MANAGEMENT OF ACUTE AND STABLE ISCHAEMIC HEART DISEASE IN PREGNANCY

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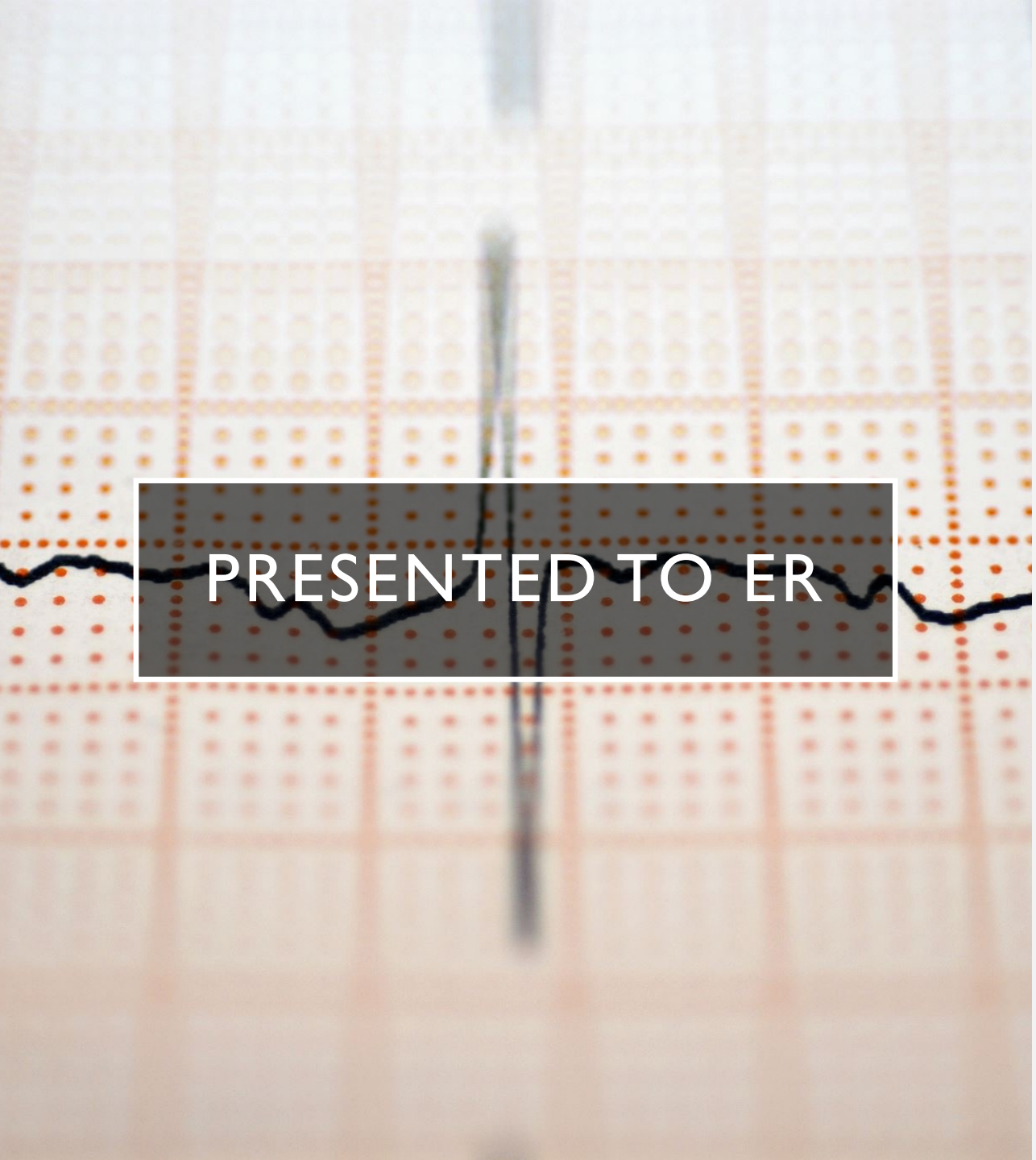
A BIT ABOUT ME

- Canadian Obstetric Internist
- ISOM Secretary
- Trained in Winnipeg (IM) and Providence, RI, USA (Obstetric Medicine)
- Work at Foothills Medical Centre in Calgary, Canada in GIM and OBIM
  - Medical consultation in pregnancy: HTN, VTE, cardiac disease, etc.
  - I am NOT a Cardiologist – no CCU, I do <u>not</u> CATH anyone
- Research in OBIM: Cardiac Disease, Thrombosis, HTN, Medical Education
- Contributor to the biannual Cardiac Problems in Pregnancy (CPP) Meetings since 2012

CASE

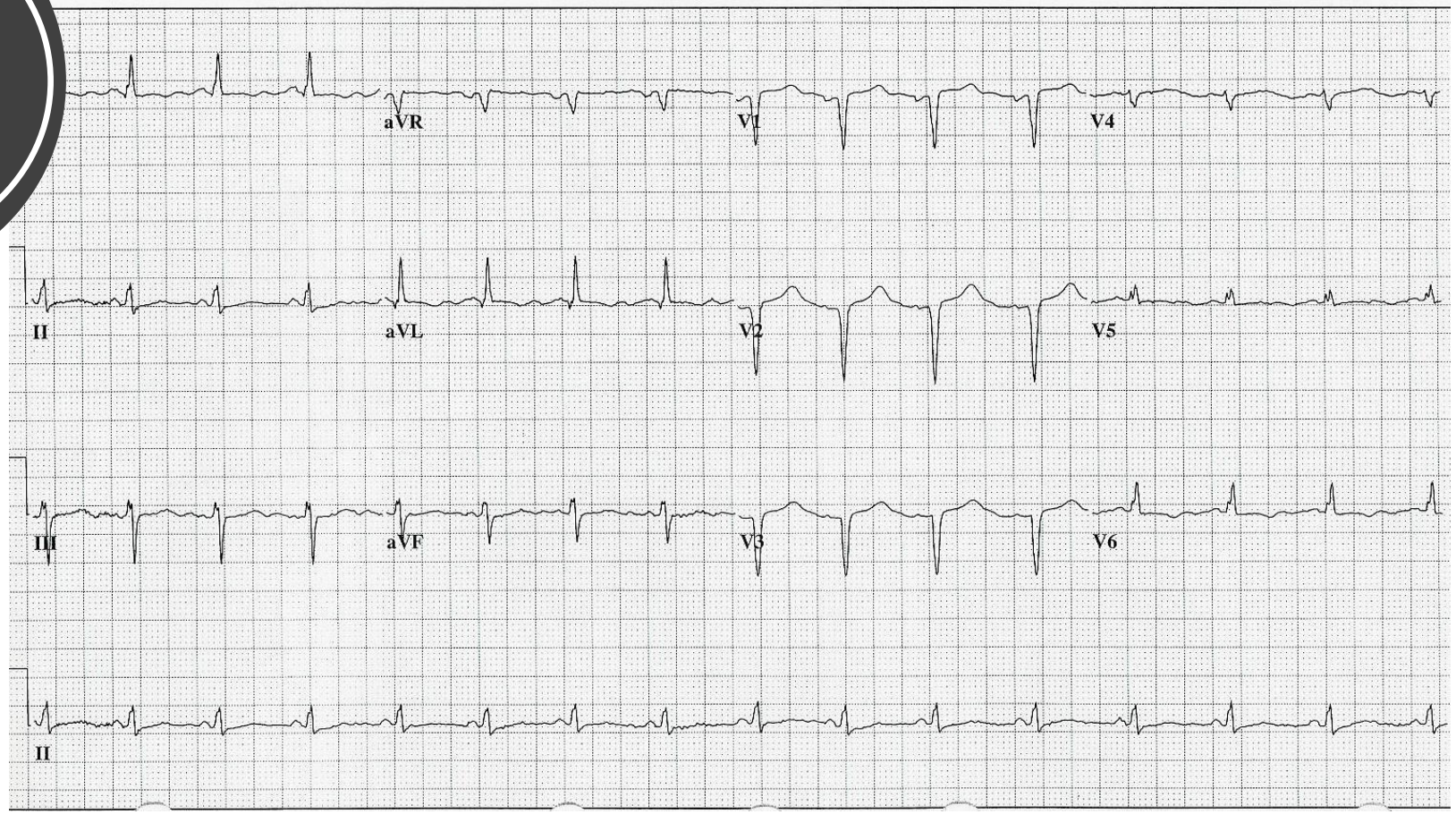
- 35 year old woman, G1P0 @ 22 weeks gestation
- Transferred from rural ER with c/o persistent chest pain
- PMH: cHTN, hypothyroidism, anxiety/depression, mild asthma
- Smoker ½ PPD
- Father had MI at age 40
- Meds: nifedipine, levothyroxine, mirtazipine, salbutamol PRN



PRESENTED TO ER

- Retrostrernal ('squeezing') CP with radiation to left arm and back
  - diaphoretic, nauseous
- BP=111/73, RR=24, HR=100 – equal pulses in both arms
- Sats initially 95% on R/A
- Heart sounds normal, lungs clear
- No calf swelling/tenderness
- FHR=145

EKG



LABS

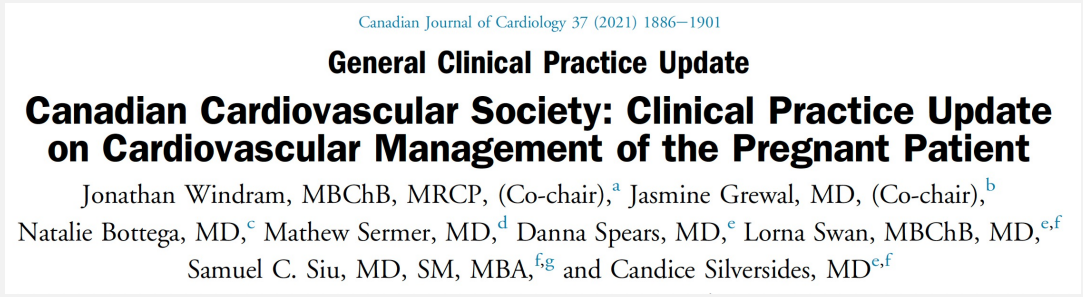
- Lytes N
- Cr=56
- Glucose=7.5
- PT/PTT=N
- D-dimer negative
- CXR normal (including mediastinum)

➢ HS-Troponin T = 425 ng/L (<5)

QUESTIONS

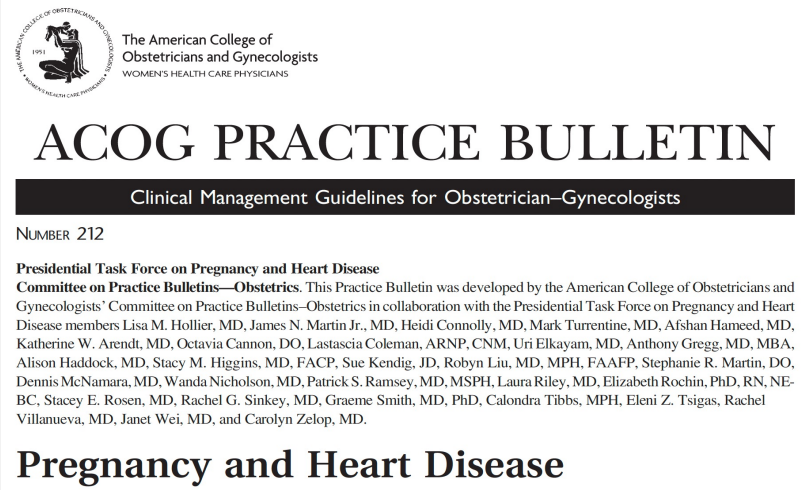
- What is the most likely cause(s) of her chest pain?
- What are the causes of elevated Troponin in pregnancy?
- What tests are safe?
  - Can she/should she have a coronary angiogram? Is PTCA +/- stenting on option?
- Which medications are recommended?
- What to do for antepartum care and peripartum management? Future pregnancy?

SOURCES OF GUIDANCE

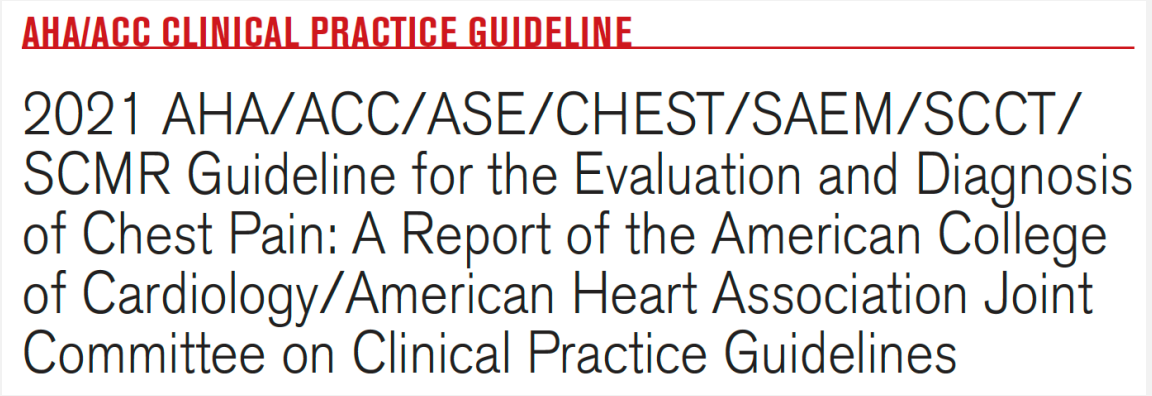


Canadian Journal of Cardiology 37 (2021) 1886e1901

Circulation. 2020;141:e884–e903.



