

A SELECTION OF TEN READINGS ON TOPICS RELATED TO "CHRONIC DISEASE MANAGEMENT 2021 UPDATE"

Some available as free full text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – GUIDANCE ON AMBULATORY BLOOD PRESSURE MONITORING

Kario K(1), Hoshida S(1), Chia YC(2)(3), Buranakitjaroen P(4), Siddique S(5), Shin J(6), Turana Y(7), Park S(8), Tsoi K(9), Chen CH(10)(11)(12), Cheng HM(10)(11)(12)(13), Fujiwara T(1), Li Y(14), Huynh VM(15), Nagai M(16), Naites J(17), Sison J(18), Soenarta AA(19), Sogunuru GP(20)(21), Sukonthasarn A(22), Tay JC(23), Teo BW(24), Verma N(25), Wang TD(26)(27)(28), Zhang Y(29), Wang JG(30). Guidance on ambulatory blood pressure monitoring: A statement from the HOPE Asia Network. J Clin Hypertens (Greenwich). 2020 Dec 14. PMID: 33319412.

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ABSTRACT

Hypertension is an important public health issue due to its association with a number of serious diseases, including cardiovascular disease and stroke. The importance of evaluating hypertension taking into account different blood pressure (BP) profiles and BP variability (BPV) is increasingly being recognised, and is particularly relevant in Asian populations given the specific features of hypertension in the region (including greater salt sensitivity and a high rate of nocturnal hypertension).

Ambulatory BP monitoring (ABPM) is the gold standard for diagnosing hypertension and assessing 24-hour BP and provides data on several important parameters that cannot be obtained using any other form of BP measurement. In addition, ABPM parameters provide better information on cardio- and cerebrovascular risk than office BP. ABPM should be used in all patients with elevated BP, particularly those with unstable office or home BP, or who are suspected to have white-coat or masked hypertension. ABPM is also an important part of hypertension diagnosis and monitoring in high-risk patients.

ABPM needs to be performed using a validated device and good practice techniques, and has a role both in hypertension diagnosis and in monitoring the response to antihypertensive therapy to ensure strict BP control throughout the 24-hour period. Use of ABPM in clinical practice may be limited by cost and accessibility, and practical education of physicians and patients is essential.

The ABPM evidence and practice points in this document are based on the Hypertension Cardiovascular Outcome Prevention and Evidence (HOPE) Asia Network expert panel consensus recommendations for ABPM in Asia.

READING 2 – 2020 HOME BLOOD PRESSURE MONITORING

Lin HJ(1), Wang TD(2), Yu-Chih Chen M(3), Hsu CY(4)(5)(6), Wang KL(7), Huang CC(8)(9)(10), Hsieh MJ(11), Chiu YW(12)(13), Chiang LT(14)(15), Chuang WP(16), Hsu PF(17), Wu CH(18), Hung CS(1), Chen KC(19)(20)(21), Wu CC(22)(23)(24), Wang YC(25)(26)(27), Chou PC(28), Yap HY(29), Cheng HM(30)(31)(32)(33). 2020 Consensus Statement of the Taiwan Hypertension Society and the Taiwan Society of Cardiology on Home Blood Pressure Monitoring for the Management of Arterial Hypertension. *Acta Cardiol Sin.* 2020 Nov;36(6):537-561. PMID:33235411.

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ABSTRACT

To facilitate the applications of home blood pressure (HBP) monitoring in clinical settings, the Taiwan Hypertension Society and the Taiwan Society of Cardiology jointly put forward the Consensus Statement on HBP monitoring according

to up-to-date scientific evidence by convening a series of expert meetings and compiling opinions from the members of these two societies.

In this Consensus Statement as well as recent international guidelines for management of arterial hypertension, HBP monitoring has been implemented in diagnostic confirmation of hypertension, identification of hypertension phenotypes, guidance of anti-hypertensive treatment, and detection of hypotensive events. HBP should be obtained by repetitive measurements based on the "722" principle, which is referred to duplicate blood pressure readings taken per occasion, twice daily, over seven consecutive days.

The "722" principle of HBP monitoring should be applied in clinical settings, including confirmation of hypertension diagnosis, two weeks after adjustment of antihypertensive medications, and at least every three months in well-controlled hypertensive patients. A good reproducibility of HBP monitoring could be achieved by individuals carefully following the instructions before and during HBP measurement, by using validated BP devices with an upper arm cuff.

