

SAVE BC

Public Forum - Welcome

May 22, 2018



SAVE BC

Study to Avoid cardioVascular
Events in British Columbia



Agenda

1. Dr. Pimstone - SAVE BC Introduction & SPOR update
2. Dr. Mancini – Risk Factors, Screening & Management of ASCVD
3. Dr. Brunham – Genetics and ASCVD Risk
4. Dr. Sedlak - Women and ASCVD Risk
5. Panel Discussion/Q&A with all presenters: write your questions
6. BREAK
7. Small-group break-out discussions: 2 rounds
8. Report back in whole group
9. Summary wrap up and raffle

SAVE BC

Early Onset Heart Disease: What's In Your Genes?

Introduction

Dr. Simon Pimstone, MD, PhD, FRCPC
Principal Investigator



SAVE BC

Study to Avoid cardioVascular
Events in British Columbia



Acknowledgements

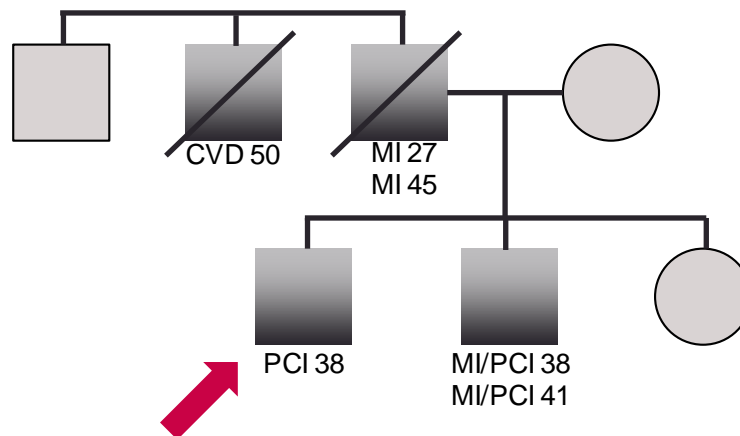
- The patients and families!
- Our funders for the forum: Amgen, Merck, Sanofi
- SPH and VGH/UBCH Foundations
- UBC Medical Students: Jian Weng, Raymond Cho, Rory Sutherland & Michal Jurkowski
- Staff at SPH Healthy Heart Program and UBC Cardiology Clinic
- HLI, PHCRI and VCHRI
- Division of General Internal Medicine (Anita Palepu)
- Alison Hoens & BC SUPPORT Unit
- SAVE BC Steering Committee
- Camp Pacific
- Volunteers: Andrew Pauls, Kelly Nguyen, Melody Feng, Jaclyn Marcil & Aisa Ahkavan

Partners and Funders



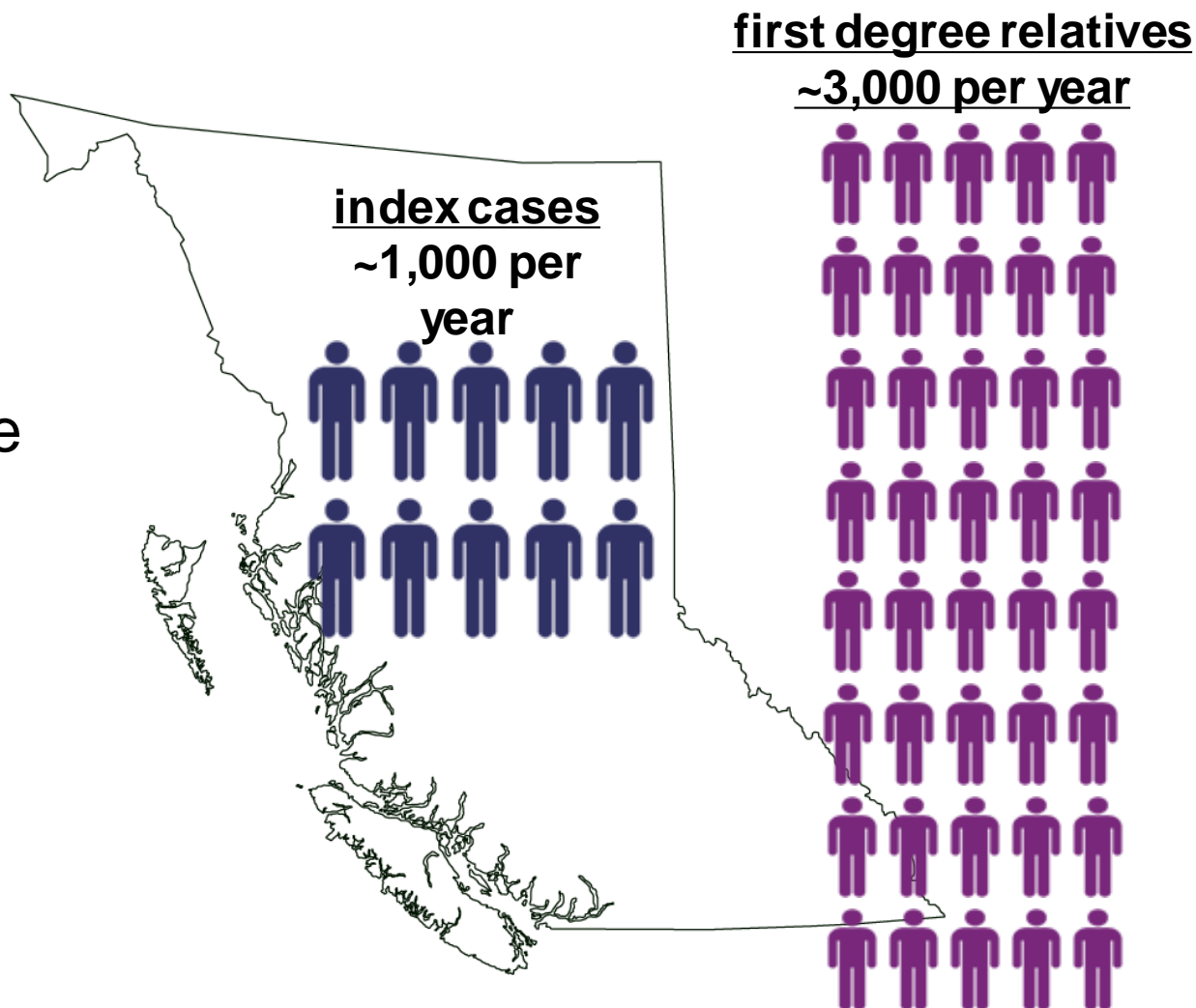
Case

- ♥ 38 yo M, mild dyslipidemia. Presents with atypical chest pain
- ♥ Coronary angiogram → obstructive RCA disease → PCI
- ♥ Older brother had acute MI with PCI at 38 yrs, recurrent MI at 41 yrs
- ♥ Father - first MI at 27 yrs, recurrent fatal MI 45 yrs
- ♥ Paternal uncle had premature CVD
- ♥ Apart from lipid levels, index case had no other prior CV risk assessment



Burden of Premature ASCVD in BC

- In BC each year, ~500 – 1,000 men ≤ 50 and women age ≤ 55 are diagnosed with ACS or stable CAD
- Each index case has 2 – 4 FDRs



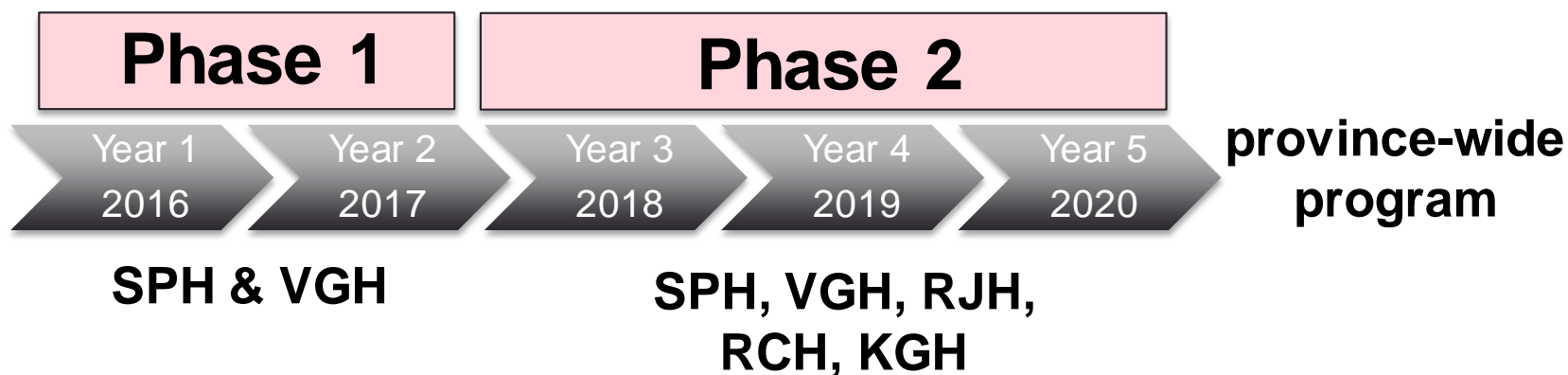
Screening of Families is Recommended

	CCS 2009/2012 Dyslipidemia /2016	ACC/AHA 2013	ESC CVD PREVENTION 1998/2007/2012/2016
Risk assessment tool	Modified FRS for patients at any age including a family history of premature CAD.	10 year and lifetime pooled ASCVD risk equations. Family history of premature CVD can be used to upscale risk.	SCORE risk
Recommendation	Premature CVD in first-degree relatives should prompt the screening of family members for significant lipoprotein disorders.	No specific recommendation for first degree relative screening.	Screening of first degree relatives in patients with premature CVD recommended.

SAVE BC Objectives:

- (i) Identify all men ≤ 50 yrs & women ≤ 55 yrs in BC, with atherosclerotic cardiovascular disease (ASCVD)**
- (ii) Screen all First Degree Relatives (FDRs) and Spouses**
- (ii) Treat all cases and FDRs/Spouses to goal**
- (iv) Look for genetic causes of early ASCVD**
- (v) Improve delivery of cost effective care for patients at risk of ASCVD**

Phased approach with a goal to be province-wide by 2020



Screening Algorithm and Data Collection

	Clinical	Laboratory	Imaging
Index			angiogram
FDR	Medical history Physical exam Family History Psychosocial stress Medication use	CBC Lipids, Lp(a) CRP, BNP Glucose, HbA1c liver enzymes renal function, ACR Testosterone, TSH blood and saliva samples for research	CACS if age > 45 CTCA if age < 45
Spouse			carotid U/S



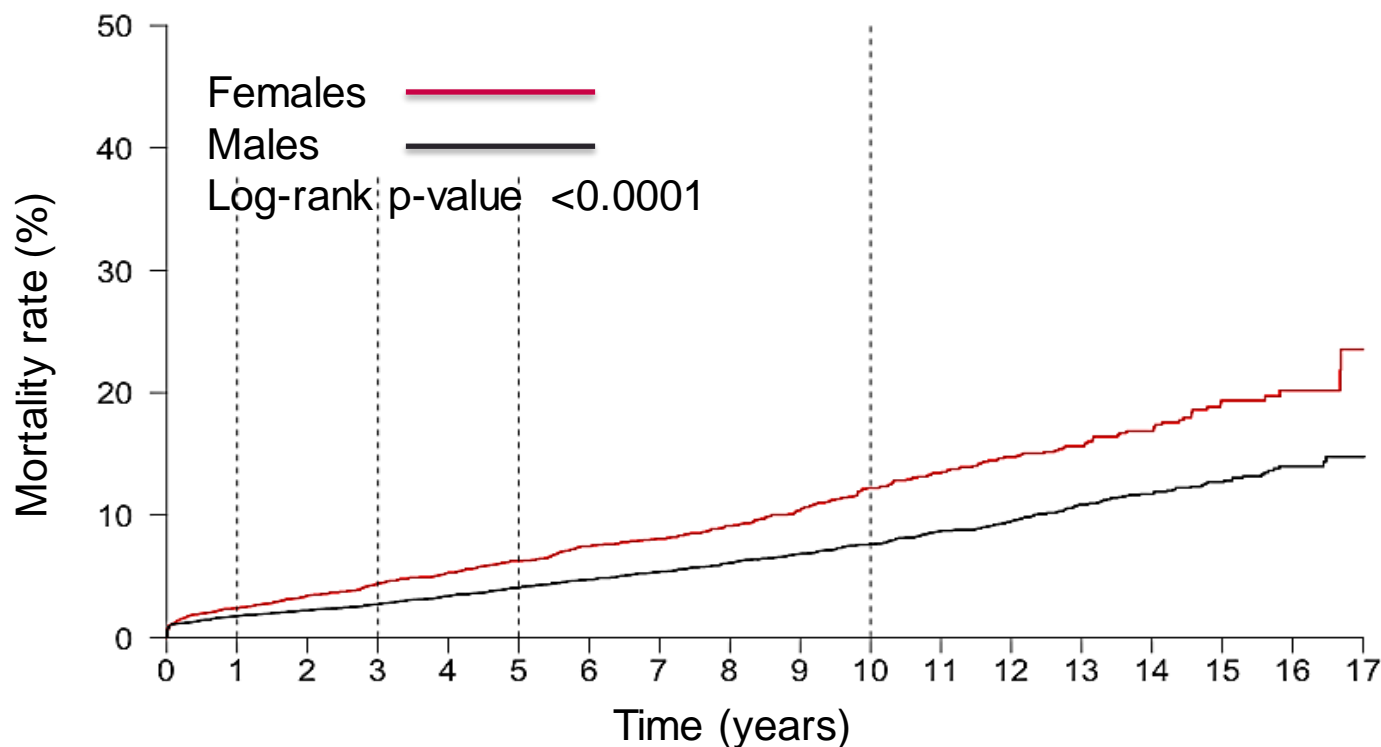
Preliminary Data on Screening for Subclinical Atherosclerosis

	Carotid ultrasound, plaques		CAC scores, percentiles		CCTA, percentiles	
	No	Yes	0-50	51-100	0-50	51-100
FDR	6 (67%)	3 (33%)	7 (50%)	7 (50%)	5 (62%)	3 (38%)
Spouses	17 (74%)	6 (26%)	1 (100%)	0 (0%)	1 (50%)	1 (50%)
Total	23 (72%)	9 (28%)	8 (53%)	7 (47%)	6 (60%)	4 (40%)