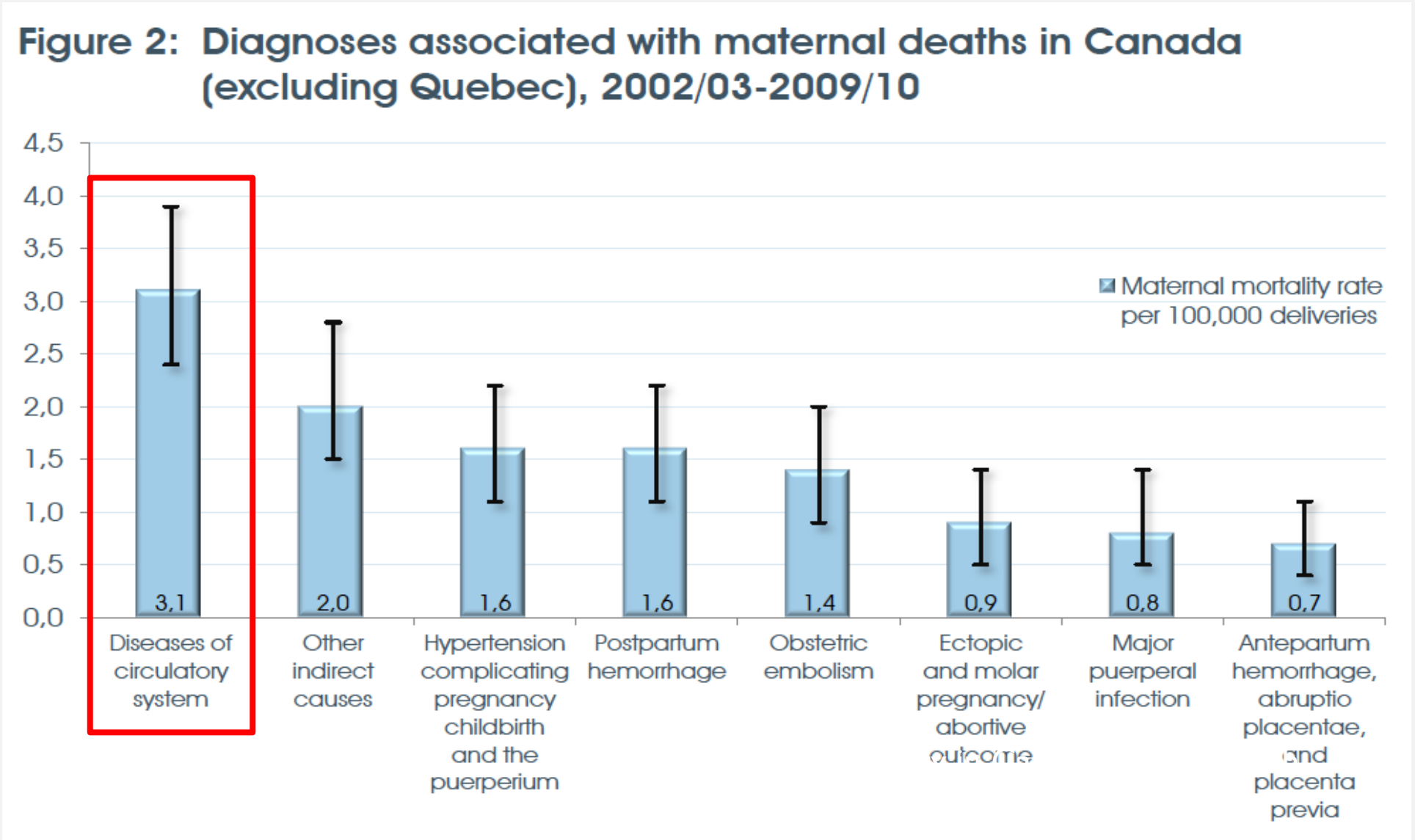
Obstetrics & Gynecology, VOL. 133, NO. 5, May 2019



Circulation. 2021;144:e368–e454

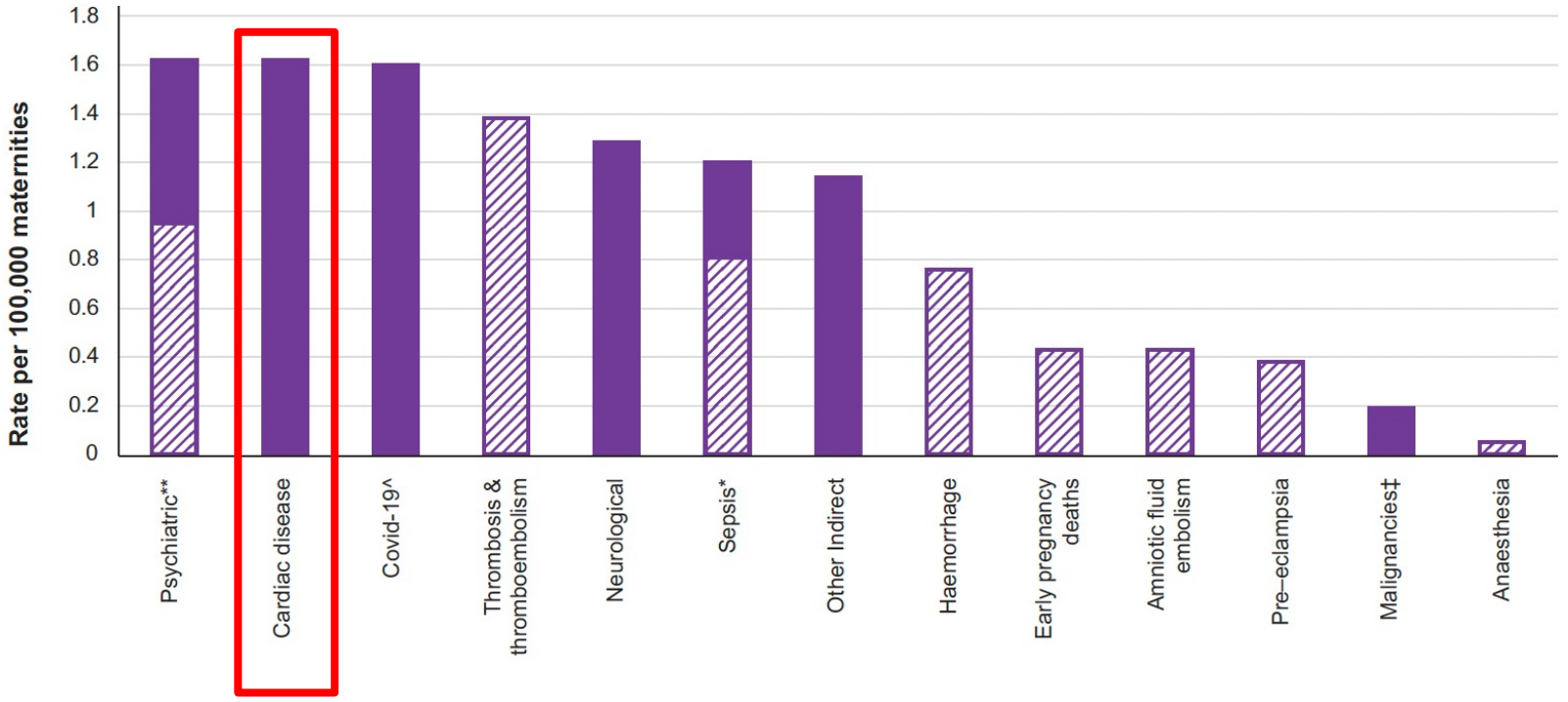
WHY IS THIS TOPIC IMPORTANT?

MATERNAL MORTALITY DUE TO CVD



MATERNAL MORTALITY DUE TO CVD

Figure 2.3: Maternal mortality by cause 2018-20

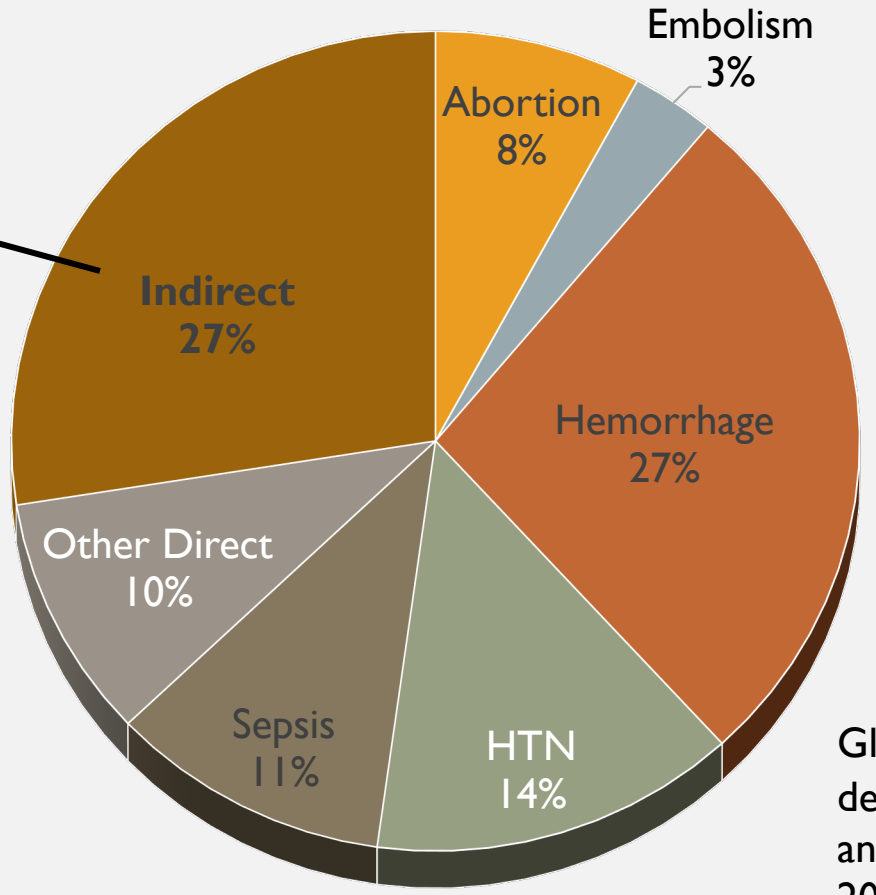


- Cardiac disease a <u>leading cause</u> of maternal mortality in developed countries

WORLDWIDE CAUSES OF MATERNAL MORTALITY

Indirect = 27.5%
An increase from 20% in 2000 (due to reduction in direct causes of maternal mortality)

14.8% were due to 'pre-existing medical conditions' including **CVD**

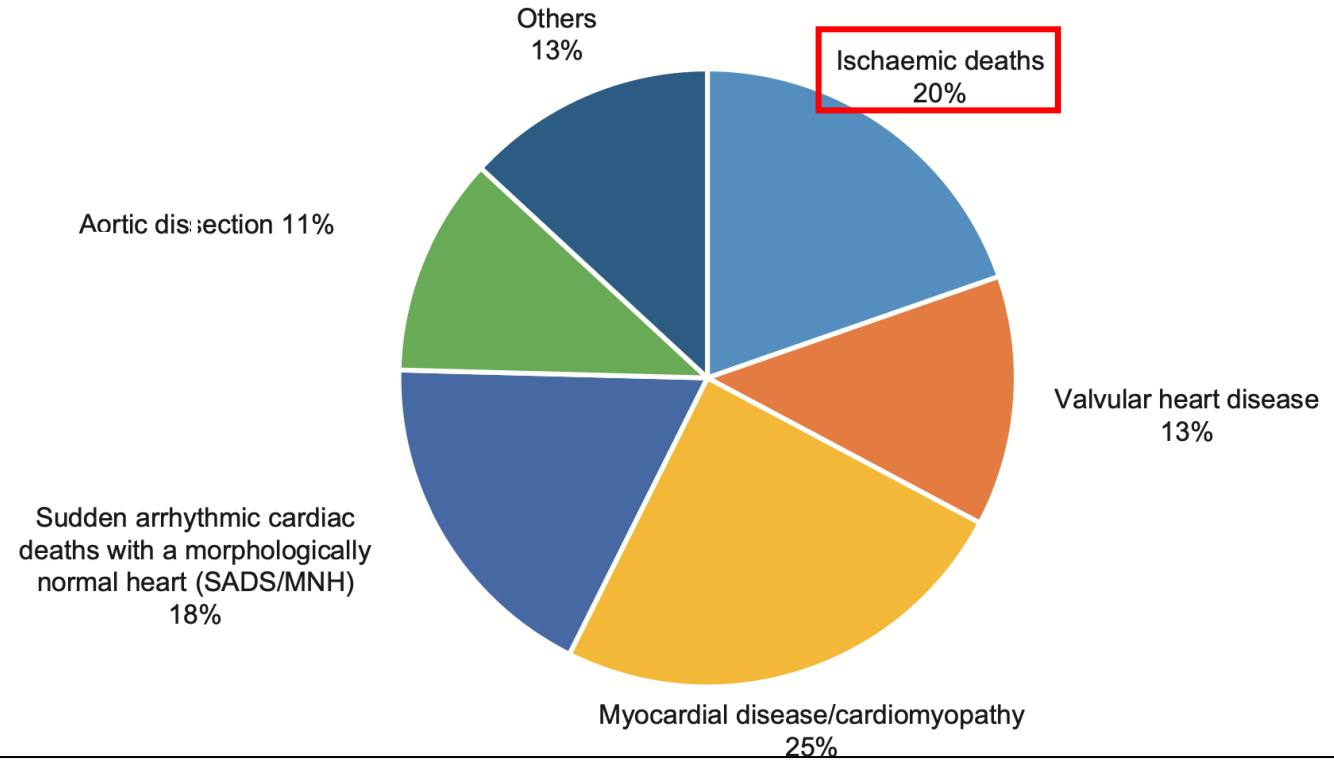


Cardiac disease is an important and increasing global cause of maternal morbidity and mortality

Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health 2014;2: e323–33

MYOCARDIAL INFARCTION IS A LEADING CAUSE OF MATERNAL CARDIAC MORTALITY

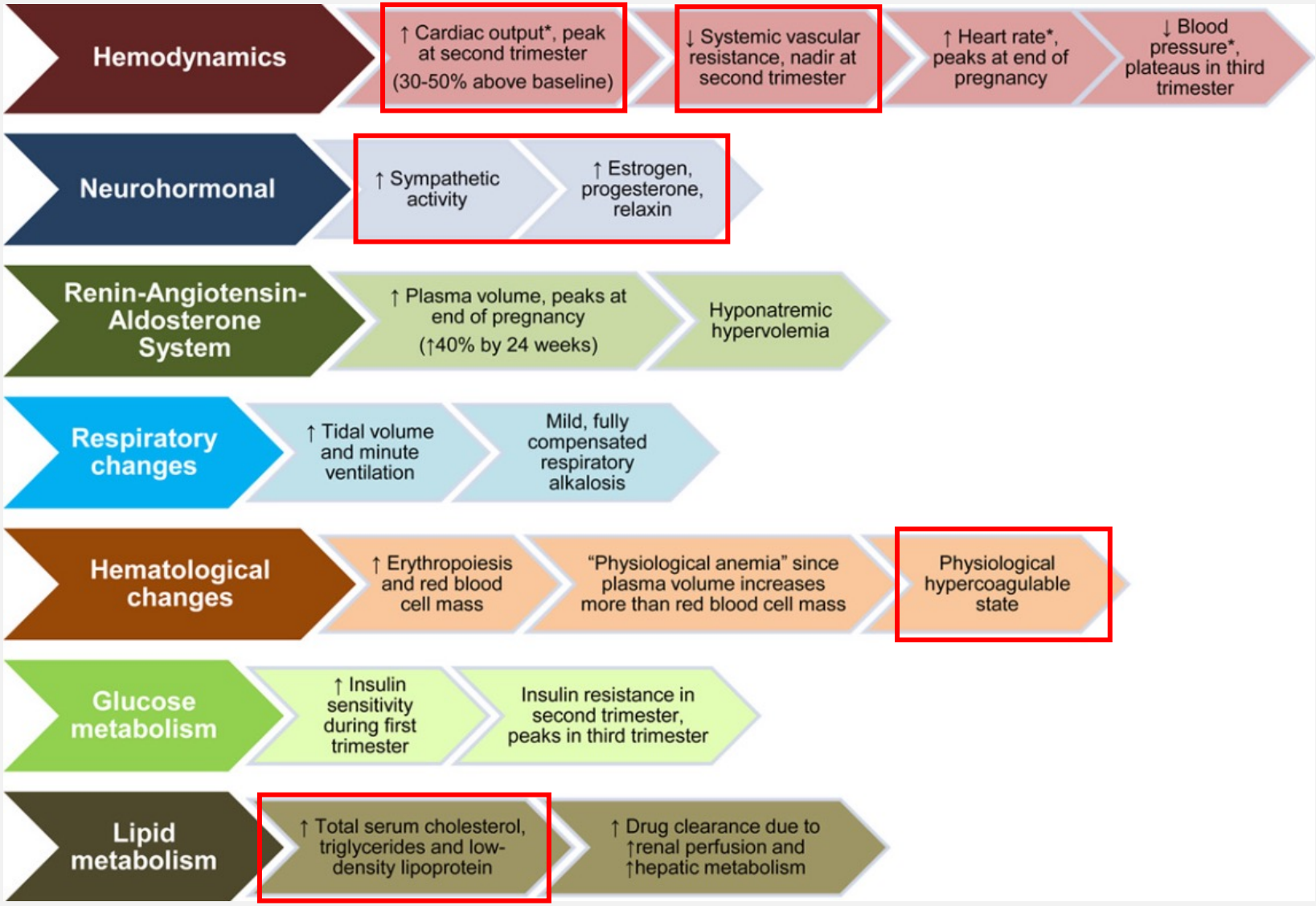
Figure 5.2: Causes of cardiovascular deaths, UK and Ireland 2018-20



"Ischaemic heart disease is often overlooked as a diagnosis in the maternity population and there needs to be a high index of suspicion in order to promptly detect and effectively institute treatments"

MI IS 3-5 FOLD MORE COMMON IN PREGNANCY – WHY?

What physiologic changes occur in normal pregnancy? (which might unmask, or lead to the new onset of, ischemic heart disease)?



Circ Cardiovasc Interv. 2020; 13:e008687

What hemodynamic and hemostatic changes occur in normal pregnancy? (which might unmask, or lead to the new onset of, ischemic heart disease)?

- **CAD:** increased HR, myocardial contractility, O2-demand, higher lipids, hypercoagulability
- **SCAD**: hormone-mediated changes to arterial media, shearing forces
- **Coronary Thrombosis/Embolism**: hypercoagulability, hemostatic agents for peripartum bleeding
- **Coronary Spasm**: vasoconstrictor medications for peripartum bleeding, preeclampsia
- **Demand Ischemia**: anemia/bleeding, severe illness

MINOCA

- *'Myocardial infarction in the absence of obstructive coronary artery disease'*
  - *ie. no coronary artery stenosis ≥ 50% in any major epicardial vessel on angiography'*

Mechanisms:

- *Vasospasm*
- *Coronary embolism/thrombosis*
- *SCAD (some cases)*
- *Supply-Demand mismatch*
- *Plaque disruption*
- *Coronary microvascular disease*

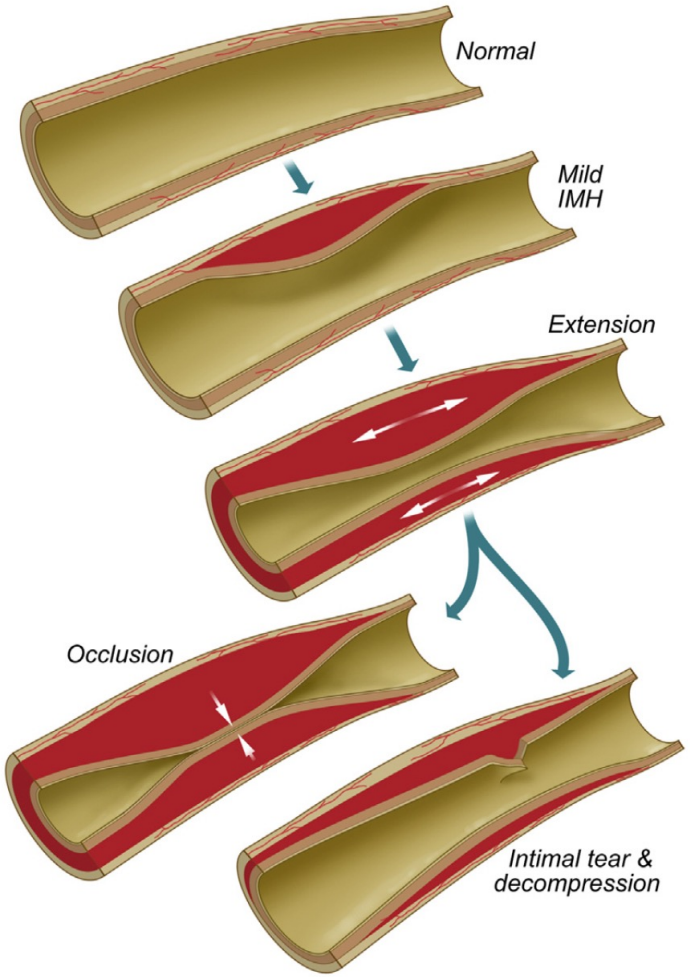
Women are less likely to manifest central chest pain

- pain in the upper back, arm, neck, and jaw, unusual fatigue, dyspnea, indigestion, nausea/vomiting, palpitations, weakness, 'sense of dread'

- **What about pregnancy?**

SCAD

- Prevalence ~ 4% of (all) patients presenting with ACS
  - the underlying cause of up to 35% of all ACS cases in women <= 50 years of age
- Patients with SCAD have lower rates of traditional cardiovascular risk
  - ➢ influenced by: sex, hormonal fluctuations, underlying arteriopathies, genetics, and environmental, physical, and emotional precipitants



JACC, VOL. 76, NO. 8, 2020

WHAT DO WE KNOW ABOUT PAMI: DATA FROM CASE SERIES

Various case reports & case series:

- Comprehensive description of risk factors, mechanisms and treatments received
- Non-consecutive patients = selection/publication bias

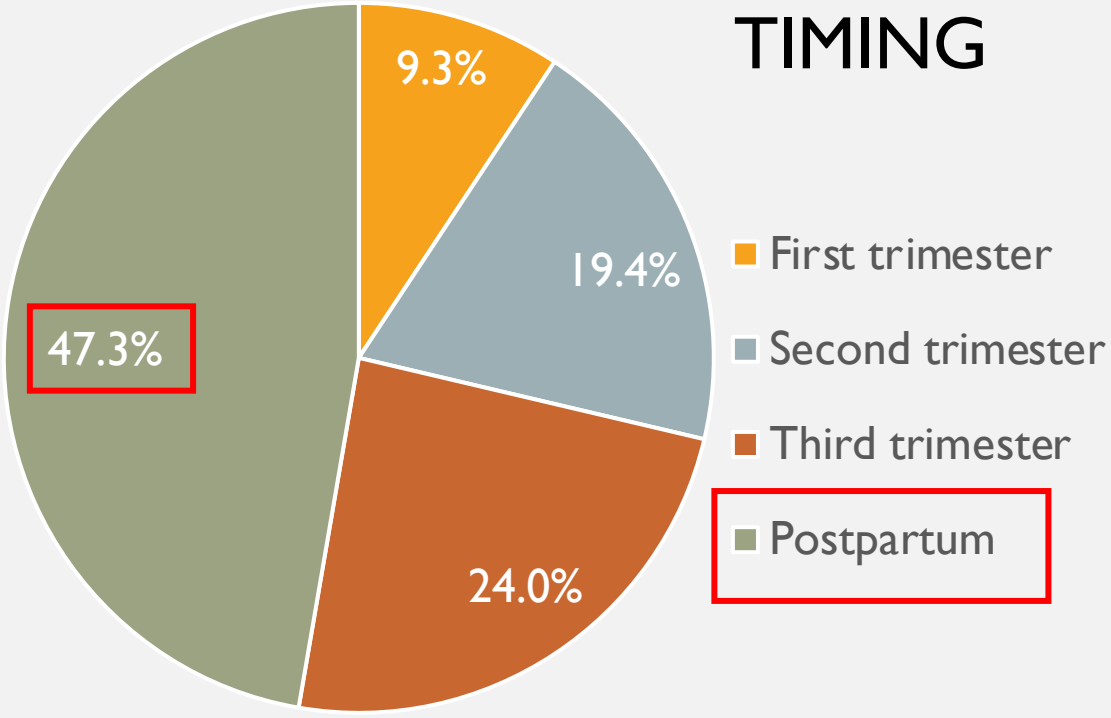
Pregnancy-Associated Acute Myocardial Infarction

A Review of Contemporary Experience in 150 Cases Between 2006 and 2011

Uri Elkayam, MD; Sawan Jalnapurkar, MD; Mohamad N. Barakkat, MD; Nudrat Khatri, MD; Angela J. Kealey, MD; Anil Mehra, MD; Arie Roth, MD

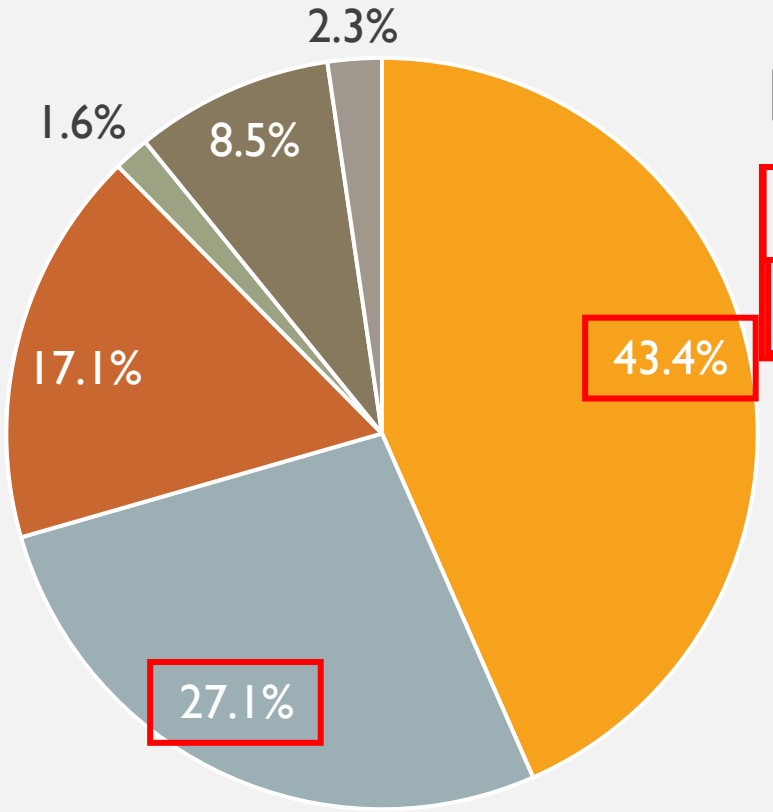
Circulation. 2014 Apr 22;129(16):1695-702.

