ACC Latin America Conference 2018

In partnership with:

GLYCEMIC CONTROL AMONG PEOPLE AT HIGH CARDIOVASCULAR RISK

Victor M. Montori, MD
Mayo Clinic
@vmontori

Disclosure

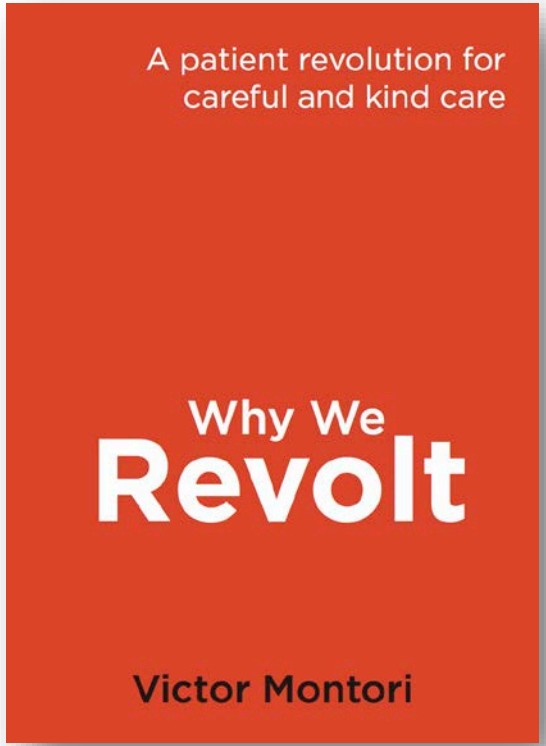
Relevant Financial Relationship(s)

- None

Off Label Usage

- None

THE PATIENT REVOLUTION.org



55 year-old man, 1.5 years after first MI

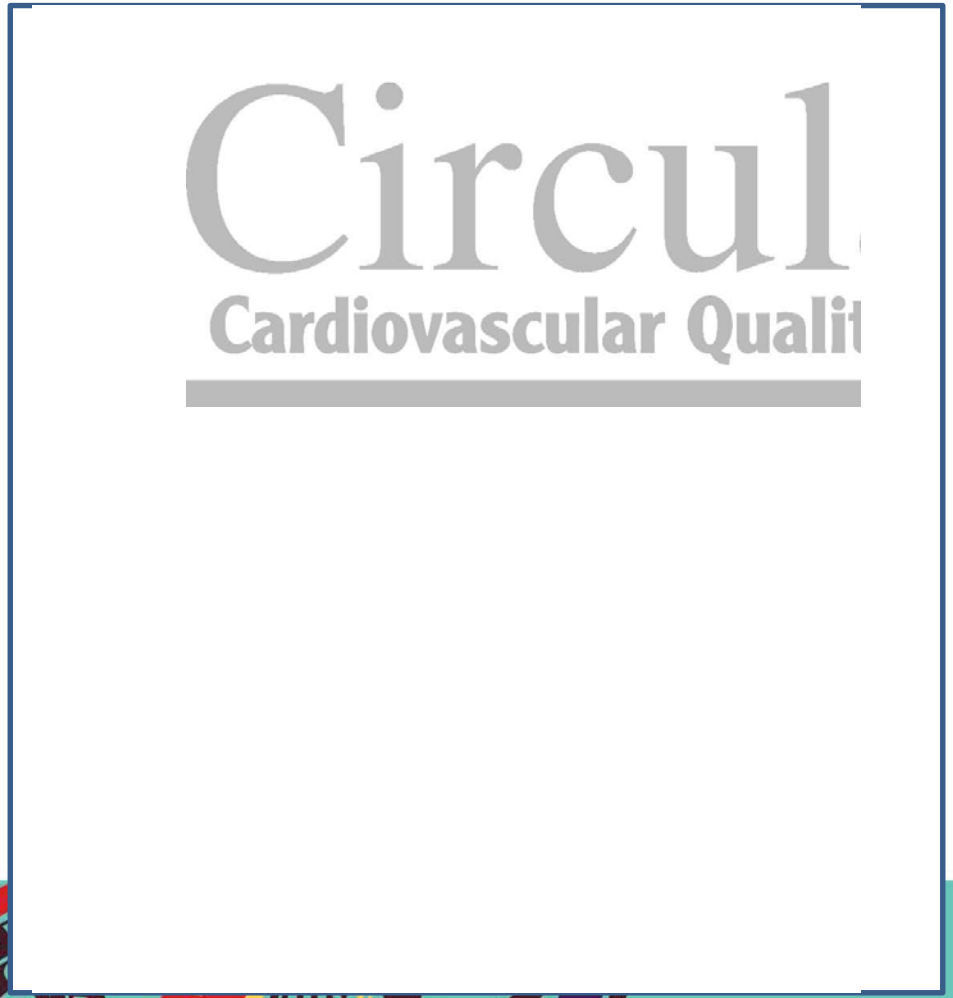
- Sedentary, accountant, married
- Obesity (BMI 35), DM2, hypertension.
- On antiplatelet, high-dose statin
- For hypertension: beta-blocker + ACEi + diuretic
- For DM2:
  - Metformin (before MI) + sitagliptin (for 1.5 years)
  - HbA1c 7.6%, Creatinine 1.7 mg/dL
  - Last review no microvascular complications

