Aims of COORDINATE: An unmet clinical need

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Objectives

- Burden of DM + ASCVD
- Aims of COORDINATE
- Barriers to guideline-directed therapies for ASCVD in DM
    - High intensity statins, ACE/ARB, CVOT DM medications
- Trial inclusion/exclusion and endpoints

Diabetes epidemiology

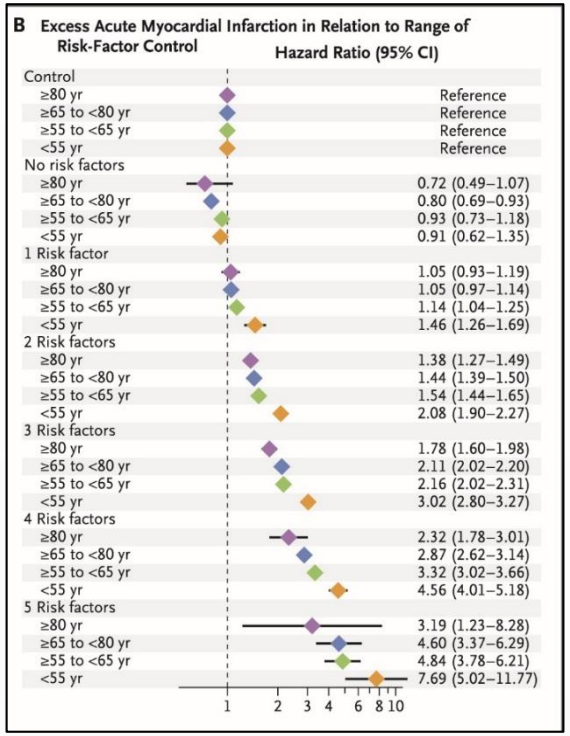
- 100 million live with diabetes ~ 10% of population.
    - Up to 80 million have ‘pre-diabetes’
- ASCVD remains the most common cause of morbidity and mortality in DM
- Once established in DM, ASCVD carries poor prognosis:
    - Higher burden of disease, complexity of atheroma, ST, ISR
    - Stroke is more disabling, longer hospitalization, worse fx outcomes
    - More likely to have unsuccessful revascularization – HR 12 for amputation

