1

MHIF FEATURED STUDY:

DAPA ACT HF

Coming soon!

EPIC message: ***Research MHIF Patient Referral***

CONDITION:	**PI:**	**RESEARCH CONTACT:**	**SPONSOR:**
Acute Heart Failure	Mosi Bennett, MD	Sarah Schwager Sarah.Schwager@allina.com | 612-863-6257	TIMI Study Group, Brigham and Women's Hospital

DESCRIPTION:

Dapagliflozin and Effects on Cardiovascular Events in Acute Heart Failure - evaluating in-hospital initiation of dapagliflozin in patients who have been stabilized during hospitalization for heart failure. All patients with heart failure, regardless of ejection fraction, are eligible to receive study medication for the two-month study follow-up.

CRITERIA LIST/ QUALIFICATIONS:

Inclusion: Acute heart failure

Exclusion:

- GFR<25
- Recent CRT, valve repair or replacement, or revascularization
- Type 1 diabetes or history of DKA

Acute heart failure is the most common cardiovascular reason for hospital admission.

HOPE DISCOVERED HERE | Minneapolis Heart Institute Foundation

2

3

University of Glasgow

Disclosures

Institutional agreements between the University of Glasgow (employer) and Abbott Vascular, AstraZeneca, Coroventis, DalCor, GSK, HeartFlow, A. Menarini Farmaceutica Internazionale, Novartis and Siemens.

Research grants from the BHF, EU and MRC

Colin Berry, 12.2021

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Objectives

1. Create awareness on small vessel disease leading to angina.
2. Describe stratified medicine, including endotypes and linked therapy.
3. Future directions: new trials, systemic disease, sex disparities, guidelines

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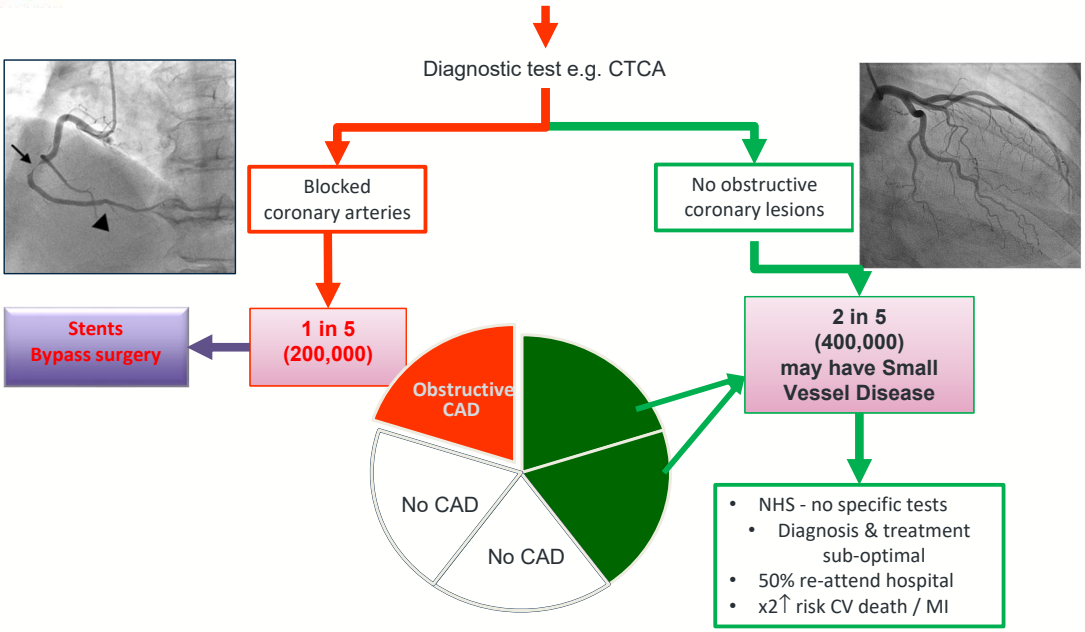
NHS **Chest Pain Clinics** **~1 million visits pa, £1 billion costs**



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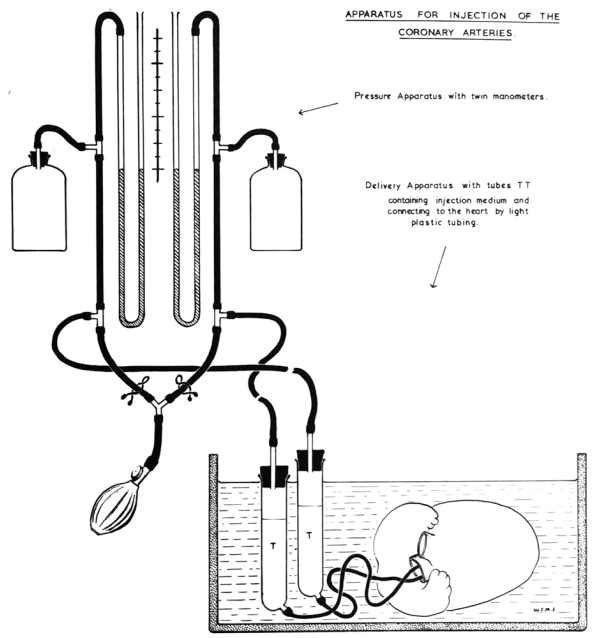
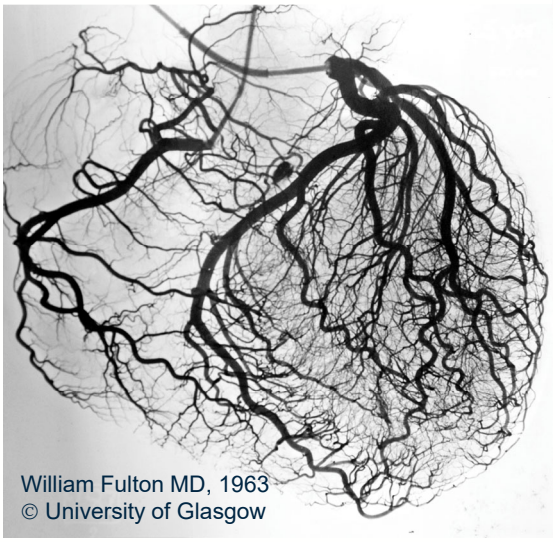
Intact perfused human heart



Human coronary circulation



3D stereo-arteriography

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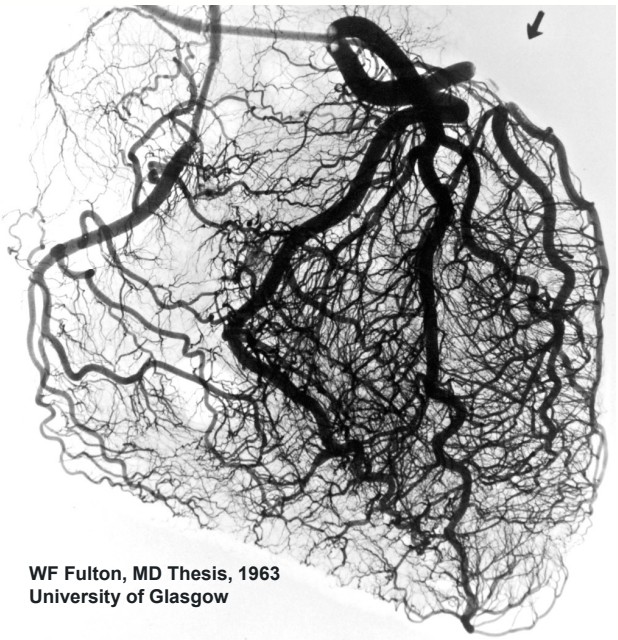
Which test first: Anatomical vs. Functional?

Anatomy

CTCA
Invasive

Microvessels invisible



WF Fulton, MD Thesis, 1963
University of Glasgow

Function

Ischaemia

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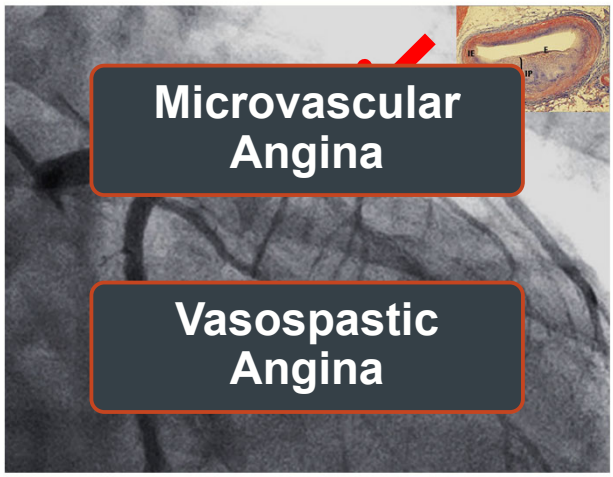
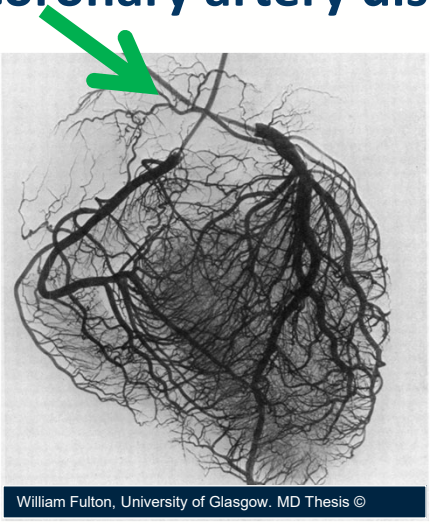
INOCA

Ischaemia and no obstructive coronary artery disease





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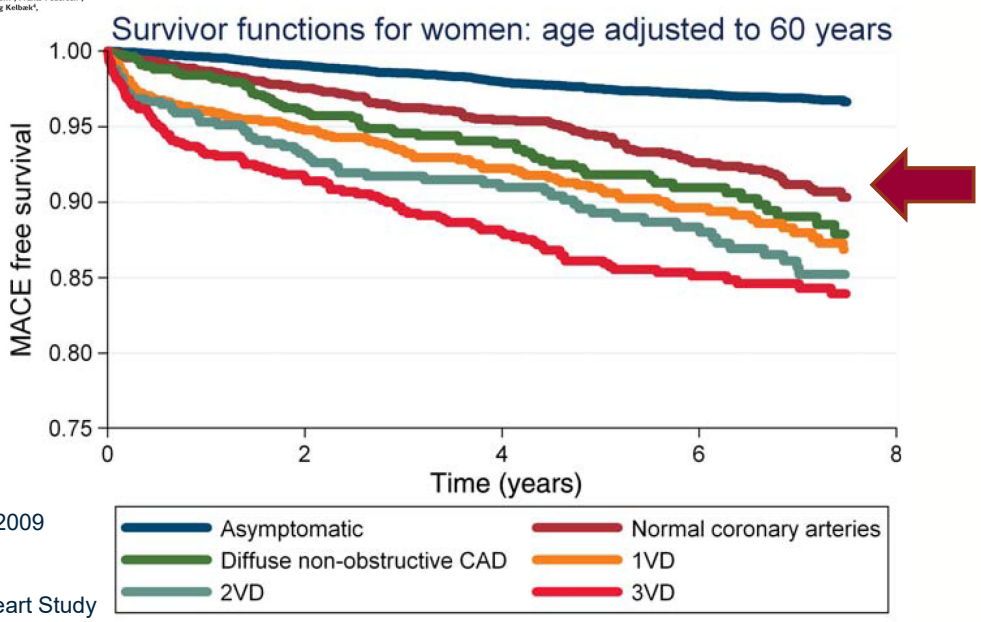
CLINICAL RESEARCH
Coronary heart disease

