Tonight’s webinar will begin shortly

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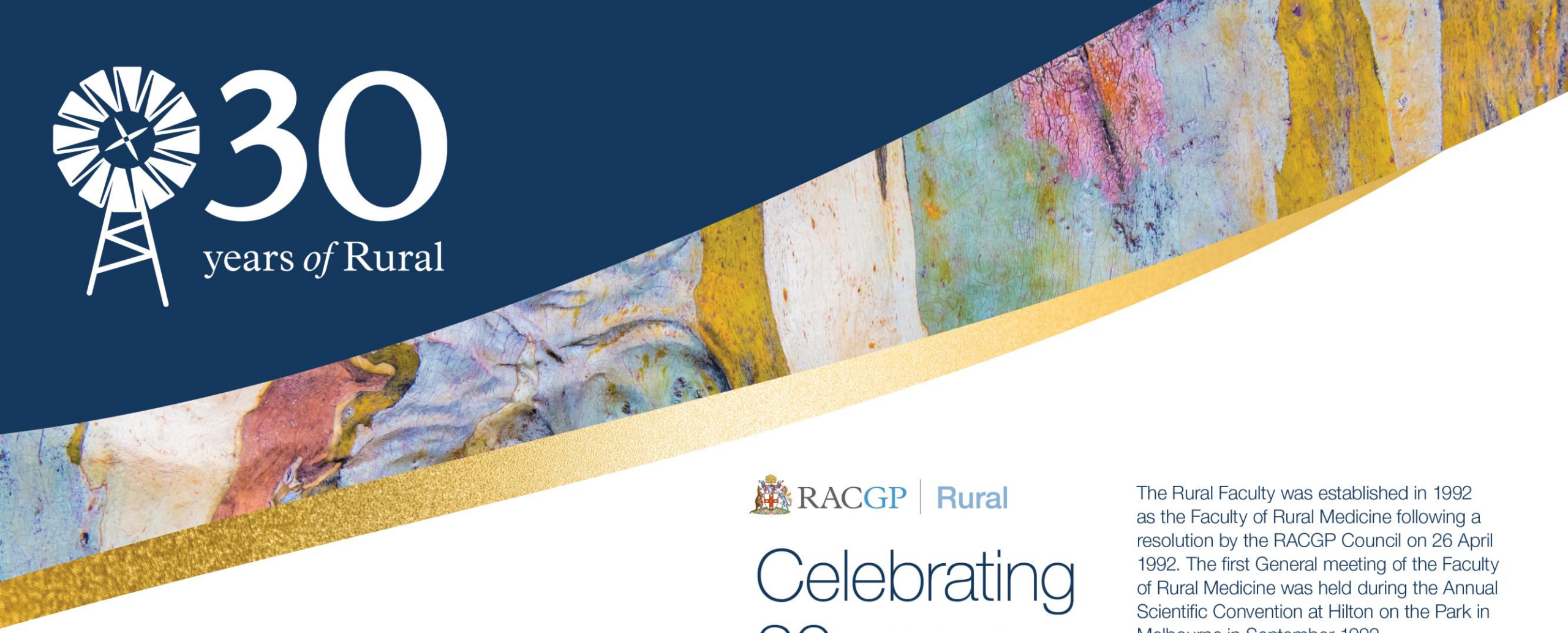

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2020
22

We will begin in 30 seconds

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We will begin in 15 seconds

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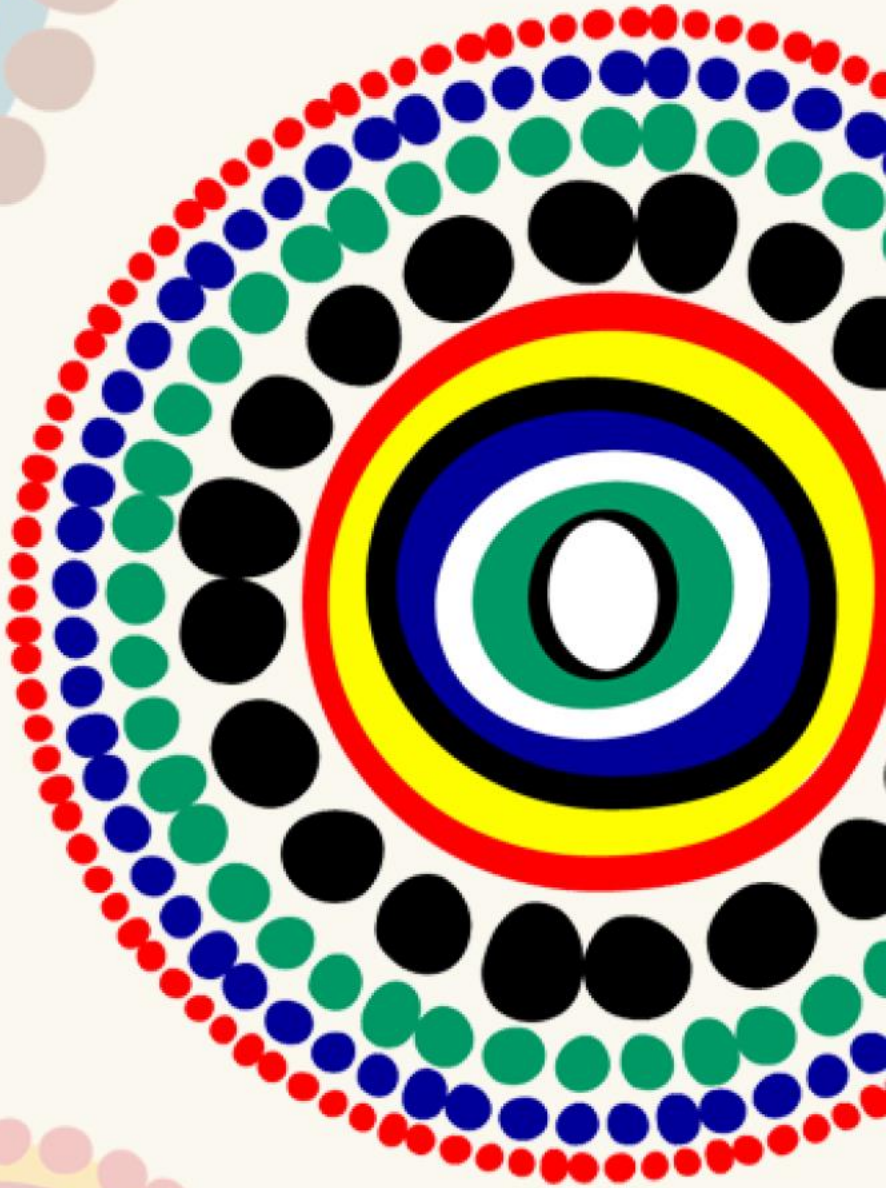

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Welcome to tonight's webinar

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Listening to the heart- Key updates on the function of the 'pump and the valves'

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Where is my control panel?

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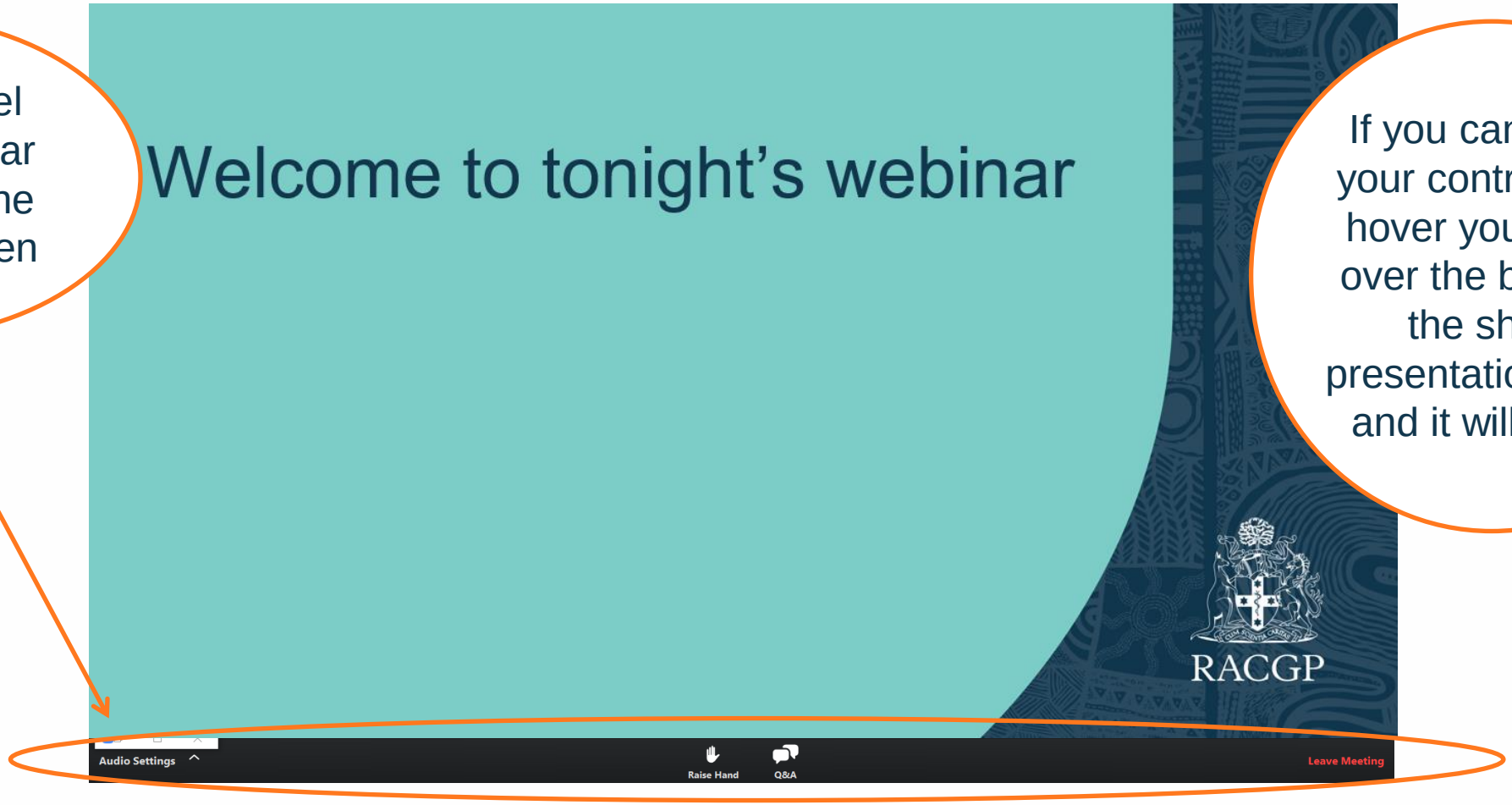


If you cannot see your control panel, hover your cursor over the bottom of the shared presentation screen and it will appear

Acknowledgement of Country

I would like to acknowledge the traditional owners of the lands from where each of us are joining this webinar today.

I wish to pay my respects to their Elders part, present and emerging.

Facilitator
Dr Atef Asham
Chair –
RACGP
Cardiology
Specific Interest
Group

Dr Gary Deed
Chair –
RACGP Diabetes
Specific Interest group

Prof Thomas (Tom) H
Marwick –
Director and Chief Executive
Baker Institute

RACGP

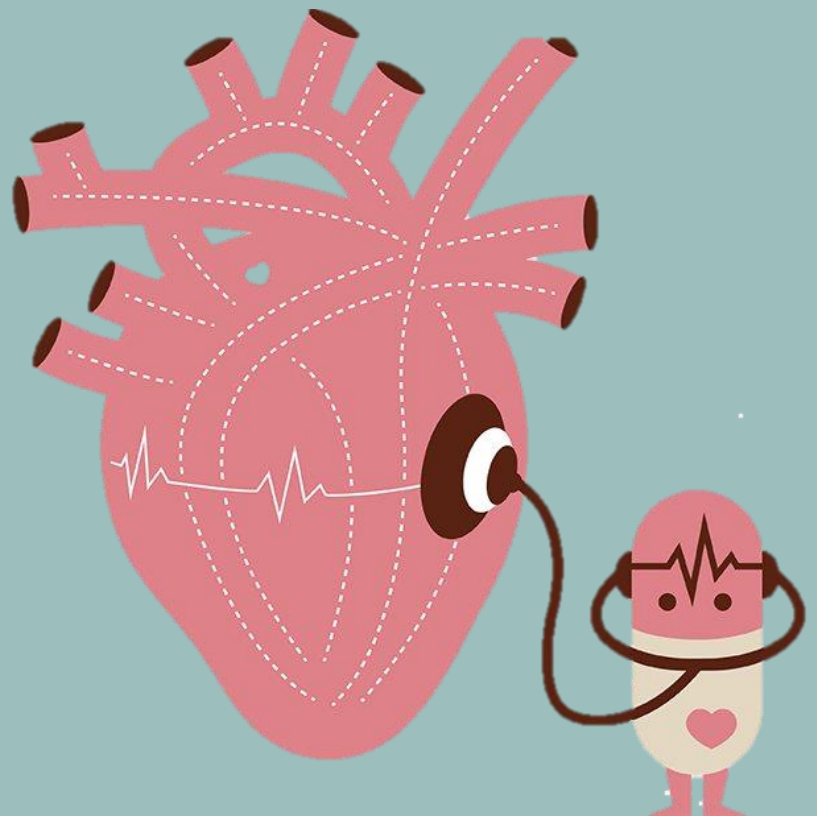
Dr. Atef M. Asham
MBBS FRACGP

Dr. Atef M. Asham graduated from Medical School in 1992. He then went on to gain a Masters degree in Cardiology in 2000. He has worked at both the Royal Melbourne Hospital and the Box Hill Hospital, as well as several general practice clinics across Victoria. As a Fellow of the Royal Australian College of General Practitioners, Dr Asham brings a solid base of knowledge and experience to this practice. His medical interests include chronic disease management, cardiovascular care, and diabetes and he speaks fluent Arabic and French

Dr Asham currently chairs the Cardiology network at the Royal College of General Practitioners (RACGPSI Cardiology), where he is also an examiner . He is a research investigator at Baker Heart and Diabetes Institute and is also collaborating with the National Heart Foundation in Cardiovascular Risk Assessment.

