

Cardiology

RESEARCH REVIEW™

Making Education Easy

Issue 101 – 2022

In this issue:

- Risk of myocarditis associated with COVID-19 vaccination or infection
- CTCA vs invasive coronary angiography in patients with stable chest pain
- PDAY risk score predicts cardiovascular events in young adults
- Trends in survival after cardiac arrest in Sweden
- MRI-guided fibrosis ablation vs conventional catheter ablation in persistent AF
- Generalisability of the EAST-AFNET 4 findings in routine practice
- Decision support tool for the diagnosis of acute HF
- Invasive vs conservative management of NSTEMI in elderly patients
- Rivaroxaban monotherapy vs dual antiplatelet therapy in patients with AF and CAD
- Outcomes in Takotsubo syndrome triggered by physical vs emotional stressors
- Age at menopause and risk of HF and AF
- Does adding salt to food increase the risk of premature mortality?

Abbreviations used in this issue

- AF = atrial fibrillation
- CABG = coronary artery bypass graft
- CAD = coronary artery disease
- CoDE-HF = Collaboration for the Diagnosis and Evaluation of Heart Failure
- COVID-19 = coronavirus disease 2019
- CTCA = computed tomography coronary angiography
- HF = heart failure
- HR = hazard ratio
- MI = myocardial infarction
- MRI = magnetic resonance imaging
- NSTEMI = non-ST-elevation MI
- NT-proBNP = N-terminal pro-B-type natriuretic peptide
- PDAY = Pathobiologic Determinants of Atherosclerosis in Youth
- PCI = percutaneous coronary intervention
- SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

Welcome to the latest issue of Cardiology Research Review.

In this issue we report a number of big data trials. Researchers in England analyse millions of patients following COVID and vaccination to put myocarditis into perspective, the DISCHARGE investigators find that CTCA works well to work up chest pain, and an analysis of the CARDIA study finds that risk factors can lead to onset of atherosclerosis at a young age. Also in this issue, a longitudinal Swedish study reports that ischaemic heart disease matters much less in cardiac arrest these days (surprisingly), an Australian study supports extending invasive management to selected elderly patients with NSTEMI, and an analysis of UK Biobank data adds to the negative press about salt and CVD.

I hope you find these and the other selected articles interesting and look forward to receiving any feedback you may have.

Kind regards,

Professor Alexander Sasse

alexandersasse@researchreview.co.nz

Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection

Authors: Patone M et al.

Summary: This English study investigated the risk of hospitalisation or death from myocarditis, pericarditis or cardiac arrhythmias after adenovirus (ChAdOx1; n=20,615,911) or messenger RNA-based (BNT162b2 or mRNA-1273; n=17,999,580) COVID-19 vaccines or a positive SARS-CoV-2 test (n=3,028,867) between Dec 2020 and Aug 2021 in people aged ≥16 years. It was estimated that there were an extra 2, 1 and 6 myocarditis events per 1 million people vaccinated with ChAdOx1, BNT162b2 and mRNA-1273, respectively, in the 28 days after a first dose, an extra 10 events per 1 million vaccinated in the 28 days after a second dose of mRNA-1273, and an extra 40 events per 1 million patients in the 28 days after a positive SARS-CoV-2 test. Increased risks of pericarditis and cardiac arrhythmias were seen after a positive SARS-CoV-2 test, but not after COVID-19 vaccination (except for an increased risk of arrhythmia after a second dose of mRNA-1273).

Comment: This is one of those *Nature Medicine* papers containing enormous amounts of UK data. 38,615,491 patients vaccinated against COVID and 3,028,867 with a positive COVID test were analysed. Of this combined group, 1615 had an admission for myocarditis, 1574 for pericarditis and 385,508 for arrhythmia. In a very condensed summary, post COVID the myocarditis incidence was 40 extra per million, compared to vaccination with 1–10 per million. Pericarditis and arrhythmia risks were not elevated post vaccination, but elevated after COVID. However, these were presentations leading to admissions, not necessarily all the patients with difficult to characterise chest pains and palpitations that we have been seeing. But it puts the post-vaccination symptoms in context with those from actual COVID disease, and overall myocarditis and pericarditis incidence was low (0.00007%).

Reference: *Nat Med* 2022;28(2):410-22

[Abstract](#)

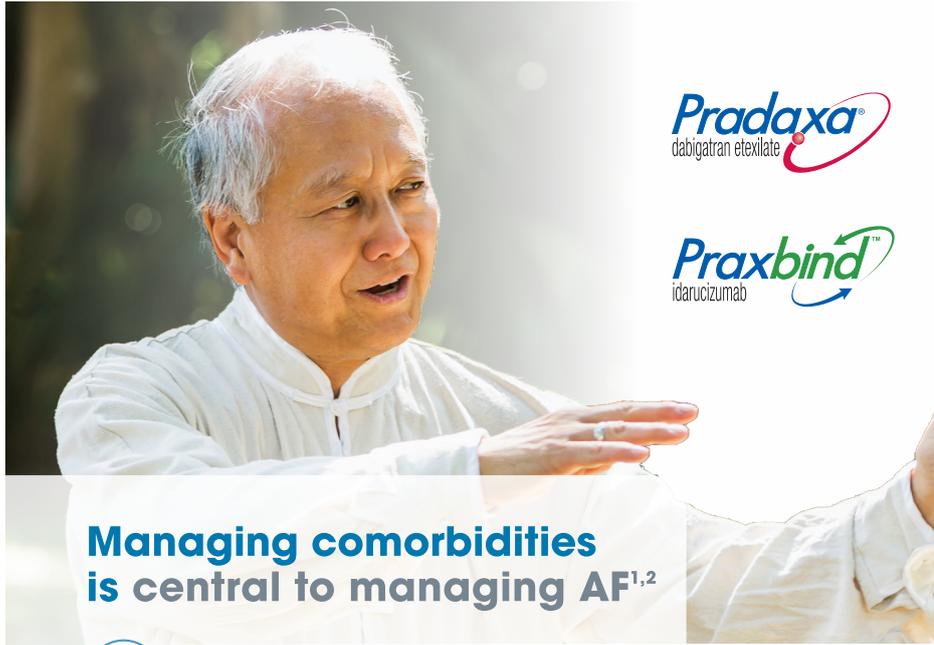
Independent commentary by Professor Alexander Sasse



