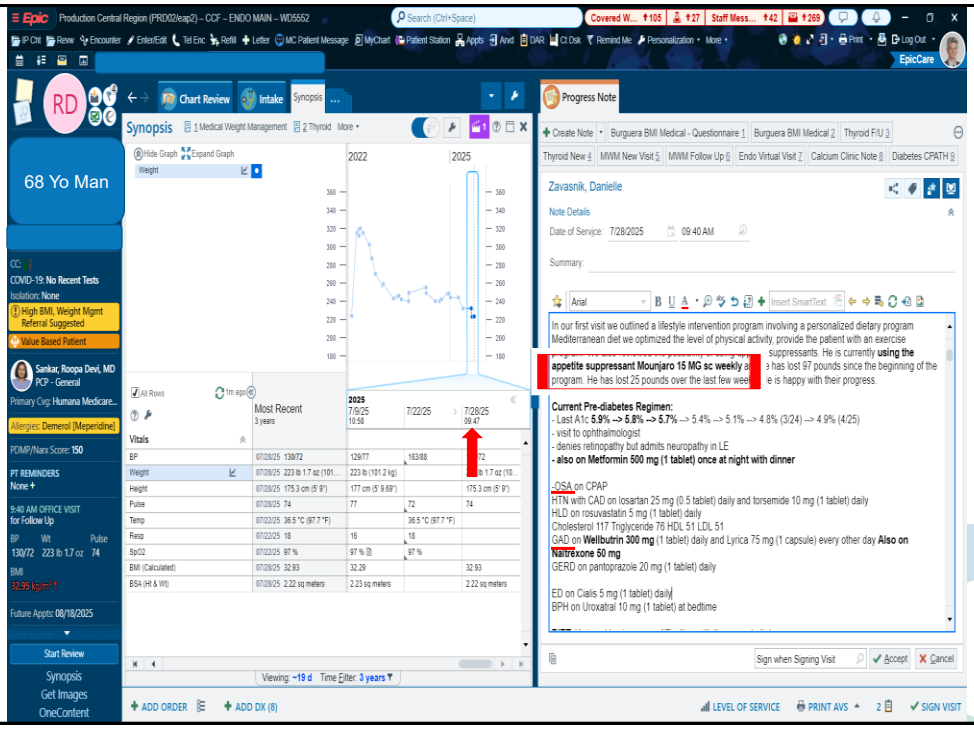
3.6% Those discontinuing the drug in less than 3 months

Healio

Treatment	Early Discontinuation	Later Discontinuation	Did Not Discontinue
Semaglutide	21.6% (1318)	31.4% (1917)	47.0% (2874)
Tirzepatide	16.4% (291)	34.1% (605)	49.4% (876)

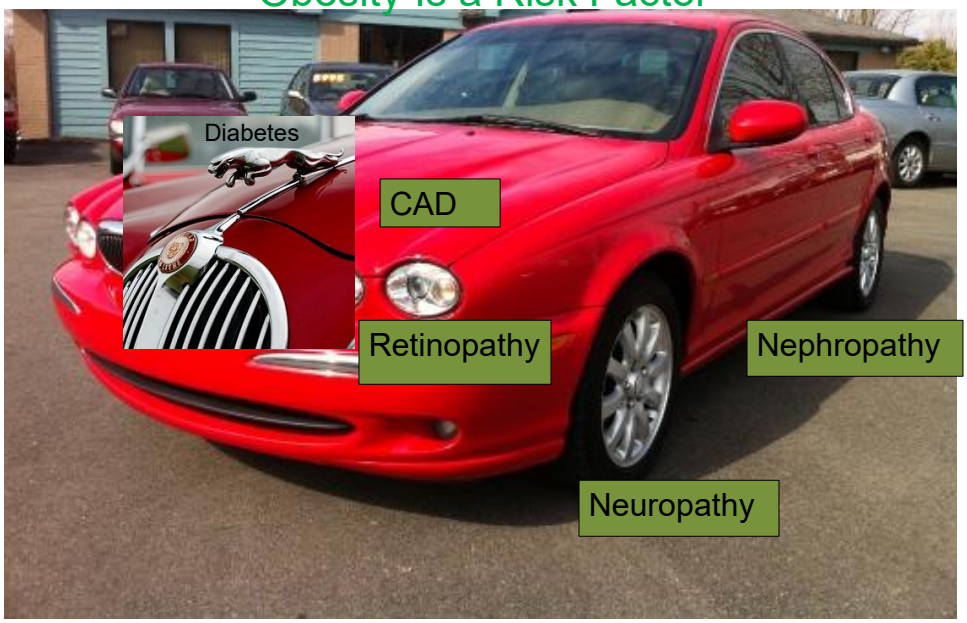
Conclusions: The average weight reduction in this cohort was lower than that observed in the main phase 3 trials, likely because of higher rates of discontinuation and lower maintenance dosages.

