# GLP 1 RA:

## The underutilized cardiometabolic drug

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# Disclosures:  none

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Objective:

- At the conclusion of this presentation, participants will be comfortable starting a GLP 1 RA.

# Heloderma Suspectum - Gila monster

**Exendin - 4 -** discovered in **1990** by VA endocrinologist Dr. John Eng

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# GLP 1 RA

- On **June 1, 2005** a new drug was launched for diabetes
  - Exenatide (BYETTA) PO BID

- In **January 2012** a new drug was launched for diabetes
  - Exenatide (BYDUREON) weekly injection

# GLP 1 RA

- In **2016** the NEJM reported the benefits of GLP 1 RA with improved MACE outcomes in the LEADER and SUSTAIN 6 trials

Steven P. Marso, M.D., et.al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med.* 2016; 375:311-322.

Steven P. Marso, M.D., et. al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. *N Engl J Med.* 2016; 375:1834-1844.

**Table 2** Summary of baseline characteristics and primary composite cardiovascular outcomes of the completed CVOTs for GLP-1 RA

| GLP-1 RA: Study name | No. of patients | Median follow-up (years) | % with CV disease* | % of statin use | Baseline age | Baseline HgA1c | Baseline BMI | Primary composite CV outcome HR (95% CI) | P value |
|---|---|---|---|---|---|---|---|---|---|
| Lixisenatide: ELIXA | 6068 | 2.1 | 100% | 93% | 60.3 | 7.7% | 30.1 | 1.02 (0.89 to 1.17) | 0.81 |
| Liraglutide: LEADER | 9340 | 3.8 | 81% | 72% | 64.3 | 8.7% | 32.5 | 0.87 (0.78 to 0.97) | 0.01 |
| Semaglutide: SUSTAIN-6 | 3297 | 2.1 | 60% | 73% | 64.6 | 8.7% | 32.8 | 0.74 (0.58 to 0.95) | 0.02 |
| Exenatide QW: EXSCEL | 14752 | 3.2 | 73.1% | 74% | 62.0 | 8.0% | 31.8 | 0.91 (0.83 to 1.00) | 0.06 |
| Albiglutide: Harmony | 9463 | 1.6 | 100% | 84% | 64.1 | 8.7% | 32.3 | 0.78 (0.68 to 0.90) | 0.0006 |
| Dulaglutide: REWIND | 9901 | 5.4 | 31.5% | 66% | 66.2 | 7.2% | 32.3 | 0.88 (0.79 to 0.99) | 0.026 |
| Oral semaglutide: PIONEER 6 | 3183 | 1.3 | 84.7% | 85% | 66.0 | 8.2% | 32.3 | 0.79 (0.57 to 1.11) | 0.17 |