Stable angina pectoris with no obstructive coronary artery disease is associated with increased risks of major adverse cardiovascular events

Lasse Jespersen[1*], Anders Hvelplund[2,3], Steen Z. Abildstrøm[1], Frants Pedersen[4], Søren Galatius[1], Jan K. Madsen[3], Erik Jørgensen[4], Henning Kelbæk[4], and Eva Prescott[1,5]

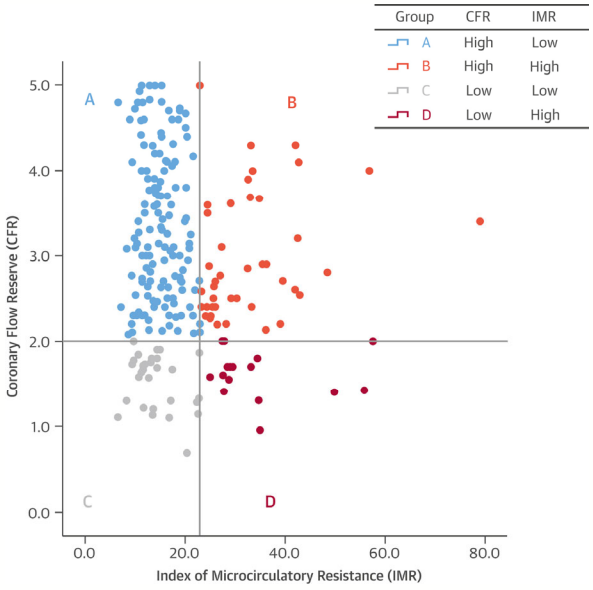
INOCA and prognosis

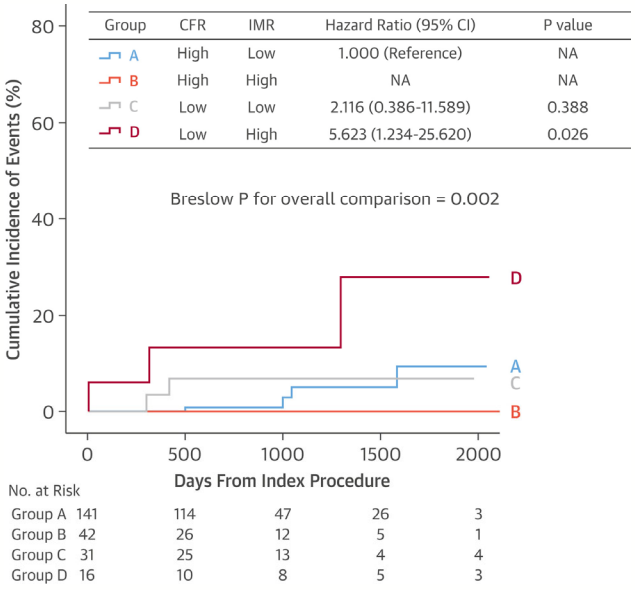


Case control study
Copenhagen,1998–2009
11,223 patients
5705 participants
Copenhagen City Heart Study

10

CFR and IMR and prognosis





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Lee JM et al JACC 2016

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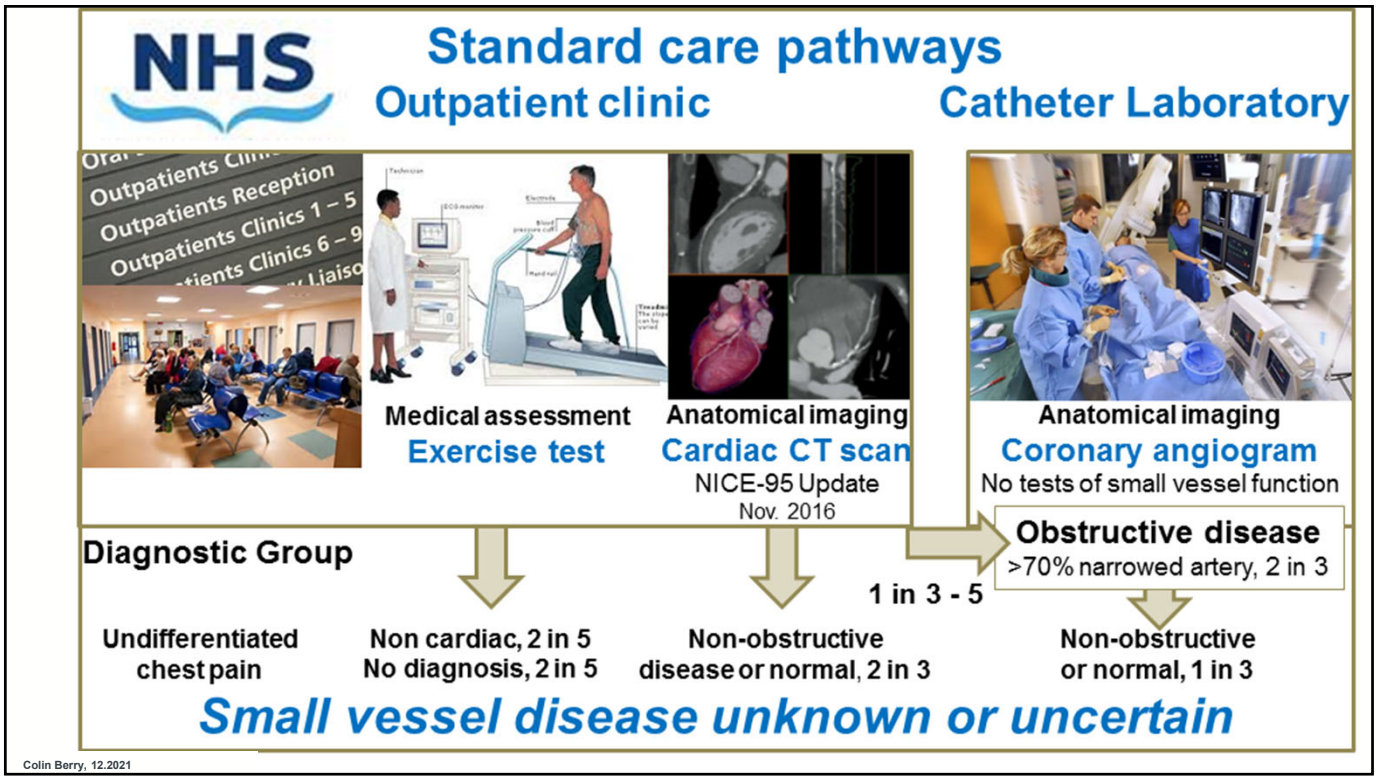

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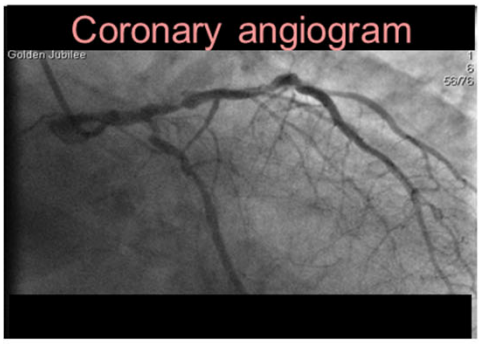
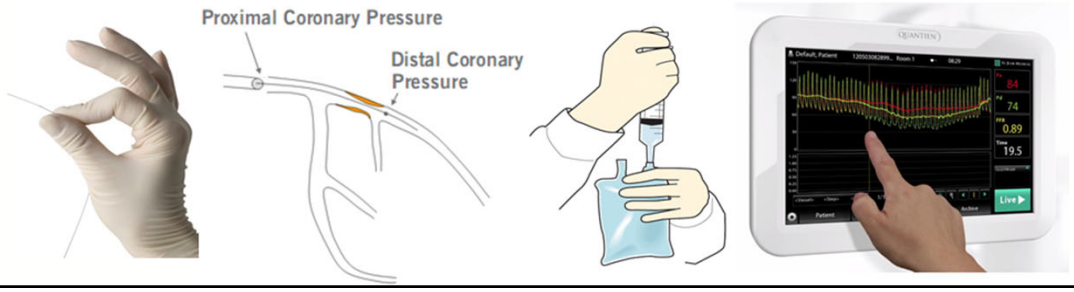
Clinical conundrums in daily practice



Diagnostic wire to assess flow-limitation



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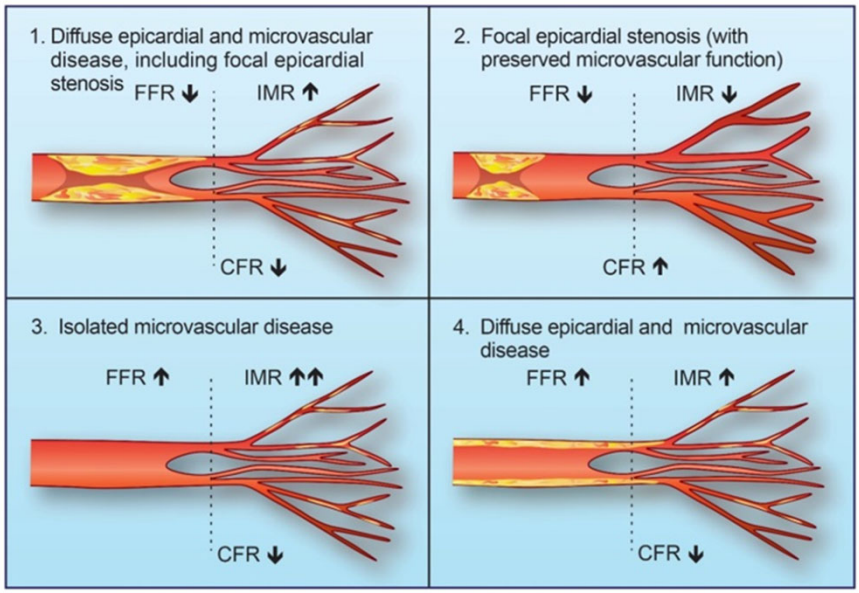
Diagnosis of coronary endotypes



