Diabetes Ther (2025) 16:1155–1176
https://doi.org/10.1007/s13300-025-01738-3

REVIEW

Advancing Cardiovascular, Kidney, and Metabolic Medicine: A Narrative Review of Insights and Innovations for the Future

Kevin Fernando · Derek Connolly · Eimear Darcy · Marc Evans · William Hinchliffe · Patrick Holmes · W. David Strain

Received: February 10, 2025 / Accepted: April 1, 2025 / Published online: April 24, 2025

ABSTRACT

Cardiovascular, kidney and metabolic (CKM) conditions are interrelated, significantly contributing to morbidity, mortality and healthcare burden. Despite therapeutic advances, traditional disease-specific approaches often fail to address their complex interplay. Key therapeutic agents—including glucagon-like peptide-1 receptor agonists (GLP-1 RAs), dual GLP-1/glucose-dependent insulinotropic polypeptide RAs, sodium glucose co-transporter inhibitors and the nonsteroidal mineralocorticoid receptor antagonist (MRA) finerenone—offer multiorgan benefits. Emerging therapies, such as triple receptor agonists and second-generation MRAs, target new pathways further expanding treatment options for CKM conditions. A holistic CKM management approach must address and recognise that conditions such as metabolic dysfunction-associated steatotic liver disease, metabolic dysfunction-associated steatohepatitis, obstructive sleep apnoea and obesity are part of the CKM spectrum. Frailty assessment is also important alongside CKM conditions, warranting comprehensive geriatric assessment and deprescribing when appropriate. Multidisciplinary care—including lifestyle interventions, pathway redesign, pharmacological advances and novel technologies—is essential for improving outcomes. As the CKM landscape evolves, future strategies should prioritise early intervention, personalised treatment and addressing unmet needs in high-risk populations. This review advocates for an integrated CKM framework, exploring treatment strategies, emerging therapies and technological innovations. It also examines the role of artificial intelligence and digital health tools in risk stratification, early diagnosis and long-term condition management, alongside ethical and regulatory considerations.

K. Fernando (✉)
NHS Lothian, Edinburgh, UK
e-mail: kevinfernando@doctors.org.uk

D. Connolly
Birmingham City Hospital, Birmingham, UK

D. Connolly
Aston University, Birmingham, UK

E. Darcy
Grange Family Practice, Omagh, UK

M. Evans
University Hospital Llandough, Cardiff, UK

W. Hinchliffe
South Tyneside and Sunderland NHS Foundation Trust, Sunderland, UK

P. Holmes
St. George's Medical Practice, Darlington, UK

W. D. Strain
University of Exeter, Exeter, UK

Keywords: Cardiovascular-kidney-metabolic conditions; Heart failure; Chronic kidney disease; Diabetes; Artificial intelligence in healthcare; Personalised medicine; Integrated care; Obstructive sleep apnoea-hypopnoea syndrome; Metabolic dysfunction-associated steatohepatitis; Metabolic dysfunction-associated steatotic liver disease; Digital health

Key Summary Points
Cardiovascular, kidney and metabolic (CKM) as a spectrum of conditions: CKM conditions share overlapping pathophysiological mechanisms, contributing to a greater disease burden. This article highlights the need for an integrated, holistic approach to their management.
Broad-spectrum therapies: Therapies such as sodium-glucose cotransporter-2 inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, GLP-1/ glucose-dependent insulinotropic polypeptide and finerenone offer multi-organ benefits, marking a shift towards therapies that target the interconnected nature of CKM conditions.
Expanding the CKM framework: Conditions such as obstructive sleep apnoea-hypopnoea syndrome and metabolic dysfunction-associated steatotic liver disease/metabolic dysfunction-associated steatohepatitis are increasingly recognised as key components of the CKM spectrum, necessitating expanded treatment strategies.
Future directions: Technology, artificial intelligence-driven healthcare and novel therapies are shaping personalised treatment to optimise outcomes across the entire CKM spectrum.

INTRODUCTION

In recent years, the concept of cardiovascular-renal-metabolic (CVRM) conditions has evolved. The American Heart Association (AHA) introduced the term cardiovascular-kidney-metabolic (CKM) syndrome in 2023 to highlight the interconnected nature of cardiovascular, kidney and metabolic health [1]. More recently, a broader framework known as cardiovascular-renal-hepatic-metabolic (CRHM) syndrome has been proposed, incorporating the liver as a central player in the interconnected pathophysiology of these organ systems [2]. This extension reflects the growing recognition of the liver's role in the complex interplay among cardiovascular, kidney and metabolic diseases [2]. CKM conditions are interlinked, sharing common pathophysiological mechanisms and risk factors, including type 2 diabetes (T2D), obesity and ageing [1, 3, 4]. Their frequent coexistence amplifies health risks and poses burdens to individuals and healthcare systems [1, 3, 4]. Suboptimal CKM health contributes to premature mortality, multiorgan complications and escalating healthcare costs [1, 5, 6]. This review explores CKM complexities, current guidelines, emerging therapies and the role of technology, aiming to provide a future-oriented framework for improving outcomes in patients with CKM conditions.

To identify relevant literature, we conducted a non-systematic search using PubMed and Google, supplemented by key references provided by the authors. A PubMed search was performed between 13 and 15 January 2025, using a combination of various keywords related to CKM and artificial intelligence (AI) in healthcare. Additionally, we reviewed reference lists of identified articles to capture further relevant literature.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Epidemiology

In the UK, T2D and obesity prevalence are rising, reflecting global trends [7]. Over 4.9 million individuals in the UK live with diabetes, 90% with T2D, a figure expected to exceed 5.5 million by 2030 [7, 8]. Diabetic kidney disease (DKD) affects ~ 40% of patients with T2D, increasing the risk of end-stage renal disease

(ESRD) and cardiovascular events, with albuminuria as a key predictor [9]. The accompanying burdens of chronic kidney disease (CKD) and cardiovascular disease (CVD) compound these challenges, straining the National Health Service (NHS). CVD remains a leading cause of death, accounting for ~ 25% of mortality, while heart failure (HF) affects > 1 million people, with 200,000 new diagnoses annually [6, 10]. CKD stages 3–5 affect 3.2 million individuals in England, projected to reach 3.9 million by 2033 [11]. Additionally, obesity, a crucial driver of metabolic disorders, affects approximately 26% of adults in England, with an additional 38% classified as overweight, highlighting the growing burden of metabolic conditions [12]. According to global data, CKM conditions, including T2D, obesity, CKD and CVD, are leading causes of death, reducing life expectancy and contributing significantly to mortality and years of life lost [13, 14].

