

# Guidelines for Lipid Lowering: Canadian, eh?

Beth Abramson MD MSc FRCP FACC

Paul Albrechtsen Professor in

Cardiac Prevention & Women's Health

Associate Professor of Medicine, U of Toronto,

Director, Cardiac Prevention & Women's CV Health, St. Michael's Hospital

## Disclosures:

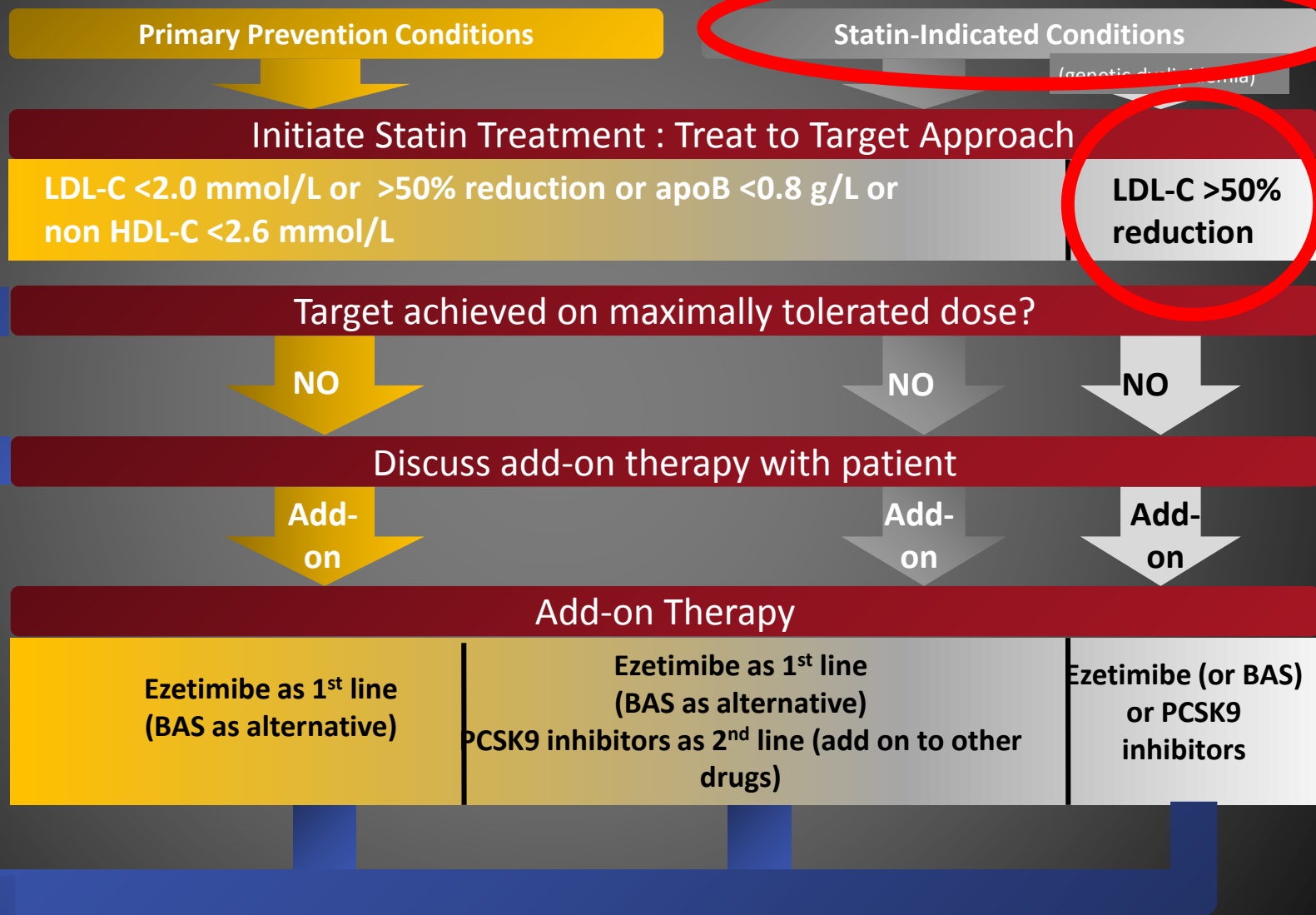
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# Learning Objectives

- To review new ESC guideline recommendations coverage re: LDL-C targets and approach post-ACS
- To review the concept of matching statin intensity with target LDL
- Discuss “fasting Vs non Fasting” lipid profile
- PCSK9i update, including high risk subgroups

# 2016 Canadian Cardiovascular Society Dyslipidemia Guidelines



# 2016 Canadian Cardiovascular Society Dyslipidemia Guidelines

Risk Assessment\*, Stratification and Treatment Consideration

No Pharmacotherapy	Primary Prevention Conditions		Statin-Indicated Conditions	
Low Risk	Intermediate Risk	High Risk		
FRS <10%	<b>FRS 10-19%</b> And LDL-C ≥3.5 mmol/L Or Non-HDL-C ≥4.3 mmol/L Or ApoB ≥1.2 g/L Or Men ≥50 and women ≥60 with one additional risk factor; low HDL-C, impaired fasting glucose, high waist circumference, smoker, hypertension	<b>FRS ≥20</b> Or <b>Alternative method</b>	<ul style="list-style-type: none"> <li>• <b>Clinical atherosclerosis</b></li> <li>• <b>Abdominal aortic aneurysm</b></li> <li>• <b>Most diabetes including:</b> <ul style="list-style-type: none"> <li>• Age ≥40y</li> <li>• Age ≥30y &amp; 15y duration (T1DM)</li> </ul> </li> <li>• <b>Microvascular disease</b></li> <li>• <b>Chronic kidney disease</b></li> </ul>	<b>LDL-C &gt;5mmol/L</b> (genetic dyslipidemia)

