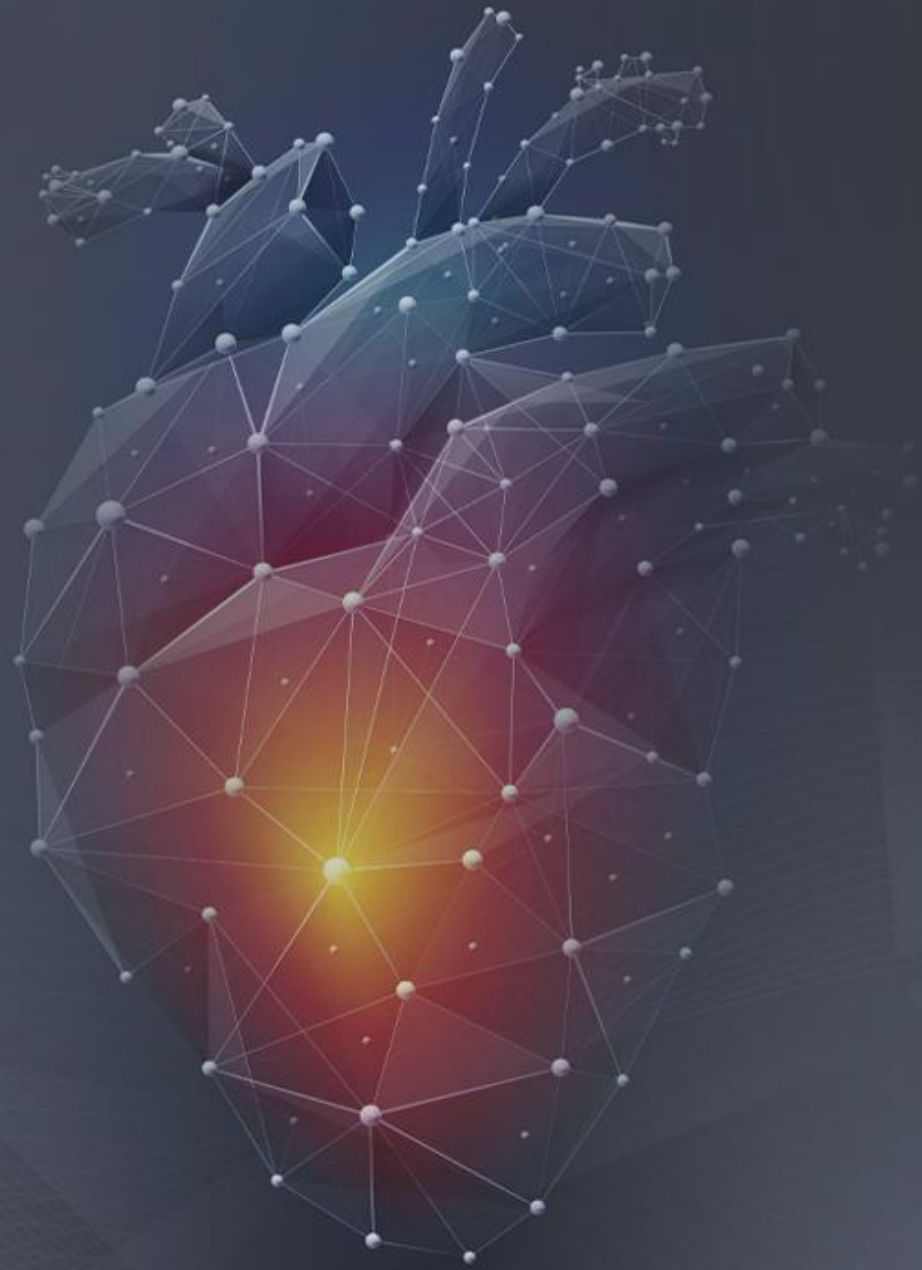
Navigating Vascular Protective Strategies in High-Risk Patients During the Current Era: Practical Applications

An Expert Case-Based Panel Discussion



Friday, June 12, 2020
6:00-7:00 pm ET

Planning Committee/Faculty

Subodh Verma (Chair)
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Cardiac Surgeon, St Michael's Hospital
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Speaker Disclosures

- Speaker name: Dr. Subodh Verma
- Relationships with financial interests:
    - Grants/Research Support: Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, HLS Therapeutics, Janssen, Merck
    - Speakers Bureau/Honoraria: AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, EOCI, HLS Therapeutics, Janssen, Merck, Novartis, Novo Nordisk, Sanofi, Sun Pharmaceuticals, TKTWG
    - Consulting Fees: Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, HLS Therapeutics, Janssen, Merck, Novo Nordisk, Sanofi

Speaker Disclosures

- Speaker name: Dr. Claudia Bucci
- Relationships with financial interests:
    - Speakers Bureau/Honoraria: Astra Zeneca, Bayer
    - Consulting Fees: Amgen, HLS Therapeutics, Novartis

Speaker Disclosures

- Speaker name: Dr. Richard Choi
- Relationships with financial interests:
  - Research Support: AstraZeneca, Bayer
  - Speakers Bureau/Honoraria/Consulting fees: AstraZeneca, Bayer, Boehringer Ingelheim/Lilly, BMS/Pfizer, HLS, Novartis, Sanofi, Servier

Speaker Disclosures

- Speaker name: Dr. Anil Gupta
- Relationships with financial interests:

Consulting Fees/Speakers Bureau/Honoraria:

AstraZeneca, Bayer, Boehringer Ingelheim/Lilly, BMS/Pfizer, HLS, Novartis, Sanofi, Servier

Disclosure of Commercial Support

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Accreditation

This event is not accredited.

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Learning Objectives

1. Review emerging strategies for managing persistent cardiovascular (CV) risk
2. Discuss considerations for managing high-risk patients in the current era: challenges and opportunities
3. Discuss practical applications for implementing vascular protective strategies during the current era through case studies

Agenda

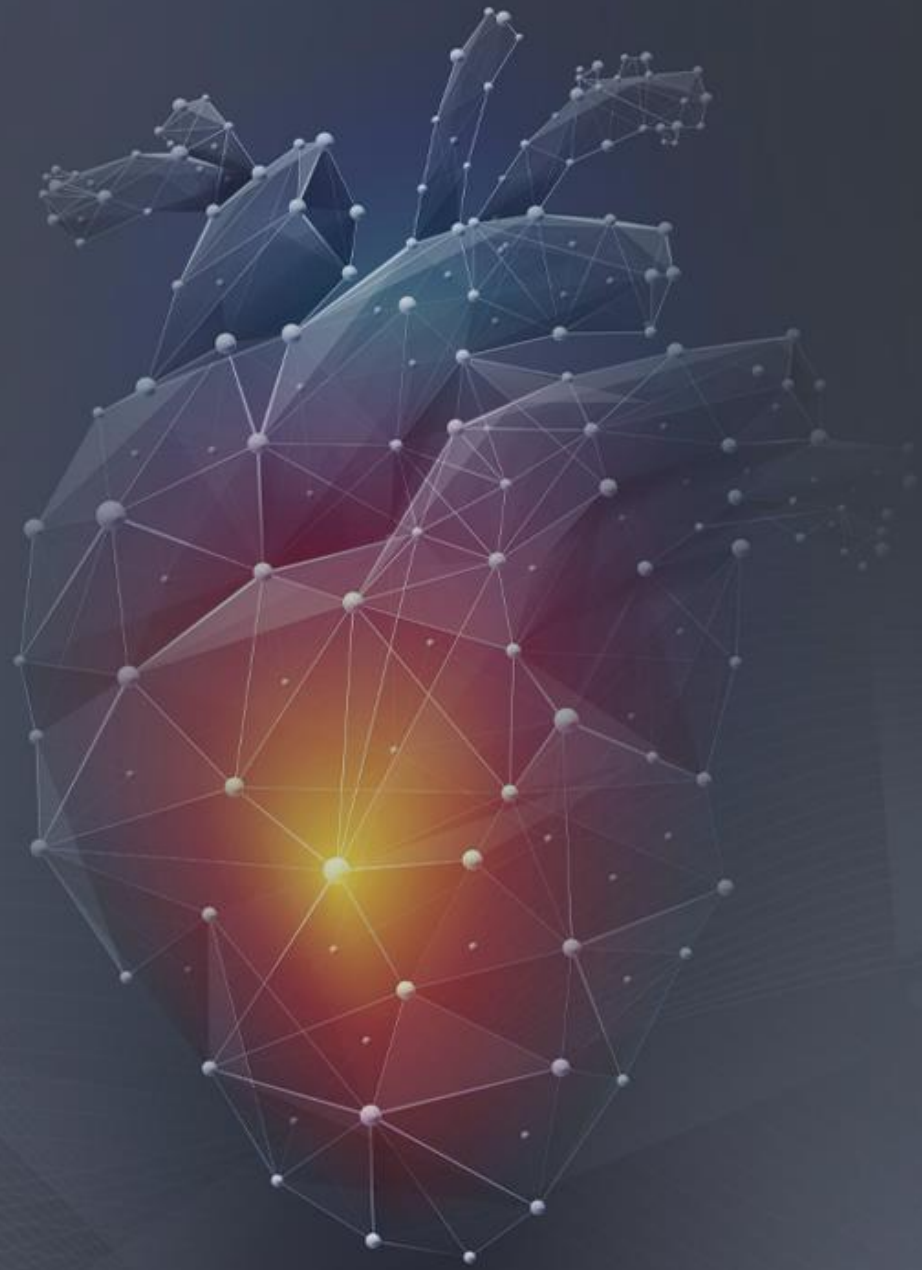
Time	Topic	Speaker
6:00 pm	Welcome and Introductions	Dr Subodh Verma
6:05 pm	Case Discussion	Dr Subodh Verma Presenters: Dr Richard Choi, Dr Claudia Bucci, Dr Anil Gupta
6:40 pm	COVID-19: Patient Reengagement	Dr Subodh Verma Presenters: Dr Richard Choi, Dr Claudia Bucci, Dr Anil Gupta
6:50 pm	Q&A	Dr Subodh Verma (moderator)
7:00 pm	Close	

Send in your questions!

- Submit your questions for the symposium Q&A by clicking on the Q&A icon on your screen

- To direct your question to a specific speaker, please **include his/her name at the beginning of your question**

Case Discussion



Subodh Verma (Chair)
MD, PhD, FRCSC, FAHA
Cardiac Surgeon, St Michael's Hospital
Professor of Surgery, and Pharmacology and Toxicology, University of Toronto
Canada Research Chair in Cardiovascular Surgery
Toronto, ON

Case Presentation: Mr. RJ

- Mr. RJ 67-year-old retired fireman
- PMHx
  - Type 2 diabetes X 8 years
  - Hypertension
  - Dyslipidemia
  - Reformed smoker
  - PCI to LAD – 2 years ago for anterior STEMI
  - RCA 50%; OM 30-50%
  - LVEF = 57%; moderate diastolic dysfunction; Anterior WMA
  - Carotid ultrasound – 50% R ICA stenosis

Case Presentation: Mr. RJ *cont'd*

Symptoms	CCS II symptoms
Investigations	SR 65/min; BP 134/80; normal physical exam EKG Anterior Q waves; LVH Awaiting stress echo, but limited access to clinic/hospital for testing
Biochemistry	A1C = 7.3% LDL-C = 2.4 mM HDL = 1.2 mM TG = 2.3 mM CBC/lytes – Normal eGFR = 54 ml/min/1.73m^2

Medications

- ASA 81mg OD
- Ramipril 10mg OD
- Bisoprolol 5mg OD
- Atorvastatin 40mg OD
- Metformin 1g BID
- Sitagliptin 100mg OD

Question

What is Mr. RJ’s risk of recurrent events?

Richard Choi
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Cardiologist, St. Joseph's Health Centre,
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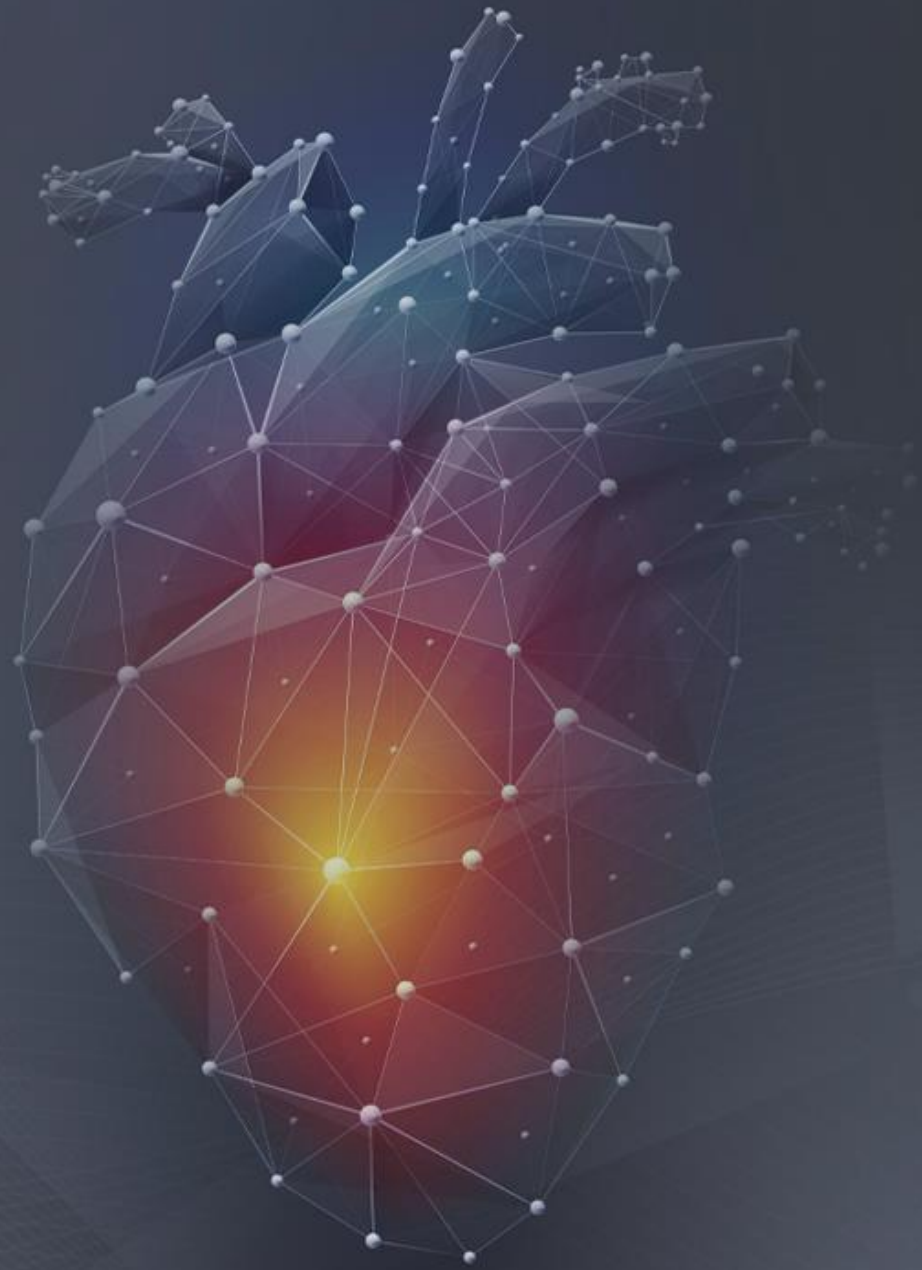


Risk of Recurrent Events

What is Mr. RJ's risk of recurrent events?