LATE TO LISTEN, LATE TO INTERVENE CASE STUDY

Dr Atef Asham



Mary 89 y/o F of European background, patient of the practice since 2016, lives at home independently with her ADLS.
Past history of hypercholesteremia, Bowen's disease and GORD (for which she takes Nexium).
Non-smoker, non-drinker, no drug use.

2016

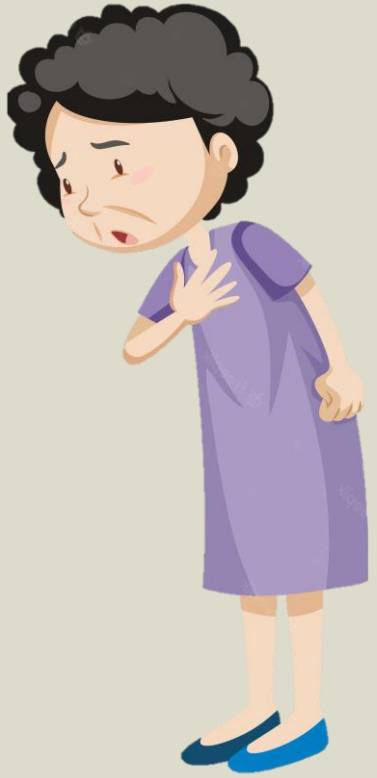
Pt undertook a general blood test → revealed iron deficiency anemia (asymptomatic) for which she received an iron infusion and gastroscopy (showing HH and gastritis) and colonoscopy (showing internal hemorrhoids).

JANUARY 2017

Pt presented with vertigo, GP listened to the heart and found a murmur, no further action was taken at the time.

JULY 2017

Presenting complaint was a productive cough.
Another GP listened to the heart, and discovered a systolic murmur.
Pt was NYHA 1 at this stage and was sent to have an echo.



Echo results show:

- Moderate AS mean gradient 32 mmHg
- Mild LV hypertrophy
- Mild LA dilation

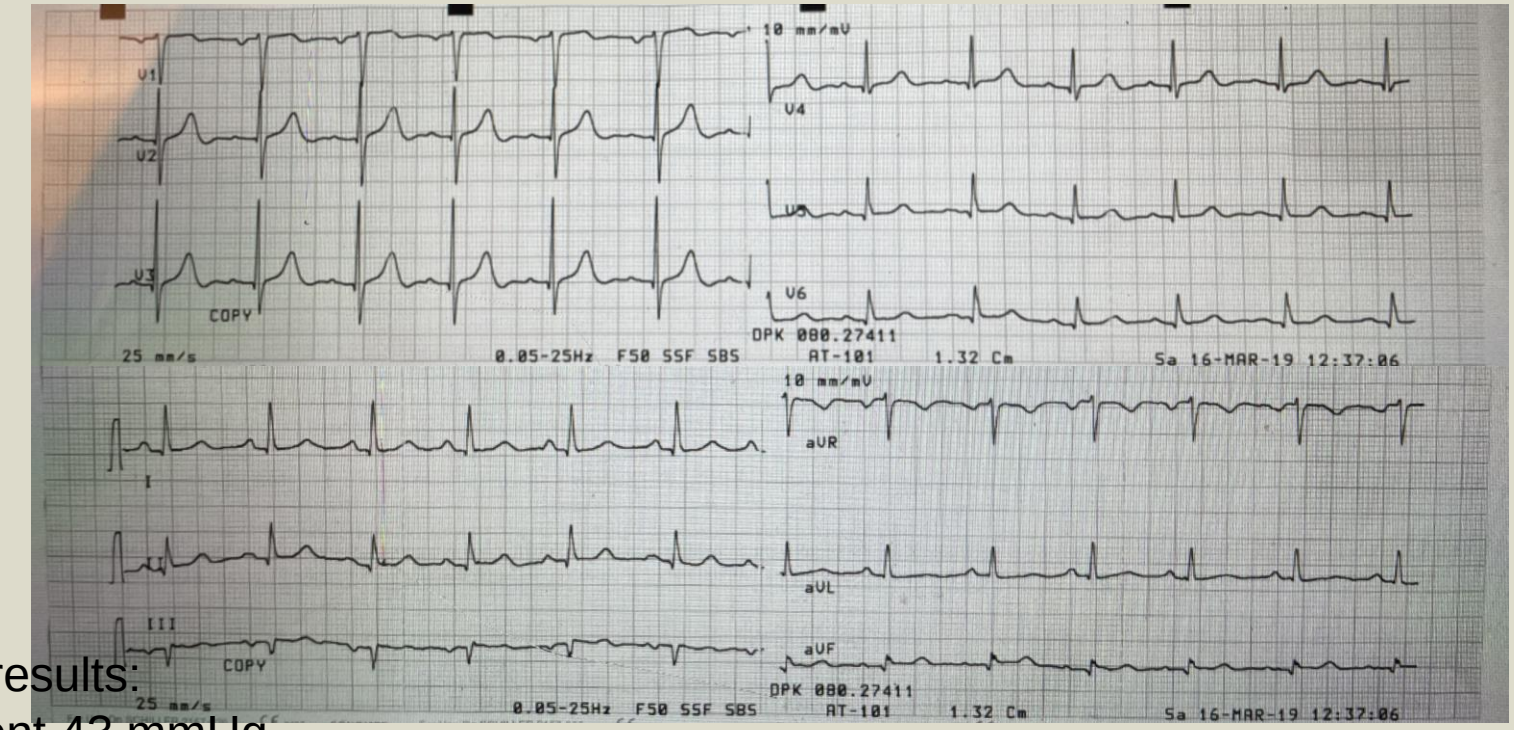
Accordingly, pt was referred for cardiology review at local public hospital

SEPTEMBER 2017

Pt presented with tiredness, diagnosed with iron deficiency anemia, received another iron infusion but declined any further endoscopy.

MARCH 2019

Mary presented with acute SOB.
Denied chest pain or palpitations.
Trop 19
ECC SR rate 90 non specific ST-T changes
Q wave inferior leads
NSTEMI and commenced on Aspirin



MAY 2019

Echo post NSTEMI results:

- Severe AS mean gradient 43 mmHg
- Moderate LV ++
- Mod LA ++
- Thickened MV + moderate restriction/calcified mitral annulus
  Moderate pulmonary hypertension

SEPTEMBER 2019

Presented with increased SOBOE
Echo results show:

- Severe AS mean gradient 44.8 mmHg
- AVA 0.59 cm2
- LA +++
- Calcified MV

DECEMBER 2019

Reviewed by cardiologist and sent for elective coronary angiogram for consideration of Transcatheter Aortic Valve Implantation (TAVI) workup.
C Angio → non obstructive CAD

JANUARY 2020

Decreased exercise tolerance and increasing tiredness → normal iron level

MARCH 2020

Review by cardiologist → found severe AS, MPG 60mmHG, MS, mild coronary artery disease and becoming progressively symptomatic → placed on waiting list for TAVI.

COVID19 pandemic hit → Pt was advised to minimize exposure and stay home.

MAY 2020

Not a candidate for TAVI as ventricular hypertrophy and cavity obliteration.

Decision for Balloon Aortic Valvuloplasty (BAV) as symptoms were progressing.

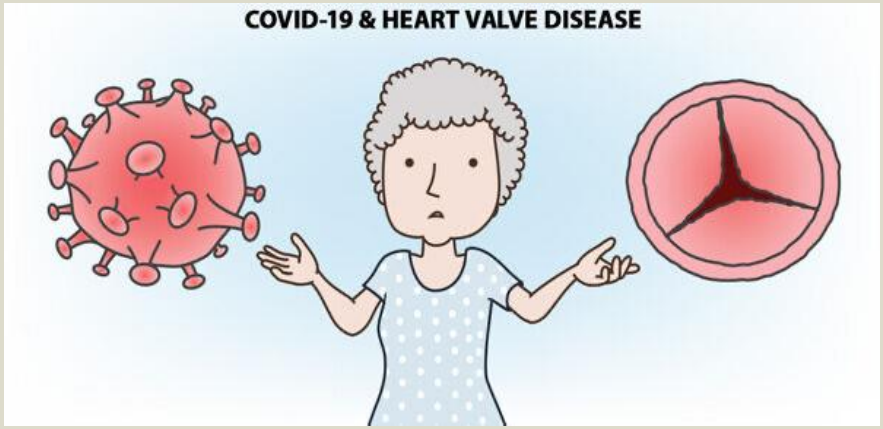
Echo showed 49 mmHg pre-BAV decreased to 27.5 mmHg post-BAV

OCTOBER 2020

Worsening of exertional dyspnea = SOB walking from room to room.
No clear signs of heart failure.
Sent for echo.
Results show AS 53 mmHg.

JUNE/JULY 2021

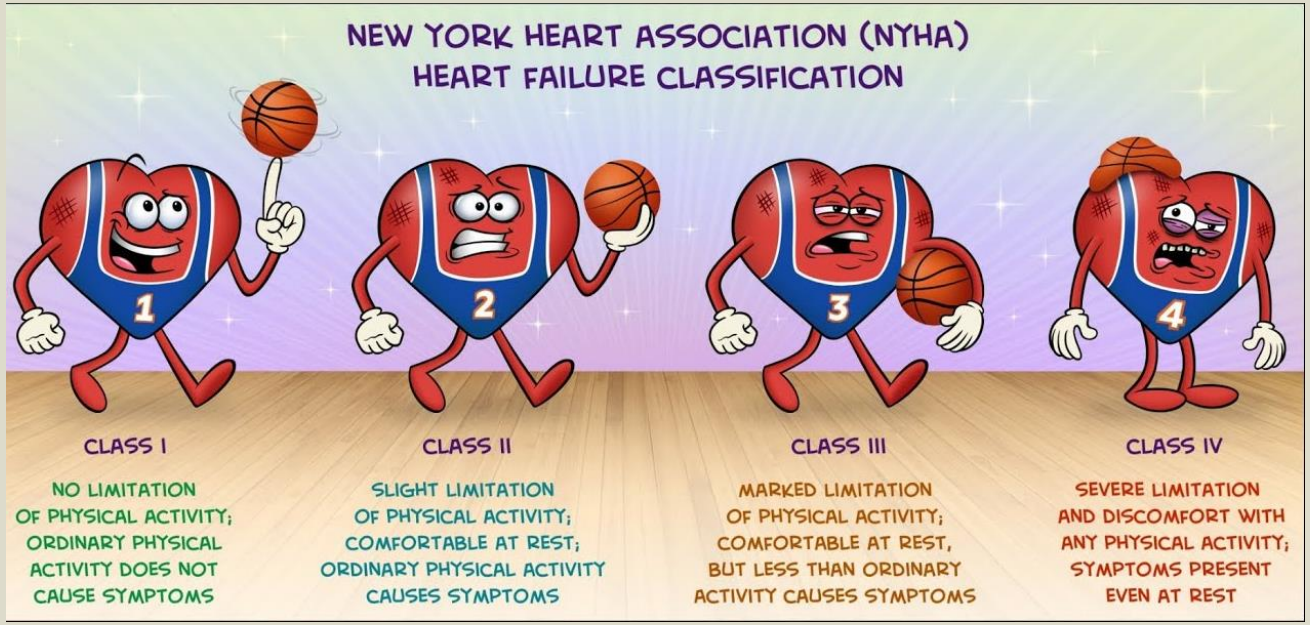
Category 2 BAV → was postponed due to COVID19



NOVEMBER 2021

Re-do BAV
(in private hospital due to increasing pressure on public system)
Mean gradient 80 mmHg decreased to 25 mmHg.

NYHA 4 at the time. Commenced on diuretics.



JANUARY 2022

Fatigue increased, SOB, decreased exercise tolerance and decreased AE entry.

Sent to hospital. NYHA 3
Commenced on valsartan. Diuretics increased.
Discharged home.

Experienced hyponatremia → treated by ceasing valsartan and fluid restriction.