Discuss Behavioural Modifications

\*Using Framingham Risk Score (FRS) or Cardiovascular Life Expectancy Model (CLEM) unless statin-indicated condition

# Recommendations for PCSK9i in FH and ASCVD

We suggest the use of PCSK9 inhibitors (evolocumab, alirocumab) to lower LDL-C for patients with heterozygous familial hypercholesterolemia whose LDL-C remains above target despite maximally tolerated statin therapy

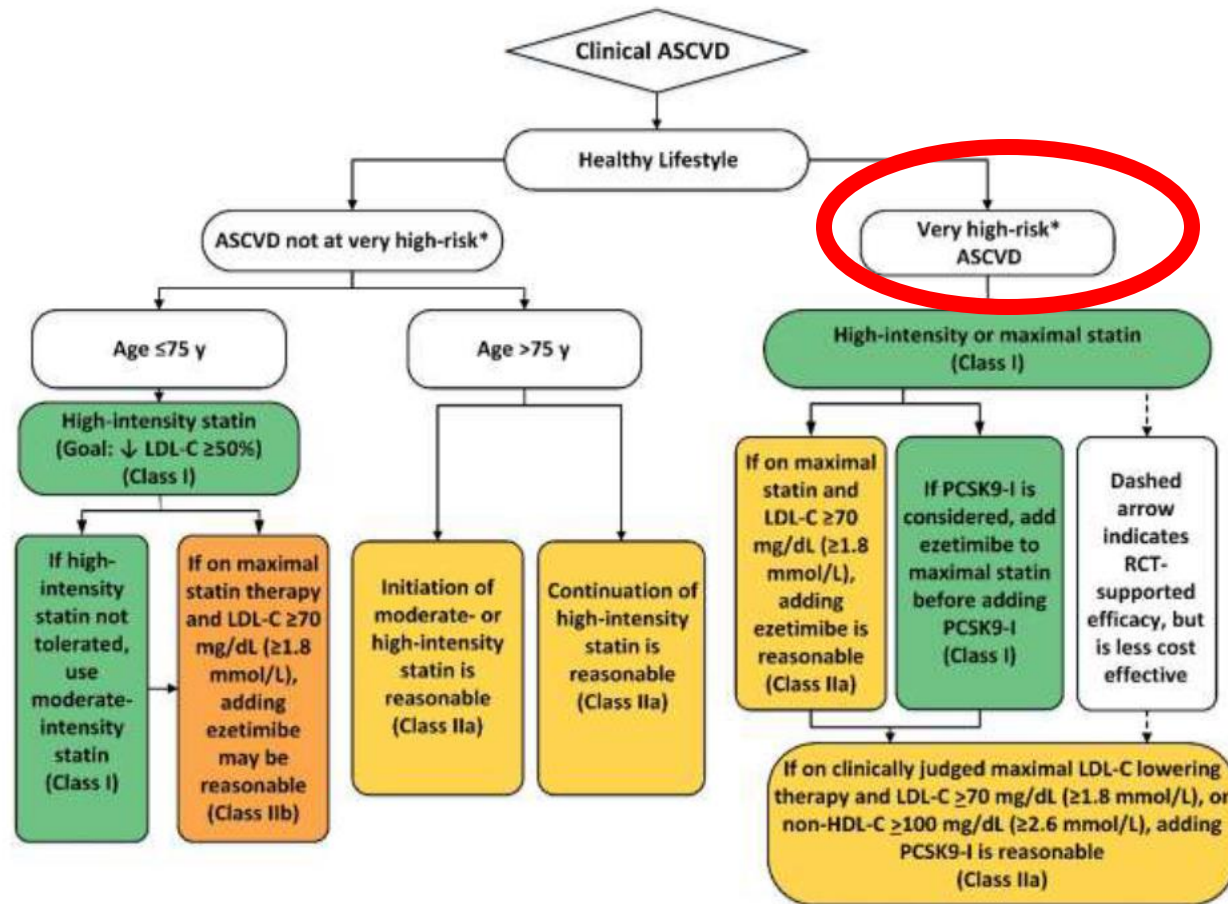
*(Conditional recommendation, moderate quality evidence)*

We suggest that PCSK9 inhibitors be considered to lower LDL-C for patients with atherosclerotic cardiovascular disease in those not at LDL-C goal despite maximally tolerated statin +/- ezetimibe therapy

*(Conditional recommendation, moderate quality evidence)*

# American Lipid Guidelines Nov. 2018 secondary prevention– treat the elderly!

Figure 1. Secondary Prevention in Patients With Clinical ASCVD



ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol, *JACC* (2018), doi: <https://doi.org/10.1016/j.jacc.2018.11.003>