Multiple reasons for ↑ risk compared to others with ASCVD

Prior MI

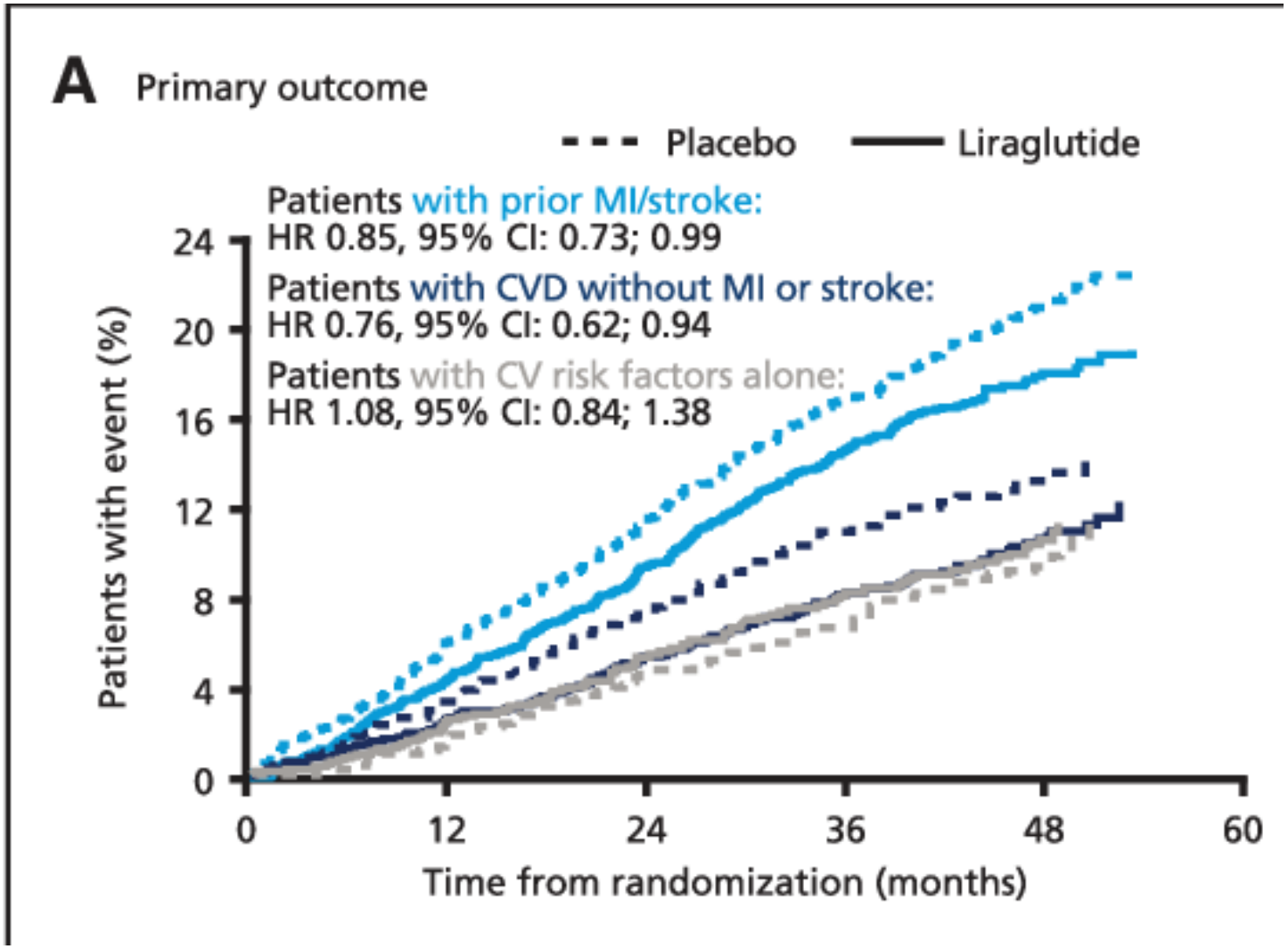
Polyvascular disease (50% carotid stenosis)

Diabetes mellitus

CKD (eGFR of 54)

LEADER - Effect of Liraglutide on MACE Endpoint - Post MI/stroke

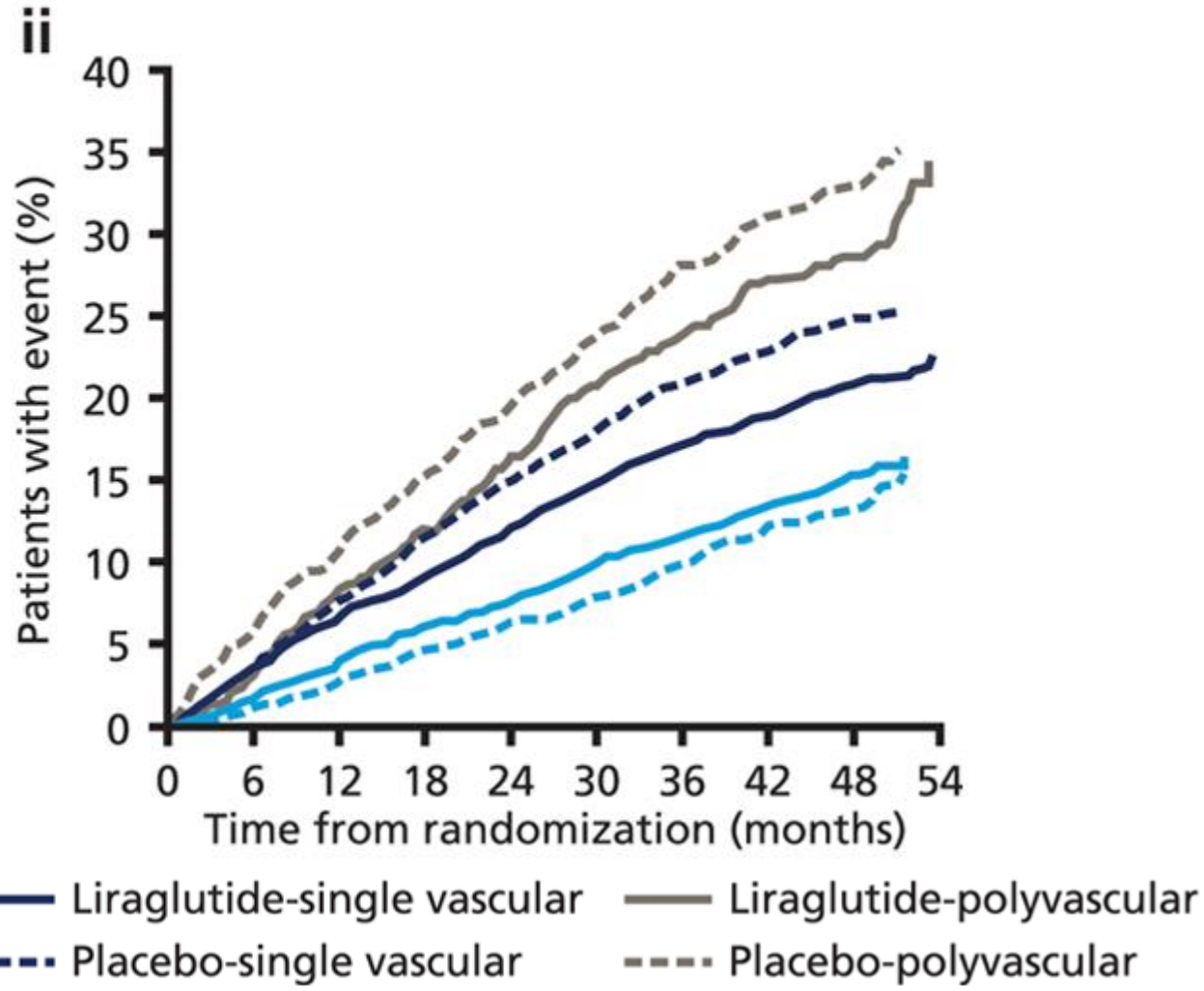
- Post hoc analysis of CV death/MI/stroke
- Stratified according to multiple RF vs established ASCVD
- Established ASCVD further stratified by way of prior MI/stroke event vs other ASCVD



Verma et al. Circulation 2018;138:2884-2894

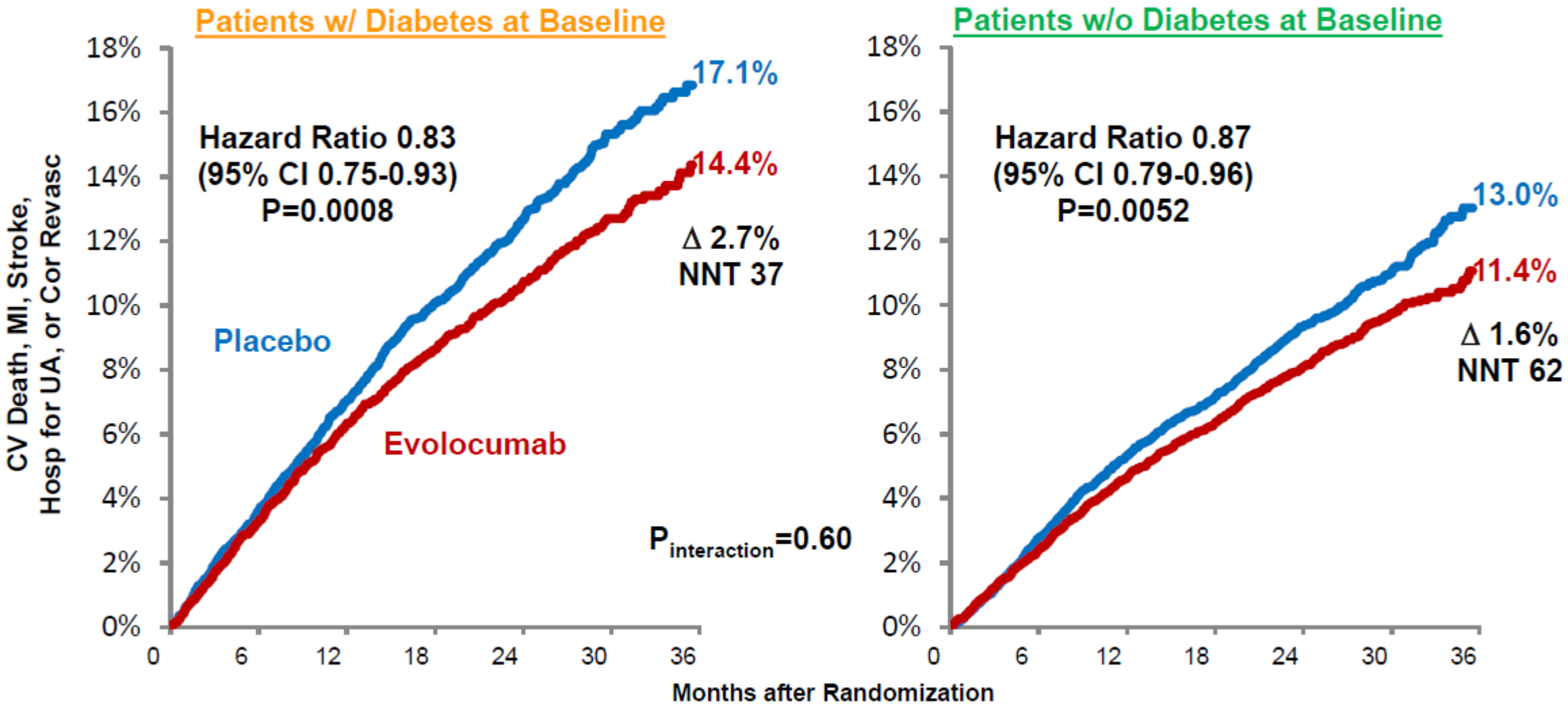
LEADER - Effect of Liraglutide on MACE Endpoint – Polyvascular

- Post hoc analysis
- Stratified according to multiple RF vs established ASCVD
- Established ASCVD further stratified by way of beds involved (1 or >1)



Verma et al. Circulation 2018;137:2179-83

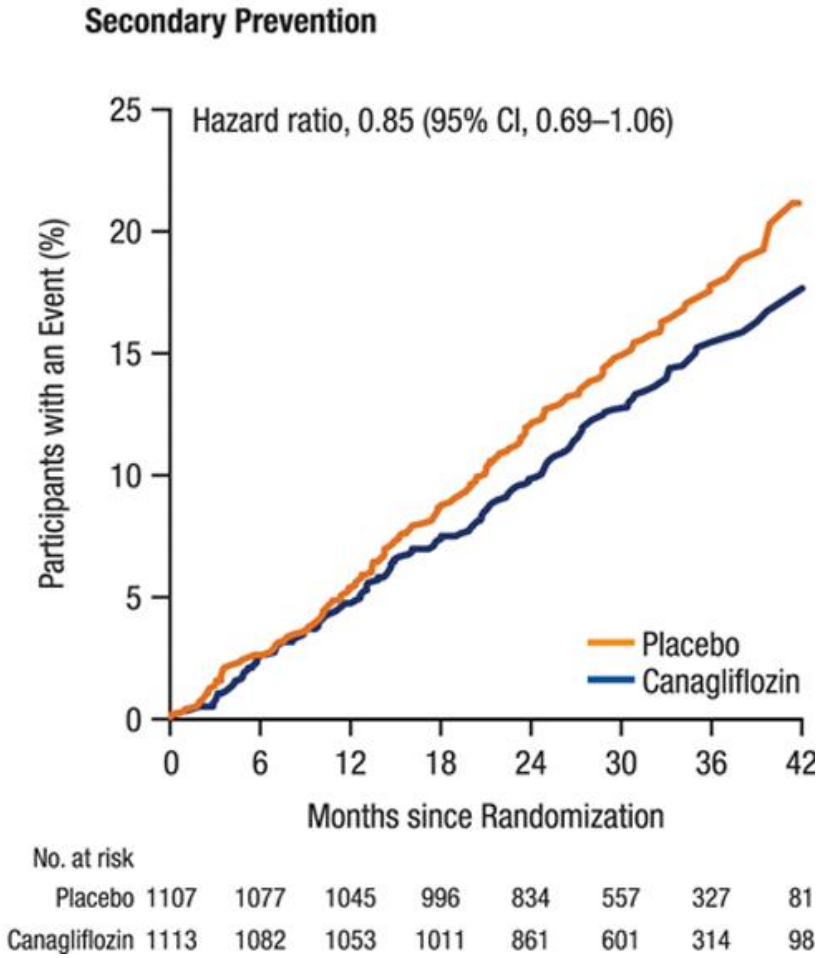
FOURIER - Effect of Evolocumab in ASCVD – DM Subgroup



Sabatine et al. Lancet DM & Endo. 2017. 5:12; 941-50

CREDENCE - Effect of SGLT2i in DM + CKD

- Renal dedicated outcome trial
- 1º endpoint was combined multiple renal endpoints + CV death
- Secondary endpoint in prespecified hierarchical analysis
  - CV death + hHF
  - CV death/MI/stroke (p=0.01)



Mahaffey et al. Circulation. 2019; 140:739

Question

Should TG matter in this patient?