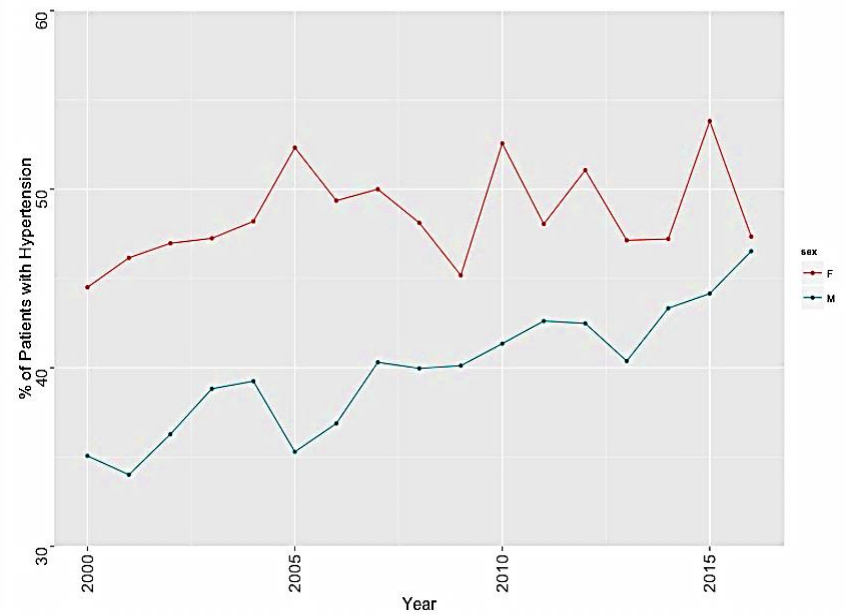
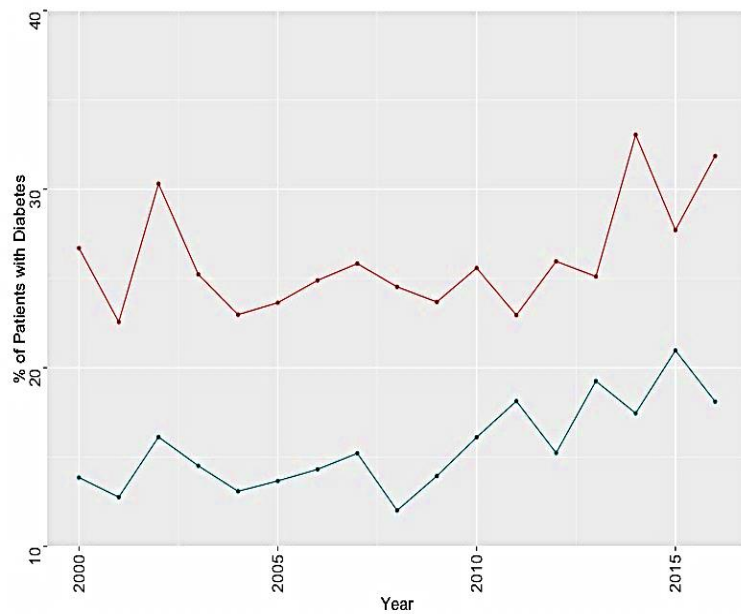
- 11 of 25 FDRs (44%) vs. 6 of 25 spouses (24%) were identified as having subclinical atherosclerosis

CSBC: Mortality Rates in BC

Mortality rate was higher for women over the study period including one month, three, five and ten year mortality rates.



Increasing Rates of Diabetes and Hypertension



SAVE BC

Early Onset Heart Disease: What's In Your Genes?

SPOR Update

Dr. Simon Pimstone, MD, PhD, FRCPC
Principal Investigator



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Why Are We Doing This Forum?

- While much research in heart disease has been conducted, little has been studied about **your priorities** as participants.
- Your thoughts are critical to design research and clinical programs that reflect your needs.



Objectives and Methods

To identify priorities of patients with heart disease and their families regarding participation in SAVE BC.

- **Stage 1: Exploration**

- **Semi-structured interviews**

- **Stage 2: Explanation and Validation**

- **Questionnaire** to validate findings.
- Identify potential areas to improve in SAVE BC and similar programs.

Stage 1: Semi-structured Interviews (N=15)

Major Themes

- A comprehensive **support network** is critical in engagement in research.
- **Mental health** support is important in engagement.
- Quality of **education** provided to patients affects level of engagement in research programs.
- Patients consider **lifestyle changes** major parts of engagement but also face many barriers in doing so.

Stage II: Support Network

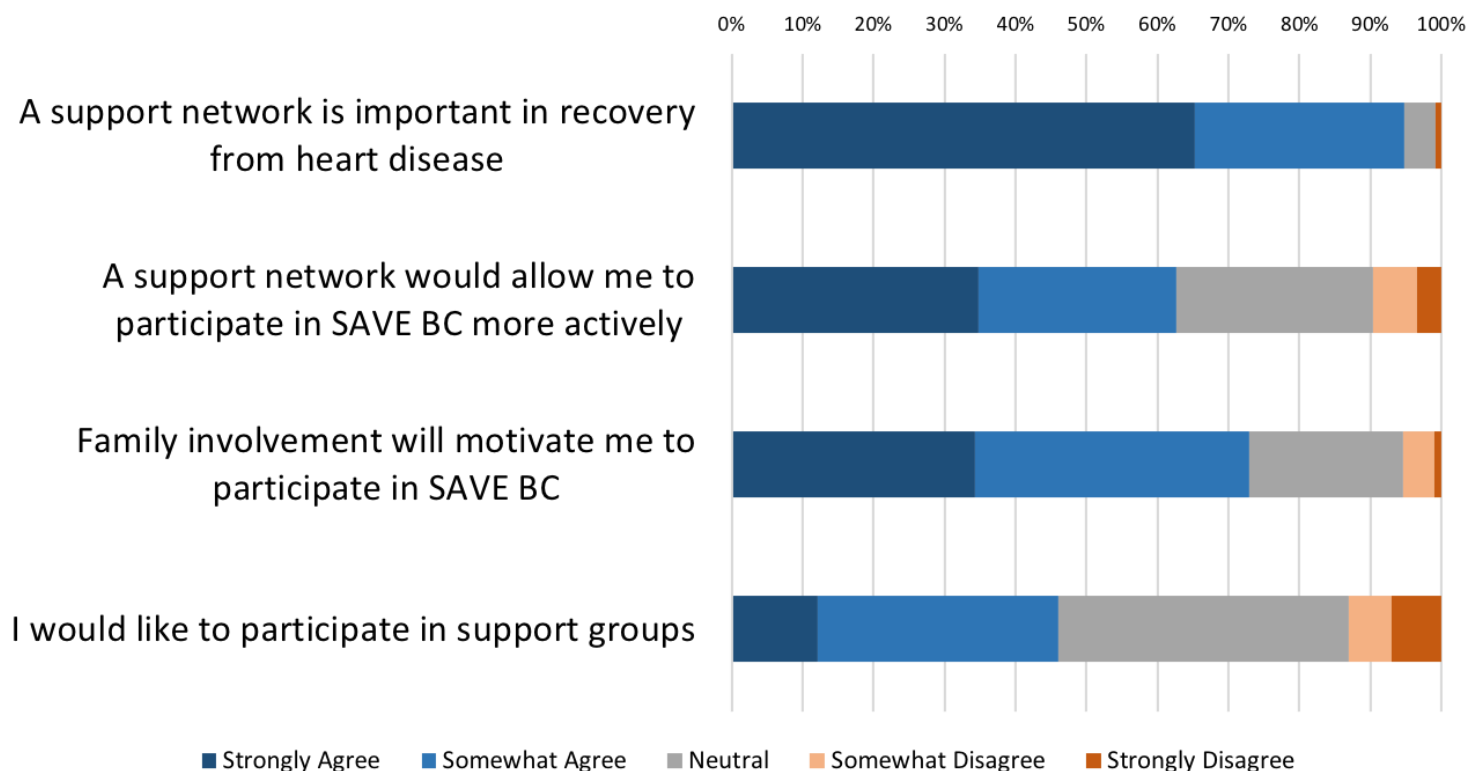


Figure 1: Participant opinions on the importance of support networks in SAVE BC participation (**N = 116**)

Stage II: Mental Health

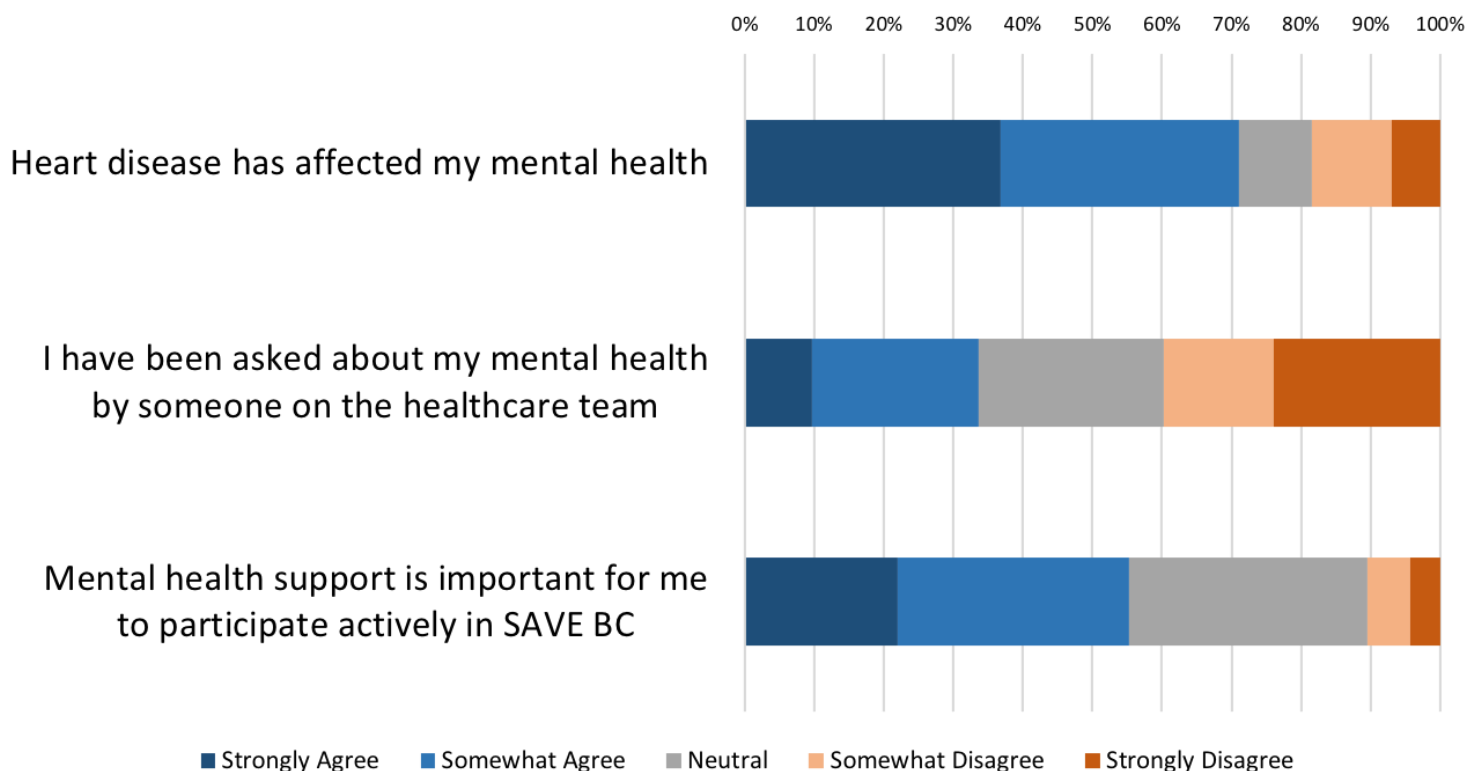


Figure 2: Participant opinions on the importance of mental health support in SAVE BC participation (**N = 116**)

Stage II: Education

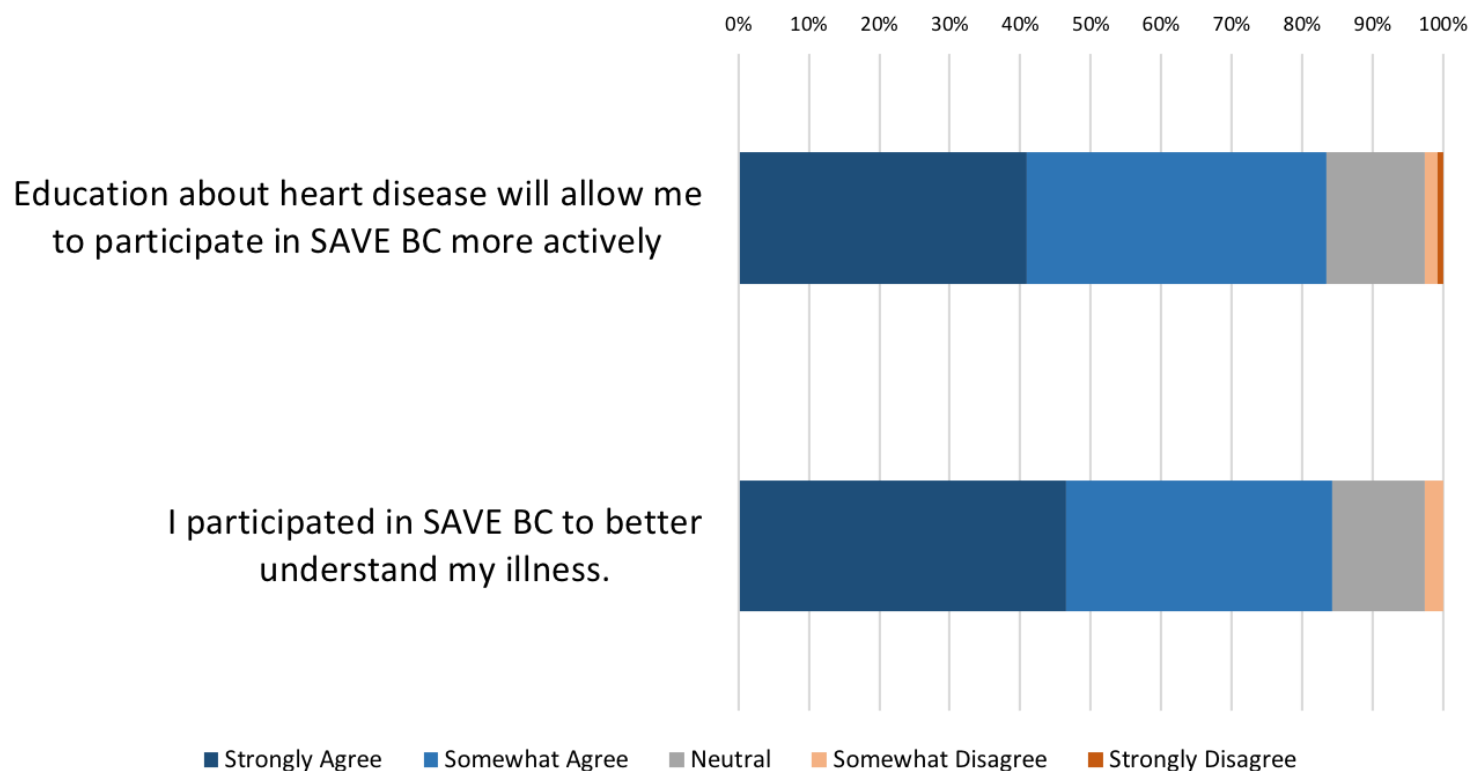


Figure 3: Participant opinions on the importance of education in SAVE BC participation (N = 116)

