

Cardiology

RESEARCH REVIEW™

Making Education Easy

Issue 94 – 2021

In this issue:

- Management of STEMI in patients with previous TAVI
- When to initiate rhythm control medication in patients with AF?
- Optimal aspirin dosage for secondary prevention
- Physical rehabilitation for older patients hospitalised with HF
- FFR- vs angiography-guided multivessel PCI
- Impact of CABG vs PCI on memory decline in older adults
- Statin therapy for primary prevention in the elderly
- Left atrial appendage closure during cardiac surgery to prevent stroke
- Aspirin vs clopidogrel for long-term monotherapy after PCI
- Long-term outcomes after CABG or PCI in patients with high-risk coronary anatomy
- Implantable vs external electrocardiographic monitoring for detection of AF
- Strain-guided management of potentially cardiotoxic cancer therapy

Abbreviations used in this issue

AF = atrial fibrillation
 CABG = coronary artery bypass grafting
 FFR = fractional flow reserve
 HF = heart failure
 HR = hazard ratio
 LVEF = left ventricular ejection fraction
 MACE = major adverse cardiovascular events
 MI = myocardial infarction
 PCI = percutaneous coronary intervention
 STEMI = ST-segment elevation MI
 TAVI = transcatheter aortic valve implantation

Welcome to the latest issue of Cardiology Research Review.

In this issue, a multicentre trial reports that management of STEMI is harder and outcomes are worse in patients with previous TAVI, the results of a Korean study suggest we should initiate rhythm control medication early in patients with AF, and the FLOWER-MI trial compares an FFR-guided strategy with an angiography-guided strategy in STEMI patients undergoing complete revascularisation. Also in this issue, a Canadian study reports the benefits of left atrial appendage closure during cardiac surgery in AF patients, a US study compares 2 dosages of aspirin for secondary prevention (let's all agree on 100mg), and the HOST-EXAM study finds that clopidogrel is superior to aspirin in patients requiring long-term antiplatelet monotherapy after PCI.

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

ST-segment elevation myocardial infarction following transcatheter aortic valve replacement

Authors: Faroux L et al.

Summary: This multicentre study evaluated the management of STEMI in patients with previous TAVI. 118 patients with STEMI after TAVI were compared with 439 patients with STEMI without previous TAVI. All patients received PCI. Median door-to-balloon time was higher in patients with previous TAVI (40 vs 30 min; $p=0.003$), as was procedural time, fluoroscopy time, dose-area product, and contrast volume (all $p<0.01$). PCI failure was more common in patients with previous TAVI (16.5% vs 3.9%; $p<0.001$). In-hospital and late mortality rates were 25.4% and 42.4%, respectively, in TAVI patients, compared with 20.6% and 38.2%, respectively, in non-TAVI patients.

Comment: TAVI valves are mounted in self- or balloon-expanding wire meshworks in the annulus and aortic sinus; recent trends encourage relatively high implantation to avoid heart block. However, consecutive coronary catheterisation, especially acutely in a STEMI, might be affected. Here 118 patients post TAVI were compared to 439 patients without TAVI in the setting of acute STEMI. PCI failure occurred more frequently in patients with previous TAVI (16.5% vs 3.9%) along with more contrast use and longer door-to-balloon time (40 vs 30 min). Mortality was higher in post-TAVI STEMI though it was difficult to compare to controls. Thrombolysis had not been a factor in this collective of patients.

Reference: *J Am Coll Cardiol* 2021;77(17):2187-99

[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](#).

RACP MyCPD Program participants can claim one credit per hour (maximum of 60 credits per year) for reading and evaluating Research Reviews. FOR MORE INFORMATION [CLICK HERE](#)

For your patient living with heart failure,
Time is essential.



For the treatment of chronic heart failure
 (NYHA Class II-IV) with reduced ejection fraction ¹

NYHA - New York Heart Association. **Reference 1.** ENTRESTO® New Zealand Data Sheet. ENTRESTO® (sacubitril/valsartan) tablets is a prescription medicine which is fully funded under special authority criteria (www.pharmac.govt.nz). Before prescribing please read the Data Sheet available at www.medsafe.govt.nz for information on dosage, contraindications, precautions, interactions and adverse effects. Novartis New Zealand Limited, Auckland. Phone 09 523 8500. NZ-00873 October 2020, TAPS NA12478, BGA201003

For more information, please go to www.medsafe.govt.nz

www.researchreview.co.nz

a RESEARCH REVIEW™ publication



Jardiance®
(empagliflozin)

FULLY FUNDED
with Special Authority criteria*
February 1st, 2021

NEW. For your patients with type 2 diabetes†

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

Click below to download your JARDIANCE resources

PRESCRIBING GUIDE **PATIENT BOOKLET**

Treatment timing and the effects of rhythm control strategy in patients with atrial fibrillation

Authors: Kim D et al.

