# Artificial Intelligence in Echocardiography

## ESC-2023


*Marina Leitman, MD*

# DASE-AI
# Detect Aortic Stenosis by Echo with Artificial Intelligence

**Professor Geoffrey Strange**

The University of Notre Dame, Sydney (Australia)

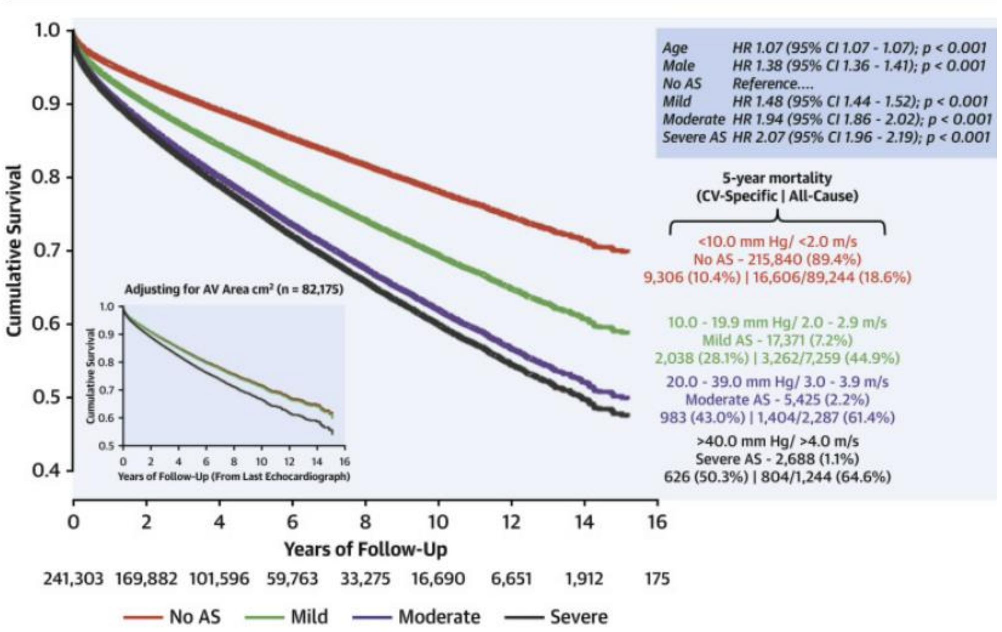
# Controversies in Aortic Stenosis

## Sex differences in aortic stenosis: from pathophysiology to treatment

Sahrai Saeed, Marc R Dweck & John Chambers

## Poor Long-Term Survival in Patients With Moderate Aortic Stenosis

Geoff Strange, PhD,[a] Simon Stewart, PhD,[b] David Celermajer, MD, PhD,[c] David Prior, MBBS, PhD,[d] Gregory M. Scalia, MBBS (Hons), MMedSc,[e] Thomas Marwick, MBBS, PhD,[f] Marcus Ilton, MD,[g] Majo Joseph, MBBS,[h] Jim Codde, PhD,[i] David Playford, MBBS, PhD,[a] on behalf of the National Echocardiography Database of Australia contributing sites




## Comorbidities and Symptom Status in Moderate and Severe Aortic Stenosis

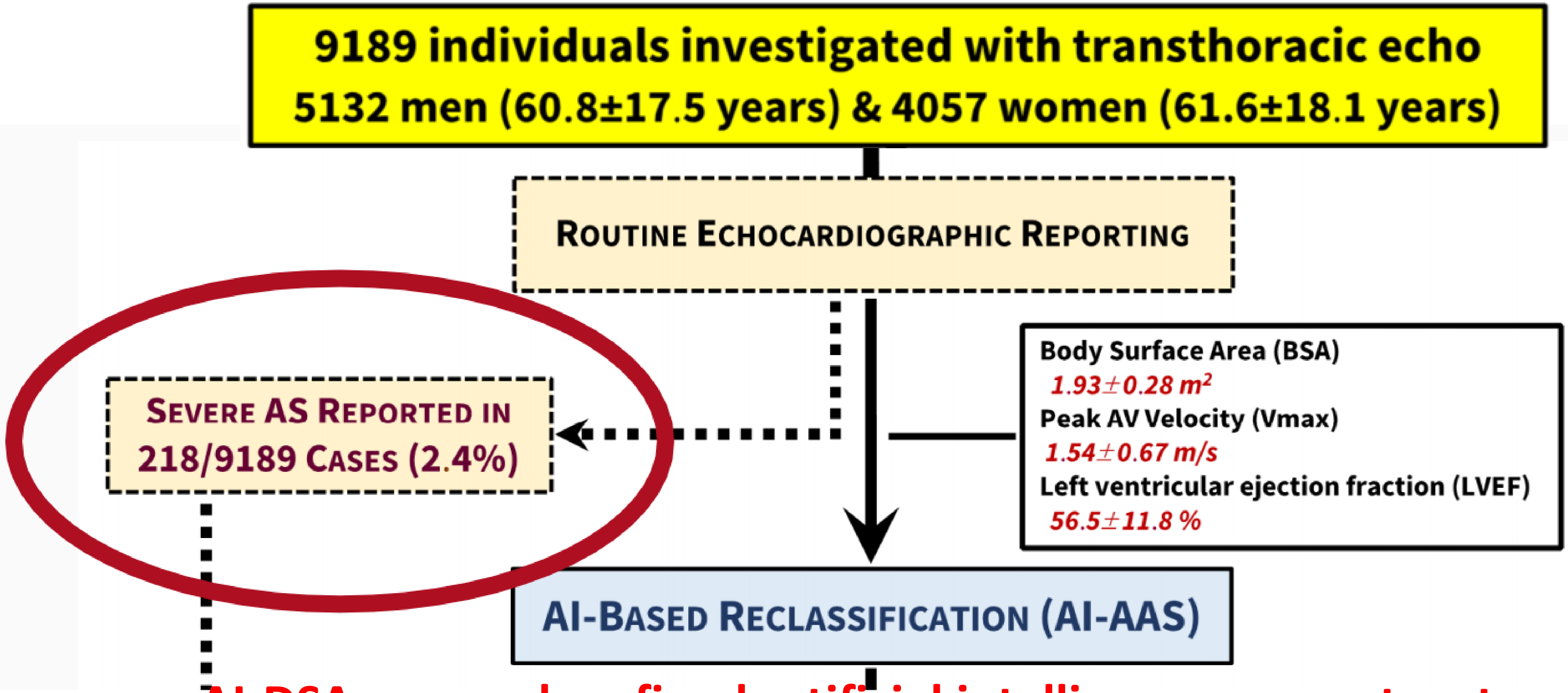
### A Multicenter Clinical Cohort Study

David Playford, MBBS, PhD,[a,b] Nisha Schwarz, PhD,[a] Enayet Chowdhury, P
MyNgan Duong, PhD,[a] Leighton Kearney, MBBS, PhD,[a,c] Simon Stewart, PH

Open access Valvular heart disease
openheart

## Enhanced detection of severe aortic stenosis via artificial intelligence: a clinical cohort study

Geoff Strange ,[1,2] Simon Stewart ,[3,4] Andrew Watts ,[5] David Playford [6]



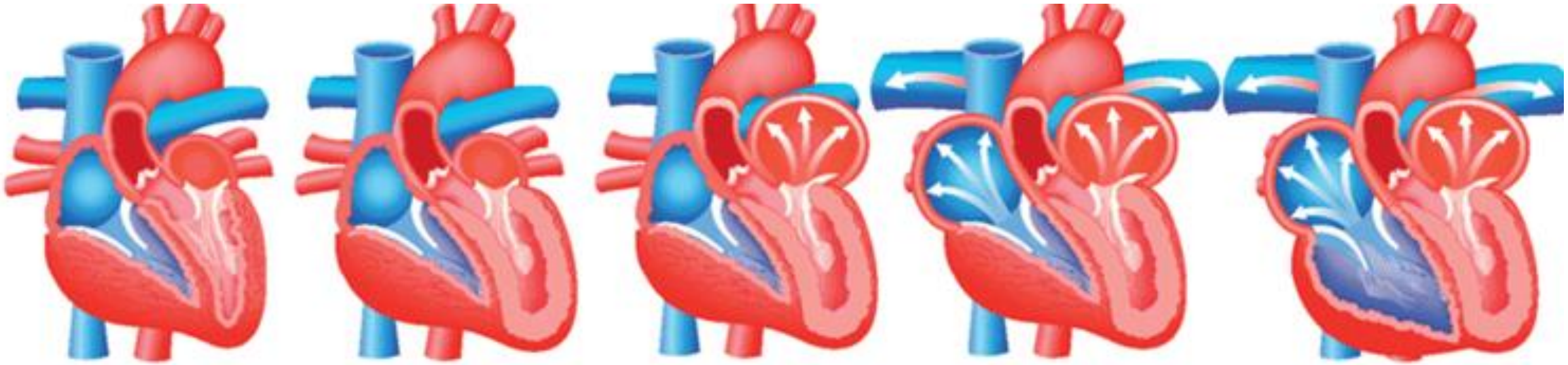

severe patients with AS from the AI-DSA-derived phenotype, if the peak velocity was ≥4.0 m/s, the mean gradient was ≥40mm Hg and/or the AVA≤1.0cm2
.