Stage II: Lifestyle Changes

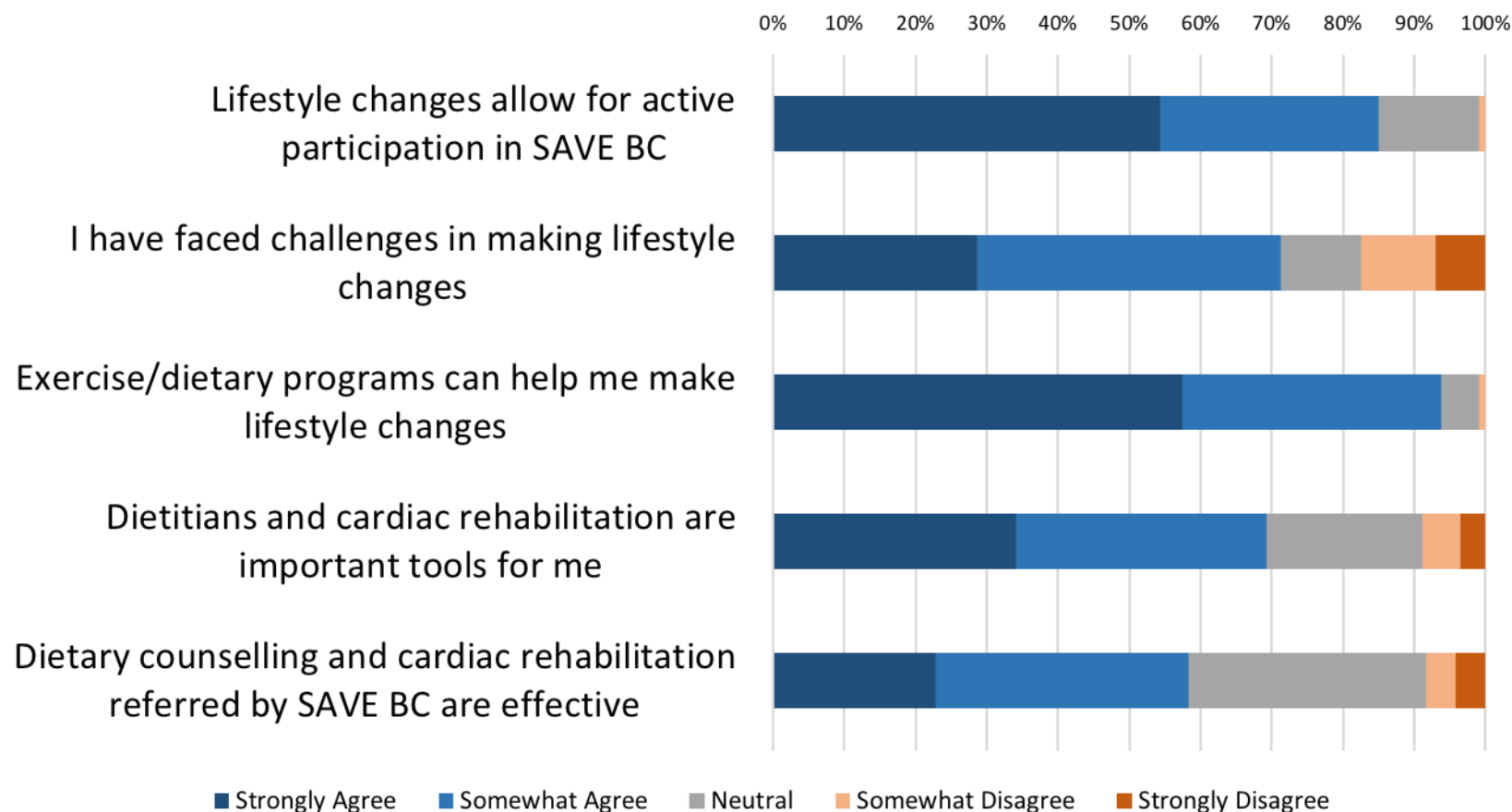


Figure 4: Participant opinions on the importance of support for lifestyle changes in SAVE BC participation (N = 116)

SAVE BC: Early Onset Heart Disease: What's in your Genes?

Risk Screening and Management

G. B. John Mancini, MD, FRCPC, FACC
Professor of Medicine
Director



SAVE BC

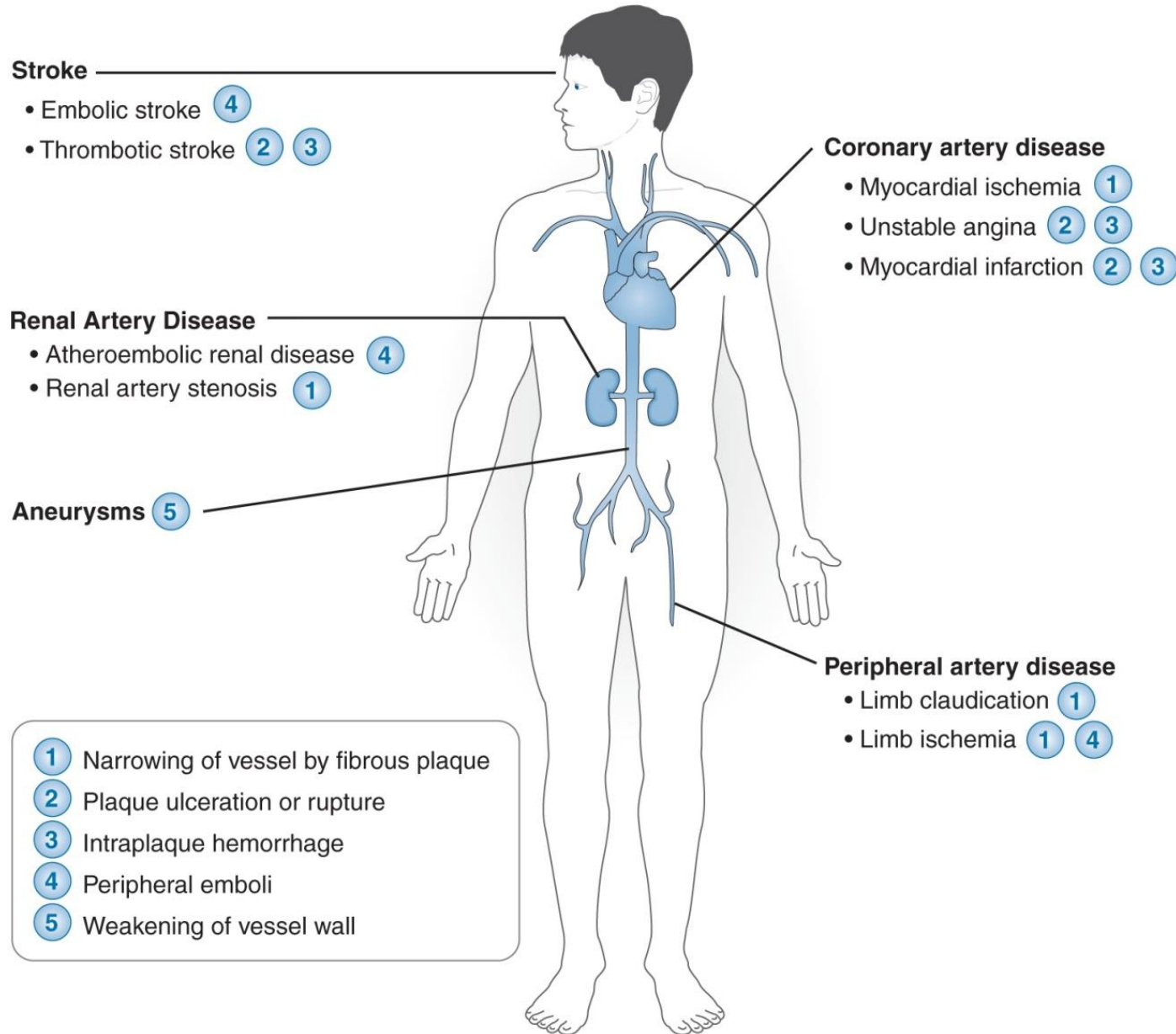
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Outline

- What is atherosclerosis?
- What are the risk factors?
- How important is this as a public health issue?
- Has the management of risk factors led to progress?
- How do clinicians balance this progress with overall costs?

Atherosclerosis: Hardening of the Arteries



What are the risk factors?

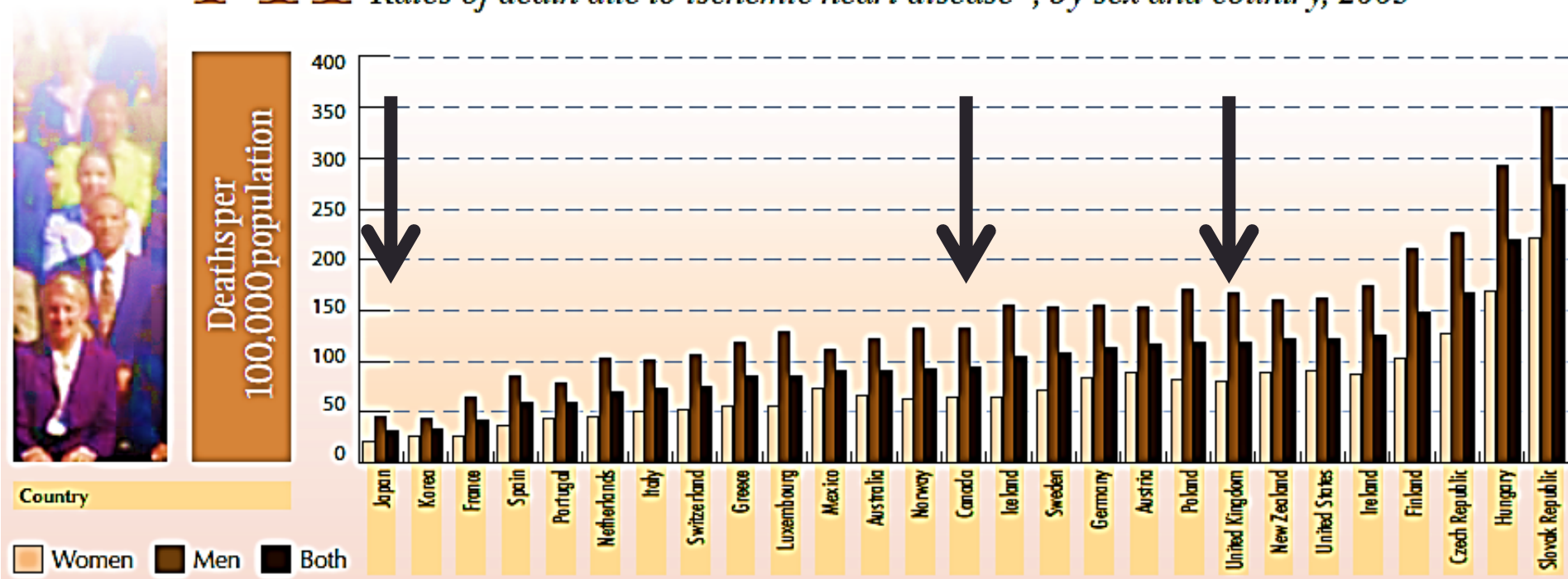
• **TRADITIONAL RISK FACTORS**

- Age
- Family history (“genetics”)
- Smoking
- Hypertension
- Diabetes
- Dyslipidemia
- Sedentary lifestyle/lack of exercise
- Obesity

• **Emerging/Novel Risk Factors**

- Biomarkers of inflammation and other processes directly/indirectly related to atherosclerosis
- Inflammatory disease states (HIV on therapy, Rheumatoid Arthritis, Systemic Lupus Erythematosus, COPD, IBD, Psoriasis etc etc)
- A VERY long list!

Figure 4-11 *Rates of death due to ischemic heart disease*, by sex and country, 2003*



HEART DISEASE *in* CANADA

It is the **2nd** leading cause of death *among Canadians*

Also known as **ischemic heart disease** or **coronary heart disease**, **heart disease** refers to the buildup of plaque in the heart's arteries that could lead to a heart attack, heart failure, or death.