Summary: This nationwide cohort study in Korea investigated the impact of treatment timing in patients receiving rhythm control for AF. 22,635 patients with AF who were newly treated with rhythm control (antiarrhythmic drugs or ablation) or rate control strategies were followed up for a median 2.1 years. The primary composite outcome was death from cardiovascular causes, ischaemic stroke, hospitalisation for HF, or acute MI. Among patients with early treatment of AF (initiated within 1 year after diagnosis), rhythm control was associated with a lower risk of the primary composite outcome than rate control (HR 0.81, 95% CI 0.71–0.93; $p=0.002$). No difference in the risk of the primary composite outcome was found between rhythm and rate control strategies in patients with late treatment of AF (initiated >1 year after diagnosis).

Comment: Rate control, sure, but when and if to start rhythm control medication in AF? This large retrospective population-based Korean study looked at outcomes (MACE and hospitalisation) of early (<1 year from onset) compared to late rhythm control in AF. Interestingly, initiating rhythm control early had better outcomes, mostly driven by fewer strokes, HF and MIs. The authors discuss early substrate remodelling or simply more intensive care as potential reasons. Rhythm control >1 year after AF onset was not better than rate control only.

Reference: *BMJ* 2021;373:n991
[Abstract](#)

Comparative effectiveness of aspirin dosing in cardiovascular disease

Authors: Jones WS et al., for the ADAPTABLE Team

Summary: This US study investigated the optimal dose of aspirin for secondary prevention in patients with established atherosclerotic cardiovascular disease. 15,076 patients were randomised to receive aspirin 81mg or 325mg daily and were followed-up for a median 26.2 months. The primary composite outcome (death from any cause or hospitalisation for MI or stroke) occurred in 7.28% of patients taking aspirin 81mg and 7.51% of patients taking aspirin 325mg (HR 1.02, 95% CI 0.91–1.14). Hospitalisation for major bleeding occurred in 0.63% and 0.60% of patients in the respective groups (HR 1.18, 95% CI 0.79–1.77).

Comment: How much aspirin for secondary prevention? The US is still undecided between 81mg and 325mg. The outcome was death, MI or stroke, and the trial ran for about 3 years. 15,076 patients were randomised and got a \$US25 remuneration for trial participation. The primary end-point occurred in 7.28% of the 81mg group and 7.51% of the 325mg group. Major bleeds were not different, and long-term adherence to 81mg was better. Can we now all agree on 100mg aspirin?

Reference: *N Engl J Med* 2021;384(21):1981–90
[Abstract](#)



^{#1}38% RRR in CV death in patients with established CV disease (CAD, PAD, MI or stroke) and T2D (HR=0.62; $p<0.001$).^{#2}
*JARDIANCE is a funded medicine. Restrictions apply: Pharmaceutical Schedule, Hospital Medicines List. †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 2019 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: *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) death:* 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. **DOSAGE AND ADMINISTRATION:** Recommended starting dose is 10mg once daily taken with or without food. Dose can be increased to 25mg once daily. No dose adjustment is necessary for patients based on age, patients with eGFR ≥ 30 mL/min/1.73m² 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 CKD stage 4 or 5 (severely impaired renal function including patients receiving dialysis; eGFR <30 mL/min/1.73m² or CrCl <30 mL/min). **WARNINGS AND PRECAUTIONS:** Patients with type 1 diabetes; diabetic ketoacidosis; necrotising fasciitis of the perineum (Fournier's gangrene); discontinue when eGFR is below 30 mL/min/1.73m²; 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); 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 1,5-anhydroglucitol assay. **ADVERSE REACTIONS:** *Very common:* hypoglycaemia (when used with combination with SU or insulin). *Common:* hypoglycaemia (combination with metformin; pioglitazone with or without metformin; metformin and linagliptin); vaginal moniliasis, vulvovaginitis, balanitis and other genital infections; UTIs (including pyelonephritis and urosepsis); pruritus; allergic skin reactions (e.g. rash, urticaria); increased urination; thirst; serum lipids increased; volume depletion (patients aged ≥ 75 years). For other adverse reactions, see full Data Sheet. **ACTIONS:** Empagliflozin is a reversible, highly potent and selective 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 SGLT2. Through inhibition of SGLT2, excessive glucose is excreted in urine. **PRESCRIPTION MEDICINE.** JARDIANCE® is a funded medicine - Restrictions apply: Pharmaceutical Schedule, Hospital Medicines List. BOEHRINGER INGELHEIM (N.Z.) Ltd. Level 3, 2 Osterley Way, Manukau Auckland 2104. TAPS MR7142/PC-NZ-100168 BOEO00370

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


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

For more information, please go to www.medsafe.govt.nz

Physical rehabilitation for older patients hospitalized for heart failure

Authors: Kitzman DW et al.