Professor Alexander Sasse is Consultant Cardiologist and Clinical Director of the Cardiology Department at Wellington Hospital/CCDHB. His clinical interests include the various modalities of cardiac imaging, structural heart disease and intervention, general cardiology and the prevention of stroke. He went to Medical School in Bonn and did his training at the RWTH Aachen (Germany) and has been a Cardiologist since 2004. In 2007 he moved to Wellington and has been there since. Appointments include being a senior lecturer at Wellington School of Medicine (University of Otago) since 2007, and adjunct Professor at the School of Biological Sciences (Victoria University) Wellington since 2012.

RACP MyCPD Program participants can claim **one credit per hour** (maximum of 60 credits per year in Category One – Educational Activities) **for reading and evaluating Research Reviews.**

Please [CLICK HERE](#) to download CPD Information



Managing comorbidities is central to managing AF^{1,2}



Diabetes mellitus (DM)

- There is a **~2x increased risk of AF** in people with DM vs no DM.²⁻⁴
- Patients with AF and DM have a **1.7x increased risk of stroke** vs no DM.⁵
- In patients with type 2 diabetes and incident AF, increased HbA1c levels are associated with a **higher risk of thromboembolism**.⁶

AF: Atrial Fibrillation. References: 1. NHA/CSANZ Atrial Fibrillation Guideline Working Group. Heart Lung Circ 2018; 27(10): 1209–66. 2. The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC). Eur Heart J 2020; ehaa612. doi: 10.1093/eurheartj/ehaa612. 3. Connolly SJ et al. N Engl J Med 2009; 361: 1139–51. 4. Brambatti M et al. Int J Cardiol 2015; 196: 127–31. 5. Stroke Risk in Atrial Fibrillation Working Group. Neurology 2007; 69: 546–54. 6. Fangel MW et al. Circ Arrhythm Electrophysiol 2019; 12(5): e007030.

PRADAXA® (dabigatran etexilate) 75 mg, 110 mg and 150 mg capsules. Before prescribing, please review the full Data Sheet which is available on request from Boehringer Ingelheim or from <https://www.medsafe.govt.nz/Medicines/infoSearch.asp> INDICATIONS: SPAF: Prevention of stroke, systemic embolism and reduction of vascular mortality in patients with non-valvular atrial fibrillation with one or more of the following risk factors: previous stroke, transient ischaemic attack, or systemic embolism, left ventricular ejection fraction < 40%, symptomatic heart failure, ≥ New York Heart Association Class 2, age ≥ 75 years, age ≥ 65 years associated with one of the following: diabetes mellitus, coronary artery disease or hypertension. VTE AFTER ORTHOPAEDIC SURGERY: Prevention of venous thromboembolic events in patients who have undergone major orthopaedic surgery. DVT/PE: Treatment of acute deep vein thrombosis (DVT) and/or pulmonary embolism (PE) and prevention of related death following treatment with a parenteral anticoagulant for at least 5 days. Prevention of recurrent DVT and/or PE and related death. DOSAGE: SPAF: Usually 150 mg twice daily. Patients aged ≥ 80 years: 110mg twice daily. Patients aged 75 to 80 years or those with moderate renal impairment (CrCl 30–50 mL/min) with low thromboembolic risk and high bleeding risk: consider 110 mg twice daily. VTE AFTER ORTHOPAEDIC SURGERY: Initially 110 mg followed by 220 mg once daily thereafter for a total of 10 days for knee replacement surgery or a total of 28–35 days for hip replacement surgery. Patients with moderate renal impairment (CrCl 30–50 mL/min): two 75 mg capsules once daily. ACUTE DVT/PE: 150 mg twice daily following treatment with a parenteral anticoagulant for at least 5 days. Therapy should be continued for up to 6 months. Patients aged ≥ 80 years: 110mg twice daily. Patients aged 75 to 80 years or those with moderate renal impairment (CrCl 30–50 mL/min) with low thromboembolic risk and high bleeding risk: consider 110 mg twice daily. RECURRENT DVT/PE: 150 mg twice daily. Therapy could be continued life-long depending on the individual patient risk. Patients aged ≥ 80 years: 110mg twice daily. Patients aged 75 to 80 years or those with moderate renal impairment (CrCl 30–50 mL/min) with low thromboembolic risk and high bleeding risk: consider 110 mg twice daily. ADMINISTRATION: Take capsule whole with a glass of water, with or without food. Do not chew or open capsule. Assess renal function: prior to treatment initiation, in clinical situations that could lead to renal function decline, and at least once a year in patients with moderate renal impairment (CrCl 30–50 mL/min). CONTRAINDICATIONS: Known hypersensitivity to dabigatran or dabigatran etexilate or to one of the excipients. Severe renal impairment (CrCl < 30 mL/min). Haemorrhagic manifestations, patients with a bleeding diathesis, or patients with spontaneous or pharmacological impairment of haemostasis. Organ lesions at risk of clinically significant bleeding, including haemorrhagic stroke within the last 6 months. Concomitant treatment with systemic ketonazolone, prosthetic heart valve replacement. WARNINGS AND PRECAUTIONS: Haemorrhagic risk*: moderate renal impairment (CrCl 30–50 mL/min), acetylsalicylic acid, NSAIDs, clopidogrel, congenital or acquired coagulation disorders, thrombocytopenia or functional platelet defects, active ulcerative gastrointestinal disease, recent gastrointestinal bleeding, recent biopsy or major trauma, recent intracranial haemorrhage, brain, spinal or ophthalmic surgery, bacterial endocarditis, age ≥ 75 years. Concomitant administration with: unfractionated heparins and heparin derivatives, low molecular weight heparins, fondaparinux, desirudin, thrombolytic agents, GPIIb/IIIa receptor antagonists, ticlopidine, dextran, sulfinpyrazone, rivaroxaban, prasugrel, ticagrelor, vitamin K antagonists, selective serotonin re-uptake inhibitors, selective serotonin norepinephrine reuptake inhibitors and the P-gp inhibitors (e.g. amiodarone, verapamil, quinidine, dronedarone, clarithromycin), itraconazole, tacrolimus, ciclosporin, ritonavir, tipranavir, nelfinavir, saquinavir and glecaprevir/pibrentasvir fixed-dose combination, P-gp inducers (e.g. rifampicin). Patients with antiphospholipid syndrome. Elevated liver enzymes > 2 ULN. Surgical interventions may require temporary discontinuation of PRADAXA®. Pregnancy. Lactation. Children. Patients < 50 kg. *For situation of life-threatening/uncontrolled bleeding, and in case of emergency surgery/urgent procedures when rapid reversal of the anticoagulant effects of PRADAXA is required, the specific reversal agent (PRAXBIND, idarucizumab) is available. ADVERSE EFFECTS: Common: Bleeding and signs of bleeding, anaemia, epistaxis, gastrointestinal haemorrhage, abdominal pain, diarrhoea, dyspepsia, nausea, hepatic function abnormal, urogenital haemorrhage. Serious: Major or severe bleeding, thrombocytopenia, neutropenia, agranulocytosis, drug hypersensitivity, angioedema, intracranial haemorrhage, haemoptysis. Others, see full Data Sheet. INTERACTIONS: See CONTRAINDICATIONS and WARNINGS AND PRECAUTIONS above. ACTIONS: Dabigatran is a potent, competitive, reversible direct thrombin inhibitor and is the main active principle in plasma. Dabigatran prolongs the aPTT, ECT and TT. PRESCRIPTION MEDICINE. PRADAXA® is fully funded with no special authority. PRADAXA® is a registered trademark of Boehringer Ingelheim. 14 May 2020.