According to 2012/13 data from the Public Health Agency of Canada's *Canadian Chronic Disease Surveillance System (CCDSS)*:



ABOUT
1 *in* 12

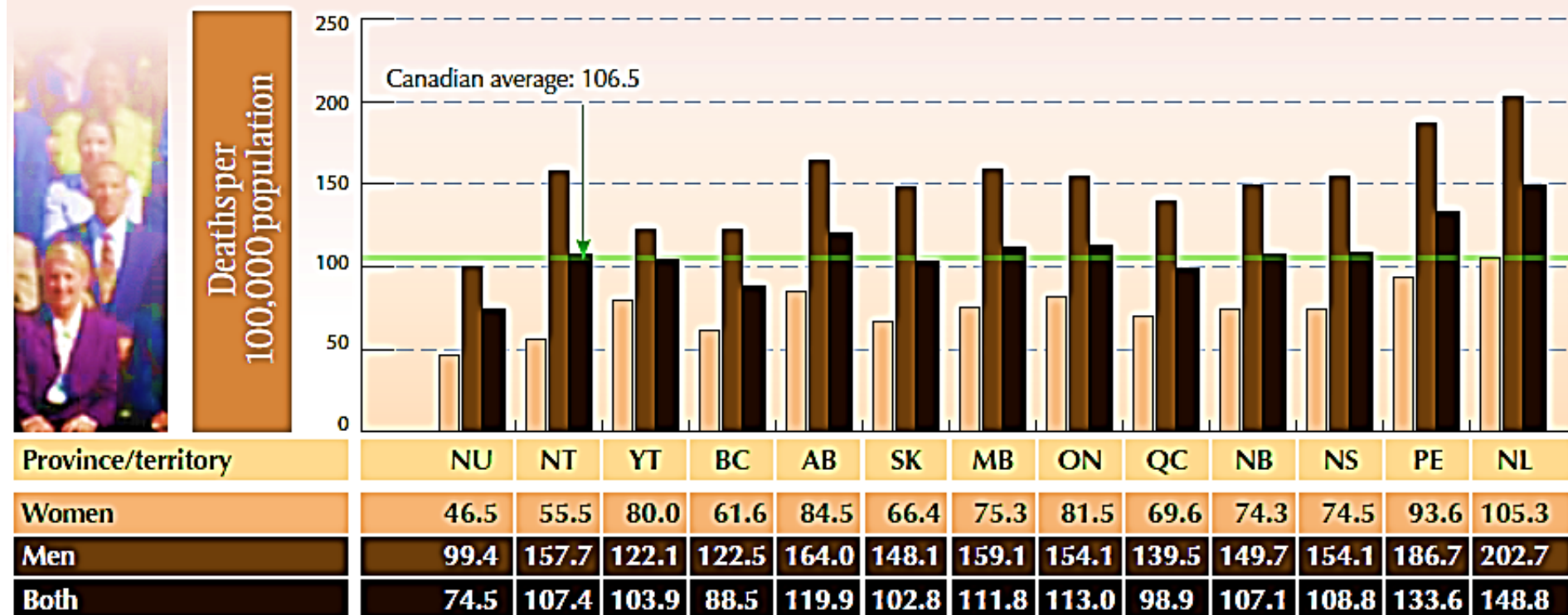
(or **2.4 million**) Canadian adults
age 20+ live with diagnosed **heart disease**

EVERY
HOUR

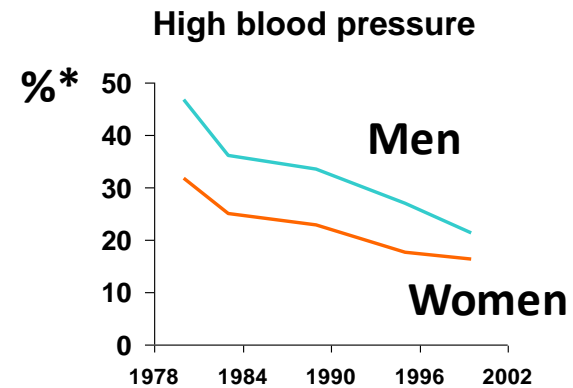
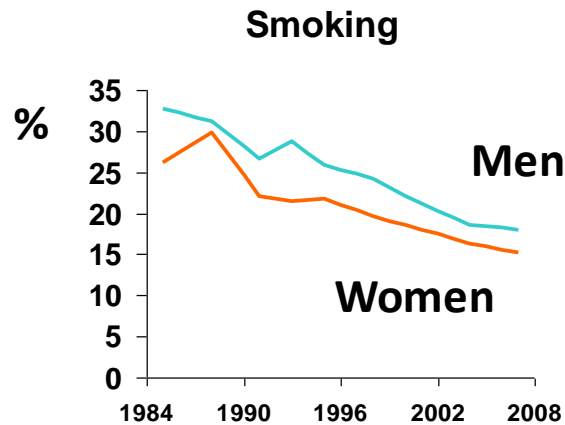
12 Canadian adults age 20+
with diagnosed **heart disease** die



Figure 4-10 *Rates of death due to ischemic heart disease*, by sex and province/territory, Canada, 2000-2004 (five year average)*



Getting Better



* Age-standardised

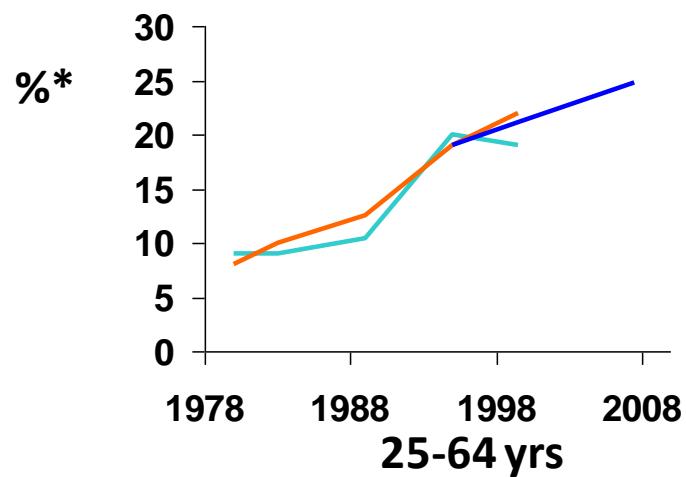


After Two Years in the USA,
Michelangelo's *David* is Being Returned
to Florence.

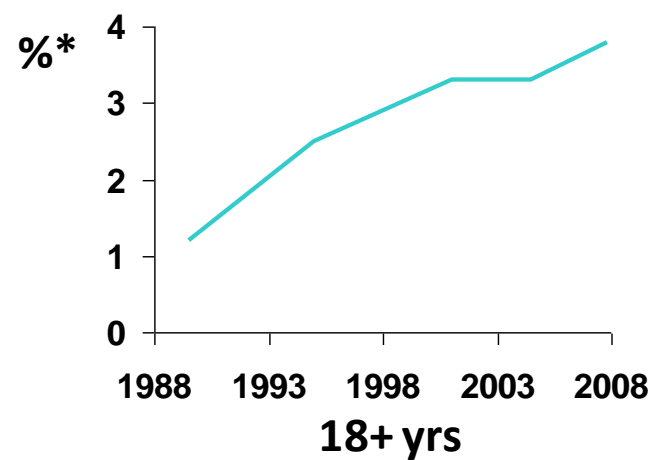


Getting Worse?

Obesity

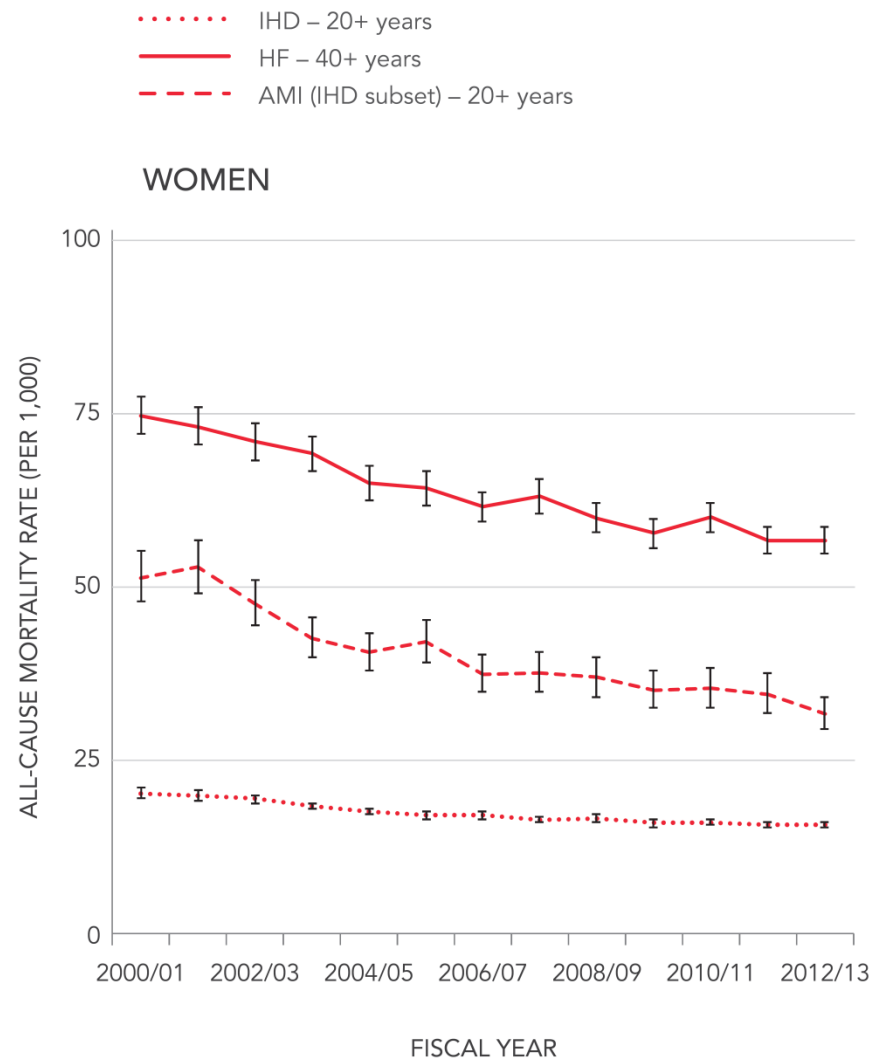
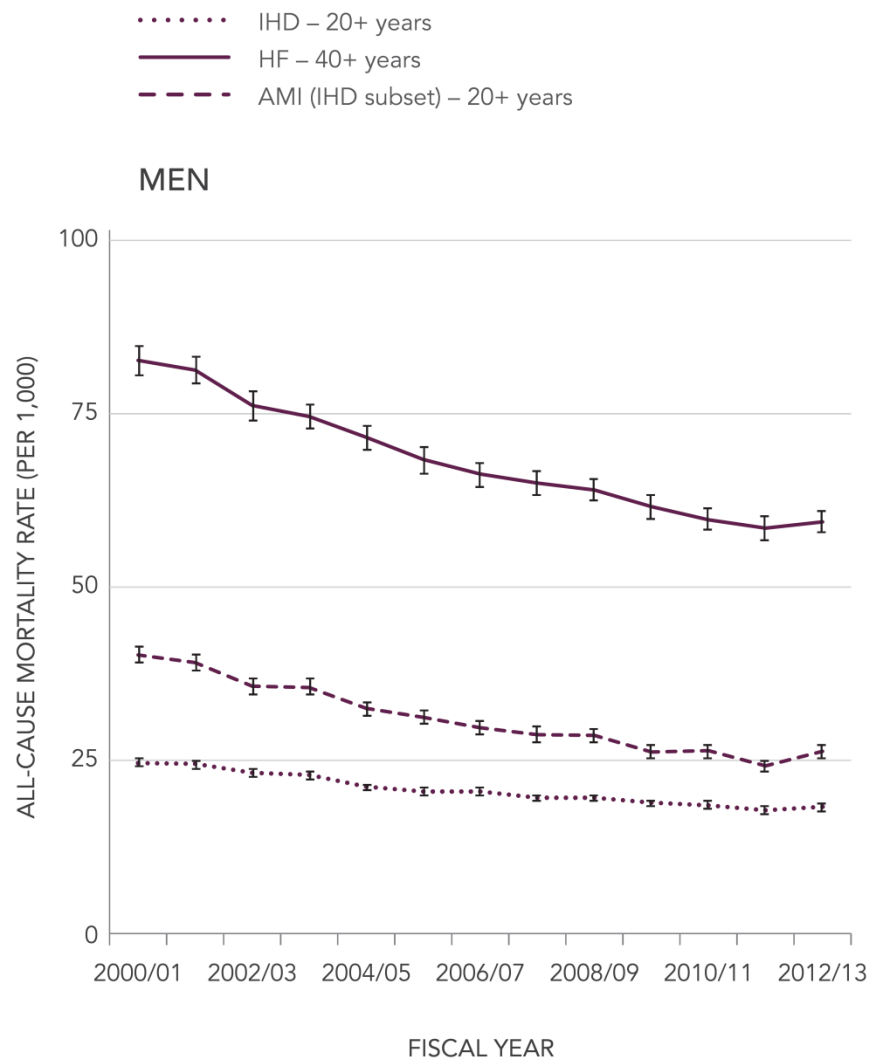


Diabetes



* Age-standardised

FIGURE 3: Age-standardized[†] all-cause mortality rates (per 1,000) among those with diagnosed ischemic heart disease (IHD) and heart failure (HF), and those who had an acute myocardial infarction (AMI), by sex, Canada,* from 2000/01 to 2012/13



WHO TO SCREEN

**Men ≥ 40 years of age;
women ≥ 40 years of age
(or postmenopausal)**

Consider earlier in ethnic groups at increased risk such as South Asian or First Nations individuals

All patients with the following conditions regardless of age:

- Clinical evidence of atherosclerosis
- Abdominal aortic aneurysm
- Diabetes
- Arterial hypertension
- Current cigarette smoking
- Stigmata of dyslipidemia (arcus cornea, xanthelasma or xanthoma)
- Family history of premature CVD*
- Family history of dyslipidemia
- Chronic kidney disease
- Obesity (BMI ≥ 30 kg/m²)
- Inflammatory bowel disease
- HIV infection
- Erectile dysfunction
- Chronic obstructive pulmonary disease
- Hypertensive diseases of pregnancy

HOW TO SCREEN

For all:

- History and physical examination
- Standard lipid panel (TC, LDL-C, HDL-C, TG)
- Non-HDL-C (will be calculated from profile)
- Glucose
- eGFR

Optional:

- ApoB
- Urine albumin:creatinine ratio
(if eGFR <60 mL/min/1.73m², hypertension or diabetes)

NON-FASTING LIPID TESTING IS ACCEPTABLE

CLINICAL ATHEROSCLEROSIS

Myocardial infarction, acute coronary syndromes
Stable angina, documented coronary disease by angiography (>10% stenoses)
Stroke, TIA, documented carotid disease
Peripheral artery disease, claudication and/or ABI < 0.9