Anil Gupta
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Staff Cardiologist, Trillium Health Partners
Lecturer, University of Toronto
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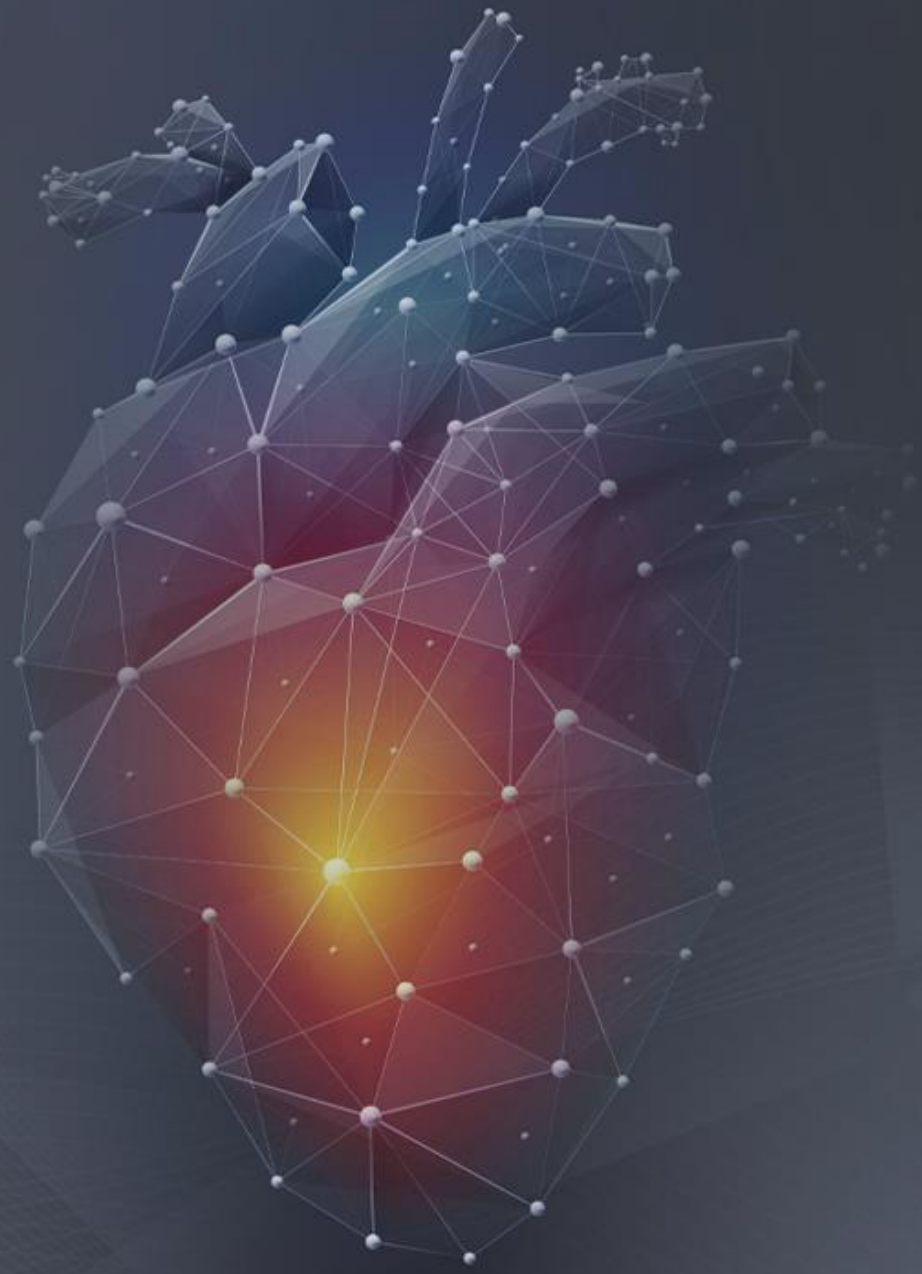
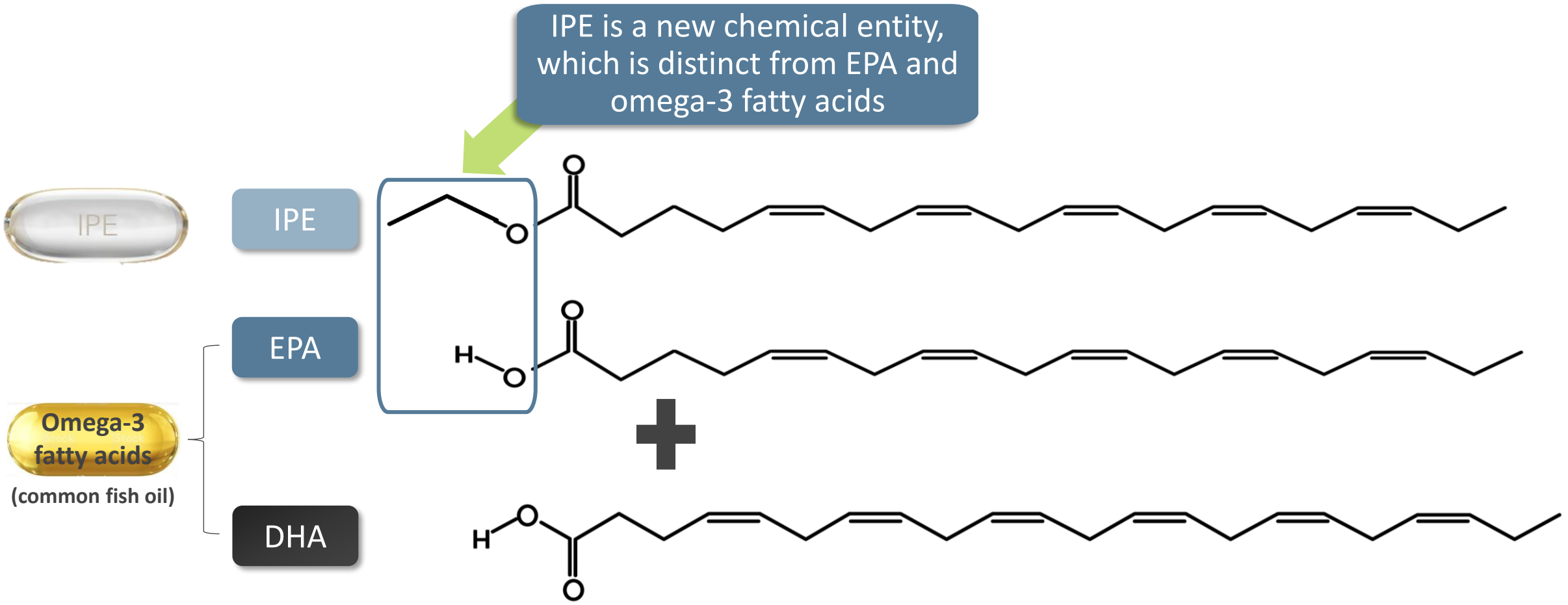


Icosapent Ethyl (IPE):
A New Chemical Entity Distinct From EPA and Omega-3 Fatty Acids



PubChem Database: DHA, CID=445580; EPA, CID=446284; IPE, CID=9831415.

Differences of IPE vs. Common Fish Oil

Common Fish Oil
(Mixtures of Omega-3 Fatty Acids)

Icosapent Ethyl

Most fish oil supplements contain DHA
- DHA is an omega-3, which can raise LDL-C

Stable EPA ethyl ester; no DHA
- Not shown to raise LDL-C

No demonstrated CV benefit in clinical trials
- Not indicated for management of CV risk

Health Canada-approved
- To reduce the risk of ischemic CV events in statin-treated patient with elevated TGs

Daily dose
- May take up to 10-40 capsules a day to equal the EPA in a daily dose of pure IPE, with an equivalent increase of DHA

Daily dose
- 4 g/day (2 x 1 g capsules BID)

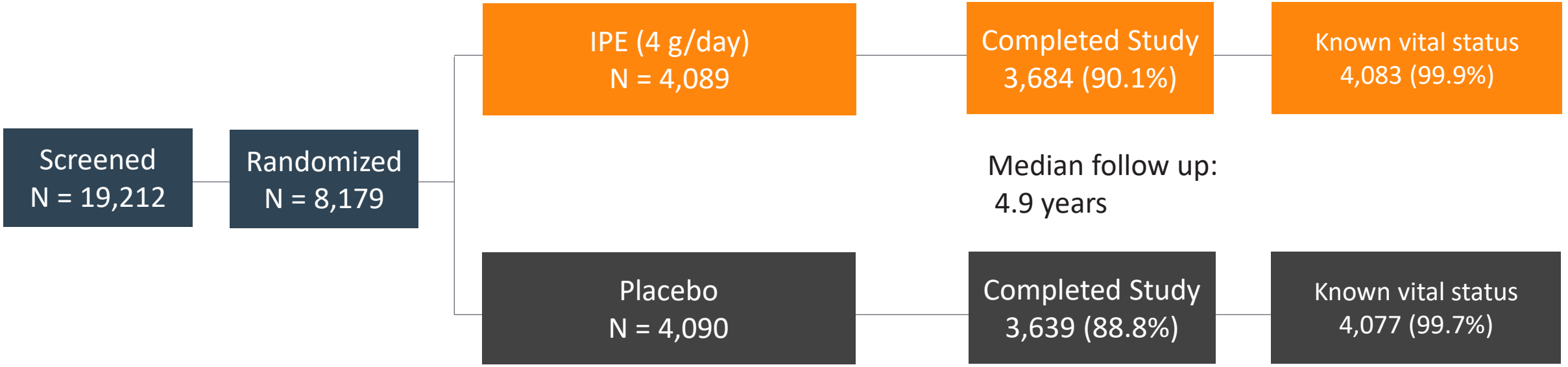
Reported to have fishy taste
- May cause fish-smelling burps

No reported fishy taste
- No fishy taste or fishy burps taking 4 g/day of pure IPE in a clinical trial

BID=twice daily.

Bhatt DL et al. *N Engl J Med*. 2019;380:11-22. Chang CH et al. *Prostaglandins Leukot Essent Fatty Acids*. 2018;129:1-12. Ganda OP et al. *J Am Coll Cardiol*. 2018;72:330-343. Healthline website: https://www.healthline.com/health-news/should-you-be-taking-prescription-strength-fish-oil. Last Accessed January 17, 2020. Icosapent ethyl Product Monograph. HLS Therapeutics. December 30, 2019. Mason RP, Sherratt SCR. *Biochem Biophys Res Commun*. 2017;483:425-429.

REDUCE-IT: A Multicenter, Randomized, Double-Blinded, Event-Driven, Placebo-Controlled Trial



Bhatt DL et al. *N Engl J Med*. 2019;380:11-22.

REDUCE-IT Key Inclusion Criteria

Prevention Cohorts		
Secondary	≥45 years with: • Established CVD (documented CAD, CVD, or PAD)	• **Fasting TG Level** ≥1.52 mmol/L and <5.63 mmol/L[a] • **LDL-C** >1.06 mmol/L and ≤2.59 mmol/L and on stable statin therapy (± ezetimibe) for ≥4 weeks prior to qualifying measurements for randomization
Primary	≥50 years with: • Diabetes • ≥1 additional risk factor for CVD	

[a] Due to the variability of TGs, a 10% allowance existed in the initial protocol, which permitted patients to be enrolled with qualifying TGs ≥1.52 mmol/L. In May 2013, the protocol was amended whereby the acceptable TG range was 1.69 mmol/L to 2.25 mmol/L, with no variability allowance.

PAD: peripheral artery disease.

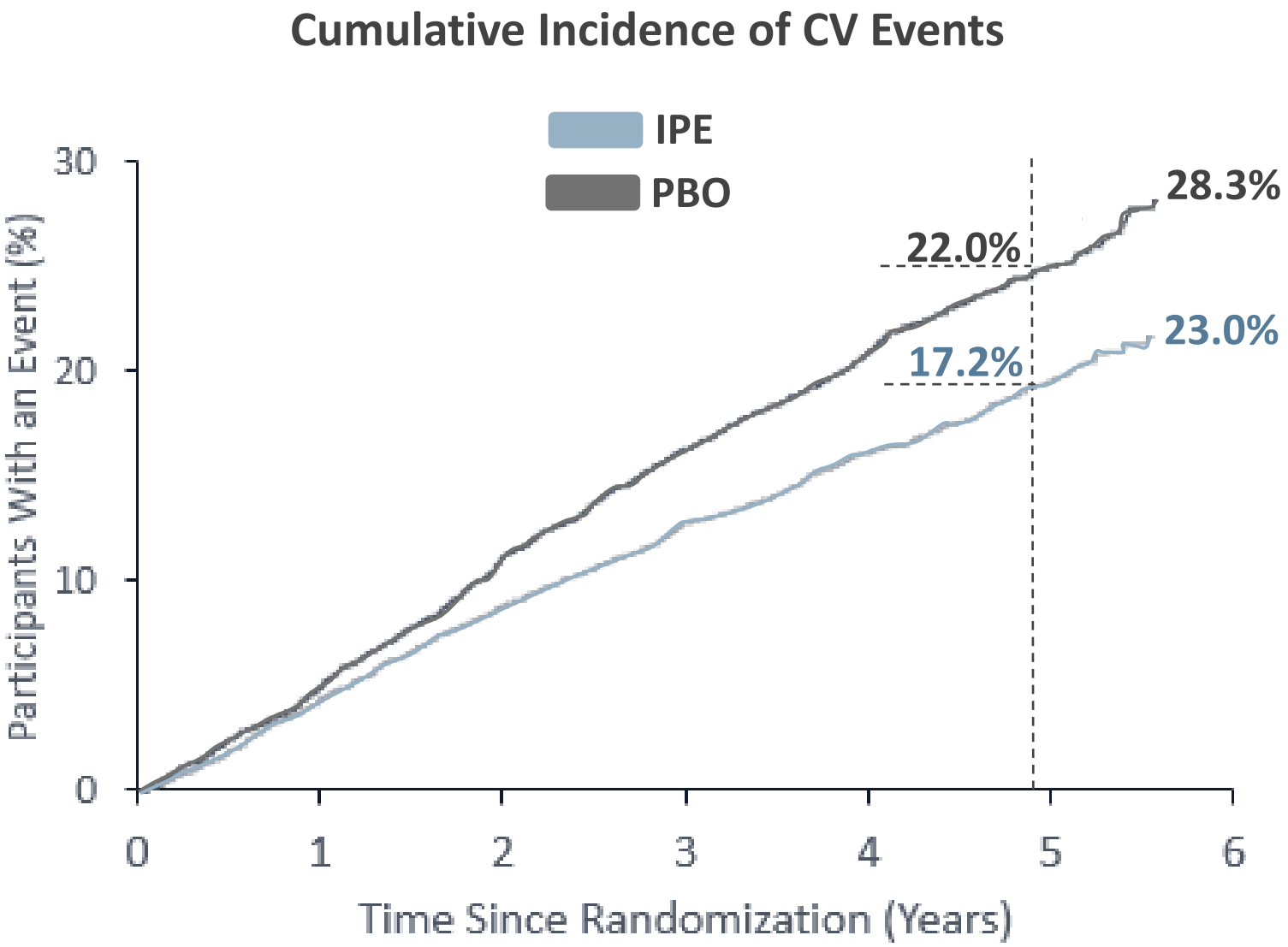
Bhatt DL et al. *N Engl J Med*. 2019;380:11-22.

REDUCE-IT: Key Baseline Characteristics (cont.)

	IPE (n = 4089)	Placebo (n = 4090)
TGs (mmol/L), Median (Q1-Q3)	2.45 (2.0 – 3.07)	2.44 (1.98 – 3.10)
HDL-C (mmol/L), Median (Q1-Q3)	1.03 (0.89 – 1.19)	1.03 (0.91 – 1.19)
LDL-C (mmol/L), Median (Q1-Q3)	1.91 (1.59 – 2.28)	1.97 (1.63 – 2.30)
TG Category, %		
<1.69 mmol/L	10.1	10.5
1.69 to <2.26 mmol/L	29.2	29.1
>2.26 mmol/L	60.7	60.4

Adapted from Bhatt DL et al. *N Engl J Med*. 2019;380:11-22.