Economic Impact

The spectrum of CKM conditions presents a significant global and national health challenge, with substantial economic costs in the UK (Fig. 1). CVD costs the NHS ~ £12 billion annually, with a broader economic impact of ~ £28 billion per year [6]. Diabetes management alone costs ~ £10.7 billion in 2021/2022, with > 40% attributed to treating complications [15]. CKD accounts for £6.4 billion in NHS costs, projected to rise to £7.8 billion by 2033 because of the increasing prevalence of advanced CKD stages [11]. Overweight and obesity-related ill health cost the NHS ~ £6.1 billion in 2014/2015, with annual spending on obesity and diabetes treatment exceeding the combined expenditure on the police, fire service and judicial system [16]. Integrated care models addressing shared risk factors, such as the disease of obesity, could reduce costs by improving patient outcomes, thereby reducing hospital admissions and the need for advanced treatments such as dialysis for ESRD.

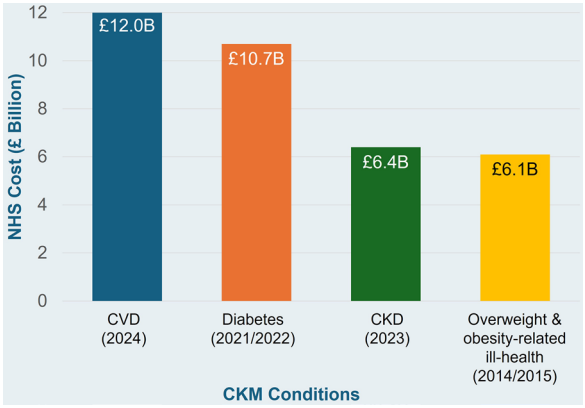

Fig. 1 Economic burden of CKM diseases in the UK. This bar chart visualises the annual financial impact of CVD, diabetes, CKD, and overweight and obesity-related ill-health on the NHS. CVD remains the costliest at ~ £12 billion per year, diabetes management accounted for ~ £10.7 billion, CKD accounted for £6.4 billion annually and overweight and obesity-related ill-health cost ~ £6.1 billion. *CKD* chronic kidney disease, *CKM* cardiovascular, kidney and metabolic, *CVD* cardiovascular disease, *NHS* National Health Service

Social Determinants of Health (SDOH)

Social determinants of health (SDOH) encompass economic, social, environmental and psychosocial factors that shape health outcomes [1]. They play a critical role in CKM health, influencing both disease risk and management strategies [1]. For instance, individuals in socioeconomically deprived areas, particularly those with lower incomes, often have limited access to healthy food and safe spaces for exercise, increasing their risk of CVD through intermediary conditions like diabetes, hypertension, obesity and dyslipidaemia [1, 17]. Low socioeconomic status is a leading cause of premature mortality, contributing to one in three early deaths in the UK [18]. Additionally, factors such as limited education, unemployment and inadequate housing can heighten stress and hinder disease management [1, 17].

To address these challenges, healthcare systems must integrate SDOH into prevention and treatment strategies [1]. Routine screening for unmet social needs within electronic health

records can help identify at-risk populations and tailor interventions [1]. In England, general practices are encouraged to adopt social prescribing, with general practitioner (GP) contracts funding 'social prescribing link workers' who connect patients to community support services such as food assistance or benefits advice [19, 20]. From 2023, integrated care systems are required to develop local plans for improving health and reducing inequalities [19]. However, inconsistent implementation, limited evaluation and the absence of a standardised framework undermine these interventions [19, 20]. Without uniform social risk assessments, it is uncertain whether current UK strategies effectively reach those most in need [20].

Advancing SDOH-focused CKM care will require leveraging technology, such as AI-driven tools, to identify social risk factors and prioritise high-risk patients. Additionally, structured screening tools like Protocol for Responding to and Assessing Patients' Assets, Risks (PRAPARE) could help systematically assess social needs and allocate resources more effectively [1, 18]. Adopting standardised, tailored screening—similar to the US approach, which is supported by federal policies—could improve treatment outcomes, reduce health disparities and promote health equity and person-centred CKM care in the UK [19, 20].

Pathophysiology

Although a detailed review of CKM physiology is beyond the scope of this paper, it is important to note that these conditions are interconnected through shared pathophysiological mechanisms, which primarily originate from both excess and dysfunctional adipose tissue [1, 3, 4, 21, 22]. Dysfunctional adipose tissue contributes to insulin resistance, a hallmark of metabolic disorders like T2D and obesity [1, 4, 21, 22]. This, in turn, leads to hyperglycaemia, which exacerbates inflammation, oxidative stress and the accumulation of advanced glycation end-products [1, 4, 21, 22]. These metabolic disturbances lead to endothelial dysfunction, vascular damage and myocardial fibrosis, ultimately increasing the risk of HF and CVD risk [1, 4, 21, 22].

The overactivity of the sympathetic nervous system (SNS) and the renin-angiotensin-aldosterone system (RAAS) further exacerbates disease progression. Hyperglycaemia activates local RAAS in the myocardium and kidneys, promoting vasoconstriction, fibrosis and impaired organ function, contributing to the onset of T2D [4, 22]. Additionally, SNS hyperactivation in HF worsens glucose homeostasis [4, 22]. RAAS and SNS overactivity also decrease the glomerular filtration rate (GFR), which in turn exacerbates fluid retention, increases vascular congestion and forms an interlocking cycle of organ dysfunction between the heart and kidneys [4, 22].

These metabolic disruptions also contribute to CKD by impairing renal microvascular function. The bidirectional HF-CKD relationship further complicates the pathology; reduced cardiac output in HF impairs renal perfusion, decreasing GFR and increasing fluid retention [1, 4, 21, 22]. Conversely, CKD exacerbates cardiovascular stress through hypertension and metabolic derangements, creating a feedback loop of cardiorenal deterioration [1, 4, 21, 22]. This interconnected nature of CKM conditions, where dysfunction in one organ system often exacerbates or drives dysfunction in another, emphasises the need for therapies targeting multiple systems to improve patient outcomes [1, 4, 21, 22].

CURRENT GUIDELINES AND EVIDENCE

The American Diabetes Association (ADA), European Society of Cardiology (ESC), European Association for the Study of Diabetes (EASD) and Kidney Disease: Improving Global Outcomes (KDIGO) have developed comprehensive guidelines for managing CKM conditions, with a focus on integrated care [23–25].