PRAXBIND® (idarucizumab, rch) 50 mg/mL solution for injection/infusion. Before prescribing, please review the full Data Sheet which is available on request from Boehringer Ingelheim or from <http://www.medsafe.govt.nz/profs/datasheet/dsform.asp> INDICATION: Specific reversal agent for dabigatran, indicated in patients treated with PRADAXA (dabigatran etexilate) when rapid reversal of the anticoagulant effects of dabigatran is required: for emergency surgery/urgent procedures, and in life-threatening or uncontrolled bleeding. The recommended dose is 5 g. Two 50 mL vials (2 x 2.5 g) constitute one complete dose. ADMINISTRATION: The complete dose of 5 g is administered intravenously, as two consecutive infusions over 5 to 10 minutes each or as a bolus injection. For instructions for use / handling and restarting antithrombotic therapy, see full Data Sheet CONTRAINDICATIONS: None. WARNINGS AND PRECAUTIONS: Idarucizumab will not reverse the effects of other anticoagulants. Known hypersensitivity (weighed against potential benefit of emergency treatment) – discontinue PRAXBIND immediately in case of anaphylactic reaction or other serious allergic reaction. Hereditary fructose intolerance, controlled sodium diet. Pregnancy. Lactation. Children. Trade name and batch number should be recorded in patient file to improve traceability. See full Data Sheet. ADVERSE EFFECTS: No adverse events causally related to PRAXBIND have been identified. INTERACTIONS: Clinically relevant interactions with other medicinal products are not expected. ACTIONS: Idarucizumab is a humanised monoclonal antibody fragment (Fab) molecule derived from an IgG1 isotype antibody molecule, directed against the thrombin inhibitor dabigatran. PRESCRIPTION MEDICINE PRAXBIND® is a funded medicine – Restrictions apply: Pharmaceutical Schedule, Hospital Medicines List. PRAXBIND® is a registered trademark of Boehringer Ingelheim. 8 July 2019.

BOEHRINGER INGELHEIM (N.Z.) Ltd. 2 Osterley Way, Manukau City Auckland T0104. PC-NZ-100292, TAPS MR8351

Pradaxa®
dabigatran etexilate

Praxbind™
idarucizumab

 **Boehringer
Ingelheim**

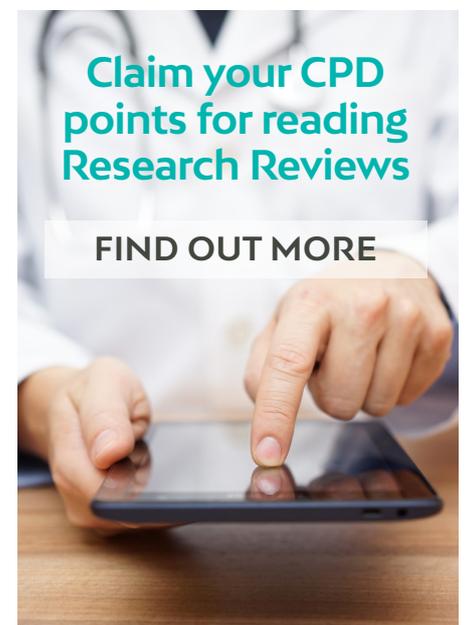
CT or invasive coronary angiography in stable chest pain

Authors: The DISCHARGE Trial Group

Summary: The DISCHARGE trial compared the utility of CTCA and invasive coronary angiography (ICA) as initial diagnostic imaging strategies for guiding the treatment of patients with stable chest pain. 3561 patients (56.2% female) who had an intermediate pretest probability of obstructive CAD and were referred for ICA at 1 of 26 European centres were included. Major adverse cardiovascular events (MACE) occurred in 2.1% of patients randomised to CTCA and 3.0% of patients randomised to ICA (HR 0.70, 95% CI 0.46–1.07; p=ns). Major procedure-related complications occurred in 0.5% and 1.9% of patients in the respective groups (HR 0.26, 95% CI 0.13–0.55), and 8.8% and 7.5% of patients in the respective groups had angina during the final 4 weeks of follow-up (odds ratio 1.17, 95% CI 0.92–1.48).