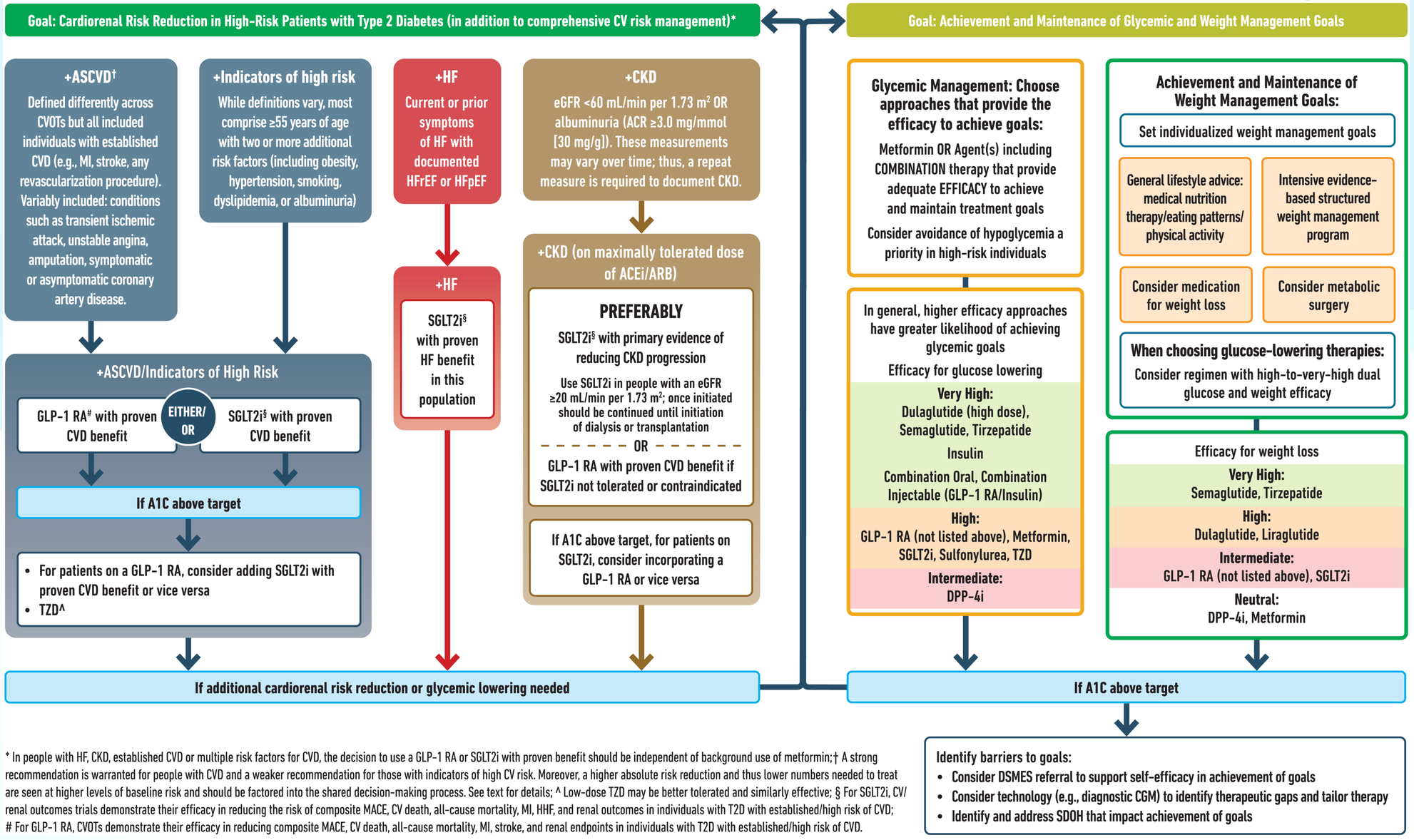
*Remaining participants with cardiovascular risk factors.
BMI, body mass index;CV, cardiovascular; HgA1c, glycated haemoglobin.

Sheahan KH, *et al*. *Postgrad Med J* 2020;**96**:156–161. doi:10.1136/postgradmedj-2019-137186

# USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

**HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)**

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)




* 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.

From: **Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)** Diabetes Care. 2022;45(11):2753-2786. doi:10.2337/dci22-0034

# GLP 1 RA

Drug adoptions:  from inception to adoption takes <u>17 years</u>

"The answer is 17 years, what is the question: understanding time lags in translational research"

- Zoe, Slote, Morris, et al. 2011. *Journal of the Royal Society of Medicine* 104(12), 510-520.