MARCH 2022

SOBOE
Echo AS mean gradient 63 mmHg
AVA 0.8 cm2

MAY 2022

CCF

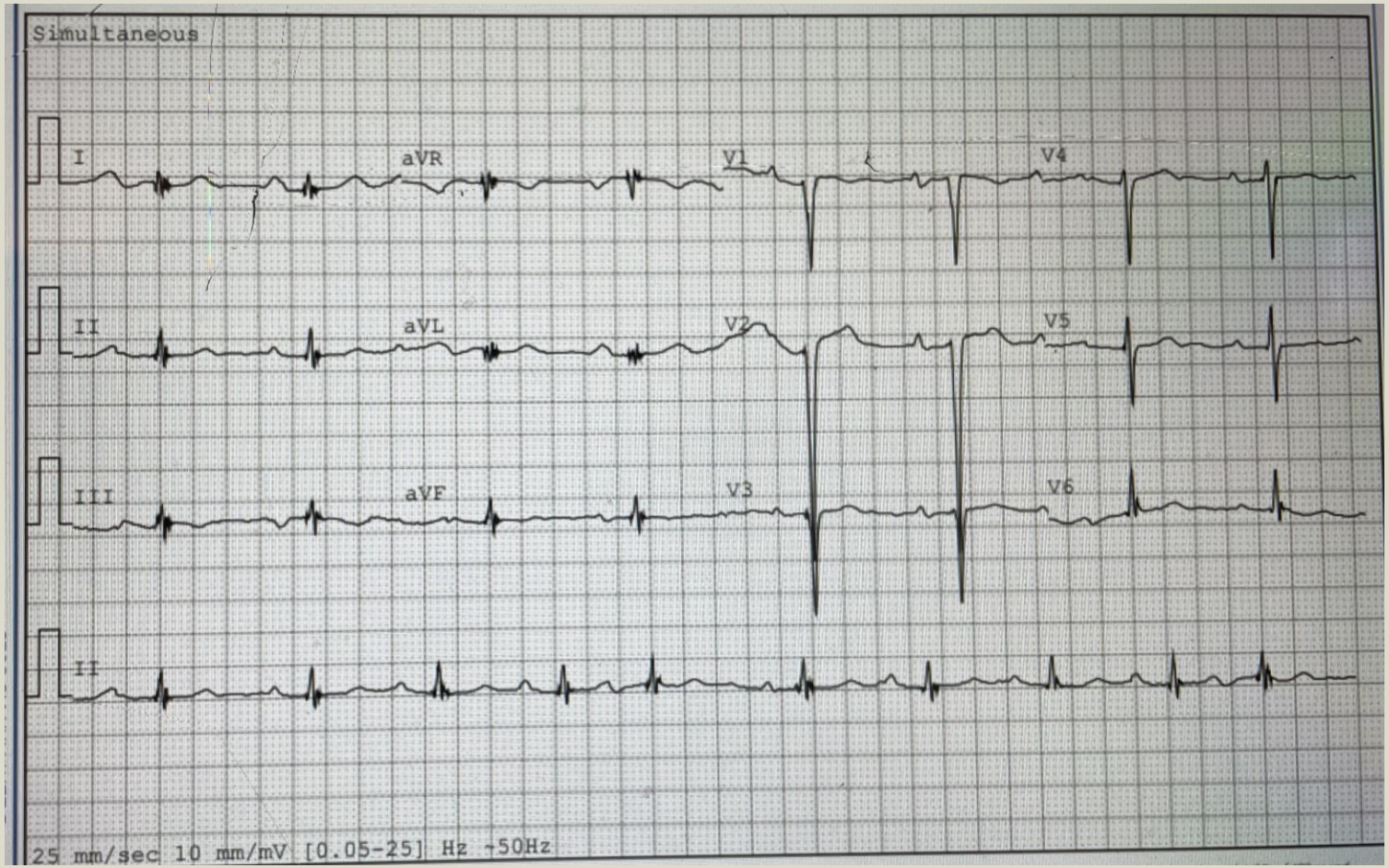
JULY 2022

Patient present with acute SOB/acute APO

<u>ECG results showed:</u>
Ant Q waves, prolonged PR, biphasic/inverted P wave (low atrial rhythm), ventricular hypertrophy
Troponin = 45

Sent to the hospital.
B Natriuretic Peptide (BNP) = 480 pmol/L

<u>Hospital echo:</u>
Severe AS 56 mmHg
AVA 0.8 cm2
Severe P+++
Moderate MS
Severe LA +++
Moderate RA ++

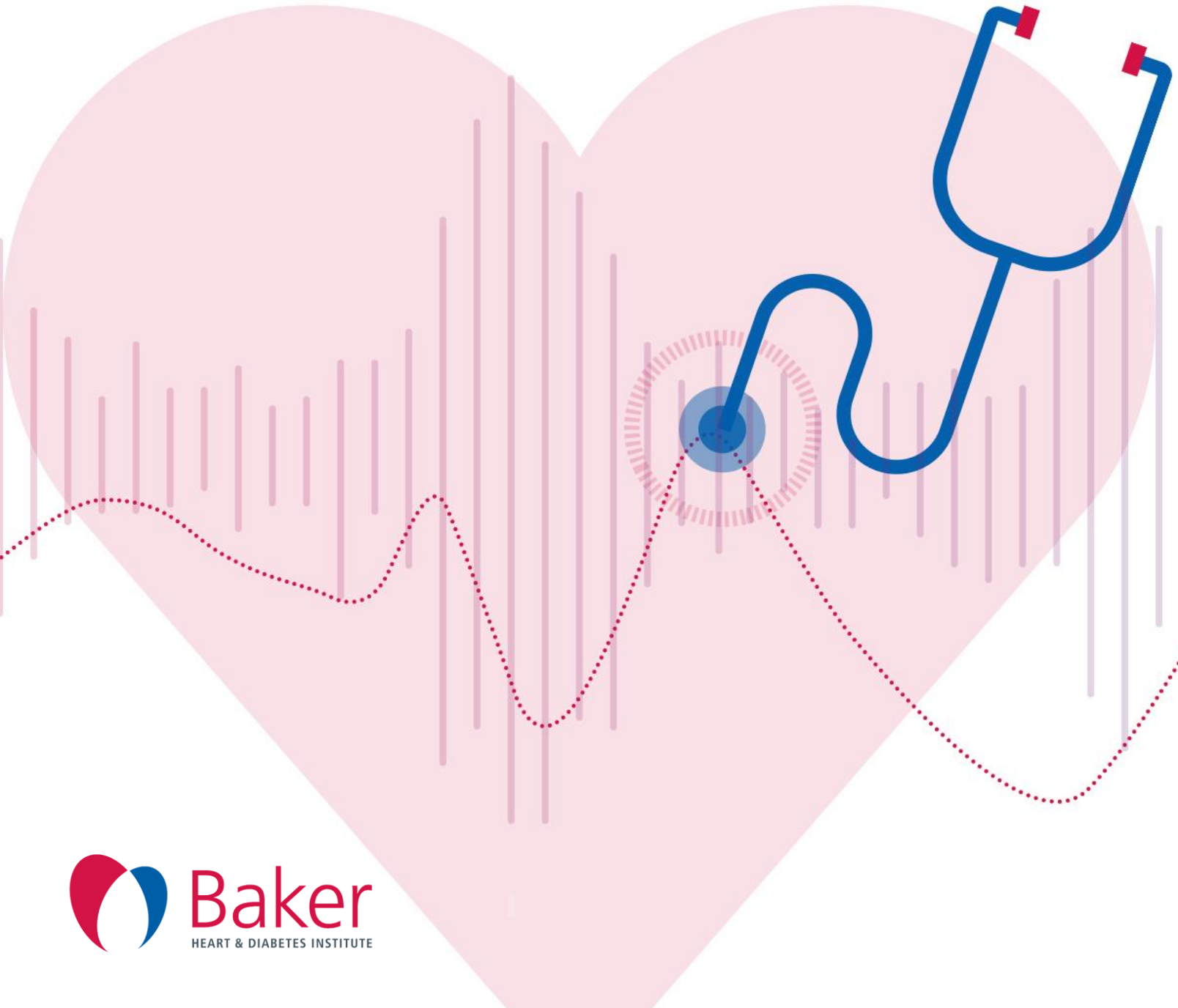


→ Initiate decision for periodic BAV for symptomatic relief. Mary unlikely to benefit as concurrent MS.

Hence, decision taken for medical management (strict fluid balance, daily weight, increasing diuretics) and sent patient home with GEM, Community CCNS (HARP) and SMART Clinic (Symptoms management in community)

Professor Thomas (Tom) H Marwick
MBBS (Hons), University of Melbourne
PhD, University of Louvain | MPH, Harvard

Tom completed training in medicine and cardiology in Australia, before undertaking an Imaging Fellowship at Cleveland Clinic, a PhD at the University of Louvain, Belgium and a Masters in Public Health at Harvard.
He is currently Director of Baker Heart and Diabetes Institute, and has divided his career mostly between Australia (former the Menzies Institute for Medical Research in Hobart, and Professor of Medicine and Head of Cardiovascular Imaging Research Centre, University of Queensland) and the USA (former Head of Cardiovascular Imaging at Cleveland Clinic).
His main contribution has been in clinical research and research training, and has supervised about 30 research higher degree students — mainly clinical — including 22 completed PhDs. He was one of the initiators of stress echocardiography, and has made contributions to the prognostic evidence underlying cardiovascular imaging. His main current research interests relate to the detection of early cardiovascular disease and cost-effective application of cardiac imaging techniques for treatment selection and monitoring.
He has published over 1000 papers, reviews, chapters and editorials, and is an Associate Editor at *JACC* and Deputy Editor at *JACC-Cardiovascular Imaging*. Dr Marwick has been the recipient of more than fifty significant research grants and several awards, including the Simon Dack Award from the American College of Cardiology, 2009 and the RT Hall Prize (2006) and Kempson Maddox Lecture (2011) of the Cardiac Society of Australia and New Zealand.



OUR HIDDEN AGEING

TIME TO LISTEN TO THE HEART

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DISCLOSURES

Disclosure of conflicts of interest

- An original unrestricted educational grant from Edwards LifeSciences supported the preparation and publication of the original report “Our hidden ageing: Time to listen to the heart”. Subsequent work has been based on studies supported by the Tasmanian Community Fund (TasELF) and philanthropy (VicELF).
- Work on heart valve disease is a component of a Cardiovascular Mission-funded trial of AI-guided echocardiography
- Marwick leads research teams studying cancer and the heart (NHMRC), cardiac resynchronisation therapy (MRFF), cardiac effects of Covid (NHMRC and NHF), and detection and management of early-stage heart failure in type 2 diabetes (Astra Zeneca and Applied Therapeutics), none of which are linked to the topic.
- He has no other financial or other conflicts to disclose with respect to the content of this talk.

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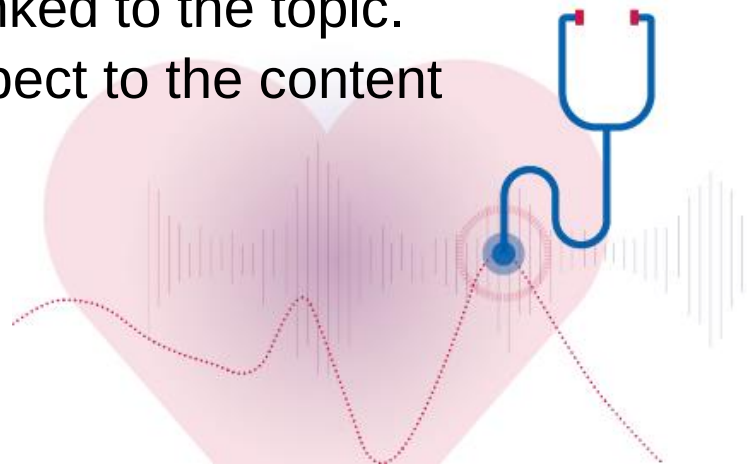

Objectives

- Review the evidence that supports timely detection and management of heart valvular disease (HVD) in the prevention of an emerging burden of social cost, morbidity, and loss of life.
- Identify and implement relevant clinical assessments for HVD, and the pathways for clinical referral.

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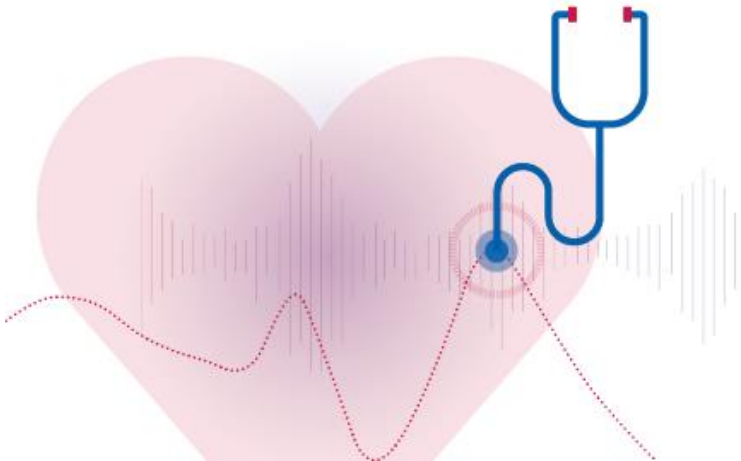

Context

- In Australia, cardiovascular disease (CVD) accounts for 30 per cent of all deaths, causing one death every 12 minutes. CVD costs $10.4 billion annually in direct health care costs.
- Heart Valve Disease (HVD) is a growing but treatable component of the CVD burden. Untreated HVD has a uniformly poor prognosis and a narrow window in which to intervene.
- How much of a problem is unrecognized HVD in Australia?

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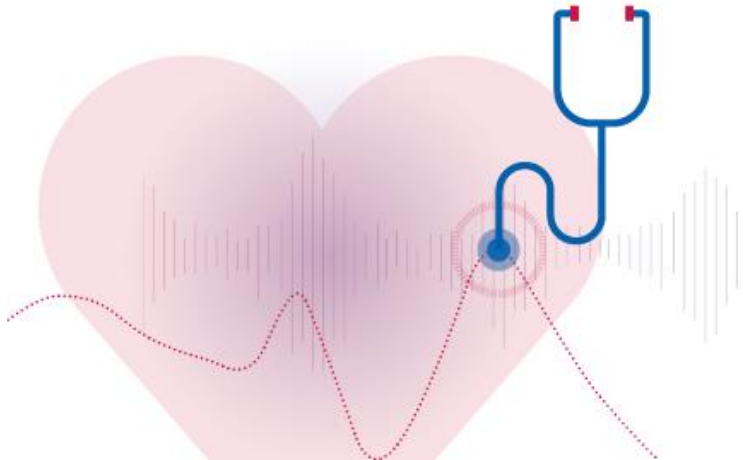

1. Epidemiology of unrecognized HVD in Australia

- Participants were comprised of two community cohorts of elderly (≥65 years old) people in Tasmania (TasELF) and Victoria (VicELF), who were prospectively recruited from the community via direct advertising and primary care practices.