Summary: This randomised controlled trial in the US evaluated a physical rehabilitation intervention for older patients hospitalised with acute decompensated HF. 349 patients were randomised to either the rehabilitation intervention or usual care (controls). The rehabilitation intervention comprised 4 physical-function domains (strength, balance, mobility, and endurance). It was initiated during or soon after hospitalisation and continued for 36 outpatient sessions after discharge. The primary outcome was Short Physical Performance Battery score (lower scores indicating worse physical dysfunction) at 3 months. At baseline, patients in each group had markedly impaired physical function (97% were frail or prefrail). At 3 months, the intervention group had a significantly better score on the Short Physical Performance Battery than the control group (mean 8.3 vs 6.9; $p<0.001$).

Comment: Older patients (73±8 years) with frailty features were randomised to cardiac rehab after HF presentation. Almost 350 patients, publication made it in the *NEJM*. Patients underwent a progressive rehabilitation intervention that included multiple physical-function domains. Participants of the 12-week rehab programme scored significantly higher on a physical performance test – pretty much across most of the participants. While readmission and mortality were not affected, the message is that even for older patients rehab helps delay frailty and improves physical function.

Reference: *N Engl J Med* 2021; published online May 16

[Abstract](#)

Multivessel PCI guided by FFR or angiography for myocardial infarction

Authors: Puymirat E et al., for the FLOWER-MI Study Investigators

Summary: This analysis of the FLOWER-MI study evaluated whether multivessel PCI guided by FFR is superior to an angiography-guided procedure in patients with STEMI. 1163 patients with STEMI and multivessel disease who had undergone successful PCI of the infarct-related artery were randomised 1:1 to receive complete revascularisation guided by either FFR or angiography. The primary outcome was a composite of death from any cause, nonfatal MI, or urgent revascularisation at 1 year. The mean number of stents placed per patient for nonculprit lesions was 1.01 in the FFR-guided group and 1.50 in the angiography-guided group. During follow-up, a primary outcome event occurred in 5.5% of patients in the FFR-guided group and 4.2% of patients in the angiography-guided group (HR 1.32, 95% CI 0.78–2.23; $p=0.31$).

Comment: The FLOWER-MI trial investigated FFR- versus angiography-guided revascularisation of non-infarct related coronaries in the context of STEMI. The FFR cut-off for intervention was 0.80. In the angiography group about 96% had an intervention, in the FFR-guided group it was also 96%. The primary outcome was MACE after 1 year, and it was not different between the 2 groups. The authors clearly note the difference between this and other FFR trials, but have no real explanation for the discrepancy.

Reference: *N Engl J Med* 2021; published online May 16

[Abstract](#)

SPECIAL REPORT ON THE 2021 NZSSD Type 2 Diabetes Management Guidelines

This Special Report by Dr Ryan Paul, who was the lead on the guidelines working party, provides a summary of and commentary on the Type 2 Diabetes Management Guidance for the busy health care worker.

[CLICK HERE](#)
to read the PDF online



Association of coronary artery bypass grafting vs percutaneous coronary intervention with memory decline in older adults undergoing coronary revascularization

Authors: Whitlock EL et al.

Summary: This retrospective cohort study compared the change in rate of memory decline in older patients undergoing CABG or PCI. 1680 community-dwelling participants in the Health and Retirement Study (HRS) who underwent CABG ($n=665$; 168 off-pump) or PCI ($n=1015$) at age ≥ 65 years were included. In the PCI group, the mean rate of memory decline (assessed by biennial cognitive test scores and proxy cognition reports) was 0.064 memory units/year before the procedure and 0.060 memory units/year after the procedure. In the CABG group, the mean rate of memory decline was 0.049 memory units/year before the procedure and 0.059 memory units/year after the procedure. The between-group difference in memory decline was not significant.

Comment: Cognitive decline following CABG has always been a concern. This trial retrospectively reviewed cognitive test performance in older patients undergoing either PCI or CABG. Patients were part of a large database (HRS) collecting data from 1992 to 2010. Different test formats were normalised. Memory decline over the years was similar in the PCI and CABG groups, the difference between the 2 groups not significant ($p=0.98$). The secondary end-point of dementia probability was not different between the 2 groups and there was also no significant difference between on- and off-pump CABG. Reassuring, but retrospective data.

Reference: *JAMA* 2021;325(19):1955-64

[Abstract](#)

Statin therapy for primary prevention in the elderly and its association with new-onset diabetes, cardiovascular events, and all-cause mortality

Authors: Lavie G et al.