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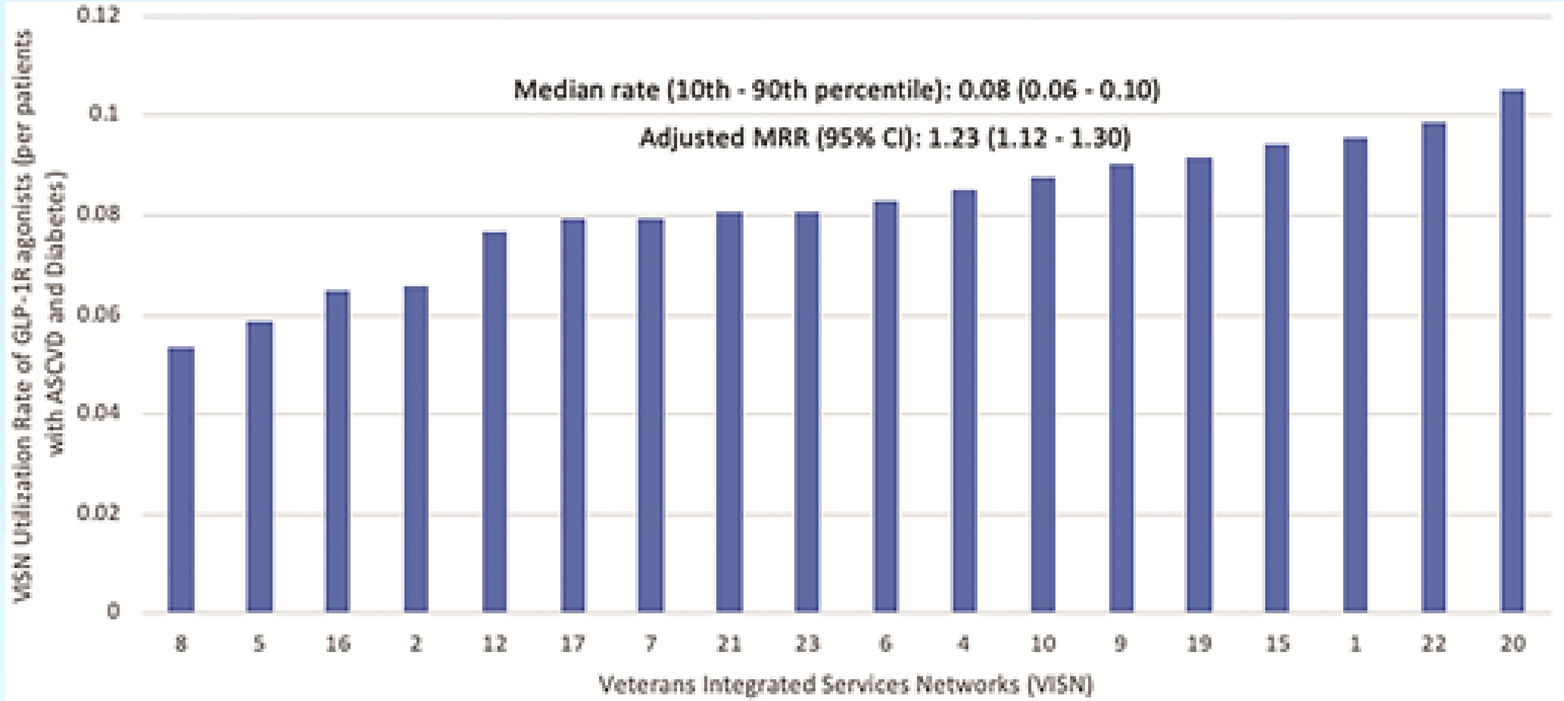