- All subjects had ≥1 CV risk factor, including hypertension (SBP >140 mmHg), type 2 diabetes mellitus, or obesity (BMI >30).

- All subjects were asymptomatic.

- None had a history of heart failure, ischaemic heart disease, cerebrovascular disease, known significant valvular disease or a life expectancy of <1 year.

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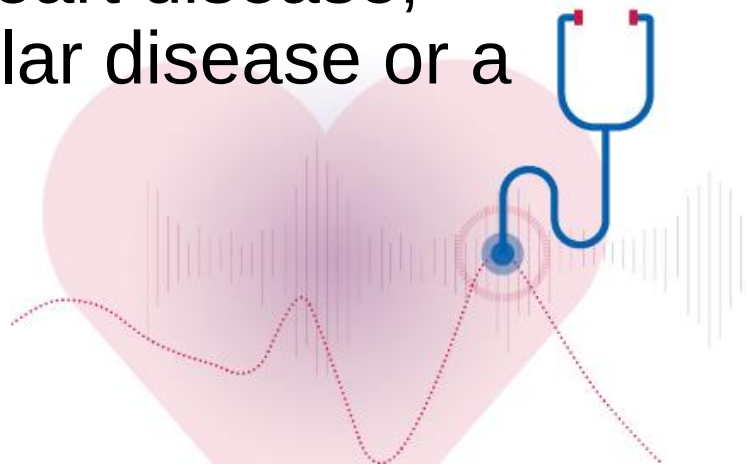

TasELF and VicELF populations

- Baseline echocardiography was obtained in 962 participants, 943 (98%) of whom had clinical data and sufficient quality scans appropriate for inclusion. 19 patients had TTE of insufficient quality for inclusion in the study.

- NT-proBNP values were available in 295 of the 943 patients (31%).

Variable	Mean ± SD
Age (Years)	70.9 (SD 4.7)
BMI	30.4 (SD 5.6)
Sex % Male (n)	50 (468)
HTN % (n)	82 (767)
T2DM % (n)	45 (422)
Atrial Fibrillation or Flutter % (n)	5 (46)
Smoking History % (n)	48 (447)

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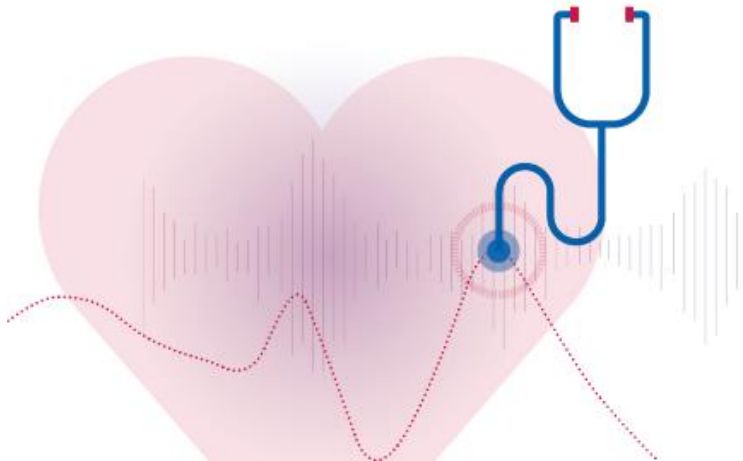

Prevalence of Undetected Valvular Disease

- At least one valvular lesion of moderate or greater severity was present in 58 participants (6%), of whom five had multiple lesions.

- Among the remaining 903, there was a high prevalence of mild valvular disease.
- Mitral regurgitation was the most common valvular pathology (36%).

Variable n, (%)	none	mild	moderate	severe
Aortic Stenosis	915 (95%)	12 (1.3%)	11 (1.1%)	2 (0.2%)
Aortic Regurgitation	766 (80%)	161 (17%)	11 (1.1%)	1 (0.1%)
Mitral Regurgitation	592 (62%)	332 (35%)	13 (1.4%)	1 (0.1%)
Mitral Stenosis	936 (98%)	2 (0.2%)	0 (0%)	0 (0%)
	< Moderate		Moderate or greater	
Tricuspid Regurgitation	919 (96%)		18 (2%)	
Pulmonic Regurgitation	897 (94%)		7 (0.7%)	

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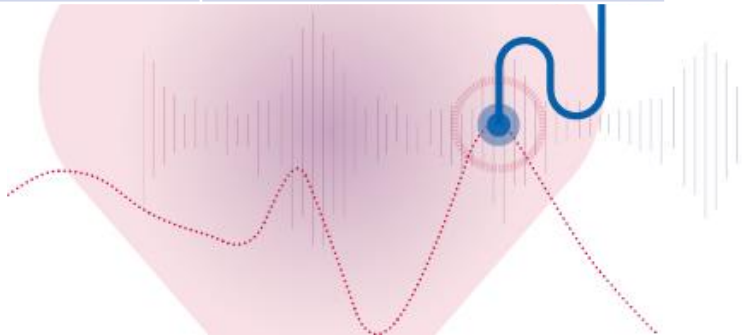

Prevalence in Prior Studies and extrapolation

	VicELF/TasELF	Framingham	OxValve	Canberra Heart Study
AR	1.2% 49,489 cases	~1% 41,241 cases	1.6% 65,986 cases	1.6% combined Aortic valve and Mitral valve. 65,986 cases.
AS	1.3% 64,335 cases	~2% (Lancet Study) 82,482 cases	0.7% 28,995 cases	
MR	1.5% 74,233 cases	~3% 123,724 cases	2.3% 94,855 cases	
TR	2% 82,482 cases	~1% 41,241 cases	2.7% 111,351 cases	

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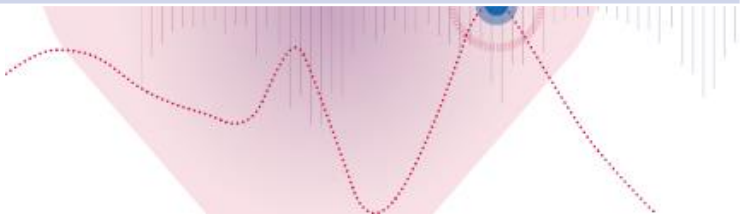
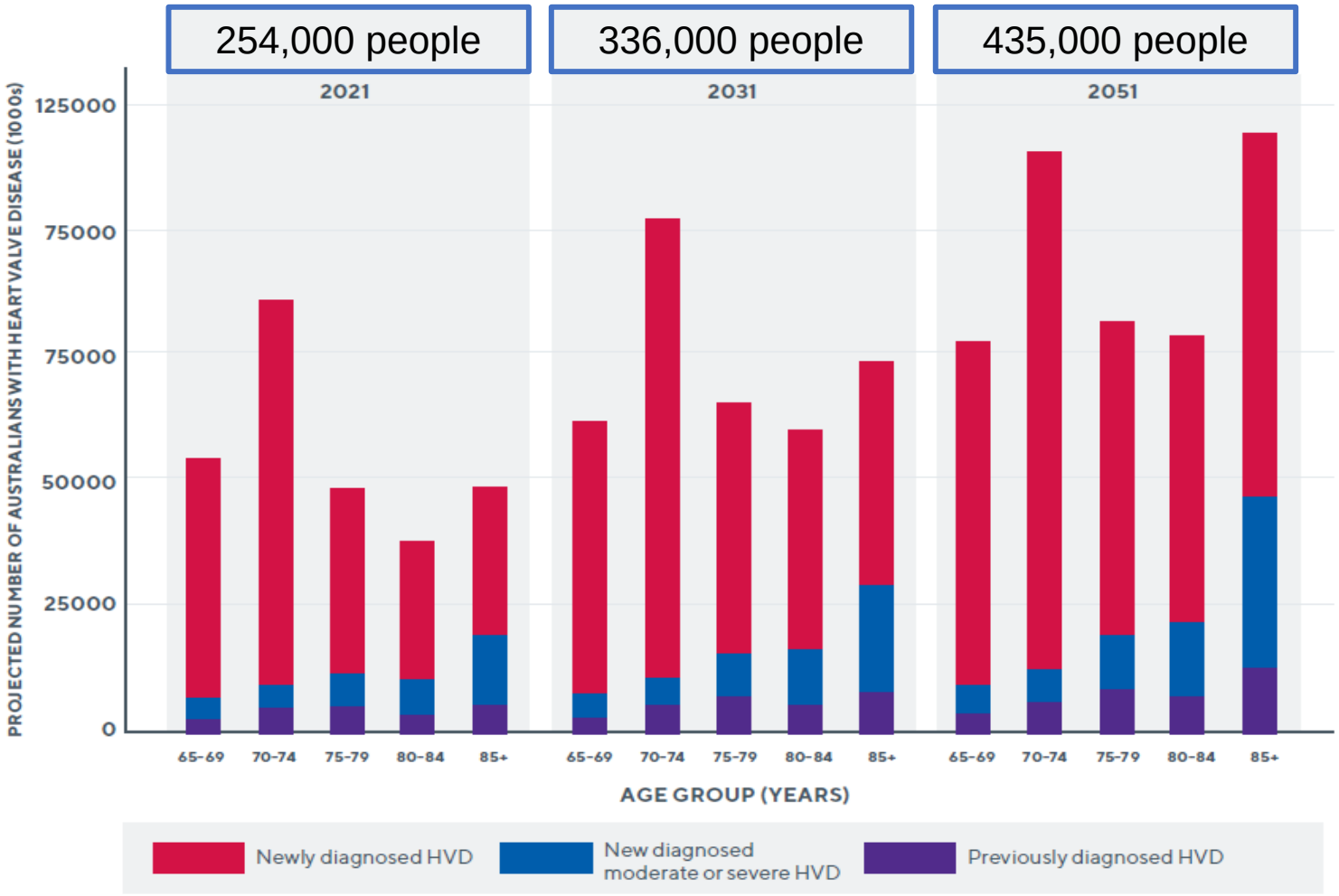


Population projection – Undiagnosed HVD



High burden of undiagnosed heart valve disease.

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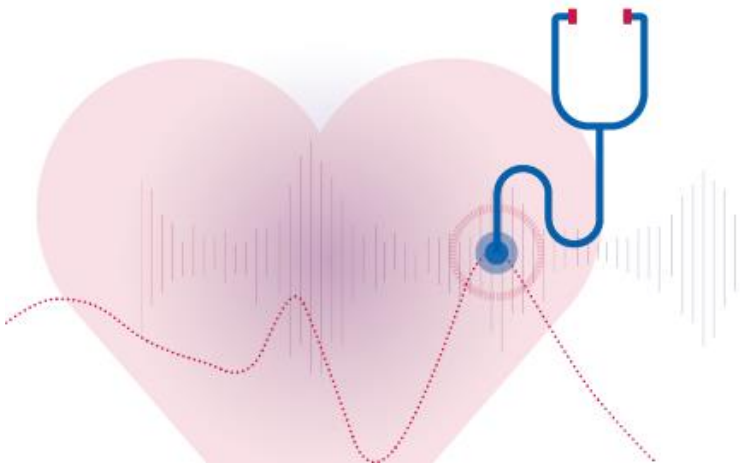
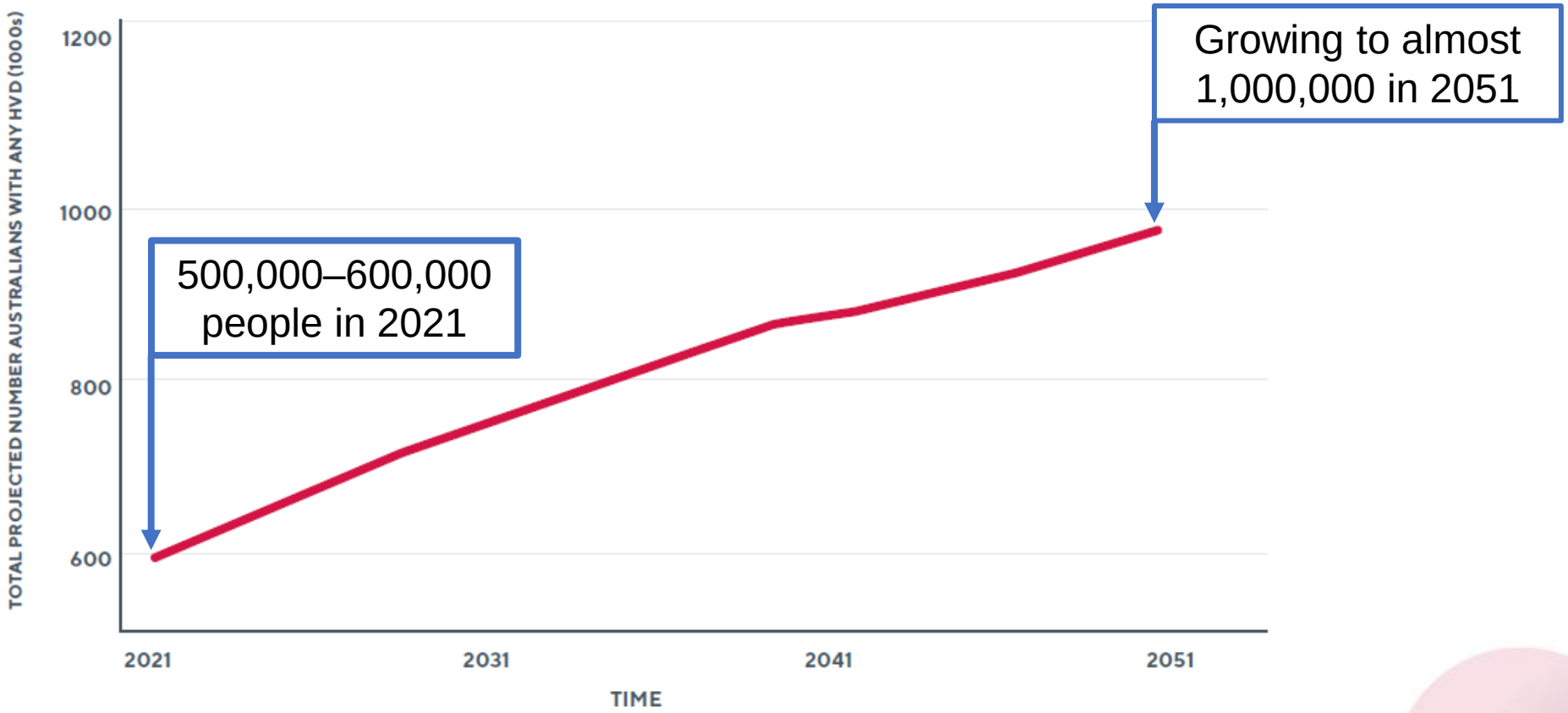