Ford, Corcoran, Berry. EHJ 2017

Colin Berry, 12.2021

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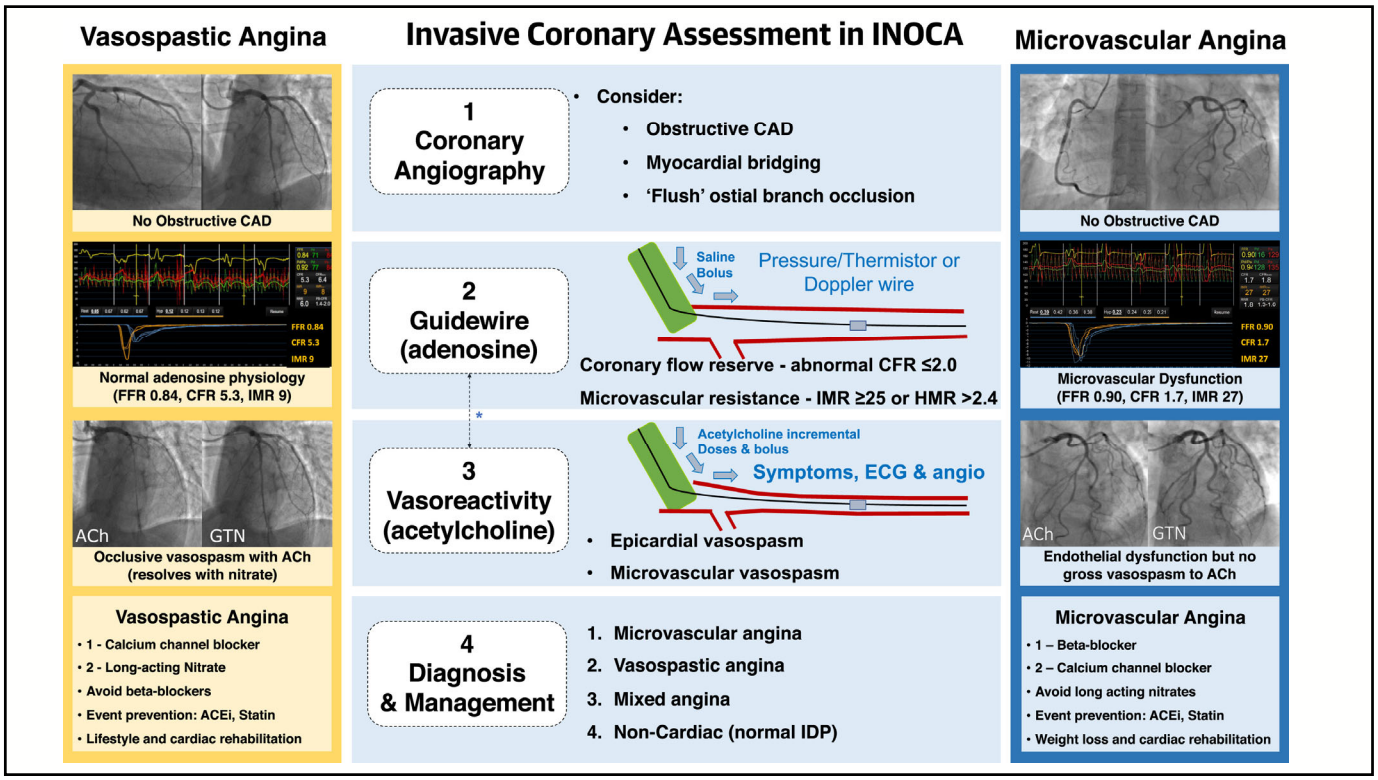
Vasospastic Angina
Invasive Coronary Assessment in INOCA
Microvascular Angina
No Obstructive CAD
1 Coronary Angiography
Consider:
Obstructive CAD
Myocardial bridging
'Flush' ostial branch occlusion
No Obstructive CAD
Normal adenosine physiology (FFR 0.84, CFR 5.3, IMR 9)
2 Guidewire (adenosine)
Saline Bolus
Pressure/Thermistor or Doppler wire
Coronary flow reserve - abnormal CFR ≤2.0
Microvascular resistance - IMR ≥25 or HMR >2.4
Microvascular Dysfunction (FFR 0.90, CFR 1.7, IMR 27)
ACh
GTN
Occlusive vasospasm with ACh (resolves with nitrate)
3 Vasoreactivity (acetylcholine)
Acetylcholine incremental Doses & bolus
Symptoms, ECG & angio
Epicardial vasospasm
Microvascular vasospasm
ACh
GTN
Endothelial dysfunction but no gross vasospasm to ACh
Vasospastic Angina
1 - Calcium channel blocker
2 - Long-acting Nitrate
Avoid beta-blockers
Event prevention: ACEi, Statin
Lifestyle and cardiac rehabilitation
4 Diagnosis & Management
1. Microvascular angina
2. Vasospastic angina
3. Mixed angina
4. Non-Cardiac (normal IDP)
Microvascular Angina
1 – Beta-blocker
2 – Calcium channel blocker
Avoid long acting nitrates
Event prevention: ACEi, Statin
Weight loss and cardiac rehabilitation

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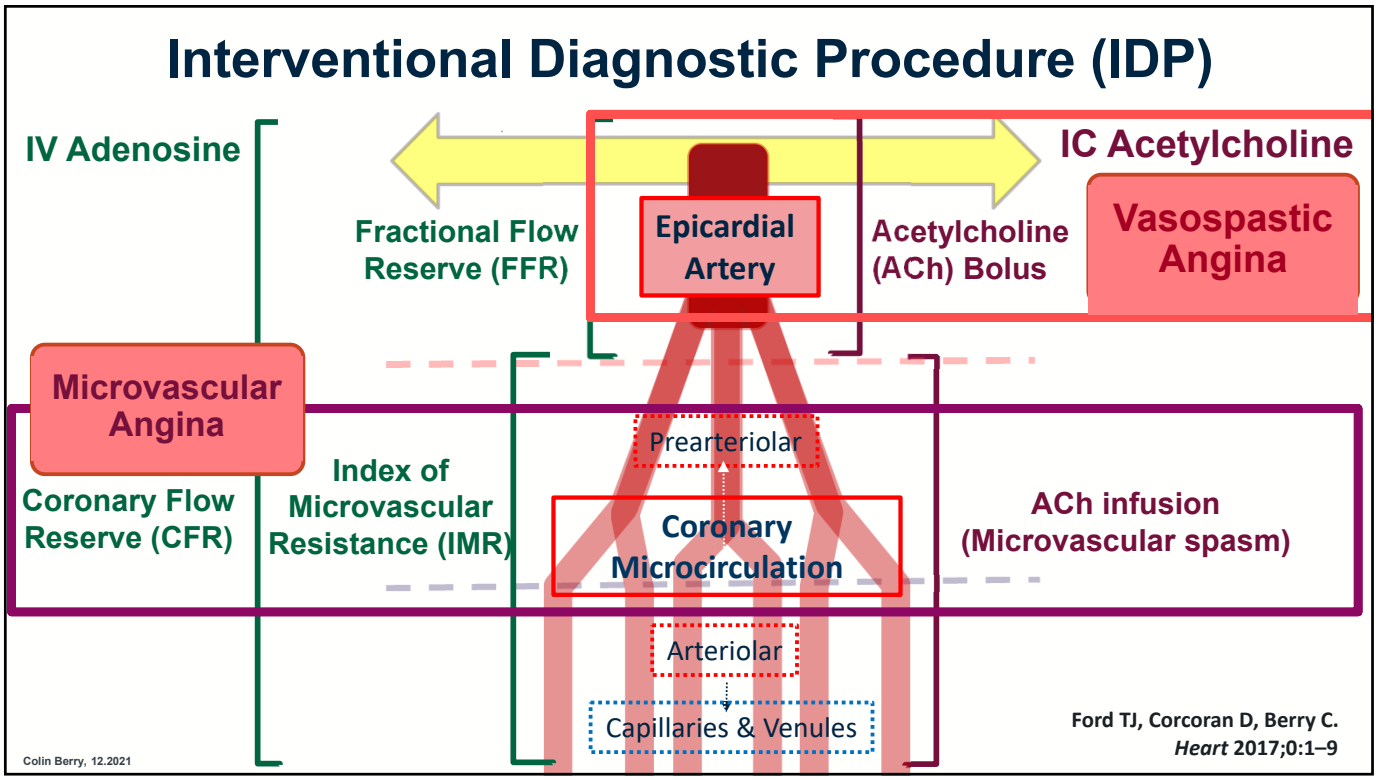
Interventional Diagnostic Procedure (IDP)
IV Adenosine
IC Acetylcholine
Fractional Flow Reserve (FFR)
Epicardial Artery
Acetylcholine (ACh) Bolus
Vasospastic Angina
Microvascular Angina
Prearteriolar
Index of Microvascular Resistance (IMR)
Coronary Flow Reserve (CFR)
Coronary Microcirculation
ACh infusion (Microvascular spasm)
Arteriolar
Capillaries & Venules
Colin Berry, 12.2021
Ford TJ, Corcoran D, Berry C.
Heart 2017;0:1–9

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Stratified Medicine

The identification of **subgroups** of patients (endotypes) within an **undifferentiated population**, identified by **disease mechanisms** and/or **therapy responses**.

MRC Framework (2015)

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British Heart Foundation

CorMicA

2015, grant rejected

"do not resubmit"

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CorMICA

Primary Endpoint = Angina Severity (SAQ SS)

Standard Care

Referred for Invasive Coronary Angiogram

Baseline (Day 0)

- Consent (N=391)
- Record Treatment/ Diagnosis
- SAQ
- EQ-5D-5L
- TSQM9
- BIPQ/
- PHQ4

Angiogram

No Obstructive CAD in 47% (N=185)

DS < 50%
FFR > 0.8

Randomise n = 151

Diagnostic procedure
Stratified Therapy, n=75

Blind, Sham Procedure
Standard Care , n=76

6 Months

- SAQ
- EQ-5D
- TSQM9
- BIPQ
- PHQ4

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CorMICA

Baseline Characteristics, n = 151

	Control (n = 76)	Intervention (n = 75)
Age	60 [53, 68]	62 [54, 69]
Female	58 (76%)	53 (71%)
BMI [Q1, Q3]	30 [26, 34]	30 [26, 35]
Current Smoker	14 (18%)	13 (17%)
Diabetes Mellitus	15 (20%)	14 (19%)
Predicted 10-year CHD risk*	18% [10, 28]	19% [12, 39]