REDUCE-IT: Primary Endpoint



Primary Endpoint
5-Point MACE[a]
(median follow-up: 4.9 years)

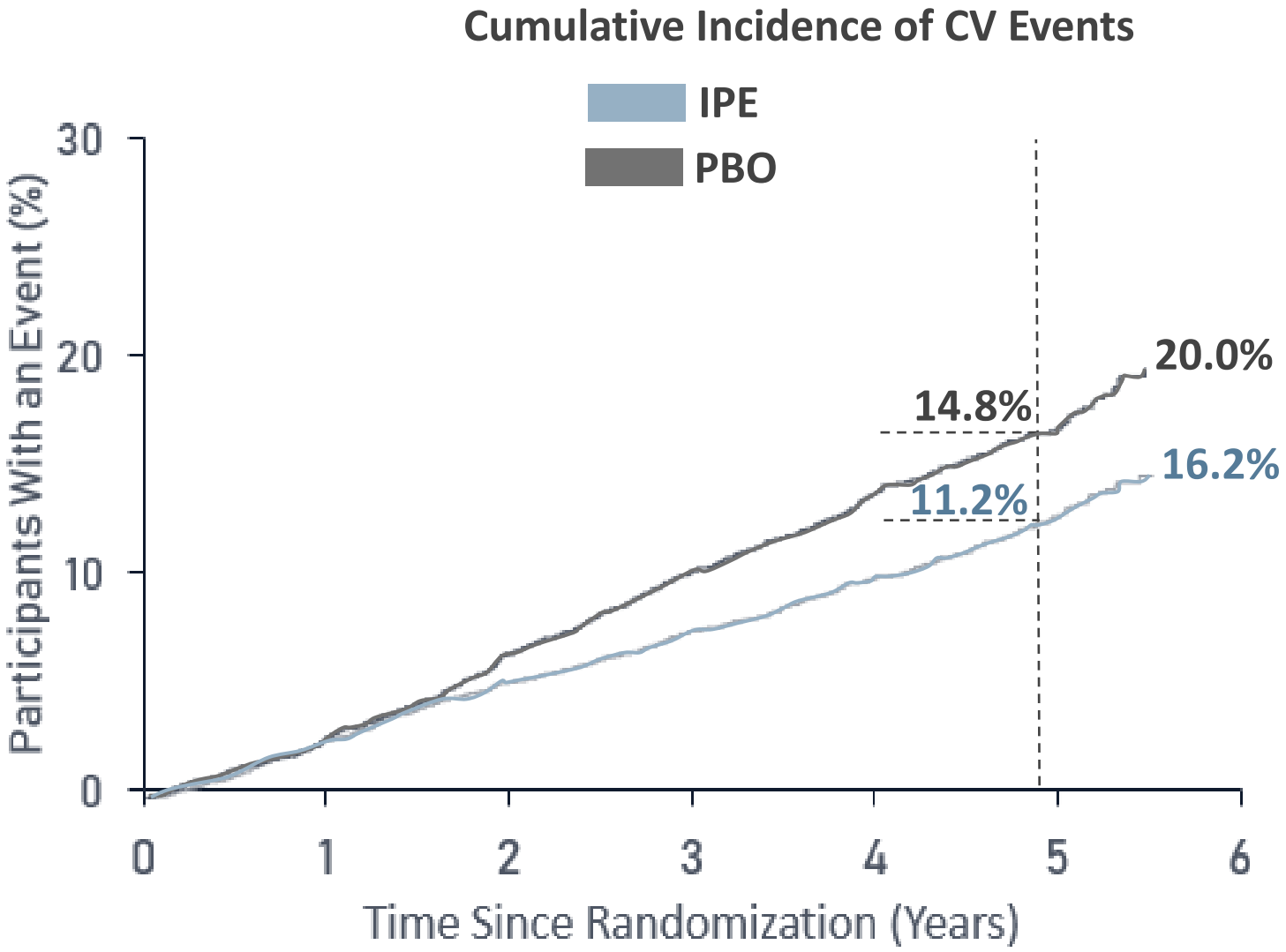
25%
RRR

NNT = 21

HR (95% CI): 0.75 (0.68-0.83)
ARR: 4.8%
***P* = .00000001**

[a] CV death, nonfatal MI, nonfatal stroke, coronary revascularization, hospitalization for unstable angina.
Adapted from Bhatt DL et al. *N Engl J Med*. 2019;380:11-22.

REDUCE-IT: Key Secondary Endpoint



Key Secondary Endpoint

3-Point MACE[a]

(median follow-up: 4.9 years)

26%
RRR

NNT = 28

HR (95% CI): 0.74 (0.65-0.83)
ARR: 3.6%
***P* = .0000006**

[a] CV death, nonfatal MI, nonfatal stroke.

Adapted from Bhatt DL et al. *N Engl J Med*. 2019;380:11-22.

REDUCE-IT: Adverse Events

Most Frequent Treatment-Emergent AEs ≥5% in Either Treatment Group	IPE, % (N = 4089)	Placebo, % (N = 4090)	*P*
Diarrhea	9.0	11.1	0.002
Peripheral edema	6.5	5.0	0.002
Constipation	5.4	3.6	<0.001
Atrial fibrillation	5.3	3.9	0.003
Anemia	4.7	5.8	0.03

Adjudicated Events Hospitalization for Atrial Fibrillation or Atrial Flutter	IPE, % (N = 4089)	Placebo, % (N = 4090)	*P*
Positively Adjudicated Atrial Fibrillation/Flutter[a]	3.1	2.1	0.004

Bhatt DL et al. *N Engl J Med*. 2019;380:11-22.

Summary (cont.)

Icosapent Ethyl met the 3-Point MACE Key Secondary Endpoint

Primary Endpoint
5-Point MACE[a]

25%
RRR
NNT=21

HR = 0.75
(95% CI, 0.68-0.83)
***P*=0.00000001**

Key Secondary Endpoint
3-Point MACE[b]

26%
RRR
NNT=28

HR = 0.74
(95% CI, 0.65-0.83)
***P*=0.0000006**

Other Secondary Endpoints

MI Fatal/Nonfatal

31%
RRR

HR = 0.69
(95% CI, 0.58-0.81)
***P*<0.001**

Stroke Fatal/Nonfatal

28%
RRR

HR = 0.72
(95% CI, 0.55-0.93)
***P*=0.01**

CV Death

20%
RRR

HR = 0.80
(95% CI, 0.66-0.98)
***P*=0.03**

[a] Nonfatal MI, nonfatal stroke, CV death, coronary revascularization, or UA requiring hospitalization. [b] nonfatal MI, nonfatal stroke, or CV death.
Bhatt DL et al. *N Engl J Med*. 2019;380:11-22.

Question

What are the various pharmacological choices available for Mr. RJ?

Claudia Bucci
PharmD
CV Pharmacist
Sunnybrook Health Sciences Centre
University of Toronto
Toronto, ON

Case Presentation: Mr. RJ

- Mr. RJ 67-year-old retired fireman
- PMHx
  - Type 2 diabetes X 8 years
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  - Dyslipidemia
  - Reformed smoker
  - PCI to LAD – 2 years ago for anterior STEMI
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Medications

- ASA 81mg OD
- Ramipril 10mg OD
- Bisoprolol 5mg OD
- Atorvastatin 40mg OD
- Metformin 1g BID
- Sitagliptin 100mg OD

Therapies for CV Risk Reduction

LIFESTYLE

- Smoking Cessation
- Blood Pressure
- Exercise
- Diet
- Weight Reduction

LIPIDS

- High Dose Statins
- Ezetimibe *(IMPROVE-IT)*
- PCSK9 Inhibitors (*FOURIER, ODYSSEY)*
- IPE *(REDUCE-IT)*

GLUCOSE-LOWERING

- SGLT-2 Inhibitors (*EMPAREG, CANVAS*)
- GLP-1 Agonists (*LEADER, SUSTAIN)*

ANTITHROMBOTIC

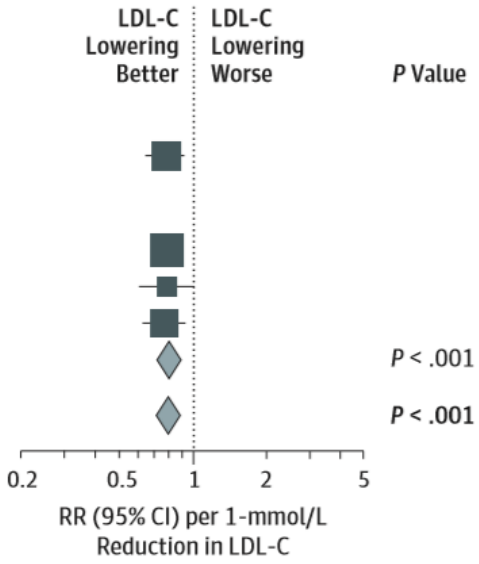
- Ticagrelor *(PLATO)*
- Long-Term DAPT *(PEGASUS)*
- Low Dose Rivaroxaban *(COMPASS)*

LDL Lowering

- Aggressive LDL lowering is beneficial, *especially* in high risk patients
  - **Canadian Lipid Guidelines (2016)** recommend LDL < 2mmol/L or 50% lowering (Consider LDL <1.8mmol/L in patients with recent ACS)
  - **ESC Lipid Guidelines (2019) Guidelines** recommend LDL < 1.4 mmol/L and 50% lowering in very high risk patients

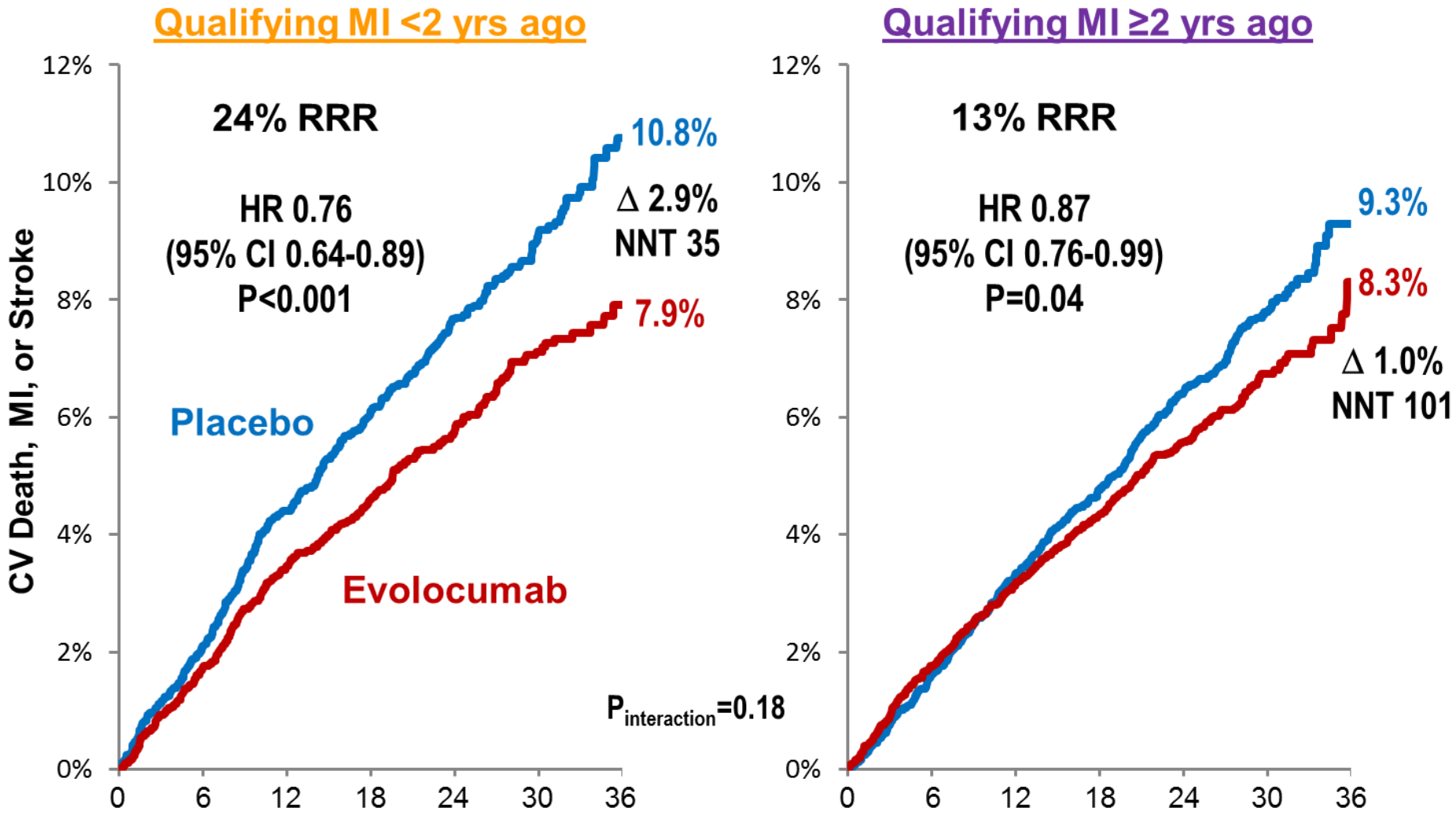
A Meta-analysis of effect of 1-mmol/L LDL-C lowering on the risk of major vascular events

Trial	Events, % per annum: Experimental Arm	Control Arm	RR (95% CI)	P Value
Statins				
CTTC <2 mmol/L subgroup	910 (4.1)	1012 (4.6)	0.78 (0.65-0.94)	
Nonstatin LDL-C lowering				
IMPROVE-IT	2455 (4.5)	2649 (4.9)	0.79 (0.67-0.93)	
FOURIER <1.8 mmol/L subgroup	81 (3.7)	103 (4.9)	0.80 (0.61-1.04)	
REVEAL	2068 (3.3)	2214 (3.5)	0.77 (0.63-0.96)	
Summary	4604	4966	0.79 (0.70-0.88)	P < .001
Overall summary	**5514**	**5978**	**0.79 (0.71-0.87)**	P < .001



Sabatine et al. *JAMA* 2018

Benefit of EvoMab Based on Time from Qualifying MI

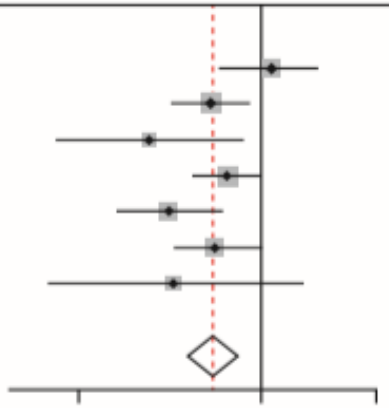


Gencer et al. JAMA Cardiology 2020

Glucose-Lowering Therapies: MACE

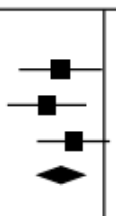
GLP-1 AGONISTS

	GLP-1 receptor agonist n/N (%)	Placebo n/N (%)	Hazard ratio (95% CI)	NNT (95% CI)	p value
Three-component MACE					
ELIXA	400/3034 (13%)	392/3034 (13%)	1·02 (0·89–1·17)		0·78
LEADER	608/4668 (13%)	694/4672 (15%)	0·87 (0·78–0·97)		0·015
SUSTAIN-6	108/1648 (7%)	146/1649 (9%)	0·74 (0·58–0·95)		0·016
EXSCEL	839/7356 (11%)	905/7396 (12%)	0·91 (0·83–1·00)		0·061
Harmony Outcomes	338/4731 (7%)	428/4732 (9%)	0·78 (0·68–0·90)		<0·001
REWIND	594/4949 (12%)	663/4952 (13%)	0·88 (0·79–0·99)		0·026
PIONEER 6	61/1591 (4%)	76/1592 (5%)	0·79 (0·57–1·11)		0·17
Overall (I^2=40·9%, p=0·118)	**2948/27977 (11%)**	**3304/28027 (12%)**	**0·88 (0·82–0·94)**	**75 (50–151)**	**<0·001**