Corresponding to office BP thresholds of 140/90 and 130/80 mmHg, the thresholds (or targets) of HBP are 135/85 and 130/80 mmHg, respectively.

HBP-based hypertension management strategies including bedtime dosing (for uncontrolled morning hypertension), shifting to drugs with longer-acting antihypertensive effect (for uncontrolled evening hypertension), and adding another antihypertensive drug (for uncontrolled morning and evening hypertension) should be considered.

Only with the support from medical caregivers, paramedical team, or tele-monitoring, HBP monitoring could reliably improve the control of hypertension.

READING 3 – ALDOSTERONE ANTAGONISTS IN ADDITION TO RENIN ANGIOTENSIN SYSTEM ANTAGONISTS

Chung EY(1), Ruospo M(2)(3), Natale P(2)(3), Bolignano D(4), Navaneethan SD(5), Palmer SC(6), Strippoli GF(2)(3)(7). Aldosterone antagonists in addition to renin angiotensin system antagonists for preventing the progression of chronic kidney disease. Cochrane Database Syst Rev. 2020 Oct 27;10:CD007004. PMID:33107592.

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ABSTRACT

BACKGROUND: Treatment with angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) is used to reduce proteinuria and retard the progression of chronic kidney disease (CKD). However, resolution of proteinuria may be incomplete with these therapies and the addition of an aldosterone antagonist may be added to further prevent progression of CKD. This is an update of a Cochrane review first published in 2009 and updated in 2014.

OBJECTIVES: To evaluate the effects of aldosterone antagonists (selective (eplerenone), non-selective (spironolactone or canrenone), or non-steroidal mineralocorticoid antagonists (finerenone)) in adults who have CKD with proteinuria (nephrotic and non-nephrotic range) on: patient-centred endpoints including kidney failure (previously known as end-stage kidney disease (ESKD)), major cardiovascular events, and death (any cause); kidney function (proteinuria, estimated glomerular filtration rate (eGFR), and doubling of serum creatinine); blood pressure; and adverse events (including hyperkalaemia, acute kidney injury, and gynaecomastia).

SEARCH METHODS: We searched the Cochrane Kidney and Transplant Register of Studies up to 13 January 2020 through contact with the Information Specialist using search terms relevant to this review. Studies in the Register are identified through searches of CENTRAL, MEDLINE, and EMBASE, conference proceedings, the International Clinical Trials Register (ICTRP) Search Portal, and ClinicalTrials.gov.

SELECTION CRITERIA: We included randomised controlled trials (RCTs) and quasi-RCTs that compared aldosterone antagonists in combination with ACEi or ARB (or both) to other anti-hypertensive strategies or placebo in participants with proteinuric CKD.

DATA COLLECTION AND ANALYSIS: Two authors independently assessed study quality and extracted data. Data were summarised using random effects meta-analysis. We expressed summary treatment estimates as a risk ratio (RR) for dichotomous outcomes and mean difference (MD) for continuous outcomes, or standardised mean difference (SMD) when different scales were used together with their 95 percent confidence interval (CI). Risk of bias were assessed using the Cochrane tool. Evidence certainty was evaluated using GRADE.

MAIN RESULTS: Forty-four studies (5745 participants) were included. Risk of bias in the evaluated methodological domains were unclear or high risk in most studies. Adequate random sequence generation was present in 12 studies, allocation concealment in five studies, blinding of participant and investigators in 18 studies, blinding of outcome assessment in 15 studies, and complete outcome reporting in 24 studies. All studies comparing aldosterone antagonists to placebo or standard care were used in addition to an ACEi or ARB (or both).