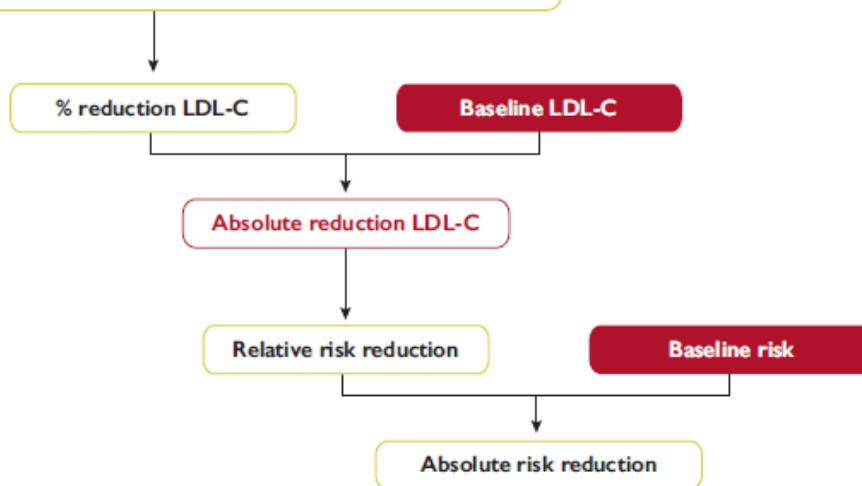


# 2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

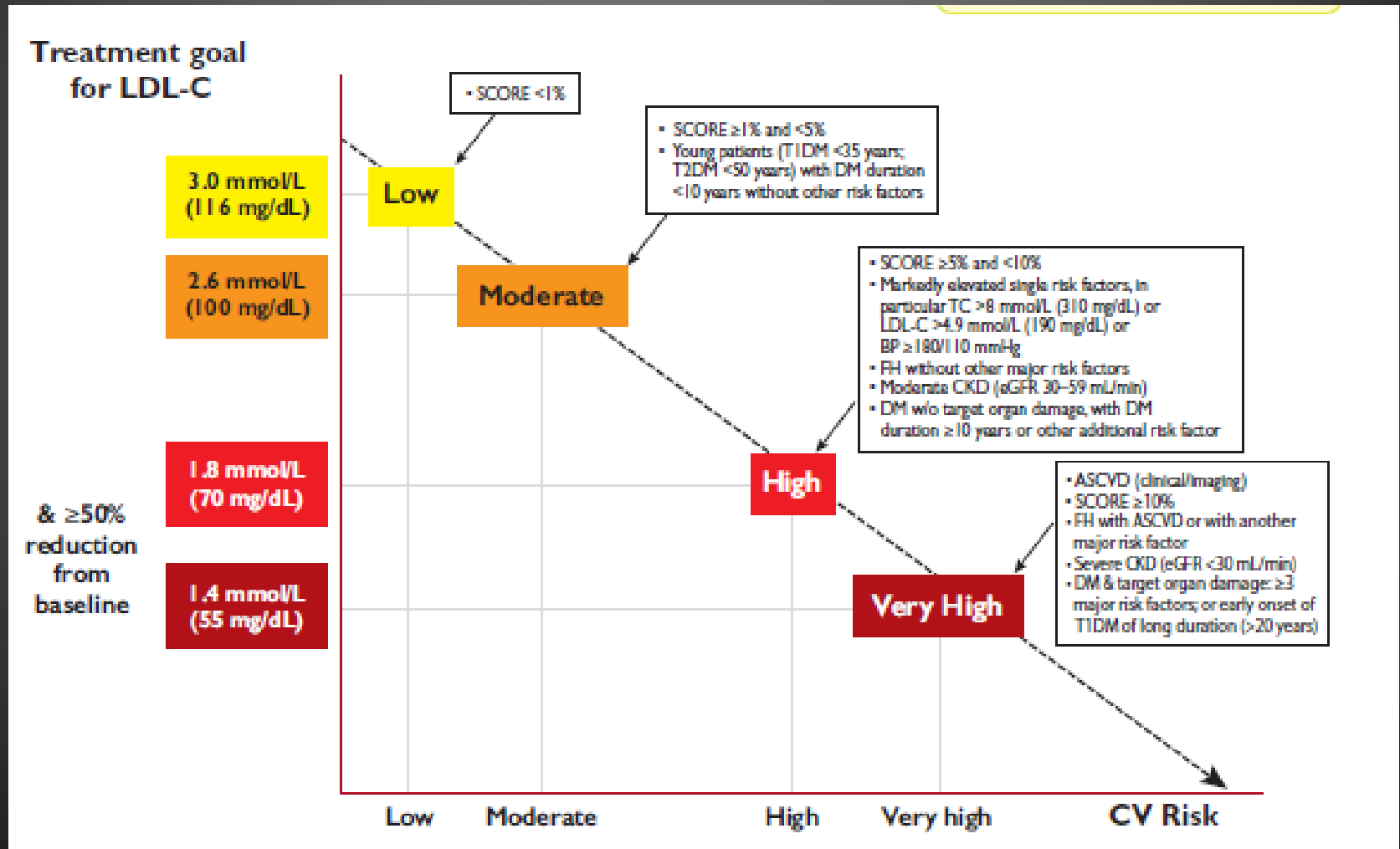
The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society

## Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	= 30%
High intensity statin	= 50%
High intensity statin plus ezetimibe	= 65%
PCSK9 inhibitor	= 60%
PCSK9 inhibitor plus high intensity statin	= 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	= 85%