SGLT2 INHIBITORS

	Patients		Events	Events per 1000 patient-years		Weight (%)	HR	HR (95% CI)
	Treatment (n)	Placebo (n)		Treatment	Placebo			
Patients with atherosclerotic cardiovascular disease								
EMPA-REG OUTCOME	4687	2333	772	37·4	43·9	29·4		0·86 (0·74–0·99)
CANVAS Program	3756	2900	796	34·1	41·3	32·4		0·82 (0·72–0·95)
DECLARE-TIMI 58	3474	3500	1020	36·8	41·0	38·2		0·90 (0·79–1·02)
Fixed effects model for atherosclerotic cardiovascular disease (p=0·0002)								**0·86 (0·80–0·93)**



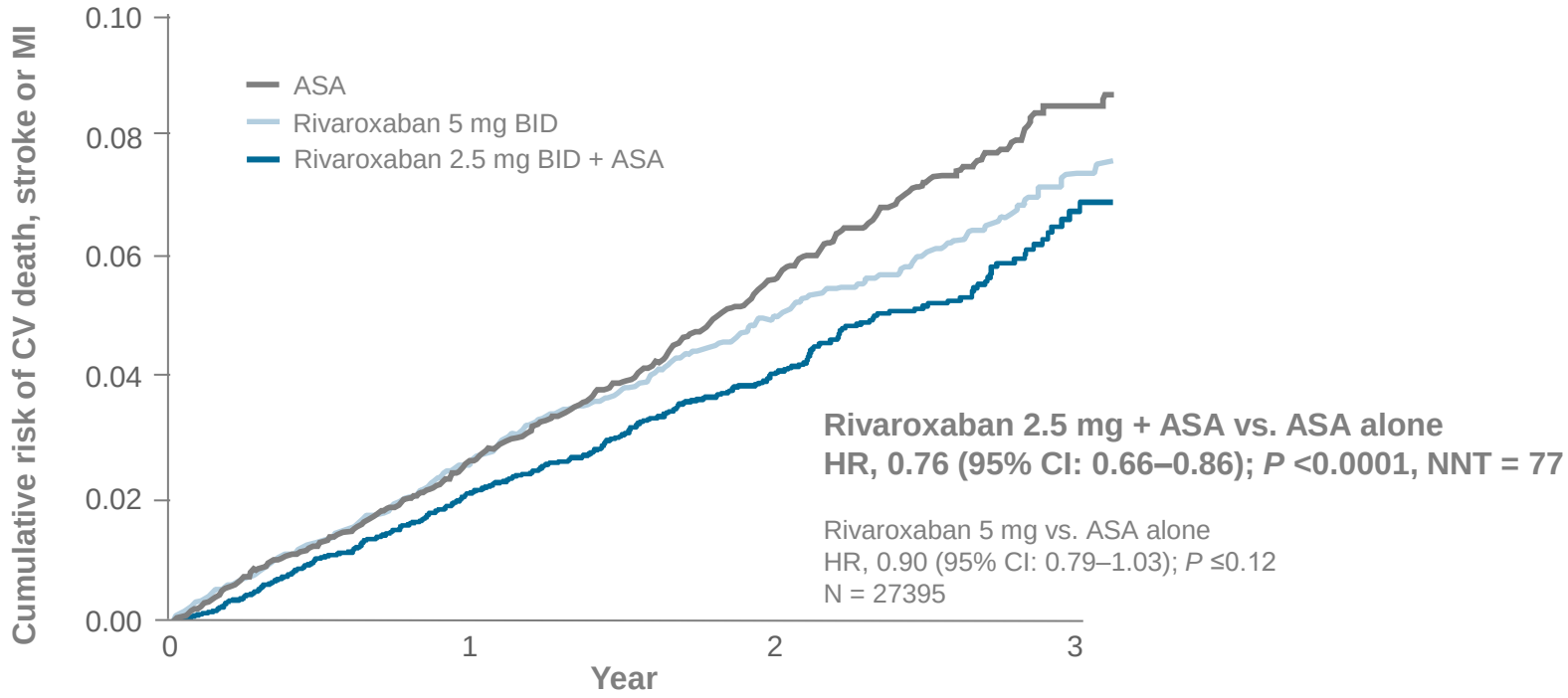
Kristensen et al. *Lancet* 2019
Zelniker et al. *Lancet* 2019

Glucose-Lowering Therapies

SGLT2 Inhibitors *(oral)*
2-3kg weight loss
BP reduction
Monitor eGFR
Sick day management
Mycotic genital infections
Rare: DKA (<0.1%), lower limb amputation (canagliflozin)

GLP-1 Agonists *(subcutaneous injections & oral semaglutide)*
1.5-3kg weight loss
Nausea, vomiting, diarrhea (rare)
Rare: gallstone disease, higher rate of retinopathy (semaglutide)

COMPASS Trial: CV Death, Stroke, MI



Vascular dose rivaroxaban 2.5 mg BID + ASA significantly reduced composite primary endpoint vs. ASA alone in patients with stable atherosclerotic vascular disease

Eikelboom JW *et al*. *N Engl J Med* 2017; 377:1319-30.

Rivaroxaban 2.5mg bid + ASA

- Reduction in CV death, MI, stroke
- Increase in major bleeding without an increase in fatal, intracranial or critical organ bleeding
- Particularly beneficial if the bleeding risk is low

Efficacy and Safety - Back to the Case…

- Increase the dose of statin, add ezetimibe if required, start IPE 2g twice daily

- Continue metformin, stop sitagliptin and add either an SGLT2 inhibitor or a GLP1 agonist
  - Remember sick day management and look at the eGFR

- Consider adding rivaroxaban 2.5mg bid to ASA given favourable risk/benefit profile

Question

The ISCHEMIA trial – why is it particularly relevant today?

Anil Gupta
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Staff Cardiologist, Trillium Health Partners
Lecturer, University of Toronto
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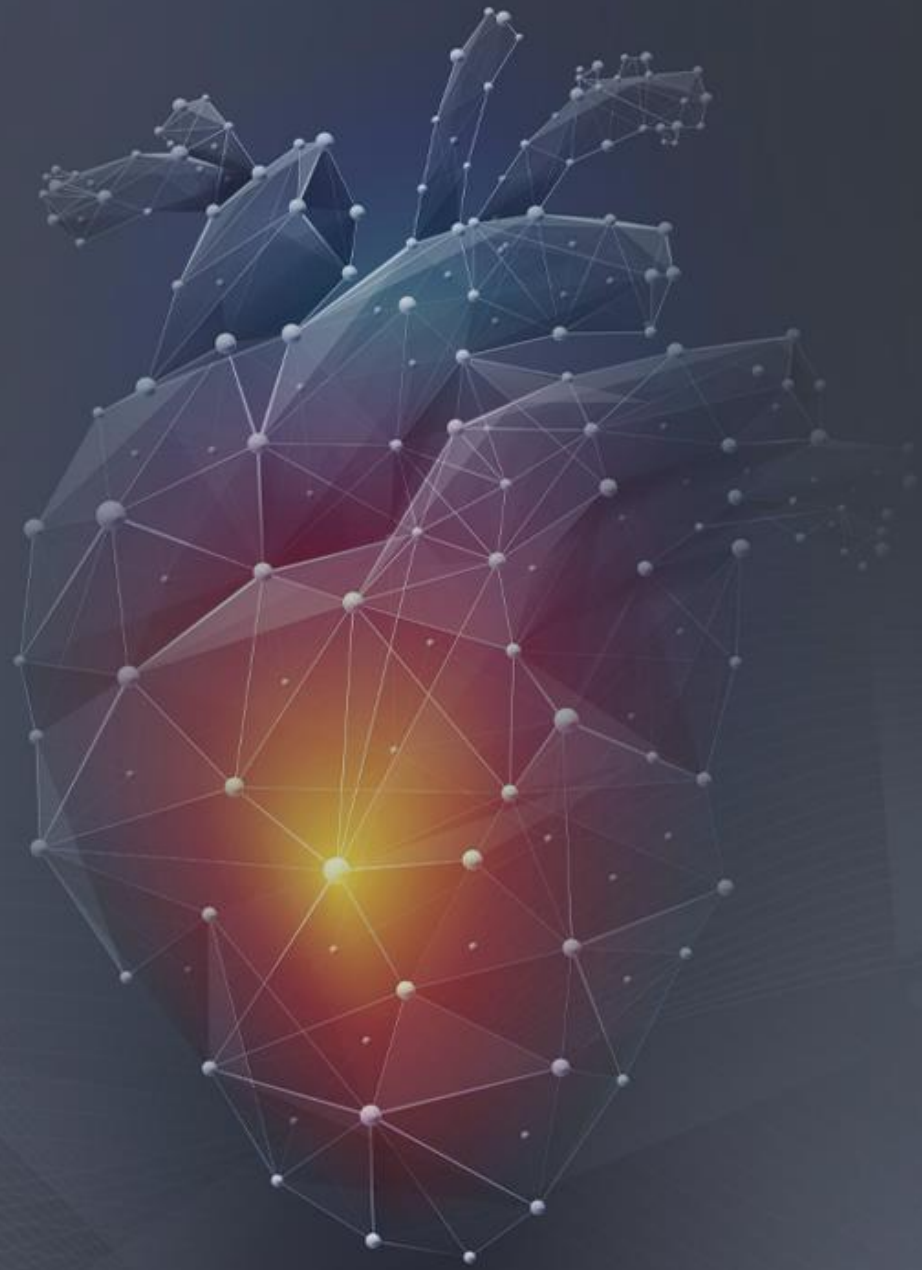
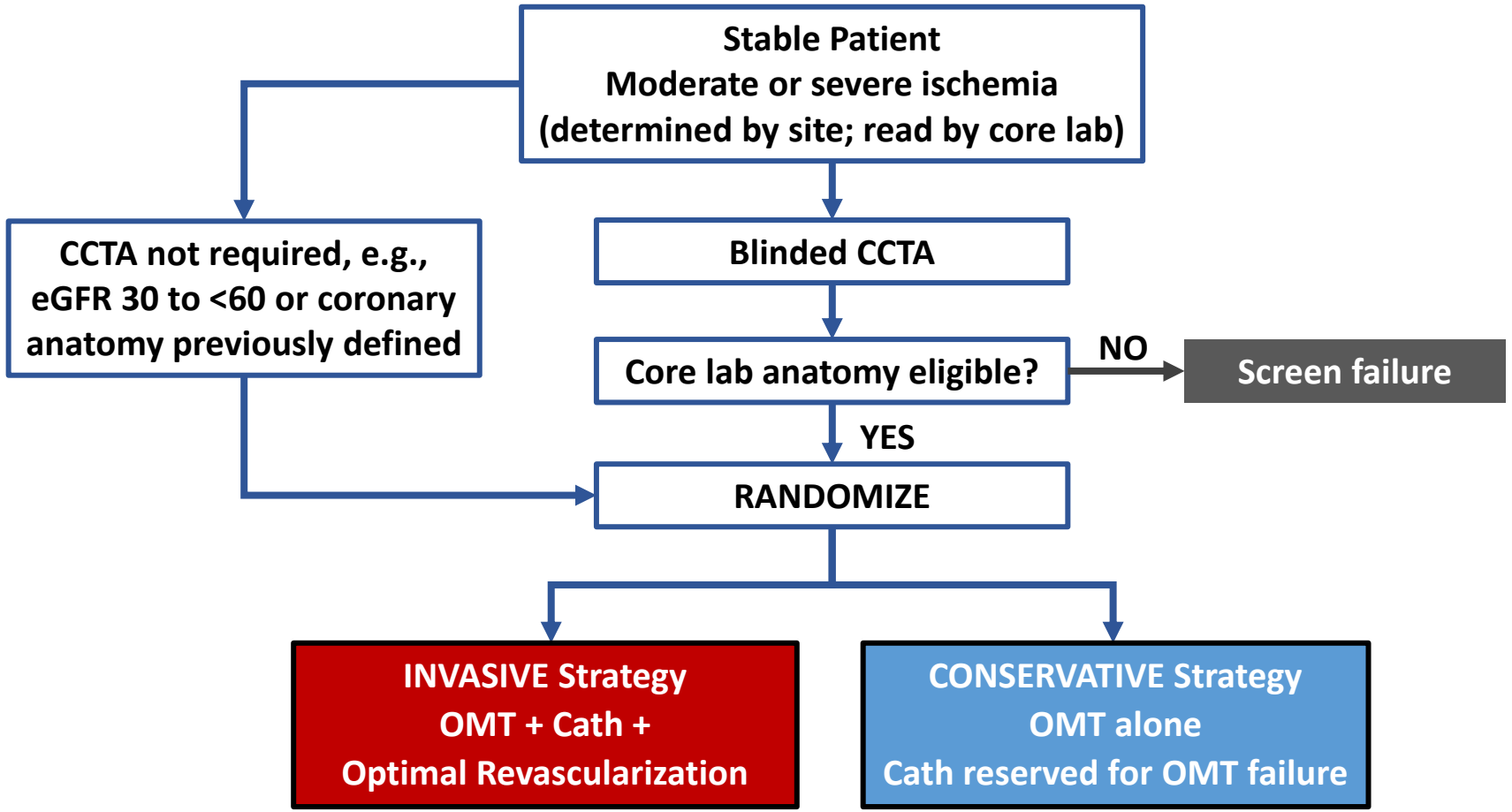


ISCHEMIA Research Question

- In stable patients with at least moderate ischemia on a stress test, is there a benefit to adding cardiac catheterization and, if feasible, revascularization to optimal medical therapy?

Study Design



Maron DJ, et al. American Heart Journal. 2018; 201;124-135.

Eligibility Criteria

Clinical and Stress Test Eligibility Criteria

Inclusion Criteria

- Age ≥21 years
- Moderate or severe ischemia*

Major Exclusion Criteria

- NYHA Class III-IV HF
- Unacceptable angina despite medical therapy
- EF < 35%
- ACS within 2 months
- PCI or CABG within 1 year
- eGFR <30 mL/min or on dialysis

CCTA Eligibility Criteria

Inclusion Criteria

- ≥50% stenosis in a major epicardial vessel (stress imaging participants)
- ≥70% stenosis in a proximal or mid vessel (ETT participants)

Major Exclusion Criteria

- ≥50% stenosis in unprotected left main

ISCHEMIA CRD

**Ischemia eligibility determined by sites. All stress tests interpreted at core labs.*

Maron DJ, et al. American Heart Journal. 2018; 201;124-135.