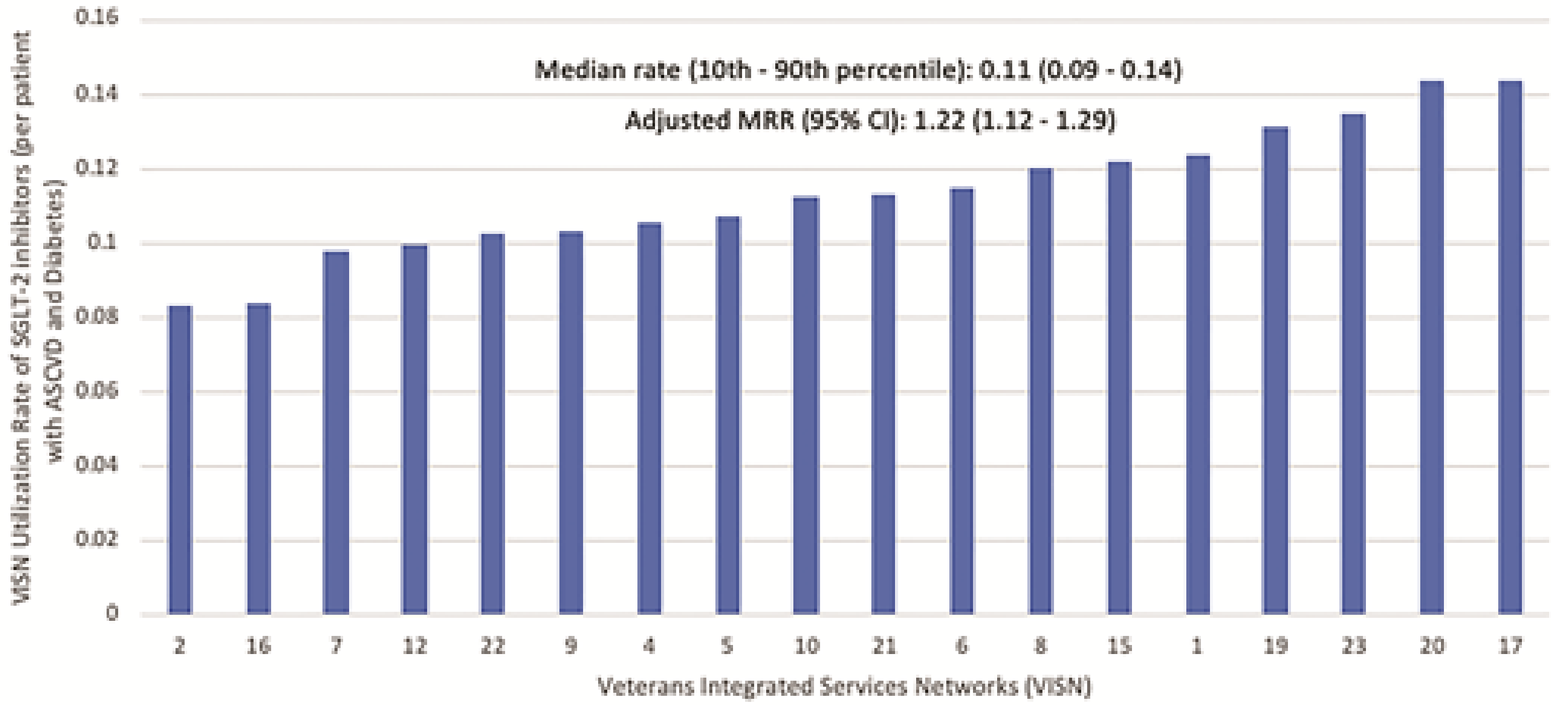
# GLP 1 RA use when indicated.