* ASSIGN CV score

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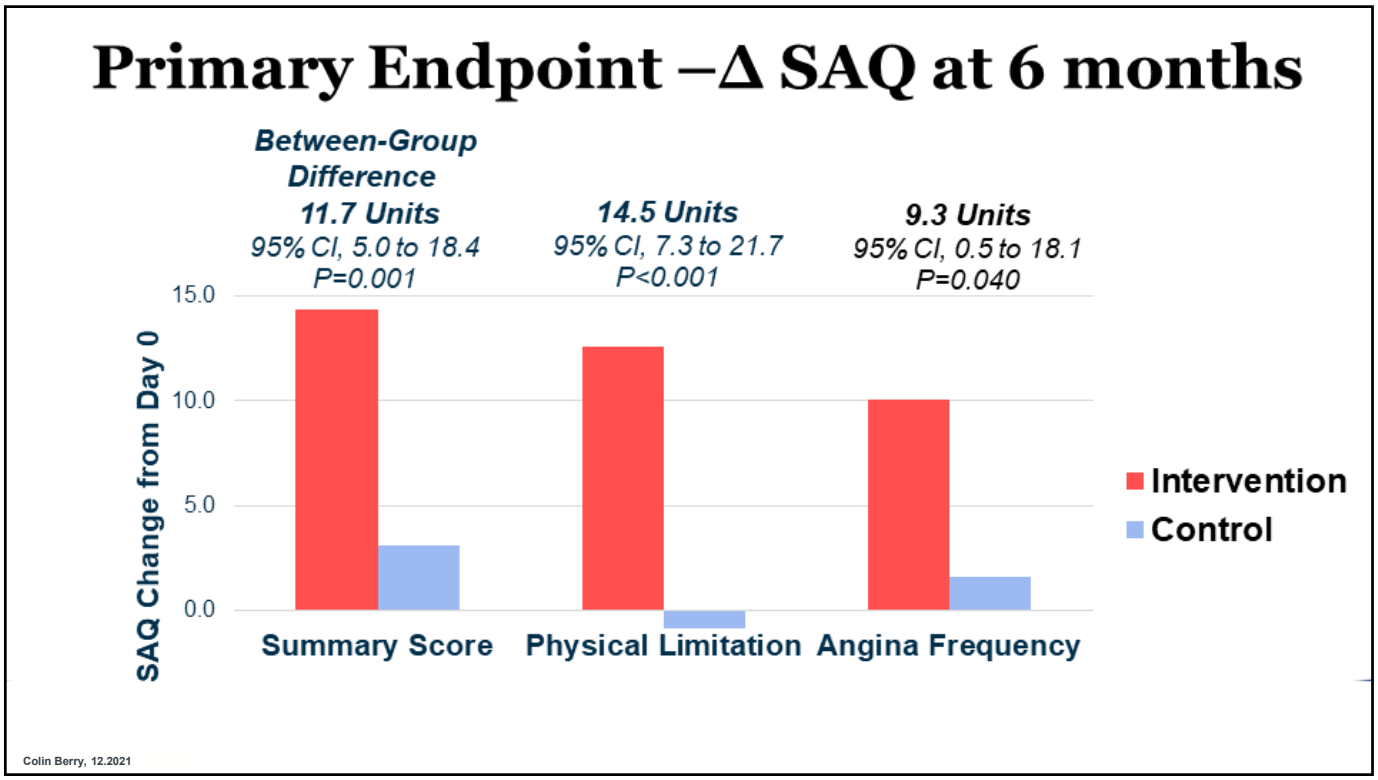
Primary Endpoint –Δ SAQ at 6 months
Between-Group Difference
11.7 Units
95% CI, 5.0 to 18.4
P=0.001
14.5 Units
95% CI, 7.3 to 21.7
P<0.001
9.3 Units
95% CI, 0.5 to 18.1
P=0.040
SAQ Change from Day 0
15.0
10.0
5.0
0.0
Summary Score
Physical Limitation
Angina Frequency
Intervention
Control
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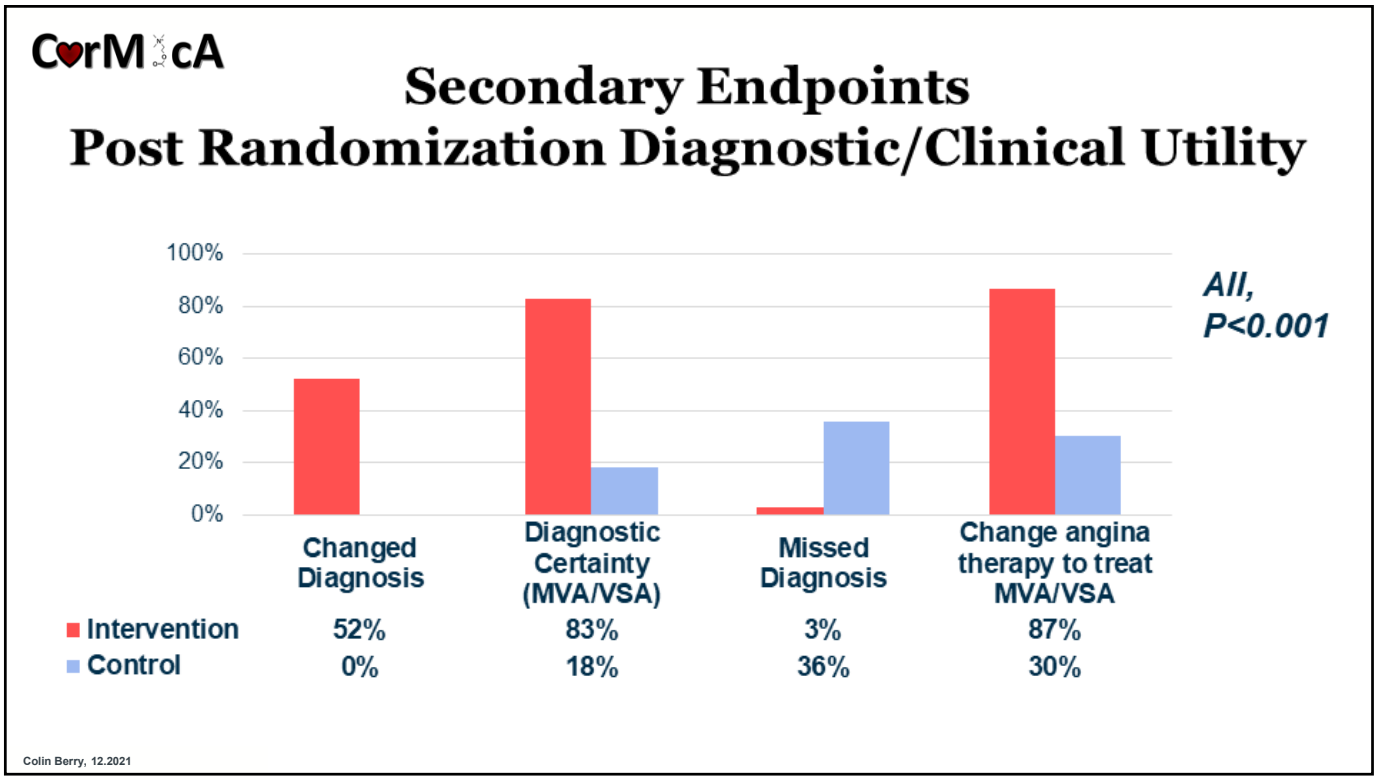
CorMicA
Secondary Endpoints
Post Randomization Diagnostic/Clinical Utility
100%
80%
60%
40%
20%
0%
All, P<0.001
Changed Diagnosis
Diagnostic Certainty (MVA/VSA)
Missed Diagnosis
Change angina therapy to treat MVA/VSA
Intervention 52% 83% 3% 87%
Control 0% 18% 36% 30%
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CorMicA

Secondary Endpoints – Health Status

	Intervention Effect	95% CI	P-Value
Quality of Life (EQ5D-5L):			
Index Score	0.1	0.01 – 0.18	0.024
VAS score	14.54	7.77 – 21.31	<0.001
Treatment satisfaction:			
Effectiveness	10.73	2.37 – 19.09	0.013
Convenience	14.34	7.30 – 21.37	<0.001
Global satisfaction	16.47	7.28 – 25.66	0.001

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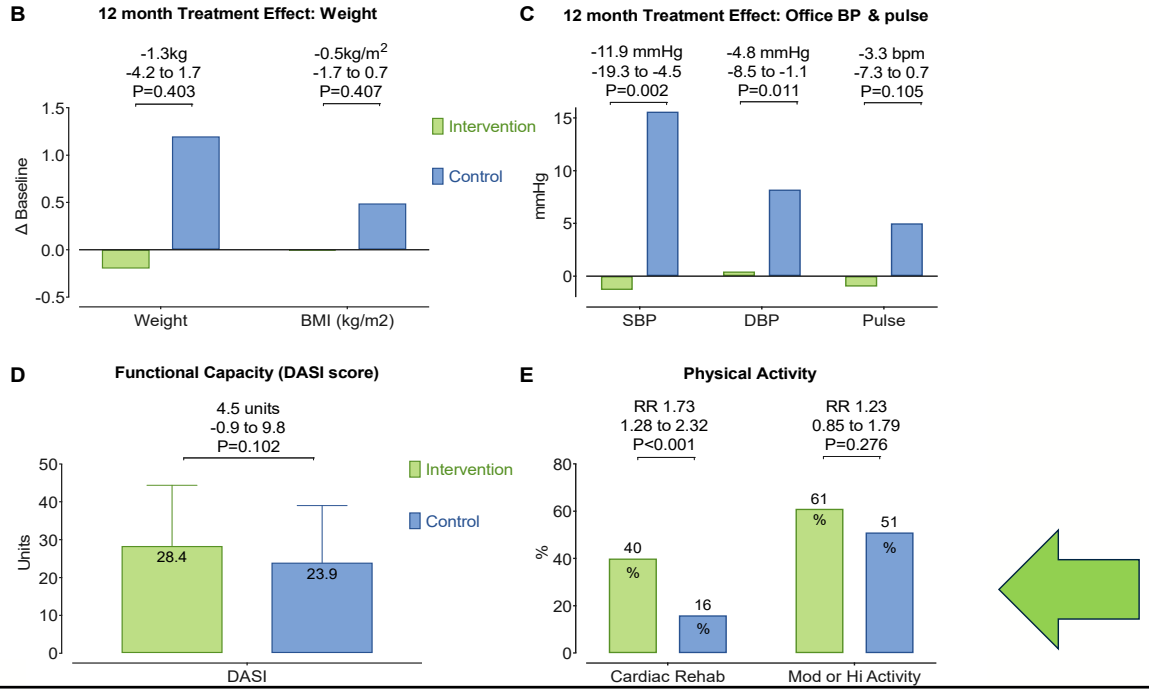
CorMicA

Mechanisms of benefit



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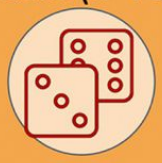
CorMicA

Invasive Coronary Function Testing in Angina (CorMicA): One Year RCT Outcomes

Randomized
151 Patients

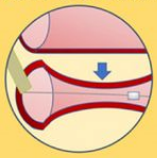
Angina & No Obstructive CAD

Intervention
Invasive Coronary Function Guided Care (n=75)



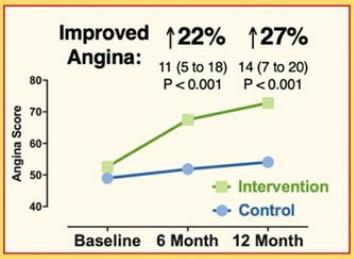
Control
Angiography guided Care (n=76)

Linked Diagnosis:
Microvascular angina
Vasospastic angina
Non-cardiac



Therapy:
Stratify Antianginals
Non-pharmacological

Main Results:



Sustained Benefits: Improved Angina and Quality of Life

Ford, Berry et al. JACC CV Int. 2019

Colin Berry, 12.2021

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European Heart Journal

ESC European Society of Cardiology

Article Navigation

GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC) FREE

Juhani Knuuti ✉, William Wijns ✉, Antti Saraste, Davide Capodanno, Emanuele Barbato, Christian Funck-Brentano, Eva Prescott, Robert F Storey, Christi Deaton, Thomas Cuisset ...
Show more