Baseline Characteristics

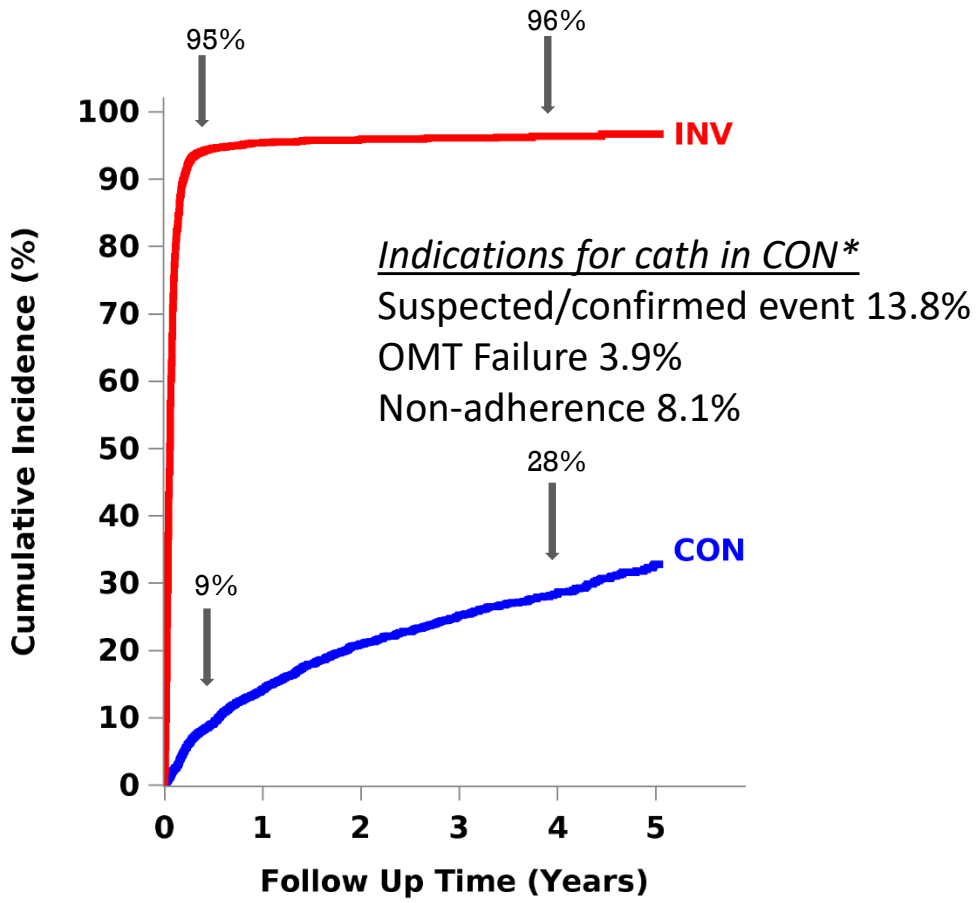
Characteristic	Total	INV	CON
Clinical			
Age at Enrollment (yrs.)			
Median	64 (58, 70)	64 (58, 70)	64 (58, 70)
Female Sex (%)	23	23	22
Hypertension (%)	73	73	73
Diabetes (%)	42	41	42
Prior Myocardial Infarction (%)	19	19	19
Ejection Fraction, Median (%) (n=4637)	60 (55, 65)	60 (55, 65)	60 (55, 65)
Systolic Blood Pressure, Median (mmHg)	130 (120, 142)	130 (120, 142)	130 (120, 142)
Diastolic Blood Pressure, Median (mmHg)	77 (70, 81)	77 (70, 81)	77 (70, 81)
LDL Cholesterol, Median (mg/dL)	83 (63, 111)	83 (63, 111)	83 (63, 109.5)
History of Angina	90%	90%	89%
Angina Began or Became More Frequent Over the Past 3 Months	29%	29%	29%
Stress Test Modality			
Stress Imaging (%)	75	75	76
Exercise Tolerance Test (ETT) (%)	25	25	24

Median values reported with 25th and 75th percentiles

Hochman JS et al. JAMA Cardiology. 2019 Mar 1;4(3):273-86.

Cardiac Catheterization and Revascularization

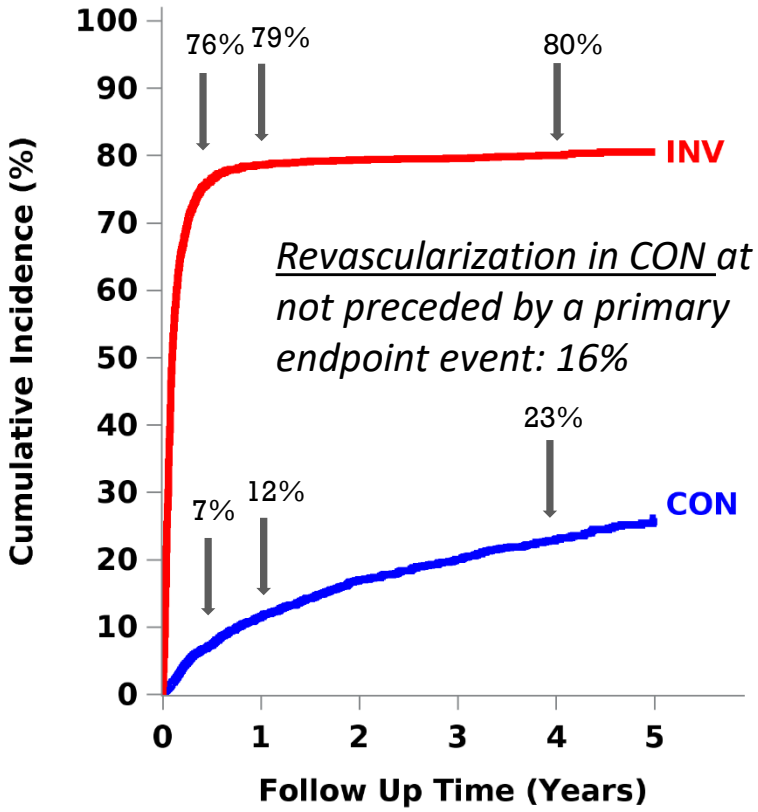
Cardiac Catheterization



*Indications for cath in CON**
Suspected/confirmed event 13.8%
OMT Failure 3.9%
Non-adherence 8.1%

CON	2591	2186	1646	1087	601	232
INV	2588	111	79	50	20	4

Revascularization



Revascularization in CON at 4 years not preceded by a primary endpoint event: 16%

CON	2591	2250	1721	1157	642	254
INV	2588	523	410	289	155	54

*Indications for Cath are percentages of CON patients whereas cumulative event rate shown at 4 years reflects censoring and the rate at that time point.

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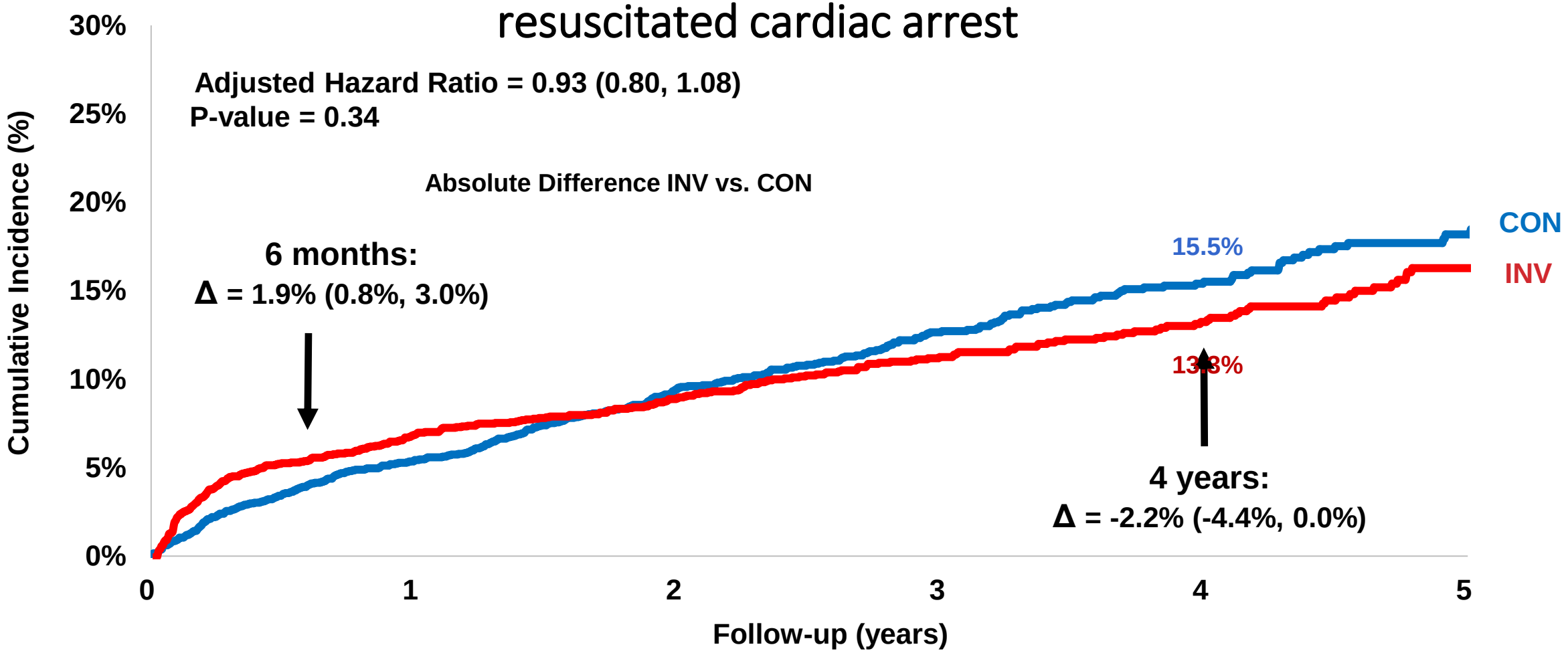
Primary Outcome: CV Death, MI, hospitalization for UA, HF or resuscitated cardiac arrest



Subjects at Risk

CON	2591	2431	1907	1300	733	293
INV	2588	2364	1908	1291	730	271

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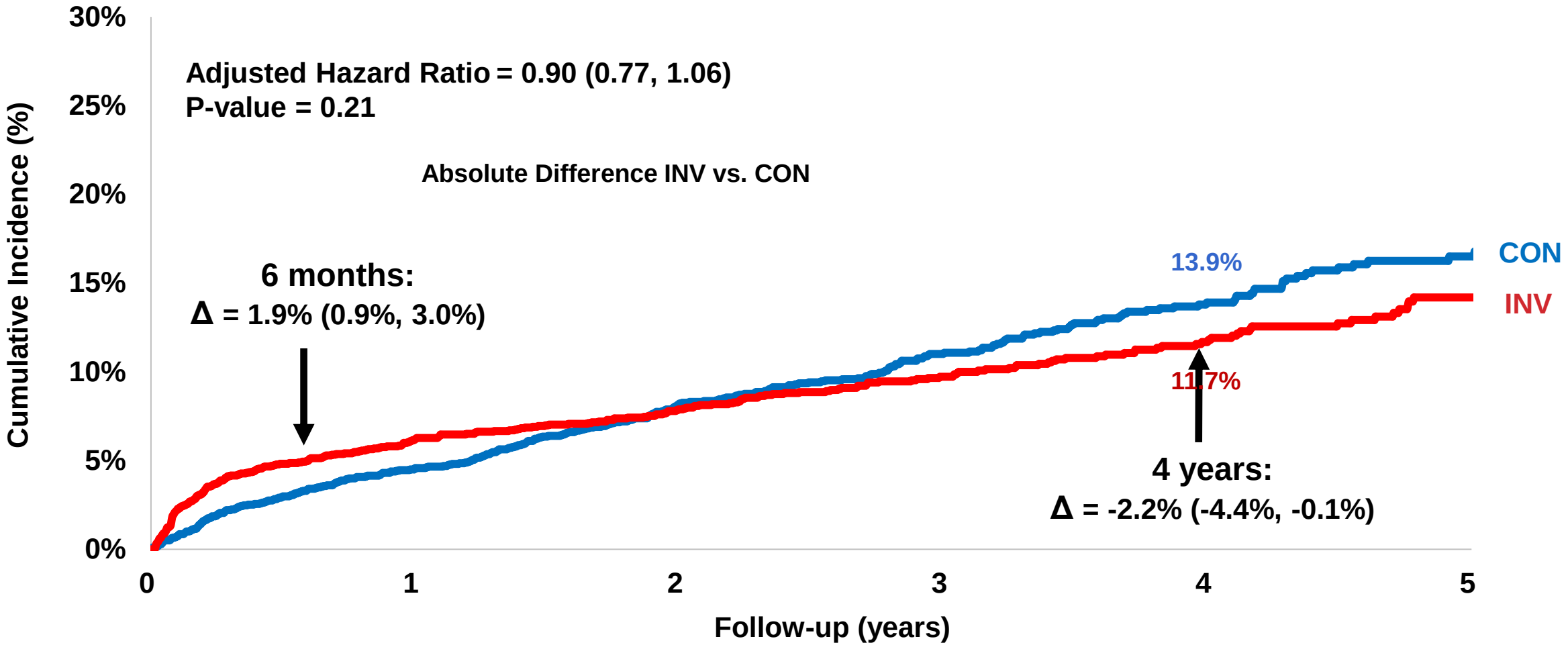
Major Secondary: CV Death or MI



Subjects at Risk

CON	2591	2453	1933	1325	746	298
INV	2588	2383	1933	1314	752	282

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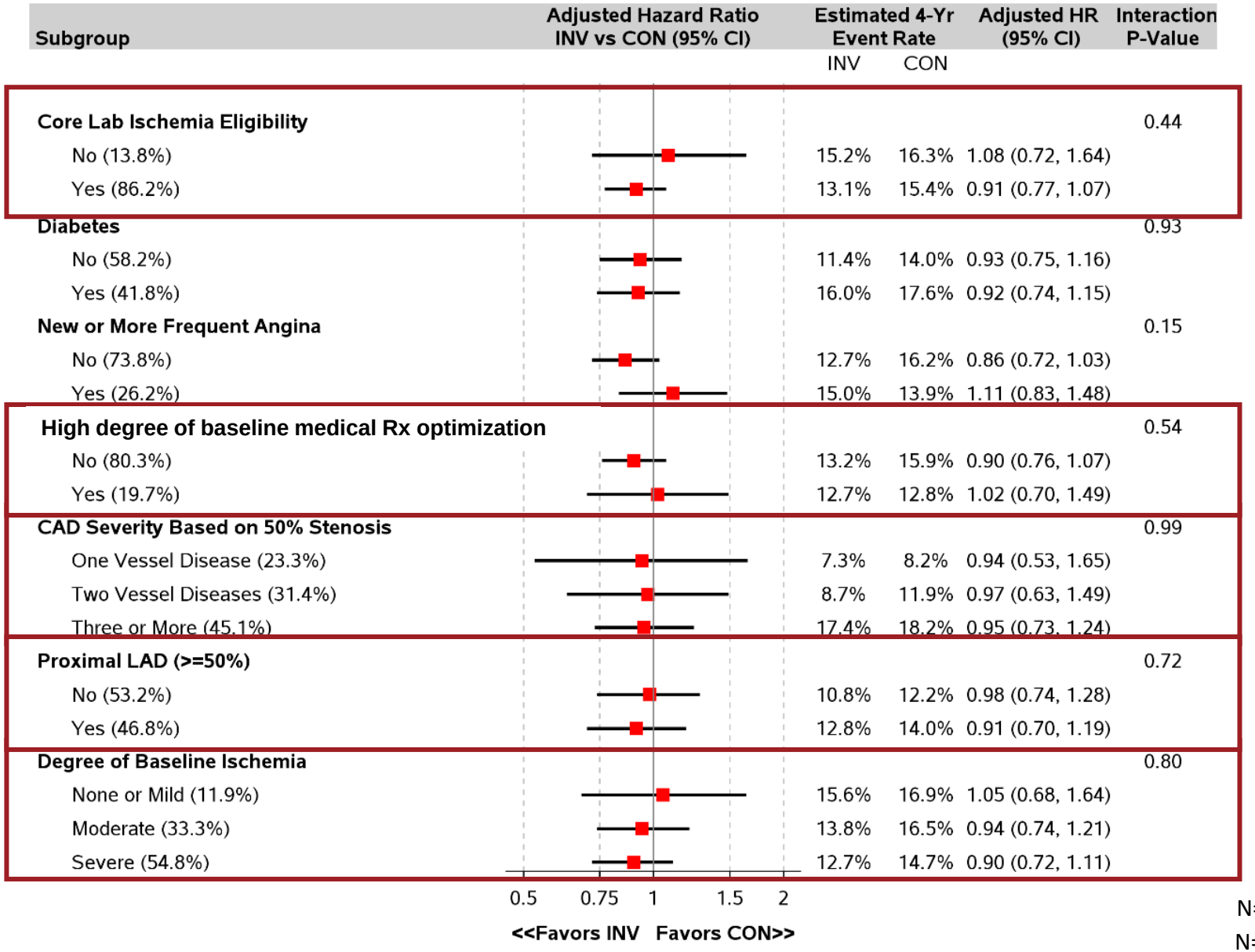
Primary endpoint
Pre-specified Important Subgroups
There was no heterogeneity of treatment effect