Burden of heart valve disease in Australia



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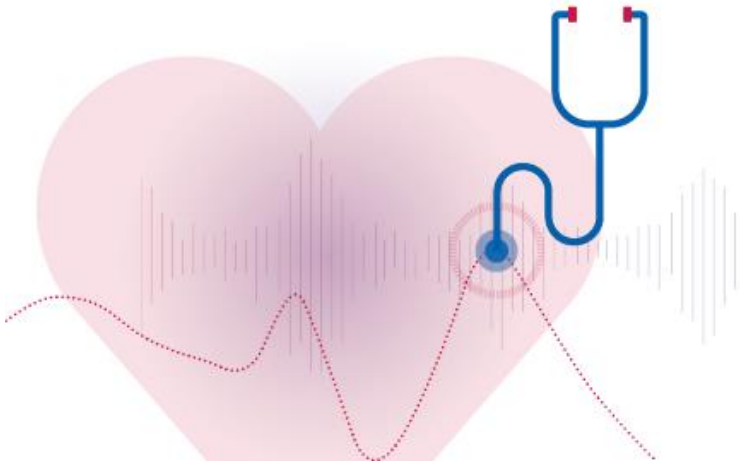

2. Diagnosis of HVD

- Heart valve disease can cause many complications, including heart failure, stroke, blood clots, and heart rhythm abnormalities, so early detection is critical.
- Timely diagnosis is based on awareness and clinical examination — especially listening to the heart sounds.

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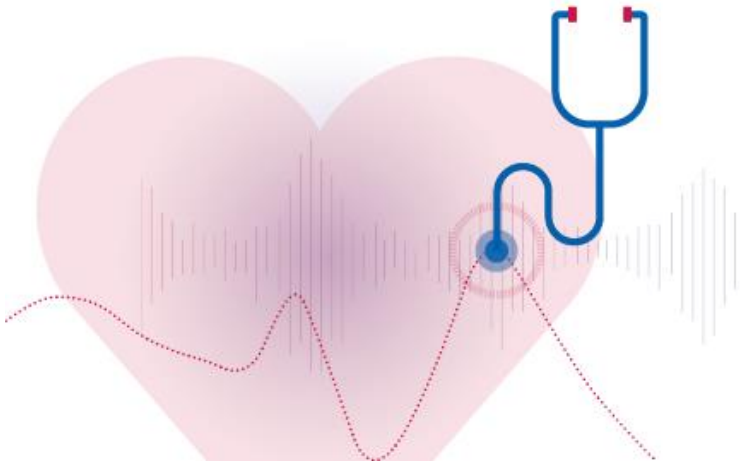

Diagnostic evaluation of HVD

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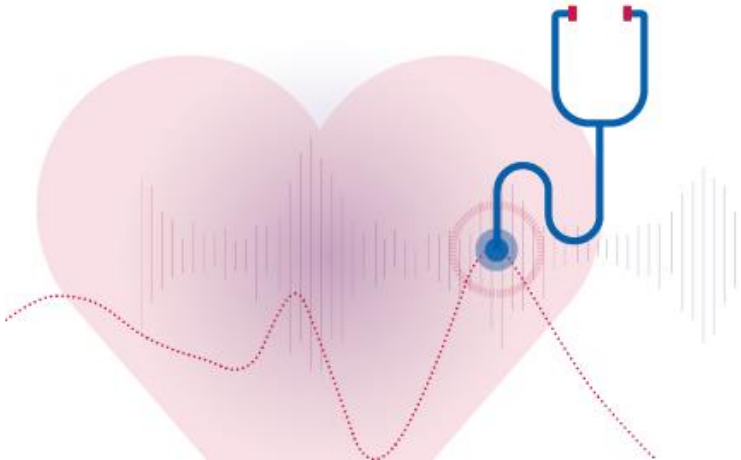

3. Prevention and treatment

- Primordial prevention of valve disease (like other forms of cardiovascular disease) is focused on healthy living.
- No specific medical treatment has been identified.
- Timely intervention (valve replacement or repair) is the best way to avoid cardiac complications.
- Avoiding complications (e.g. heart failure) is economically beneficial, even in the elderly. Independence is maintained and losses in annual value of earnings from work, as well as childcare and volunteering activities are curtailed.

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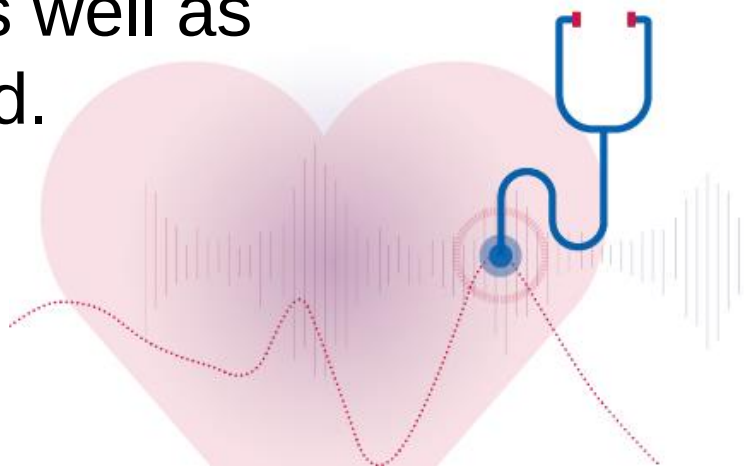
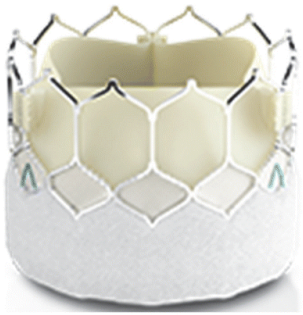
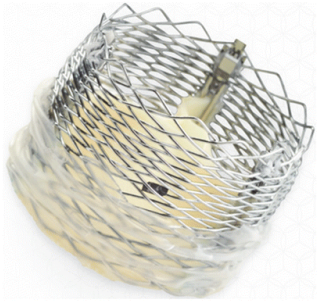


- Interventions involve replacement (operative or catheter), repair (usually for regurgitant valves) or splitting a stenotic valve with a balloon (valvuloplasty).
- The low risk and high tolerability of Transcatheter Aortic Valve Implantation [TAVI] is enabling this intervention to be undertaken earlier in the course of disease.
- Increasing the proportion of patients receiving timely TAVI will result in greater benefits including more quality of life. Is it cost-effective?

TAVR Valve	 Evolut Pro+ [23]	 SAPIEN 3 Ultra [31]	 LOTUS [28]
Mechanism	Self-expanding	Balloon Expandable	Mechanical Expanding
Highlighted Advances	External porcine pericardial wrap over lower cells; Lower profile delivery; Greater sizing range [23]	Increased outer skirt height; Lower profile delivery [31]	Easy ability to reposition; Multilayer and multipolymer external wrap over lower cells [28]
Complication Concerns Relative to Competitors	Perivalvular leak rates	Left bundle branch block rate	High pacemaker implantation rate

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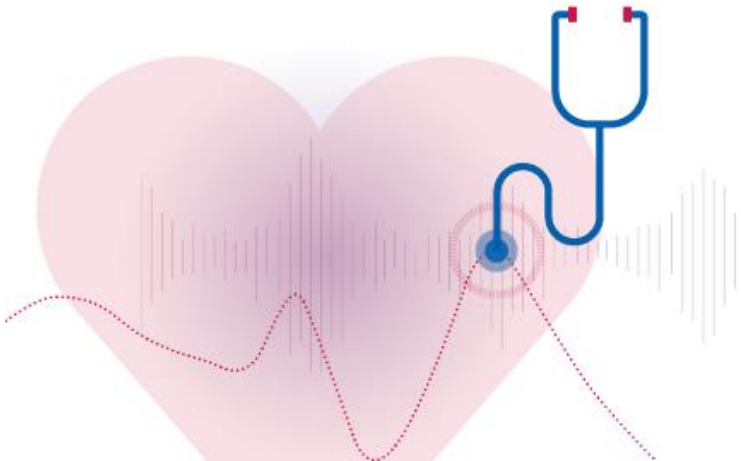

4. Social and economic considerations

- Heart disease is negatively associated with participation of the elderly in paid employment (~3–27% decline).
- Likewise, it leads to a decline in the hours that the elderly contribute to productive non-market activities (child care, adult care, volunteering).
- These findings echo similar losses reported in Europe.
- Important to acknowledge the multiple contributions of the elderly when assessing any interventions.

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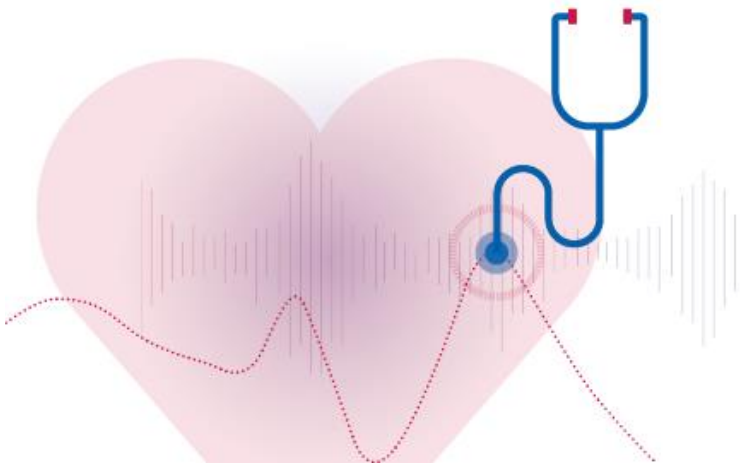
OUR HIDDEN AGEING
TIME TO LISTEN TO THE HEART



Health economics

- Increasing availability of TAVI has changed AS management over the last decade. Initially offered as an alternative to surgical AVR in severe AS patients with high surgical risk.
- Now increasing use in a wider group of patients who are younger and have lower surgical risk.
- Evaluate cost-effectiveness of offering TAVI early to patients ≥65 years with moderate AS. Compared to standard medical management group (‘watchful waiting group’).
- Examined five scenarios: offer TAVI to 10%, 25%, 50%, 75% and 90% of patients with moderate AS.

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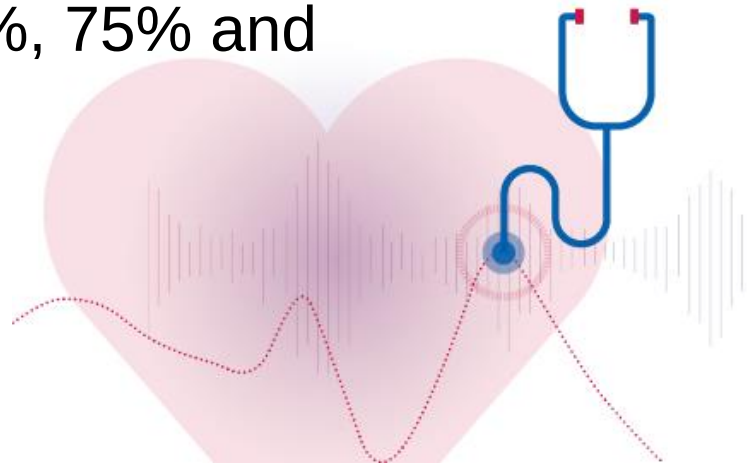

Health economics

- Increasing the proportion of patients receiving early TAVI resulted in both higher healthcare costs and greater benefits (more quality adjusted life years gained and fewer cases of heart failure).
- If early TAVI was made available to the eligible national population aged 65 years and over, substantial savings in productivity losses would accrue.