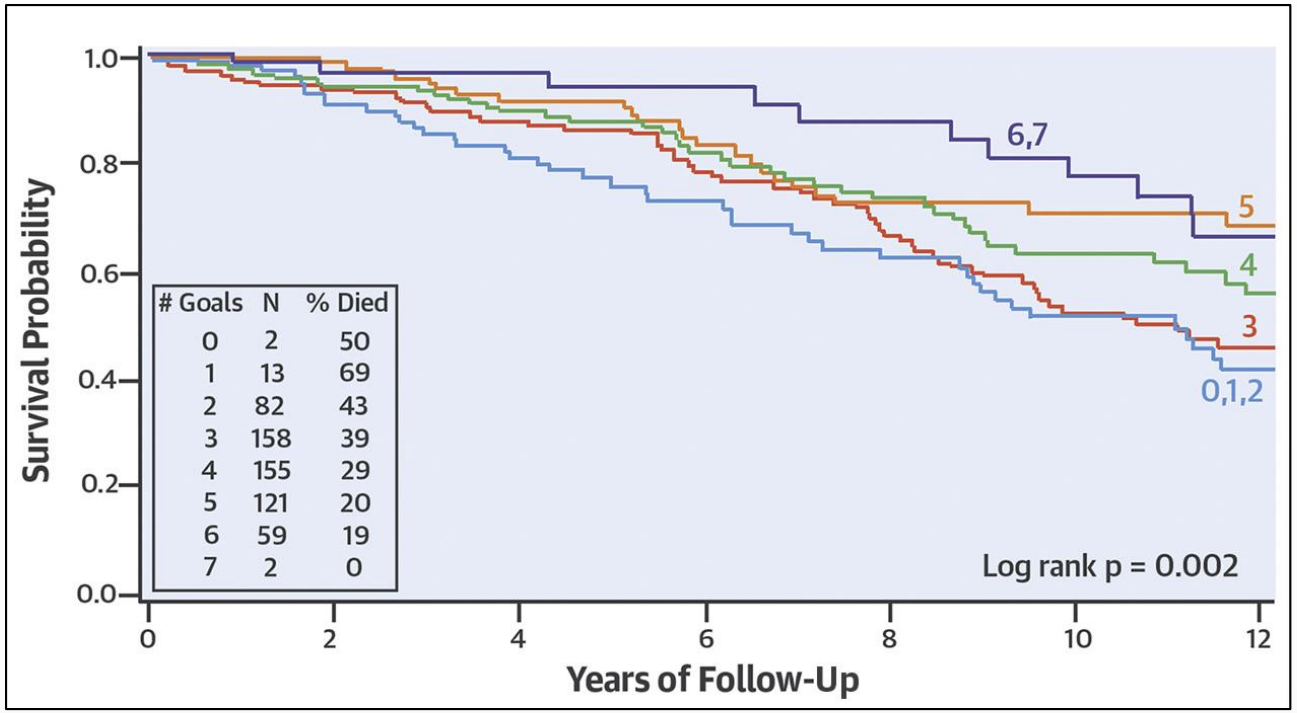
COORDINATE-Diabetes

Nelson et al. *Progress Cardiovasc Disease* 2019 (in press)

Diabetes strategies

- Treating risk factors can significantly reduce ASCVD risk





BUT <15% in NHANES are at target BP, LDL, HbA1c, smoking status…

COORDINATE-Diabetes

Rawshani et al. *NEJM* 2018; Mancini et al. *JACC* 2019

Managing CV risk is a team game

Two worlds of managing CV risk in diabetes

Diabetologist

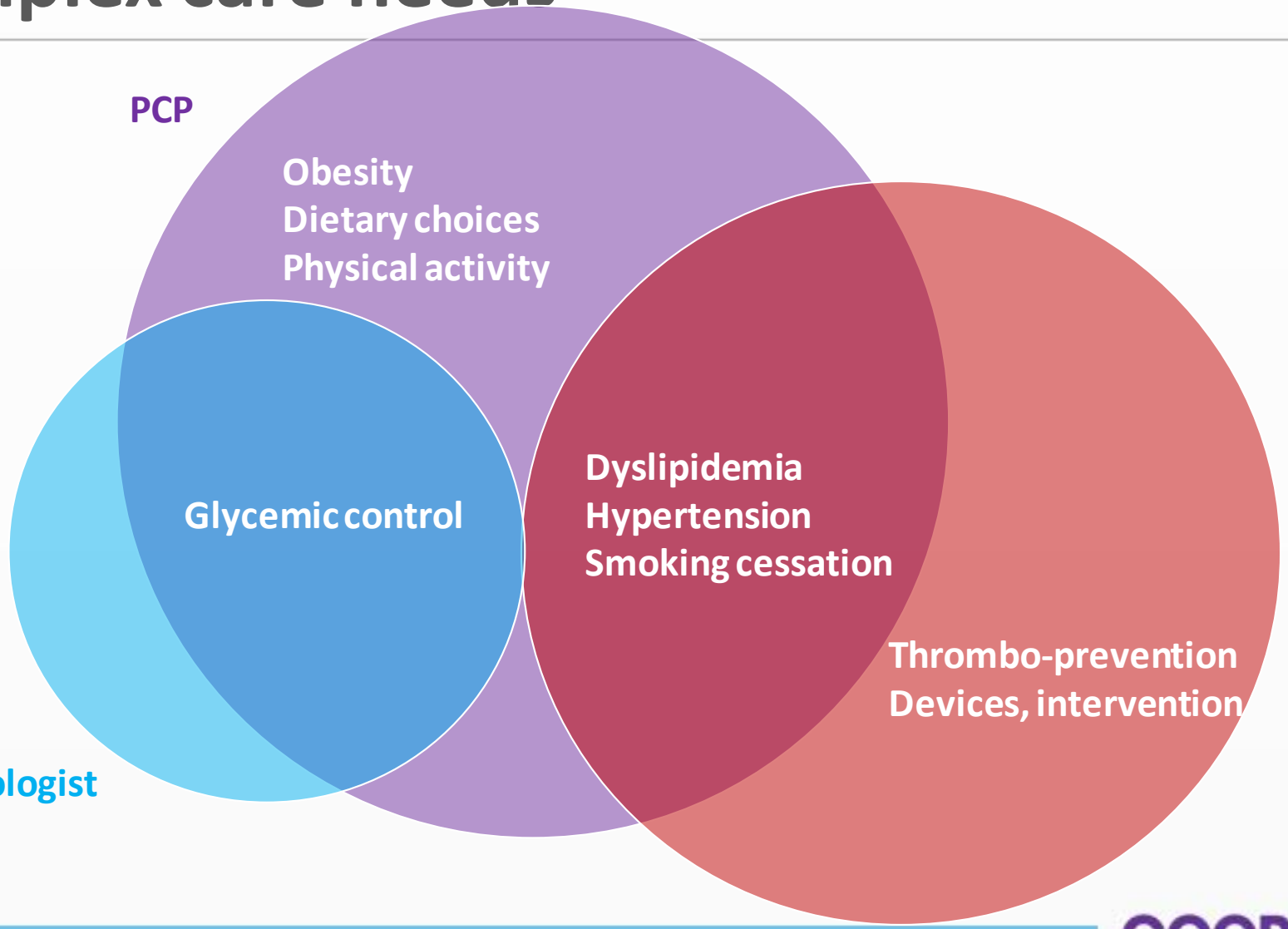
- Focus on blood sugar
- Expert in wide range of hypoglycemia medications
- Expert in global care of diabetes, microvascular complications
- Defers to cardiologist on CV protection