Summary: This retrospective cohort study in Israel investigated the use of statins for primary prevention in the elderly. 42,767 new users of statins (5970 were aged ≥ 70 years) without cardiovascular disease or diabetes mellitus were followed up for 5 years for assessment of new-onset diabetes mellitus, MACE and all-cause mortality. Adherence to statins was evaluated according to the proportion of days treated. For the highest ($\geq 75\%$) and lowest ($<25\%$) proportion of days treated categories, respective incident rates were 16.9% and 16.7% for MACE, 9.4% and 6.3% for all-cause mortality, and 1.7% and 9.4% for new-onset diabetes mellitus. In patients aged ≥ 70 years, the adjusted HRs for MACE and mortality were significantly decreased in the highest adherence group (0.71 and 0.68, respectively).

Comment: Over 70? Considering statins for primary prophylaxis, what is the evidence? Retrospectively 5970 patients over 70 with no prior cardiovascular events were identified in this study from Israel; outcomes were compared to number of days statins were prescribed ($<25\%$, 25–50%, 50–75%, $>75\%$) during 60 months of observation. With $>75\%$ statin prescription, adjusted MACE were reduced, all-cause mortality was non-significantly lower, and there was no indication for higher rates of diabetes. However inconsistent prescription ($<75\%$) was clearly less efficient. If you are prescribing statins for this indication, it will need to be persistent.

Reference: *Am J Med* 2021;134(5):643-52

[Abstract](#)



Research Review New Zealand is now on LinkedIn.

[FOLLOW US](#) TO KEEP UP TO DATE

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. **For full bio** [CLICK HERE](#).





YOUR NVAF[#] PATIENT CAN CHANGE WITH TIME, BUT THEIR PROTECTION FROM STROKE DOESN'T HAVE TO.

PROTECT YOUR NVAF[#] PATIENTS FROM STROKE WITH XARELTO.[†] XARELTO - THE ONLY NOAC REGISTERED FOR PATIENTS WITH CrCl DOWN TO 15mL/min.^{*1,2,3}

Start with Xarelto. Stay with Xarelto.



[†]Use with caution in patients with CrCl 15–29 mL/min. Contraindicated in patients with CrCl <15 mL/min.¹

²Xarelto® 20 mg once daily for patients with NVAF and CrCl ≥50 mL/min. Xarelto 15 mg once daily for patients with NVAF and CrCl 15–49 mL/min.¹

^{*}Prevention of stroke and systemic embolism in adult patients with NVAF and at least one additional risk factor for stroke.

CrCl = creatinine clearance; NOAC = non-vitamin K antagonist oral anticoagulant; NVAF = nonvalvular atrial fibrillation

References: 1. Xarelto (rivaroxaban) Data Sheet, 1 December 2020. 2. Pradaxa (dabigatran) Data Sheet, 11 March 2020. 3. Eliquis (apixaban) Data Sheet, 30 August 2019.

XARELTO® (rivaroxaban). Prescription Medicine. Oral tablets containing 2.5 mg, 10 mg, 15 mg or 20 mg rivaroxaban. **INDICATIONS:** Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery. Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack. Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and for the prevention of recurrent DVT and PE (see PRECAUTIONS for haemodynamically unstable PE patients). In combination with aspirin, for the prevention of major cardiovascular events (composite of stroke, myocardial infarction and cardiovascular death) in patients with coronary artery disease (CAD) and/or peripheral artery disease (PAD) **DOSAGE AND ADMINISTRATION:** Prevention of VTE in total hip replacement (treatment for up to 5 weeks), and total knee replacement (treatment for up to 2 weeks); 10mg once daily. Stroke prevention in atrial fibrillation, 20 mg once daily (15 mg once daily for patients with creatinine clearance 15–49 mL/min). Treatment of DVT and PE and for the prevention of recurrent DVT and PE; 15 mg tablet twice daily for the first 3 weeks followed by 20 mg tablet once daily. Following completion of six to twelve months therapy, based on an individual assessment of the risk of recurrent DVT or PE against the risk of bleeding, dose reduction to 10 mg once daily may be considered. CAD and/or PAD; 2.5 mg twice daily in combination with aspirin 100 mg once daily. Xarelto 15 mg and 20 mg tablets should be taken with food. Xarelto 2.5 mg and 10 mg tablets may be taken with or without food. Tablets may be crushed and administered orally (mixed with water or applesauce) or given through gastric tubes. See Data Sheet for full details. **CONTRAINDICATIONS:** Hypersensitivity to rivaroxaban or to any of the excipients, clinically significant active bleeding, lesions at increased risk of clinically significant bleeding and patients with spontaneous impairment of haemostasis, significant hepatic disease which is associated with coagulopathy, undergoing dialysis or severe renal impairment with a creatinine clearance < 15 mL/min, concomitant treatment with strong inhibitors of both CYP3A4 and P-glycoprotein, pregnancy, lactation. **PRECAUTIONS:** Increased bleeding risk such as general haemorrhagic risk (see Data Sheet for list), renal impairment, surgery and interventions, spinal/epidural anaesthesia or puncture, patients with prosthetic valves (not recommended), haemodynamically unstable PE patients or patients who require thrombolysis or pulmonary embolectomy, patients with non-valvular atrial fibrillation who undergo PCI with stent placement (limited data), lactose intolerance. CAD and/or PAD; patients with haemorrhagic lacunar stroke, or ischaemic non-lacunar stroke (should not be used). **INTERACTIONS WITH OTHER MEDICINES:** Care to be taken if concomitantly used with medicines affecting haemostasis; increased risk of bleeding with concomitant administration with selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), non-steroidal anti-inflammatory drugs (NSAIDs), platelet aggregation inhibitors, other anticoagulants. Strong inhibitors of both CYP3A4 and P-gp. **ADVERSE EFFECTS:** Please refer to Data Sheet for a complete list. Common adverse reactions (≥ 1/100 to < 1/10) include post procedural, eye, GI tract and urogenital tract haemorrhage, haemoptysis, increased transaminases, gingival bleeding, constipation, diarrhoea, dyspepsia, nausea, vomiting, pyrexia, oedema peripheral, confusion, pain in extremity, gastrointestinal and abdominal pain, headache, fever, decreased general strength and energy, contusion, dizziness, epistaxis, haematoma, anaemia, renal impairment and ecchymosis, cutaneous and subcutaneous haemorrhage, hypotension, rash and pruritus. Less frequent but serious adverse reactions include: urticaria, cerebral and intracranial haemorrhage, jaundice, angioedema, allergic oedema, cholestasis, hepatitis and thrombocytopenia. **Based on DS:** 1 Dec 2020.