Scenario	Total QALYs gained	Productivity savings
Early TAVI 10%	43,105	$11.28 million
Early TAVI 50%	217,055	$59.86 million
Early TAVI 90%	384,662	$117.76 million

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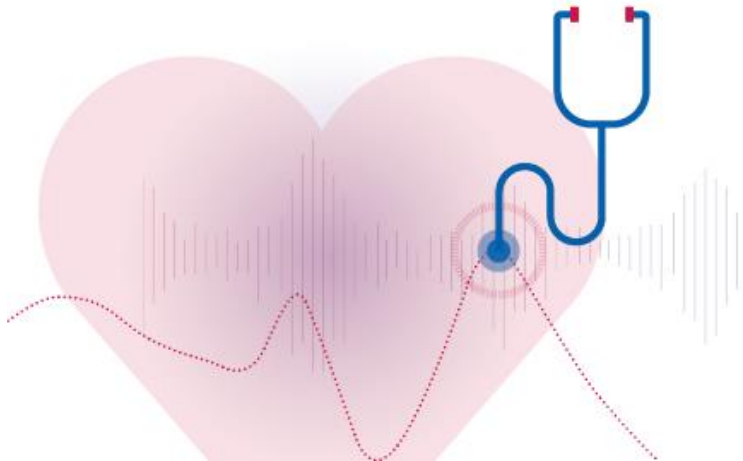
TIME TO LISTEN TO THE HEART



Conclusions

- There are more than half a million Australians living with heart valve disease.
- An estimated 254,000 cases of heart valve disease in Australia are undetected.
- The problem is increasing with the ageing of the population.
- The risk/benefit metrics of intervening for HVD – especially in the elderly - have changed with the development of percutaneous interventions.

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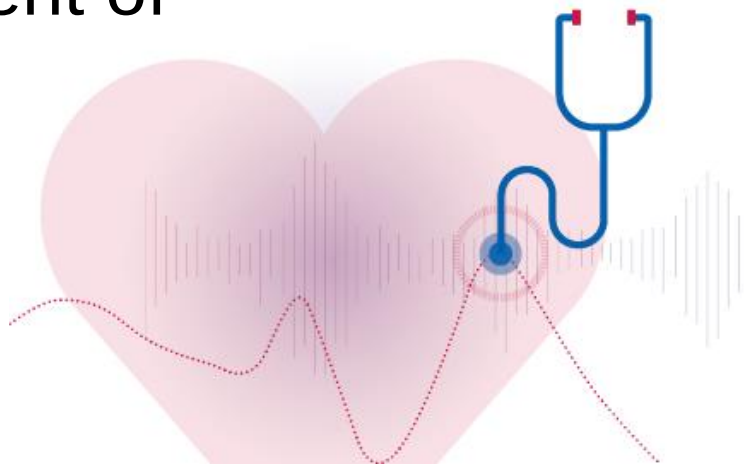
OUR HIDDEN AGEING
TIME TO LISTEN TO THE HEART



DR GARY DEED
MBBS, FACNEM, MRACGP
Mediwell Medical Clinic,
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Gary Deed is a general practitioner at Mediwell Medical Clinic and Adjunct Senior Research Fellow at Monash University, Melbourne, VIC, Australia. He completed his training in medicine at The University of Queensland, Brisbane, QLD, Australia.

Dr Deed has a passionate interest in promoting quality patient care for diabetes in general practice through education, policy development, research, strategic collaboration, and development of resources including guidelines.

Dr Deed is Chair of the Diabetes Specific Interest Network for the Royal Australian College of General Practitioners. He also holds a ministerial appointment to the Commonwealth Diabetes Implementation Reference Group for Australia. Dr Deed helps to co-ordinate the National Health and Medical Research Council-funded STAREE (Statins in Reducing Events in the Elderly) trial. He has published peer-reviewed journal articles in diabetes, and he is a reviewer/editor for *Diabetes Therapy* and adviser/editor for *Endocrinology Today*.

UPDATE ON T2DM MANAGEMENT

Dr Gary Deed

GP with specific interest in chronic illness, diabetes, obesity, fatigue disorders. Developing evidence-based guidelines and strategies

DISCLOSURES

Disclosure of conflicts of interest

- Member of the Australian Diabetes Society. He is a GP in a multidisciplinary practice at Coorparoo in Brisbane, He has been a member of National and International advisory boards in diabetes and educational development and delivery: AstraZeneca, Abbott, Boehringer Ingelheim, Inova, Lilly, Nevro, Novartis, Novo-nordisk, MSD, Sanofi.
- He is a member of an NHMRC funded research team based at Monash University for STAREE; a JDRF funded research team based at Sydney University for National Screening for type 1 diabetes; START trial with George Institute
- He has no other financial or other conflicts to disclose with respect to the content of this talk.

Objectives

- Understand how guidelines with emerging evidence, influences therapeutic recommendations in T2D
- Describe the rationale for individualising treatment options for differing presentations with common diabetes co-morbidities such as HF & CKD

GP – Call to action

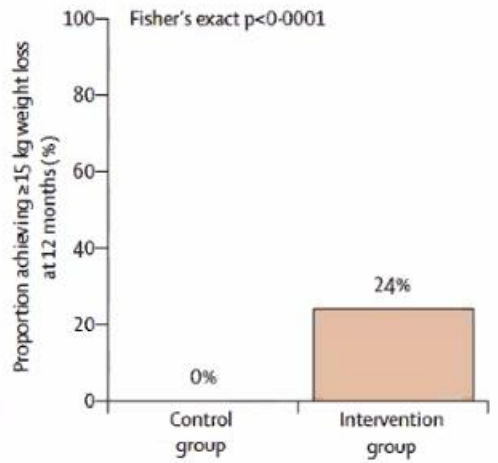
- Support possible early remission
  Weight management focus
- Commence individualized therapy using updated evidence of non-glycaemic benefits

Type 2 diabetes remission is defined as a sustained improvement in blood glucose where HbA1c levels remain below 6.5% (48mmol/mol) for at least 3 months in the absence of glucose-lowering medications.

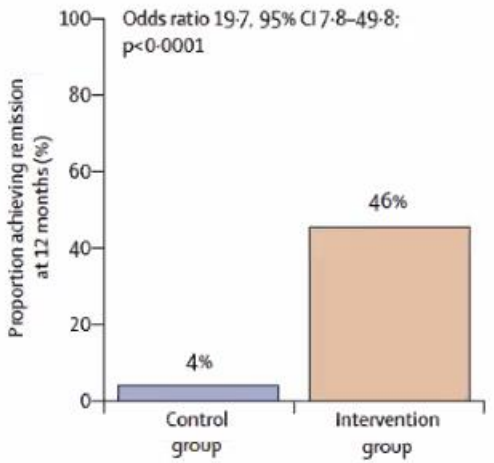
https://www.diabetesaustralia.com.au/wp-content/uploads/2021_Diabetes-Australia-Position-Statement_Type-2-diabetes-remission_2.pdf

NEW EVIDENCE: DIRECT STUDY

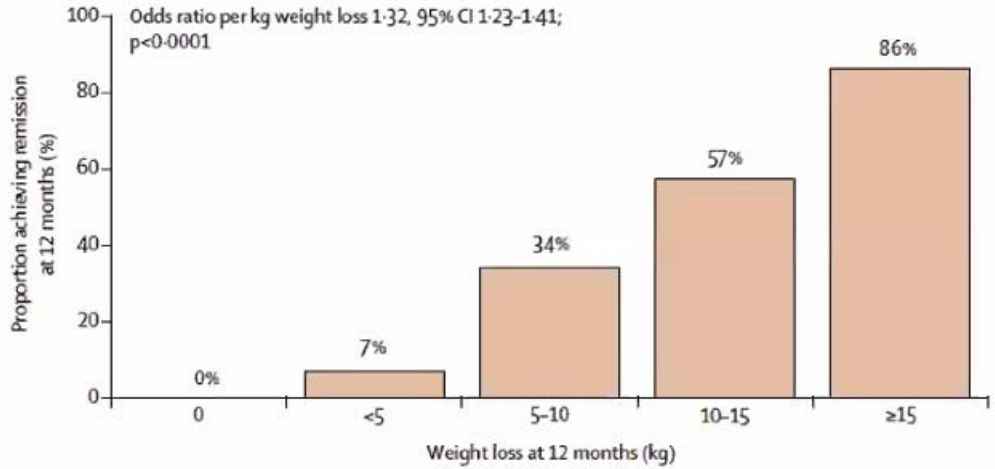
Diabetes Remission Clinical Trial (DiRECT)



Achievement of at least 15 kg weight loss at 12 months



Achievement of remission of diabetes

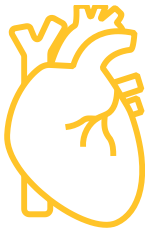


Remission of diabetes, in relation to weight loss achieved at 12 months (both groups combined).

References: Lean ME et al. Lancet. 2018; 391:541–51.

SIMPLE ADVICE CAN CHANGE OUTCOMES

Modest weight loss (5–10%) has clinically significant benefits[1,2]



Improved cardiovascular risk factors[1]

- Blood pressure

Reduced risk of type 2 diabetes in at-risk populations[2]

TGA: Anti-obesity medication*	Pharmacy based interventions
Bupropion/naltrexone	VLED DIET REPLACEMENTS
Liraglutide	SUPPORTIVE PROGRAMMES TO ADDRESS OVERWEIGHT AND OBESITY
Orlistat	
Phentermine	

1. Wing RR *et al. Diabetes Care* 2011; 34:1481–6. 2. Hamman RF *et al. Diabetes Care* 2006; 29:2102–7; Taylor VH et al. Canadian Adult Obesity Clinical Practice Guidelines: The role of mental health in obesity management. https://obesitycanada.ca/guidelines/mentalhealth [Accessed August 2021]. .

METABOLIC GRADIENT EFFECT OF WEIGHT LOSS

Weight loss has dose-dependent and tissue-dependent biological effects

Effects of moderate and subsequent progressive weight loss

	5% weight loss	11% weight loss	16% weight loss
Adipose tissue insulin sensitivity	✓	✓	✓
Liver insulin sensitivity	✓	✓	✓
Muscle insulin sensitivity	✓	✓ ✓	✓ ✓ ✓
β cell function	✓	✓ ✓	✓ ✓ ✓
Intra-abdominal adipose tissue volume	✓	✓ ✓	✓ ✓ ✓
Intrahepatic triglyceride content	✓	✓ ✓	✓ ✓ ✓
Adipose tissue biology*		✓	✓ ✓
Inflammatory markers		✓	✓ ✓

*Upregulation of genes involved in cholesterol flux, downregulation of genes involved in lipid synthesis, extracellular matrix remodelling and oxidative stress.

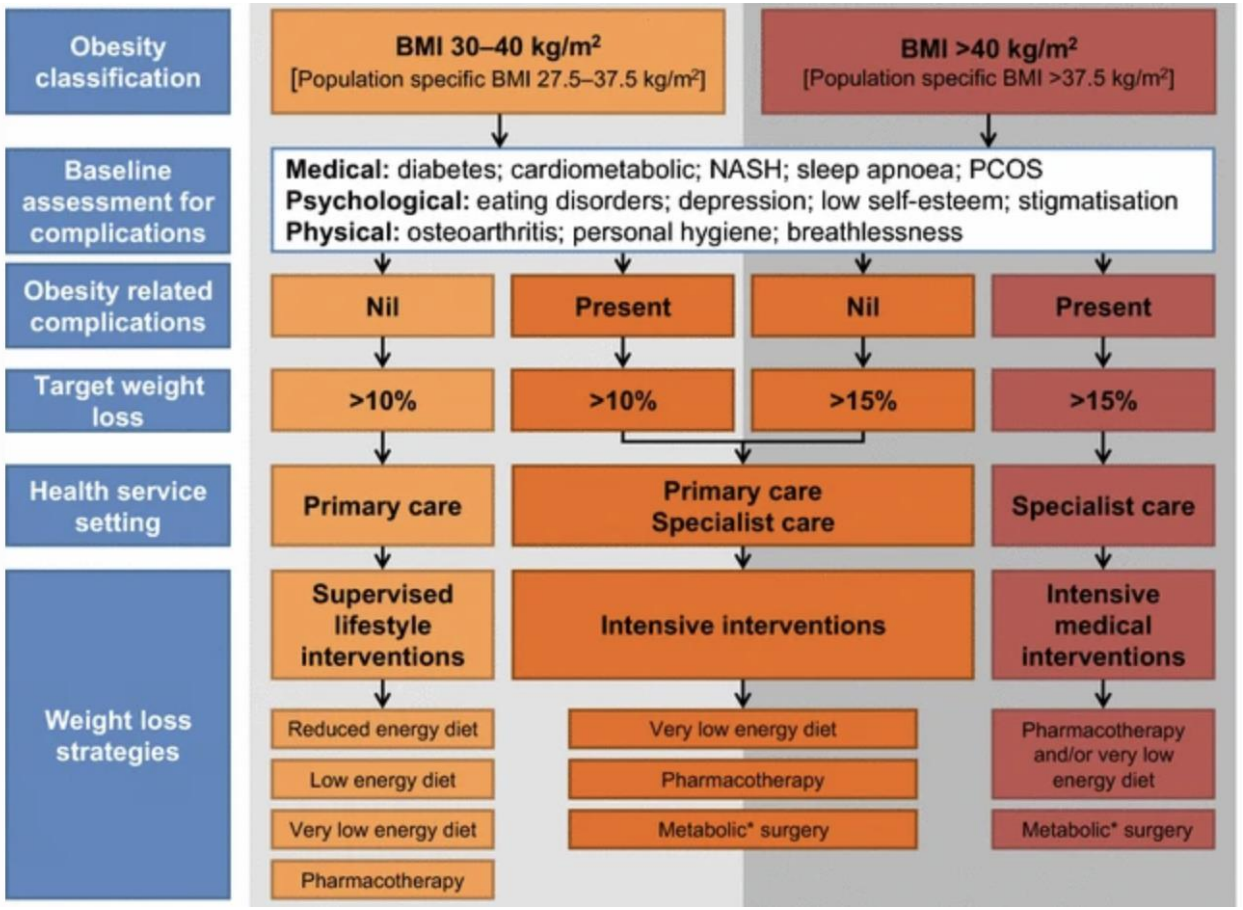
References: Magkos *et al. Cell Metab* 2016;23:591–601

Apply updated principles of management

Obesity Management

Type 2 diabetes remission is possible through weight loss achieved following intensive dietary changes or bariatric surgery.