ABDOMINAL AORTIC ANEURYSM

Abdominal aorta > 3.0 cm or
Previous aneurysm surgery

DIABETES MELLITUS

≥ 40 years of age or
> 15 years duration and age ≥ 30 years or
Microvascular complications

CHRONIC KIDNEY DISEASE

> 3 months duration and
ACR > 3.0 mg/mmol or
eGFR < 60 ml/min/1.73m²

LDL-C ≥ 5.0 MMOL/L

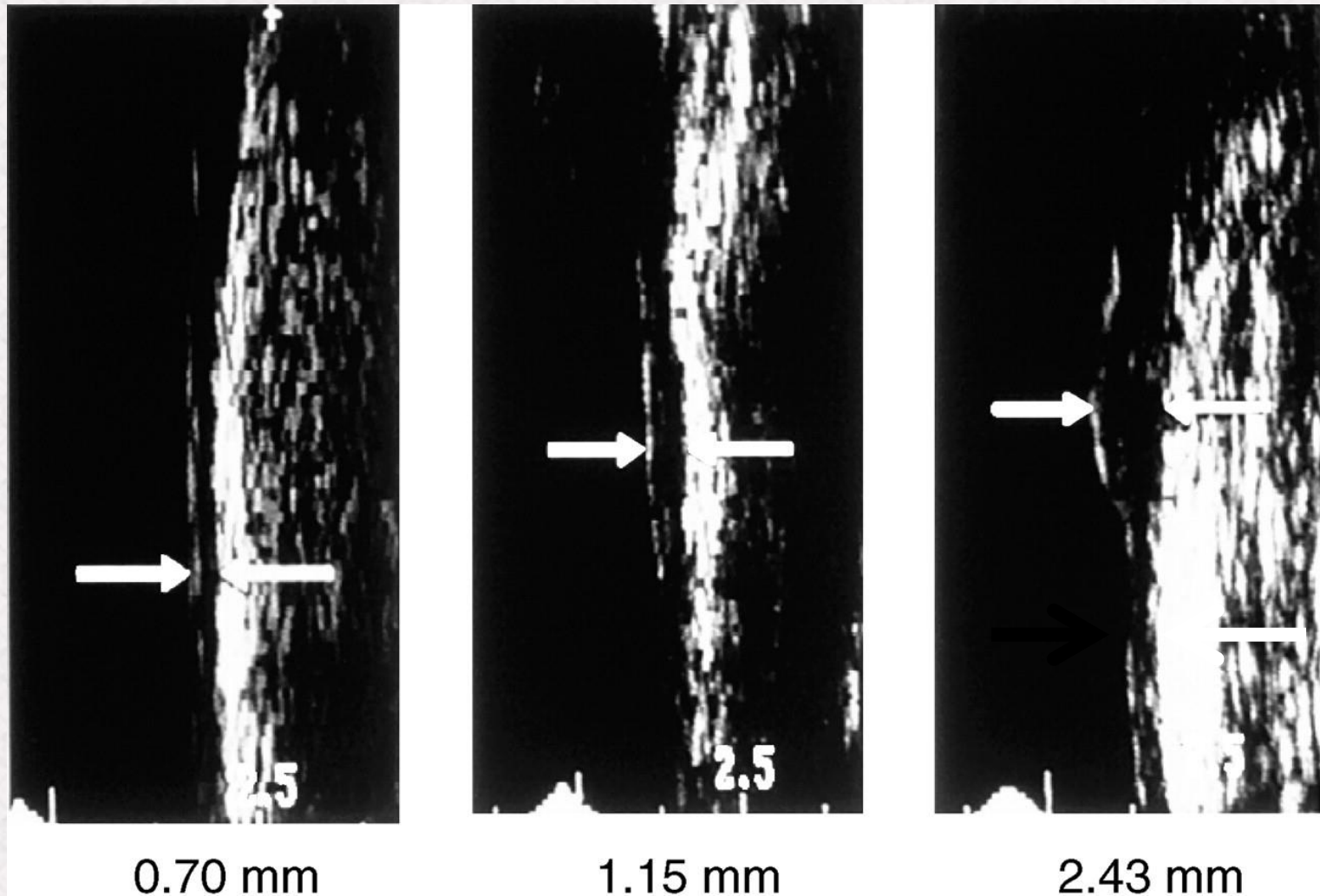
LDL-C ≥ 5.0 mmol/L or
Document familial hypercholesterolemia
Excluded 2nd causes

Who to Treat

1. Statin indicated conditions
2. Primary prevention patients at high cardiovascular risk
(NEED TO DO A CALCULATION e.g. FRS >20%)
3. Primary prevention patients at intermediate cardiovascular risk (FRS 10 – 20%) with elevated LDL (>3.5mmol/L) or other risk factors

When you and your physician may not be sure, other tests may be ordered to help make a personalized treatment decision.

Examples of B Mode Ultrasound Images Captured on Videotape. 38



Crouse J R J. Lipid Res. 2006;47:1677-1699

CT CARDIAC WWO
CONTRAST W/3D
///Cardiac/3.0/

R

L

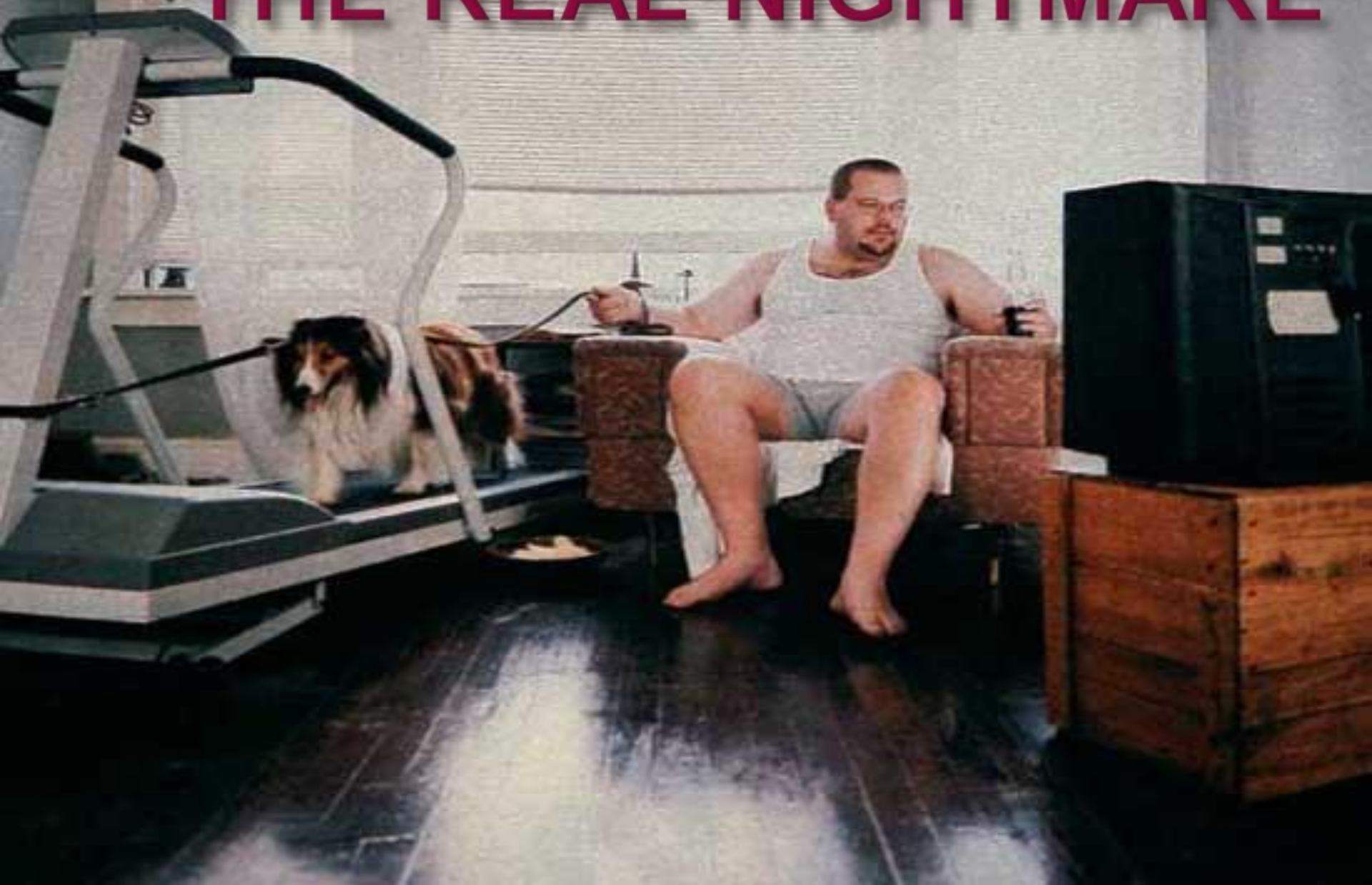
7 cm

kVP:135
mA:440
msec:250
mAs:110
Thk:3 mm
Aquilion

Region	Agatston	Volume
LM	0	0
RCA	404	378
LAD	669	542
CX	988	783
PDA	0	0
Other1	0	0
Other2	0	0
Other3	0	0
Total	2111	1683

Vitrea (R)
Phase %075
W/L:300/40
#16 at 1782.5mm

THE REAL NIGHTMARE





Review

- What is atherosclerosis?
 - Hardening of the arteries, head to toe.
- What are the risk factors?
 - Address all modifiable risk factors!
- How important is this as a public health issue?
 - 12 adults with IHD die/hour in Canada
- Has the management of risk factors led to progress?
 - Improving: smoking, BP, lipids
 - Worsening: obesity, diabetes,
- How do clinicians balance this progress with overall costs?
 - Careful attention to national guidelines and judicious use of specialized tests

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Genetics and ASCVD Risk

Dr. Liam Brunham, MD, PhD, FRCPC
Principal Investigator

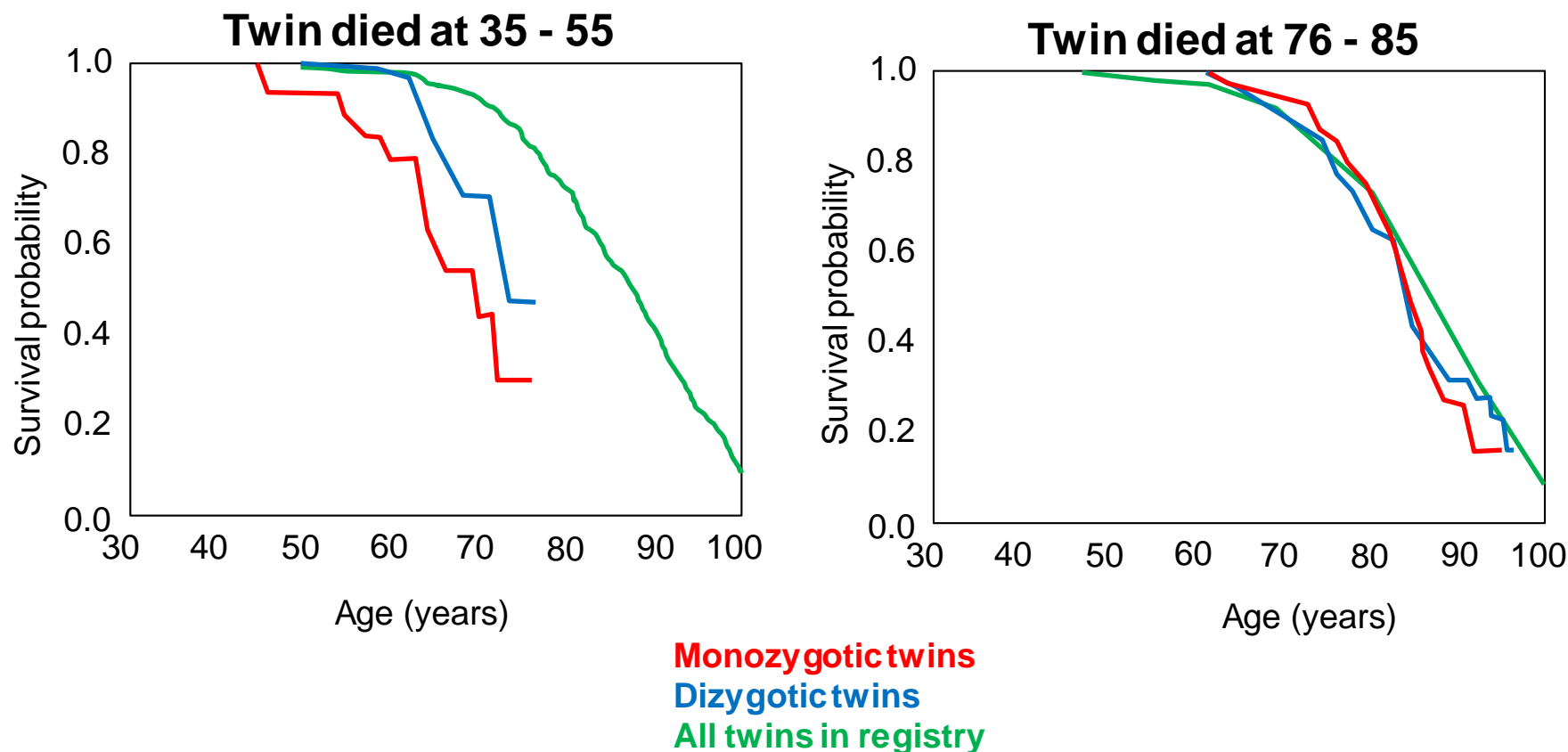


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Premature ASCVD is Highly Heritable



Age-Specific Probabilities of Death from Coronary Heart Disease in Subjects Whose Twins Died of the Disease