Xarelto 10 mg, 15 mg and 20 mg tablets are fully funded – no special authority. Xarelto 2.5mg tablets are not funded and are not marketed by Bayer in New Zealand. This medicine has risks and benefits. Before prescribing, please review Data Sheet for further information. Full Data Sheet is available from www.medsafe.govt.nz or Bayer New Zealand Limited, B:HIVE, Smales Farm, 74 Taharoto Rd, Takapuna, Auckland 0622. Telephone 0800 233 988. PP-XAR-NZ-0141-2. TAPS NA 12768. March 2021. BY10147.

For more information, please go to www.medsafe.govt.nz

www.researchreview.co.nz

Left atrial appendage occlusion during cardiac surgery to prevent stroke

Authors: Whitlock RP et al., for the LAAOS III Investigators

Summary: This study in Canada investigated the use of left atrial appendage closure (LAAC) during cardiac surgery to prevent stroke in patients with AF. 4770 patients with AF and a CHA₂DS₂-VASc score of ≥2 who were scheduled to undergo cardiac surgery for another indication were randomised to undergo LAAC or no closure (controls) during surgery. All patients were expected to receive usual care, including oral anticoagulation, during a mean 3.8 years of follow-up. Stroke or systemic embolism occurred in 4.8% of patients in the LAAC group and 7.0% of controls during follow-up (HR 0.67, 95% CI 0.53–0.85; p=0.001). The incidence of perioperative bleeding, HF, or death did not differ significantly between groups.

Comment: What is the role of surgical LAAC to reduce the risk of stroke? Important note, the aim was not to replace anticoagulation but to continue standard practise plus LAAC. Patients undergoing cardiac surgery with AF and a CHA₂DS₂-VASc score of at least 2 were 1:1 randomised; surgical technique with or without device was variable, and purse-string closure was not allowed. About 80% of patients remained on oral anticoagulation. 114 in the LAAC group had a stroke or embolism (4.8%) compared to 168 (7.0%) controls. Subgroup analysis confirmed the benefits of LAAC, especially in older, male, hypertensive and HF patients. These are fascinating results – will LAAC during surgery in AF patients become a standard feature?

Reference: *N Engl J Med* 2021;384:2081–91
[Abstract](#)

Aspirin versus clopidogrel for chronic maintenance monotherapy after percutaneous coronary intervention (HOST-EXAM)