The 2023 ESC Guidelines for managing CVD in patients with diabetes recommend glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter-2 inhibitors (SGLT2is) as first-line therapies for diabetes with atherosclerotic cardiovascular disease (ASCVD), shown to significantly reduce cardiovascular risk independently of glucose control [24]. SGLT2is

are strongly recommended for all patients with diabetes and HF, irrespective of left ventricular ejection fraction [24]. For DKD, both SGLT2is and finerenone are recommended to reduce cardiovascular and kidney failure risk alongside standard treatments like RAAS inhibitors and lipid lowering therapies [24]. The ADA 2024 Standards of Care similarly recommend SGLT2i for diabetes-related HF and CKD [23]. These guidelines advocate for early CVD screening in patients with diabetes and a holistic approach, including lifestyle changes such as the Mediterranean diet and physical activity [23, 24]. Furthermore, the ADA and EASD joint recommendations on managing hyperglycaemia in T2D emphasise the use of GLP-1 RAs and SGLT2is as foundational therapies in patients with ASCVD [25]. The ADA/KDIGO 2022 consensus similarly recommends a comprehensive strategy for diabetes in CKD, including SGLT2is, GLP-1 RAs, statins, lifestyle modifications and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for hypertension and albuminuria [26].

While there is broad consensus on SGLT2is and GLP-1 RAs for CKM complications, certain areas, like the use of finerenone in patients without diabetes with CKD, are still emerging, with ongoing studies investigating its broader applications [27, 28]. Overall, while guidelines from ADA, ESC, EASD and KIDIGO align on SGLT2i and GLP-1 RAs for ASCVD, HF and CKD, differences exist regarding specific populations and emerging therapeutic options, suggesting a need for further research and potential guideline updates [23–26].

CURRENT THERAPEUTIC CONSIDERATIONS

Recent advances in managing CKM conditions emphasise the importance of evidence-based therapies tailored to individual patient profiles. Key agents, including GLP-1 RAs, dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) RAs, SGLT2is and finerenone, offer significant benefits across the CKM spectrum [4, 29].

- GLP-1 RAs, including liraglutide, semaglutide and dulaglutide, reduce ASCVD risk and improve glucose control, also offering significant cardiovascular benefits by reducing major adverse cardiovascular events (MACE) in patients with T2D and ASCVD [25]. Additionally, subcutaneous semaglutide has demonstrated cardiorenal benefits in the recently published FLOW trial (NCT03819153), reducing the risk of major kidney disease events and cardiovascular mortality in patients with T2D and CKD [30]. Evidence from the SELECT trial demonstrates that subcutaneous semaglutide also improves cardiovascular outcomes in people with obesity and CVD [31]. Furthermore, oral semaglutide has also demonstrated cardiovascular benefits reducing MACE risk by 14% in the SOUL trial (NCT03914326) [32]. By addressing multiple metabolic and cardiovascular conditions, GLP-1 RAs can help reduce polypharmacy, even when it is considered appropriate, thereby simplifying treatment and contributing to deprescribing efforts.
- Dual GLP-1/GIP RAs, such as tirzepatide, provide enhanced metabolic benefits, including greater weight loss and improved insulin sensitivity compared to GLP-1 RAs alone [33]. Emerging data suggest benefits in metabolic dysfunction-associated steatotic liver disease (MASLD), obstructive sleep apnoea-hypopnoea syndrome (OSAHS) and heart failure with preserved ejection fraction (HFpEF), extending their utility beyond diabetes management by addressing both metabolic and cardiovascular complications [33–37].
- SGLT2is, such as dapagliflozin, canagliflozin and empagliflozin, are first-line therapies for patients with diabetes and CKD, HF or ASCVD [38]. Their benefits extend beyond glucose control, offering reductions in HF hospitalisations, MACE and CKD progression [25, 38].
- Finerenone, a non-steroidal mineralocorticoid receptor antagonist (MRA), is a key therapy for patients with DKD, with preclinical data showing potent anti-inflammatory and antifibrotic effects [1, 22, 39–41]. Clinical tri-

als, such as FIDELIO-DKD (NCT02540993) and FIGARO-DKD (NCT02545049), have demonstrated its efficacy in reducing the risk of cardiovascular events and CKD progression [40, 41]. The FINEARTS-HF (NCT04435626) trial further established finerenone's cardiovascular benefits, showing a significant reduction in the risk of cardiovascular events in patients with HF with mildly reduced or preserved ejection fraction [42]. Ongoing trials are exploring its broader use. FINE-ONE (NCT05901831) is assessing finerenone in CKD with type 1 diabetes (T1D), while CONFIDENCE (NCT05254002) is investigating its combination with the SGLT2i empagliflozin in CKD and T2D to determine potential additive benefits [43, 44].

While effective, benefits of these therapies must always be balanced against potential adverse effects. GLP-1 RAs and GLP/GIP agonists may cause gastrointestinal disturbances, which may impact tolerability; however, these mostly occur during dose escalation, usually fade with time and are typically mild to moderate in severity [45]. SGLT2is are associated with genitourinary infections and, uncommonly, euglycaemic ketoacidosis [46]. Counselling regarding good personal hygiene, adequate hydration and the use of sick day guidance can mitigate these adverse effects. Finerenone carries a small risk of hyperkalaemia, necessitating regular potassium monitoring [40, 47].

Pharmacological advances, such as GLP-1 RAs, GLP-1/GIP RAs, SGLT2is and finerenone, complement lifestyle modifications by supporting weight loss and improving metabolic outcomes [23–25]. When combined with proactive weight management, these interventions offer a comprehensive approach consistent with current guidelines for preventing and managing CKM conditions [23–25].

In CKM management, addressing underlying metabolic abnormalities early is crucial. Obesity, insulin resistance and central adiposity—key contributors to hyperglycaemia—often develop decades before the clinical diagnosis of T2D [48]. Early intervention through lifestyle changes, including dietary adjustments, physical activity and behavioural support, can reverse these metabolic disturbances, improving glycaemic control and reducing cardiovascular and renal risks [23–25, 48]. Weight loss interventions, in particular, extend beyond glycaemic control, preventing or even reversing of microvascular complications that are associated with diabetes, such as CKD [48]. Numerous studies have shown that early weight loss and lifestyle modifications significantly reduce the risk of progression to more severe CKM conditions, supporting their role as a cornerstone of preventive care [48].

EMERGING THERAPIES

The management of CKM conditions is evolving rapidly, with several novel therapies in the pipeline that show promise for improving patient outcomes. These include triple hormone receptor agonists (GLP-1/GIP/glucagon), lysophosphatidic acid (LPA) receptor antagonists and second-generation selective MRAs, which aim to target new pathways involved in the pathophysiology of CKM conditions (Table 1) [9, 49, 50].

Triple-hormone Receptor Agonists

Triple-hormone receptor agonists target the GLP-1, GIP and glucagon receptors, offering a potential advancement beyond GLP-1 RAs in managing diabetes, obesity and cardiovascular risk [49, 51, 52]. While GLP-1 RAs already provide significant benefits in glycaemic control, weight loss and cardiovascular protection, triple agonists may further enhance energy expenditure and promote lipid metabolism, leading to superior reductions in liver fat and improvements in glucose homeostasis [49, 51–53].