AI-DSA – a newly refined artificial intelligence support system

**4.1% identified by the AI vs 2.4% by the human alone**

**72% of additional patients inside guidelines found by the AI**

# AI-DSA – a newly refined artificial intelligence support system



| Stages/Criteria | Stage 0 | Stage 1 | Stage 2 | Stage 3 | Stage 4 |
|---|---|---|---|---|---|
| | No Cardiac Damage | LV Damage | LA or Mitral Damage | Pulmonary Vasculature or Tricuspid Damage | RV Damage |
| Echocardiogram | | Increased LV Mass Index >115 $g/m^2$ (Male) >95 $g/m^2$ (Female) | Indexed left atrial volume >34 $mL/m^2$ | Systolic Pulmonary hypertension ≥60 mmhg | Moderate-Severe right ventricular dysfunction |
| | | E/e' >14 | Moderate-Severe mitral regurgitation | Moderate-Severe tricuspid regurgitation | |
| | | LV Ejection Fraction <50% | Atrial Fibrillation | | |

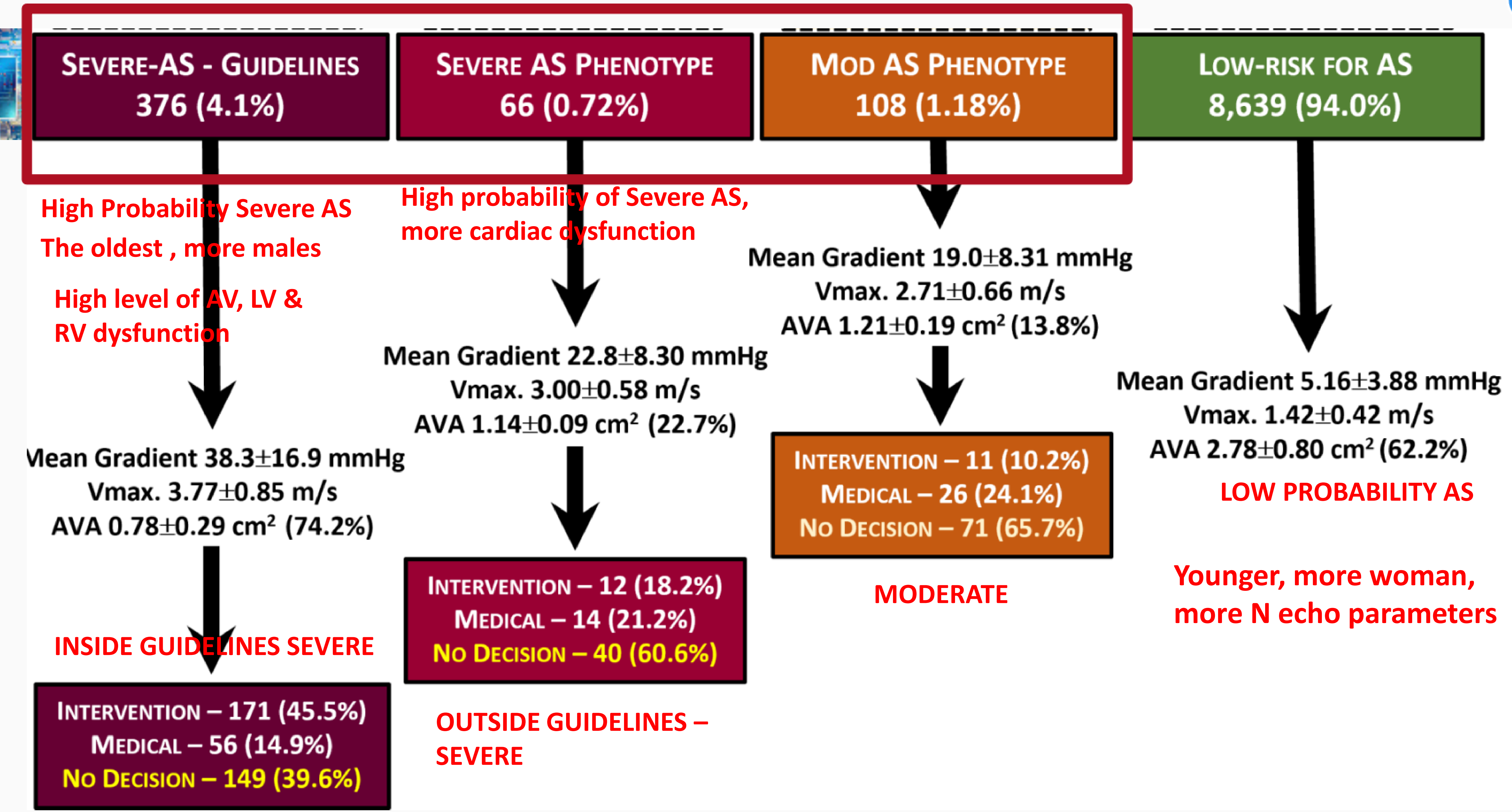
Genereux P et al. Eur Heart J. 2017

HIGH PROBABILITY SEVERE AS INSIDE GUIDELINES

HIGH PROBABILITY SEVERE AS OUTSIDE GUIDELINES

HIGH PROBABILITY MODERATE AS INSIDE GUIDELINES

LOW PROBABILITY AS =LOW RISK
MILD AS/ NO AS



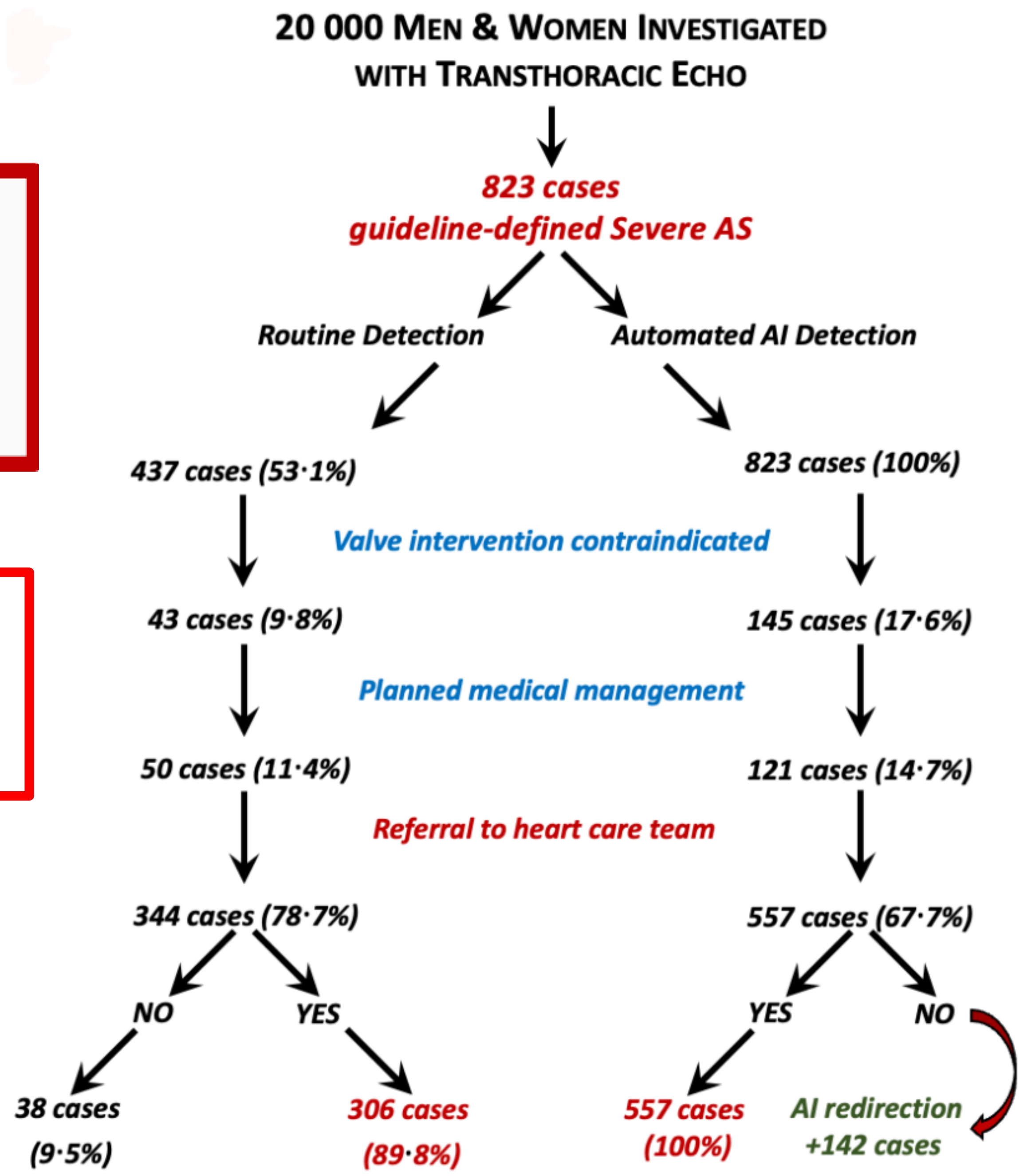
SEVERE-AS - GUIDELINES
376 (4.1%)
SEVERE AS PHENOTYPE
66 (0.72%)
MOD AS PHENOTYPE
108 (1.18%)
LOW-RISK FOR AS
8,639 (94.0%)
High Probability Severe AS
The oldest , more males
High level of AV, LV &
RV dysfunction
Mean Gradient 38.3±16.9 mmHg
Vmax. 3.77±0.85 m/s
AVA 0.78±0.29 cm² (74.2%)
INSIDE GUIDELINES SEVERE
INTERVENTION – 171 (45.5%)
MEDICAL – 56 (14.9%)
NO DECISION – 149 (39.6%)
High probability of Severe AS,
more cardiac dysfunction
Mean Gradient 22.8±8.30 mmHg
Vmax. 3.00±0.58 m/s
AVA 1.14±0.09 cm² (22.7%)
INTERVENTION – 12 (18.2%)
MEDICAL – 14 (21.2%)
NO DECISION – 40 (60.6%)
OUTSIDE GUIDELINES –
SEVERE
Mean Gradient 19.0±8.31 mmHg
Vmax. 2.71±0.66 m/s
AVA 1.21±0.19 cm² (13.8%)
INTERVENTION – 11 (10.2%)
MEDICAL – 26 (24.1%)
NO DECISION – 71 (65.7%)
MODERATE
Mean Gradient 5.16±3.88 mmHg
Vmax. 1.42±0.42 m/s
AVA 2.78±0.80 cm² (62.2%)
LOW PROBABILITY AS
Younger, more woman,
more N echo parameters

**AI-Enhanced Human Diagnosis:**
EchoSolv™ would redirect **2.1-fold more women** (29·8% to 62·1%) and **1.6-fold more men** (44·9% to 73·5%) towards definitive management (review +/- AVR).