None of the studies were powered to detect differences in patient-level outcomes including kidney failure, major cardiovascular events or death. Aldosterone antagonists had uncertain effects on kidney failure (2 studies, 84 participants: RR 3.00, 95 percent CI 0.33 to 27.65, $I^2 = 0$ percent; very low certainty evidence), death (3 studies, 421 participants: RR 0.58, 95 percent CI 0.10 to 3.50, $I^2 = 0$ percent; low certainty evidence), and cardiovascular events (3 studies, 1067 participants: RR 0.95, 95 percent CI 0.26 to 3.56; $I^2 = 42$ percent; low certainty evidence) compared to placebo or standard care. Aldosterone antagonists may reduce protein excretion (14 studies, 1193 participants: SMD -0.51, 95 percent CI -0.82 to -0.20, $I^2 = 82$ percent; very low certainty evidence), eGFR (13 studies, 1165 participants, MD -3.00 mL/min/1.73 m², 95 percent CI -5.51 to -0.49, $I^2 = 0$ percent, low certainty evidence) and systolic blood pressure (14 studies, 911 participants: MD -4.98 mmHg, 95 percent CI -8.22 to -1.75, $I^2 = 87$ percent; very low certainty evidence) compared to placebo or standard care. Aldosterone antagonists probably increase the risk of hyperkalaemia (17 studies, 3001 participants: RR 2.17, 95 percent CI 1.47 to 3.22, $I^2 = 0$ percent; moderate certainty evidence), acute kidney injury (5 studies, 1446 participants: RR 2.04, 95 percent CI 1.05 to 3.97, $I^2 = 0$ percent; moderate certainty evidence), and gynaecomastia (4 studies, 281 participants: RR 5.14, 95 percent CI 1.14 to 23.23, $I^2 = 0$ percent; moderate certainty evidence) compared to placebo or standard care. Non-selective aldosterone antagonists plus ACEi or ARB had uncertain effects on protein excretion (2 studies, 139 participants: SMD -1.59, 95 percent CI -3.80 to 0.62, $I^2 = 93$ percent; very low certainty evidence) but may increase serum potassium (2 studies, 121 participants: MD 0.31 mEq/L, 95 percent CI 0.17 to 0.45, $I^2 = 0$ percent; low certainty evidence) compared to diuretics plus ACEi or ARB. Selective aldosterone antagonists may increase the risk of hyperkalaemia (2 studies, 500 participants: RR 1.62, 95 percent CI 0.66 to 3.95, $I^2 = 0$ percent; low certainty evidence) compared ACEi or ARB (or both). There were insufficient studies to perform meta-analyses for the comparison between non-selective aldosterone antagonists and calcium channel blockers, selective aldosterone antagonists plus ACEi or ARB (or both) and nitrate plus ACEi or ARB (or both), and non-steroidal mineralocorticoid antagonists and selective aldosterone antagonists.

AUTHORS' CONCLUSIONS: The effects of aldosterone antagonists when added to ACEi or ARB (or both) on the risks of death, major cardiovascular events, and kidney failure in people with proteinuric CKD are uncertain.

Aldosterone antagonists may reduce proteinuria, eGFR, and systolic blood pressure in adults who have mild to moderate CKD but may increase the risk of hyperkalaemia, acute kidney injury and gynaecomastia when added to ACEi and/or ARB.

READING 4 – ALIKIREN MONOTHERAPY LOWERED BP SAFELY

Zhao Q(1), Shen J(2)(3), Lu J(1), Jiang Q(1), Wang Y(1). Clinical efficacy, safety and tolerability of Aliskiren Monotherapy (AM): an umbrella review of systematic reviews. BMC Cardiovasc Disord. 2020 Apr 17;20(1):179. PMID: 32303191.

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ABSTRACT

BACKGROUND: Aliskiren is a newly developed drug. Its role in lowering BP has been recognised. However, the role of aliskiren in treating heart and renal diseases are still controversial.

OBJECTIVE: To evaluate the existing evidence about clinical efficacy, safety and tolerability of aliskiren monotherapy (AM).

METHODS: An umbrella review of systematic reviews of interventional studies. We searched PubMed, Embase and Cochrane Library up to June 2019. Two reviewers applied inclusion criteria to the select potential articles independently. The extract and analyse of accessible data were did by two reviewers independently too. Discrepancies were resolved with discussion or the arbitration of the third author.

RESULTS: Eventually, our review identified 14 eligible studies. Results showed that for essential hypertension patients, aliskiren showed a great superiority over placebo in BP reduction, BP response rate and BP control rate.

Aliskiren and placebo, ARBs or ACEIs showed no difference in the number or extent of adverse events.

For heart failure patients, AM did not reduce BNP levels (SMD -0.08, -0.31 to 0.15) or mortality rate (RR 0.76, 0.32 to 1.80), but it decreased NT-proBNP (SMD -0.12, -0.21 to -0.03) and PRA levels (SMD 0.52, 0.30 to 0.75), increased PRC levels (SMD -0.66, -0.8 to -0.44).

For patients who suffered from hypertension and diabetes and/or nephropathy or albuminuria at the same time, aliskiren produced no significant effects (RR 0.97, 0.81 to 1.16).