Comment: Different paths are taken for the workup of stable chest pain; this study compared CTCA to ICA as initial tests. The primary endpoint was the prevention of MACE. 3561 patients with intermediate pretest probability were randomised in 26 European centres. While MACE did not differ between CTCA and ICA, there were significantly more adverse events in the ICA group. 22.3% of CTCA patients underwent consecutive ICA. CTCA patients had less PCI (10.8% vs 14.4%) or CABG surgery (2.2% vs 3.5%). Overall, a CTCA-first strategy compared favourably with ICA, preventing MACE at a similar level but with less adverse outcomes. Functional testing was not the subject of this study.

Reference: *N Engl J Med* 2022;386:1591-1602
[Abstract](#)



Jardiance®
(empagliflozin)

FULLY FUNDED
with Special Authority criteria*
for the treatment of T2D

For your patients with type 2 diabetes[†]

THE POWER TO ACCOMPLISH MORE
Above and beyond glycaemic control^{‡,1,2}

Not an actual patient.

PDAY risk score predicts cardiovascular events in young adults

Authors: Gidding SS et al.

Summary: The CARDIA study used the PDAY risk score to predict atherosclerotic cardiovascular disease (ASCVD) events in young adults. Cardiovascular risk data, coronary artery calcium (CAC) scores, and ASCVD data were collected for 5004 young adults at age 18 and 30 years, with 30-year follow-up. Each standard deviation increase in PDAY score at each examination was significantly associated with future ASCVD. Hazard ratios (per standard deviation) increased from 1.74 to 2.04 from year 0 to year 15, and C-statistics ranged from 0.771 to 0.794. CAC measurement at age 33–45 years improved risk prediction only if the score was zero.

Comment: Another risk score, this one predicts atherosclerosis in under 40-year-olds. In a very unusual approach, the PDAY score is based on postmortem data of men and women who died accidentally. The score was applied to 5004 patients originally recruited in 1985–1986 and was tested to see if it predicted ASCVD in mid-life. Measured were age, high-density lipoprotein (HDL) and non-HDL cholesterol, hypertension, male gender, male obesity and smoking, though they were weighted differently. When CAC scoring was added to the assessment, it produced only a small improvement in ASCVD risk prediction. The paper is very complex, but the score seems to work. Personally I was again reminded that these (partially) preventable risk factors have a relevant effect even at a young age.

Reference: *Eur Heart J* 2022;**43(30):2892-900**
[Abstract](#)

Independent Content: The selection of articles and writing of summaries and commentary in this publication is completely independent of the advertisers/sponsors and their products.

Privacy Policy: Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time.

Disclaimer: This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

Research Review publications are intended for New Zealand health professionals.