Severe (**area less than 1.0 cm2,** mean gradient greater than 40 mm Hg or jet velocity greater than 4.0 m/s)

Pibarot, 2012

Bonow et al. Guidelines 2006



University of Glasgow
School of Cardiovascular & Metabolic Health

NHS
Greater Glasgow and Clyde

# OPERA-AI: Artificial Intelligence Reporting of Handheld Echocardiography in Suspected Heart Failure


**Dr Ross T. Campbell**

School of Cardiovascular & Metabolic Health

University of Glasgow & Queen Elizabeth University Hospital, Glasgow



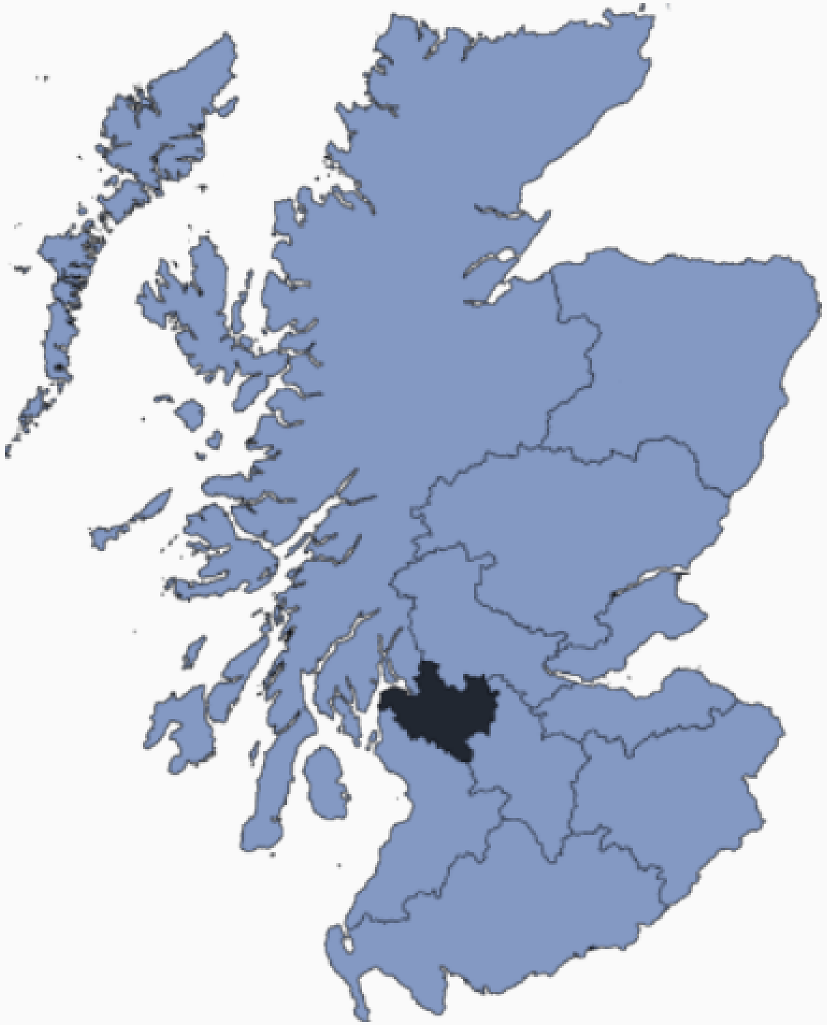
**Doctor Ross Campbell**

University of Glasgow, Glasgow (United Kingdom of Great Britain & Northern Ireland)


OPERA

27/08/2023

# Study setting



- **NHS Greater Glasgow & Clyde (Scotland)**
  - Population 1.2 million (~20% of national population)
- **Healthcare free at point of care**
- **Centralised HF referral pathway**
  - GP/ primary care to secondary care
  - NT-proBNP triage

# Carried out during COVID 19 pandemic

NHS
SCOTLAND
**NHS Louisa Jordan**



# Study Design

## Patients

- Patients attending clinical pathway for assessment of suspected HF
  - Signs/ symptoms of HF
  - Elevated NT-proBNP

## Echocardiogram

Handheld (Philips Lumify) | Cart (GE Vivid E95)

**Performed by accredited sonographer**

## Analyses

- Clinical analysis Cart
- Core lab analysis handheld + Cart
- US2.Ai analysis handheld + Cart

# Methods- AI software

**US2.Ai software allows automated echocardiogram analysis & reporting[1]**

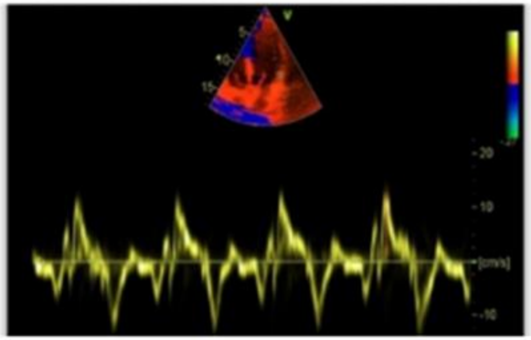
- Identifies appropriate images & performs analysis
- Generates echocardiogram report
  - Including diagnostic parameters for HFpEF

US2.AI Report

US2.AI

Main Findings

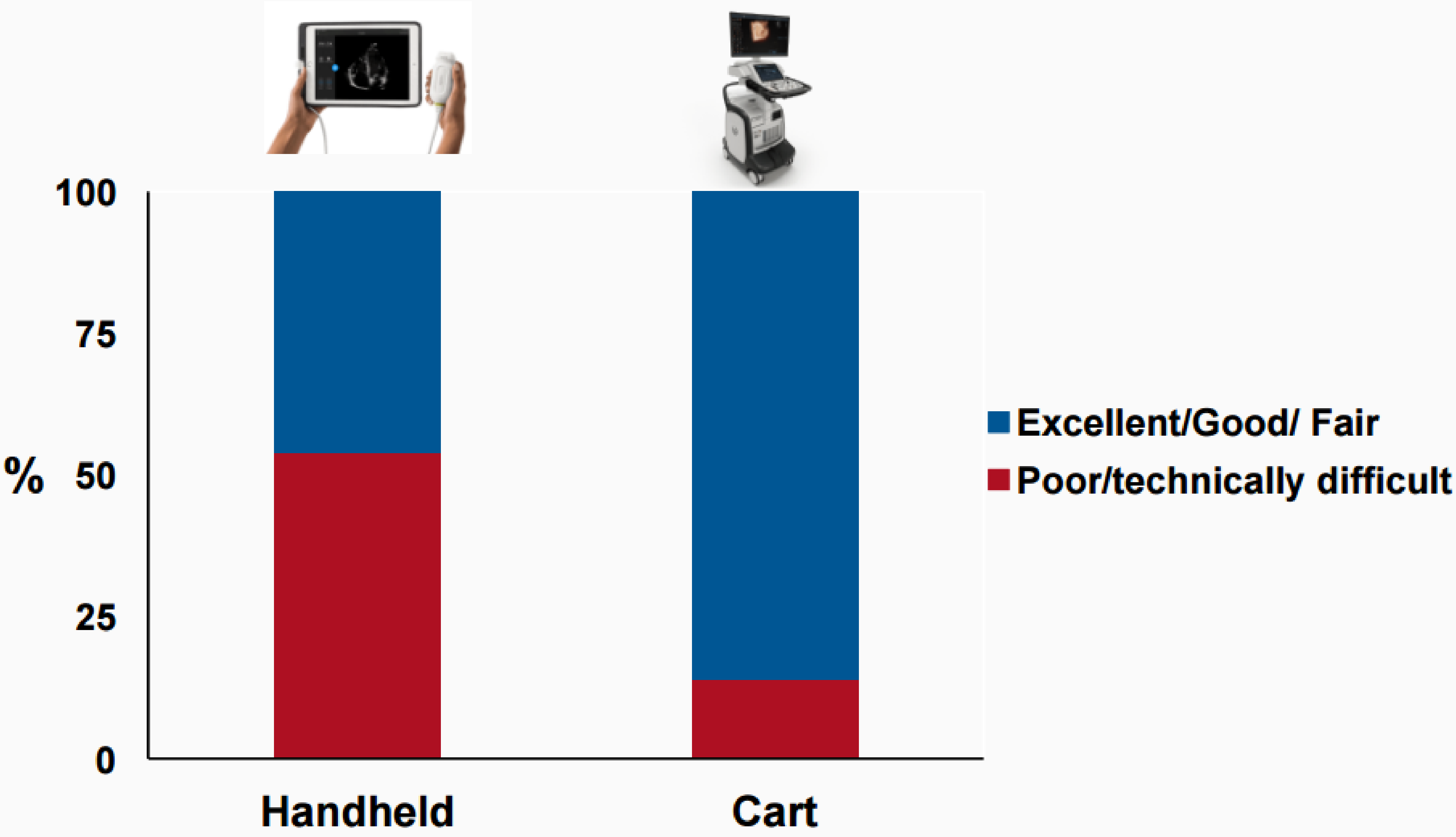
| | |
|---|---|
| LV Systolic Function | Normal |
| LV Diastolic Function | Normal |
| RV Function | Normal |
| LV Geometry | Normal |
| LV Size | Normal |
| RV Size | Abnormal |
| RA Size | Abnormal |
| LA Size | Normal |
| LVMi | 79.1 g/m² |
| RWT | 0.33 |
| MV-E | 0.71 m/s |
| MV-A | 0.52 m/s |
| E/A ratio | 1.4 |
| DecT | 239.4 ms |
| e' septal | 11.5 cm/s |
| e' lateral | 13.5 cm/s |
| E/e' mean | 5.7 |
| s' septal | 12.1cm/s |
| a' septal | 8.6 cm/s |
| s' lateral | 13.0cm/s |
| e' mean | 12.5 cm/s |
| a' lateral | 8.2 cm/s |