CONCLUSION: We found solid evidence to support the benefits of aliskiren in the treatment of essential hypertension, aliskiren can produce significant effects in lowering BP and reliable safety. However, the effects of aliskiren in cardiovascular and renal outcomes were insignificant.

TRIAL REGISTRATION: Study has been registered in PROSPERO (CRD42019142141).

READING 5 – SGLT2 REDUCES PROTEINURIA AND ARE NEPHROPROTECTIVE

Piperidou A(1), Loutradis C(1), Sarafidis P(2). SGLT-2 inhibitors and nephroprotection: current evidence and future perspectives. J Hum Hypertens. 2021 Jan;35(1):12-25. PMID:32774748.

URL: doi: 10.1038/s41371-020-00393-4 (Free full text).

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ABSTRACT

Chronic kidney disease (CKD) is a major public health issue and an independent risk factor for cardiovascular and all-cause mortality. Diabetic kidney disease develops in 30-50 percent of diabetic patients and it is the leading cause of end-stage renal disease in the Western world. Strict blood pressure control and renin-angiotensin system (RAS) blocker use are the cornerstones of CKD treatment; however, their application in everyday clinical practice is not always ideal and in many patients CKD progression still occurs.

Accumulated evidence in the past few years clearly suggests that sodium-glucose co-transporter-2 (SGLT-2) inhibitors present potent nephroprotective properties.

In clinical trials in patients with type 2 diabetes mellitus, these agents were shown to reduce albuminuria and proteinuria by 30-50 percent and the incidence of composite hard renal outcomes by 40-50 percent. Furthermore, their mechanism of action appears rather solid, as they interfere with the major mechanism of proteinuric CKD progression, i.e., glomerular hypertension and hyperfiltration.

The present review summarises the current evidence from human trials on the effects of SGLT-2 inhibitors on nephroprotection and discusses their position in everyday clinical practice.

READING 6 – IMPROVEMENT OF NUTRITIONAL INTAKE FOR LOW-INCOME URBAN DWELLERS WITH HYPERTENSION

Azizan NA(1)(2), Majid HA(1)(3)(4), Nahar Mohamed A(5), Su TT(6). Improvement of nutritional intake for the low-income urban dwellers with hypertension in Malaysia. SAGE Open Med. 2020 Sep 20;8:2050312120960563. PMID:33014371.

URL: doi: 10.1177/2050312120960563 (Free full text).

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ABSTRACT

OBJECTIVE: To ascertain the effect of dietary practice modification and a peer-support home blood pressure monitoring program on the nutritional intake (macronutrients and micronutrients), blood pressure and biochemical profiles of hypertension patients in a low-income community setting.

METHODS: This is a pre- and post-measurement intervention study conducted in low-income community housing projects in Kuala Lumpur, Malaysia. A total of 90 participants aged 18 years and above with hypertension received intervention. The participants were divided into small groups and received instructions on the use of home blood pressure measurement. They also attended a series of talks on dietary intake modification and exercise demonstration for the first six months (active phase). In another six months (maintenance phase), they received only pamphlet and SMS reminders. Their anthropometry, blood pressure, dietary, and biochemical parameter changes were measured at baseline, six months, and 12 months of intervention.

RESULTS: Macronutrients and micronutrients showed a significant improvement at the end of 12-month dietary intervention. The energy, carbohydrate, protein, total fat, sodium, and potassium are showing significant reduction from baseline to end of the 12-month intervention. There is no significant reduction in blood pressure. Fasting blood glucose, renal sodium, triglyceride, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol showed a significant improvement, after controlling for age and reported physical activity.

CONCLUSION: The intervention improved the nutritional intake and biochemical profiles of the low-income urban population with hypertension. This promising result should be replicated in a larger scale study.

READING 7 – GOUT PREVALENCE, INCIDENCE, TREATMENT PATTERNS AND RISK FACTORS

Dehlin M(1), Jacobsson L(1), Roddy E(2)(3). Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. Nat Rev Rheumatol. 2020 Jul;16(7):380-390. PMID:32541923.

URL:doi: 10.1038/s41584-020-0441-1 (Payment required).

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ABSTRACT

Gout is the most common inflammatory arthritis and occurs when hyperuricaemia, sustained elevation of serum urate levels resulting in supersaturation of body tissues with urate, leads to the formation and deposition of monosodium urate crystals in and around the joints.