# European Goal 1.4 in those with ASCVD!



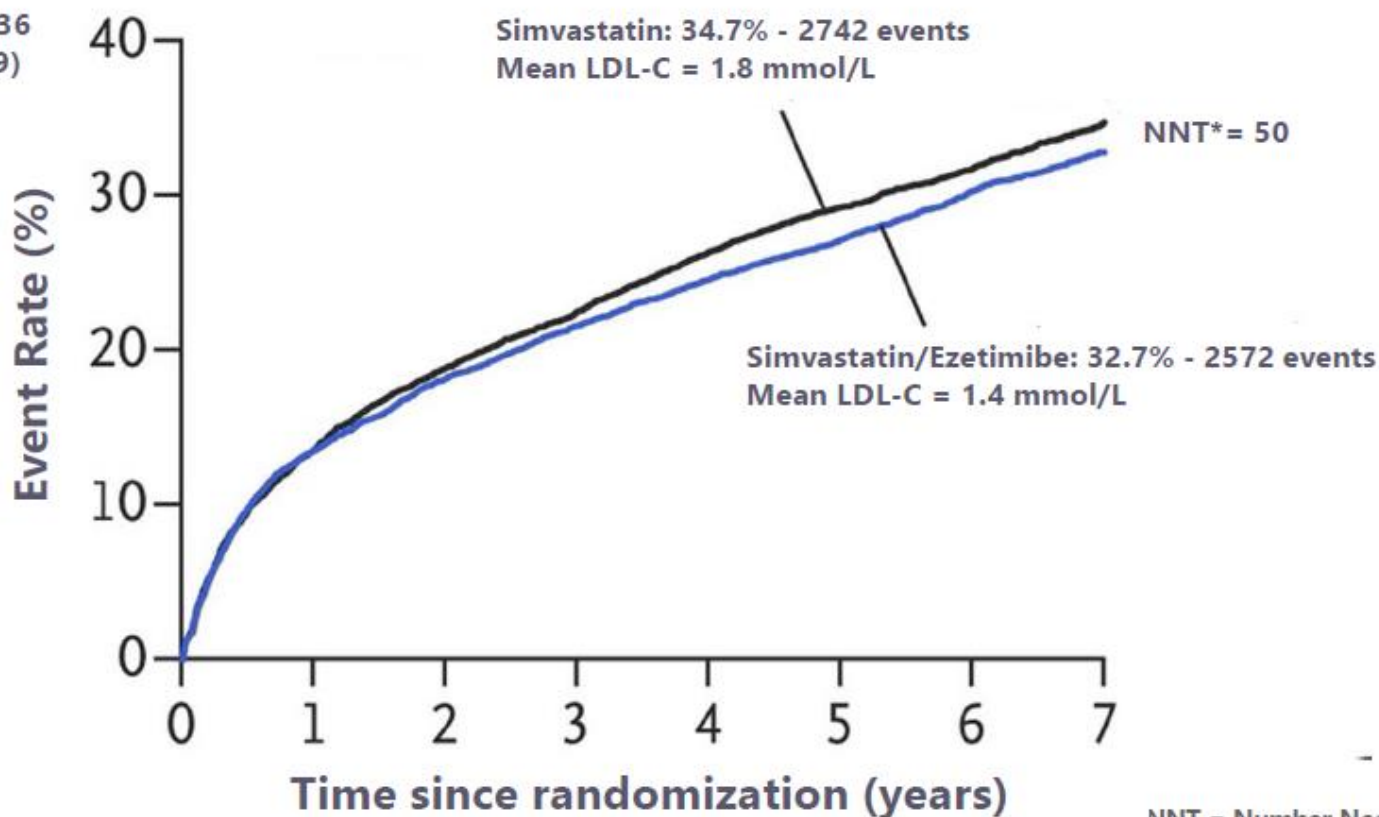




# IMPROVE-IT

**Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization ( $\geq 30$  days), or stroke**

Hazard Ratio, 0.936  
(95% CI, 0.89-0.99)  
 $p=0.016$



NNT = Number Needed to Treat



# You need to match the strength of your medication with goals of care



too big



too small

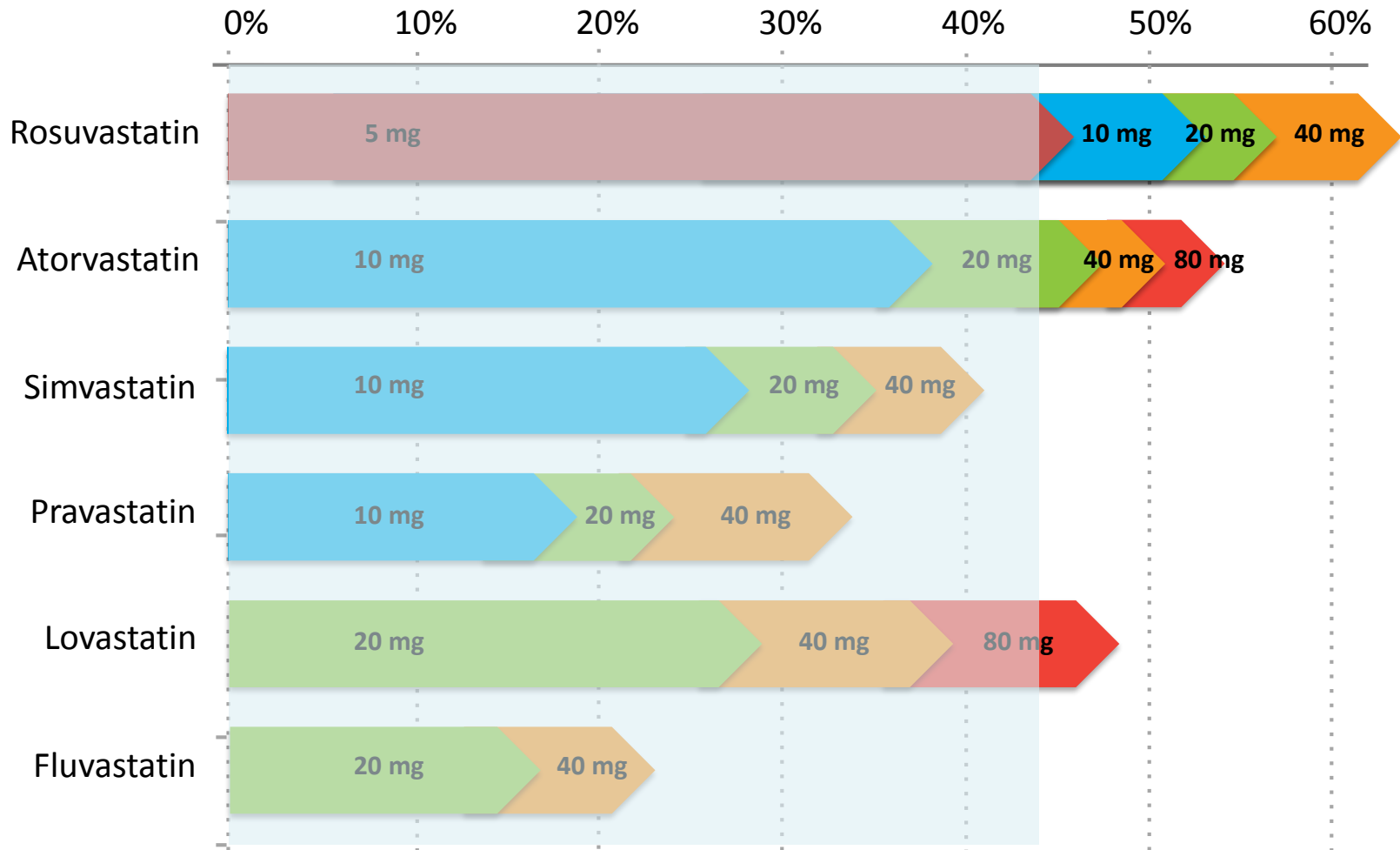
# Prospective meta-analysis: 90,056 participants in 14 randomized statin trials