European Heart Journal, ehz425, https://doi.org/10.1093/eurheartj/ehz425
Published: 31 August 2019

Colin Berry, 12.2021

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ESC guidelines, Chronic Coronary Syndromes
Angina without obstructive disease in the epicardial coronary arteries - INOCA

Recommendations	Class	Level
Guidewire-based CFR and/or microcirculatory resistance measurements should be considered in patients with persistent symptoms, but coronary arteries that are either angiographically normal or have moderate stenoses with preserved iwFR/FFR.	IIa	B
Intracoronary acetylcholine with ECG monitoring may be considered during angiography, if coronary arteries are either angiographically normal or have moderate stenoses with preserved iwFR/FFR, to assess microvascular vasospasm.	IIb	B
Transthoracic Doppler of the LAD, CMR, and PET may be considered for non-invasive assessment of CFR.	IIb	B

Colin Berry, 12.2021

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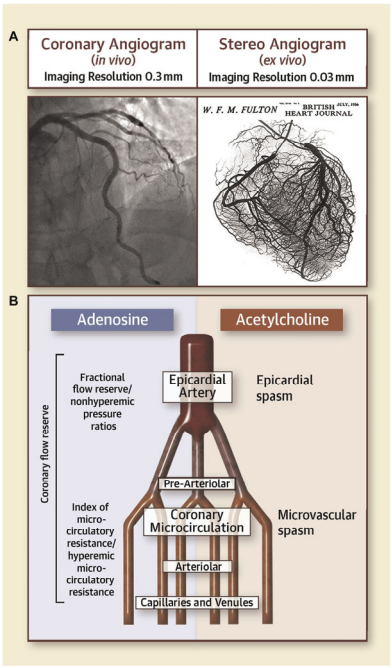
STATE-OF-THE-ART REVIEW

COVADIS
Assessment of Vascular Dysfunction in Patients Without Obstructive Coronary Artery Disease
Why, How, and When

Thomas J. Ford, MD, PhD,[a,b,c] Peter Ong, MD, PhD,[d] Udo Sechtem, MD,[d] John Beltrame, MD, PhD,[e] Paolo G. Camici, MD,[f] Filippo Crea, MD, PhD,[g] Juan-Carlos Kaski, MD, DSc,[h] C. Noel Bairey Merz, MD,[i] Carl J. Pepine, MD, PhD,[j] Hiroaki Shimokawa, MD, PhD,[k] Colin Berry, MD, PhD,[a,l]
on behalf of the COVADIS Study Group

CENTRAL ILLUSTRATION: Limited Visualization of the Coronary Microvasculature With Invasive Coronary Angiography



Ford, T.J. et al. J Am Coll Cardiol Intv. 2020;13(16):1847-64.

Colin Berry, 12.2021

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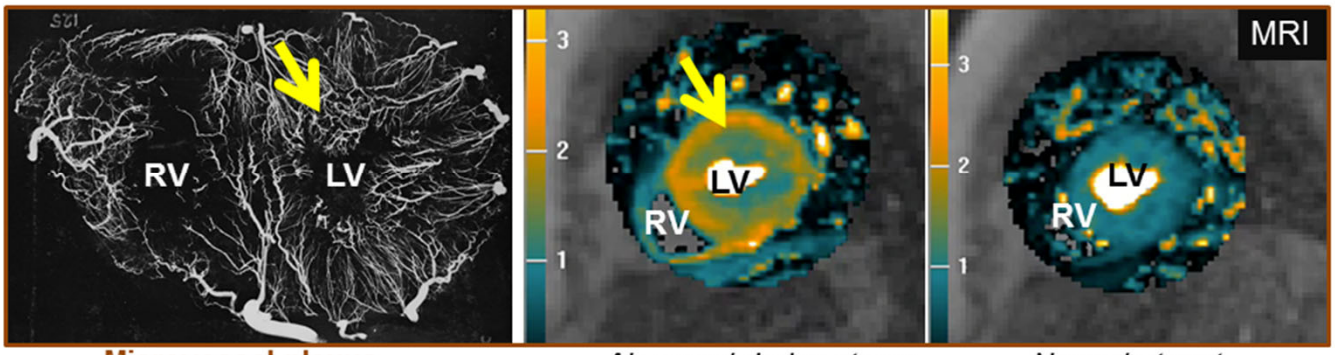
Non-invasive imaging of CMD

Pathological validation of perfusion MRI



Microvessel plexus subendocardium
Human coronary arteriogram
Ex vivo, Fulton, Glasgow 1963

Abnormal during stress
↓ subendocardial perfusion

Normal at rest

LV – left ventricle, RV – ventricle, LCA – left coronary artery, RCA – right coronary artery, GCV – great cardiac vein, RA – right atrium

Arai & Hsu, US NIH
Corcoran, Orchard, Berry, University of Glasgow

Colin Berry, 12.2021

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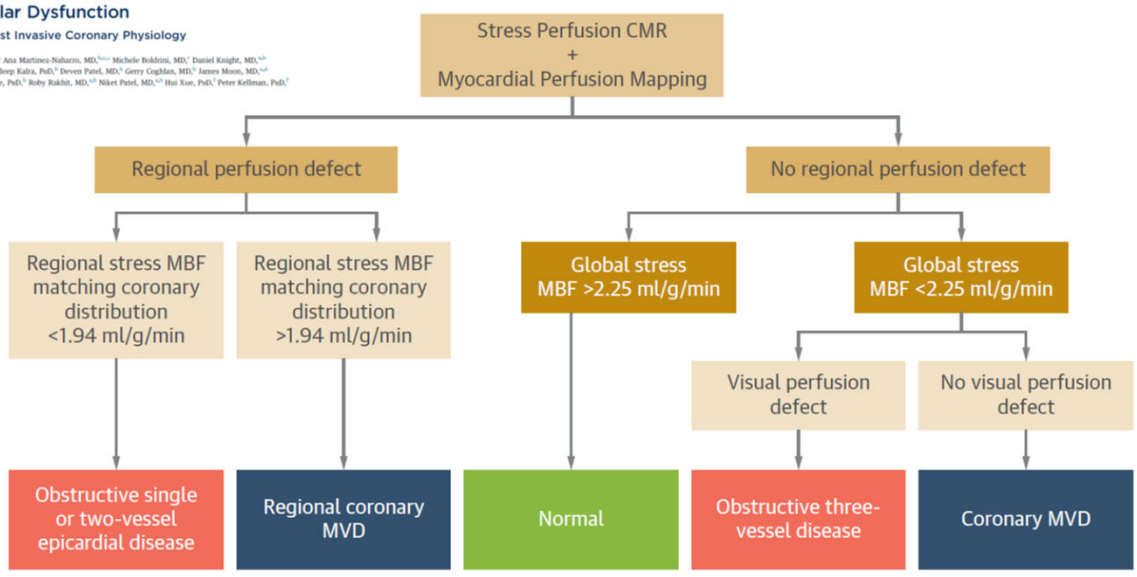
ORIGINAL RESEARCH

Automated Pixel-Wise Quantitative Myocardial Perfusion Mapping by CMR to Detect Obstructive Coronary Artery Disease and Coronary Microvascular Dysfunction

Validation Against Invasive Coronary Physiology

Tushar Kotecha, MBChB, Ana Martinez-Naharro, MD, Michele Boldrini, MD, Daniel Knight, MD, Philip Hawkins, PsD, Sundeep Kalra, PsD, Deven Patel, MD, Gerry Coghlan, MD, James Moon, MD, Sven Plein, PsD, Tim Lockie, PsD, Roby Rakhit, MD, Niket Patel, MD, Hui Xue, PsD, Peter Kellman, PsD, Marianna Fontana, PsD

CMR



Kotecha et al iJACC 2021

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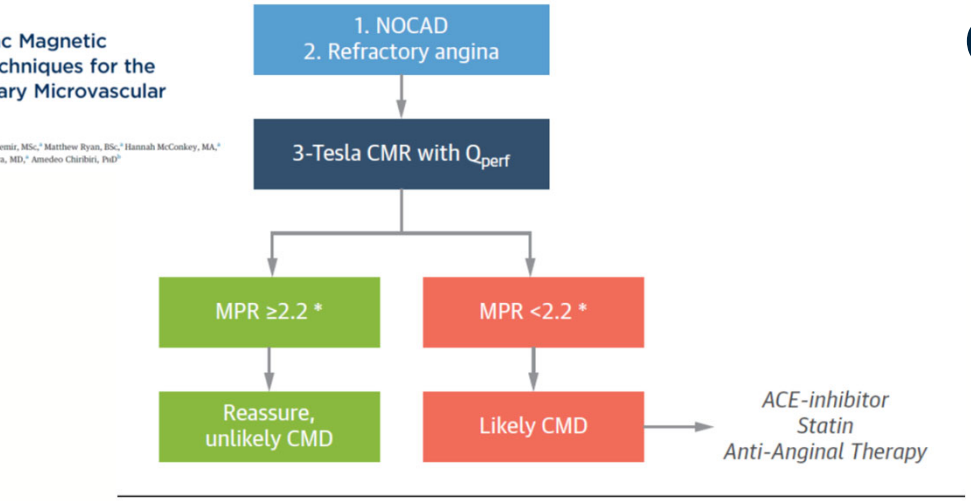
CLINICAL RESEARCH

High-Resolution Cardiac Magnetic Resonance Imaging Techniques for the Identification of Coronary Microvascular Dysfunction

Haseeb Rahman, PsD,[a] Cian M. Scannell, MRes,[b] Ozan M. Demir, MSc,[a] Matthew Ryan, BSc,[a] Hannah McConkey, MA,[a] Howard Ellis, BSc,[a] Pier Giorgio Masci, PsD,[b] Divaka Perera, MD,[a] Amedeo Chiribiri, PsD[b]

CMR



The **asterisk** indicates that an MPR value can be substituted with an MPR_{ENDO} value of 2.41, which will have greater sensitivity at the cost of specificity. An MPR threshold of 2.19 has sensitivity and specificity values of 70% and 90%, and an MPR_{ENDO} threshold of 2.41 has sensitivity and specificity values of 95% and 72%, respectively.

ACE = angiotensin-converting enzyme; CMD = coronary microvascular dysfunction; CMR = cardiac magnetic resonance; NOCAD = nonobstructive coronary artery disease; Q_{perf} = quantitative perfusion; other abbreviations as in Figure 2.

Rahman et al iJACC 2021

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University of Glasgow

British Heart Foundation

Directions
Guidelines, sex disparities, MINOCA, systemic disease.