Recent reports of the prevalence and incidence of gout vary widely according to the population studied and methods employed but range from a prevalence of <1 percent to 6.8 percent and an incidence of 0.58-2.89 per 1,000 person-years.

Gout is more prevalent in men than in women, with increasing age, and in some ethnic groups. Despite rising prevalence and incidence, suboptimal management of gout continues in many countries.

Typically, only a third to half of patients with gout receive urate-lowering therapy, which is a definitive, curative treatment, and fewer than a half of patients adhere to treatment.

Many gout risk factors exist, including obesity, dietary factors and comorbid conditions. As well as a firmly established increased risk of cardiovascular disease and chronic kidney disease in those with gout, novel associations of gout with other comorbidities have been reported, including erectile dysfunction, atrial fibrillation, obstructive sleep apnoea, osteoporosis and venous thromboembolism.

Discrete patterns of comorbidity clustering in individuals with gout have been described. Increasing prevalence and incidence of obesity and comorbidities are likely to contribute substantially to the rising burden of gout.

READING 8 – NON-ALCOHOLIC FATTY LIVER DISEASE AND CARDIOVASCULAR RISKS

Miptah HN(1), Ramli AS(2)(3), Mohamad M(4), Hashim H(5), Tharek Z(1). Non-alcoholic fatty liver disease (NAFLD) and the cardiovascular disease (CVD) risk categories in primary care: is there an association? BMC Fam Pract. 2020 Nov 20;21(1):238. PMID:33218301.

URL: doi: 10.1186/s12875-020-01306-7 (Free full text).

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ABSTRACT

BACKGROUND: Non-alcoholic fatty liver disease (NAFLD) is an emerging novel cardiovascular disease (CVD) risk factor. Its prevalence is increasing globally. However, there is paucity in the evidence showing the association between NAFLD and CVD risk in primary care setting. Therefore, the objectives of this study were to determine the prevalence and factors associated with NAFLD among patients with ≥ 1 risk factor for NAFLD or CVD attending primary care clinics.

METHODOLOGY: A cross sectional study was conducted in two clinics at a university primary care centre. Patients aged ≥ 18 years with ≥ 1 risk factor for NAFLD or CVD were recruited. Participants with history of established liver disease or chronic alcohol use were excluded. Socio-demographics, clinical related data, anthropometric measurements and blood investigation results were recorded in a proforma. Diagnosis of NAFLD was made using abdominal ultrasound. The 10-year CVD risk was calculated using the general Framingham Risk Score (FRS). Multiple logistic regression (MLogR) was performed to identify independent factors associated with NAFLD.

RESULTS: A total of 263 participants were recruited. The mean age was 52.3 ± 14.7 years old. Male and female were equally distributed. Majority of the participants were Malays (79.8 percent). The overall prevalence of NAFLD was 54.4 percent (95 percent CI 48,60 percent). Participants in the high FRS category have higher prevalence of NAFLD (65.5

percent), followed by those in the moderate category (55.4 percent) and the low category (46.3 percent), $p=0.025$. From MLogR, independent factors associated with NAFLD were being employed (OR=2.44, 95 percent CI 1.26,4.70, $p=0.008$), obesity with BMI ≥ 27.5 (OR=2.89, 95 percent CI 1.21,6.91, $p=0.017$), elevated fasting glucose ≥ 5.6 mmol/L (OR=2.79, 95 percent CI 1.44,5.43, $p=0.002$), ALT ≥ 34 U/L (OR=3.70, 95 percent CI 1.85,7.44, $p<0.001$) and high FRS category (OR=2.82, 95 percent CI 1.28,6.23, $p=0.010$).

CONCLUSION: NAFLD is highly prevalent among patients with ≥ 1 risk factor for NAFLD or CVD in these primary care clinics. Patients who were obese, have elevated fasting glucose, elevated ALT and in the high FRS category were more likely to have NAFLD. This study underscores the importance of targeted screening for NAFLD in those with risk factors in primary care. Aggressive intervention must be executed in those with NAFLD in order to reduce CVD complications and risk of progression.

READING 9 – SGLT2 PREVENTS CARDIOVASCULAR DISEASE

Kario K(1), Ferdinand KC(2), O’Keefe JH(3). Control of 24-hour blood pressure with SGLT2 inhibitors to prevent cardiovascular disease. *Prog Cardiovasc Dis.* 2020 May-Jun;63(3):249-262. PMID:32275926.