PAMI – ELKAYAM CASE SERIES



TIMING

- First trimester
- Second trimester
- Third trimester
- Postpartum



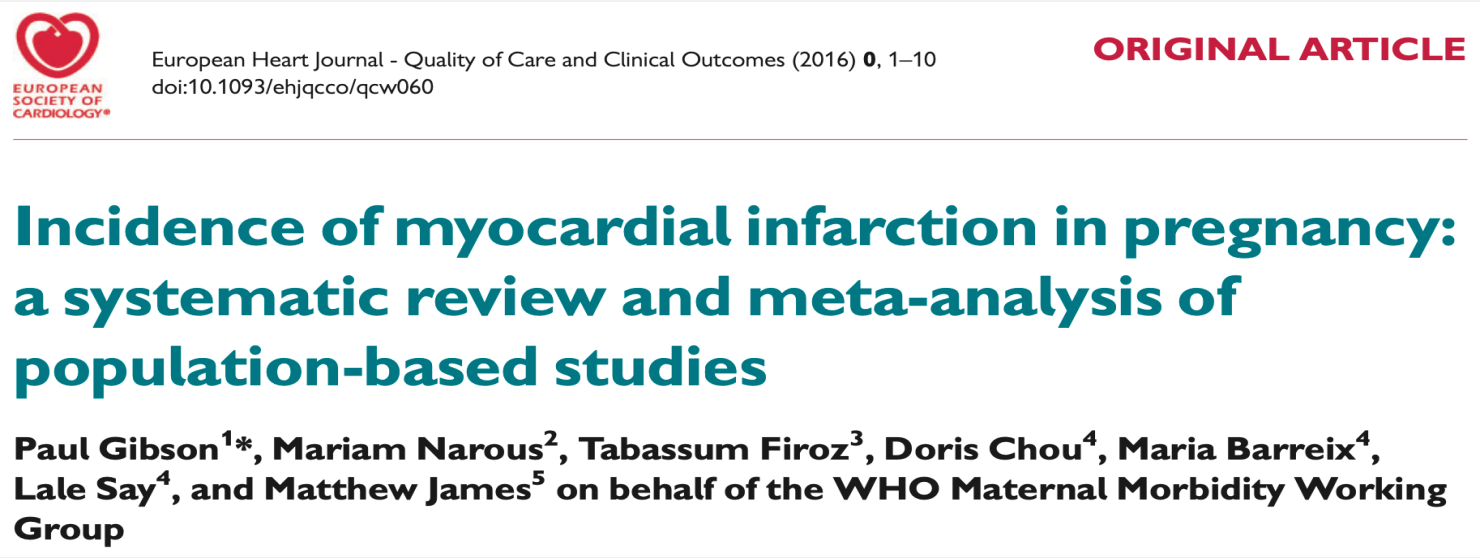
MECHANISM

- Coronary dissection
- CAD — 70%
- Thrombosis
- Spasm
- Normal coronaries
- Takotsubo

Circulation. 2014 Apr 22;129(16):1695-702.

PAMI: POPULATION-BASED STUDIES

- A number of large, database-derived studies
  - Provide information on epidemiology of PAMI



European Heart Journal - Quality of Care and Clinical Outcomes (2016) **0**, 1–10
doi:10.1093/ehjqcco/qcw060

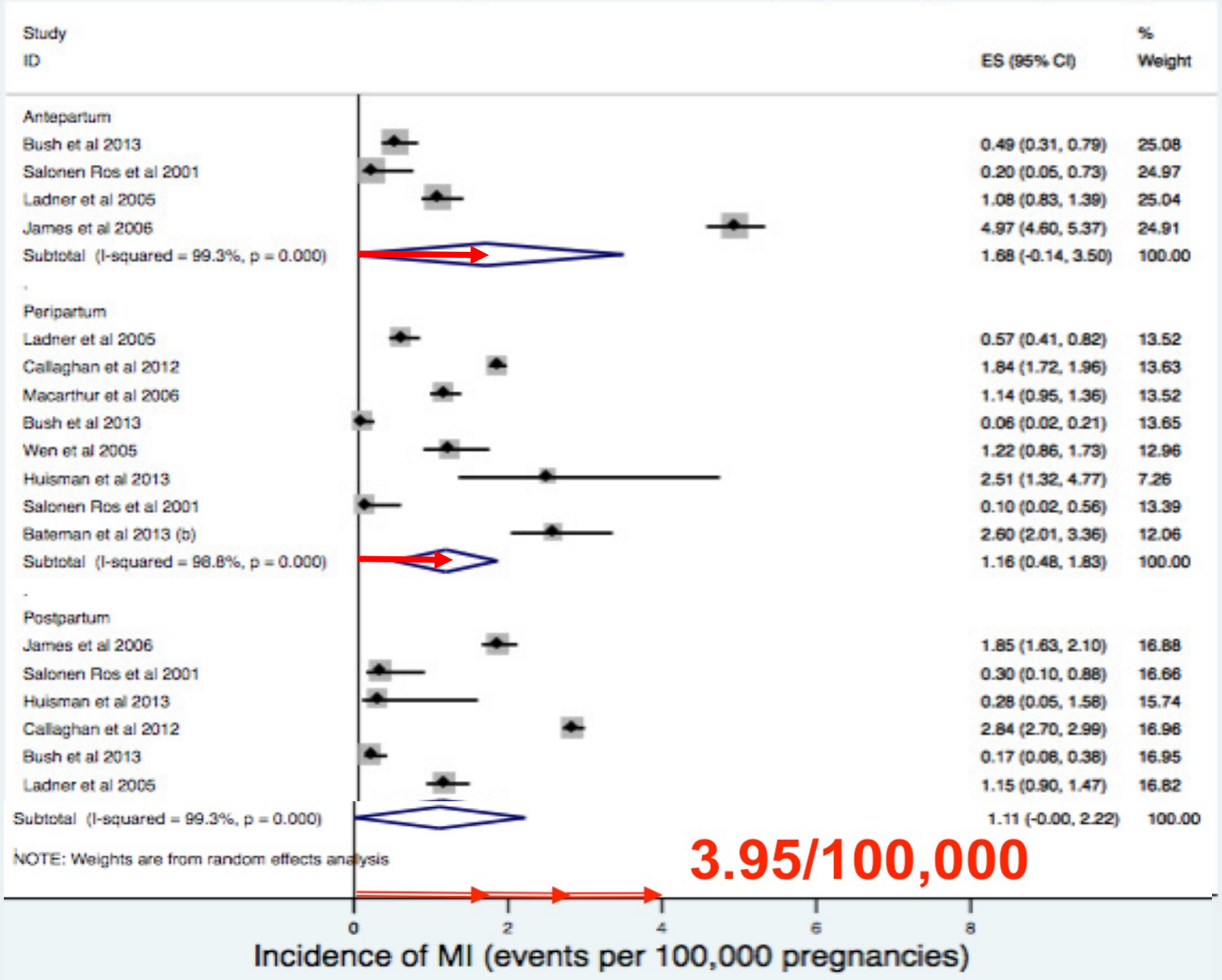
ORIGINAL ARTICLE

Incidence of myocardial infarction in pregnancy: a systematic review and meta-analysis of population-based studies

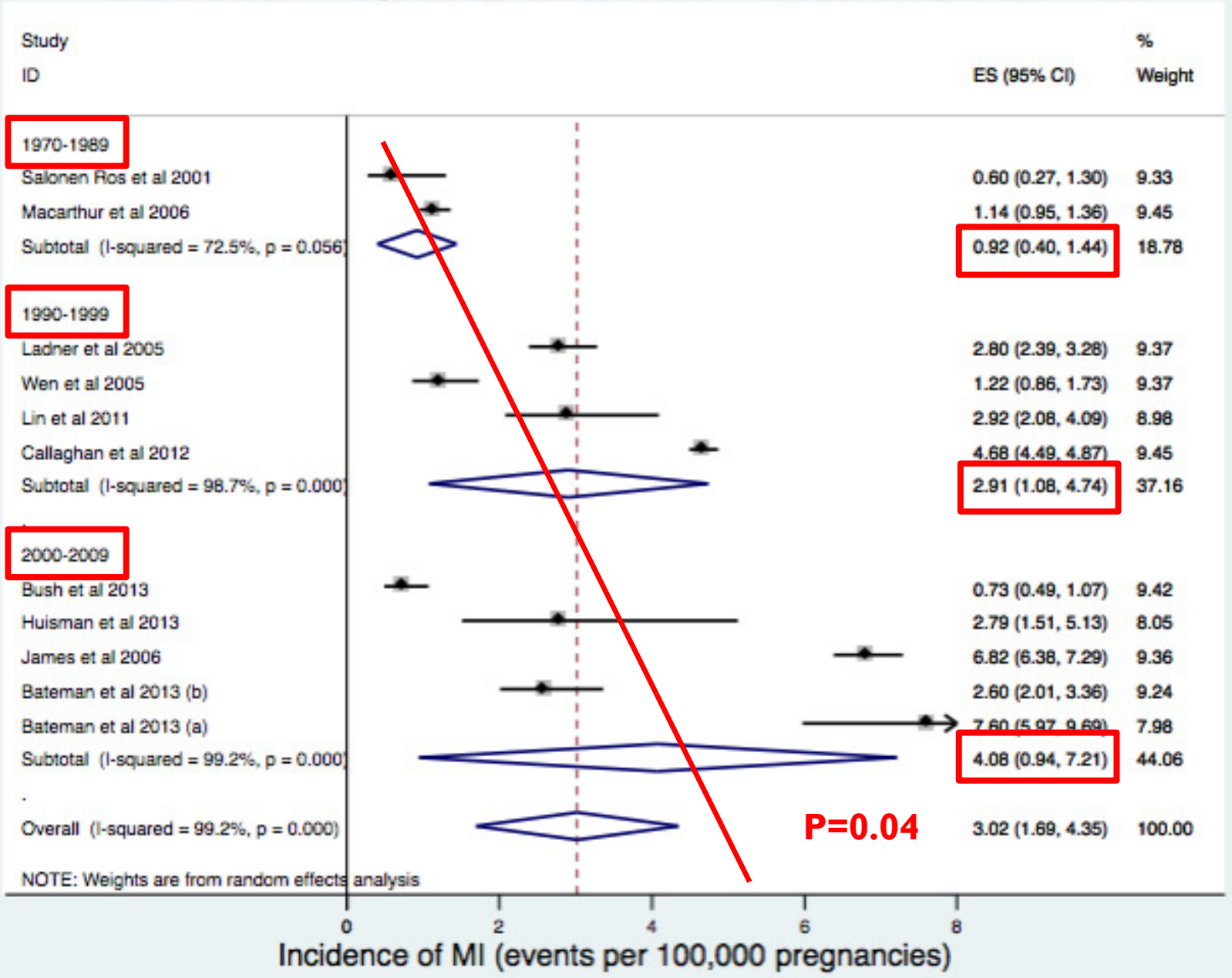
Paul Gibson[1]*, Mariam Narous[2], Tabassum Firoz[3], Doris Chou[4], Maria Barreix[4], Lale Say[4], and Matthew James[5] on behalf of the WHO Maternal Morbidity Working Group

European Heart Journal - Quality of Care and Clinical Outcomes (2016):1-10.