- **For each 1 mmol/L LDL-C lowering**
  - 12% reduction in all cause mortality ( $p < 0.0001$ )
  - 19% reduction in coronary mortality ( $p < 0.0001$ )
  - 23% reduction in MI and coronary death ( $p < 0.0001$ )
  - 24% reduction in revascularizations ( $p < 0.0001$ )
  - 17% reduction in fatal or non-fatal stroke ( $p < 0.0001$ )
  - 21% reduction in any major vascular event ( $p < 0.0001$ )
  - no increase in non-vascular mortality or cancers



# Don't start below LDL reduction of 50%



■ \*As per Canadian Product Monographs

1. Crestor (rosuvastatin) Product Monograph. AstraZeneca. May 1, 2013
2. Lipitor (atorvastatin) Product Monograph. Pfizer. Sep. 4, 2012.
3. Pravachol (pravastatin) Product Monograph Bristol-Myers Squibb Canada. Jan. 11, 2013.
4. Mevacor (lovastatin) Product Monograph. Merck. Jul. 24, 2012.

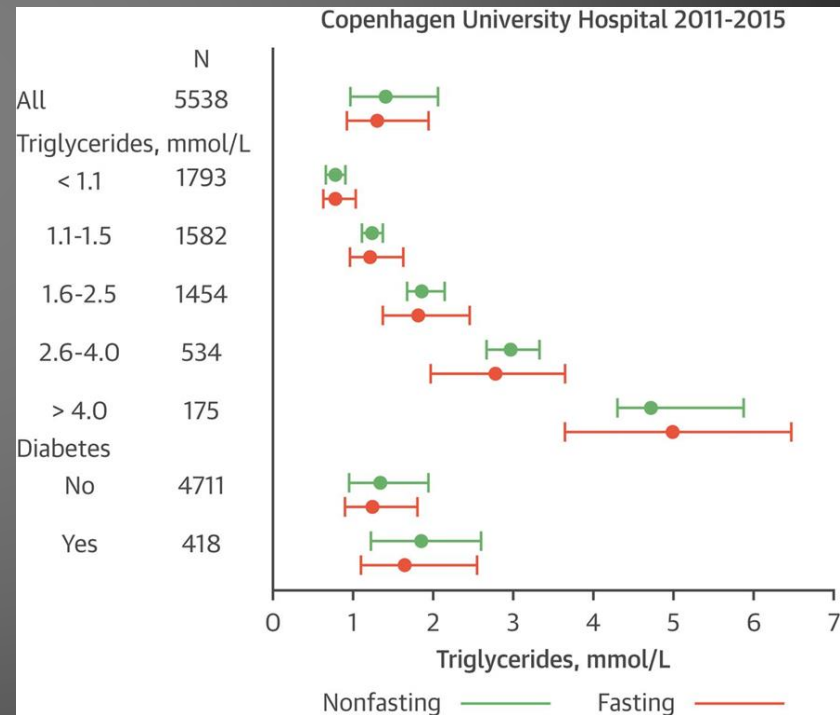
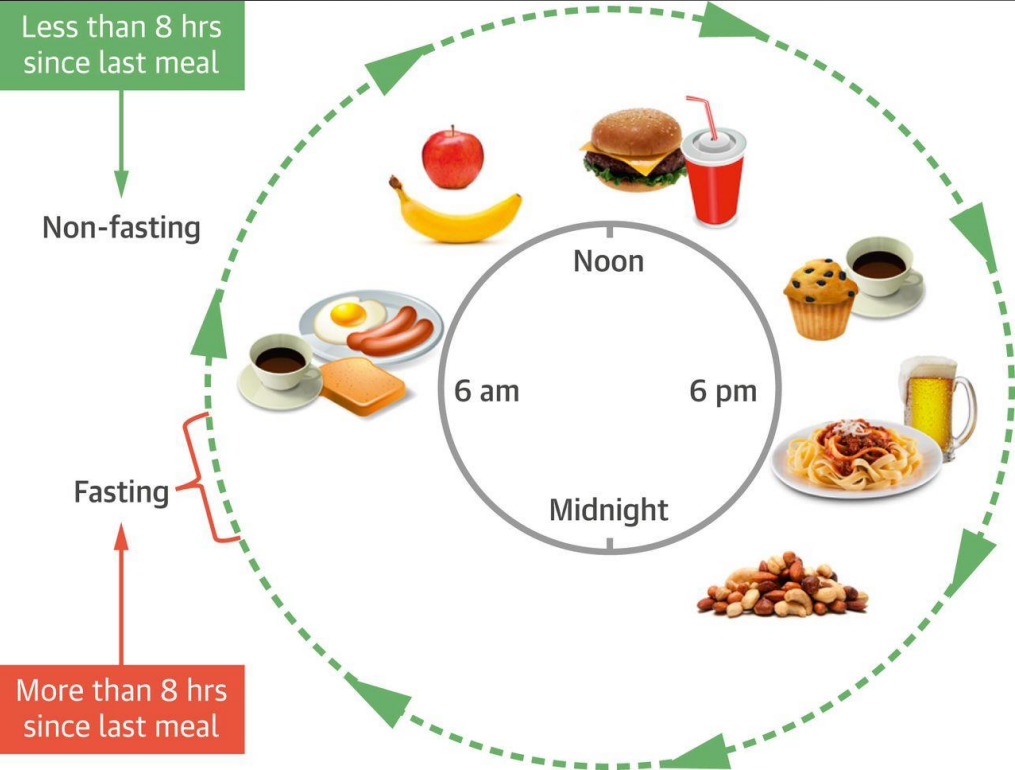
5. Zocor (simvastatin) Product Monograph. Merck. Jun. 6, 2012.
6. Lescol (fluvastatin) Product Monograph. Novartis. Sep. 27, 2012.
7. Adapted from Jones P, et al. for the CURVES Investigators. Am J Cardiol. 1998;81:582-587.