48



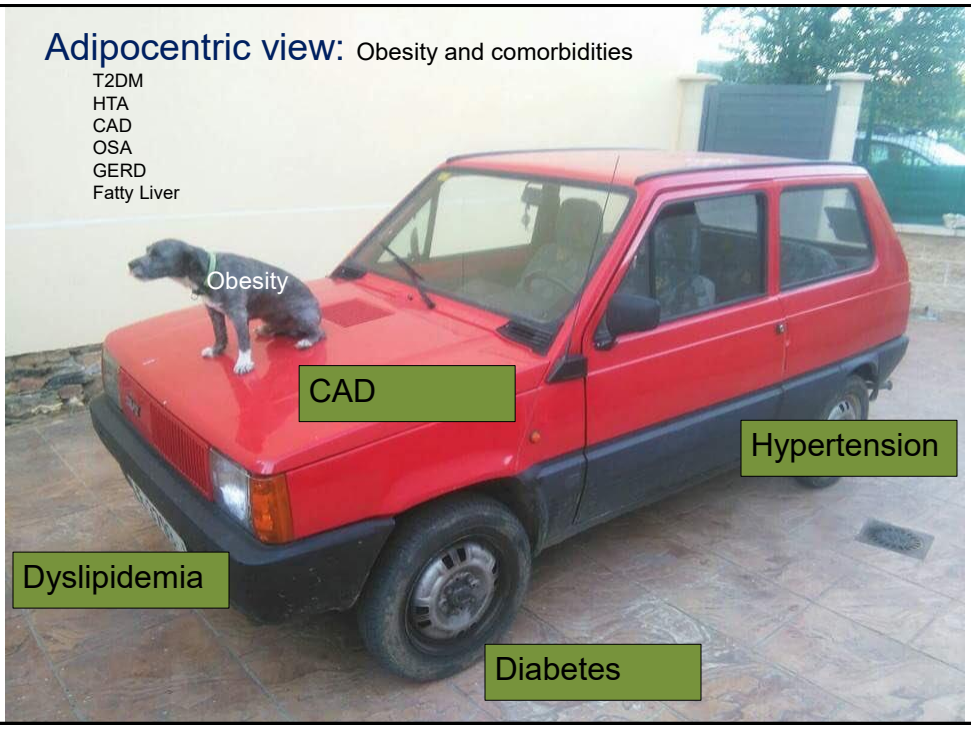
49

Glucocentric View: Pt with T2DM
Obesity Is a Risk Factor



50

51


Adipocentric view: Obesity and comorbidities
T2DM
HTA
CAD
OSA
GERD
Fatty Liver
Obesity
CAD
Hypertension
Dyslipidemia
Diabetes

52

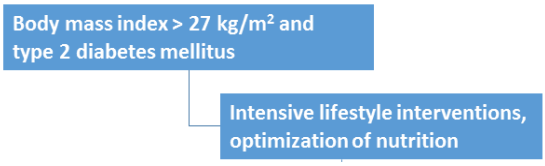
We Need to Address Obesity and Diabetes

53

- An optimal approach to patients with obesity and T2D:
  - control of glycemia and its associated comorbidities
- Obesity a key player
- Many of our first-line oral treatments for type 2 DM are associated with weight gain
- Worsen control of glycemia → insulin→ further exacerbating the weight gain
  - ***It seems counterintuitive to treat a disease for which obesity is one of the main risk factors, with medications that promote weight gain***

54

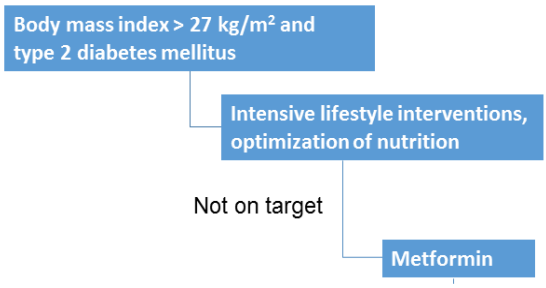
Antiobesity drugs in the management of type 2 diabetes: A shift in thinking?