- Use of GLP 1 RA where indicated is 10-15%

# GLP 1 RA



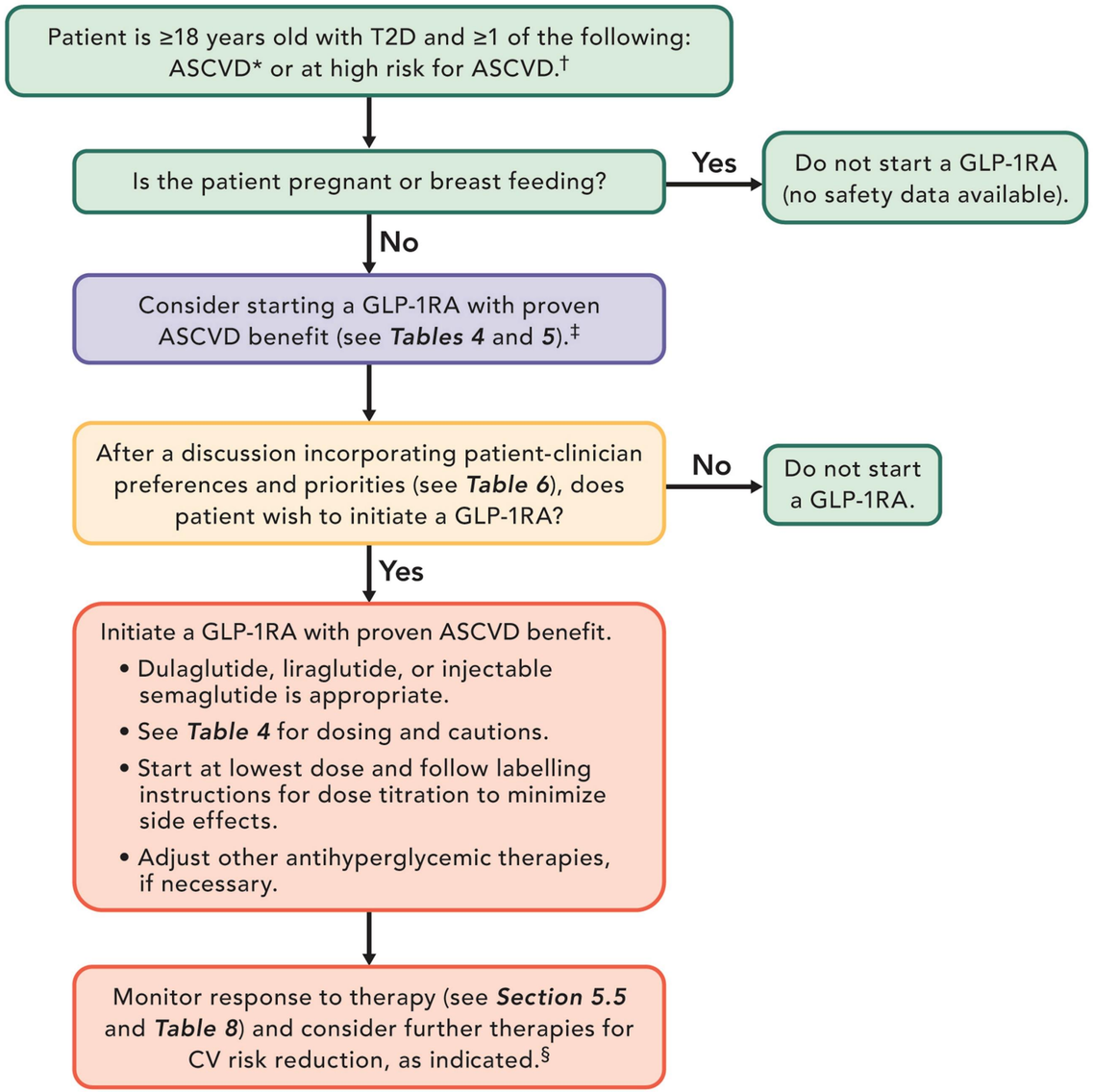

EPIDEMIOLOGY/HEALTH SERVICES RESEARCH| JANUARY 17 2022

**Utilization Rates of SGLT2 Inhibitors and GLP-1 Receptor Agonists and Their Facility-Level Variation Among Patients With Atherosclerotic Cardiovascular Disease and Type 2 Diabetes: Insights From the Department of Veterans Affairs**

Dhruv Mahtta

# GLP 1 RA:

# ACC Decision Pathway 2020




*ASCVD is defined as a history of an acute coronary syndrome or MI, stable or unstable angina, coronary heart disease with or without revascularization, other arterial revascularization, stroke, or peripheral artery disease assumed to be atherosclerotic in origin.

†Patients at high risk for ASCVD include patients with end organ damage such as left ventricular hypertrophy or retinopathy or with multiple CV risk factors (e.g., age, hypertension, smoking, dyslipidemia, obesity).

‡ Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

§ This may include the addition of an SGLT2 inhibitor in the appropriate patient (see ***Section 5.3.3***).

ASCVD = atherosclerotic cardiovascular disease; GLP-1RA = glucagon-like peptide-1 receptor agonist; MI = myocardial infarction; SGLT2 = sodium-glucose cotransporter-2; T2D = type 2 diabetes

# GLP 1 RA - when starting, explain the benefits

- Weight loss as it reduces the brain’s desire to eat
- Protects the heart, kidneys and liver
- Helps reduce blood sugar
- Generally does not cause low blood sugar
- May be able to remove other medications

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# GLP 1 RA - explain the risks

- Nausea
- Diarrhea
- Constipation
- Stomach pain - if severe, call office and stop it