1. Tromp, J. *et.al.*, (2022) Lancet digital health, 4(1), 46-54. https://doi.org/10.1016/S2589-7500(21)00235-1

**Us2.ai- current echo solutions that focus on semi-automation or black box AI or just single measurements**

# Image quality assessment



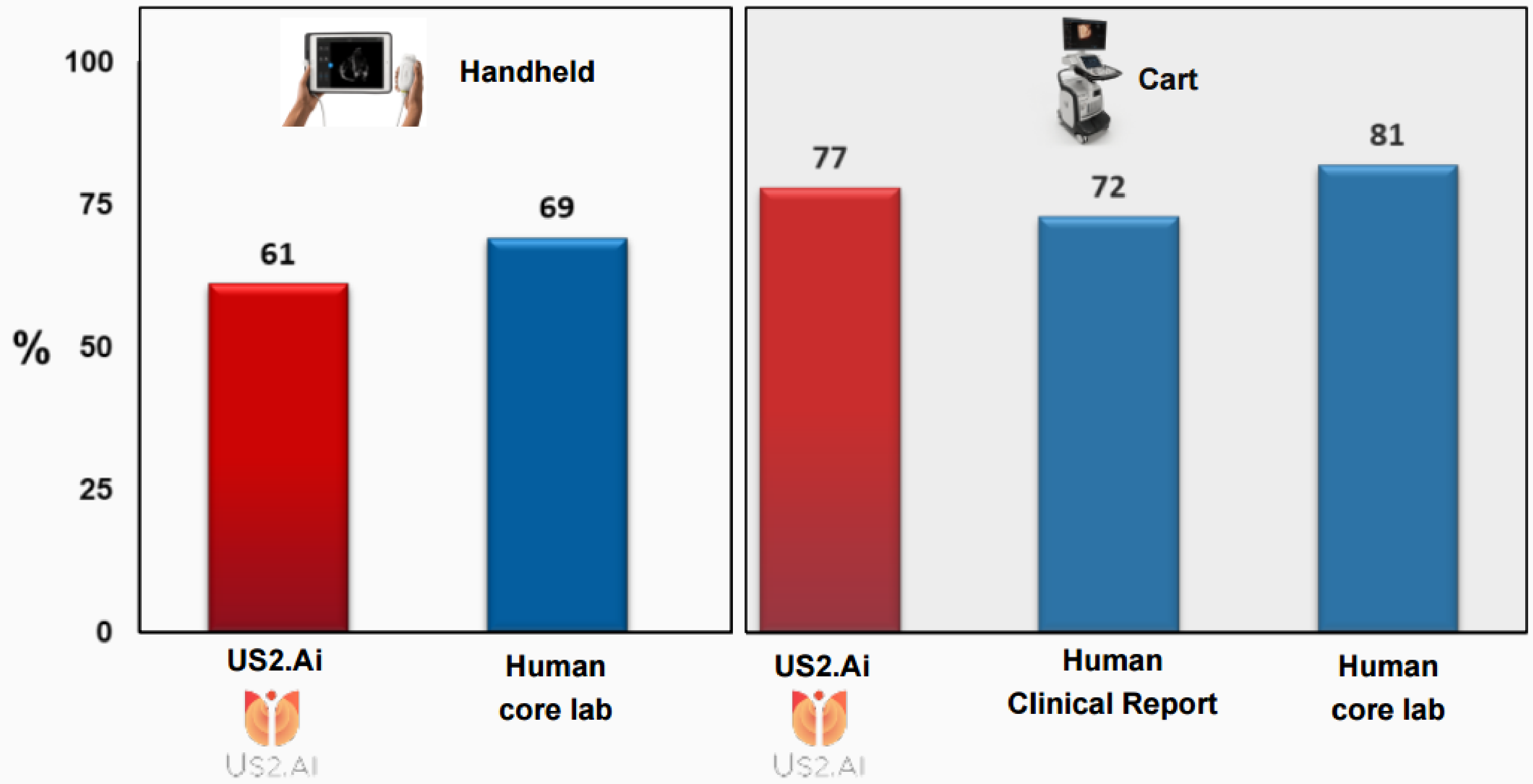
- **Comparison of interchangeability of LVEF (Simpson's biplane)**

US2.Ai AI algorithm analysis of handheld

Vs

Two accredited sonographer analysis of cart

## Percentage of scans with reportable LVEF



US2.Ai AI algorithm analysis of handheld

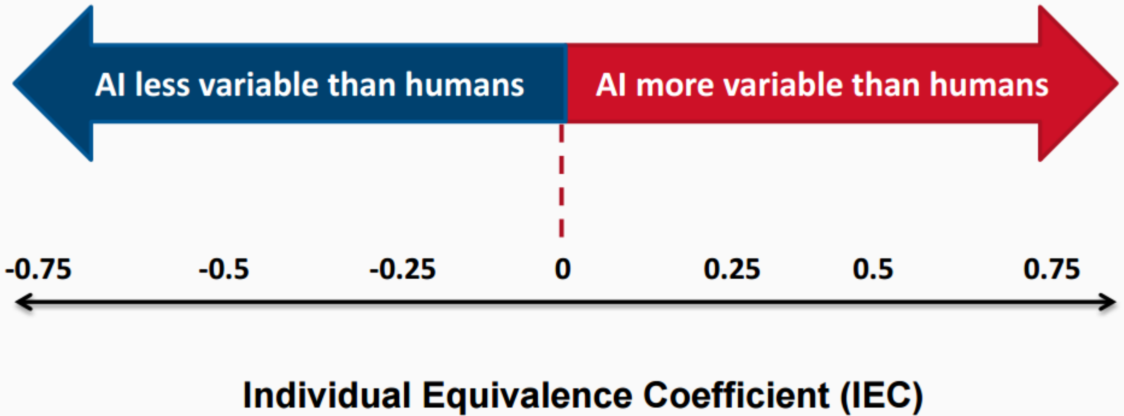

Vs

Comparison LVEF

Two accredited sonographer analysis of cart

| Individual equivalence coefficient (95% CI) for LVEF | **-0.42 (CI: -0.62, -0.19)** |
|---|---|
| < 0.25 upper limit of 95% CI = interchangeable | |

**US2.AI LVEF from handheld images was interchangeable with Cart human LVEF**



CAVA-ADHF

DZHK TRIAL 10

Mr Alexander Jobs

Heart Center of Leipzig, Leipzig (Germany)

# Decongestion guided by inferior vena cava ultrasound measurements in acute decompensated heart failure

On behalf of the CAVA-ADHF investigators

Alexander Jobs, MD

alexander.jobs@medizin.uni-leipzig.de

Heart Center Leipzig at University of Leipzig and University Heart Center Lübeck, Germany