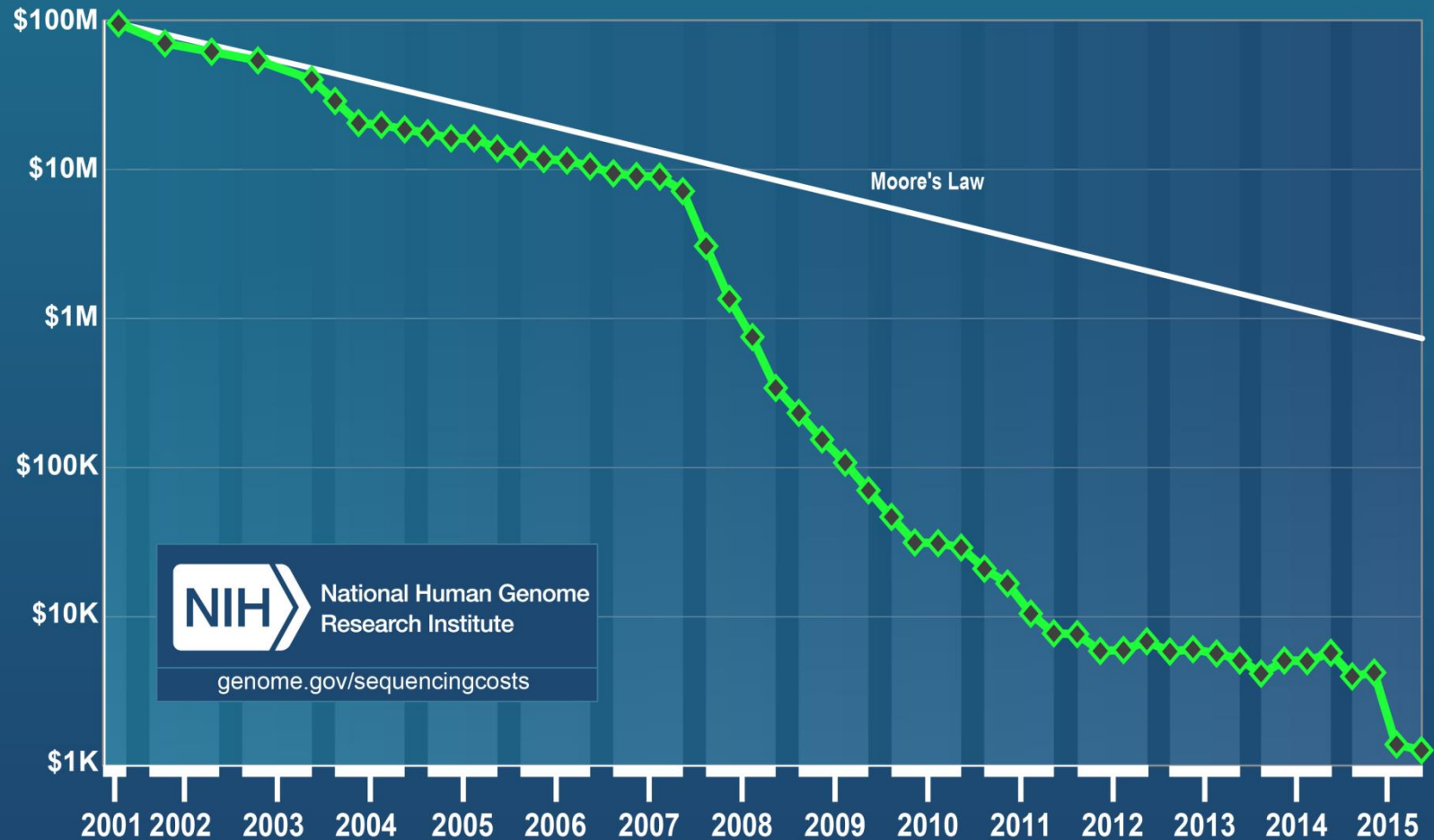
2001



2018



Cost per Genome





4608 LANGARA AVENUE, Vancouver, British Columbia V6R1E1

Photos

\$8,688,000

MLS® Number: R2223859

3 2



Favourite



Compare



Print



Financial



Multimedia

Property Type

Single Family

Building Type

House

Title

Freehold

Land Size

7150 sqft

Built in

1935

SHARE THIS LISTING:

Judy (Pei-Hu) Yu

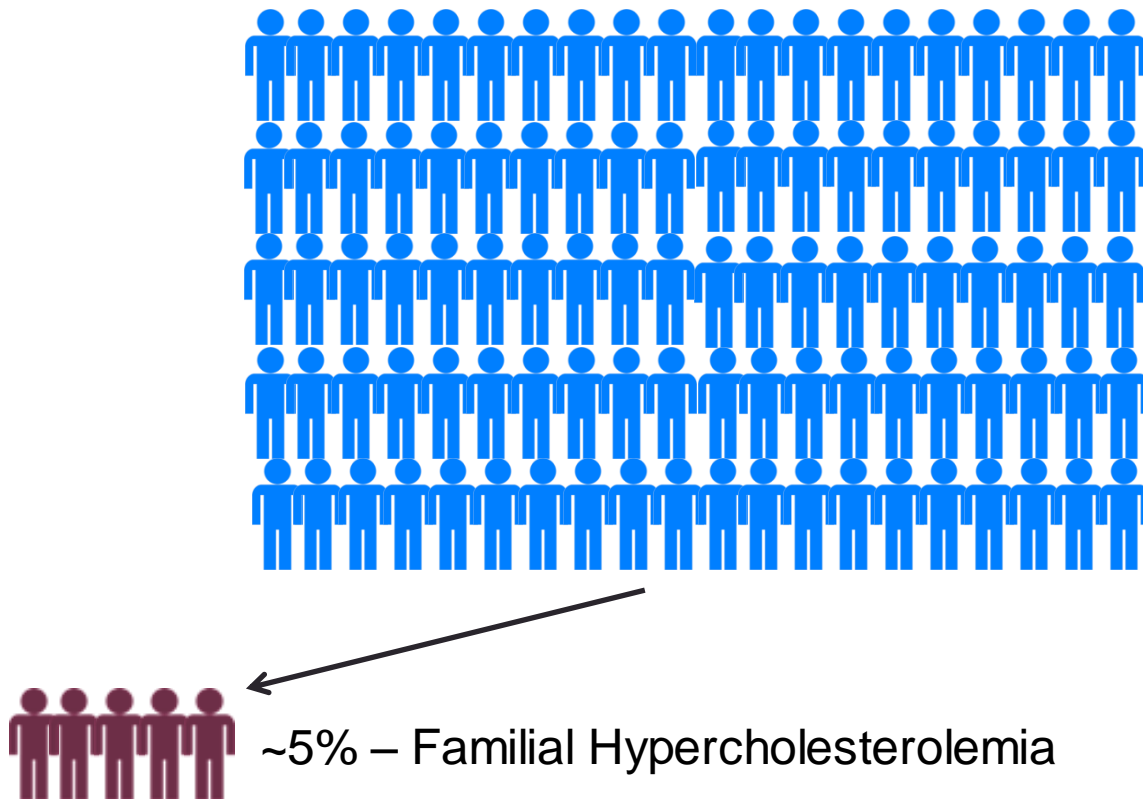
604-671-0271

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**Sutton Group-West
Coast Realty**

Genetic Testing on 100 Individuals with Early Onset Heart Disease



Familial Hypercholesterolemia (FH)

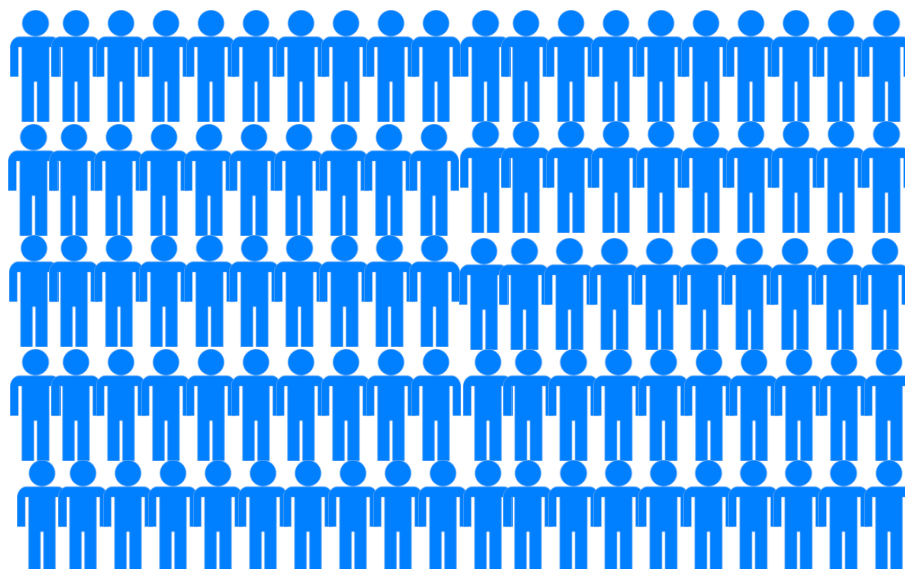
- ♥ One of the most common inherited forms of high cholesterol (1 in 250 individuals)
- ♥ Elevated LDL cholesterol (usually $> 5\text{mmol/L}$) and **~10x increased risk of heart attack**
- ♥ Most commonly caused by mutations in the LDL Receptor (*LDLR*) gene
- ♥ $>90\%$ of patients are undiagnosed



LDL – The Bad Guy



Genetic Testing on 100 Individuals with Early Onset Heart Disease



~5% – Familial Hypercholesterolemia



~10% – High lipoprotein(a) [due to *LPA* gene variant]

Lipoprotein(a) – The Really Bad Guy (or Girl)



The New York Times

WELL

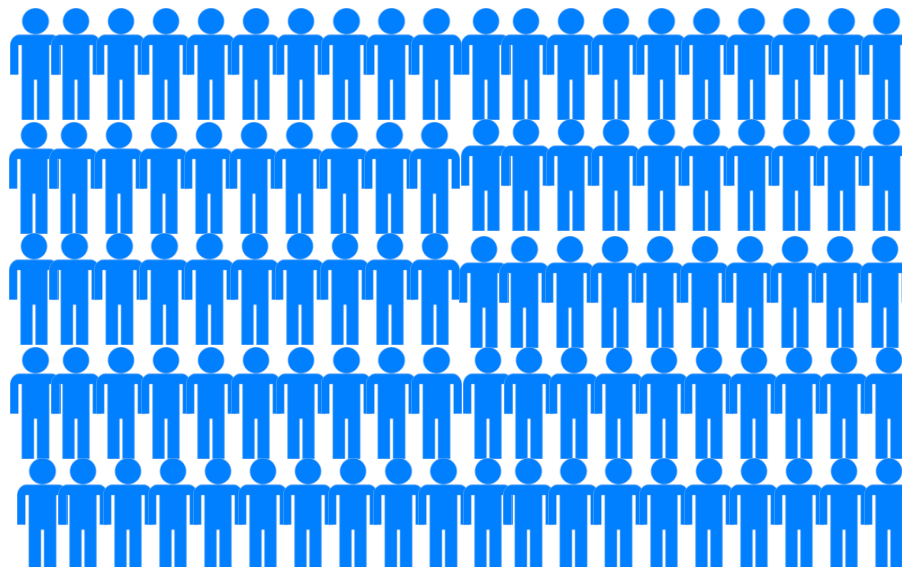
A Heart Risk Factor Even Doctors Know Little About

By ANAHAD O'CONNOR JAN. 9, 2018



Bob Harper, the celebrity fitness trainer from the TV show “The Biggest Loser,” suffered a heart attack last year. He eventually found out the cause was a particle in the blood called lipoprotein(a), which few doctors test for. Hilary Swift for The New York Times

Genetic Testing on 100 Individuals with Early Onset Heart Disease



~5% – Familial Hypercholesterolemia

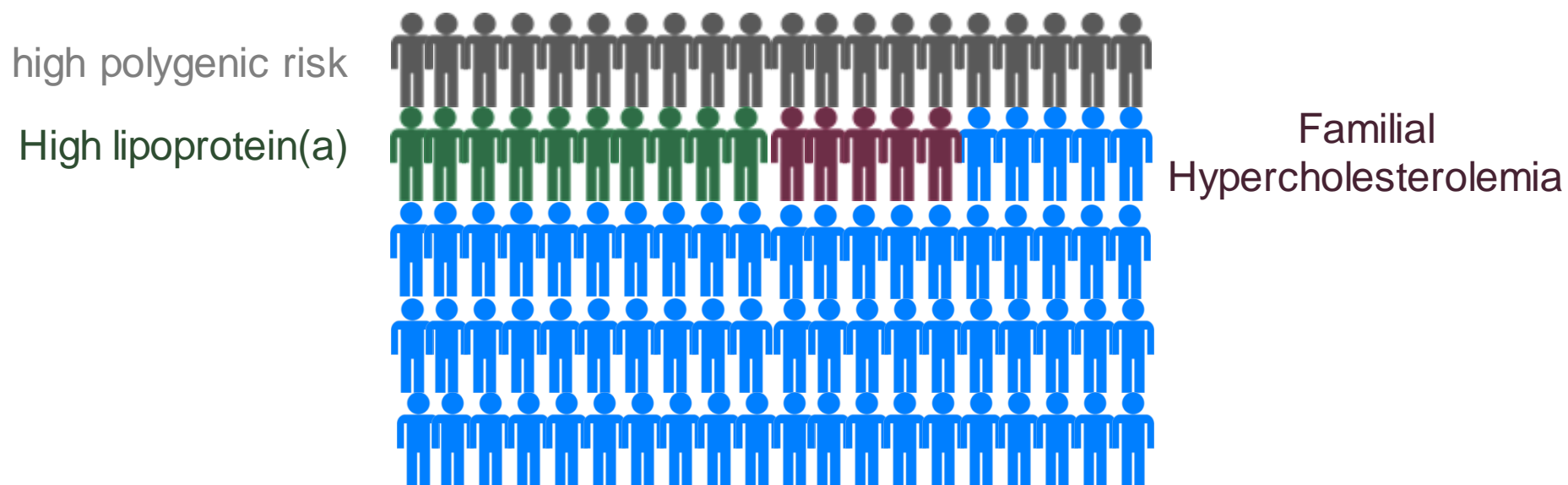


~10% – High lipoprotein(a) [due to *LPA* gene variant]



~20% – high polygenic risk

Genetic Testing on 100 Individuals with Early Onset Heart Disease

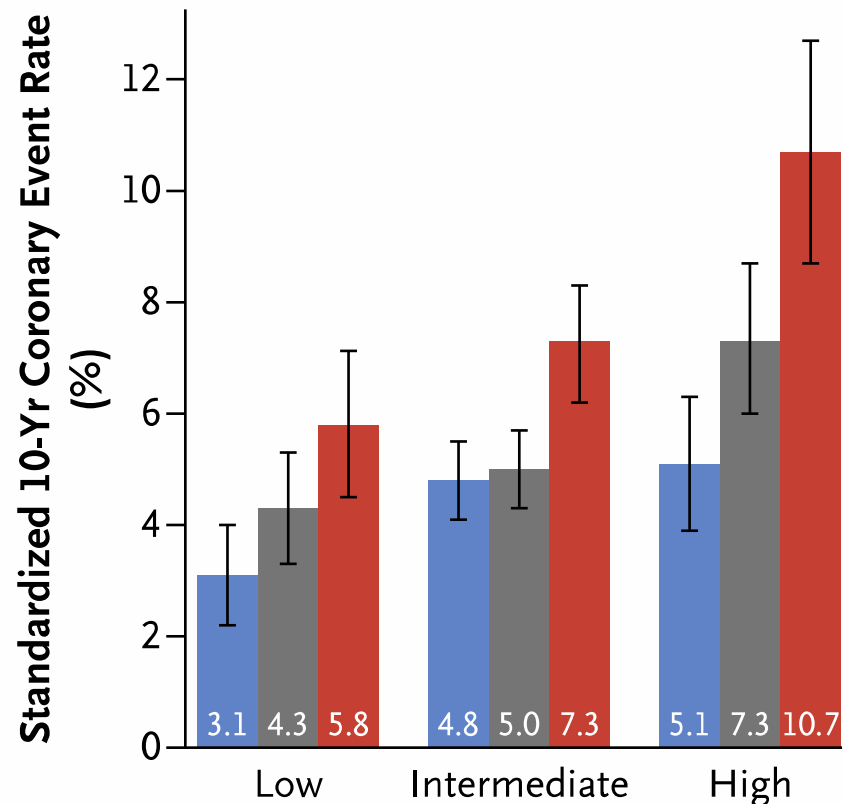


**~65 – 70% have
no known cause**

What can I do if I have high genetic risk for heart disease?