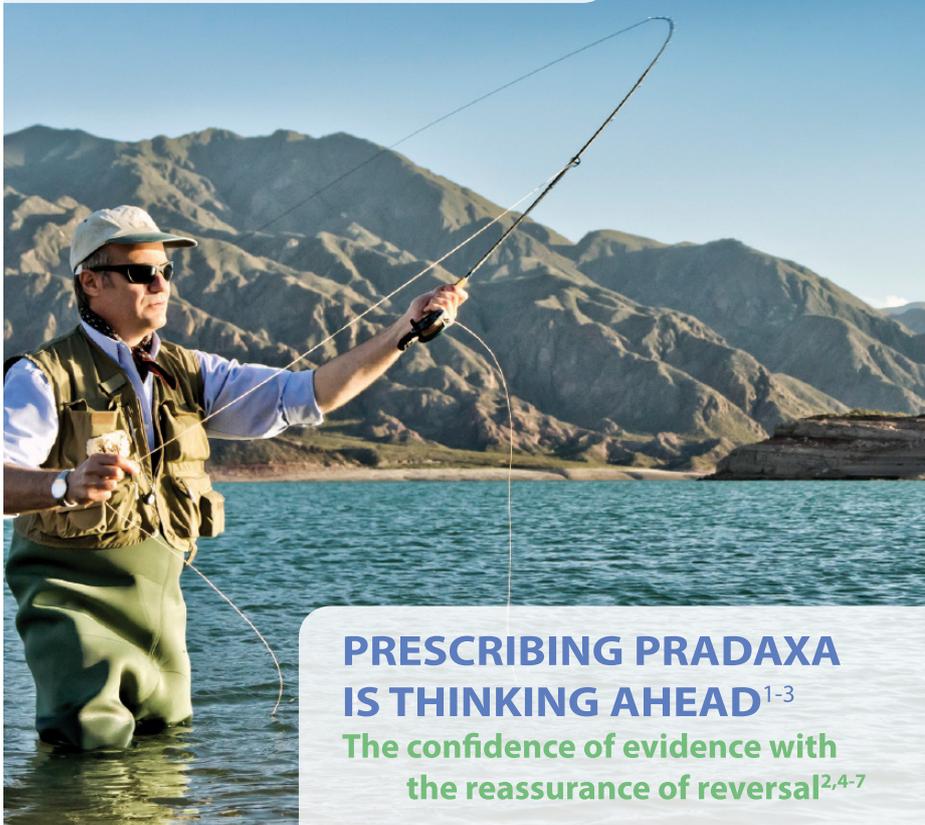
Authors: Koo BK et al.

Summary: The HOST-EXAM trial compared the use of long-term monotherapy with aspirin versus clopidogrel after PCI. At 37 sites in South Korea, 5438 patients who received dual antiplatelet therapy (DAPT) without clinical events for 6–18 months after PCI with a drug-eluting stent (DES) were randomised to receive monotherapy with either clopidogrel 75mg once daily or aspirin 100mg once daily for a further 24 months. The primary end-point was a composite of all-cause death, non-fatal MI, stroke, readmission for acute coronary syndrome, and major bleeding. During follow-up, the primary outcome occurred in 152 (5.7%) patients in the clopidogrel group and 207 (7.7%) in the aspirin group (HR 0.73, 95% CI 0.59–0.90; p=0.0035).

Comment: Another permutation of antiplatelets, this time after DES and a course of DAPT; patients were randomised to aspirin or clopidogrel monotherapy. Prospective, randomised, multicentre trial in Korea. The end-point was the usual MACE and bleeding events. And clopidogrel as monotherapy did better, with 5.7% vs 7.7% in the aspirin group reaching an end-point. The authors suggest using long-term clopidogrel instead of aspirin.

Reference: *Lancet* 2021; published online May 16
[Abstract](#)

**PRADAXA®: The only NOAC with a
SPECIFIC REVERSAL AGENT***



**PRESCRIBING PRADAXA
IS THINKING AHEAD¹⁻³**
The confidence of evidence with
the reassurance of reversal^{2,4-7}

NOAC: Non-Vitamin K Oral Anticoagulant. NVAf: Non Valvular Atrial Fibrillation. *Praxbind consent to market 2015. References: 1. Pradaxa New Zealand approved data sheet March 2020. 2. Pollack CV, et al. N Engl J Med 2017;377:431-41. 3. Connolly SJ, et al. N Engl J Med 2009;361:1139-51. 4. Larsen TB, et al. BMJ 2016;353:113189 (and supplementary material). 5. Nielsen PB, et al. BMJ 2017;353:j510. 6. Roger KC, et al. Cardiol Rev 2016; 24(6):310-15. 7. Praxbind New Zealand approved data sheet Sept 2020.

PRADAXA® (dabigatran etexilate) 110 mg and 150 mg capsules ABRIDGED PRESCRIBING INFORMATION. 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> INDICATION: Prevention of stroke, systemic embolism and reduction of vascular mortality in patients with nonvalvular 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. DOSAGE: 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. 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 ketoconazole. 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, sulfonpyrazone, 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, skin haemorrhage, urogenital haemorrhage, haematuria. 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. 27 November 2020

PRAXBIND® (idarucizumab, rch) 50 mg/mL solution for injection/infusion. ABRIDGED PRESCRIBING INFORMATION 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. DOSAGE: 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 2014.

PC-NZ-100139, TAPS MR781



For more information, please go to www.medsafe.govt.nz

Long-term clinical outcomes following revascularization in high-risk coronary anatomy patients with stable ischemic heart disease

Authors: Baine KR et al.