Incidence of Pregnancy-Associated MI, by Pregnancy Stage

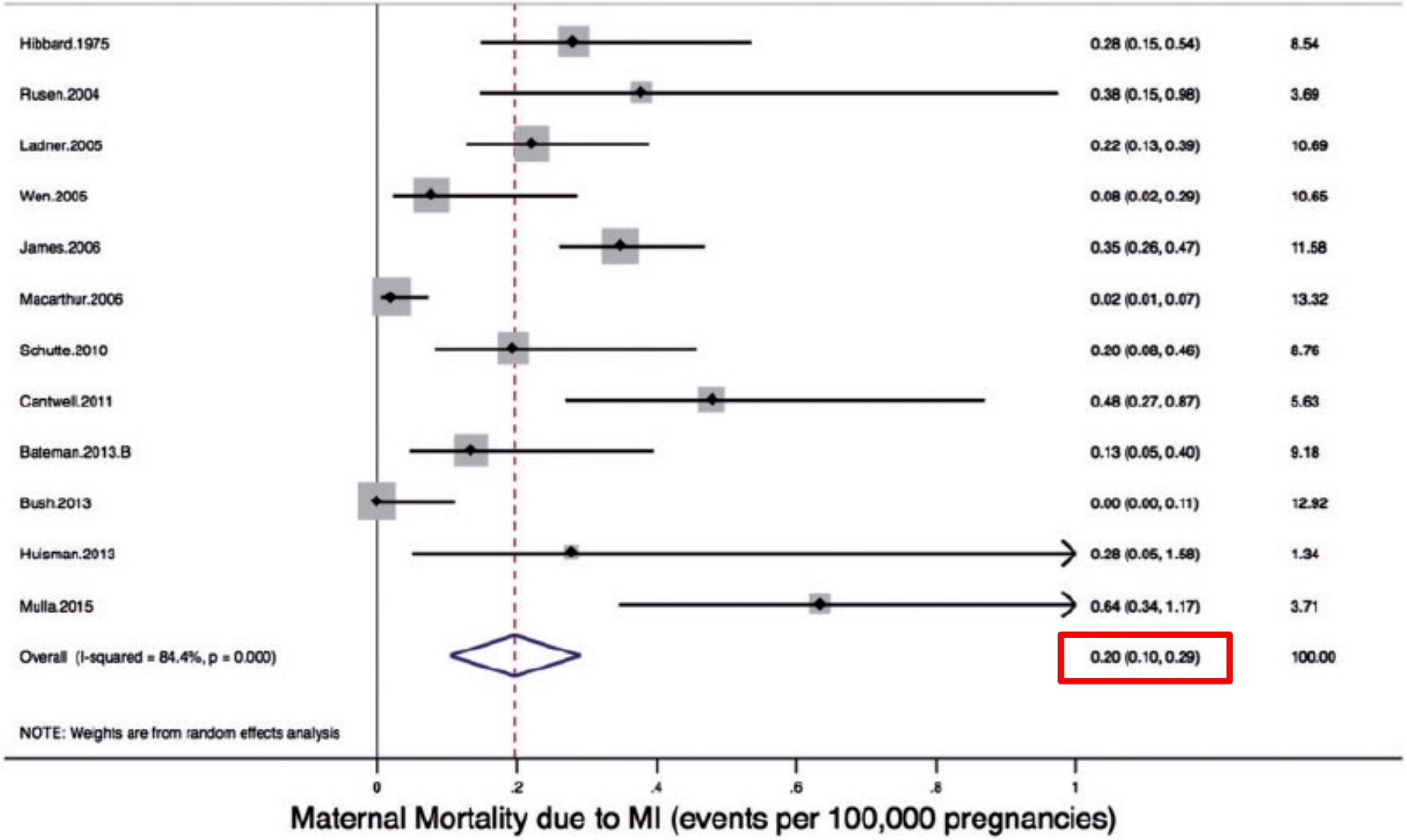


Incidence of Pregnancy-Associated MI, by Study Start Date

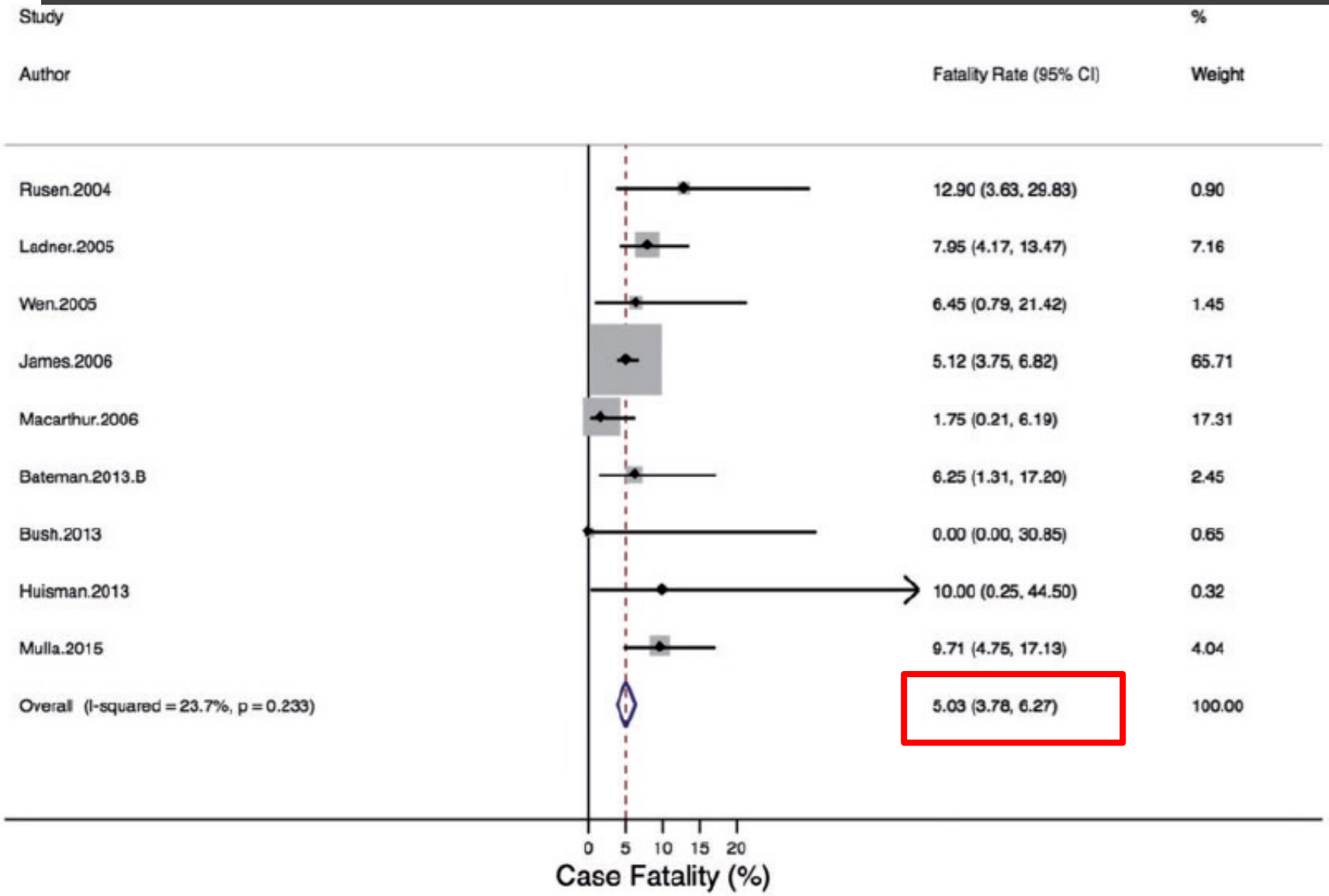


Increasing prevalence of PAMI over time

MATERNAL MORTALITY FROM PAMI: 0.2 PER 100,000



CASE FATALITY: 5%



KEY FINDINGS IN SR

- The incidence of pregnancy-associated MI was 3-4/100,000 pregnancies
  - Appears to be higher in the USA, increasing over the last 30 years
  - Fairly equally distributed between antepartum, peripartum, and postpartum
    - Higher day-to-day risk peripartum and postpartum
- The incidence of maternal mortality due to MI is about 0.2/100,000 pregnancies; case-fatality rate of ~ 5%
- **Limitations**
  - **Lack of sensitivity (missed cases)**
  - **Lack of detail on MI characteristics, risk factors and treatment received**

CONSECUTIVE CASE SERIES: 2003-2017, ALBERTA, CANADA (GIBSON ET AL, IN SUBMISSION)

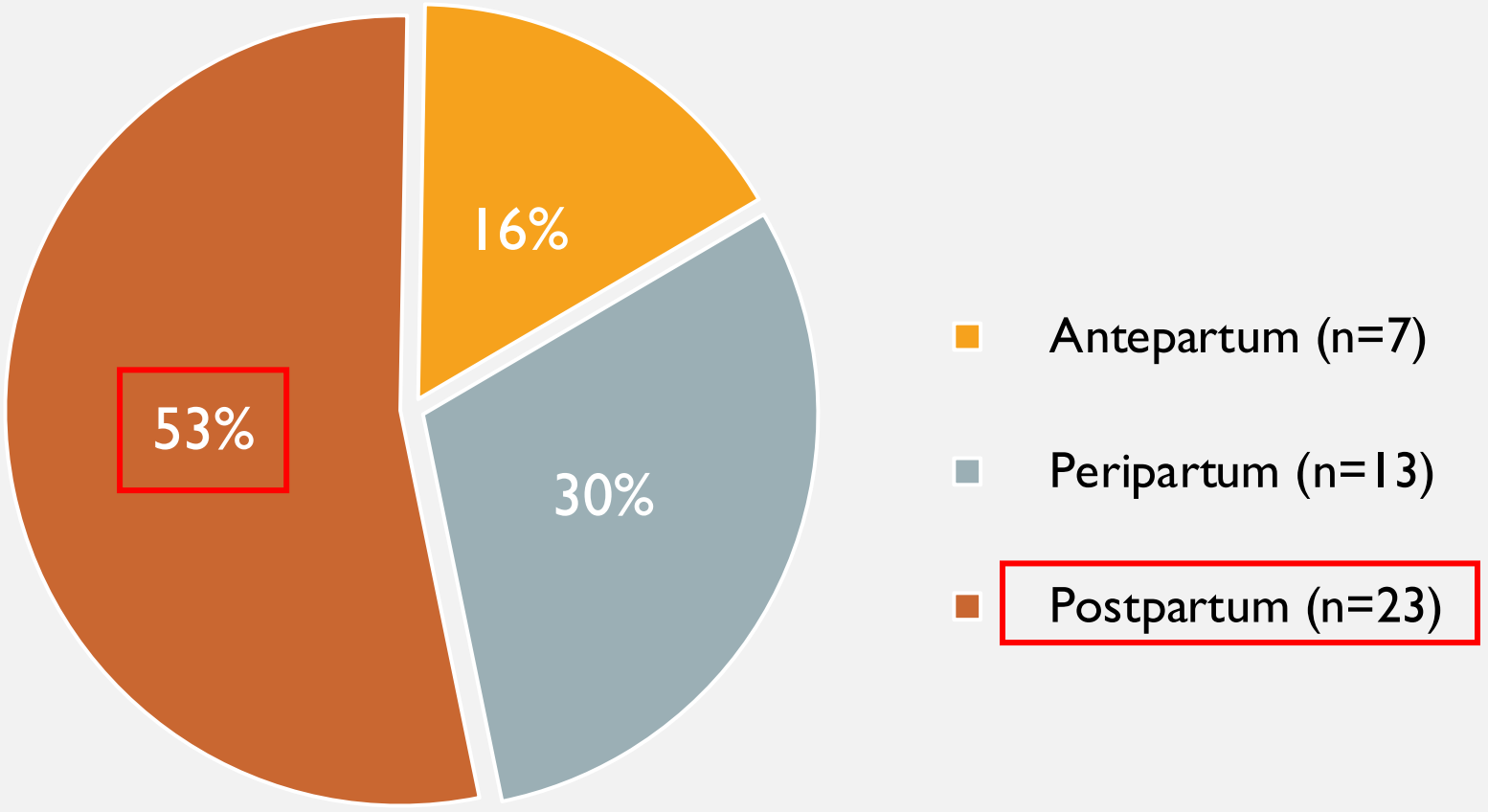
- Consecutive case series of a large population (> 4M)
- Identified by corporate data and review of maternal mortality cases, as well as linkage to provincial angiography/CCU database (high sensitivity)
- ➢ Robust data collection over time (17 years)
- Cases validated by original record review
  - Confirmed 'real' PAMI
  - Original angiographic images reviewed (when available)
- Details of testing, treatment and outcomes collected

CONSECUTIVE CASE SERIES: 2003-2017, ALBERTA, CANADA (GIBSON ET AL, IN SUBMISSION)

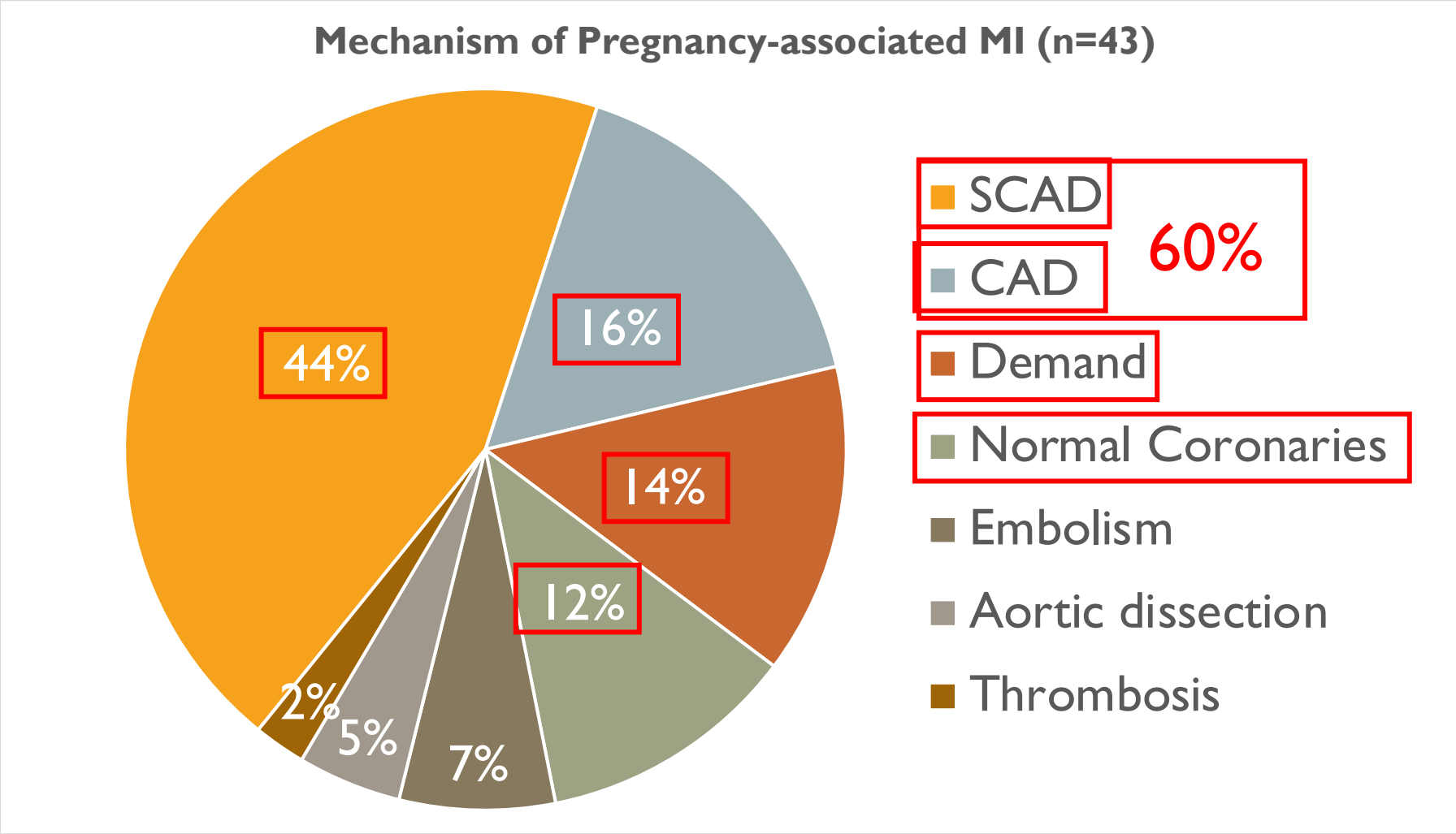
Main Findings:

- N=43 cases of PAMI (2003-2017)
  - Crude incidence of ~ **5.64/100,000 births**
- Rates of PAMI increased over the study period
- Maternal mortality was ~ 9%

TIMING OF PAMI



MECHANISM OF PREGNANCY-ASSOCIATED MI



Mechanism of Pregnancy-associated MI, by timing

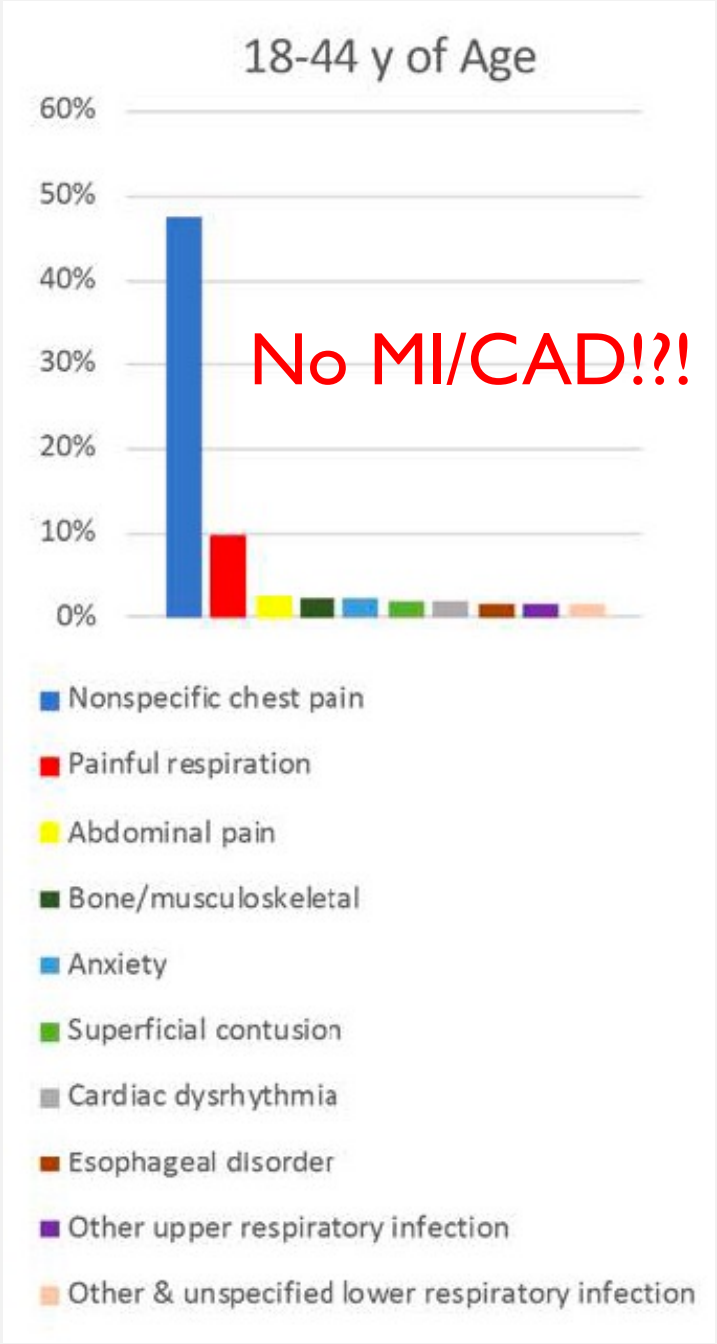
Antepartum (n=7)	Peripartum (n=13)	Postpartum (n=23)
CAD (43%)	Demand (38%)	SCAD (74%)

Demand Ischemia		
Prolonged peripartum hypotension d/t regional anesthesia		
HELLP/DIC/pulmonary edema		
Severe anemia from massive peripartum hemorrhage (x3)		
Fatal antepartum acetaminophen overdose		

DDX FOR CHEST PAIN

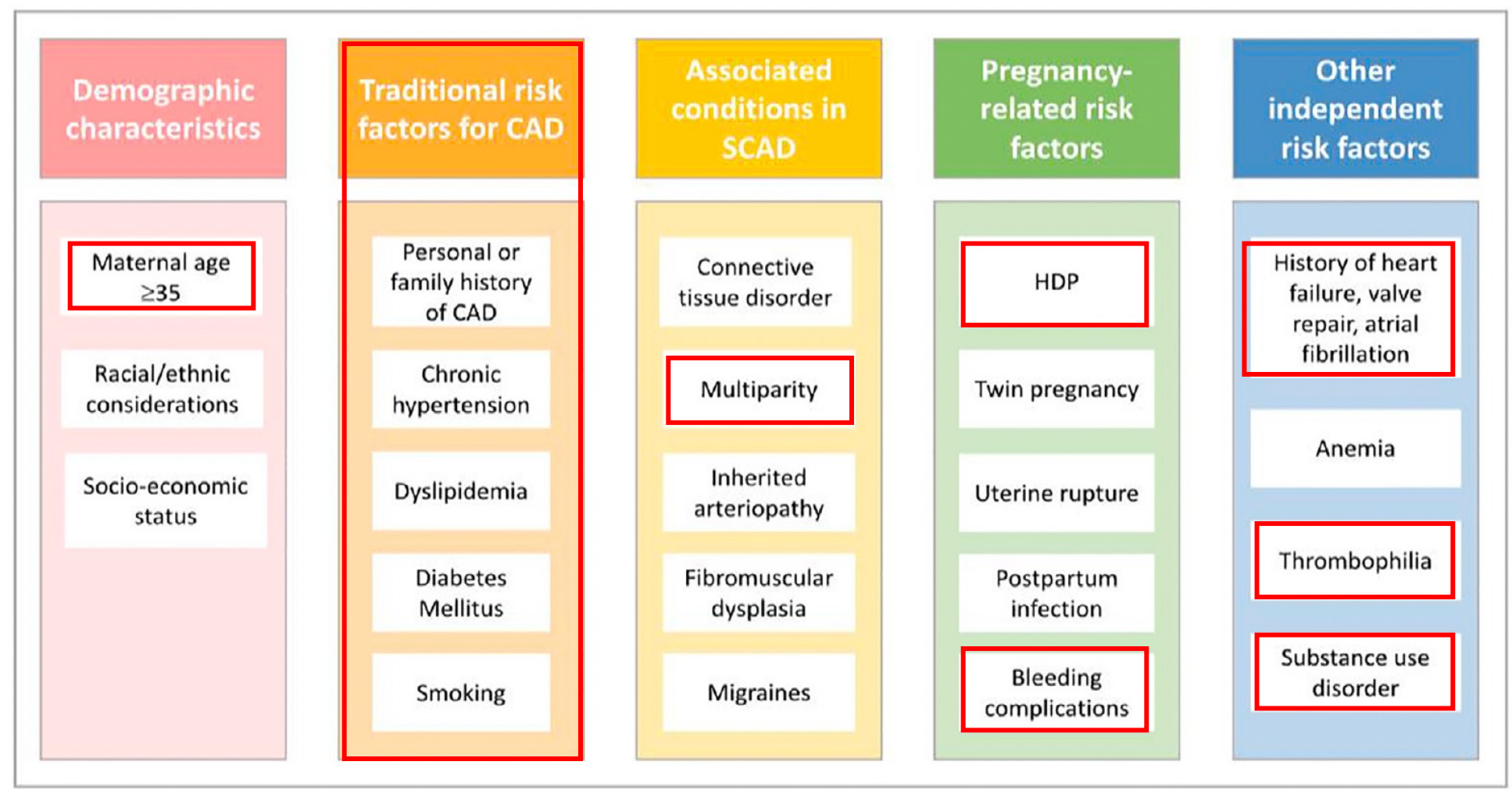
MANY causes in pregnancy …

- GERD
- MSK
- DO NOT want to miss
  - MI
  - PE
  - Aortic dissection



Circulation. 2021;144:e368–e454

RISK FACTORS FOR PAMI



Curr Prob Cardiol, Nov 2022

APPROACH TO SUSPECTED MI IN PREGNANCY

Ischemic Heart Disease

Preconception Red Flags

- Established vascular disease
- Previous coronary event
- Evidence of residual ischemia
- Left ventricular dysfunction
- Hypertension, Dyslipidemia, Diabetes, Smoking
- Family history of premature coronary artery disease

Red Flags During Pregnancy

- Acute chest pain
- Escalating exertional symptoms
- Reduction in left ventricular ejection fraction
- Elevated troponin
- New ischemic electrocardiographic changes

➢ Need to maintain 'high index of suspicion'

Canadian Journal of Cardiology
37 (2021) 1886e1901

https://www.heart.org/-/media/Images/News/2023/November-2023/1106SSAIElectrocardiogram_SC.jpg?sc_lang=en

EKG CHANGES IN PREGNANCY

Normal Changes in Cardiac Exam and Testing during Pregnancy and Delivery	Abnormal Cardiac Exam and Testing during Pregnancy and Delivery
• Q waves in leads III and aVF • T wave inversions in leads III, V1 – V3 • Transient ST depressions with cesarean delivery	• ST elevations • ST depressions that are persistent or occur in the setting of chest pain • T wave inversions, especially if deep and/or present in leads other than V1 – V3

Circ Cardiovasc Interv. 2020;13:e008687

WHAT ABOUT BIOMARKERS?

TROPONIN LEVELS IN NORMAL PREGNANCY

High-Sensitivity Troponin T and I Among Pregnant Women in the US—The National Health and Nutrition Examination Survey, 1999-2004

JAMA Cardiol. 2023;8(4):406-408

- hs-cTn levels were comparable among pregnant and nonpregnant women across all trimesters (and across 4 different assays)
- Pregnant women did not have elevated hs-cTn levels compared with nonpregnant women, before or after adjustment for demographic and clinical factors
  - **pregnancy alone does not result in significant changes in troponin levels**

WHAT ABOUT IN PREECLAMPSIA

Cardiac-specific troponins in uncomplicated pregnancy and pre-eclampsia: A systematic review

Plos One, 2021

- Found that HS-TnI levels were higher in women with preeclampsia than in those with an uncomplicated pregnancy
  - Patients with pregnancy-induced hypertension (median 11 ng/L) and pre-eclampsia (mean 12ng/L) had higher concentrations of cardiac troponin compared with normal individuals (mean 1 ng/L)