# GLP 1 RA - Risk Mitigation

- Check renal labs and monitor for dehydration
  - Most side effects are eased by slow titration
  - Reducing food intake 30-50%, especially carbs
  - Rarely needs to be stopped
  - Elderly tend to have higher incidence of side effects

# GLP 1 RA - write the “Script”

- Advise if it’s too costly, do not fill it!
- But cost is not the barrier to care!
  - Getting approval requires persistence but most do get approved eventually
  - Many are covered without prior authorization
  - Some employer’s insurance will cover GLP 1 RA
  - VA: it's on the formulary

# GLP 1 RA - write the “Script”

- Older GLP 1 RA are often covered
- Prior authorization does work
- Patient assistance does work for most patients with Medicare
- Commercial insurance can have a co-pay card

# GLP 1 RA - once approved start the medication

- Semaglutide 0.25 sc weekly
- Liraglutide 0.6 mg sc weekly
- Dulaglutide 0.75 mg sc weekly
- Tirzepatide 2.5 mg sc weekly (Cardiac studies are on the way)

# GLP 1 RA - now that it's started what do you do with the other medications?

What's the biggest concern?

- Other diabetic meds and hypoglycemia
  - Insulin: reduce 10-20%
  - Sulfonylurea (SU): needs to be stopped anyway, so stop them
  - Stop DPP4

# GLP 1 RA - starting it, a few quick examples

Example 1

Make it easy on yourself to start:

- Diabetic on metformin with ASCVD
  - Add Glp1 RA and titrate
  - Age, kidney function, hepatic function – rarely prevent use
  - Recommend exercise
  - Appropriate protein intake (.8g per kg body weight) as you reduce carbs

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# GLP 1 RA - starting it, a few quick examples

Example 2

Make it easy on your self to start:

- Diabetic on metformin and SU with ASCVD
  - Add Glp1 RA, stop SU and titrate
  - Recommend exercise
  - Appropriate protein intake (.8g per kg body weight) as you reduce carbs
  - Check renal labs

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# GLP 1 RA - starting it, a few quick examples

Example 3

Make it easy on your self to start:

- Diabetic on metformin, stable insulin regimen with ASCVD
  - Add Glp1 RA, reduce insulin by 10-20% and titrate
  - Recommend exercise
  - Appropriate protein intake (.8g per kg body weight) as you reduce carbs
  - Check renal labs