August 27th, 2023

# Background: Congestion as major problem

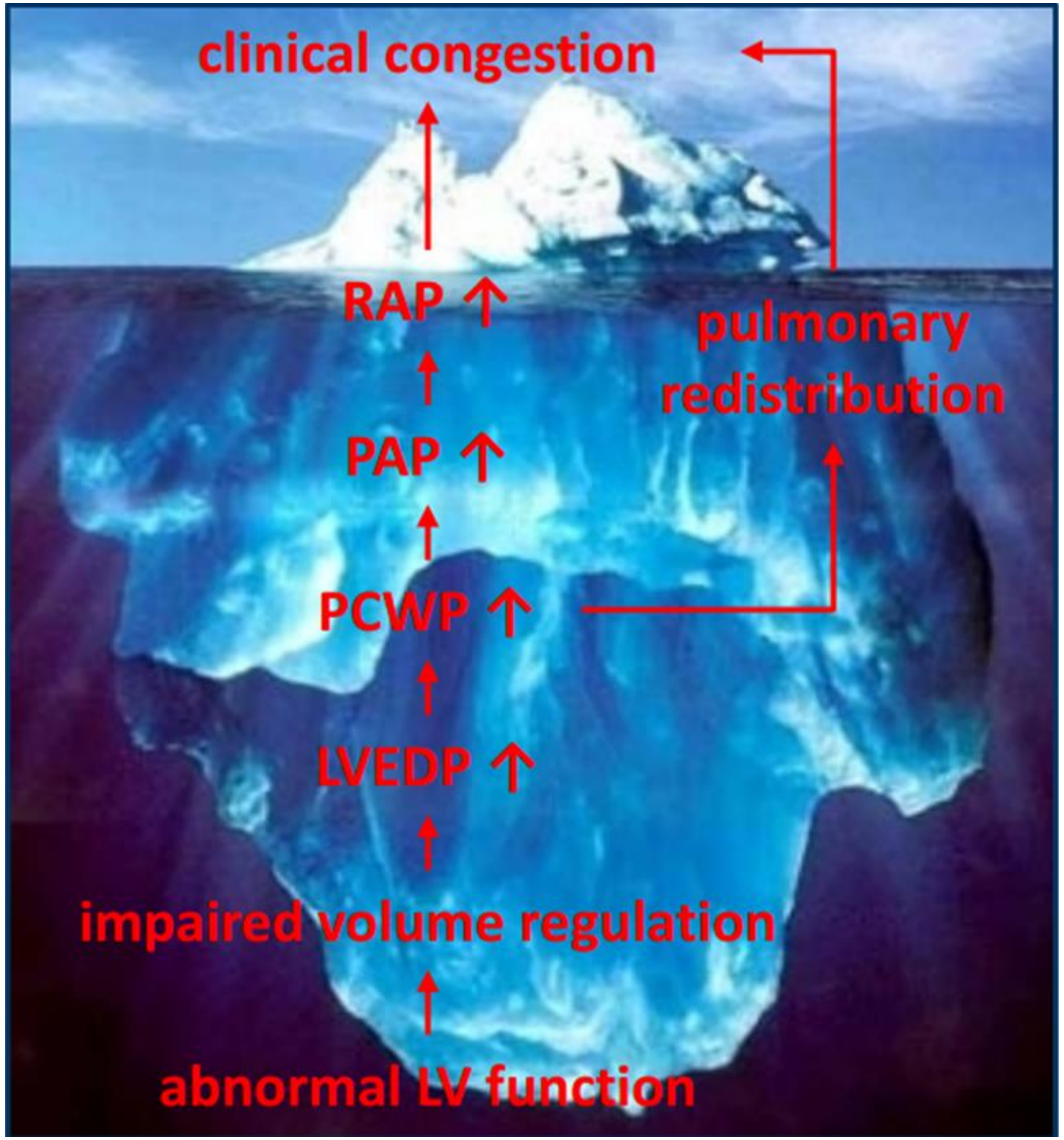
HEART FAILURE WITH

SYSTOLIC LV DYSFUNCTION →

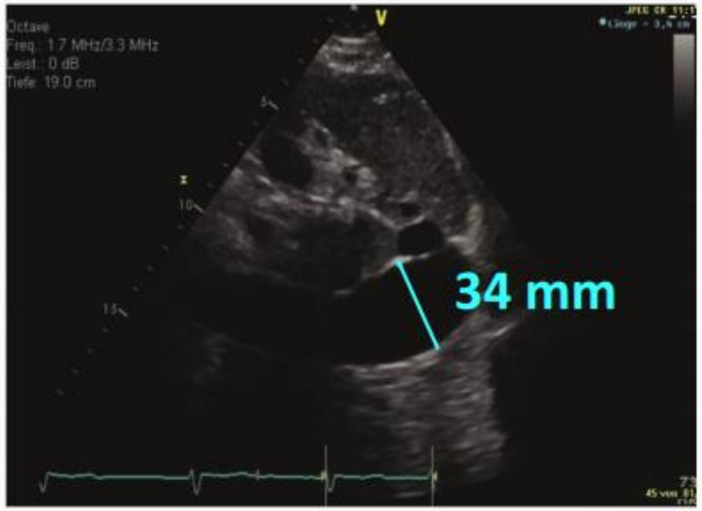
HIGH LVEDP→ HIGH PCWP →

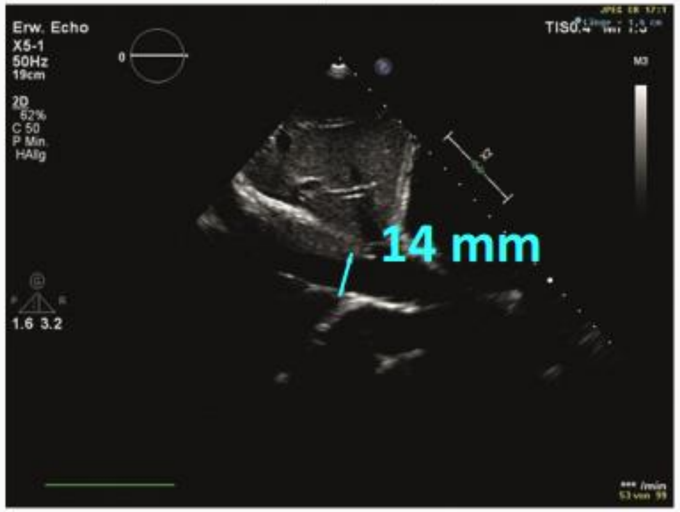
HIGH PAP → HIGH RAP →

RIGHT HEART FAILURE



# IVC measurements as surrogate of RAP




$$IVCCI = \frac{(IVCmax - IVCmin)}{IVCmax} \times 100$$

| RAP | Normal (0-5 mm Hg) | Intermediate (5-10 mm Hg) | | High (10-20 mm Hg) |
|---|---|---|---|---|
| IVCmax | ≤21 mm | ≤21 mm | >21 mm | >21 mm |
| IVCCI | >50% | <50% | >50% | <50% |

# Objective of CAVA-ADHF

CAVA-ADHF
DZHK TRIAL 10

DZHK
DEUTSCHES ZENTRUM FÜR HERZ-KREISLAUF-FORSCHUNG E.V.

**To determine whether decongestion guided by ultrasound assessment of IVC diameters in addition to clinical assessment leads to greater reductions in NT-proBNP levels from baseline to hospital discharge as compared with decongestion guided by clinical assessment alone.**

# Design


15 trial sites in Germany

CAVA-ADHF
DZHK TRIAL 10

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**Patient admitted for ADHF**

↓

Informed consent

↓

Baseline assessments including NT-proBNP

↓

Randomisation

**Usual-care (n = 194)**
Treating physicians **unaware** of daily IVC ultrasound findings.

Treatment goal for discharge:

1. Relief of symptoms and signs of congestion

**IVC ultrasound-guided (n = 194)**
Treating physicians **aware** of daily IVC ultrasound findings.

Treatment goal for discharge:

1. Relief of symptoms and signs of congestion
2. IVCmax ≤21 mm
3. IVCCI >50%

↓

Discharge assessments including NT-proBNP

↓

180 to 210 days after randomisation
Telephone interview for assessment of clinical endpoints

# Baseline Characteristics

CAVA-ADHF
DZHK TRIAL 10
DZHK
DEUTSCHES ZENTRUM FÜR HERZ-KREISLAUF-FORSCHUNG E.V.

| | Usual-care (n = 192) | IVC ultrasound-guided (n = 192) |
|---|---|---|
| **Age, years**; mean (SD) | 72.7 (12.4) | 73.8 (11.6) |
| **Female sex** | 30.4% | 29.7% |
| **NYHA functional class** | | |
| III | 69.5% | 71.9% |
| IV | 30.5% | 28.1% |
| **LV-EF, %;** median (IQR) | 40 (25 to 54) | 37.5 (27 to 51) |
| **NT-proBNP**, ng/l; median (IQR) | 4,335 (2,256 to 9,060) | 4,909 (2,534 to 10,141) |
| **eGFR**, ml/min/1.73m²; median (IQR) | 51 (40-69) | 53 (41-67) |
| **Previous hospitalization for HF** | 76.9% | 80.3% |
| **Atrial fibrillation or flutter** | 69.3% | 64.7% |

CAVA-ADHF
DZHK TRIAL 10

DZHK
DEUTSCHES ZENTRUM FÜR HERZ-KREISLAUF-FORSCHUNG E.V.

# Conclusion

**Among patients with ADHF, the addition of IVC ultrasound to clinical assessment, in comparison to clinical assessment alone, did not improve decongestion as assessed by the change in NT-proBNP levels from baseline to discharge.**

# Increased Mortality Associated with Mild, Moderate and Severe Mitral Regurgitation

Professor David Playford

**David Playford**

MBBS PhD FRACP FCSANZ FESC FACC

Professor of Cardiology, The University of Notre Dame Australia

Co-Founder and Chief Investigator, National Echo Database Australia

David Playford, Simon Stewart, Sarah Harris, Greg Scalia, David Celermajer, Liza Thomas, Kai Chan and Geoff Strange

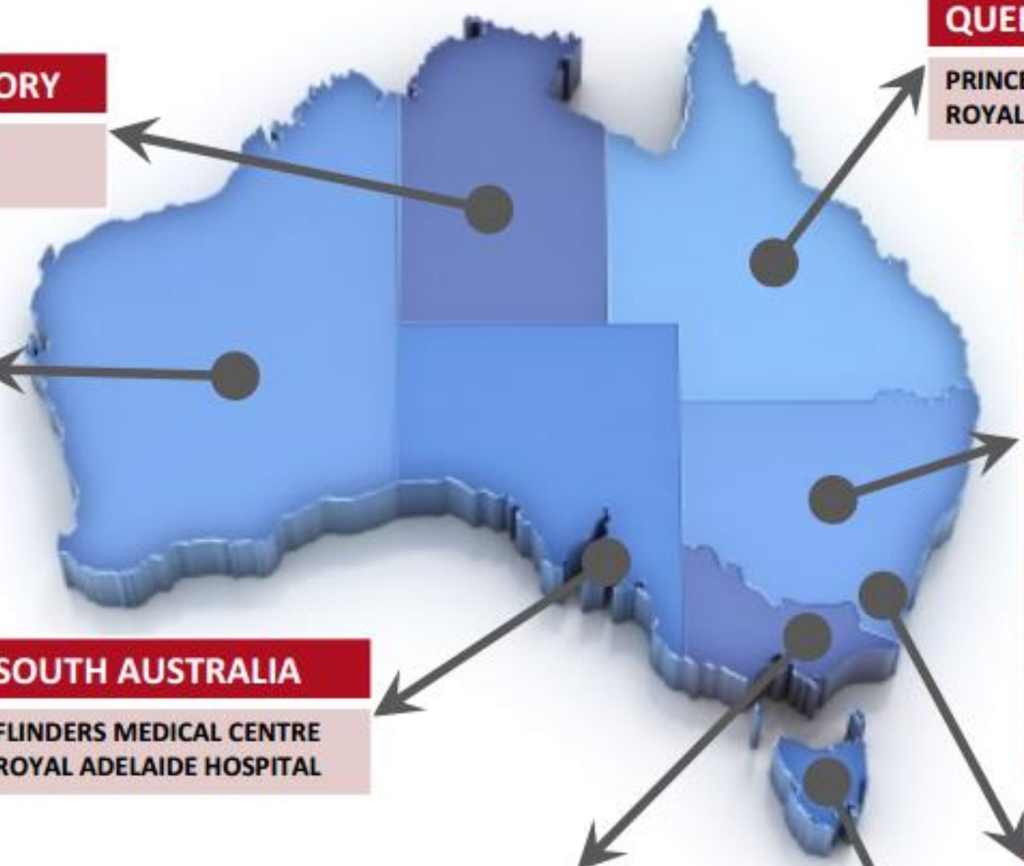
On behalf of the NEDA Contributing Sites