Australian Obesity Management Algorithm



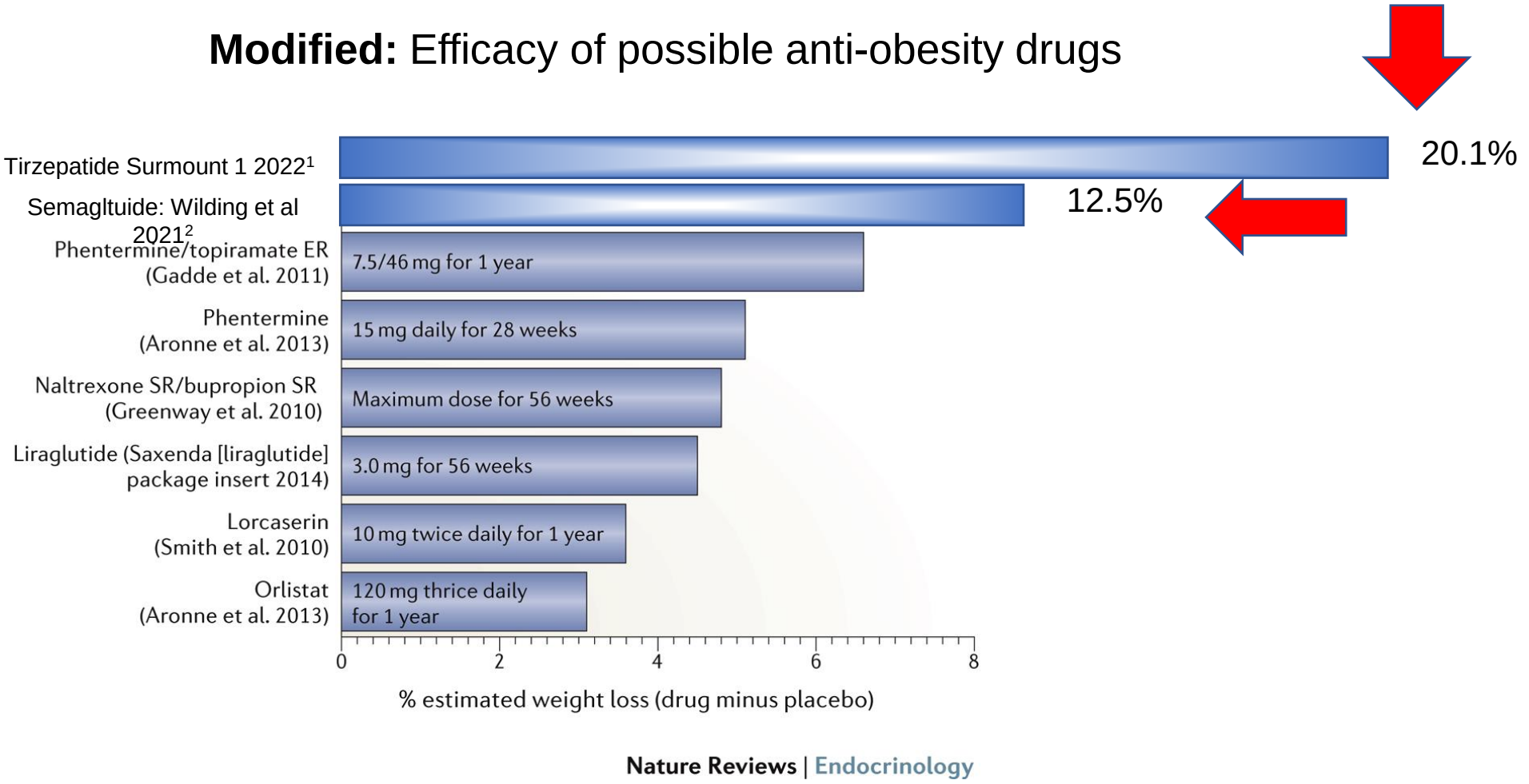
https://static1.squarespace.com/static/5e3b5875edc1485d14d6fe3a/t/5f333410b37c0216c50936dc/1597191187793/Australian+Obesity+Management+Algorithm+update_22Jun2020.pdf

Emerging WEIGHT MANGEMENT Options

- GLP-1RA
  - Semaglutide – FDA approved at dose of 2.4mgs weekly but recent failed PBAC approval. “Off-Label issues “
  - Nausea and GIT upsets
  - Category D for pregnancy

- Twincretin: GLP-1RA Plus GIP analogues
  - Tirzepatide – not yet FDA/TGA approved for obesity

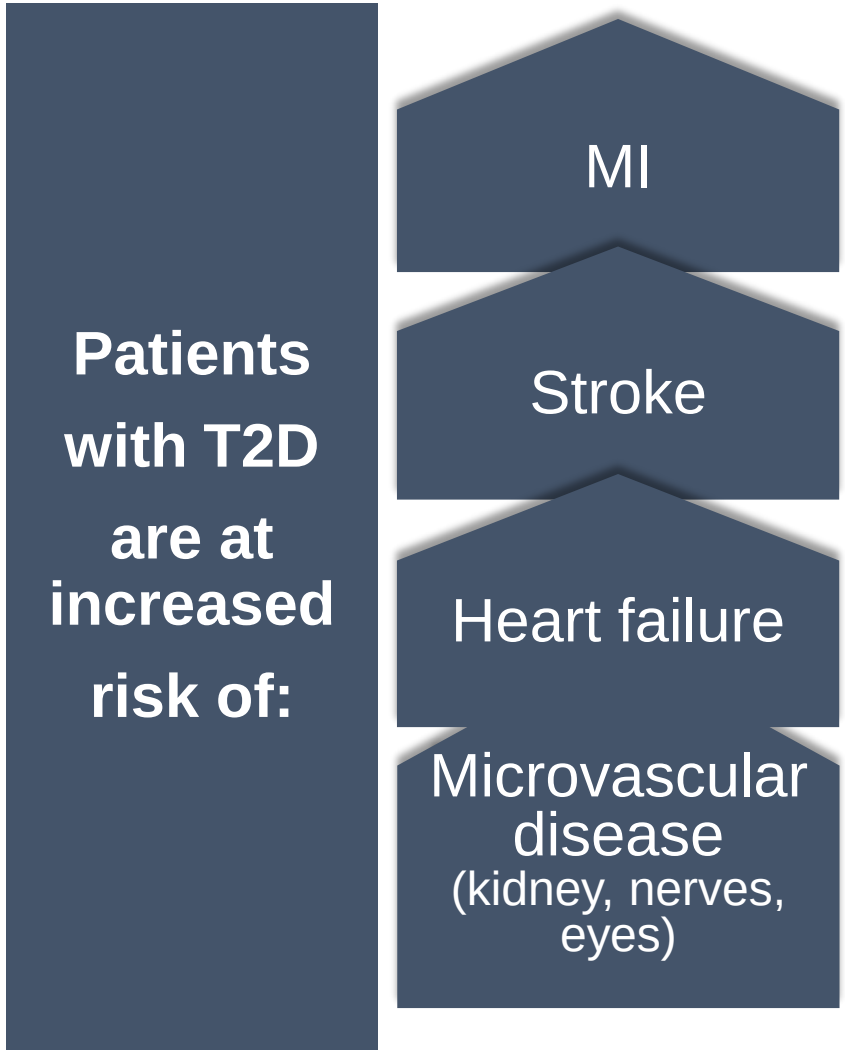
Modified: Efficacy of possible anti-obesity drugs



Srivastava, G. & Apovian, C. M. (2017) Current pharmacotherapy for obesity *Nat. Rev. Endocrinol.* doi:10.1038/nrendo.2017.122

1. **Tirzepatide Once Weekly for the Treatment of Obesity** A. M. Jastreboff, L. J. Aronne, N. N. Ahmad, S. Wharton, L. Connery, B. Alves, et al.New England Journal of Medicine 2022
2. Once-Weekly Semaglutide in Adults with Overweight or Obesity J. P. H. Wilding, R. L. Batterham, S. Calanna, M. Davies, L. F. Van Gaal, I. Lingvay, et al. New England Journal of Medicine 2021 Vol. 384 Issue 11 Pages 989-1002

Emerging evidence supports not just controlling HbA_{1c} but preventing these interlinked micro- & macro-vascular events



54%
increased risk of MI (median 5.5 years) compared to those without T2D[2]

72%
increased risk of stroke (median 5.5 years) compared to those without T2D[2]

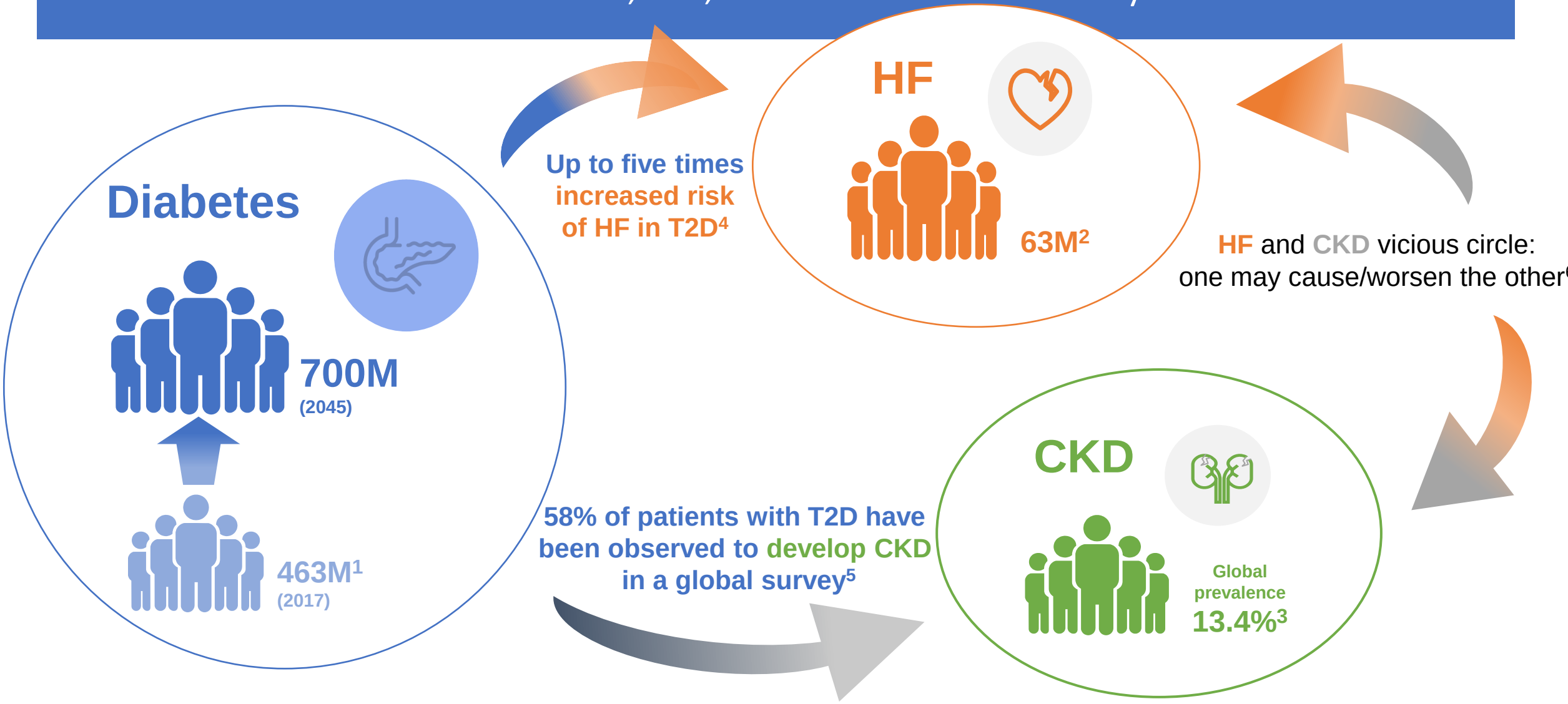
33%
increased risk of hospitalization for heart failure (at 4 years) compared to those without T2D[3]

>50%
develop microvascular disease within 10 years[1]

CV, cardiovascular; HbA_{1c}, glycated haemoglobin; MI, myocardial infarction; T2D, type 2 diabetes.

1. Litwak L, et al. *Diabetol Metab Syndr.* 2013;5:57. 2. Shah AD, et al. *Lancet Diabetes Endocrinol.* 2015;3:105-113. 3. Cavender MA, et al. *Circulation*. 2015;132:923-931.