[†]38% RRR in CV death in patients with established CV disease (CAD, PAD, MI or stroke) and T2D (HR=0.62; p<0.001).[‡] *JARDIANCE is a funded medicine. Restrictions apply: Pharmaceutical Schedule, Hospital Medicines List. Jardiance is fully funded for the treatment of T2DM. Jardiance is not funded for the treatment of heart failure with reduced ejection fraction. [†]In adult patients with insufficiently controlled type 2 diabetes and CAD, PAD, or a history of MI or stroke. [‡]The absolute risk for CV death was reduced from 5.9% in patients receiving standard of care plus placebo to 3.7% in patients receiving standard of care plus JARDIANCE[®] (p<0.001).^{1,2} 1.JARDIANCE[®] Data Sheet 2021 2.Zinman B et al. N Engl J Med. 2015;373(22):2117-2128
JARDIANCE[®] empagliflozin 10mg, 25mg film coated tablets. Before prescribing, please review full Data Sheet which is available on request from Boehringer Ingelheim or from <http://www.medsafe.govt.nz/profs/datasheet/dsform.asp> **INDICATION:** Type 2 diabetes mellitus - Glycaemic control: Treatment of type 2 diabetes mellitus (T2DM) to improve glycaemic control in adults as: Monotherapy - When diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance; Add-on combination therapy - With other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control. **Prevention of cardiovascular (CV) events:** In patients with T2DM and established CV disease to reduce the risk of CV death. To prevent CV deaths, Jardiance should be used in conjunction with other measures to reduce CV risk in line with the current standard of care. **Heart failure:** In adult patients with heart failure (NYHA class II-IV) and reduced ejection fraction, with or without type 2 diabetes mellitus: -to reduce the risk of hospitalisation for heart failure; -to slow kidney function decline. **DOSE AND ADMINISTRATION:** Type 2 diabetes mellitus: Recommended starting dose is 10mg once daily. Patients with type 2 diabetes mellitus tolerating 10mg once daily and requiring additional glycaemic control, increase dose to 25mg once daily. **Heart failure:** Recommended dose is 10mg once daily. Can be taken with or without food. No dose adjustment is recommended based on age, patients with eGFR ≥30mL/min/1.73m² (T2DM) or ≥20mL/min/1.73m² (HF), or hepatic impairment. When Jardiance is used in combination with a sulfonylurea (SU) or with insulin, a lower dose of the sulfonylurea or insulin may be considered. **CONTRAINDICATIONS:** Hypersensitivity to empagliflozin or any of the excipients; patients with severe renal impairment (T2DM: eGFR <30mL/min/1.73m²). **WARNINGS AND PRECAUTIONS:** Patients with type 1 diabetes; ketoacidosis; necrotising fasciitis of the perineum (Fournier's gangrene); contraindicated when eGFR <30mL/min/1.73m² (T2DM); not recommended when eGFR <20mL/min/1.73m² (HF); assess renal function before treatment and regularly thereafter; patients for whom a drop in BP could pose a risk (e.g. those with known CV disease, on anti-hypertensive therapy with a history of hypotension, or aged ≥75 years); complicated urinary tract infections (UTIs); rare hereditary conditions of galactose intolerance, e.g. galactosaemia; pregnancy; lactation; children (<18 years). **INTERACTIONS:** Diuretics; insulin and SU: interference with 15-nhydroxyglucitol assay. **ADVERSE REACTIONS:** Very common: hypoglycaemia (when used with metformin in combination with SU or insulin - patients with T2DM); volume depletion (patients with HF). Common: hypoglycaemia (combination with metformin; pioglitazone with or without metformin; metformin and linagliptin - patients with T2DM); hypoglycaemia (patients with HF); vaginal moniliasis, vulvovaginitis, balanitis and other genital infections; UTIs (including pyelonephritis and urosepsis); pruritus (patients with T2DM); allergic skin reactions (e.g. rash, urticaria); increased urination (patients with T2DM); thirst (patients with T2DM); serum lipids increased; volume depletion (patients aged ≥75 years); constipation. For other adverse reactions, see full Data Sheet. **ACTIONS:** Empagliflozin is a reversible competitive inhibitor of sodium-glucose co-transporter 2 (SGLT2), which is responsible for glucose absorption in the kidney. It improves glycaemic control in patients with type 2 diabetes by reducing renal glucose reabsorption. Through inhibition of SGLT2, excessive glucose is excreted in the urine. Empagliflozin also reduces sodium reabsorption and increases the delivery of sodium to the distal tubule. This may influence several physiological functions including, but not restricted to, increasing tubuloglomerular feedback and reducing intraglomerular pressure, lowering both pre- and afterload of the heart, and downregulating sympathetic activity. **PRESCRIPTION MEDICINE - JARDIANCE is a funded medicine - Restrictions apply: Pharmaceutical Schedule, Special Authority. Jardiance is fully funded for the treatment of T2DM. Jardiance is not funded for the treatment of heart failure with reduced ejection fraction. JARDIANCE[®] is a registered trademark of Boehringer Ingelheim. BOEHRINGER INGELHEIM (N.Z.) Ltd. Level 3, 2 Oysterly Way, Manukau, Auckland 2104. TAPS MR8157/PC-NZ-100168 April 2022 BOE000418**

Boehringer Ingelheim
Boehringer Ingelheim (NZ) Ltd.
PO Box 76216 Manukau City,
Auckland 2241. Phone 0800 802 461

Lilly
Eli Lilly and Company (NZ) Ltd.
PO Box 109197 Newmarket,
Auckland 1149. Phone 0800 500 056
NZBN 9429039560643

Kindly Supported by



Trends in survival after cardiac arrest: A Swedish nationwide study over 30 years

Authors: Jerkeman M et al.

Summary: This analysis of the Swedish cardiopulmonary resuscitation registry evaluated trends in characteristics, management, and survival after out-of-hospital cardiac arrest (OHCA) or in-hospital cardiac arrest (IHCA). 106,296 cases of OHCA where resuscitation was attempted were reported in 1990–2020 and 30,032 cases of IHCA where resuscitation was attempted were reported in 2004–2020. 30-day survival after OHCA increased from 5.7% in 1990 to 10.1% in 2011 and remained unchanged thereafter. Odds ratios for 30-day survival in 2017–2020 versus 1990–1993 were 2.17 overall, 2.36 for men, and 1.67 for women. Bystander cardiopulmonary resuscitation (CPR) increased from 30.9% to 82.2%. The odds ratio for 30-day survival after IHCA in 2017–2020 versus 2004–2007 was 1.18, with the probability of survival increasing by 46.6% in 2011–2020. Approximately 90% of survivors of OHCA and IHCA had no or mild neurological sequelae.

Comment: Sweden has been running a national registry on cardiac arrests since 1990, and this paper describes developments in OHCAs and IHCA in a health system that is quite comparable to that of New Zealand. By its nature the paper is mostly descriptive. Survival of patients has improved significantly, at least for patients with shockable rhythm (from 14.4% to 35.8%). Women make up about one-third of cardiac arrests and their outcomes tend to be worse. 30-day survival increased by a factor of 2.2 after OHCA and 1.2 after IHCA, in particular men and younger patients had the most improvements. Myocardial ischaemia as the main cause reduced drastically from 67% to 28%. Rates of bystander CPR have also markedly changed from 31% to 82%. This study provides a wealth of data to guide future policy decisions.

Reference: *Eur Heart J* 2022; published online Aug 4

[Abstract](#)

Effect of MRI-guided fibrosis ablation vs conventional catheter ablation on atrial arrhythmia recurrence in patients with persistent atrial fibrillation

Authors: Marrouche NF et al.

Summary: The multicentre DECAAF II trial investigated the efficacy and safety of MRI-guided fibrosis ablation in patients with persistent AF. 843 patients with symptomatic or asymptomatic persistent AF who were undergoing AF ablation at 44 centres in 10 countries were randomised to pulmonary vein isolation (PVI) plus MRI-guided atrial fibrosis ablation (n=421) or standard PVI alone (n=422). Delayed-enhancement MRI was performed in both groups before ablation to assess baseline atrial fibrosis and 3 months after ablation to assess ablation scar. The primary end-point (time to first atrial arrhythmia recurrence after the 90-day blanking period post-ablation) did not differ significantly between groups (43.0% of fibrosis-guided PVI patients and 46.1% of PVI-only patients). Patients in the fibrosis-guided PVI group had a higher rate of safety outcomes (2.2% vs 0%; p=0.001). Six patients in the fibrosis-guided ablation + PVI group had an ischaemic stroke compared with none in PVI-only group.