# Fasting Vs Non Fasting...





# Fasting Vs Non Fasting in Context



# For Most Patients Non Fasting is Appropriate ...

- Except “type A” patients...
- +/- 10% with non fasting





# PCSK9 Inhibitor OUTCOME Studies

5 years now...  
Both in NEJM

## Evolocumab

### FOURIER

Outcome Study (5 yrs), N=27 500

- **Inclusion criteria:** High-risk 2<sup>o</sup> prevention population with LDL-C  $\geq$  1.8 mmol/L or non-HDL  $\geq$  2.6 mmol/L
- Evolocumab 140mg Q2W or 420mg QM + optimal LLT
- **1<sup>o</sup> endpoint:** Time to CV death, MI, hospitalization for unstable angina, stroke, or coronary revascularization

## Alirocumab

### ODYSSEY Outcomes

Outcome Study (64 months), N=18 000

- **Inclusion criteria:** Hospitalized for ACS within past 1-12 months
- LDL  $\geq$  1.8mmol/L or Non-HDL-C  $\geq$  2.5 mmol/L
- Alirocumab 75mg Q2W, up-titrate to 150mg Q2W as needed
- **1<sup>o</sup> endpoint:** Time to CHD death, any non-fatal MI, fatal and non-fatal ischemic stroke, unstable angina requiring hospitalization

ACS: acute coronary syndrome; CHD: coronary heart disease; CV: cardiovascular; LLT: lipid lowering therapy; MI: myocardial infarction

ORIGINAL ARTICLE

## Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome

G.G. Schwartz, P.G. Steg, M. Szarek, D.L. Bhatt, V.A. Bittner, R. Diaz, J.M. Edelberg, S.G. Goodman, C. Hanotin, R.A. Harrington, J.W. Jukema, G. Lecorps, K.W. Mahaffey, A. Moryusef, R. Pordy, K. Quintero, M.T. Roe, W.J. Sasiela, J.-F. Tamby, P. Tricoci, H.D. White, and A.M. Zeiher, for the ODYSSEY OUTCOMES Committees and Investigators\*