Cardiologist

- Focus on hypertension, lipids, diet
- Expert in lipid-lowering therapies
- Management of cardiovascular disease
- Defers to diabetologist on diabetes drugs

A cardiologist is 3 x more likely to see a DM + ASCVD patient than an endocrinologist…

Complex care needs



Gap 1: statins

- Non-persistence affects up to 60% of 2° prevention
    - Intolerance causes ~ half of non-persistence

- **BUT** carefully designed trials suggest the absolute effect is ~5%
- Intentional and deliberate re-challenges successful in >70% of patients

Intervention: statins

- LMS module:
    - Evidence for statin usage
    - Strategies to overcome statin intolerance
- Patient facing materials: importance and rationale of statin usage

Gap 2: ACE/ARB

- Demonstrable benefit for DM and ASCVD, independently

- **BUT** up to 1/3 of patients with DM/ASCVD are not on RAAS blockade
- Hyperkalemia, reduced GFR, intolerance all limit adherence
- Careful commencement even in reduced GFR is often successful

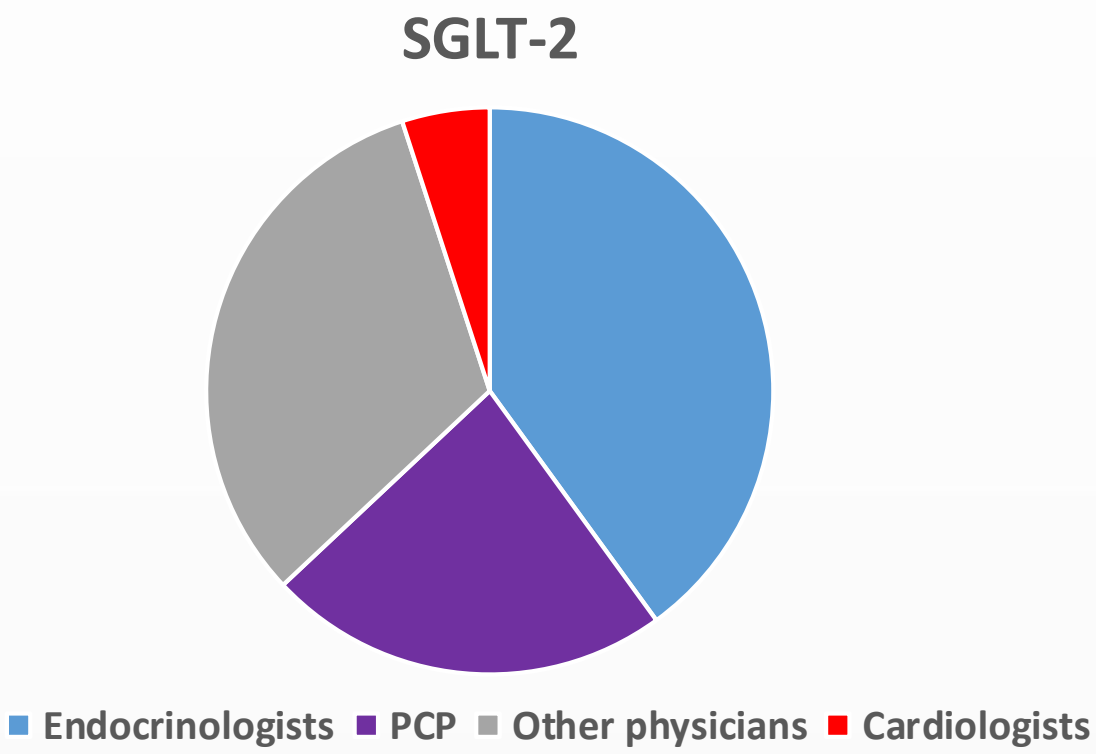
Intervention: ACE/ARB

- LMS module:
    - Evidence for ACE/ARB usage
    - Strategies to commence with reduced GFR/perceived intolerance
- Patient facing materials: importance and rationale of ACE/ARB usage