Subgroup	Adjusted Hazard Ratio INV vs CON (95% CI)	Estimated 4-Yr Event Rate INV	Estimated 4-Yr Event Rate CON	Adjusted HR (95% CI)	Interaction P-Value
Core Lab Ischemia Eligibility					0.44
No (13.8%)		15.2%	16.3%	1.08 (0.72, 1.64)	
Yes (86.2%)		13.1%	15.4%	0.91 (0.77, 1.07)	
Diabetes					0.93
No (58.2%)		11.4%	14.0%	0.93 (0.75, 1.16)	
Yes (41.8%)		16.0%	17.6%	0.92 (0.74, 1.15)	
New or More Frequent Angina					0.15
No (73.8%)		12.7%	16.2%	0.86 (0.72, 1.03)	
Yes (26.2%)		15.0%	13.9%	1.11 (0.83, 1.48)	
High degree of baseline medical Rx optimization					0.54
No (80.3%)		13.2%	15.9%	0.90 (0.76, 1.07)	
Yes (19.7%)		12.7%	12.8%	1.02 (0.70, 1.49)	
CAD Severity Based on 50% Stenosis					0.99
One Vessel Disease (23.3%)		7.3%	8.2%	0.94 (0.53, 1.65)	
Two Vessel Diseases (31.4%)		8.7%	11.9%	0.97 (0.63, 1.49)	
Three or More (45.1%)		17.4%	18.2%	0.95 (0.73, 1.24)	
Proximal LAD (>=50%)					0.72
No (53.2%)		10.8%	12.2%	0.98 (0.74, 1.28)	
Yes (46.8%)		12.8%	14.0%	0.91 (0.70, 1.19)	
Degree of Baseline Ischemia					0.80
None or Mild (11.9%)		15.6%	16.9%	1.05 (0.68, 1.64)	
Moderate (33.3%)		13.8%	16.5%	0.94 (0.74, 1.21)	
Severe (54.8%)		12.7%	14.7%	0.90 (0.72, 1.11)	

N=3739 for Prox LAD Y/N
N=2982 for # diseased vessels

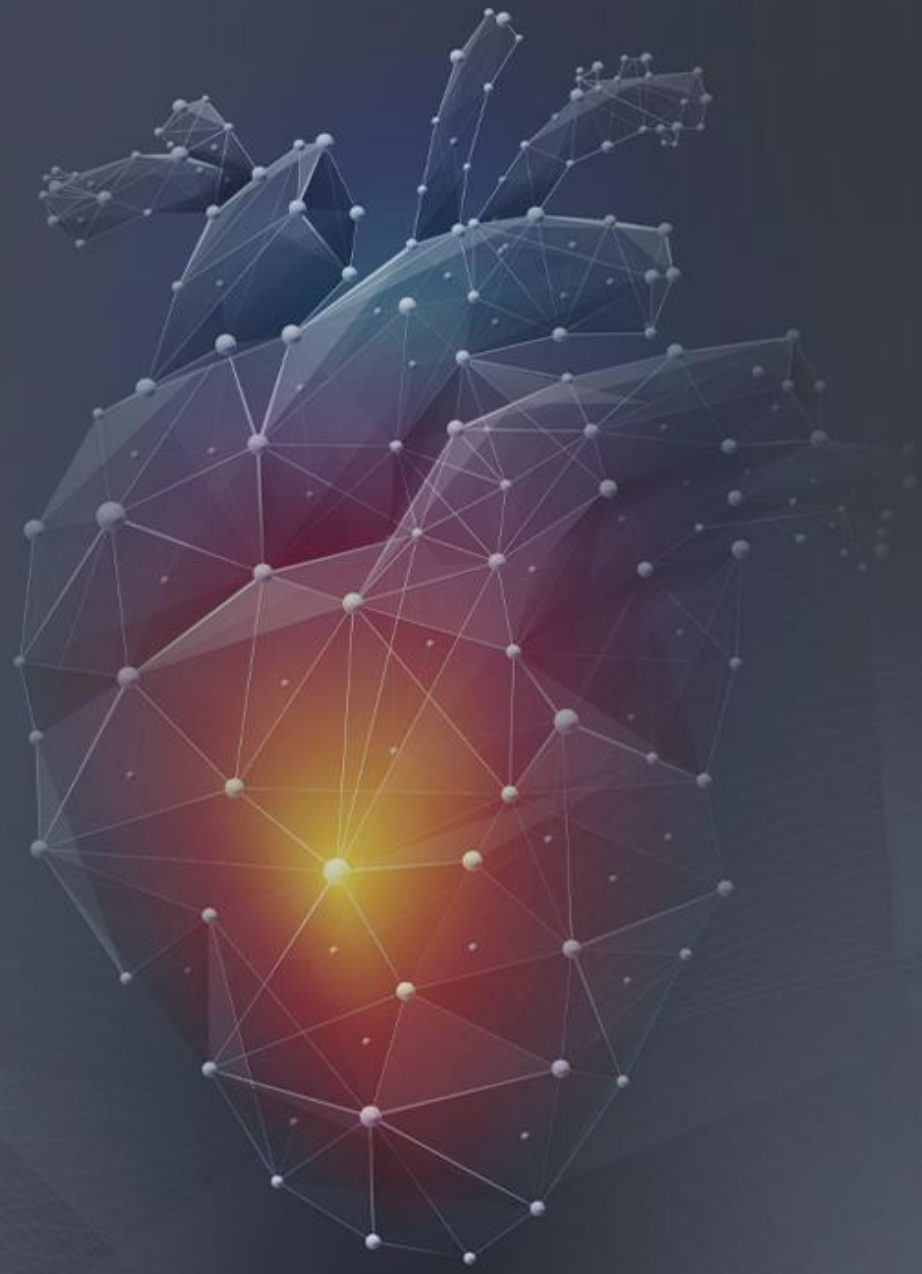
ISCHEMIA

Conclusions

- ISCHEMIA is the largest trial of an invasive vs conservative strategy for patients with SIHD

- Overall, an initial INV strategy as compared with an initial CON strategy did not demonstrate a reduced risk over median 3.3 years for
  - Primary endpoint - CV death, MI, hospitalization for UA, HF, RCA
  - Major Secondary endpoint - CV death or MI

COVID-19: Patient Reengagement



Question

Given the circumstances surrounding COVID-19, how do we start reengaging our patients?

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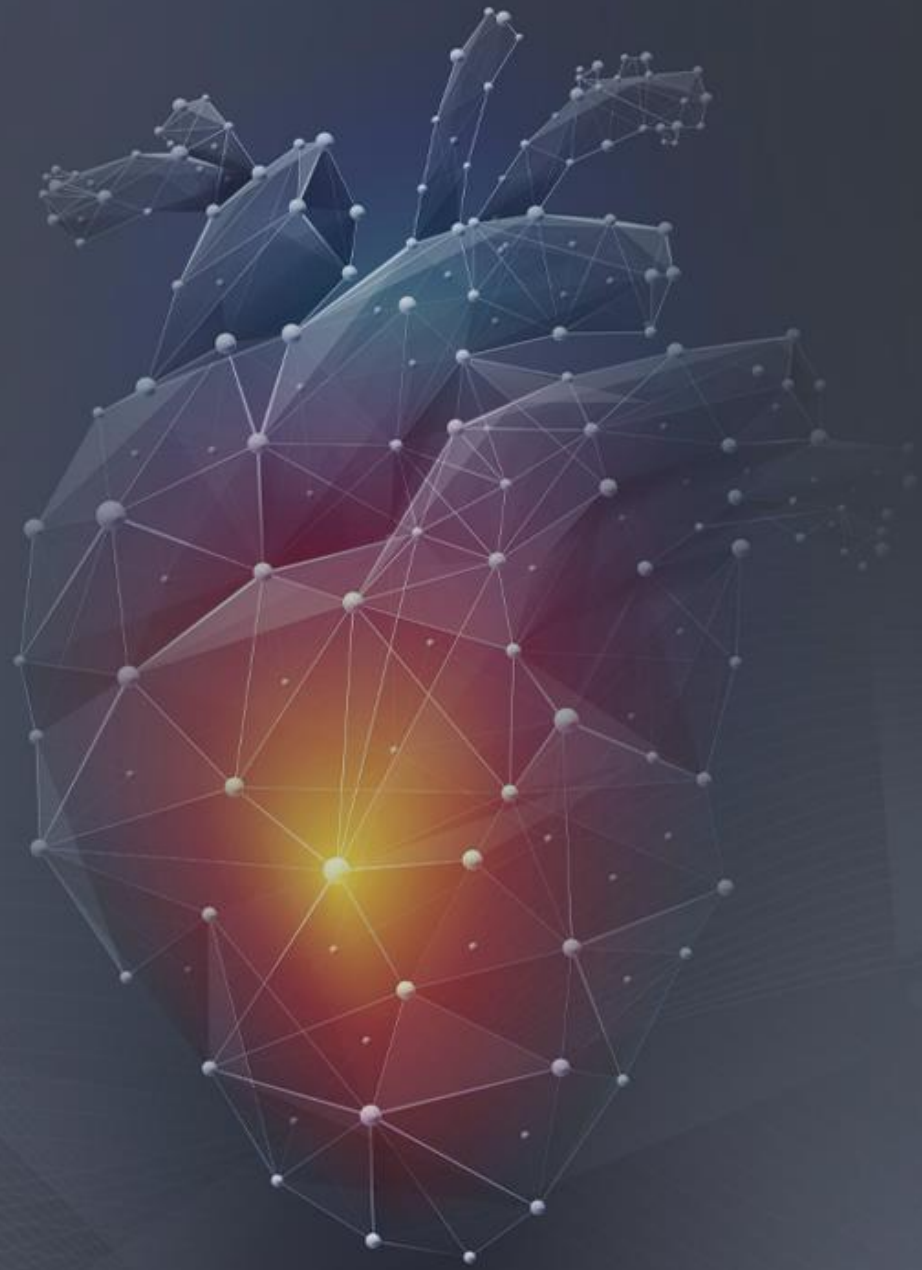
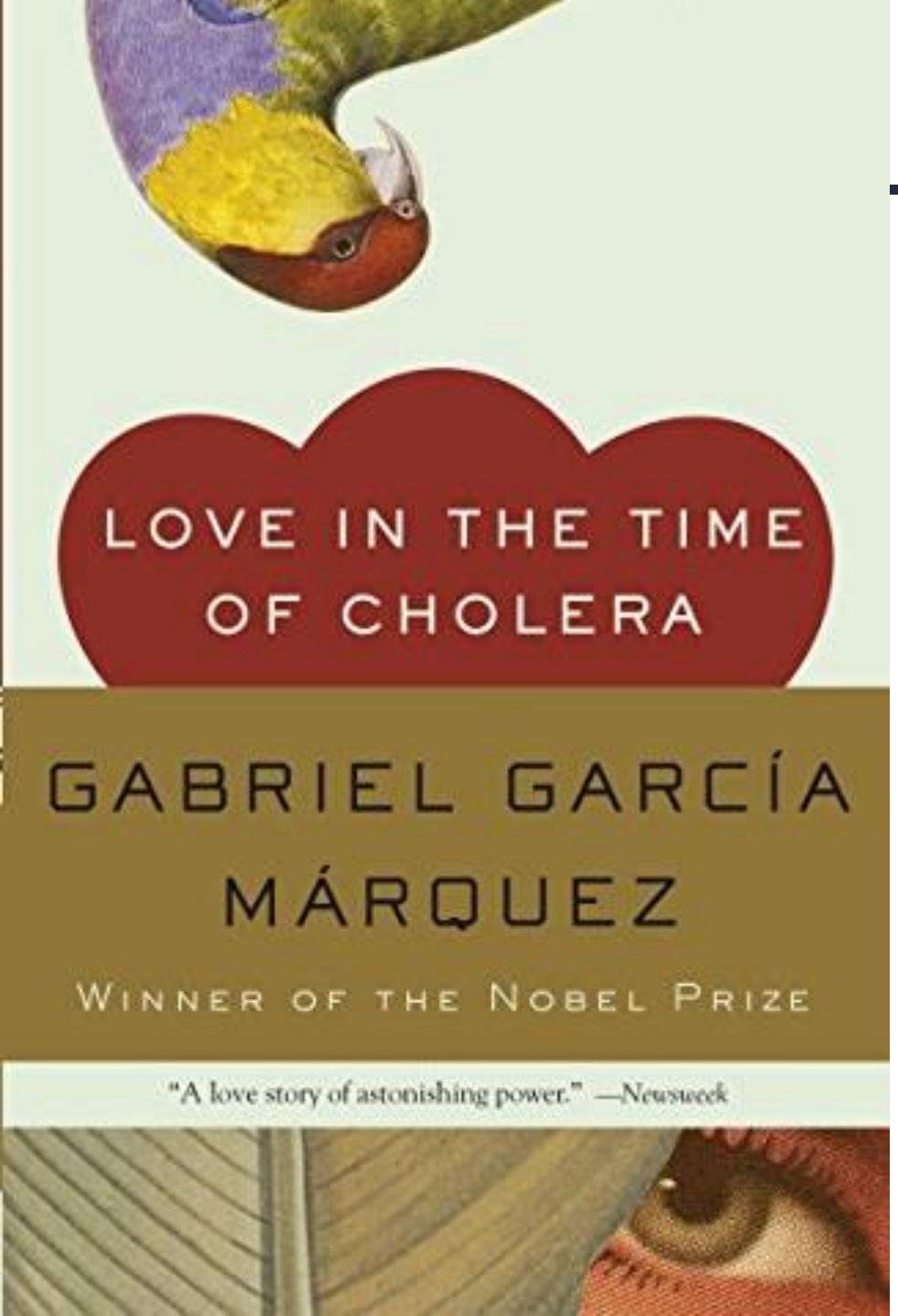
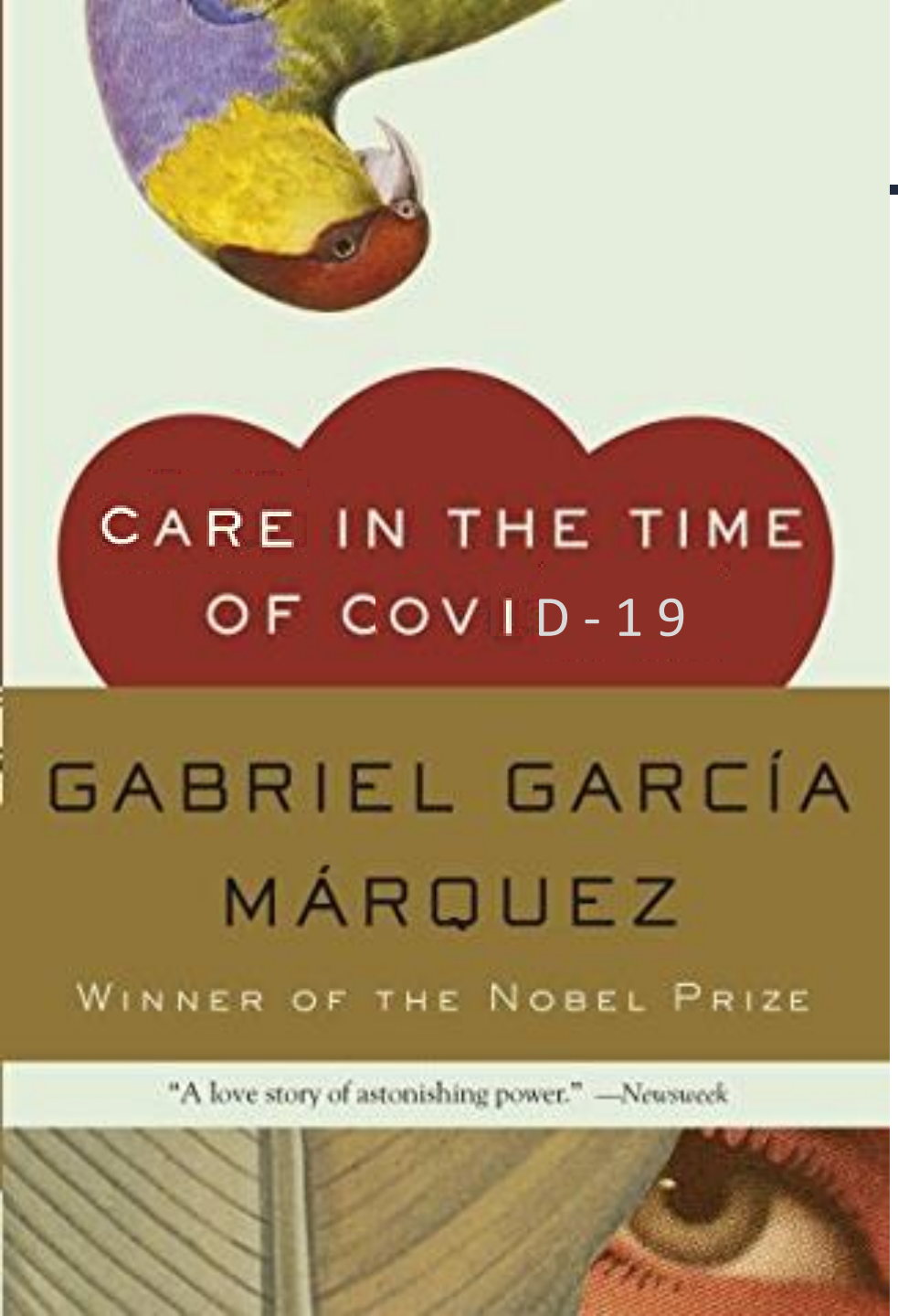