Colin Berry, 12.2021

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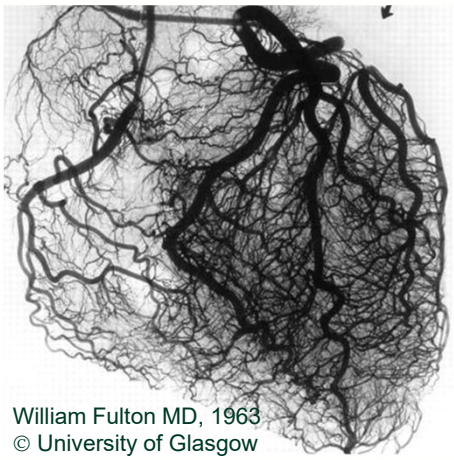
False negative - anatomical imaging

Stereo-arteriogram

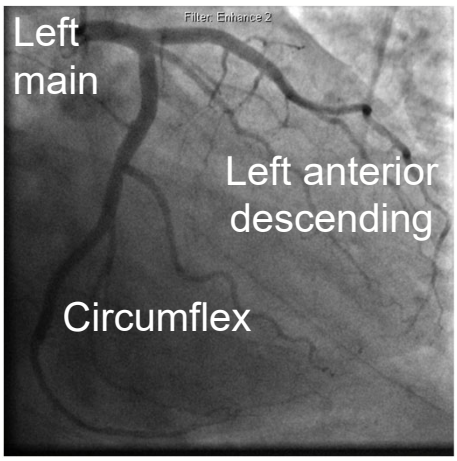
40 µm



William Fulton MD, 1963
© University of Glasgow

Coronary angiogram

0.5 mm



Colin Berry, 12.2021

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Sex differences, IHD

CorMicA all-comers registry

	Obstructive CAD N = 206	INOCA N = 185	P-value
Age	63 (9.6)	61.3 (10.0)	0.081
Female	38%	68%	<0.001
Prev MI	29%	16%	0.008
10-year CVD risk	24% [10, 28]	20% [12, 39]	0.003

Colin Berry, 02.09.2019

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Stratified Medical Therapy Using Invasive Coronary Function Testing in Angina
The CorMicA Trial

Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial

In context	CorMicA	ORBITA
Age, years	61	66
Sex, % female	74	27
Angina		
Summary Score	51	?
Limitation	52	70
Frequency	59	71
Stability	45	66
EQ5D - QoL	0.6	0.8
Enrolment, years	1	3·5
Centres, n	2	5

Colin Berry, 12.2021

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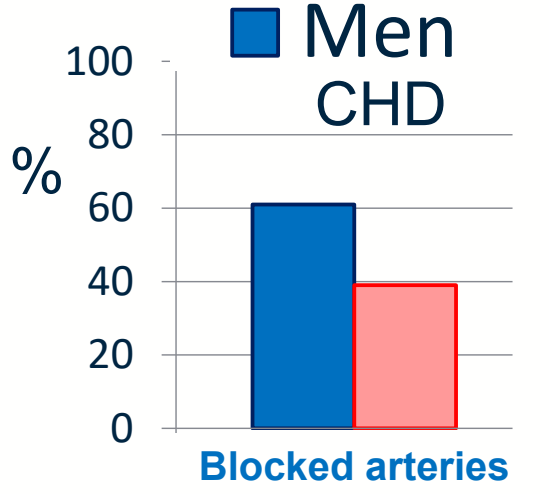
IHD differs in women vs. men

Angina by cause



SCOT-HEART, 2015

Colin Berry, 12.2021

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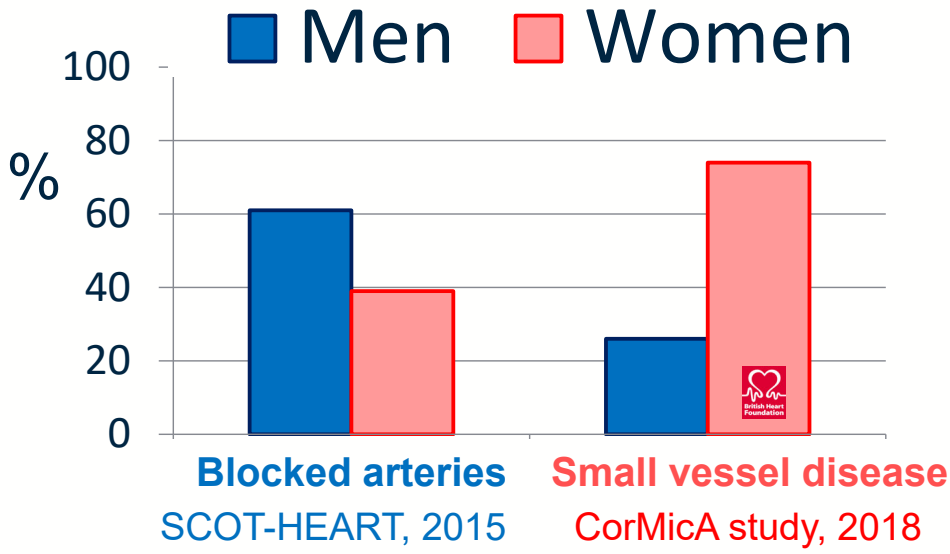
IHD differs in women vs. men

Angina by cause



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Ischaemic heart disease

CHD
Coronary Heart Disease

INOCA
Ischemia with no obstructive coronary arteries

Sex Bias: Terminology in Clinical Trials
SCOTHEART – Angina due to CHD …. If No, angina excluded
Option to stop therapy

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OPEN ACCESS

ORIGINAL ARTICLE

Symptoms and quality of life in patients with suspected angina undergoing CT coronary angiography: a randomised controlled trial

Michelle C Williams,[1] Amanda Hunter,[1] Anoop Shah,[1] Valentina Assi,[2] Stephanie Lewis,[2] Kenneth Mangion,[3] Colin Berry,[3] Nicholas A Boon,[1] Elizabeth Clark,[1] Marcus Flather,[4] John Forbes,[5] Scott McLean,[6] Giles Roditi,[3] Edwin JR van Beek,[1] Adam D Timmis,[7] David E Newby,[1] on behalf of the Scottish COmputed Tomography of the HEART (SCOT-HEART) Trial Investigators

Heart 2017

	All patients	Standard care+CTCA	Standard care	Difference (95% CIs)	p Value (for difference)
Change at 6 weeks	n=3427	n=1755	n=1672		
Physical limitation	−0.3±0.4 (2076)	−0.5±0.5 (1082)	−0.0±0.5 (994)	−0.72 (−2.08 to 0.63)	0.2957
Angina stability	16.3±0.6 (3190)	16.7±0.9 (1637)	15.8±0.9 (1553)	1.03 (−0.61 to 2.68)	0.2184
Angina frequency	11.5±0.4 (3264)	11.2±0.6 (1684)	11.8±0.6 (1580)	−0.84 (−2.20 to 0.54)	0.2277
Treatment satisfaction	−7.0±0.3 (3247)	−7.0±0.4 (1675)	−7.0±17.1 (1572)	0.03 (−1.07 to 1.14)	0.9525
Quality of life	9.3±0.4 (3261)	8.7±0.5 (1681)	9.9±0.6 (1580)	−1.31 (−2.66 to 0.05)	0.0585
Change at 6 months	n=3035	n=1562	n=1473		
Physical limitation	2.3±0.4 (1814)	1.6±0.6 (937)	3.0±0.6 (877)	−1.74 (−3.34 to −0.14)	0.0329
Angina stability	13.0±0.6 (2833)	13.4±0.9 (1462)	12.5±0.9 (1371)	1.27 (−0.27 to 2.80)	0.1059
Angina frequency	18.7±0.4 (2895)	18.3±0.6 (1498)	19.2±0.6 (1397)	−1.55 (−2.85 to −0.25)	0.0198
Treatment satisfaction	−4.7±0.3 (2872)	−5.0±0.4 (1485)	−4.3±0.4 (1387)	−0.97 (−2.14 to 0.21)	0.1060
Quality of life	17.0±0.4 (2865)	15.5±0.6 (1484)	18.6±0.6 (1381)	−3.48 (−4.95 to −2.01)	<0.0001

Mean±SE (n).

Angina frequency, limitation, QoL — *Worse in CTCA group*

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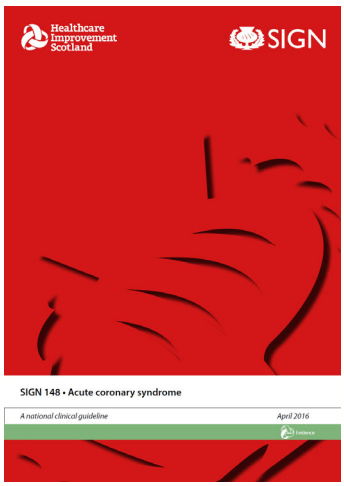
Sex bias in UK guidelines?



‘Syndrome X’ (therapeutic nihlism)
…. no mention of microvascular angina, MINOCA, or SCAD

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ESC – new guidelines

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

SPECIAL ARTICLE
Coronary artery disease

An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary Arteries in Collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group

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CorMicA

Angina without obstructive disease in the epicardial coronary arteries - Microvascular angina

Recommendations	Class	Level
Guidewire-based CFR and/or microcirculatory resistance measurements should be considered in patients with persistent symptoms, but coronary arteries that are either angiographically normal or have moderate stenoses with preserved iwFR/FFR.	IIa	B
Intracoronary acetylcholine with ECG monitoring may be considered during angiography, if coronary arteries are either angiographically normal or have moderate stenoses with preserved iwFR/FFR, to assess microvascular vasospasm.	IIb	B
Transthoracic Doppler of the LAD, CMR, and PET may be considered for non-invasive assessment of CFR.	IIb	B

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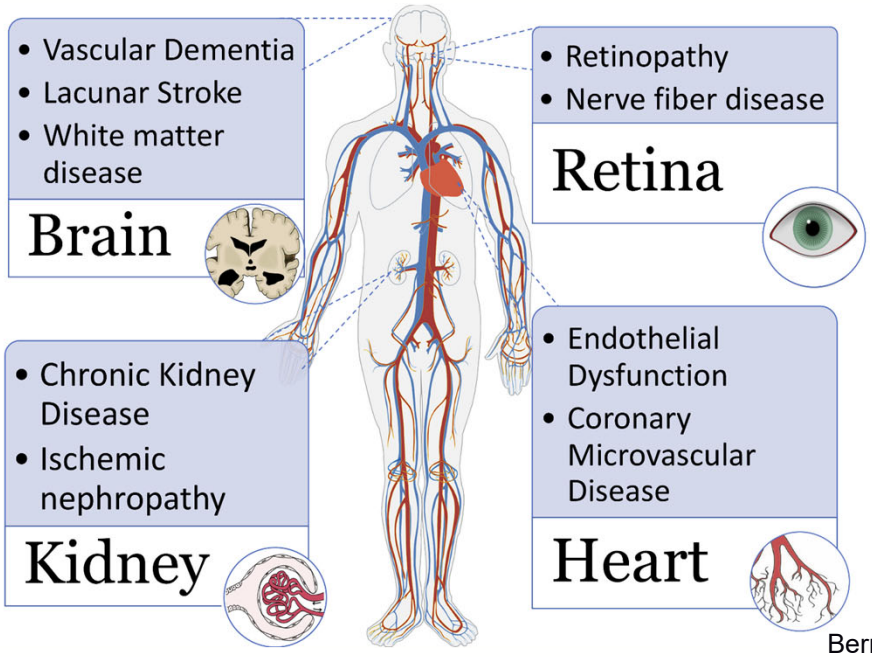
Microvascular angina – a multisystem disorder?