➢ VERY MODEST ELEVATIONS

EXPERT PANEL

CARDIO-OBSTETRICS

The Utilization and Interpretation of Cardiac Biomarkers During Pregnancy

JACC: Advances Expert Panel

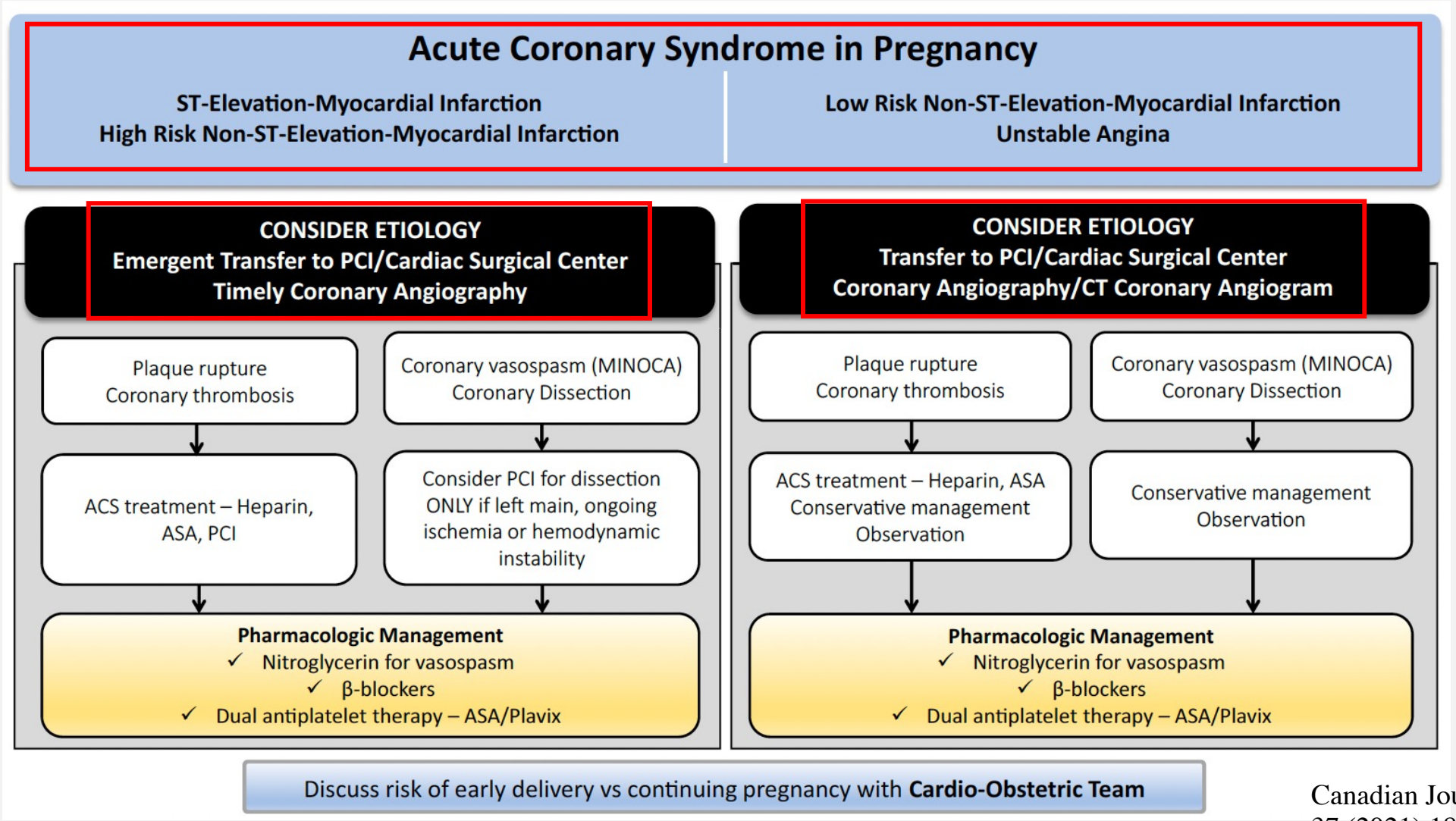
Amy A. Sarma, MD,[a,b] Niti R. Aggarwal, MD,[c] Joan E. Briller, MD,[d] Melinda Davis, MD,[e] Katherine E. Economy, MD,[b,f] Afshan B. Hameed, MD,[g] James L. Januzzi, MD,[a,b,h] Kathryn J. Lindley, MD,[i] Deirdre J. Mattina, MD,[j] Brandon McBay, MPH,[a] Odayme Quesada, MD,[k,l] Nandita S. Scott, MD,[a,b] On behalf of the American College of Cardiology Cardiovascular Disease in Women Committee and Cardio-obstetrics Work Group

- If pre-existing/suspected CV disease
  - biomarkers (troponins and NT-BNP) **retain their negative predictive value**
- Elevated natriuretic peptides and troponin may occur (without clear clinical significance) in the immediate postpartum period
- Clear elevations (in the setting of clinical suspicion) should prompt further investigation into possible CV pathology
- **Other causes**: myocarditis/PPCM, arrhythmias, PE, sepsis, renal failure, COVID-19 (ie. sensitive but NOT specific for MI)

JACC Advances: Vol 1, No 2; 2022

APPROACH TO ACS IN PREGNANCY

CCS, 2021



Canadian Journal of Cardiology
37 (2021) 1886e1901

CORONARY ANGIOGRAPHY IN PREGNANCY

Concerns:

- Fetal radiation exposure
- Procedural complications (initiation/propagation of coronary dissection)

➢ Facilitates Rx tailored to mechanism and option for immediate revascularization/stabilization

➢ Technique: prefer access via UE (radial), low-pressure injections, limited guidewire manipulation

https://tedrogersresearch.ca/app/uploads/2021/11/coronary-angiography.jpg

ESTIMATED FETAL RADIATION EXPOSURE

Estimated Fetal Dose (mGy)* According to Exam:

- Chest x-ray (2 views): 0.0005-0.01
- Chest CTA for pulmonary embolus: 0.01-0.66
- Coronary CTA (prospective gating): 1†
- Coronary CTA (retrospective gating): 3†
- Coronary angiography: 0.074
- Percutaneous coronary intervention: dependent on procedure with reports of <1
- Fluoroscopy of the groin to heart catheter passage: 0.094 to 0.244 per minute

Circ Cardiovasc Interv. 2020;13:e008687

RISKS OF FETAL RADIATION EXPOSURE FROM ANGIO

"The US National Council on Radiation Protection states that the risk of induced miscarriages or major congenital malformations in embryos or fetuses exposed to doses of

50 mGy (5 rads) or less

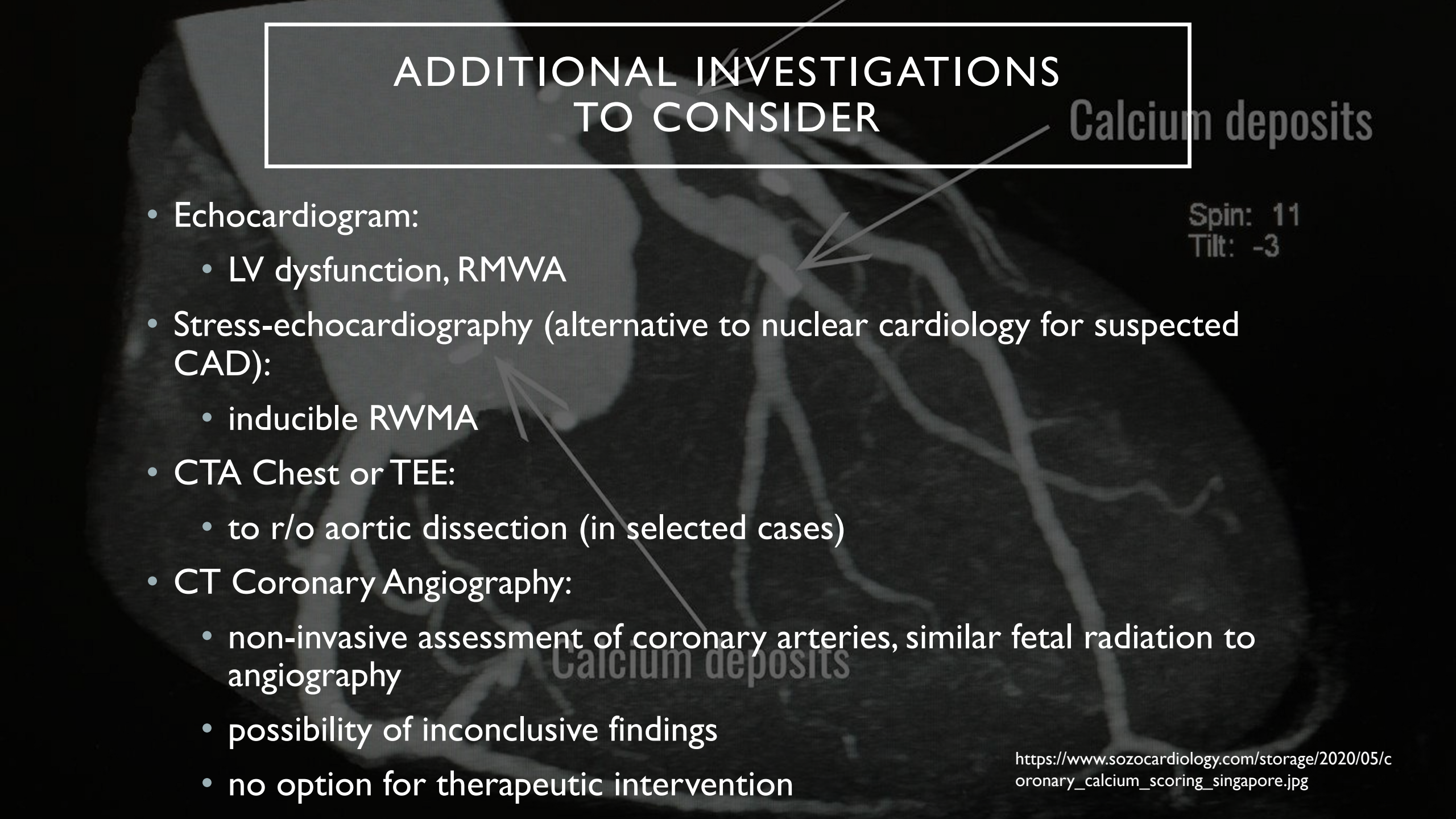
(Angio w PTCA ~1 mGy = 2%)

is negligible compared to the spontaneous risk among nonexposed women."

Koren et al., CMAJ, 2008

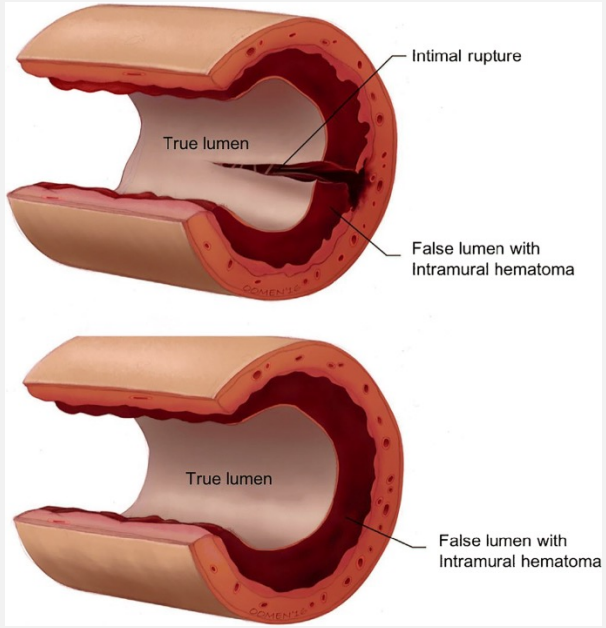
ADDITIONAL INVESTIGATIONS TO CONSIDER

- Echocardiogram:
  - LV dysfunction, RMWA
- Stress-echocardiography (alternative to nuclear cardiology for suspected CAD):
  - inducible RWMA
- CTA Chest or TEE:
  - to r/o aortic dissection (in selected cases)
- CT Coronary Angiography:
  - non-invasive assessment of coronary arteries, similar fetal radiation to angiography
  - possibility of inconclusive findings
  - no option for therapeutic intervention



https://www.sozocardiology.com/storage/2020/05/coronary_calcium_scoring_singapore.jpg

MANAGEMENT OF SCAD (AHA, 2020)



https://media.springernature.com/lw685/springer-static/image/art%3A10.1007%2Fs11883-020-00866-4/MediaObjects/11883_2020_866_Fig1_HTML.png

- Conservative (medical) management is recommended for most patients
- Radial forces generated by balloon inflation or stent expansion may broaden the dissection (resulting in procedural failure)
  - PCI should ONLY be performed for LM dissection, hemodynamic instability, recurrent chest pain, or ongoing ischemia
- Treatment: antiplatelet agents combined with β-blockers

https://assets.clevelandclinic.org/transform/e7d4ade3-65ba-443f-ac44-45332ce27114/heartMedications-1202286466-770x533-1_jpg

Drugs that are considered safe

Arrhythmia

Adenosine, Bisoprolol, Digoxin*, Lidocaine, Metoprolol, Nadolol, Propranolol

Hypertension/Heart failure

Labetalol, Methyl-dopa, Metoprolol, Nifedipine, Bumetanide, Carvedilol, Furosemide, Dobutamine, Dopamine, Norepinephrine

Anticoagulation/Antiplatelets/ Thrombolytics

Aspirin, Low molecular weight heparin, Unfractionated heparin

Drugs with limited/conflicting data/use with caution

Arrhythmia

Diltiazem, Flecainide, Procainamide, Propafenone, Sotalol, Verapamil

Hypertension/Heart failure

Amlodipine, Hydralazine, Nitrates, Nitroprusside, Hydrochlorothiazide, Metalozone, Milrinone, Torsemide

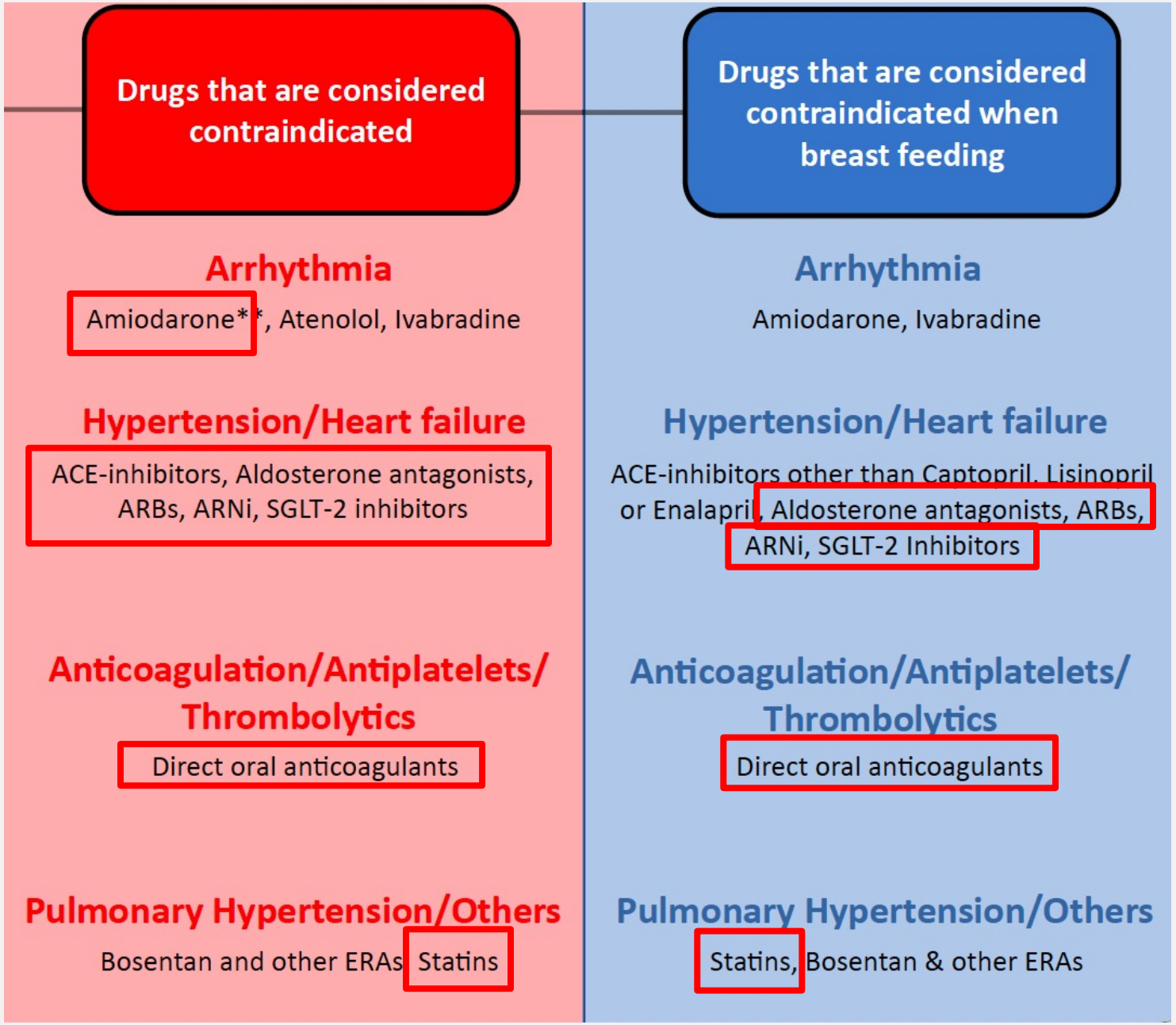
Anticoagulation/Antiplatelets/ Thrombolytics