Early-phase clinical trials, particularly with retatrutide, have shown significant efficacy in reducing blood glucose and body weight in T2D as well as other metabolic benefits including reduction in liver fat [52, 53]. A similar compound, LY3437943, has demonstrated potential for managing glycaemia and facilitating weight loss in preclinical studies [54]. These therapies' ability to concurrently target

Table 1 Emerging therapies in CKM conditions. This table summarises emerging therapies under investigation for CKM conditions, including triple receptor agonists, LPA receptor antagonists, second-generation MRAs and SGLT2i combinations. These treatments target key pathways such as fibrosis, metabolic dysfunction and renal protection, with the potential to improve patient outcomes by addressing multiple disease mechanisms. *CKD* chronic kidney disease, *CKM* cardiovascular, kidney and metabolic, *GIP* glucose-dependent insulinotropic polypeptide, *GLP-1* glucagon-like peptide-1, *HF* heart failure, *LPA* lysophosphatidic acid, *MRA* mineralocorticoid receptor antagonist, *SGLT2i* sodium-glucose cotransporter-2 inhibitors

Therapy Class	Therapeutic target & Mechanism	Potential Benefits	Key Agents & Trials
Triple Receptor Agonists	Activate GLP-1, GIP, and glucagon receptors to enhance glycaemic control, promote weight loss, and provide cardiometabolic benefits.	• Improves blood sugar levels • Reduces body weight significantly • Potential cardiovascular protection	• Retatrutide • LY3437943
LPA Receptor Antagonists	Block LPA1 receptor, reducing fibrosis, inflammation, and vascular dysfunction, key drivers of CKD and HF.	• Antifibrotic effects in kidney and heart • Potential to slow CKD and HF progression	• BMS-986020
Second-Generation Selective MRAs	More selective MRAs designed to lower the risk of hyperkalaemia while maintaining renal protective effects.	• Reduces albuminuria in diabetic kidney disease • Lower risk of electrolyte disturbances	• Esaxerenone (ESAX-DN trial) • Balcinrenone (MIRO-CKD and BALANCED-HF trials)
Ongoing Studies Involving SGLT2i	Combine SGLT2i with other agents to enhance kidney and cardiovascular protection.	• Improves CKD outcomes • Potential synergistic effects with other therapies	• ZENITH-CKD • EASi-KIDNEY

metabolic dysfunction and cardiorenal risk factors represents a promising strategy, although additional trials are needed to confirm their long-term safety and efficacy in diverse patient populations.

LPA Receptor Antagonists

LPA is a biologically active lysophospholipid involved in a variety of physiological processes, including fibrosis, inflammation and vascular dysfunction [55, 56]. There are six known LPA receptors (LPA1-LPA6), which mediate diverse physiological functions [55, 56]. A promising avenue of research involves LPA receptor antagonists, which target the LPA1 receptor implicated in the pathogenesis of CKD and HF [50, 55–57]. Preclinical studies and early-phase clinical trials, such as with BMS-986020, demonstrate that LPA1 antagonists can modulate collagen dynamics and exhibit antifibrotic effects, presenting potential benefits for conditions like CKD and HF [58]. These agents could complement existing therapies by targeting the inflammatory and fibrotic processes driving disease progression, although further investigation is necessary to assess their broader clinical use.

Second-generation Selective MRAs

Renin-angiotensin system inhibitors are standard therapy for DKD, offering benefits such as blood pressure reduction and albuminuria regression [9]. However, steroidal MRAs like spironolactone and eplerenone are limited in DKD because of the risk of hyperkalaemia [9]. Second-generation non-steroidal MRAs, such as esaxerenone and balcinrenone, offer greater selectivity, potentially reducing this risk while maintaining efficacy [9].

Esaxerenone has shown promise in hypertension, with a phase 3 trial (ESAX-DN) demonstrating albuminuria reduction, though further development has been limited [59]. Balcinrenone is being evaluated for CKD and HF in the MIRO-CKD (NCT06350123) and BALANCED HF (NCT06307652) trials, which are investigating the safety and efficacy of

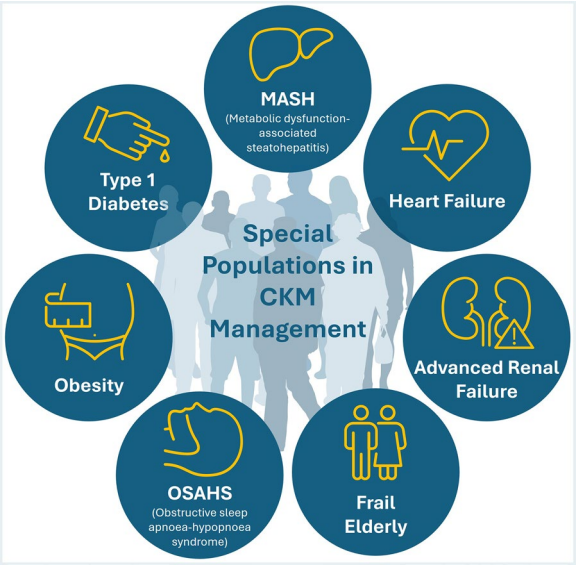

Fig. 2 Special populations in CKM management. This figure highlights key patient populations requiring tailored CKM management approaches. Conditions such as MASH, heart failure, frailty, obesity, type 1 diabetes, advanced renal failure and OSAHS share overlapping risk factors and contribute to the progression of cardiovascular, kidney and metabolic conditions. Addressing their specific needs through integrated care is essential for improving patient outcomes. *CKM* cardiovascular, kidney, metabolic, *MASH* metabolic dysfunction-associated steatohepatitis, *OSAHS* obstructive sleep apnoea-hypopnoea syndrome

balcinrenone combined with dapagliflozin [60, 61]. These agents may become key treatments in cardiorenal disease.

Ongoing Studies Involving SGLT2i

Combining therapies with distinct mechanisms of action is a promising strategy to improve patient outcomes by synergistically targeting multiple disease pathways [62]. This approach may enhance efficacy, reduce required drug doses and mitigate the risk of treatment resistance [62]. Several ongoing trials are exploring the potential of combining SGLT2is with other therapies for patients with CKD and related long-term conditions. ZENITH-CKD (NCT04724837) is evaluating zibotentan (a selective endothelin A receptor antagonist) combined with dapagliflozin versus dapagliflozin alone in patients with CKD [63], while EASi-KIDNEY (NCT06531824) is investigating the dual therapy of vicadrostat (a selective aldosterone synthase inhibitor) and empagliflozin for improving CKD outcomes [64].

SPECIFIC PATIENT POPULATIONS

Management of CKM conditions requires an individualised tailored approach to address the distinct challenges presented by specific patient groups (Fig. 2). This section explores key populations, outlining advances and unmet needs.

Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) and Metabolic Dysfunction-associated Steatohepatitis (MASH)

Metabolic dysfunction-associated steatohepatitis (MASH), formerly known as non-alcoholic steatohepatitis (NASH), falls into the broader MASLD spectrum [65]. This updated terminology highlights the metabolic origins of the condition, aiding patient identification and reducing stigma. MASLD is the most common liver disease in Western countries, affecting up to 30% of adults, while MASH, its progressive fibrotic form, affects ~ 5% [66]. MASH is closely linked to CKM conditions, driven by shared risk factors such as obesity, insulin resistance and dyslipidaemia, and is particularly common in individuals with T2D and obesity [66–68]. Notably, CVD is the leading cause of death in patients with MASH, emphasising its importance within CKM care [67, 68].

Despite its significant cardiometabolic implications, no therapies are currently approved in the UK specifically for MASH [65, 66]. However, in the US, resmetirom—an oral, liver-directed, thyroid hormone receptor beta-selective agonist—is the first MASH therapy approved by the Food and Drug Administration and should be considered for the treatment of non-cirrhotic MASH with significant liver fibrosis (stage ≥ 2) [65]. Meanwhile, several other agents, including dual GLP-1/GIP (e.g., tirzepatide), dual

GLP-1/glucagon (e.g., survodutide) and triple GLP-1/GIP/glucagon (e.g., retatrutide) agonists, show promise, demonstrating metabolic and hepatic benefits such as reductions in liver fat and fibrosis [65]. Nevertheless, the EASL-EASD-European Association for the Study of Obesity (EASO) guidelines recommend GLP-1 RAs only for their approved indications, such as T2D or obesity, rather than as targeted treatments for MASH [65].

Lifestyle modification remains the cornerstone of MASLD/MASH management. A sustained weight loss of 5% to reduce liver fat, 7–10% to improve liver inflammation and ≥ 10% to improve fibrosis is recommended [65]. Additional interventions, such as the Mediterranean diet, have been shown to reduce liver fat, even without weight loss [65]. Proactive screening for liver fibrosis in high-risk individuals, using the Fibrosis-4 (FIB-4) score initially and, if elevated, a further non-invasive assessment such as vibration-controlled transient elastography (VCTE), is critical for mitigating the heightened cardiometabolic risks associated with MASH [65].

Heart Failure

HF subtypes present distinct challenges, reflecting their varied underlying pathologies. HFpEF is frequently associated with hypertension, obesity and diabetes, while heart failure with reduced ejection fraction (HFrEF) is more commonly linked to ischaemic heart disease and renal impairment [69–71]. Both subtypes often coexist with other CKM conditions; approximately 25–40% of patients with HF have diabetes, and approximately 40–50% have CKD, highlighting the complex interplay between these conditions and the need for integrated management [72].

The National Institute for Health and Care Excellence (NICE) guideline NG106 recommends N-terminal pro-B-type natriuretic peptide (NT-proBNP) testing to evaluate suspected HF [73]. For patients with HFrEF, current guidelines advocate quadruple therapy, which includes an RAAS inhibitor (or angiotensin receptor-neprilysin inhibitor), a β-blocker, an MRA and an SGLT2i—collectively termed the "four pillars" of HFrEF management [74, 75]. Early initiation of quadruple therapy after discharge, ideally within 30 days, aligns with recent expert consensus recommending rapid sequencing of the four foundational treatments for HFrEF to maximise prognostic benefits [74, 76]. However, these therapies remain underutilised, often because of polypharmacy concerns and clinical inertia [74]. Addressing these barriers through early, aggressive optimisation of evidence-based treatments is critical to improving outcomes for patients with HF.

Advanced Renal Failure

Patients with an estimated glomerular filtration rate (eGFR) below 25 ml/min/1.73m^2, those on dialysis and kidney transplant recipients (KTR) represent a distinct and high-risk population within CKM management. These individuals face a significantly increased risk of cardiovascular complications and mortality; however, evidence-based treatment options and guideline-directed medical therapies remain limited because of their frequent exclusion or underrepresentation in major clinical trials [1, 77, 78].

For example, there is limited evidence regarding the use of SGLT2is, GLP-1 RAs and dual GIP/GLP-1 RAs in patients with an eGFR < 20 ml/min/1.73m^2 and in end-stage kidney disease (ESKD) [29]. Nevertheless, emerging preclinical and clinical data suggest that SGLT2is may offer cardiovascular and renal benefits even in advanced CKD, despite their diminished glycosuric and natriuretic effects [29]. The ongoing RENAL LIFECYCLE trial (NCT05374291) is investigating the effects of dapagliflozin on cardiovascular and renal outcomes in this high-risk population [79].

Similarly, GLP-1 RAs have shown potential cardiovascular and metabolic benefits in patients with T2D and advanced CKD, including ESKD [29, 78]. A recent meta-analysis indicated that, although gastrointestinal side effects may occur, GLP-1 RAs improve blood glucose control, promote weight loss and may provide cardiovascular benefits [29, 78].

For patients on dialysis, mineralocorticoid receptor antagonists (MRAs) have also been explored as a potential strategy to reduce

cardiovascular risk. The ALCHEMIST trial, which investigated spironolactone in haemodialysis patients, failed to meet its primary endpoint. However, it did demonstrate a reduction in heart failure hospitalisations, highlighting a promising therapeutic avenue that warrants further investigation [80].

The global rise in CKD prevalence is contributing to an increasing number of patients reaching CKD stage 5 and requiring kidney replacement therapy [77]. Currently, an estimated 10 million individuals worldwide qualify for kidney replacement therapy, and this figure is projected to increase by 50% to 100% by 2030 [77]. Given the persistent lack of data from large cardiovascular outcome trials, there is an urgent need for dedicated studies evaluating cardiometabolic therapies in advanced CKD.

Frail Elderly

By 2072, the UK population aged ≥ 65 is projected to reach 22.1 million, representing 27% of the total population [81]. Older adults, often with multiple long-term conditions, present unique challenges in CKM management due to frailty and polypharmacy [82, 83]. Frailty, characterised by loss of functional and homeostatic reserve leading to functional and physiological vulnerability, worsens cardiovascular outcomes, especially in those over 75 with multiple long-term conditions [82–84].

Individualised strategies, guided by tools like the electronic Frailty Index and Rockwood Scale, are essential to address age-related decline and to ensure ongoing appropriate polypharmacy [83]. Inappropriate polypharmacy can accelerate frailty progression, with each additional drug increasing the risk by 27% [85]. In this context, deprescribing has emerged as an important strategy, with emerging evidence suggesting it may improve quality of life and survival, particularly in older adults with multiple long-term conditions [86]. Careful medication review is therefore essential to optimise treatment while reducing unnecessary drug burden.