Gap 3: CVOT DM drugs

- Robust evidence base for SGLT-2i and GLP-1RA in DM + ASCVD

- **BUT** contemporary registries suggest <10% of eligible patients are prescribed
- Of those who receive prescriptions, <5% are from the cardiologist



COORDINATE-Diabetes

Wittbrodt E *Diab Obes Metabolism* 2019; Vaduganathan M *J Am Coll Cardiol.* 2018

Intervention: SGLT-2i/GLP-1RA

- LMS module:
    - Evidence for SGLT-2i/GLP-1RA usage
    - Practical guidance for SGLT-2i/GLP-1RA
- Patient facing materials: importance and rational of ACE/ARB usage
- System issues: strategies for pre-authorization, tips for navigating co-pays and vouchers, insurance limitations

What are the issues?

Multifactorial

System	Provider	Patient
• Communication and coordination with providers • Pre-authorization barriers • Co-pay and affordability	• Knowledge base • Comfort zone in diabetes medication prescriptions • Interdisciplinary boundaries	• Knowledge base/literacy • Degree of patient activation • Barriers to adherence

COORDINATE-DM

COORDINATE-Diabetes is a cluster-randomized clinical trial to test the effectiveness of an innovative, clinic-level educational intervention to improve the management of patients with T2DM and CVD.

Primary outcome

Proportion of patients achieving guideline-recommended management for T2DM and CVD at 12 months, as initiated or confirmed by a cardiologist for all of the following (composite score of 3):

1. Use of a regimen which includes an anti-hyperglycemic agent indicated and/or guideline recommended to reduce cardiovascular risk*
    - Acceptable alternative: metformin monotherapy with HbA1c<7%
2. Guideline-recommended medical therapy* with ACEi/ARB
3. Guideline-recommended medical therapy* with high-intensity statin: atorvastatin 40-80mg daily OR rosuvastatin 20-40mg daily

Primary outcome (continued)

*As new consensus or evidence emerges and guidelines are updated, the composite score and requisites will be evaluated by the Steering Committee for needed updates on an ongoing basis.

For the first component of the primary outcome (related to anti-hyperglycemic agents), patients will be evaluated according to the list of “indicated and/or guideline recommended” agents in effect **at the time of their 12 month follow-up**. Medications started during the 12 month study period that receive FDA indication/guideline recommendation during that time will count towards the primary outcome.

Secondary outcome

Assessment of cardiology provider behavior as measured by the following **cardiologist-initiated** medications for diabetes suggested by guidelines and FDA approved for CVD risk reduction:

- Proportion of patients achieving guideline-recommended therapy for T2DM
- Proportion of patients with an ACEi/ARB treatment
- Proportion of patient with a high-intensity statin treatment

Variations on the Primary Outcome:

- Proportion of patients achieving a composite score of ≥ 2

Secondary outcome (continued)

Intermediate Outcomes:

- Changes from baseline to 12 months in the following: sBP, dBP, HbA1c, LDL-C (when available)
- Change from baseline to 12 months in proportion of patients achieving the following targets (individually and in combination): sBP<130 mmHg, dBP<80 mmHg, HbA1c<8%, LDL-C<70 mg/dL (when available)

Clinical time-to-event outcomes:

- Composite of all-cause death; hospitalization for: MI, stroke, decompensated heart failure, or urgent revascularization (coronary, peripheral, carotid)
- Each of the clinical time-to-event outcomes will also be assessed individually

Population

Inclusion Criteria

- ≥ 18 years old
- Diagnosis of Type 2 diabetes
- History of at least one:
  - Coronary artery disease
  - Peripheral arterial disease
  - Cerebrovascular disease
- English speaking

Exclusion Criteria

- Unlikely to comply with study procedures
- Life expectancy < 1year
- Already prescribed at baseline:
  - All 3 guideline recommended therapies
  - SGLT-2i or GLP-1RA
- Absolute contraindication to any of the 3 guideline recommended therapies

Definition

Coronary artery disease

- prior MI, coronary revascularization (CABG or PCI), and/or obstructive CAD (≥50%) as documented by angiography or CTA

Peripheral arterial disease

- defined as claudication with ABI<0.9, prior peripheral revascularization, and/or amputation due to circulatory insufficiency

Cerebrovascular disease

- Stroke and/or carotid artery stenosis (≥50%)

Summary

- High burden of DM & CVD
- Gap in prescription of guideline-directed therapies
- Multiple barriers to adoption: system, provider, patient.
    - Multifaceted intervention required
- Basics of the COORDINATE Trial