A Healthy Lifestyle Can Attenuate High Genetic Risk

■ Favorable lifestyle ■ Intermediate lifestyle ■ Unfavorable lifestyle



Genetic Risk

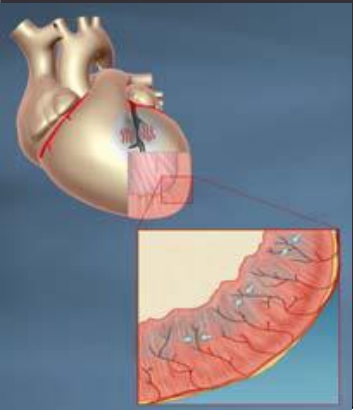
Khera et al. *NEJM* 2016

Summary

- Most common causes of early onset heart disease include:
 - Familial Hypercholesterolemia (high LDL)
 - High lipoprotein(a)
 - High burden of polygenic variants
- With appropriate treatment and a healthy lifestyle, a high genetic risk can be significantly reduced
- No known genetic cause is found in more than half of patients with early onset heart disease → this is part of what we hope to learn in SAVE BC

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Heart Disease in Women: Ms. Understood



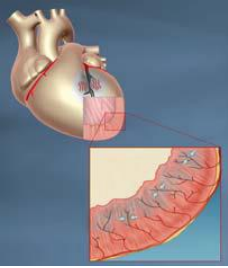
Tara L. Sedlak, MD, FRCPC
Medical Director, Leslie Diamond
Women's Heart Health Clinic



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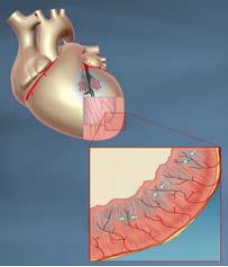




Facts: Women & Heart Disease

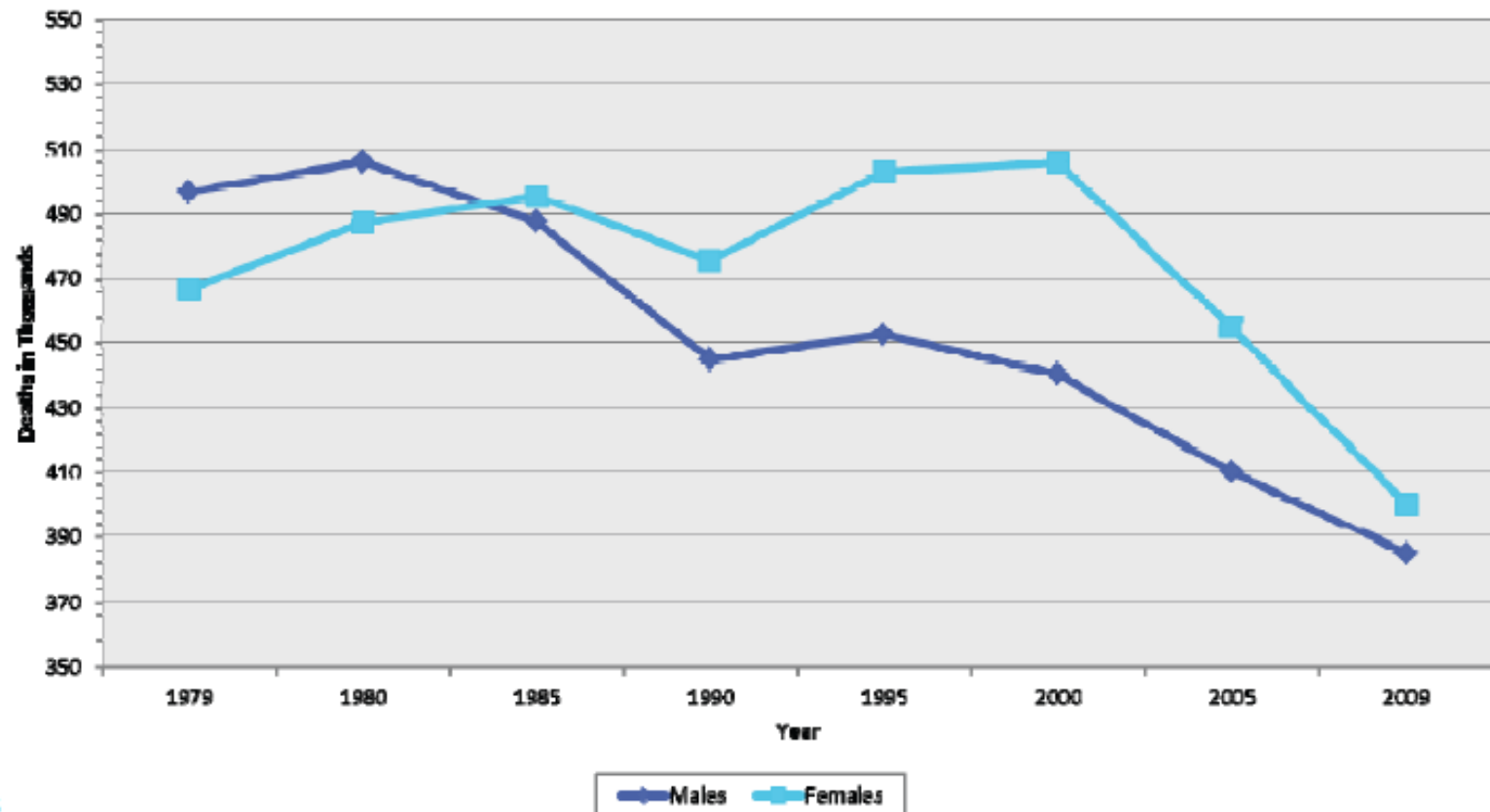


- Cardiovascular disease is the leading killer amongst women in Canada
- Women are 6 times more likely to die of cardiovascular disease than breast cancer
- Every 20 minutes a woman in Canada dies from heart disease
- Two-thirds of heart disease research focuses on men

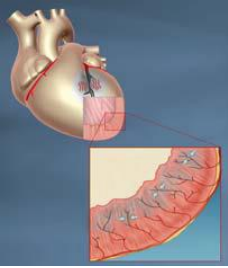


Heart Disease Trends

Cardiovascular Disease Mortality Trends for Males and Females United States: 1979–2009



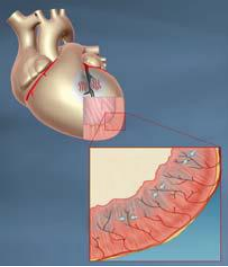
Source: NCHS.



Ms. Understood #1

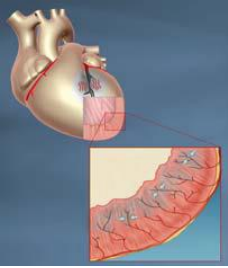


- 50-year-old female
- Asymptomatic, walks 3 times/week
- High cholesterol
- 2 pregnancies
 - 38 years old: pre-eclampsia (toxemia)
 - 40 years old: pre-eclampsia 34 weeks, gestational diabetes controlled with diet, induced at 37 weeks
- Concerned regarding family history
 - Mother had a heart attack at the age of 52



Ms. Understood #1

Women have the same cardiac risk factors as men

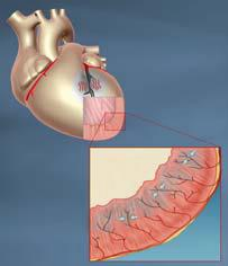


Risk factors for heart disease

- 8 risk factors that account for 80% of the risk for heart disease

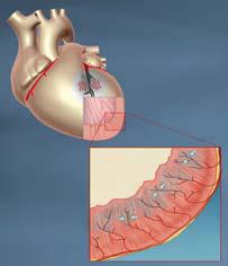
- **Smoking**
- High blood pressure
- High cholesterol
- Inactivity
- Obesity
- **Diabetes**
- Poor diet
- **Psychosocial stress**

**Two fold higher
risk in women**



Novel risk factors in women

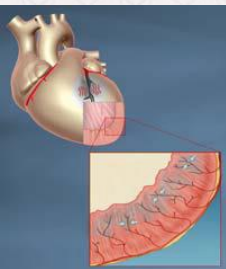
- Pre-eclampsia (toxemia during pregnancy)
 - Doubles risk of a future cardiac event
 - Worse with increased severity of pre-eclampsia
- Gestational diabetes
 - Doubles risk of future cardiac event



Ms. Understood #2



- 48-year-old female, smoker
- History of anxiety on treatment
- Severe retrosternal chest pain before work
- Tries tums with no relief
- Deep breathing – again no relief
- Calls EMS – come to her house – tell her she is having an anxiety attack – take an ativan
- Calls them back 6 hours later – brought to ED
- Diagnosed with acute heart attack



Ms. Understood #2

Women with a heart attack have completely different symptoms than men

Learn the signs of heart attack



Chest discomfort

Pressure, squeezing, fullness or pain, burning or heaviness



Sweating



Upper body discomfort

Neck, jaw, shoulder, arms, back



Nausea



Shortness of breath



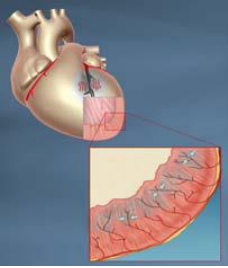
Light-headedness

Call 9-1-1 right away.

Ms. Understood

Women's hearts are victims of a system that is ill-equipped to diagnose, treat and support them

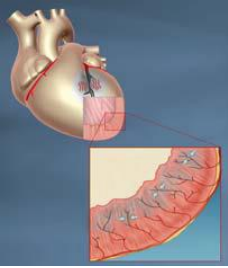
Heart & Stroke **2018** Heart Report



What does research show?

- Chest pain as main symptom
 - 53% of women, 56% of men
- Throat, jaw and neck discomfort
 - More common in women than men
- Weakness, fainting (atypical symptoms)
 - More commonly found in elderly
 - Since women have heart attacks 10 years later than men
 - more commonly have these non-classic symptoms

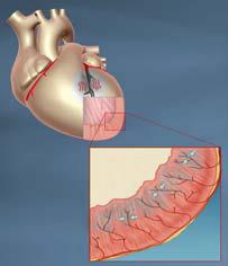
Women describe their symptoms differently but the symptoms are actually similar



Facts: Women & Heart Disease

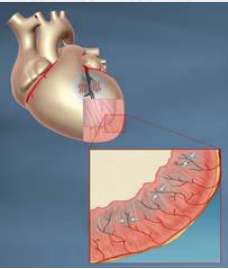


- 60% of heart disease in women presents as a heart attack
- Early heart attack signs are missed in 78% of women
- Women are less likely than men to seek medical attention and when they do seek help, they are less likely to receive a diagnosis for their heart condition



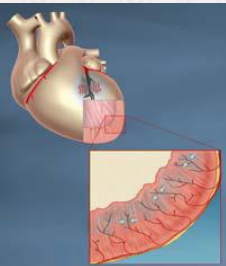
Ms. Understood #3

- 57-year-old female, history of hypertension
- Following an elective surgery, she began experiencing severe left sided chest pressure
- Stress test: lack of blood supply to the heart
- Urgent angiogram: normal coronary arteries
- Told chest pain was not cardiac
- 2 more visits to ED, saw 2 more cardiologists
- Gastroenterology work-up: normal
- Referred to the Leslie Diamond Women's Heart Health Clinic in Vancouver, BC



Ms. Understood #3

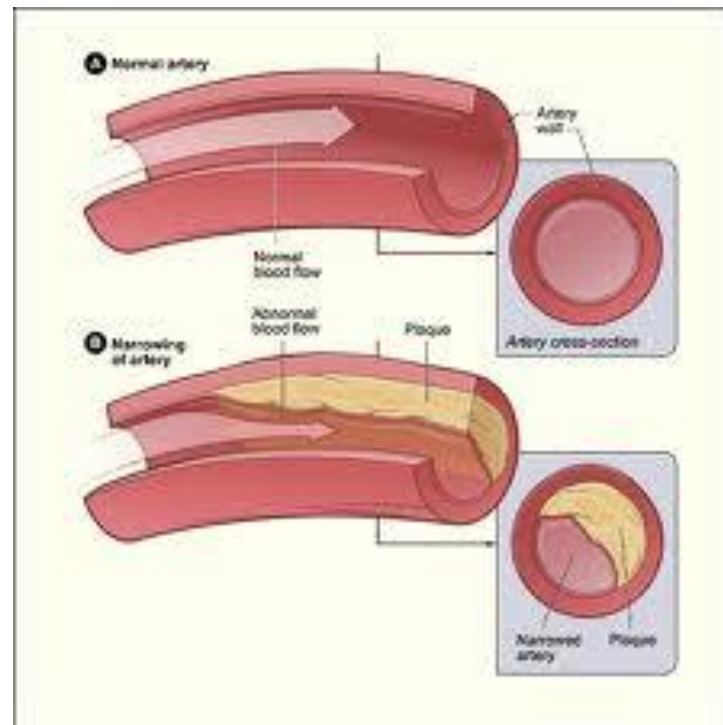
Plaque (cholesterol) is the only cause of chest pain/heart attack in women