Beyond medication management, targeted pharmacological interventions can benefit frail patients. The post hoc DAPA-HF analysis demonstrated that dapagliflozin is effective and well tolerated in frail patients with HFrEF, highlighting the potential benefits of initiating treatment like SGLT2is in this population despite clinical reluctance [87]. Additionally, non-pharmacological strategies, such as cardiac rehabilitation programs evaluated in the REHAB-HF trial, show promise in improving physical function, quality of life and frailty metrics in older adults [82, 88]. Further research is needed to optimise both pharmacological and non-pharmacological strategies to improve overall well-being in this special population.

Notably, frailty can be potentially modifiable following a comprehensive geriatric assessment, which includes a multidisciplinary evaluation of physical, psychosocial, functional and environmental factors [89]. This process may involve assessments such as falls risk evaluation, medication review and occupational therapy assessment [89].

Obesity

A recent Lancet Commission redefined clinical obesity as a chronic disease resulting from excess adiposity that impacts organ and tissue function [90]. It critiques the current body mass index (BMI)-based definition, noting it fails to differentiate between fat and lean mass, consider fat distribution or account for tissue or organ dysfunction and functional status [90]. The Commission recommends classifying obesity as either clinical (with functional alterations in organs) or preclinical (without such alterations) [90]. Diagnosis now requires confirming excess body fat through BMI, body measurements or direct fat measurement (e.g., DEXA scan), with specific waist circumference and ratio thresholds for accurate assessment [90].

The National Child Measurement Programme (NCMP) found that 9.6% of reception-age children in England (ages 4–5) were obese in 2023/2024 [91]. This highlights the alarming rise in childhood obesity, underscoring the need to prioritise early, proactive education to promote healthy lifestyle habits from a young age. Obesity increases cardiovascular risk, accelerates CKD progression and drives metabolic dysfunction. Multidisciplinary

interventions focused on weight loss are essential, particularly for patients living with T2D. Weight loss of 5–10% is well established to improve metabolic health, while 10–15% or more can modify disease progression or even achieve remission [25]. NICE recommends setting an initial weight loss target of 5–10% for people living with obesity [92]. Behavioural interventions, supported by structured weight management programs and person-centred, stigma-free communication, can improve treatment adherence [93–95]. GLP-1 and GLP-1/GIP RAs can complement lifestyle interventions for individuals with overweight or obesity and at least one weight-related condition [96].

NICE guidance (NG246) also advocates a personalised, multi-component approach to obesity management, combining lifestyle modifications, pharmacological treatments and, where appropriate, non-pharmacological options [97]. Lifestyle interventions should include a balanced, calorie-controlled diet, regular physical activity tailored to the individual's capacity and behavioural strategies such as goal setting and self-monitoring [97]. Pharmacotherapy, including GLP-1 RAs and GLP-1/GIP RAs, may be considered when lifestyle changes alone are insufficient, with treatment decisions based on the patients' clinical profile, benefits and risks [97]. For individuals with severe obesity (BMI ≥ 40 kg/m^2 or ≥ 35 kg/m^2 with obesity-related comorbidities), bariatric surgery may be an option following multidisciplinary assessment, with long-term post-surgical support essential for sustained weight management [97].

Type 1 Diabetes

T1D affects approximately 1 in 500 children and young people under 15 years in the UK, with an annual incidence of 25.6 per 100,000 in the general population [98]. Between 2023 and 2024, most people registered with T1D in England were aged 40 years and younger, accounting for 44.7% of cases [99]. Patients living with T1D face significantly higher risks of cardiovascular and renal complications compared to the general population [98, 100]. Despite advancements in managing T2D, treatment options for CKM complications in T1D remain limited. Current guidelines emphasise the importance of intensive glycaemic control, supported by structured education and lifestyle optimisation, to reduce long-term complications [101]. Continuous glucose monitoring (CGM) is recommended for enhancing glycaemic stability and preventing microvascular and macrovascular damage [101].

Although SGLT2is have shown benefits in other populations, their use in T1D is more controversial because of the increased risk of ketoacidosis [102]. This highlights the need for careful consideration and monitoring regarding these therapies, which remain off license. The ongoing lack of targeted therapies to address the specific cardiovascular and renal risks in T1D underscores the need for further research and the development of more effective treatment strategies tailored to this population [103]. Encouragingly, FINE-ONE (NCT05901831) is assessing finerenone in CKD with T1D, offering a potential new avenue for managing renal complications in this group [44].

Obstructive Sleep Apnoea-Hypopnoea Syndrome

OSAHS, affecting up to 1.5 million adults in the UK, is an under-recognised sleep-related breathing disorder linked to obesity, T2D, CVD and CKD [104–106]. It is characterised by recurrent upper airway obstruction during sleep, leading to intermittent hypoxia, oxidative stress and autonomic dysregulation, all of which contribute to hypertension, insulin resistance, endothelial dysfunction and systemic inflammation [104–107].

OSAHS is associated with a 37% increased risk of developing T2D, with reportedly 58–86% of T2D patients having OSAHS and 15–30% of OSAHS patients having T2D [105, 108]. OSAHS is also strongly linked to hypertension, HF, atrial fibrillation, coronary artery disease and stroke [109]. It is present in 30–50% of hypertensive patients, 70–85% of those with resistant hypertension and > 90% of those with refractory hypertension [107]. The intermittent hypoxia and sympathetic nervous system activation characteristic of OSAHS contribute to vascular dysfunction, increased arterial stiffness and the

development of arrhythmias, which all worsen cardiovascular outcomes [109].

Similarly, OSAHS accelerates CKD progression through nocturnal hypoxia, blood pressure fluctuations and sympathetic overactivity driving glomerular damage, albuminuria and renal decline [110]. Interestingly, the relationship between OSAHS and CKD is bidirectional, with CKD also exacerbating the severity of OSAHS, creating a cycle that further worsens both renal and cardiovascular outcomes [110].

Screening for OSAHS should be prioritised, using tools such as the Epworth Sleepiness Scale and STOP-Bang questionnaire to identify high-risk individuals [111]. Continuous positive airway pressure (CPAP) remains the gold standard for managing moderate-to-severe OSAHS; however, adherence can be challenging, making lifestyle modifications including weight loss, alcohol reduction and smoking cessation essential complementary strategies [111]. A multidisciplinary approach, integrating OSAHS management into CKM care pathways, is key to improving long-term patient outcomes.

TECHNOLOGY IN CKM MANAGEMENT

The integration of technology, particularly AI, is revolutionising the management of CKM conditions. AI and digital health tools are enhancing early diagnosis, risk stratification and personalised treatment while addressing challenges such as inappropriate polypharmacy and disease complexity (Fig. 3) [112–114].

Artificial Intelligence in CKM

AI has demonstrated transformative potential in CKM care by leveraging large datasets to predict disease progression, optimise treatment and improve outcomes [112, 114–117].