Comment: A convincing hypothesis, the amount of atrial scarring should affect the outcome in AF ablation. Here 44 centres enrolled 843 patients and measured atrial scar with MRI. They then randomised patients to standard PVI or fibrosis-guided PVI. Arrhythmia recurrence rates were 46% in the standard PVI group and 43% in the fibrosis-guided PVI group, so not different (p=0.63). Hence fibrosis-guided ablation is not recommended by the authors. However, my comment would be that (1) fibrosis measurement via MRI is not as easy/reproducible as these trials make you believe, and (2) it does not necessarily disprove the fibrosis to AF link, but rather shows – yet again – that the type of PVI does not matter so much.

Reference: *JAMA* 2022;327(23):2296-305

[Abstract](#)

New Zealand Research Review subscribers can claim CPD/CME points for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our [CPD page](#).



Iron deficiency is exposing your heart failure patients to major risks^{1,2}

Ferinject® could help keep HF patients out of hospital.^{1,2} There's no time to lose for heart failure patients with iron deficiency. Ferinject® alleviates symptoms of HF and improves exercise capacity and quality of life.³⁻⁵

Screen, diagnose, treat & follow up.

Because in heart failure - *Iron Matters*



References: 1. Anker SD et al. *Eur J Heart Fail* 2018;20:125–33. 2. Ponikowski P, et al; *Lancet* 2020;396:1895-904. 3. Ponikowski P et al. *Eur Heart J* 2015;36(11):657–68. 4. Anker SD et al. *N Engl J Med* 2009;361:2436–48. 5. Van Veldhuisen DJ et al. *Circulation* 2017;136:1374–83. **FERINJECT®** (ferric carboxymaltose) solution for intravenous (IV) use. **Presentation:** 10mL vial containing 500mg of iron. **Therapeutic Indications:** Ferinject® is indicated for the treatment of iron deficiency when oral iron preparations are ineffective, cannot be used, or there is a clinical need to deliver iron rapidly. The diagnosis must be based on laboratory tests **Dosage:** The dosage must be calculated individually for each patient and must not be exceeded. Maximum single dose of 1000mg iron per week or 20 mg iron/kg body weight. IV injection: Administer >500mg-1000mg iron over 15 minutes, administer >200-500mg iron at 100mg iron/min. IV infusion: >500mg-1000mg iron over 15 minutes; >200mg-500mg iron over 6 minutes. 100mg-200mg iron over 3 minutes. **Contraindications:** Hypersensitivity to any of the ingredients; anaemia not attributed to iron deficiency; evidence of iron overload or disturbances in utilisation of iron. **Special warnings and precautions for use:** Parenteral iron preparations can cause hypersensitivity reactions – monitor patients for 30 minutes after each administration; paravenous leakage can lead to skin discolouration and irritation; iron overload; hypophosphataemia and hypophosphataemic osteomalacia; hepatic impairment; acute or chronic infections; contains sodium; not recommended in children < 14 years; Pregnancy category B3 – not recommended if <16 weeks gestation, monitor unborn baby. **Adverse effects:** Common: headache, dizziness, hypertension, flushing, nausea, injection/infusion site reactions, hypophosphataemia. Uncommon: hypersensitivity Rare: anaphylactoid reactions. Please review Data Sheet before prescribing, available at www.medsafe.govt.nz or call 0800 996 312 for further information. FERINJECT® is listed on the HML and is a fully funded Prescription Medicine – special authority criteria apply. Based on data sheet June 2021. FERINJECT® is a registered trademark of Vifor Pharma Group used under license by Aspen New Zealand, C/O Pharmacy Retailing (NZ) Ltd, Auckland. TAPS BG2176-MAY22. NZ-FCM-2200008. INSIGHT 11664



Learn more at www.aspenhub.co.nz Click the link to request a password from Aspen

Generalizability of the EAST-AFNET 4 trial: Assessing outcomes of early rhythm-control therapy in patients with atrial fibrillation

Authors: Dickow J et al.

Summary: The EAST-AFNET 4 trial demonstrated the clinical benefits of early rhythm-control (ERC) therapy in patients with new-onset AF and concomitant cardiovascular conditions. This study evaluated the generalisability of the EAST-AFNET 4 findings in routine practice. 109,739 patients with newly diagnosed AF were identified from a US administrative database and classified as receiving ERC (AF ablation therapy or antiarrhythmic drug therapy) within the first year after AF diagnosis (n=27,106) or not receiving ERC (control group, n=82,633). 72.9% of patients met inclusion criteria for EAST-AFNET 4. Cox proportional hazards regression analysis showed that ERC was associated with a reduced risk of the primary composite outcome of all-cause mortality, stroke, or hospitalisation for HF or MI (HR 0.85, 95% CI 0.75–0.97; p=0.02). Results were largely consistent between patients who were eligible for EAST-AFNET 4 trial inclusion and those who were not.

Comment: The EAST-AFNET 4 trial had previously suggested a benefit for ERC in AF, including early ablation (in 25%) or medical rhythm control strategies. These study results were analysed by retrospective review of US data. 27,106 patients would qualify as ERC treatment compared to 82,633 receiving usual AF care; patients were grouped according to whether they met original EAST-AFNET 4 criteria. The primary outcome was a composite of all-cause mortality, stroke, or hospitalisation with the diagnoses of HF or MI, and the ERC had a better outcome compared to usual care (HR 0.85, 95% CI 0.75–0.97), although mortality was not affected in the 2.6-year follow-up. While the patients were not randomised to the 2 groups (leading to a certain bias) the authors feel their data support the EAST-AFNET 4 results suggesting an early strategy for rhythm control in AF.