# National Echo Database Australia - Contributing Sites

Population:
~25,000,000
Aged > 18 years:
~ 20,000,000

**33 main contributing sites** representing every state and territory of Australia

**Individual linkage with mortality** via the National Deaths Index



**NORTHERN TERRITORY**
ROYAL DARWIN HOSPITAL
NT CARDIAC

**WESTERN AUSTRALIA**
FIONA STANLEY HOSPITAL
FREMANTLE HOSPITAL
ROYAL PERTH HOSPITAL
HEARTS WEST
CARDIOVASCULAR SERVICES

**SOUTH AUSTRALIA**
FLINDERS MEDICAL CENTRE
ROYAL ADELAIDE HOSPITAL

**VICTORIA**
BARWON HEALTH
BAKER INSTITUTE
ST VINCENT'S HOSPITAL
WESTERN HEALTH

**QUEENSLAND**
PRINCE CHARLES HOSPITAL
ROYAL BRISBANE HOSPITAL

**NEW SOUTH WALES**
BLACKTOWN HOSPITAL
JOHN HUNTER HOSPITAL
NEPEAN HOSPITAL
ROYAL PRINCE ALFRED
WESTMEAD HOSPITAL
ROYAL NORTH SHORE HOSPITAL
CROWN MEDICAL NETWORK
HACKWORTHY CARDIOLOGY
ST VINCENTS CLINIC
CONCORD HOSPITAL
CANTERBURY HOSPITAL
BOWRAL AND DISTRICT HOSPITAL
CAMPBELLTOWN HOSPITAL
FAIRFIELD HOSPITAL
BANKSTOWN-LIDCOMBE HOSPITAL

**ACT**
CANBERRA HOSPITAL

**TASMANIA**
ROYAL HOBART HOSPITAL
CHARLES CLINIC HEART CARE

# Background and Study Objective

- **Background**: Prognostic implications of severe MR are well recognised, but **mortality implications of mild and moderate MR** are uncertain

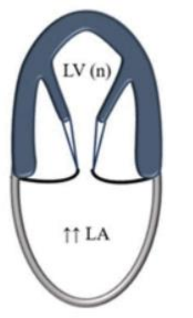
- **Objective**: To determine **prognostic impact of worsening degrees of MR**, including:
  - MR due to mitral leaflet disease (MLD)
  - Atrial functional MR (aFMR)
  - Ventricular functional MR (vFMR)

**MLD definition:**

Any mitral leaflet **abnormality** reported, extracted using NLP

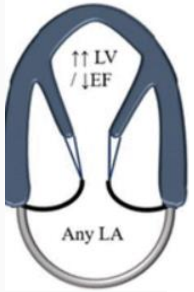
**Atrial FMR definition*:**

Severe LA dilatation and normal LVEF and no/mild LV dilatation




**Ventricular FMR definition*:**

Moderate or severe LV dilatation and/or LVEF <50%






* full definitions available on request

# Study Population

- NEDA v2.0 (census 21/05/2019), last echo, **excluding prior mitral valve intervention**

**National Echo Database of Australia (v2.0)**
1,077,145 echo study reports from 631,824 men & women aged ≥18 years linked to mortality
(1st echo to Study Census - 01/01/2000 to 26/06/2019)

Excluded sequentially from primary analyses:
- Echo studies without complete data (i.e. echo completed outside 01/01/2000 to 21/05/2019 inclusive) (n=17,786 from 10,287 individuals)
- Repeat echo studies n= 437,822 (41.3%) (Range 1-52 with 386,414 having ≤5 repeat investigations) – LAST ONLY
- **Mitral Valve Intervention: n= 9,375**

**608,570 people screened for mitral valve disease/MR via Natural Language Processing between 01/01/2000 to 21/05/2019 inclusive**

**319,808 Men aged 61.8±17.1 years & 288,762 Women aged 62.1±18.5 years**
**153,612 all-cause deaths during median 1,541 [IQR 820 – 2,629] years follow-up**

**No/Trivial MR**
M: 243,774 (53.3%)
W: 213,215 (46.7%)
MLD: 120,047 (26.3%)

102,950 (16.9%)

**Mild MR**
M: 51,613 (50.1%)
W: 51,337 (49.9%)
MLD: 57,200 (55.6%)

38,504 (6.3%)

**Moderate MR**
M: 18,931 (49.2%)
W: 19,573 (51.8%)
MLD: 27,721 (72.0%)

10,127 (1.7%)

**Severe MR**
M: 5,490 (54.2%)
W: 4,637 (45.8%)
MLD: 7,995 (78.9%)

| | |
|---|---|
| **No/trivial MR:** | **75.1%** |
| **Mild MR:** | **16.9%** |
| **Moderate MR:** | **6.3%** |
| **Severe MR:** | **1.7%** |

- Echo reports examined for **Mitral Leaflet Disease (MLD) and MR severity** using a **Natural Language Processing (NLP)** custom engine developed by Echo IQ Ltd

- Individual patient-level linkage to mortality via the **Australian National Deaths Index**

# Characteristics of men and women with mild to severe MR

- **Increasing age with worsening MR severity**
- **Atrial Fibrillation (AF) increasingly common with worse MR severity**
- **Increased ventricular dimension, LV mass, atrial volumes, pulmonary pressure and TR severity with worsening MR severity**

| | MEN (N=319,808) | | | | WOMEN (n=288,762) | | | |
|---|---|---|---|---|---|---|---|---|
| | No MR (n=243,774) | Mild MR (n=51,613) | Moderate MR (n=18,931) | Severe MR (n=5,490) | No MR (n=213,215) | Mild MR (n=51,337) | Moderate MR (n=19,573) | Severe MR (n=4,637) |
| Age at Echo, years | 59.0 ± 17.0 | 69.5 ± 14.2 | 73.5 ± 13.4 | 72.9 ± 14.3 | 58.7 ± 18.3 | 70.3 ± 15.5 | 75.3 ± 14.3 | 75.9 ± 15.3 |
| Atrial Fibrillation, n(%) | 16,427 (6.7%) | 7,551 (14.6%) | 5,027 (26.6%) | 1,646 (30.0%) | 11,742 (5.5%) | 5,093 (9.9%) | 4297 (22.0%) | 1304 (28.1%) |
| LVSD, cm | 3.2 ± 0.7 | 3.4 ± 0.9 | 3.9 ± 1.1 | 4.4 ± 1.3 | 2.8 ± 0.6 | 2.8 ± 0.7 | 3.1 ± 0.9 | 3.5 ± 1.1 |
| LVMi, g/m² | 91.9 ± 25.6 | 114.0 ± 34.8 | 122.0 ± 36.8 | 132.2 ± 37.3 | 78.5 ± 22.4 | 98.3 ± 33.7 | 105.3 ± 35.0 | 116.0 ± 36.8 |
| LVEF, % | 61.2 ± 11.1 | 58.6 ± 15.4 | 49.1 ± 17.4 | 44.0 ± 19.1 | 65.1 ± 9.5 | 64.6 ± 12.7 | 58.1 ± 15.4 | 51.8 ± 18.0 |
| Septal e' Velocity, cm/s | 8.4 ± 2.9 | 6.9 ± 2.4 | 6.6 ± 2.4 | 6.4 ± 2.5 | 8.8 ± 3.1 | 7.2 ± 2.7 | 6.7 ± 2.5 | 6.3 ± 2.5 |
| LAVi, ml/m² | 33.5 ± 16.2 | 69.6 ± 37.5 | 79.8 ± 48.7 | 84.9 ± 54.2 | 31.6 ± 15.3 | 61.0 ± 32.5 | 73.51 ± 42.4 | 88.6 ± 55.6 |
| Moderate-Severe TR, n(%) | 4,105 (16.8%) | 4,614 (19.2%) | 5,134 (48.8%) | 1,865 (58.0%) | 5,553 (18.9%) | 6,241 (23.5%) | 6,199 (52.3%) | 1,929 (63.6%) |
| Estimated RVSP, mmHg | 35.2 ± 10.6 | 39.8 ± 11.6 | 43.6 ± 13.2 | 48.3 ± 14.9 | 35.0 ± 10.8 | 39.4 ± 11.9 | 43.5 ± 13.5 | 49.4 ± 15.4 |

# Mitral Regurgitation Characteristics

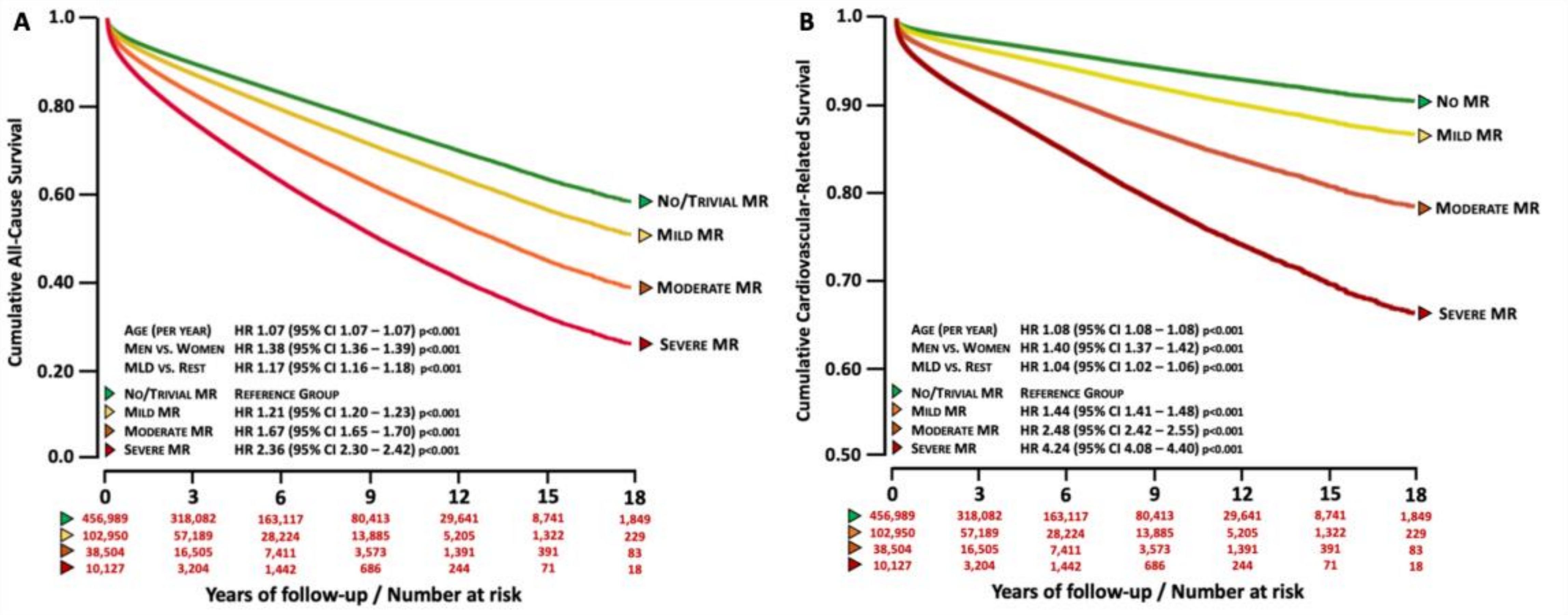
- Mitral leaflet thickening commonly reported (~20% without MR, ~60% with severe MR)
- Mitral valve prolapse much more common with severe MR
- Mitral stenosis more common in women, particularly with severe MR
- vFMR more associated with severe MR and aFMR with mild MR