What is appropriate for his diabetes at this point?

a) Add liraglutide to reduce his CV risk, A1c, and weight
b) Stop metformin (elevated Cr) and add insulin lantus to reduce his A1c and CV risk
c) Advice to promote activity and healthier diet and review HbA1c in 3-6 months
d) Start logging blood sugars 1-2 times per day
e) Lower the statin dose

My clinical approach

1. Promote health: diet, activity, **stress**, tobacco
2. Estimate and reduce CVD risk
   - ✓ Statin (even high doses), aspirin
   - ✓ Glucoretics? GLP-1 agonists?
   - ✓ Treat hypertension
3. Glycemic control:
   - Involve patients in target (nl-8%) and how http://diabetesdecisionaid.mayoclinic.org
   - Treat symptomatic hyper; avoid hypoglycemia
5. Failure: intensification vs. adherence



Rodriguez-Gutierrez and Montori; Circ Cardiovasc Qual Outcomes. 2016;9

Antidiabetes agents with positive CV Outcome Trials

- Pioglitazone (IRIS)*

* Inconsistent results within the class

- Canagliflozin (CANVAS)*
- **Empagliflozin** (EMPA-REG)
- Dapagliflozin (DECLARE-TIMI 58)

- **Liraglutide** (LEADER)*
- Semaglutide (SUSTAIN-6)

EMPA-REG

Empagliflozin (HbA1c 0.5%)

- RCT at low risk of bias (blinding)
- 7028 >5y DM2 (A1c 7-10%)+ CV
- Empagliflozin (10 or 25 mg) vs. Placebo
- At 2.5y: 14% RRR in CV death, nonfatal MI, nonfatal stroke, from 12 % to 10.5%
- **Certainty:** Consistent with prior trials and CANVAS (cana), but not with DECLARE (dapa), a 17160-patient 4y trial: no effect on MACE/CV death

Participants with additional:	Placebo	Empagli-flozin
Glucose-lowering medications added in concordance with an escalated 'standard of care'	31.5%	19.5%
Insulin	11.5%	5.8%
Dipeptidyl peptidase 4-inhibitor	8.3%	5.6%
Sulfonylurea	7.0%	3.8%
Thiazolidinedione	2.9%	1.2%

Concerns: change in protocol, posthoc outcomes, 40% deaths uncertain

N Engl J Med 2015;373:2117-28.

Liraglutide (HbA1c 0.5%)

RCT at low risk of bias (blinding)
9340 DM2 (A1c 7-10%)+ 80% CV
Liraglutide (1.8 mg daily) vs. placebo
At 3.5y: 13% RRR in CV death, nonfatal MI, nonfatal stroke from 15% to 13%

Concerns: Differences between arms in diabetes treatments
Adverse effects in patients with advanced heart failure?
Class effect?
Exenatide weekly (EXSCEL, n=14752) Neg
Semaglutide weekly (SUSTAIN-6, n=3297) **Pos**
Lixisenatide daily (ELIXA, n=6068 ACS) Neg

N Engl J Med 2016;375:311-22.