AI applications in cardiovascular care include detecting arrhythmias, assessing HF risk and identifying subclinical atherosclerosis [112, 115, 118]. Algorithms analysing electrocardiogram and imaging modalities, such as echocardiography and coronary computed tomography, have significantly improved diagnostic precision and risk stratification [115]. For example, AI can

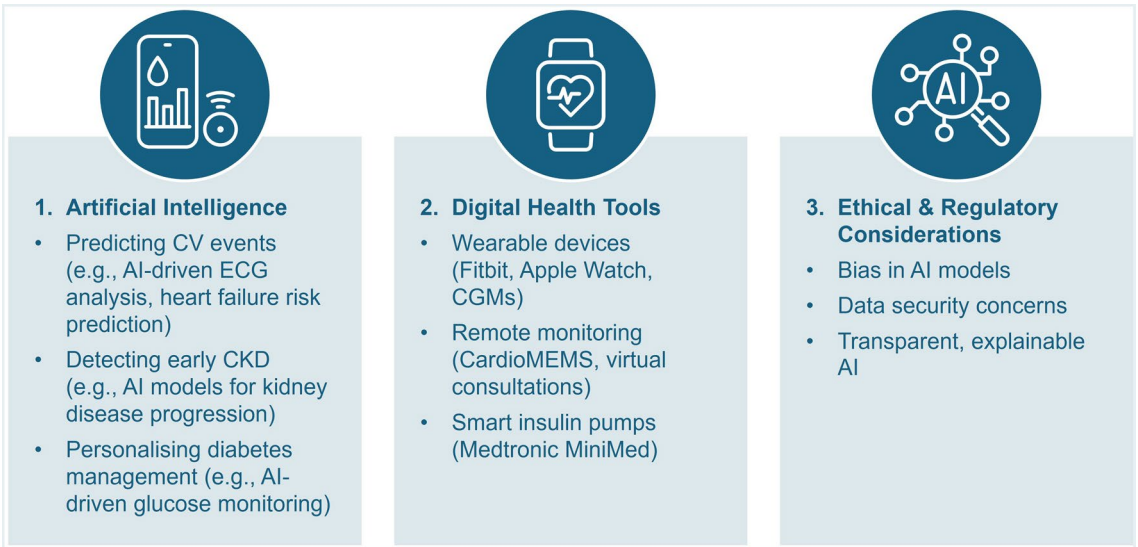

Fig. 3 The role of AI and Digital Health in CKM Management. This figure summarises ways in which AI and digital health tools are being implemented within CKM management to improve patient care. There are also some ethical and regulatory aspects that must be taken into consideration. *AI* artificial intelligence, *CGMs* continuous glucose monitor, *CKD* chronic kidney disease, *CKM* cardiovascular, kidney and metabolic, *CV* cardiovascular, *ECG* electrocardiogram

predict future cardiovascular events by integrating biomarkers, lifestyle factors and imaging data [114, 118]. Additionally, machine learning models aid in decision-making for therapies like anticoagulation in atrial fibrillation, enabling personalised treatment strategies [119]. In CVD, AI-driven models may also help clinicians determine when to withdraw medications like diuretics or beta-blockers to minimise pill burden.

AI plays a key role in detecting early kidney disease, predicting progression and optimising dialysis schedules [113, 116]. For instance, AI algorithms can analyse electronic health records to predict acute kidney injury or CKD progression more accurately than traditional risk scores [113, 120]. In transplantation, AI enhances donor-recipient matching and assists in evaluating eligibility [121, 122]. Tools like KidneyIntelX personalise treatment in DKD by predicting outcomes and guiding medication adjustments [123].

In metabolic diseases, AI-driven models predict the onset and progression of T2D by analysing patient data, including blood glucose trends and lifestyle factors [117]. Combined with CGMs, AI algorithms provide real-time feedback to optimise glycaemic control [124]. For patients with well-controlled blood glucose, AI can recommend treatment de-escalation, such as reducing insulin or transitioning to non-insulin therapies like GLP-1 RAs or SGLT2is. Additionally, AI supports personalised weight management strategies for metabolic syndrome and T2D [125].

Digital Health Tools in CKM Management

Digital health technologies complement AI in CKM management by enhancing patient engagement and enabling continuous monitoring.

- Wearable Devices: Tools like Fitbit, Apple Watch and CGMs provide actionable insights into physical activity, heart rate and glucose levels [124, 126, 127]. CGMs such as Dexcom G6 and Abbott's FreeStyle Libre improve glycaemic control in diabetes, while smart insulin pumps like Medtronic MiniMed enable automated insulin delivery [124, 127].
- Telemedicine and Remote Monitoring: Platforms for virtual consultations improve access to care for patients with diabetes, HF and CKD, particularly those in remote areas [128–131]. Devices like the CardioMEMS heart sensor allow real-time monitoring of HF patients, reducing hospital readmissions through timely interventions [127, 132].
- Other digital technologies such as the Clinical Digital Resource Collaborative (CDRC) and CVDPREVENT can support primary care teams to deliver gold-standard patient care or explore GP practice data to improve cardiovascular healthcare respectively [133, 134].

Ethical and Regulatory Challenges

The use of AI in CKM care introduces ethical and regulatory challenges, particularly related to bias, transparency and data security. AI models may exhibit bias if trained on unrepresentative datasets, potentially leading to inaccurate predictions for underrepresented groups, such as ethnic minorities and women [91, 135, 136]. Inclusive datasets and ongoing validation are needed to ensure equitable AI performance across populations.

Additionally, the integration of AI in clinical decision-making raises concerns about the impact on the person-centred clinician-patient relationship [137]. AI's role in treatment decisions could alter patient perceptions of care, leading to potential disengagement or mistrust if not effectively communicated [137]. Furthermore, AI's reliance on large-scale patient data raises issues around privacy and security. Compliance with regulations and implementing robust data protection frameworks are crucial to safeguard sensitive patient information and maintain public trust [118, 135]. Another concern is the "black box" nature of some AI systems, where decision-making processes lack transparency [135]. This can undermine clinician trust and hinder AI adoption. Developing transparent, explainable AI tools is critical for improving transparency, maintaining trust and ensuring clinicians can interpret AI-driven decisions within the context of patient care [137].

As AI evolves from detection to decision-making, questions arise about its regulation

as a medical intervention. The Medicines and Healthcare products Regulatory Agency (MHRA) is addressing this by developing a strategic approach to ensure safety while fostering innovation [138]. Its "AI Airlock" initiative tackles regulatory challenges for AI-integrated medical devices, providing a framework for their safe clinical use [138, 139]. The MHRA's efforts underscore the importance of establishing clear guidelines for AI-driven decision support in healthcare.