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Berry, et al JAHA 2018

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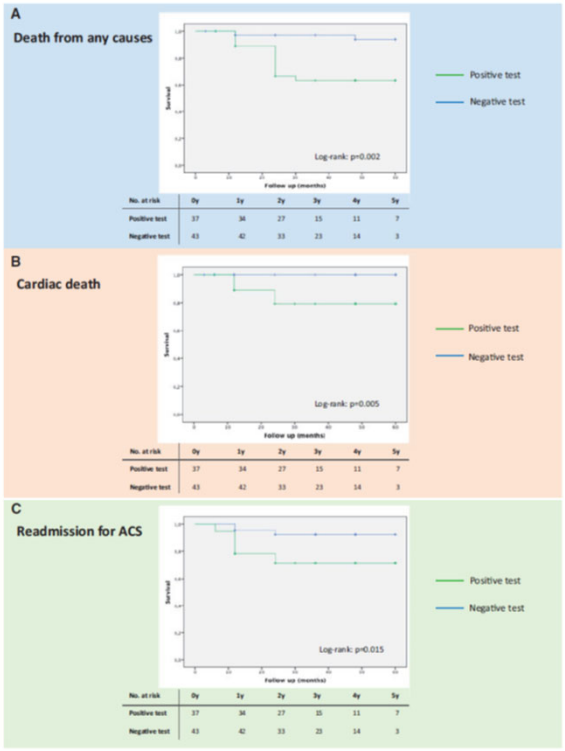
MINOCA
Vasospasm & prognosis

n = 80

n = 37 +

5 years



Montone, Crea EHJ 2018

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University of Glasgow

British Heart Foundation

Future directions: clinical trials

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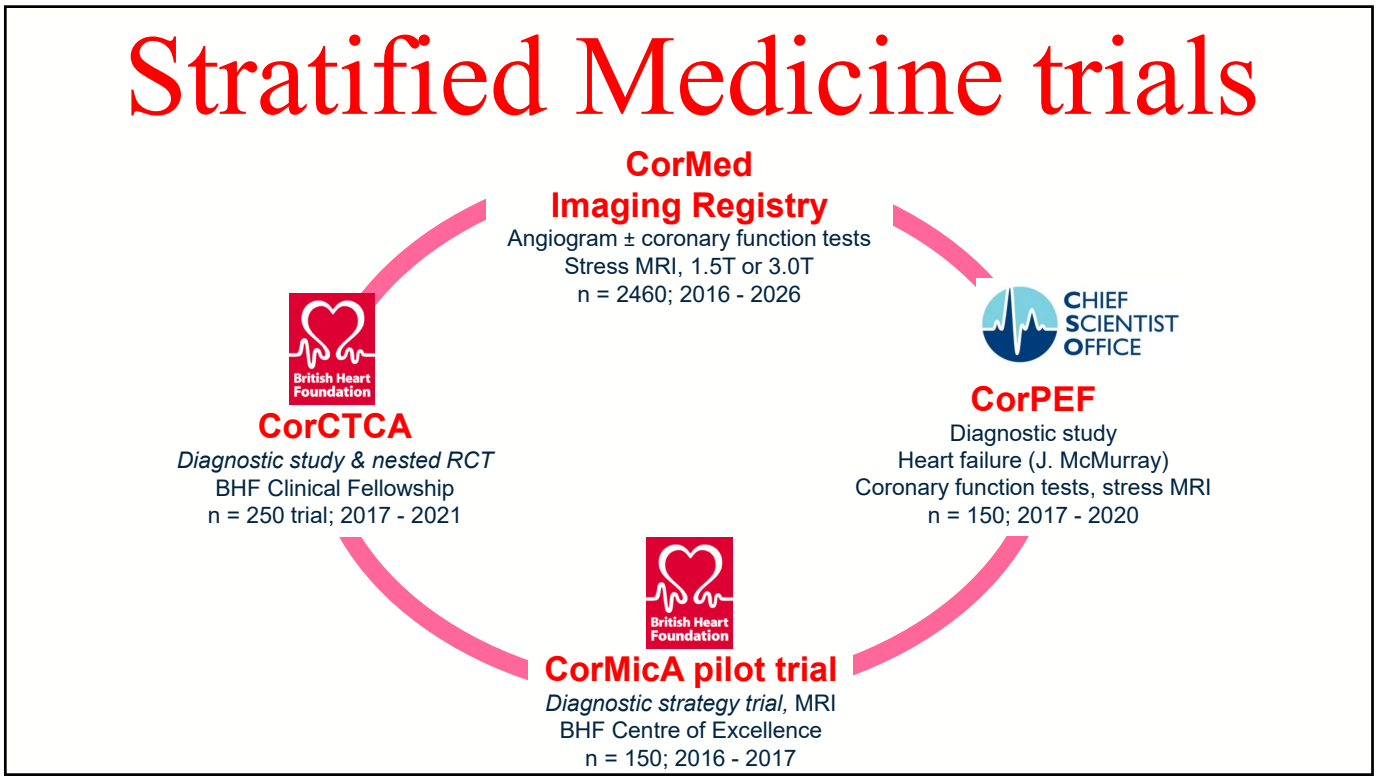
Stratified Medicine trials
CorMed
Imaging Registry
Angiogram ± coronary function tests
Stress MRI, 1.5T or 3.0T
n = 2460; 2016 - 2026
British Heart Foundation
CorCTCA
Diagnostic study & nested RCT
BHF Clinical Fellowship
n = 250 trial; 2017 - 2021
CHIEF SCIENTIST OFFICE
CorPEF
Diagnostic study
Heart failure (J. McMurray)
Coronary function tests, stress MRI
n = 150; 2017 - 2020
British Heart Foundation
CorMicA pilot trial
Diagnostic strategy trial, MRI
BHF Centre of Excellence
n = 150; 2016 - 2017

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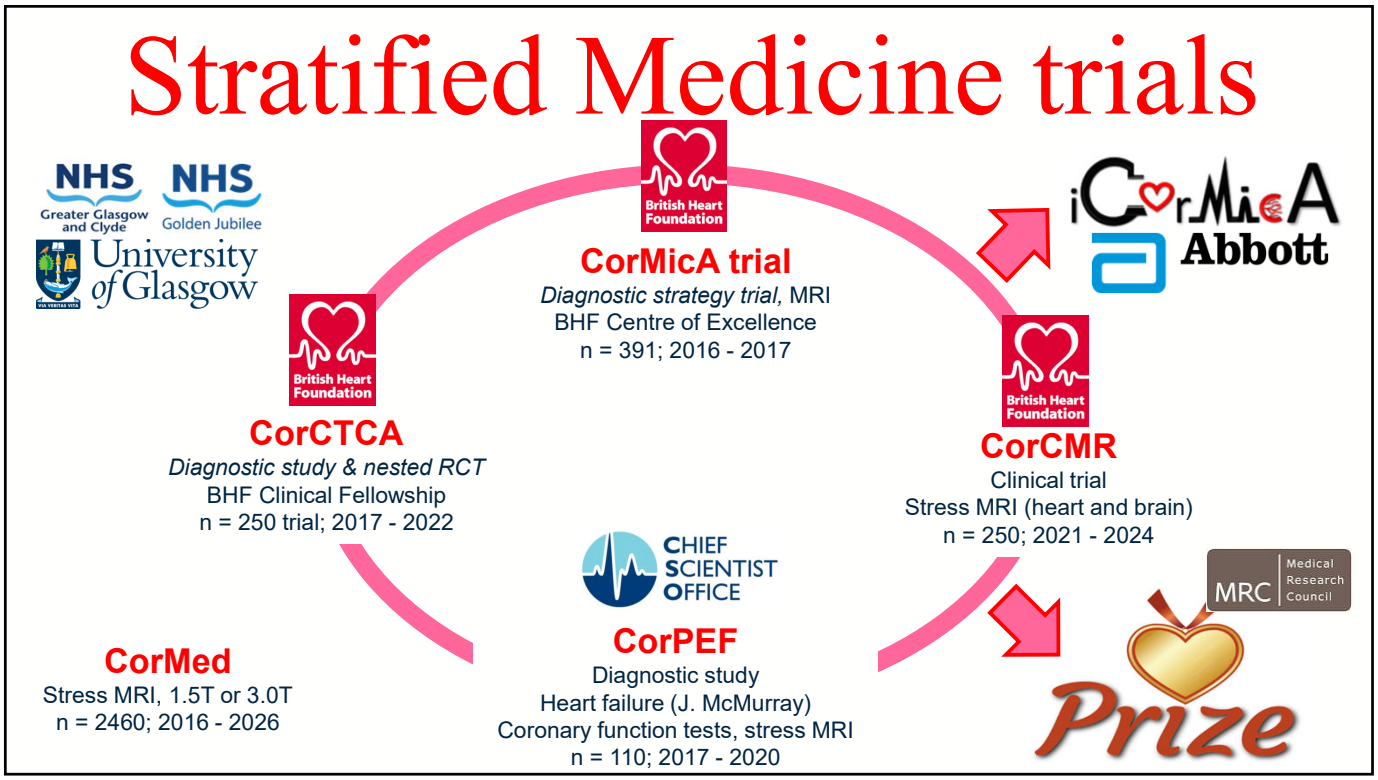
Stratified Medicine trials
NHS Greater Glasgow and Clyde
NHS Golden Jubilee
University of Glasgow
British Heart Foundation
CorMicA trial
Diagnostic strategy trial, MRI
BHF Centre of Excellence
n = 391; 2016 - 2017
iCorMicA
Abbott
British Heart Foundation
CorCTCA
Diagnostic study & nested RCT
BHF Clinical Fellowship
n = 250 trial; 2017 - 2022
British Heart Foundation
CorCMR
Clinical trial
Stress MRI (heart and brain)
n = 250; 2021 - 2024
CHIEF SCIENTIST OFFICE
CorPEF
Diagnostic study
Heart failure (J. McMurray)
Coronary function tests, stress MRI
n = 110; 2017 - 2020
MRC Medical Research Council
Prize
CorMed
Stress MRI, 1.5T or 3.0T
n = 2460; 2016 - 2026

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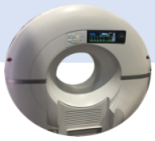
The BHF COR-CTCA Trial

The BHF **COR**onary Microvascular Function and **CT** Coronary **A**ngiography Trial: Rationale and Design

British Heart Foundation

CTCA for suspected angina

No obstructive CAD



~ >3 in 4 patients

Sidik, Berry et al. Am Heart J 2020

Colin Berry, 12.2021

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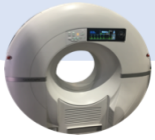
The BHF COR-CTCA Trial

The BHF **COR**onary Microvascular Function and **CT** Coronary **A**ngiography Trial: Rationale and Design