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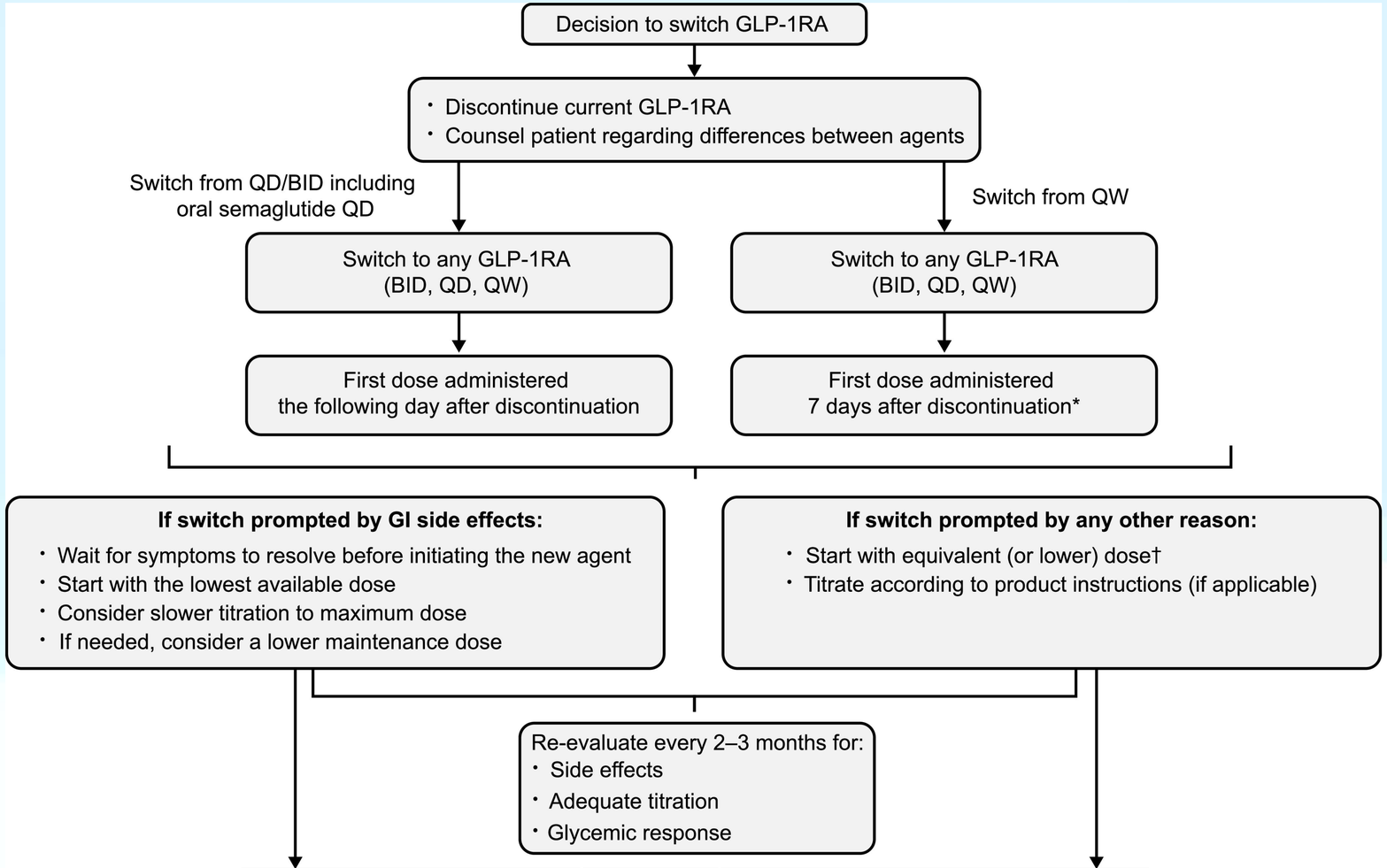
# GLP 1 RA: switching between them




| Agent | Frequency | Equivalent Dose† | | | |
|---|---|---|---|---|---|
| Exenatide | QW | | | 2 mg | |
| Dulaglutide | QW | | 0.75 mg | 1.5 mg | |
| Semaglutide | QW | | 0.25 mg | 0.5 mg | 1 mg |
| Liraglutide | QD | 0.6 mg | 1.2 mg | 1.8 mg | |
| Lixisenatide | QD | 10 µg | 20 µg | | |
| Oral semaglutide | QD | 3 mg | 7 mg | 14 mg | |
| Exenatide | BID | 5 µg | 10 µg | | |

Clin Diabetes. 2020 Oct; 38(4): 390–402. Switching Between Glucagon-Like Peptide-1 Receptor Agonists: Rationale and Practical Guidance Jaime P. Almandoz et al

# SUMMARY
# Why should I start GLP 1 RA's?

1. Helps your patient feel better
2. Guideline supported therapy for cardiometabolic patients
3. Most patients get approved with persistence
4. Low side effect profile
5. Helps your patient feel better

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**Thank you for listening and being here today**

**Also, thanks to the following:**

- ✓To my colleague and friend Dr. Vijay Rao and the ACC
- ✓To my Cardiometabolic Center Alliance (CMCA) team at Major Health Partners
- ✓To Dr. Mikhail Kosiborod and Saint Lukes in Kansas for developing the CMCA
- ✓To Indiana Heart Physicians and the Franciscan Alliance

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# Resources:

- Cardiometabolic Center Alliance, Saint Luke’s Hospital, Kansas City, MO
- JACC 2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients with Type 2 Diabetes: A Report of the American College of Cardiology Solution Set Oversight Committee
- J Diabetes Complications 2022 DCRM Multispecialty Practice Recommendations for the management of diabetes, cardiorenal, and metabolic diseases
- Heart in Diabetes Conference 2023

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