Burguera B, Khawla F. Ali, Brito JP **Antiobesity drugs in the management of type 2 diabetes: A shift in thinking?** Clev Clin J Med. In press. July 2017

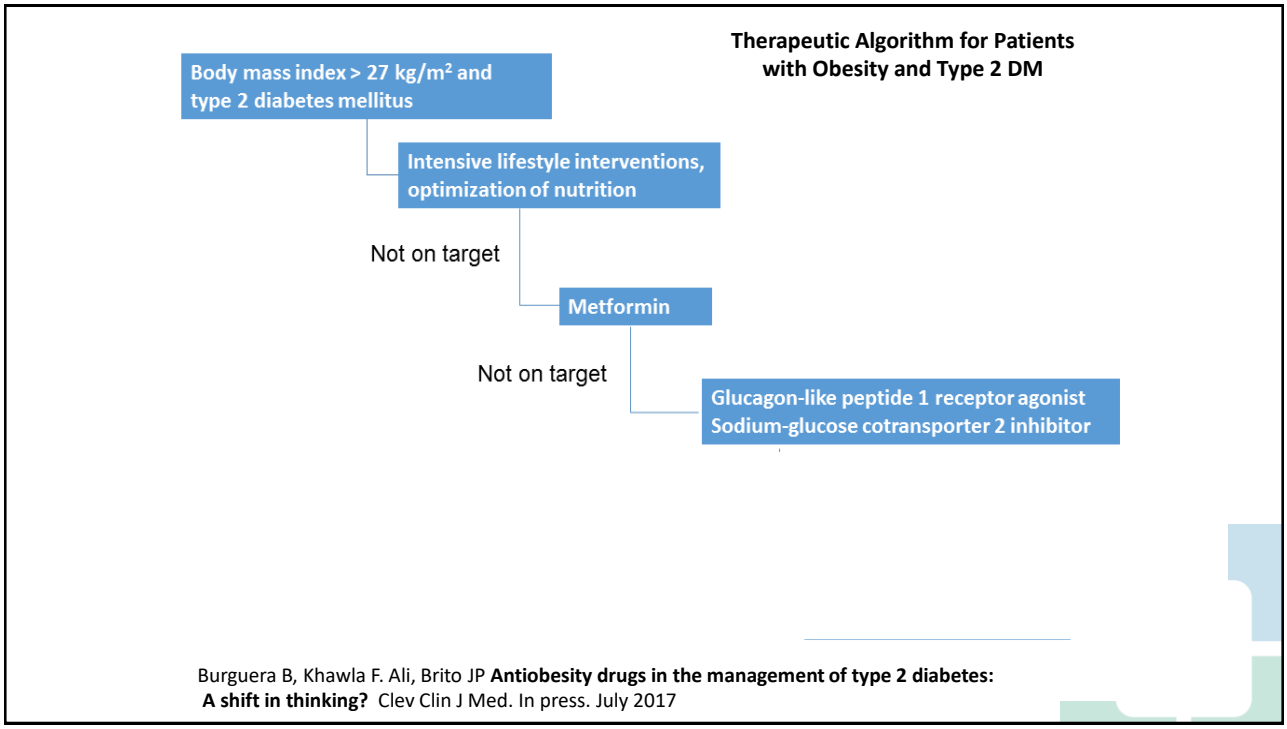
55

Therapeutic Algorithm for Patients with Obesity and Type 2 DM



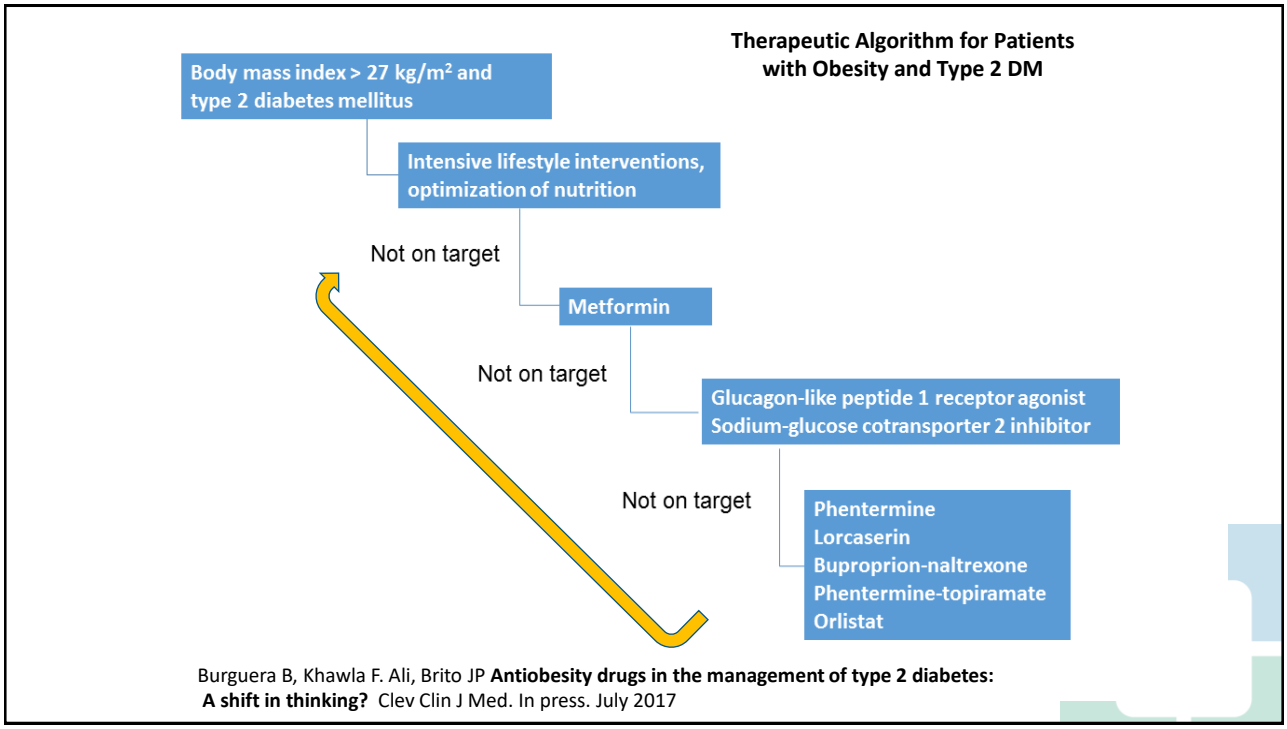
Burguera B, Khawla F. Ali, Brito JP **Antiobesity drugs in the management of type 2 diabetes: A shift in thinking?** Clev Clin J Med. In press. July 2017