FDA and metformin

Obtain eGFR before starting metformin + yearly

- >45 Use (careful with contrast studies)
- 30-45 Question use
- <30 Don't use

04/20/2016 - http://www.fda.gov/Drugs/DrugSafety/ucm493244.htm

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Why not do everything to the patient?

For a patient at 30% at 10 years

Statin low dose reduce by 25% to 22.5% (-7.5)

20%

Statin high dose reduce by 15% to 19.1% (-3.9)

Aspirin reduces risk by 15%* to 16% (-3)

Antihypertensive treatment by 20% to 13% (-3)

Glycemic control by 15% to 11% (-2)

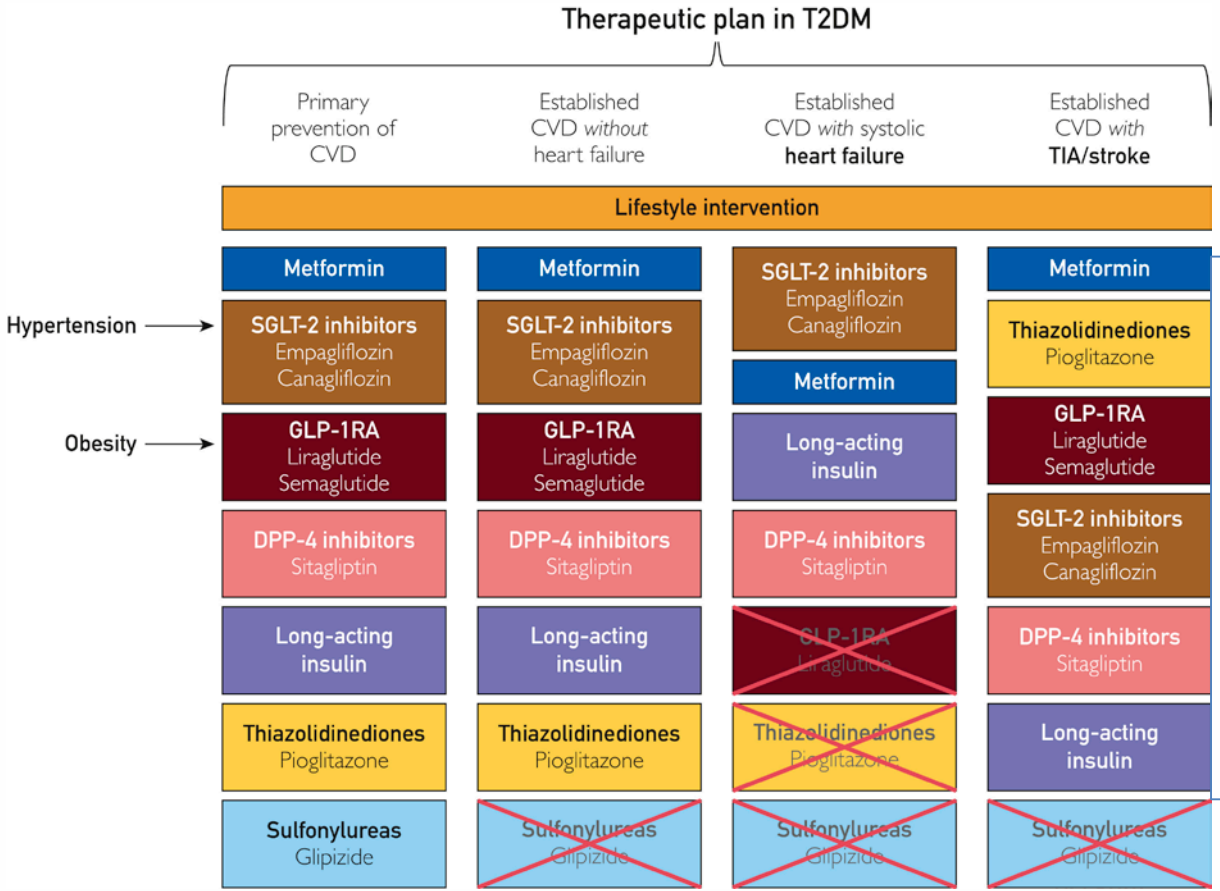
10%

Liraglutide by 13% to 9.6% (-1.4)