CV Risk Reduction

- How do we reengage and provide CV care?



CV Risk Reduction

- How do we reengage and provide CV care?
- Heart failure has been the most difficult
  - Decompensated HF best evaluated in person
  - BP, HR and labs guide decision making and prognosis altering therapies
- CAD – symptom based decision making on medical vs cath guided therapy is viable option
- Lipids – low risk proposition if labs available
- Arrhythmias – remote rhythm monitoring
- Hypertension – home monitoring
- DM and CV risk – counselling for SGLT2/GLP-1

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Learnings From COVID-19 and Where We Go From Here

- New therapies have been shown to lower CV risk
- There is increasing comfort using technology in patient populations
- Virtual care can be used to optimize the use of guideline-based therapies – for both initiation and monitoring

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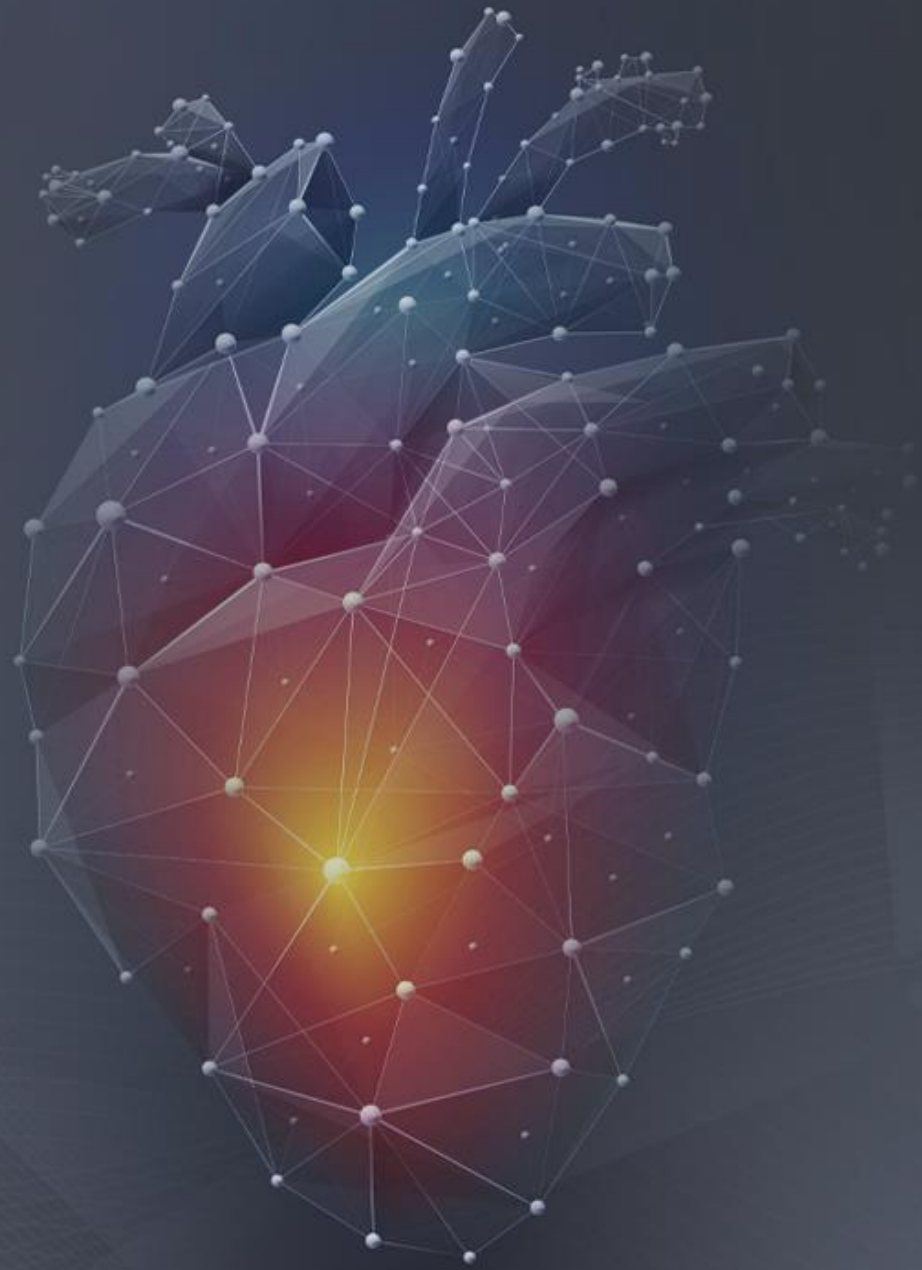


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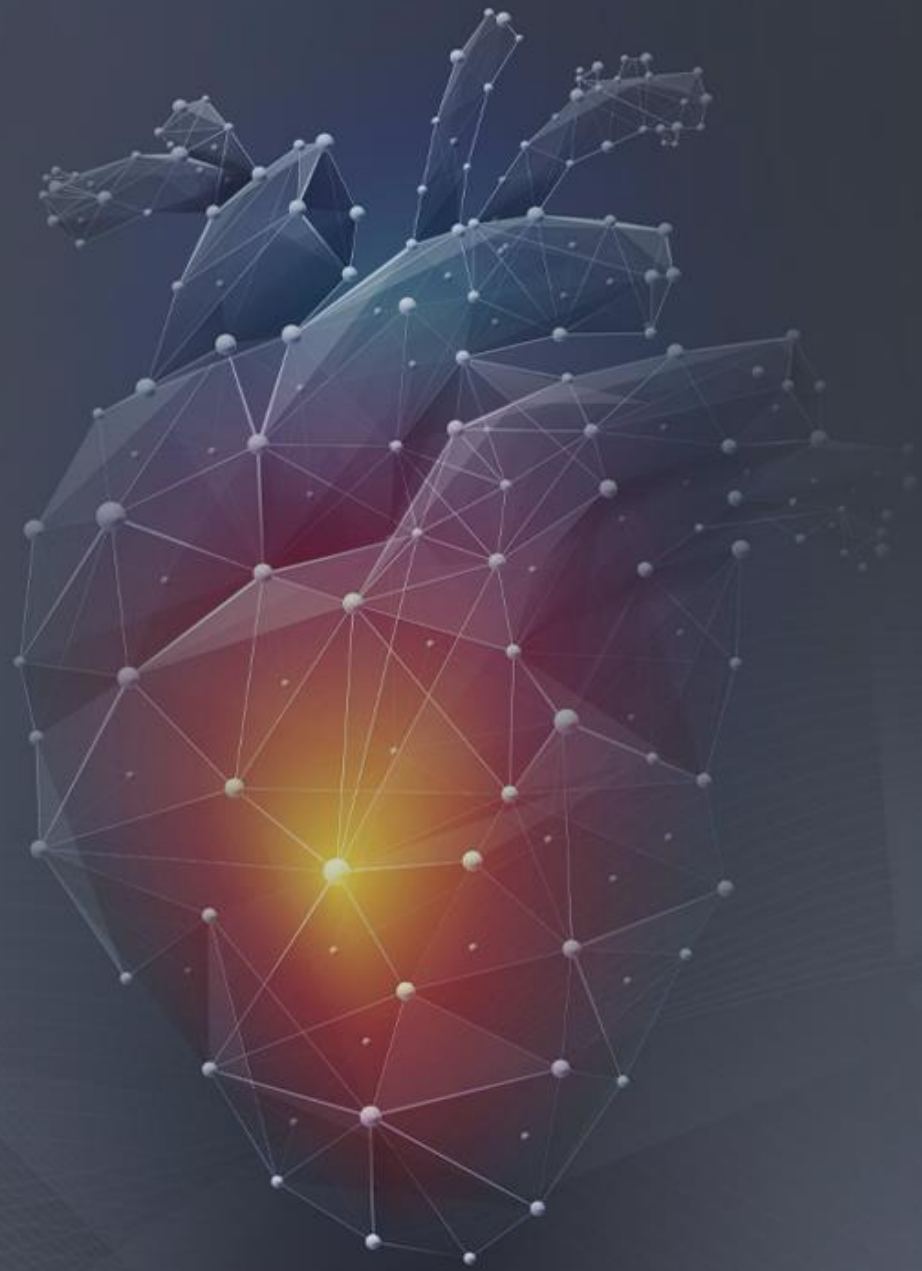
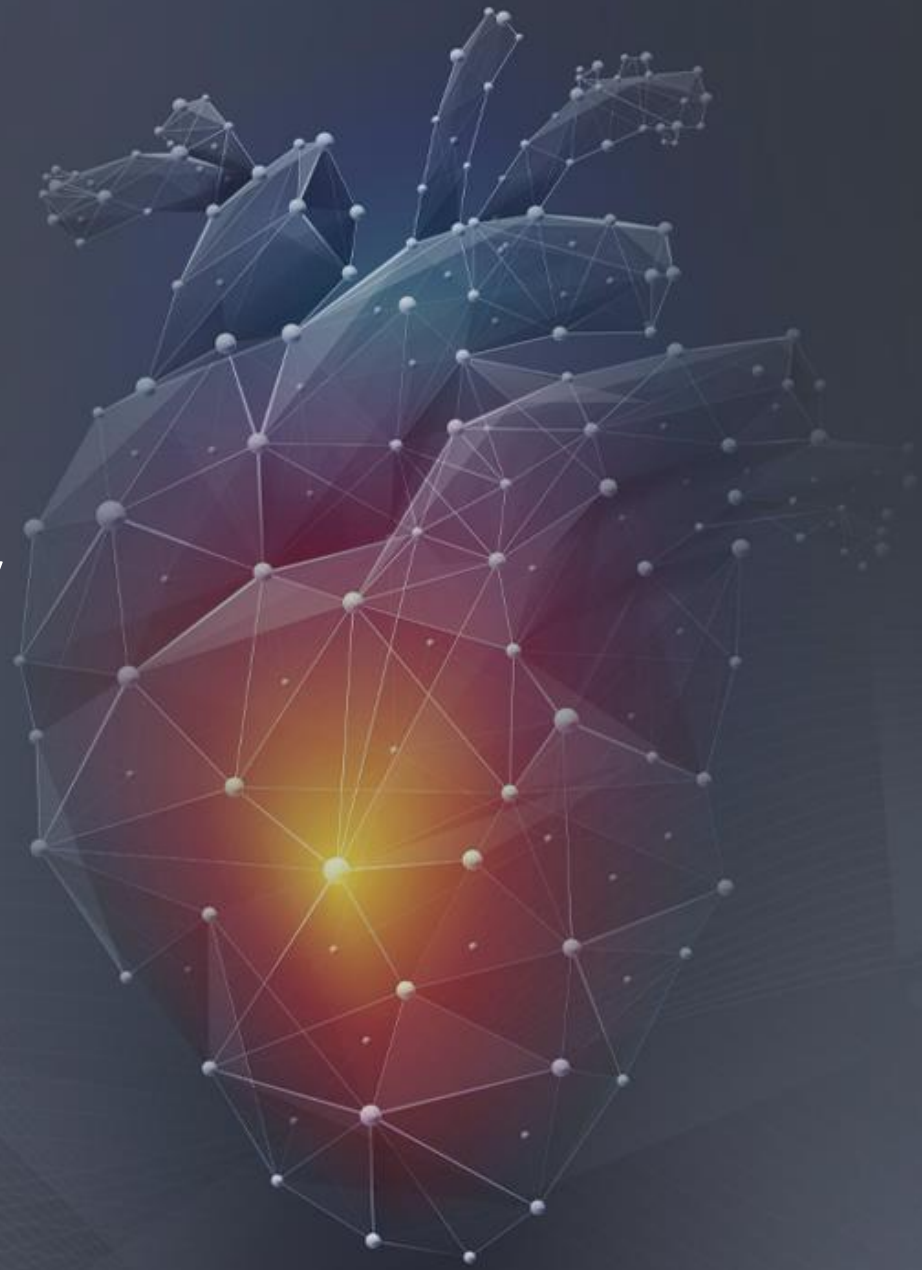
Q&A



Thank you!

Please complete the online evaluation survey to follow via e-mail.



HLS Therapeutics Inc.