British Heart Foundation

CTCA for suspected angina

No obstructive CAD



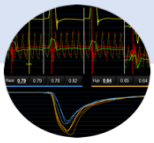
Invasive coronary angiography

Enrolled n = 250

Randomization

Intervention n = 125

Control n = 125



Management

Stratified medicine

Angiography guided

Outcomes

Health status PROMS

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Sidik, Berry et al. Am Heart J 2020

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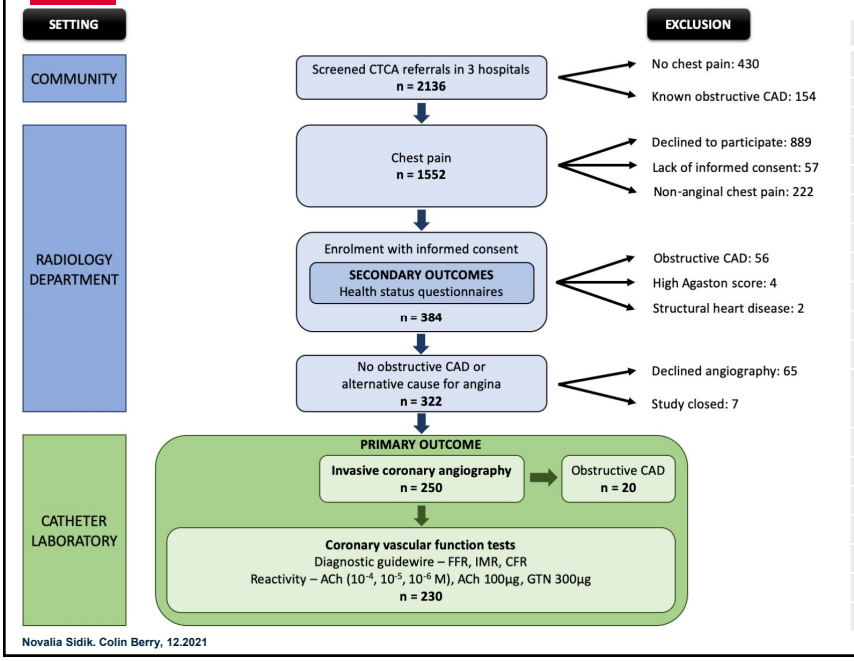
CorCTCA trial



CorCTCA population at baseline	N = 250
Age, years	60 ± 9
Female	156 (62%)
BMI, kg/m^2	30.9 ± 6.0
Current smoker	53 (21%)
History of MI	8 (3%)
Prior coronary stent	3 (1%)
History of stroke	15 (6%)
Type 2 diabetes mellitus	30 (12%)
Hypertension	120 (48%)
Dyslipidaemia	147 (59%)
Family history CHD	145 (58%)
Predicted 10-year likelihood of coronary heart disease event, JBS3	12.3 ± 8.9
Aspirin	156 (62%)
Beta-blocker	154 (62%)
Calcium-channel blocker	65 (26%)
Nitrate	41 (16%)
Statin	160 (64%)
ACE inhibitor / ARB	74 (30%)
Total cholesterol, mmol/l	5.1 ± 1.2

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3900
Angina, coronary angiography → **Registry**

n = 25+ per centre
Obstructive CAD

Angina, No Obstructive CAD

1500
Randomise, double-blind

IDP
all patients

n = 750, IDP

Stratified medicine

n = 750, IDP sham

Standard care

Seattle Angina Score
Primary outcome, 1 year

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Schedule of Assessments

These activities can take place on the same day		Letter +/- phone call	Letter +/- phone call	Letter/ phone call/ clinic visit	Letter +/- phone call	Clinic/ phone call/ letter	
Screening	Visit 1	Follow-up 1 at 1 month	Follow-up 2 at 3 months	Follow-up 3 at 6 months	Follow-up 4 at 9 months	Follow-up 5 at 12 months	Follow-up 6 & 7 at 5 & 10 years
•Informed Consent •Medical History •Vital signs •Health Questionnaires	•12 lead ECG •Blood Samples •Coronary Angiogram •Randomisation •Small vessel function tests •Clinical diagnosis with linked treatment plan	•iCorMicA Symptom Log	•iCorMicA Symptom Log	•Health Questionnaires •Medication list •Follow-up for health events	•iCorMicA Symptom Log	•Vital signs •Physical examination •Medical History •Health Questionnaires •Blood samples •Medication list	•Follow-Up review •Health Questionnaires

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Outcomes

Primary

Seattle Angina Questionnaire (SAQ) Summary Score @ 1 year.

Secondary

Health status questionnaires, safety, healthcare resource use.

Exploratory

CV risk factor control, potential biomarkers.

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NHS Greater Glasgow and Clyde

University of Glasgow

MRC Medical Research Council

Prize

PRECISION MEDICINE WITH ZIBOTENTAN IN MICROVASCULAR ANGINA

Dr Andrew Morrow, MRC Clinical Fellow

Prize

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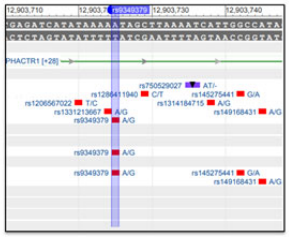
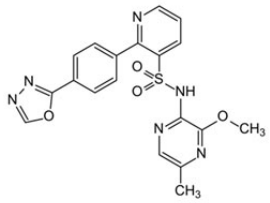
PRIZE Study: Precision Medicine



rs9349379 (G allele)

↑PHACTR1 expression

↑Circulating ET-1



ET-A antagonist

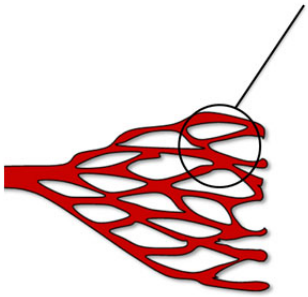
ZIBOTENTAN

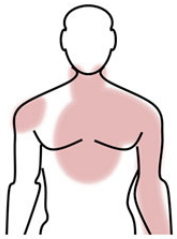
Vascular smooth muscle membrane | ET-A

↑ET-A receptor activation
Enhanced Ca2+ signalling
↑Contraction
↑Proliferation

↑Microvascular resistance

↓Myocardial perfusion





Microvascular angina

Prize

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Precision medicine with zibotentan in microvascular angina

Prize

MRC Medical Research Council

Exclusion n=212

Drop out n=44

Screening
Informed consent
n=356

Genotyping

n=144

Medical optimisation

Single blind placebo

n=50 Zibotentan 10mg OD

n=50 Placebo

Zibotentan 10mg OD

Placebo

Final visit

TIME	Week 0-6	Week 7-9	Week 10-22	Week 23-34
VISIT	1	2	3	4	5
	C, Q, GB, B ETT, PD	C, Q, B	C, Q, B ETT, PD, PK +- spCMR	C, Q, B ETT, PD, PK +- spCMR	C, Q, B ETT, PD, PK +- spCMR

Blood (B), Clinical examination (C), Exercise tolerance test (ETT; Bruce protocol), GB – genomic blood test, Quality of life questionnaire (Q)
Stress perfusion cardiac magnetic resonance imaging (spMRI; optional sub-study), Pharmacokinetic and Pharmacodynamic sampling (PK/PD);

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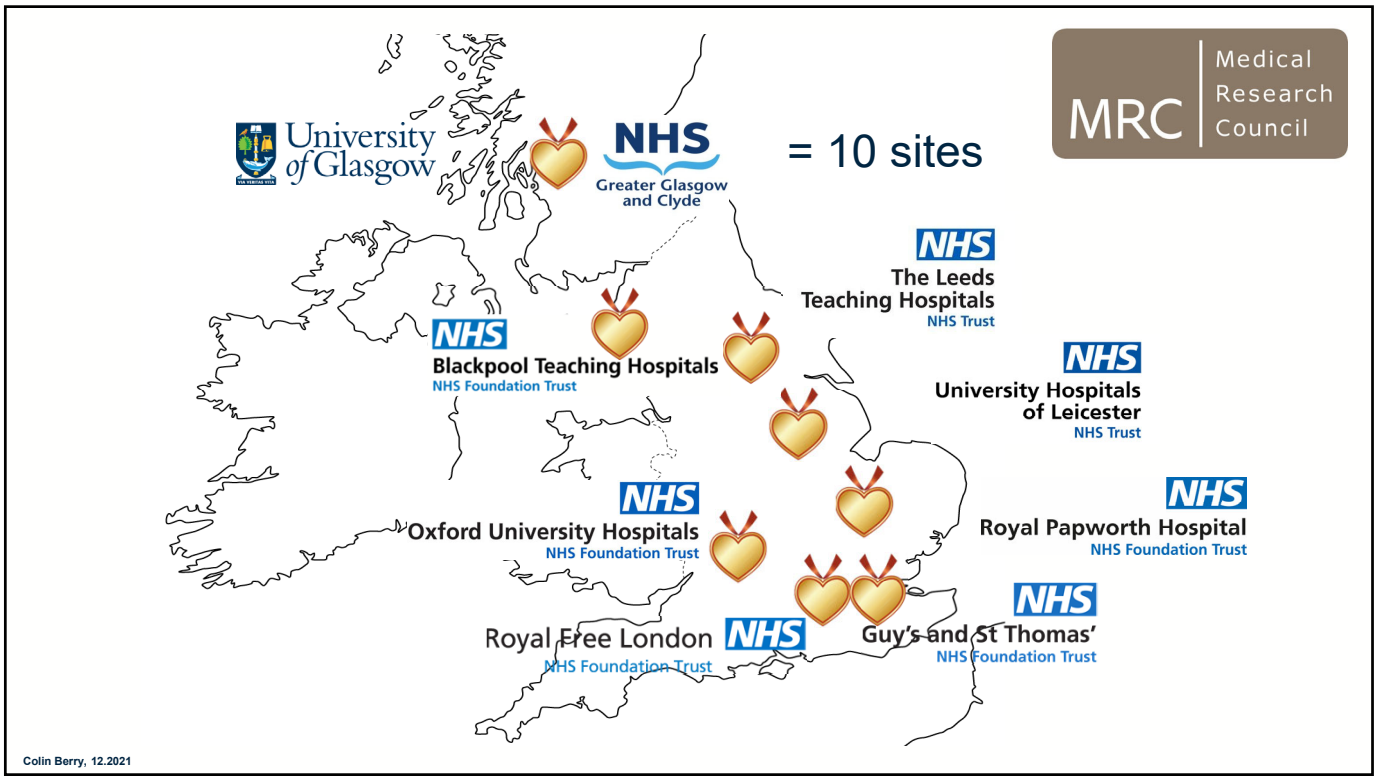

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Conclusions

1. **INOCA**: common (>obstructive CAD), under-recognition diagnosis & treatment.
2. **CorMicA trial:** *stratified medicine changes diagnosis, treatment, improves symptoms*
3. **Future directions**: educate on sex disparities, MINOCA, therapy development, and trials.

Colin Berry, 12.2021

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British Medical Association (BMA) Women's Health Report, August 2018

No mention of heart disease in women.

Colin Berry, 02.2021

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