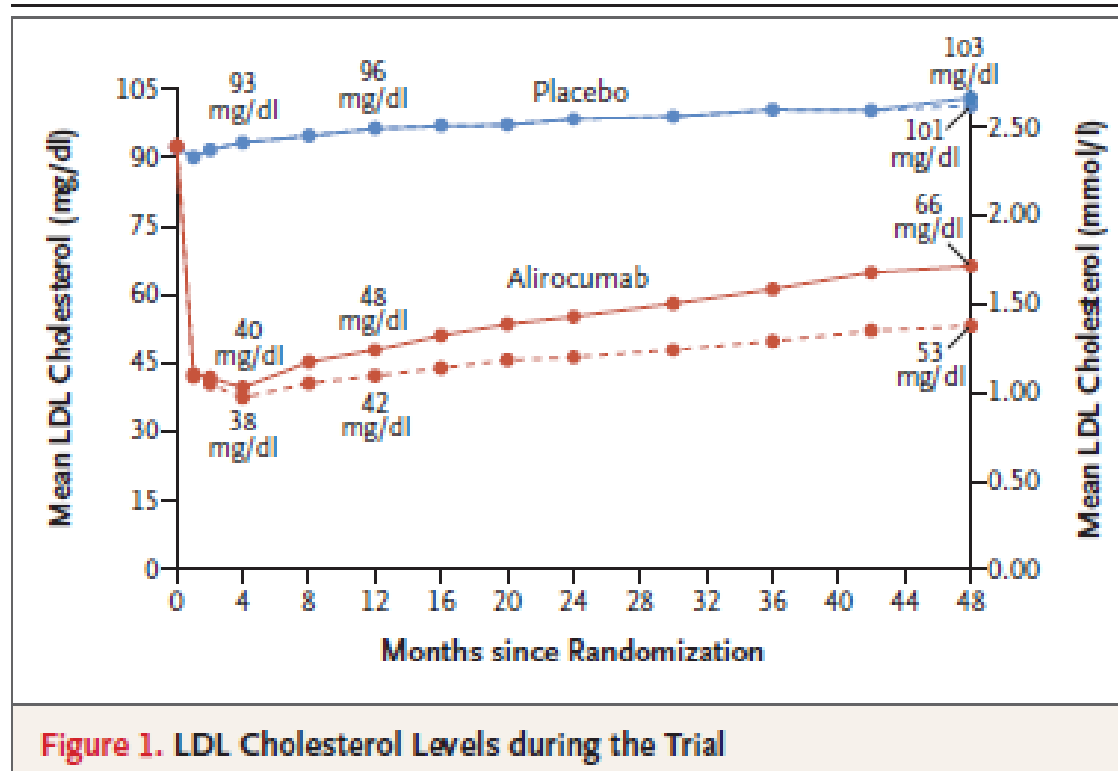


Figure 1. LDL Cholesterol Levels during the Trial

2.6 mmol/L

1.7 mmol/L

1.3 mmol/L

# Fourier Analysis Recent Vs Remote MI

## Baseline Characteristics

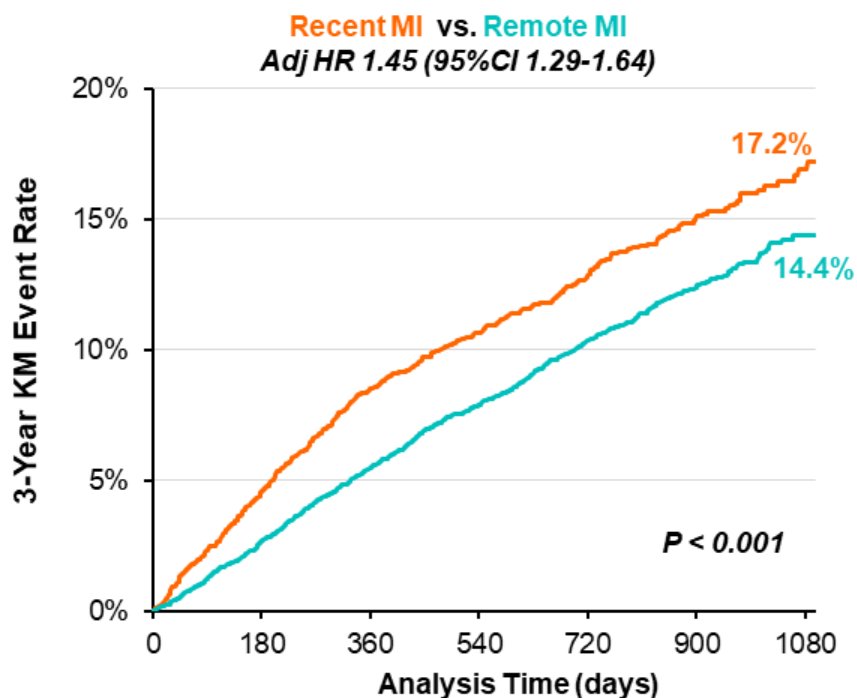
Characteristics	Recent MI N=5711	Remote MI N=16,609	P-Value
Median time from MI (months)	4.8	59	NA
Mean age (years)	60	63	< 0.001
Male, %	78	79	0.14
Hypertension, %	73	81	< 0.001
Diabetes mellitus, %	30	37	< 0.001
History of stroke, %	5	8	< 0.001
History of PAD, %	5	9	< 0.001
Prior CABG, %	15	24	< 0.001
Mean LDL-C [mg/dL(mmol/L)]	95 (2.5)	99 (2.6)	< 0.001
High intensity statin, %	77	69	< 0.001

Gencer B, et al. Poster presented at American Heart Association Scientific Sessions 2019; November 16–18, 2019, Philadelphia, PA.