| | MEN (N=319,808) | | | | WOMEN (n=288,762) | | | |
|---|---|---|---|---|---|---|---|---|
| | No MR (n=243,774) | Mild MR (n=51,613) | Moderate MR (n=18,931) | Severe MR (n=5,490) | No MR (n=213,215) | Mild MR (n=51,337) | Moderate MR (n=19,573) | Severe MR (n=4,637) |
| Mitral Thickening, n(%) | 44,948 (18.4%) | 21,549 (41.8%) | 10,344 (54.6%) | 3,238 (59.0%) | 42,106 (19.7%) | 22,395 (43.6%) | 11,109 (56.8%) | 2,944 (63.5%) |
| Mitral Calcification, n(%) | 16,289 (6.7%) | 9,879 (19.1%) | 4,879 (25.8%) | 1,312 (23.9%) | 17,890 (8.4%) | 12,438 (24.2%) | 6,694 (34.2%) | 1,731 (37.3%) |
| Mitral Prolapse, n(%) | 7,029 (2.9%) | 1,724 (3.3%) | 1,806 (9.5%) | 1,236 (22.5%) | 6,212 (2.9%) | 2,010 (3.9%) | 1,729 (8.8%) | 872 (18.8%) |
| Mitral Endocarditis, n(%) | 812 (0.3%) | 295 (0.6%) | 197 (1.0%) | 188 (3.4%) | 495 (0.2%) | 261 (0.5%) | 188 (1.0%) | 118 (2.5%) |
| Mitral Stenosis*, n(%) | 705 (0.3%) | 272 (0.5%) | 257 (1.4%) | 122 (2.2%) | 1,316 (0.6%) | 668 (1.3%) | 756 (3.9%) | 329 (7.1%) |
| Any form of MLD, n(%) | 61,558 (25.3%) | 27,481 (53.2%) | 13,169 (69.6%) | 4,194 (76.4%) | 58,489 (27.4%) | 29,719 (57.9%) | 14,552 (74.4%) | 3,801 (82.0%) |
| Ventricular FMR, n(%) | 4,903 (2.7%) | 1,616 (6.7%) | 952 (16.5%) | 294 (22.7%) | 3,828 (2.5%) | 752 (3.5%) | 455 (9.1%) | 151 (18.1%) |
| Atrial FMR, n(%) | 5,018 (2.8%) | 6,676 (29.7%) | 844 (17.6%) | 66 (6.6%) | 4,652 (3.1%) | 5,921 (28.4%) | 982 (21.5%) | 72 (10.5%) |

* Mitral Stenosis: Mean antegrade MV gradient >5mmHg

MLD = Mitral Leaflet Disease
FMR = Functional Mitral Regurgitation

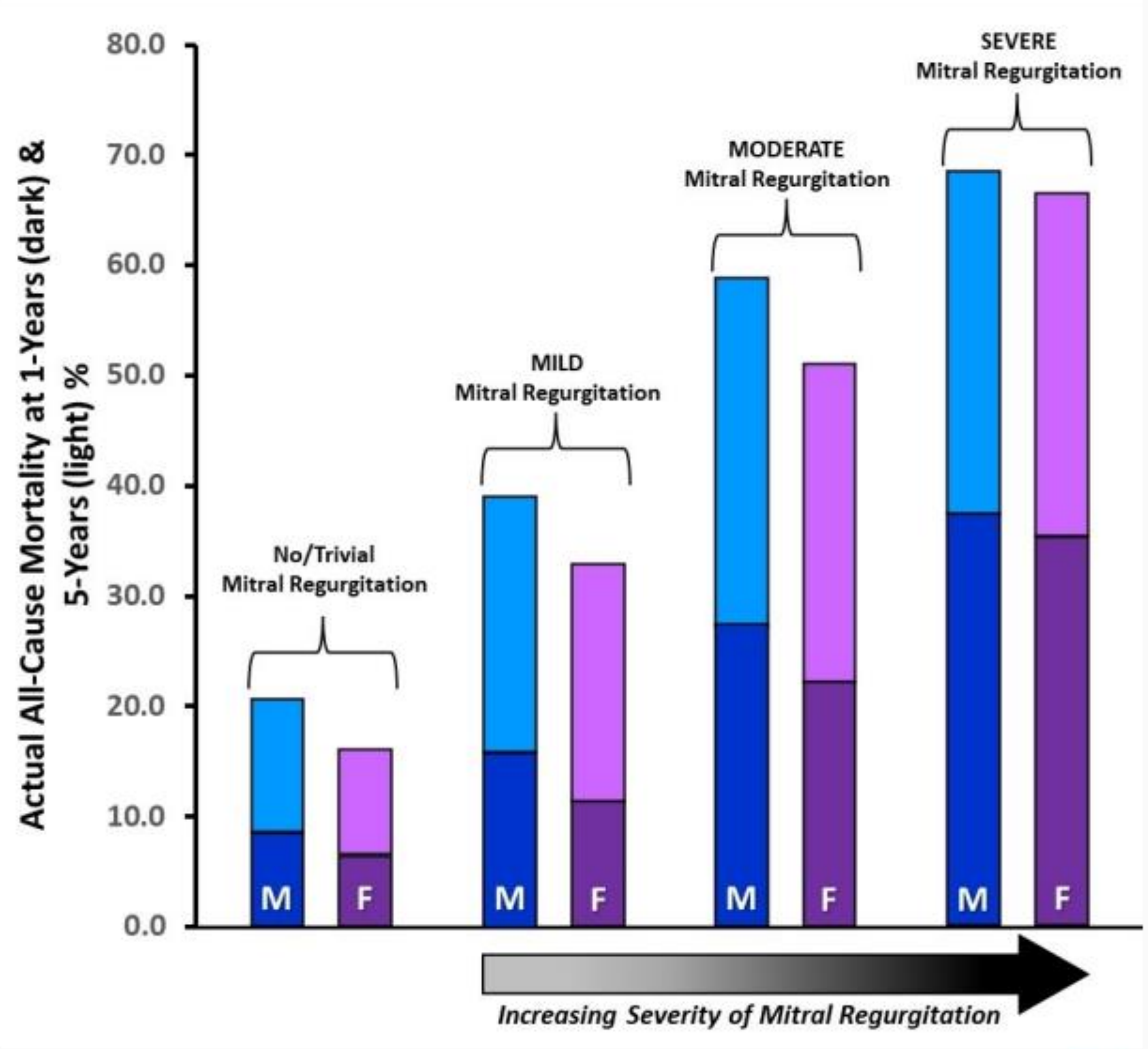
# Adjusted long-term all-cause (A) and Cardiovascular-related (B) mortality according to MR severity




**Pattern of mortality persisted after adjustment for age, sex, mitral leaflet disease, atrial fibrillation, aFMR & vFMR, LV ejection fraction, TR peak velocity and time of echo**

# Summary

- **Increasing severity of MR is associated with rising mortality**
- Minor sex difference observed **(M>F)** except for severe MR
- Uncorrected **severe MR** has a poor prognosis
- **Mild and moderate MR** are also associated with mortality
- Mortality in mild and moderate MR may be due to **phenotypic cardiac changes**, further investigation is warranted



# Limitations

- **Clinical information** (e.g. comorbidity, drug treatment, procedures) not captured in NEDA v2.0
- **Other external factors** may be responsible for the mortality association despite persistence with adjustment
- **No independent image-based adjudication of MR severity** – although systematic over- or under-estimation unlikely
- **Quantitation data for MR severity not readily available** despite its use for grading MR severity
- Small proportion of acute MR unlikely to affect results (and more likely to be severe)