Reference: *J Am Heart Assoc* 2022;11(11):e024214

[Abstract](#)

[CLICK HERE](#)

to read previous issues of Cardiology Research Review



This Research Review has been endorsed by The Royal New Zealand College of General Practitioners (RNZCGP) and has been approved for up to 1 CME credit for the General Practice Educational Programme (GPEP) and Continuing Professional Development (CPD) purposes. You can record your CME credits in your [RNZCGP Dashboard](#)



Time spent reading this publication has been approved for CNE by The College of Nurses Aotearoa (NZ) for RNs and NPs. For more information on how to claim CNE hours please [CLICK HERE](#).



Development and validation of a decision support tool for the diagnosis of acute heart failure

Authors: Lee KK et al.

Summary: This meta-analysis and modelling study evaluated the diagnostic performance of NT-proBNP thresholds for acute HF and developed a decision support tool (CoDE-HF) that combined NT-proBNP levels with clinical characteristics to determine the probability of acute HF. Of 10,369 patients with suspected acute HF who participated in 14 trials, 43.9% had an adjudicated diagnosis of acute HF. An NT-proBNP threshold of 100 pg/ml achieved optimal rule-out criteria, and an NT-proBNP threshold of 1000 pg/ml achieved optimal rule-in criteria. However, performance was poor in certain patient subgroups. The CoDE-HF decision tool used NT-proBNP concentrations as a continuous measure together with objective clinical variables known to be associated with acute HF (age, estimated glomerular filtration rate, haemoglobin, body mass index, heart rate, blood pressure, peripheral oedema, chronic obstructive pulmonary disease, and ischaemic heart disease). It had excellent diagnostic performance across all patient subgroups, and ruled in and ruled out acute HF more accurately than use of NT-proBNP thresholds alone.

Comment: While the use of NT-proBNP is well established in the diagnosis of HF, this study evaluated the performance of NT-proBNP for the diagnosis of acute HF in different subgroups. Essentially they did a meta-analysis but went back to patient-level data on 10,369 patients. A NT-proBNP threshold of 100 pg/ml achieved the best rule-out results with a negative predictive value of 97.8% and a sensitivity of 99.3%. For rule-in a threshold of 1000 pg/ml was seen as optimal with a positive predictive value of 74.9% and specificity of 76.1%. Both cut-offs worked less well in older patients. From the data a decision tool (CoDE-HF) was developed by incorporating and weighing clinical factors. It apparently performed well and further prospective studies are planned to see if CoDE-HF can guide clinical decisions.

Reference: *BMJ* 2022;377:e068424

[Abstract](#)

Invasive versus conservative management in patients aged ≥85 years presenting with non-ST-elevation myocardial infarction

Authors: Kunniardy P et al.

Summary: This retrospective cohort study in Australia compared outcomes after invasive versus conservative management of NSTEMI in elderly patients. Outcomes for 1052 patients aged ≥85 years who presented to a tertiary centre with NSTEMI in 2008–2018 were analysed. 99 (9.4%) patients underwent early coronary angiography (they tended to be younger, male, and live independently without mobility or cognitive issues). Overall, 47% of patients died during a mean follow-up of 1.3 years. Cox regression analysis adjusted for age, pre-morbid functional status, cognition and cardiovascular risk factors showed that invasive management was the strongest predictor of survival (HR 0.47, 95% CI 0.26–0.85; p=0.01). Invasive management was associated with a trend to increased risk of in-hospital bleeding (6.1% vs 2.6%; p=0.054) but there was no significant between-group difference in stroke (2.0% vs 3.8%; p=0.37).

Comment: Acute coronary syndrome pathways were initially quite restrictive regarding invasive management of elderly patients. Concerns were comorbidity and the ability to benefit compared to the risk. This Australian study retrospectively analysed patients 85 years or older presenting with NSTEMI. They found 1052 patients and (only) 9.4% underwent invasive management – these patients being younger, having less comorbidity and being more likely male. After a follow-up of 1.3 years, 47% of patients had died. After trying to adjust for cofounders by statistical means the invasive management was the strongest predictor for survival (HR 0.47, p=0.01). Bleeding increased from 2.6% to 6.1% with invasive management, but the rate of stroke did not differ between groups. While this study does not replace a randomised trial it supports extending invasive management to selected elderly patients with NSTEMI.

Reference: *Intern Med J* 2022;52(7):1167-73

[Abstract](#)

Rivaroxaban monotherapy vs combination therapy with antiplatelets on total thrombotic and bleeding events in atrial fibrillation with stable coronary artery disease

Authors: Naito R et al.

Summary: This post hoc secondary analysis of the AFIRE trial evaluated the use of rivaroxaban alone or in combination with antiplatelet therapy in patients with AF and CAD. 2215 patients with AF and stable CAD who had undergone PCI or CABG surgery at least 1 year earlier or who had angiographically confirmed CAD not requiring revascularisation were randomised to receive rivaroxaban alone or in combination with antiplatelet therapy. 12.2% of patients in the rivaroxaban monotherapy group and 19.2% in the combination therapy group had a thrombotic, bleeding, or fatal event during a median follow-up of 24.1 months. Mortality rates were 3.7% and 6.6% in the respective groups. Overall, rivaroxaban monotherapy was associated with a lower risk of total events compared with combination therapy (HR 0.62, 95% CI 0.48–0.80; $p < 0.001$).