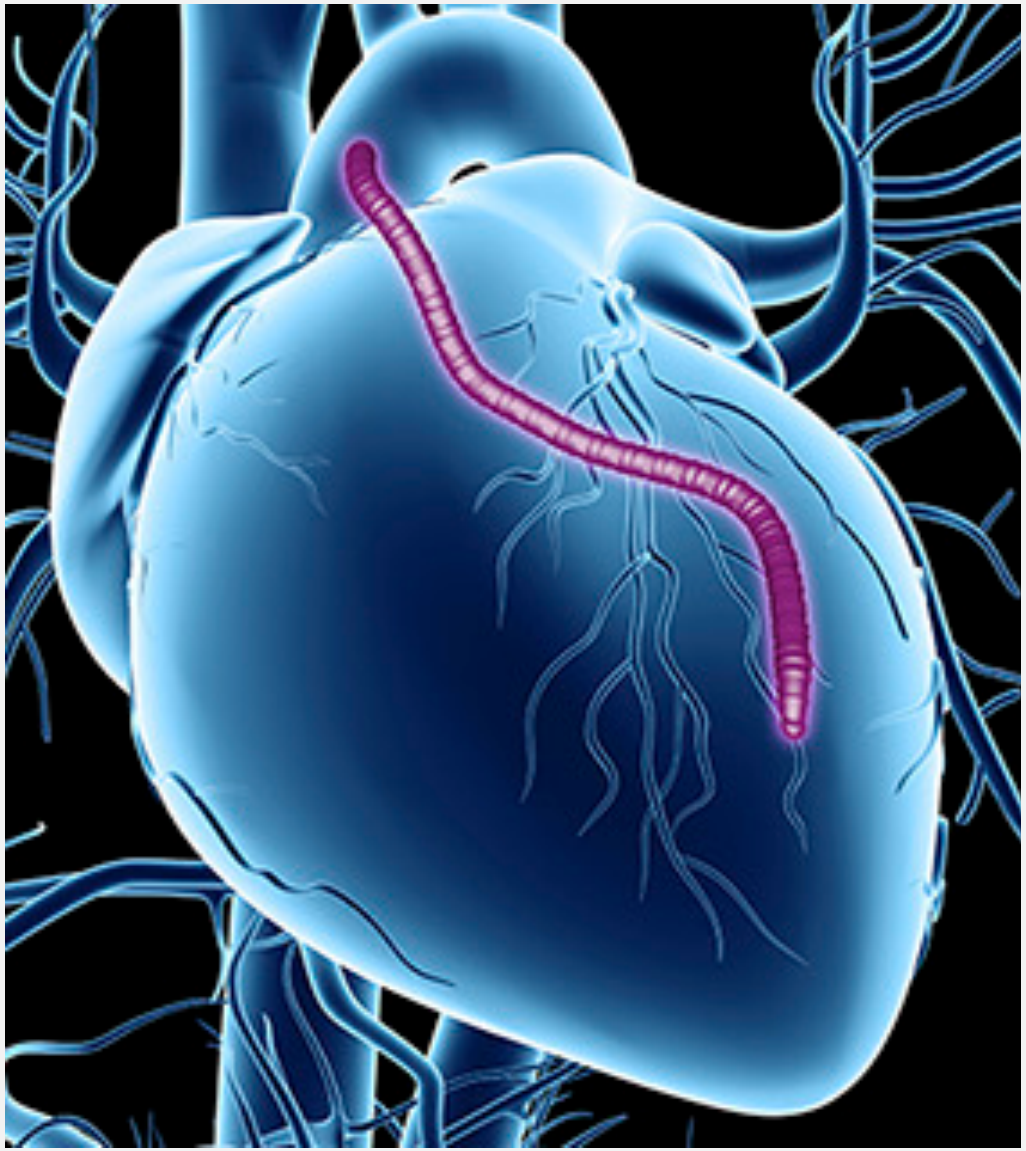
Clopidogrel, Ticagrelor, Warfarin
Argatroban, Bivalirudin, Fondaparinux
Alteplase, Streptokinase, Tenecteplase

Pulmonary Hypertension/Others

Epoprostenol, Iloprost, Sildenafil, Treprostinil

Canadian Journal of Cardiology 37 (2021) 1886e1901


Drugs that are considered contraindicated
Arrhythmia
Amiodarone**, Atenolol, Ivabradine
Hypertension/Heart failure
ACE-inhibitors, Aldosterone antagonists, ARBs, ARNi, SGLT-2 inhibitors
Anticoagulation/Antiplatelets/ Thrombolytics
Direct oral anticoagulants
Pulmonary Hypertension/Others
Bosentan and other ERAs Statins
Drugs that are considered contraindicated when breast feeding
Arrhythmia
Amiodarone, Ivabradine
Hypertension/Heart failure
ACE-inhibitors other than Captopril, Lisinopril or Enalapril, Aldosterone antagonists, ARBs, ARNi, SGLT-2 Inhibitors
Anticoagulation/Antiplatelets/ Thrombolytics
Direct oral anticoagulants
Pulmonary Hypertension/Others
Statins, Bosentan & other ERAs



https://www.uab.edu/news/images/2018/bypass_2.jpg

SURGICAL REVASCULARIZATION?

- Scattered case reports/series
- Risk of maternal mortality ~ 2%, higher if emergent
- Risk of fetal loss ~16-33%
  - may be improved with warm cardioplegia, shorter 'on pump' times and higher flow rates
- Option for "mini-thoracotomy" and CABG without cardioplegia/CPB in some cases
  - Likely to reduce risk of fetal damage/loss

➢ Largely reserved for double/triple vessel disease, SCAD of LAD or LM, failed PTCA or complication

DELIVERY AFTER ANTEPARTUM MI

- Prefer delay >= 2 weeks from cardiac event
- Mode of delivery (generally) by obstetric indications
- Individualized intrapartum plan:
  - Continue ASA and beta-blockers, hold clopidogrel x 5-7d (?)
  - Continuous cardiac monitoring (where available)
  - 'Cardiac' anesthesia = early regional w careful hemodynamics
  - Assisted/extended second stage?
  - AVOID ergots – prefer oxytocin, carboprost, misoprostil for peripartum hemorrhage
  - Consider recovery in a monitored unit (ie. CCU) if available

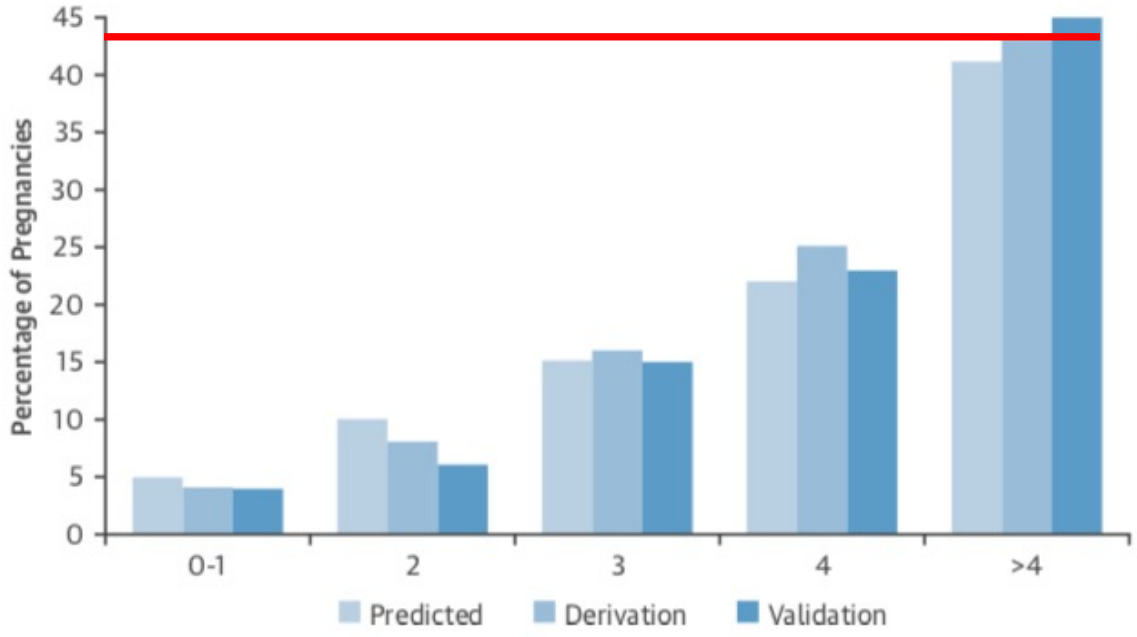
WHAT ABOUT FUTURE PREGNANCY IN WOMEN WITH CAD/PRIOR MI?

https://static5.depositphotos.com/1007995/474/i/450/depositphotos_4748447-stock-photo-worried-woman.jpg

CARPREG II

(JACC. 2018 MAY, 71 (21) 2419–2430)

FIGURE 4 CARPREG II Risk Prediction Index: Incidence of Adverse Cardiac Events Stratified According to CARPREG II Risk Scores



PREDICTOR	POINTS
Prior cardiac events or arrhythmias	3
Baseline NYHA III-IV or cyanosis	3
Mechanical valve	3
Ventricular dysfunction	2
High risk left-sided valve disease/ left ventricular outflow tract obstruction	2
Pulmonary hypertension	2
Coronary artery disease	2
High risk aortopathy	2
No prior cardiac intervention	1
Late pregnancy assessment	1

All HIGH RISK!

The CARPREG (Cardiac Disease in Pregnancy Study) II risk score is based on 10 predictors, shown in the **box.** Each predictor is assigned a weighted point score. The sum of points represents the risk score. Risk scores are categorized into the 5 groups (x-axis). The predicted **(light blue)** and the observed frequency of primary cardiac events in the derivation **(medium blue)** and validation **(dark blue)** groups are shown on the y axis. NYHA = New York Heart Association.

PREGNANCY AFTER MI

Pregnancy in women with pre-existent ischaemic heart disease: A meta-analysis, 2019 (BMJ) n=116

- 21% chance of having an uncomplicated pregnancy
  - **Obstetric complications occurred in 58%** and fetal/neonatal complications in 42%
  - **Primary (ischaemic) endpoints occurred in 9% (n=11)**
- Women with atherosclerosis had more cardiovascular complications
- There were two **(2%) maternal cardiac deaths = HIGH RISK**

PLANS FOR FUTURE PREGNANCY AFTER MI

https://www.mfmnyc.com/wp-content/uploads/2016/08/ shutterstock_154584407.jpg

- Preconception counselling is necessary
  - Assessment of:
    - Risk factors
    - EKG and echocardiographic findings
  - Optimization of cardiac risk factors
  - Residual ischemic disease should be addressed
  - Management plan for pregnancy: ASA & B-blockers
- All future pregnancies must be followed by a high-risk (CardioOB) pregnancy team

TAKE HOME POINTS

- CVD is a leading cause of maternal mortality – and PAMI is an important (and increasing) mechanism
- Pregnancy is associated with a significant (3-5X) increase in risk of MI
- The mechanism of PAMI appears to be variable (by timing in pregnancy)
  - SCAD > CAD > demand, spasm, thrombosis, embolism
- Diagnosis starts with clinical suspicion
  - then EKG, biomarkers, coronary angiography
- Treatment is ADAPTED for pregnancy
  - coronary assessment/revascularization, specific medical Rx
- There is a substantial risk of recurrent morbidity/mortality in subsequent pregnancy
  - Need VERY close assessment/monitoring by Cardio-Obstetrics team


Save the Date!
CPP 2025
The 9th International Congress on Cardiac Problems in Pregnancy
24-27 April, 2025
Vienna, Austria
CPP

THANK YOU FOR YOUR TIME AND ATTENTION!