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ABSTRACT

The presence of hypertension (HTN) in patients with diabetes mellitus (DM) further worsens cardiovascular disease (CVD) prognosis. In addition, masked HTN and abnormal circadian blood pressure (BP) variability are common among patients with DM.

Clinical trial data show that sodium-glucose cotransporter 2 inhibitors (SGLT2i) improve CVD prognosis and prevent progression of renal dysfunction in high-risk patients with type 2 DM (T2DM).

Consistent reductions in 24-hour, daytime and nocturnal BP have been documented during treatment with SGLT2i in patients with DM and HTN, and these reductions are of a magnitude that is likely to be clinically significant. SGLT2i agents also appear to have beneficial effects on morning, evening and nocturnal home BP. Greater reductions in BP during treatment with SGLT2i have been reported in patient subgroups with higher body mass index, and in those with higher baseline BP.

Other documented beneficial effects of SGLT2i include reductions in arterial stiffness and the potential to decrease the apnoea-hypopnea index in patients with DM and obstructive sleep apnoea.

Recent guidelines highlight the important role of SGLT2i as part of the pharmacological management of patients with DM and HTN, and recommend consideration of SGLT2i early in the clinical course to reduce all-cause and CVD mortality in patients with T2DM and CVD.

Overall, available data support a role for SGLT2i as effective BP-lowering agents in patients with T2DM and poorly controlled HTN, irrespective of baseline glucose control status. Sustained improvements in 24-hour BP and the 24-hour BP profile are likely to contribute to the CVD benefits of SGLT2i treatment.

READING 10 – USE OF GLP1 RECEPTOR AGONISTS IN PATIENTS WITH T2DM AND CARDIOVASCULAR DISEASE

Honigberg MC(1), Chang LS(2), McGuire DK(3), Plutzky J(4), Aroda VR(2), Vaduganathan M(4). Use of Glucagon-Like Peptide-1 Receptor Agonists in Patients With Type 2 Diabetes and Cardiovascular Disease: A Review. JAMA Cardiol. 2020 Jun 7;10.1001/jamacardio.2020.1966. PMID:32584928.

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ABSTRACT

IMPORTANCE: Recent randomised clinical trials have demonstrated that glucagon-like peptide-1 receptor agonists (GLP-1RAs) reduce cardiovascular events in at-risk individuals with type 2 diabetes. Despite these findings, GLP-1RAs are underused in eligible patients, particularly by cardiologists.

OBSERVATIONS: To date, randomised clinical trials of albiglutide, dulaglutide, liraglutide, and injectable semaglutide have reported favourable cardiovascular outcomes. Most recently approved for clinical use, oral semaglutide has a favourable safety profile and is currently undergoing regulatory evaluation and further study for cardiovascular outcomes. Professional society guidelines now recommend GLP-1RA therapy for cardiovascular risk mitigation in patients with type 2 diabetes and established atherosclerotic cardiovascular disease (ASCVD) or multiple ASCVD risk factors, independent of glucose control or background antihyperglycemic therapy (other diabetes medications being used). Additional conditions suitable for GLP-1RA therapy include obesity and advanced chronic kidney disease (estimated glomerular filtration rate <30 mL/min/1.73 m²), for which cardiovascular risk-reducing options are limited. Out-of-pocket costs and secondary advantages (e.g., weight loss) may inform shared decision-making discussions regarding potential therapies. GLP-1RA therapy has a favourable safety profile. Its most common adverse effect is gastrointestinal upset, which typically wanes during the early weeks of therapy and may be mitigated by starting at the lowest dose and escalating as tolerated. Depending on baseline glycaemic control, sulfonylureas and insulin may need to be decreased before GLP-1RA initiation; without concurrent use of insulin or sulfonylureas, GLP-1RAs are not associated with hypoglycaemia. Multidisciplinary follow-up and collaborative care with primary care physicians and/or endocrinologists are important.

CONCLUSIONS AND RELEVANCE: Findings from this review suggest that GLP-1RAs are safe, are well tolerated, and improve cardiovascular outcomes, largely independent of their antihyperglycemic properties, but they remain underused by cardiologists. This review provides a practical resource for cardiologists for initiating GLP-1RAs and managing the therapy in patients with type 2 diabetes and established ASCVD or high risk for ASCVD.