Summary: This Canadian study analysed data from a large angiographic disease-based registry to examine the impact of revascularisation on long-term outcomes in patients with high-risk coronary anatomy and stable ischaemic heart disease (SIHD). 9016 patients with SIHD with high-risk coronary anatomy (3 vessel disease with ≥70% stenosis in all 3 epicardial vessels, or left main disease ≥50% stenosis) were included. 5487 (61.0%) patients received revascularisation with either CABG or PCI, while 3529 (39.0%) patients were managed conservatively. During a median follow-up of 6.2 years, the primary composite end-point of all-cause death or MI occurred less often in patients receiving coronary revascularisation than in patients managed conservatively (HR 0.62, 95% CI 0.58–0.66; p<0.001). No significant differences in risk reduction were seen between PCI and CABG.

Comment: Stenting in SIHD; the ultimate controversy in cardiology. Trial outcomes very much depend on definitions, as well as inclusion and exclusion bias. Canadian registry data of 9016 patients managed with PCI, CABG or conservatively; median follow up 6.2 years. Mortality and MI had a significantly lower risk in the intervention arms (HR 0.62, p<0.001); outcomes were similar for PCI and CABG. Benefits were evident early on and sustained. Included were patients with high-risk coronary anatomy, the word 'FFR' does not feature in the paper. Encouraging data for revascularisation, just mind the definitions.

Reference: *J Am Heart Assoc* 2021;10:e018104
[Abstract](#)



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](#).



ANZET21

15th Annual
Australia & New Zealand
Endovascular Therapies Meeting

Friday 6 August – Sunday 8 August 2021
Adelaide Convention Centre

www.anzet.com.au

Praluent®
alirocumab

THEY SURVIVED A CV EVENT¹
NOW PROTECT THEM WITH PRALUENT^{1,2*}

*Praluent significantly reduced the relative risk of the primary MACE endpoint vs. placebo (HR 0.85, 95% CI 0.78-0.93) P=0.0003.^{1,2} †Praluent is indicated to reduce the risk of CV events (myocardial infarction, stroke, unstable angina requiring hospitalisation) in adults with established cardiovascular disease, in combination with optimally dosed statins and/or other lipid lowering therapies.¹

Had an MI 6 months ago and not at LDL-C goal

Praluent® is an unfunded medicine - a prescription charge will apply.

STUDY DESIGN: ODYSSEY OUTCOMES trial involved 18,924 patients with recent ACS (1-12 months prior) and elevated atherogenic lipoproteins (92.1% qualified on the basis of LDL-C \geq 1.8 mmol/L) despite receiving statin therapy at high-intensity dose or at the maximum tolerated dose. Patients were randomly assigned to receive alicumab (n=9462) or placebo (n=9462) every 2 weeks. The median duration of follow-up was 2.8 years. The primary MACE endpoint was a composite of CHD death, nonfatal myocardial infarction, fatal and nonfatal ischaemic stroke, or unstable angina requiring hospitalisation and occurred in 903 patients (9.5%) on alicumab and 1052 (11.1%) on placebo. The incidence of adverse events was similar in the two groups, with the exception of local injection-site reactions (3.8% in the alicumab group vs. 2.1% in the placebo group, P<0.001).²

CLICK HERE TO REVIEW FULL DATA SHEET BEFORE PRESCRIBING OR CONTACT SANOFI MEDICAL INFORMATION ON 0800 283 684 FOR FURTHER INFORMATION.

References: 1. Praluent Approved Data Sheet, February 2020. 2. Schwartz GG et al. N Eng J Med 2018; 379:2097-107. Abbreviations: CV events = cardiovascular events; ACS = acute coronary syndrome; CHD = coronary heart disease; CI = confidence interval. HR = hazard ratio; LDL-C = low density lipoprotein cholesterol; MACE = major adverse cardiovascular event; MI = myocardial infarction.