Empagliflozin by 14% to 8.3% (-1.3)

Burden of treatment, cost to patient, and value to patient
CV risk to take low dose statins >20%

*ASCEND Trial, NEJM 379;16



Burden of treatment?

- Administration
- Side effects (worry)

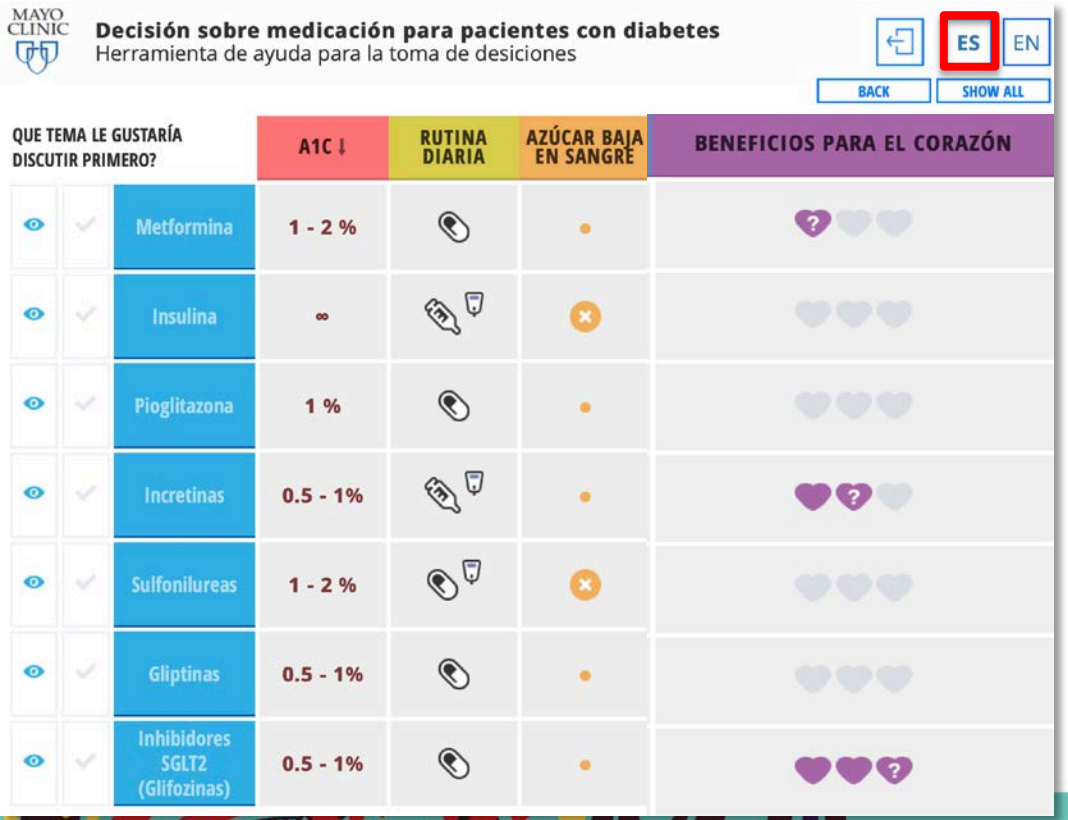
  SGLT-2i (class effects)*

  - Amputations (2:1000py)
  - DKA (1:1000py)
  - Genital infex (10:1000py)
- Cost

*BMJ 2018; 363

Mayo Clinic Proceedings 2018 93, 1629-1647

http://diabetesdecisionaid.mayoclinic.org



What is the situation that requires action?

Which response makes the most intellectual, emotional, and practical sense?

Questions & Discussion