# Mortality due to rheumatic heart disease

Professor Ganesan Karthikeyan

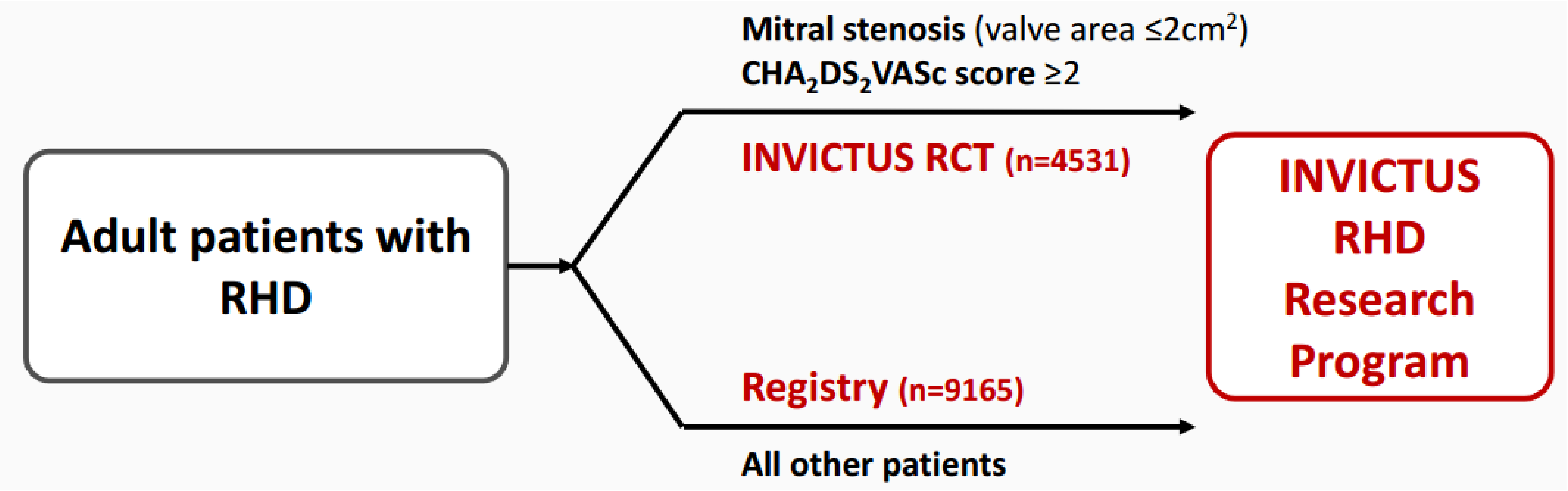
Primary results from the INVICTUS rheumatic heart disease research program from 24 countries

**Ganesan Karthikeyan**, Connolly S, Ntsekhe M, Rangarajan S, and Yusuf S for the INVICTUS Steering Committee and Investigators

25th August 2023

# RHD affects over 40 million people, mainly in LMICs

## In 2018, the WHO adopted a resolution calling for high quality data to guide policy and action




- **Primary outcome**
  - All-cause mortality (vascular* and non-vascular)
  - *Death due to HF, sudden death, stroke

**Secondary outcomes**
- Hospitalization for HF
- Stroke or TIA
- Infective endocarditis
- Recurrent rheumatic fever

# Participating sites

- **13,696** participants over **6 years**
- 138 sites in 24 LMICs
- Africa, Asia, Middle-East, and Latin America
- PHRI, Hamilton, Coordinating Centre

# Key differences by country income status

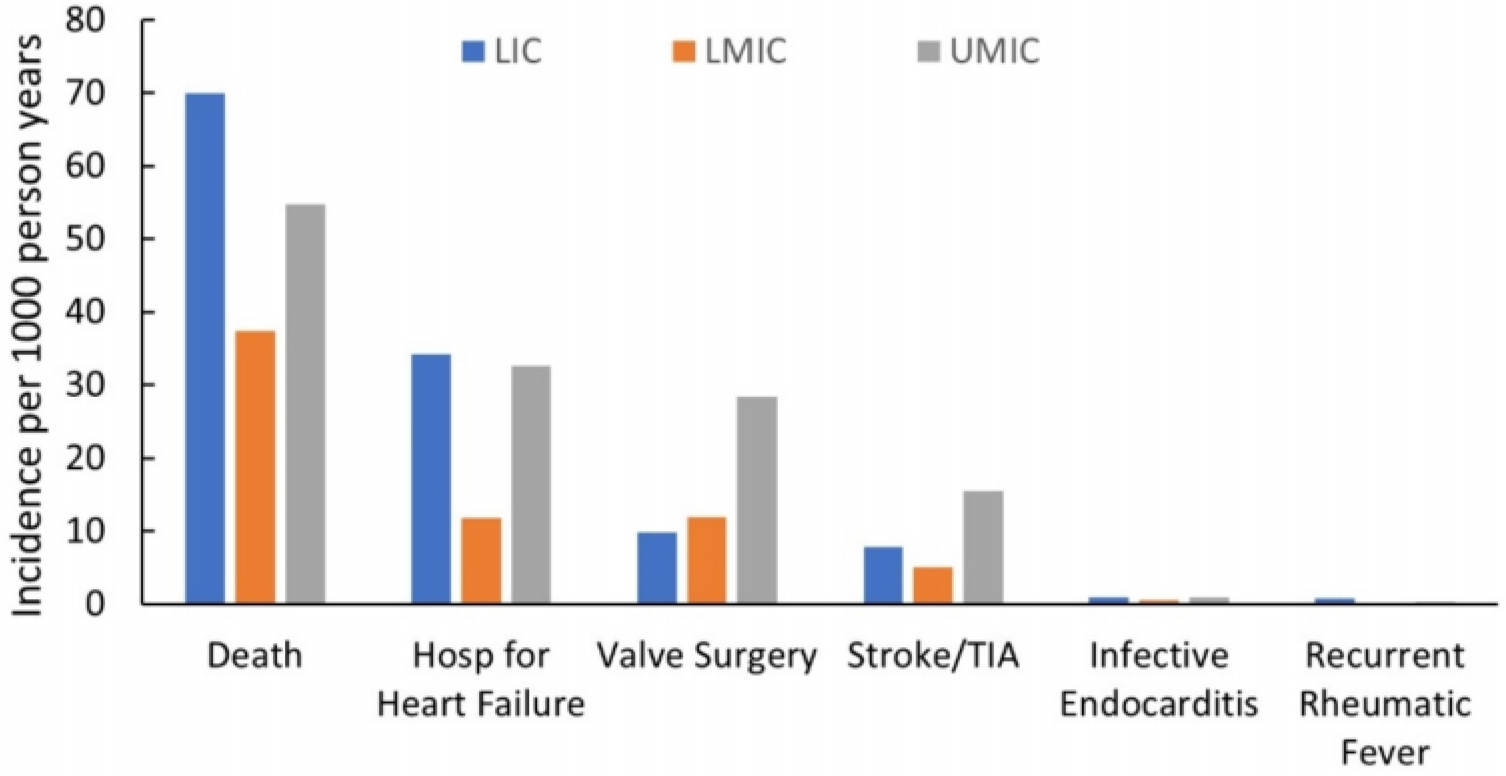
| | LIC (n=2769) | LMIC (n=8453) | UMIC (n=2474) |
|---|---|---|---|
| Age, years, mean | 33.1 | 43.9 | **52.3** |
| Atrial fibrillation, n (%) | 719 (26.0) | 2874 (34.0) | 889 (**35.9**) |
| Mitral regurgitation, n (%) | 1249 (45.1) | 3723 (44.0) | 920 (37.2) |
| Aortic regurgitation, n (%) | 546 (19.7) | 1367 (16.2) | 370(15.0) |
| Aortic stenosis, n (%) | 29 (1.1) | 206 (2.4) | 96 (3.9) |
| Pulmonary hypertension, n (%) | 1087 (39.2) | 3411 (40.4) | 803 (**32.5**) |
| Diuretic use, n (%) | 2182 (78.8) | 6626 (78.4) | 1554 (**62.8**) |
| Secondary prophylaxis, n (%) | 1748 (63.1) | 3522 (41.7) | 385 (15.6) |
| Prior valvuloplasty or surgery | 378 (13.7) | 1348 (16.0) | 1124 (**45.4**) |

*p value for trend <0.0001 for all comparisons*

| | Overall (n=13696) | LIC (n=2769) | LMIC (n=8453) | UMIC (n=2474) |
|---|---|---|---|---|
| Smoking, n (%) | 1299 (9.5) | 103 (3.7) | 587 (6.9) | 609 (24.6) |
| Hypertension, n (%) | 2490 (18.2) | 222 (8.0) | 1223 (14.5) | 1045 (42.2) |
| Diabetes, n (%) | 633 (4.6) | 48 (1.7) | 347 (4.1) | 238 (9.6) |
| Stroke/TIA/SE, n (%) | 1201 (8.8) | 167 (6.0) | 568 (6.7) | 466 (18.8) |
| Coronary artery disease, n (%) | 145 (1.1) | 18 (0.7) | 46 (0.5) | 81 (3.3) |

*p value for trend <0.0001 for all comparisons*

N=13,696, median 3.1 years (2.2, 4.0 years), 95% follow-up 14.2% patients died




Valve surgery: 3.3% (LIC), 4% (LMIC), and 7.2% (UMIC)

Death d/t any cause 4.7% /y (1943)

HF hospitalization 2.0%/ y (805)

Cardiovascular death 3.2%/y (1312)
- Heart failure 1.6%/y (667)
- Sudden death 0.9%/y (352)
- Stroke 0.2%/y(79)

# Predictors of mortality

| | HR (95% CI) | p value |
|---|---|---|
| Age (10-year increase) | 1.07 (1.03-1.11) | <0.0001 |
| **Congestive heart failure** | **1.68** (1.50, 1.87) | <0.0001 |
| **Pulmonary hypertension** | **1.52** (1.37, 1.69) | <0.0001 |
| **Atrial fibrillation** | **1.30** (1.15, 1.46) | <0.0001 |
| **Left ventricular dysfunction** | **1.18** (1.05, 1.32) | 0.0049 |
| Smoking | 1.20 (1.03, 1.39) | 0.0179 |
| Diabetes | 1.56 (1.30, 1.87) | <0.0001 |
| Prior stroke/TIA | 1.24 (1.08, 1.42) | 0.0022 |
| Coronary artery disease | 1.57 (1.14, 2.18) | 0.0059 |
| **Higher country income group**<br>- UMIC vs. LIC<br>- LMIC vs. LIC | <br>**0.57** (0.34, 0.94)<br>**0.49** (0.31, 0.76) | <br>0.0287<br>0.0016 |
| Secondary antibiotic prophylaxis* | 0.71 (0.59, 0.85) | 0.0002 |

LIC

UMIC

# Conclusions and implications

- Mortality in RHD is mainly due to **heart failure**
- May be due to **lower utilization of valve surgery and valvuloplasty** and limited access to **hospitalization** for HF

The greatest reduction in morbidity and mortality may be achieved by

1. Increasing the availability and access to timely **valve interventions and surgery**, and
2. Improving access and outcomes of **hospital care** for HF

***THANK YOU FOR YOUR ATTENTION***