PRALUENT® (alirocumab (rch)) Abridged Data Sheet

INDICATIONS Primary hypercholesterolaemia: In adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet: -in combination with a statin, or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with maximum tolerated dose of a statin or, -alone or in combination with other lipid lowering therapies in patients who are statin intolerant or for whom a statin is contraindicated. **Prevention of cardiovascular events:** to reduce the risk of cardiovascular events (myocardial infarction, stroke, unstable angina requiring hospitalisation) in adults with established cardiovascular disease, in combination with optimally dosed statins and/or lipid-lowering therapies (see full Data Sheet) **DOSE AND ADMINISTRATION** Usual starting dose is 75 mg subcutaneously once every 2 weeks. May increase to 150 mg every 2 weeks if inadequate LDL-C response. Patients requiring larger LDL-C reduction (>60%) may be started on 150 mg subcutaneously once every 2 weeks, or 300 mg once every 4 weeks (monthly), administered subcutaneously. Measure lipid levels after 4 weeks of initiating/titrating Praluent, to assess response and adjust dose if needed. Patients should be treated with the lowest dose necessary to achieve the desired LDL-C reduction. If additional LDL-C reduction is needed in patients treated with 75 mg once every 2 weeks or 300 mg once every 4 weeks (monthly), the dosage may be adjusted to the maximum dosage of 150 mg once every 2 weeks. Allow to warm at room temperature for 30-40 min before injecting; do not warm in any other way. Inject into thigh or abdomen or upper arm that is not tender, bruised, red or hard (rotate site). See full DS. **CONTRAINDICATIONS** Hypersensitivity to the active substance or to any of the excipients. **PRECAUTIONS** Allergic reactions, immunogenicity, very low LDL-C levels (long-term effects unknown), pregnancy, lactation, children (<18 years). Severe hepatic (Child-Pugh C) or severe renal impairment (eGFR < 30 mL/min/1.73 m²) not studied. **INTERACTIONS** Not anticipated. **ADVERSE EFFECTS** Common adverse reactions: injection site reactions, pruritus, upper respiratory tract signs and symptoms. Others, see full DS. **MEDICINE CLASSIFICATION** Prescription Medicine **SPONSOR** sanofi-aventis new zealand limited, Level 8, 56 Cawley Street, Ellerslie, Auckland. **Before prescribing Praluent, please refer to the data sheet (available at www.medsafe.govt.nz) for information on dosage, contraindications, precautions, interactions and adverse effects. Date of Preparation: 25 March 2020. Based on Full DS, with most recent amendment on 27 February 2020. sanofi-aventis new zealand limited, Level 8, 56 Cawley Street, Ellerslie, Auckland. TAPS PP7286 MAT-NZ-2100029. Date of preparation February 2021.**



For more information, please go to www.medsafe.govt.nz

Effect of implantable vs prolonged external electrocardiographic monitoring on atrial fibrillation detection in patients with ischemic stroke

Authors: Buck BH et al.

Summary: The PER DIEM trial investigated whether 12 months of monitoring with an implantable loop recorder detects more occurrences of AF than 30 days of conventional external loop recorder monitoring in patients with a recent ischaemic stroke. 300 patients without known AF who had an ischaemic stroke within the previous 6 months were randomised to electrocardiographic monitoring with either an implantable loop recorder (12 months) or an external loop recorder (30 days). The primary outcome (definite or highly probable AF) was observed in 15.3% of patients in the implantable loop recorder group and 4.7% of patients in the external loop recorder group (risk ratio 3.29, 95% CI 1.45-7.42; p=0.003).

Comment: How to best screen for AF following an ischaemic stroke? This study compared a 30-day external loop recorder to a 1-year implantable recorder. Definite AF was defined for AF episodes >2 min. Somewhat unsurprisingly the implantable device detected AF in 15.3%, compared to 4.7% in the external device group (HR 3.3, p=0.003); device results were not different when comparing the first 30 days only. Longer monitoring leads to more AF detection, is 24-48h enough then? Does longer monitoring improve outcome? Either way we might have to look harder for AF.

Reference: JAMA 2021;325(21):2160-8

[Abstract](#)

Strain-guided management of potentially cardiotoxic cancer therapy

Authors: Thavendiranathan P et al., for the SUCCOUR Investigators

Summary: The SUCCOUR trial investigated whether global longitudinal strain (GLS)-guided cardioprotective therapy (CPT) prevents reduction in LVEF and development of cancer therapy-related cardiac dysfunction (CTRCD) in high-risk patients receiving potentially cardiotoxic chemotherapy. 331 anthracycline-treated patients with an additional risk factor for HF were randomised to receive CPT guided by either \geq 12% relative reduction in GLS or >10% absolute reduction of LVEF. Patients were followed for LVEF and CTRCD over 1 year. Change in LVEF did not differ significantly between groups. However, there was significantly greater use of CPT in the GLS-guided group, and fewer patients in the GLS-guided group developed CTRCD (5.8% vs 13.7%; p=0.02).

Comment: Cardiotoxic cancer therapy requires early detection and precise measurement of LV function. GLS measures LV function by quantifying LV wall deformation. In this prospective, controlled trial, anthracycline-treated patients were randomised to GLS- or LVEF-guided initiation of CPT (usually an ACE inhibitor or beta-blocker). The results are a bit difficult to interpret, but essentially GLS was felt to be more sensitive to detect LV dysfunction; 13.7% in the LVEF group developed cardiotoxicity compared to 5.8% in the GLS group. The use of GLS is recommended, but the threshold for CPT is still debated.

Reference: J Am Coll Cardiol 2021;77(4):392-401

[Abstract](#)

CLICK HERE
to read previous issues of Cardiology Research Review

CONGRATULATIONS TO
Ruth Spearing (Haematologist at CDHB)
and **Peter Shapkov** (Breast Surgeon at Waitemata DHB)
who were winners in our prize draw by taking part in our recent Research Review Annual Subscriber Update.

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.**