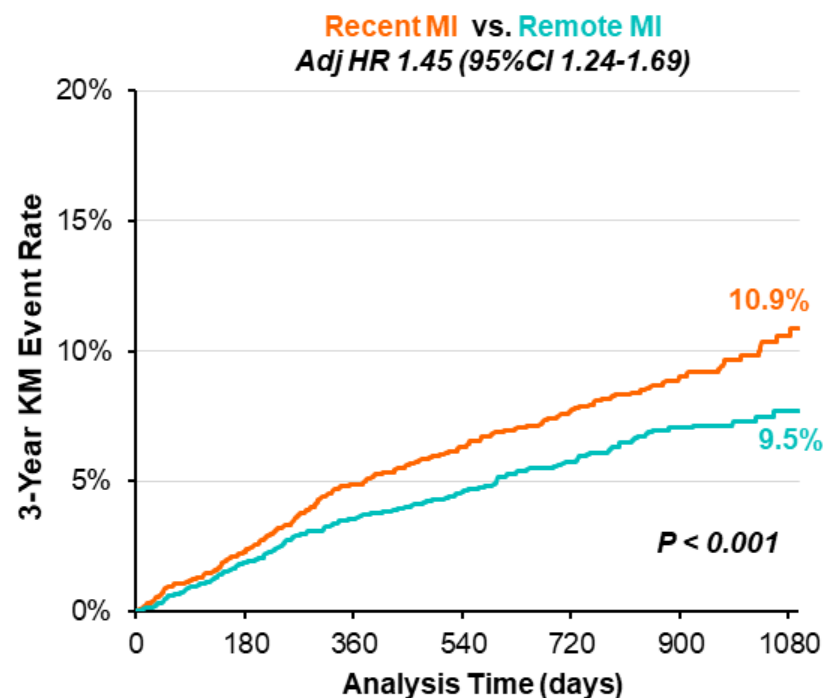
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# 3-Year Event Rate in Recent vs. Remote MI

## Incidence of the PEP



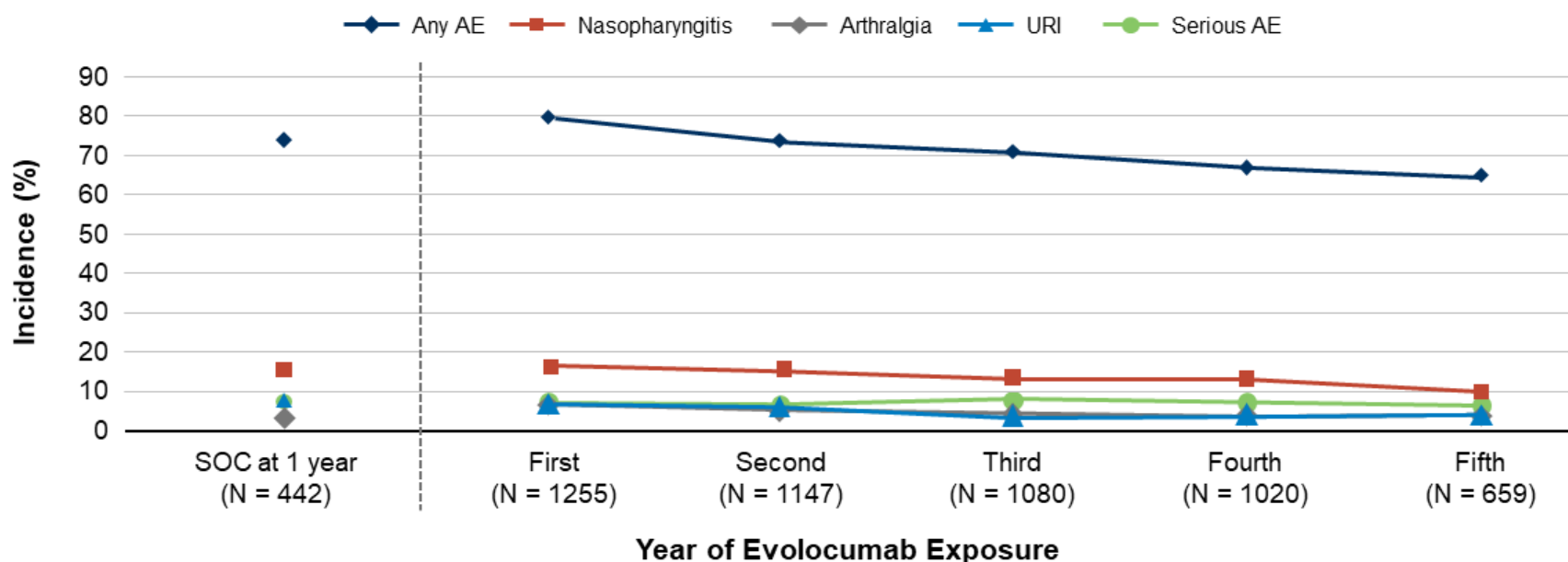
## Incidence of the Key SEP





# Rates of Adverse Events Over 5 Years in OSLER-1 Did Not Change Over Time

## Adverse Events Over Time



Over 5 years of evolocumab exposure, AEs occurred in 65% of patients; similar to previous years (67%-80%) and to Year 1 SOC control group (74%).

AE = adverse event; SOC = standard of care; URI = upper respiratory infection.

Koren MJ, et al. *J Am Coll Cardiol*. 2019;74(17):2132-2146.

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# Practical Implications of Getting High Risk Patients to Goal :

- lipid profile but regardless of levels start high-intensity statin
- re-check lipids in 4 weeks:
- if not at goal start ezetimibe (or prior if pt. willing)
- If at goal but long term time horizon discuss adding ezetimibe regardless
- re-check lipids in 4 weeks, if not at goal start PCSK9i

# Putting it into perspective...

## Core Components of Cardiac Rehab/Secondary Prevention Programs, a Quality Indicator of Care:

- Nutritional Counseling
- **Lipid Management**
- Hypertension Management
- Smoking Cessation
- Weight Management
- Diabetes Management
- Psychosocial Management
- Physical Activity Counselling
- Exercise Training

# SMH Cardiac Rehab Reopened.... Patient Focussed, Evidence Based



TORONTO  
HEART CENTRE

- Educational sheets /advice available for download
- Coping with Covid
- Weight loss
- Activity
- Smoking cessation
- Lipid management
- Diabetes Management
- Stress Management

[beth.abramson@unityhealth.to](mailto:beth.abramson@unityhealth.to)