Comment: AF and recent stents frequently cause concerns about anticoagulation, however this paper looks at the patients that are medically managed with stable CAD and concomitant AF. Rivaroxaban monotherapy was compared to rivaroxaban with antiplatelet medication by randomising a total of 2215 patients either way. The primary end-point was a composite of thrombotic, bleeding, and fatal events. In these patients with stable CAD, rivaroxaban monotherapy was associated with less adverse events (12.2% vs 19.2%) and a lower mortality rate (3.7% vs 6.6%). Overall the findings support giving rivaroxaban alone instead of in conjunction with antiplatelet medication in this group of patients with stable CAD. Whether this is a class effect for non-vitamin K antagonist oral anticoagulants was not tested by the study.

Reference: *JAMA Cardiol* 2022;7(8):787-94

[Abstract](#)

Type of stressor and medium-term outcomes after Takotsubo syndrome: What becomes of the broken hearted? (ANZACS-QI 59)

Authors: Looi J-L et al.

Summary: This NZ study compared outcomes in patients with Takotsubo syndrome (TS) triggered by acute physical or emotional stressors. Of 632 patients presenting with TS in 2006–2018 (mean age 65 years, 95.9% female), 27.4% had an associated acute physical stressor, 46.4% had an emotional stressor and 26.2% had no evident stressor. In-hospital mortality was similar in the respective groups (1.7%, 1.2%, and 0.3%). During a median 4.4 years of follow-up post-discharge, mortality was higher in TS patients with physical stress (HR 4.46, 95% CI 3.10–6.42) or MI (HR 4.23, 95% CI 3.81–4.70) than in patients without known cardiovascular disease (CVD). However, mortality in patients with TS associated with emotional stress or no stressor was similar to that in patients without known CVD. Recurrence was similar in the 3 groups.

Comment: TS is a regional cardiomyopathy triggered by stress, but does the type of stress affect the outcome? Stressors were categorised as emotional or acute physical illness. 632 patients (96% female) were enrolled in this NZ study, 27.4% had a physical, 46.4% an emotional and 26.2% no apparent stressor. Following discharge and compared to a reference group with no presumed CVD, patients with MI and TS with physical stressor had a similar mortality risk (HR 4.5 and 4.2); TS with emotional or no stressor had a mortality similar to the no-CVD group (HR 1.11 and 1.08). Recurrence rate (6.4%) was not affected by the type of stressor. Mortality in the physical stress TS patients seemed to be driven by non-cardiac causes.

Reference: *Heart Lung Circ* 2022;31(4):499-507

[Abstract](#)

Age at menopause and risk of heart failure and atrial fibrillation

Authors: Shin J et al.

Summary: This nationwide cohort study in Korea evaluated the impact of premature or early menopause on the risk of HF and AF. Reproductive histories were collected for 1,401,175 postmenopausal women enrolled with the Korean National Health Insurance Service. 42,699 (3.0%) women developed HF and 44,834 (3.2%) developed AF during a mean follow-up of 9.1 years. Multivariable Cox proportional hazard models found that women with premature menopause were at increased risk for HF (HR 1.33, 95% CI 1.26–1.40) and AF (HR 1.09, 95% CI 1.02–1.16) compared with women without premature menopause. There was a significantly increasing trend in HRs for the risk of both HF and AF in women aged 45–49, 40–44, and <40 years at menopause compared with women aged ≥ 50 years at menopause (p -trend < 0.001).

Comment: Two chronic heart diseases, HF and AF, but how are they affected by premature menopause (<40 years of age)? The study enrolled 1,401,175 postmenopausal women in Korea via their public health records. Mean follow up was 9.1 years. Women with premature menopause more commonly presented with HF (HR 1.33) and AF (HR 1.09, both $p < 0.001$); when adjusted for cofounders the statistical relation did not change much. Also, when comparing different age groups of menopause onset, early onset had significantly higher rates of AF and HF. The findings in this study are clear and well presented. Maybe age at menopause should be a routine part of risk assessment and taken into account more often for clinical decisions.

Reference: *Eur Heart J* 2022; published online Aug 4

[Abstract](#)

Adding salt to foods and hazard of premature mortality

Authors: Ma H et al.

Summary: This analysis of UK Biobank data investigated whether adding salt to food increases the risk of premature mortality. 501,379 individuals completed a questionnaire on the frequency of adding salt to food (but not adding salt to cooking) at baseline and were followed up for a median 9.0 years, during which time 18,474 premature deaths occurred. Multivariable hazard ratios for all-cause premature mortality across the increasing frequency of adding salt to foods were 1.00 (reference), 1.02 (95% CI 0.99–1.06), 1.07 (95% CI 1.02–1.11), and 1.28 (95% CI 1.20–1.35) (p -trend < 0.001). The association was significantly modified by fruit and vegetable intake. Compared with the never/rarely group, always adding salt to foods decreased life expectancy by 1.50 years in 50-year-old females and by 2.28 years in 50-year-old males.

Comment: Salt and CVD, there are quite a few publications coming out lately. Here 501,379 patients enrolled in the UK Biobank had filled out a salt questionnaire, describing salt use as 'never/rarely', 'sometimes', 'usually' and 'always'. This was backed up by sodium urine analysis and follow-up questionnaires. Median follow-up was 9 years. Mortality was increased in the 'usually' (HR 1.07, 95% CI 1.02–1.11) and 'always' (HR 1.28, 95% CI 1.20–1.35) groups – all groups were extensively adjusted for cofounders. The mortality was more often from CVD in these groups, including a higher frequency of strokes. However, the association between salt and mortality was not shown in patients with body mass index > 30 kg/m². High intakes of potassium-containing vegetables and fruits attenuated the salt effect. 'Sometimes' adding a bit of salt seems ok, but 'usually' doing it not so much.

Reference: *Eur Heart J* 2022;43(30):2878-88

[Abstract](#)



Research Review New Zealand is on LinkedIn.
[FOLLOW US](#) TO KEEP UP TO DATE