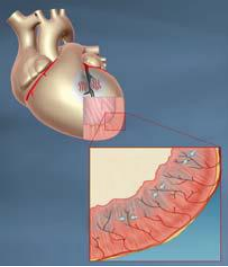


Causes of a heart attack/chest pain: Atherosclerosis



- Cholesterol plaque causing narrowing of the coronary or “heart” arteries
 - >90% of men with a heart attack
 - 70% of women with a heart attack
- Normal arteries
 - 5% of men
 - **20-30% of women**

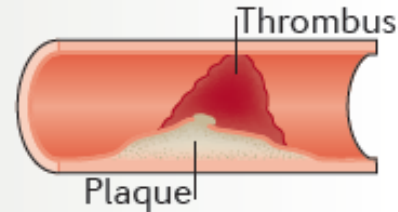




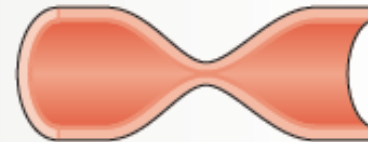
Causes of a heart attack in women



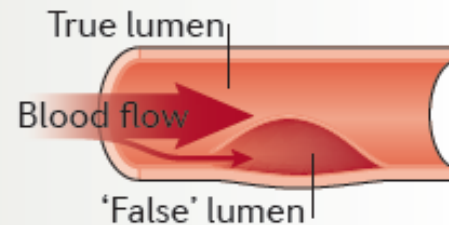
Thrombus formation on a ruptured or eroded plaque



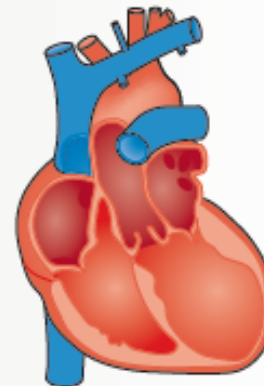
Coronary vasospasm



Spontaneous coronary artery dissection



Stress-related (Takotsubo) cardiomyopathy





Obstructive Coronary Disease

More prevalent
in men

Coronary Microvascular Dysfunction

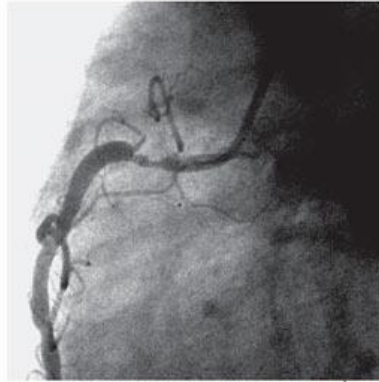
More prevalent
in women

A Hidden Risk

While an angiogram, in which dye is injected into the coronary arteries, helps doctors to determine whether the blockages are forming in the larger vessels of the heart, the test does not reveal the smaller vessels, microvasculature. Blockages in these small vessels, which seem to be more common in women, can become an undetected threat.

75

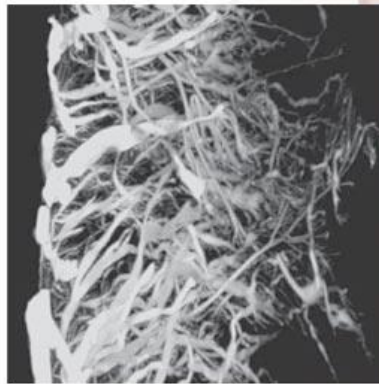
TYPICAL ANGIOGRAM



Minneapolis Heart Institute and Foundation

Larger vessels stand out while smaller ones, because of their microscopic size and the motion of the heart, are lost in a blur.

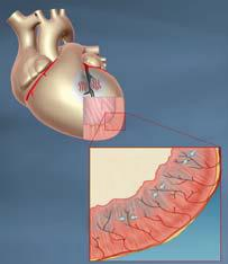
MICROVASCULATURE



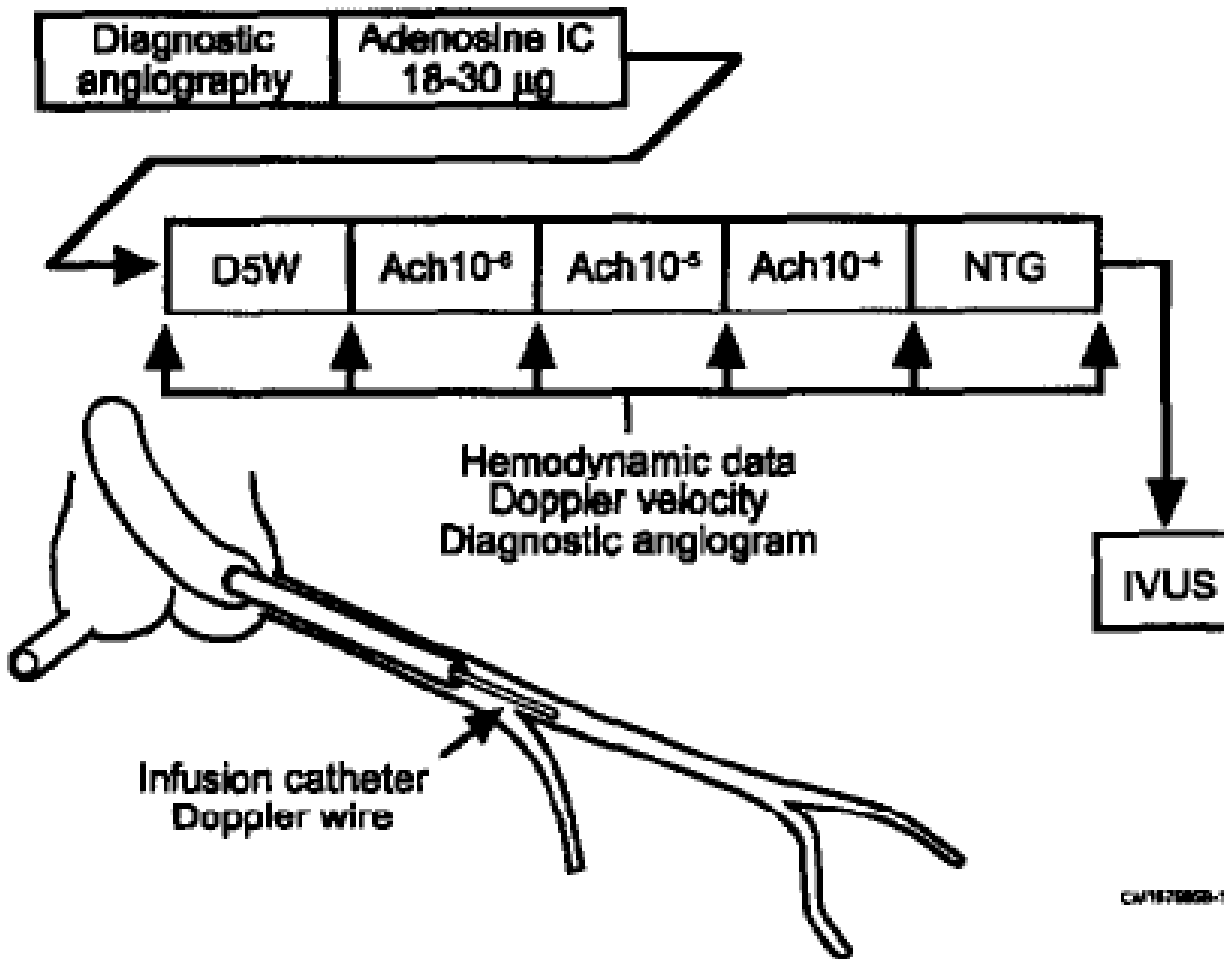
Minneapolis Heart Institute and Foundation

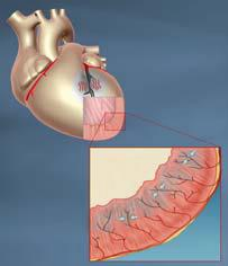
Other imaging techniques used on hearts removed from the body reveal the vast network of vessels unseen by the angiogram. This image shows the microvessels in a pig's heart.

Plaque
deposit



Diagnosis of microvascular?



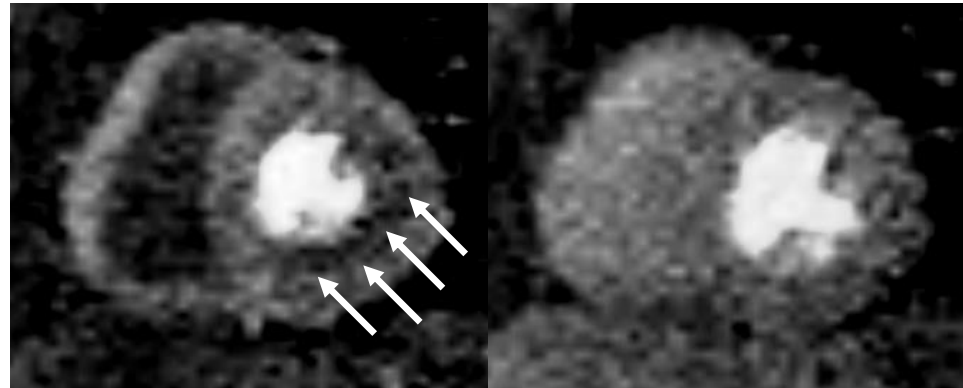


Diagnosis of microvascular?

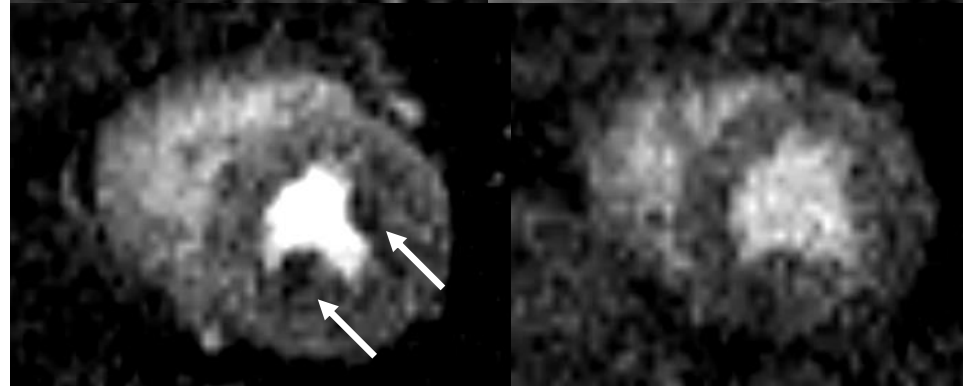
Stress Perfusion

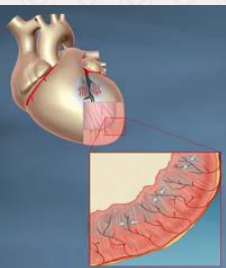
Rest Perfusion

Patient A



Patient B





Facts: Women & Heart Disease



- Only 37% of young women believe that heart disease can be different for women compared to men
- Only 28% of women know that heart disease and stroke are the leading cause of women's death worldwide
- Only 20% of women's doctors talk to them regularly about their heart health

Ms. Understood

Women's hearts are victims of a system that is ill-equipped to diagnose, treat and support them



The Future



- Build awareness
- Invest in women
- Empower women
- Emphasize more research in women
- Create dedicated Women's Heart Health Centers



British Columbia
Women's Heart
Health Network

Heart Program
for Women
(BCWH)

Cardiac Rehab
for Women
(VGH)

Leslie Diamond
Women's Heart
Health Clinic (VGH)

Cardiac Obstetrics
Clinic
(SPH)

Cardiologists	✓	✓	✓	✓
Nurse/NP	✓		✓	✓
Dieticians		✓	✓	
Exercise therapists		✓		
Counselors/SW	✓	✓	✓	✓
MOAs	✓	✓	✓	✓
Affiliations	Gyne/Endocrine	Psychiatry	Interventional Card	Obs/MFM/Genetics

Q&A

Panel:

- Dr. Simon Pimstone
- Dr. Liam Brunham
- Dr. John Mancini
- Dr. Tara Sedlack

Small-Group Discussions

- Two rounds of conversation
- Choose your topics
 - Approx. 15 people per group
- Law of two feet
- Move to new topic for Round 2
 - Review the notes from Round 1
- Reconvene here after Round 2
 - Report-back

Operating Values

- Respect is our guiding principle
- One person speaks at a time
- We balance “air time”
- We welcome different perspectives and opinions
- We respect the confidentiality of this space, not attributing comments to an individual or sharing identifiable information

Small-Group Discussion Topics

Topic	Question
Cardiovascular Research	What topics related to heart disease in adults under age 55 are most important for researchers to focus on?
Social Supports	What are some social supports that you rely on, in relation to your experience with cardiovascular disease?
Mental Health	How has your emotional well-being changed after you or a loved one was diagnosed with heart disease?
Lifestyle Changes	What are some things that might help you make changes to your lifestyle?
Education	Where do you go to get information about heart disease?
Open Discussion	As a patient / family member interested in cardiovascular health, I think researchers and clinicians should consider...

Small-Group Discussion Locations

Topic	Room
Cardiovascular Research	LSC 1330
Social Supports	LSC 1416
Mental Health	LSC 1410
Lifestyle Changes	LSC 3
Education	LSC 1510
Open Discussion	LSC 1 (here)

Small-Group Discussion Topics

Topic	1 st Question
Cardiovascular Research	What topics related to heart disease in adults under age 55 are most important for researchers to focus on?
Social Supports	What are some social supports that you rely on, in relation to your experience with cardiovascular disease?
Mental Health	How has your emotional well-being changed after you or a loved one was diagnosed with heart disease?
Lifestyle Changes	What are some things that might help you make changes to your lifestyle?
Education	Where do you go to get information about heart disease?
Open Discussion	As a patient / family member interested in cardiovascular health, I think researchers and clinicians should consider...