56



Burguera B, Khawla F. Ali, Brito JP **Antiobesity drugs in the management of type 2 diabetes: A shift in thinking?** Clev Clin J Med. In press. July 2017

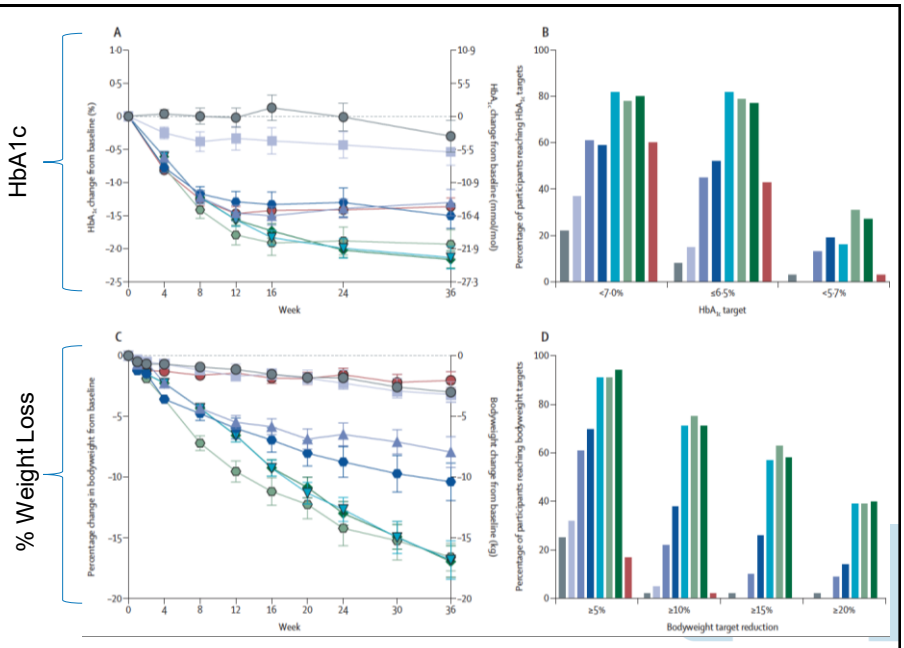
57



Burguera B, Khawla F. Ali, Brito JP **Antiobesity drugs in the management of type 2 diabetes: A shift in thinking?** Clev Clin J Med. In press. July 2017

58

Retatrutide (GLP1-GIP-GCGR) Triple Agonist and Treatment of Patients with T2D and Obesity:
a Phase 2 Trial



Level 2-3 hypoglycemia
2-4%

Rosenstock J et al. Lancet. 2023
Aug 12;402(10401):529-544

59

Goals for the Treatment and Management of T2DM with Patients with Obesity:

- The care of patients with obesity and T2DM requires a personalized intervention
- Interdisciplinary approach
- Therapeutic goals:
  - Weight loss must be a priority when establishing a care plan for the control of HbA1C and prevention of hypoglycemias
- Consider the use of anti-obesity medications early on in the plan assessment
- Surgical Metabolic Interventions
- Blood pressure and lipid panel improve with weight loss
- Medical coverage from insurance companies and governmental agencies

60