NEWER Evidence: Diabetes, HF, and CKD are closely connected



CKD, chronic kidney disease; HF, heart failure; T2D, Type 2 diabetes

1. International Diabetes Federation. *IDF Diabetes Atlas, 9th edn.* Brussels, Belgium: International Diabetes Federation; 2019; 2. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. *Lancet* 2017;390:1211–1259; 3. Hill NR, et al. *PLoS One* 2016;11:e0158765; 4. Nichols GA, et al. *Diabetes Care* 2004;27:1879–1884; 5. Parving HH, et al. *Kidney Int* 2006;69:2057–2063; 6. Ronco C, et al. *J Am Coll Cardiol* 2008;52:1527–1539

Metformin

SU

Insulin

Less commonly used: acarbose, DPP-4 inhibitor, SGLT2 inhibitor GLP-1RA, or TZD. Only acarbose is PBS reimbursed for monotherapy.

Conditional recommendation for

DUAL THERAPY: Choice of treatment – add on an oral agent or injectable therapy

Choice of dual therapy should be guided by clinical considerations (presence of, or high risk of, cardiovascular disease, heart failure, chronic kidney disease, hypoglycaemia risk, obesity), side effect profile, contraindications and cost.

SGLT2 inhibitor

GLP-1RA

DPP-4 inhibitor

SU

Insulin

Less commonly used are: acarbose or TZD.

Recommendation for addition of

Conditional recommendation for

Conditional recommendation against

MULTIPLE THERAPIES: Choice of treatment : include additional oral agent or GLP-1 RA or insulin

Choice of agents should be guided by clinical considerations as above. Note: combinations not approved by PBS include GLP-1RA with SGLT2i. Consider revewing any previous medication that has not reduced HbA1c by ≥0.5% after 3 months and take into consideration **glycaemic AND non-glycaemic benefits**.

SGLT2 inhibitor

GLP-1RA

DPP-4 inhibitor

SU

Insulin

Less commonly used are: acarbose or TZD.

NON-GLYCAEMIC PLEOTROPHIC EFFECTS

ADVANCING EVIDENCE in T2D

GLP-1RA and SGLT2i

Network meta-analysis including 21 CVOTs of SGLT2i, GLP-1RA and DPP-4i [1]

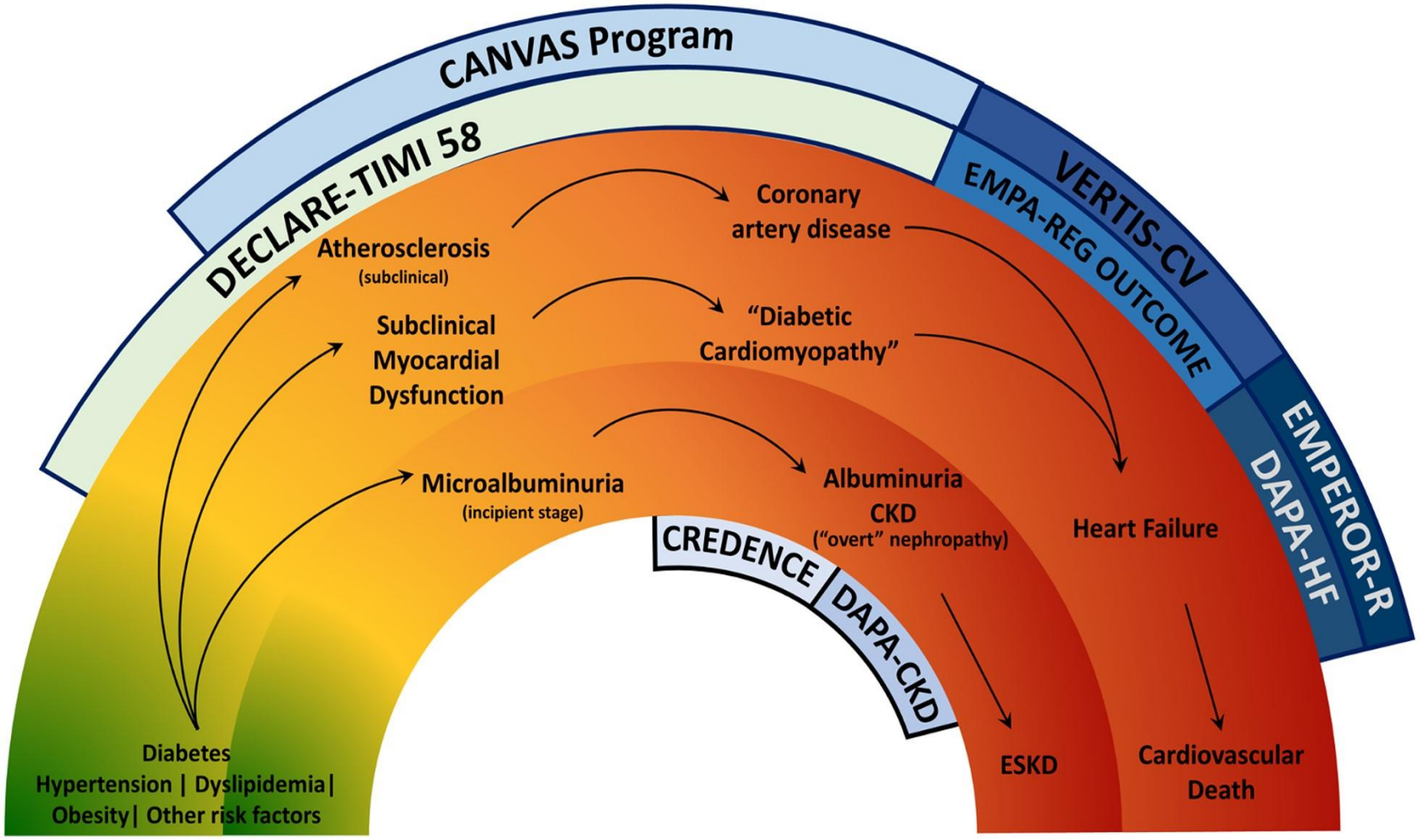
- SGLT2i and GLP-1RA ↓ risks of **MACE**, **death** from any cause, **HHF** and composite outcome of **renal events**
- GLP-1RA class was superior with ↓ the risk of **STROKE**
- SGLT2i led to significantly ↓ risks of **HHF and RENAL events**

Efficacy levels of GLP-1RA and SGLT2i in reducing MACE were more pronounced in *elderly patients, in Asians and white people*, in those with *pre-existing ASCVD*, and in those with *diabetes for longer durations*

MACE - Major Adverse Cardiovascular Events HHF – Hospitalisation for heart failure ASCVD – Atherosclerotic cardiovascular disease

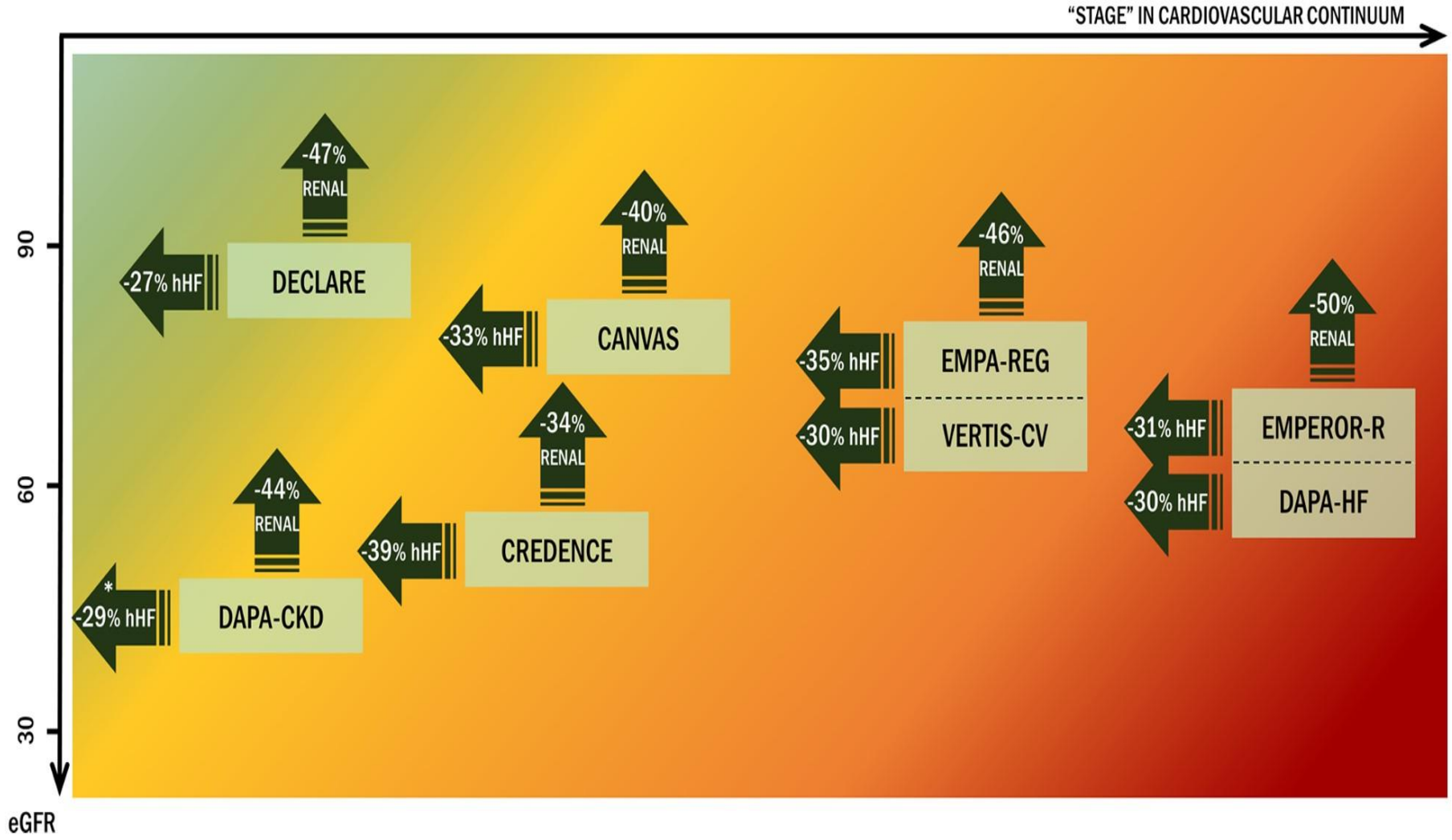
1. Lin, Donna Shu-Han, et al (2021). The efficacy and safety of novel classes of glucose-lowering drugs for cardiovascular outc**MACE**omes: a network meta-analysis of randomised clinical trials. Diabetologia, 64(12), 2676–2686.

Figure 1 Clinical trials of SGLT2 inhibitors across the cardiorenal continuum.



Eur. J. Prev. Cardiol., Volume 29, Issue 9, July 2022, Pages 1352–1360, https://doi.org/10.1093/eurjpc/zwab034

Figure 2 Summary of the effects of SGLT2i on heart failure hospitalization and renal outcomes (RENAL) in different ...



Eur. J. Prev. Cardiol., Volume 29, Issue 9, July 2022, Pages 1352–1360, https://doi.org/10.1093/eurjpc/zwab034

NON-GLYCAEMIC PLEOTROPHIC EFFECTS

TGA INDICATIONS

ADVANCING EVIDENCE including people without diabetes

SGLT2I & Heart failure

- EMPAGLIFLOZIN and DAPAGLIFLOZIN are indicated in adults for the treatment of symptomatic heart failure with reduced ejection fraction, as an adjunct to standard of care therapy. (TGA product information accessed AUG 2022)

SGLT2I & CVD death

- Empagliflozin indicated in patients with type 2 diabetes mellitus and established cardiovascular disease to reduce the risk of cardiovascular death

SGLT2I & CKD

- DAPAGLIFLOZIN is indicated to reduce the risk of progressive decline in kidney function in adults with proteinuric chronic kidney disease (CKD Stage 2,3 or 4 and urine ACR ≥ 30 mg/g)

TGA Product information – Empagliflozin, Dapagliflozin Aug 2022

COVID 19 and Diabetes

- " Diabetes should be considered as a risk factor for a rapid progression and bad prognosis of COVID-19" [1]
- People over the age of 40 with type 1 diabetes have worse outcomes and higher mortality[2]
- COVID-19 can increase a person's risk of diabetes after infection. People recovering from Covid need monitoring for diabetes as 40% more likely to develop diabetes up to a year later in older males in these studies[3,4]

1. Diabetes is a risk factor for the progression and prognosis of COVID-19 W. Guo, M. Li, Y. Dong, H. Zhou, Z. Zhang, C. Tian, et al. Diabetes/metabolism research and reviews 2020 Pages e3319-e3319
2. Age and Hospitalization Risk in People With Type 1 Diabetes and COVID-19: Data From the T1D Exchange Surveillance Study C. Demeterco-Berggren, O. Ebekozien, S. Rompicherla, L. Jacobsen, S. Accacha, M. P. Gallagher, et al. The Journal of Clinical Endocrinology & Metabolism 2021 Vol. 107 Issue 2 Pages 410-418
3. Xie, Y. & Al-Aly, Z. *Lancet Diabetes Endocrinol.* https://doi.org/10.1016/S2213-8587(22)00044-4 (2022)
4. Wander, P. L. *et al. Diabetes Care* **45**, 782–788 (2022).

SUMMARY

Emerging evidence shows that

- Newer classes of drugs may need to be considered BEYOND just glucose lowering abilities
- Choices should be driven by indidualised risk evaluation, patient choices and comorbidities
- Significant clinical effects may now be seen in people without diabetes in HFrEF, CKD & weight management

Q&A and panel discussion

RACGP