CONCLUSION

To improve outcomes for patients with CKM conditions, a comprehensive approach is needed that combines evidence-based therapies, technological innovations and a focus on prevention. By addressing the interconnected nature of these conditions, healthcare systems can streamline care pathways and enhance the patient journey, improving the sustainability of existing systems and ultimately helping to improve both the quality and quantity of life for people living with CKM conditions.

Call to Action for Future Cardiovascular, Kidney, and Metabolic (CKM) Care:

1. **Integrate evidence-based therapies:** Optimising CKM care requires the integration of pharmacological treatments in an evidence-informed yet person-centred manner alongside lifestyle interventions for optimal patient outcomes.
2. **Leverage technology for personalised care:** The use of artificial intelligence and digital health tools can optimise treatment plans, enabling more precise, patient-centred care and improving disease management across CKM conditions.
3. **Prioritise lifestyle interventions and early diagnosis:** Early detection and interventions targeting shared risk factors, such as the disease of obesity, insulin resistance and inflammation, remain key to managing and preventing CKM conditions effectively.
4. **Promote multidisciplinary care:** A coordinated, holistic approach that addresses the interconnected nature of cardiovascular, kidney, and metabolic conditions will enhance care delivery and improve patient outcomes.

Medical writing/Editorial assistance. Medical writing and Editorial assistance in the preparation of this article was provided by Nida Khan, Dhara Mistry and Angharad Kerr of LCW Consulting Ltd. No funding or sponsorship was received for this assistance.

Author Contribution. Kevin Fernando, Derek Connolly, Eimear Darcy, Marc Evans, William Hinchliffe, Patrick Holmes and W. David Strain contributed to the article in a substantive and meaningful manner. All authors have read and agreed to the published version of the manuscript.

Funding. No funding or sponsorship was received for this study or publication of this article. The Rapid Service Fee was funded by the authors.

Declarations

Conflict of interest. Marc Evans is an Editor-in-Chief of Diabetes Therapy. Marc Evans was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. W. David Strain is an Editorial Board member of Diabetes Therapy. W. David Strain was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Kevin Fernando, Derek Connolly, Eimear Darcy, William Hinchliffe and Patrick Holmes have nothing to declare.

Ethical approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

REFERENCES

1. Cardiovascular-Kidney-Metabolic Health: a presidential advisory from the American Heart Association [Internet]. https://doi.org/10.1161/CIR.0000000000001184. Accessed 17 Dec 2024.

2. Kadowaki T, Maegawa H, Watada H, Yabe D, Node K, Murohara T, et al. Interconnection between cardiovascular, renal and metabolic disorders: a narrative review with a focus on Japan. Diabetes Obes Metab. 2022;24(12):2283–96.

3. Usman MS, Khan MS, Butler J. The interplay between diabetes, cardiovascular disease, and kidney disease. ADA Clin Compend. 2021;2021(1):13–8.

4. A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) syndrome: a scientific statement from the American Heart Association | Circulation [Internet]. https://doi.org/10.1161/CIR.0000000000001186?rfr_dat=cr_pub++0pubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org. Accessed 17 Dec 2024.

5. Norhammar A, Bodegard J, Eriksson JW, Haller H, Linssen GCM, Banerjee A, et al. Cost of healthcare utilization associated with incident cardiovascular and renal disease in individuals with type 2 diabetes: a multinational, observational study across 12 countries. Diabetes Obes Metab. 2022;24(7):1277–87.

6. BHF CVD Statistics UK Factsheet January 2025 [Internet]. https://www.bhf.org.uk/-/media/files/for-professionals/research/heart-statistics/

bhf-cvd-statistics-uk-factsheet.pdf?rev=81a8015761aa4ced8bc39d7045202be5&hash=9D78ACBF5EB80FA8A9BE28C90BFBE171. Accessed 31 Jan 2025.

7. Diabetes UK [Internet]. Diabetes diagnoses double in the last 15 years. https://www.diabetes.org.uk/about-us/news-and-views/diabetes-diagnoses-doubled-prevalence-2021. Accessed 17 Dec 2024.

8. Diabetes UK [Internet]. How many people in the UK have diabetes? https://www.diabetes.org.uk/about-us/about-the-charity/our-strategy/statistics. Accessed 17 Dec 2024.

9. Sarafidis P, Iatridi F, Ferro C, Alexandrou ME, Fernandez-Fernandez B, Kanbay M, et al. Mineralocorticoid receptor antagonist use in chronic kidney disease with type 2 diabetes: a clinical practice document by the European Renal Best Practice (ERBP) board of the European Renal Association (ERA). Clin Kidney J. 2023;16(11):1885–907.

10. Burden of CVD | Background information | CVD risk assessment and management | CKS | NICE [Internet]. https://cks.nice.org.uk/topics/cvd-risk-assessment-management/background-information/burden-of-cvd/. Accessed 17 Dec 2024.

11. Economics-of-Kidney-Disease-full-report_accessible.pdf [Internet]. https://www.kidneyresearchuk.org/wp-content/uploads/2023/06/Economics-of-Kidney-Disease-full-report_accessible.pdf. Accessed 17 Dec 2024.

12. Stiebahl S. Obesity statistics. 2025. https://commonslibrary.parliament.uk/research-briefings/sn03336/. Accessed 10 Mar 2025.

13. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1204–22.

14. Foreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. Lancet Lond Engl. 2018;392(10159):2052–90.

15. Hex N, MacDonald R, Pocock J, Uzdzinska B, Taylor M, Atkin M, et al. Estimation of the direct health and indirect societal costs of diabetes in the UK using a cost of illness model. Diabet Med. 2024;41(9): e15326.

16. GOV.UK [Internet]. Health matters: obesity and the food environment. https://www.gov.uk/government/publications/health-matters-obesity-and-the-food-environment/health-matters-obesity-and-the-food-environment-2. Accessed 29 Jan 2025.

17. Brandt EJ, Tobb K, Cambron JC, Ferdinand K, Douglass P, Nguyen PK, et al. Assessing and addressing social determinants of cardiovascular health: JACC state-of-the-art review. J Am Coll Cardiol. 2023;81(14):1368–85.

18. Painter H, Parry E, McCann L, Dehn Lunn A, Ford J. Social needs screening in primary care: a tool in the fight for health equity? Public Health Pract. 2024;1(7): 100466.

19. A framework for NHS action on social determinants of health | The Health Foundation [Internet]. 2022. https://www.health.org.uk/reports-and-analysis/briefings/a-framework-for-nhs-action-on-social-determinants-of-health. Accessed 26 Mar 2025.

20. Fisher R, Gottlieb LM, Marchis ED, Alderwick H. Assessing patients' social risks: what can England learn from emerging evidence in the US? Br J Gen Pract. 2023;73(733):370–2.

21. Massy ZA, Drueke TB. Combination of cardiovascular, kidney, and metabolic diseases in a syndrome named cardiovascular-kidney-metabolic, with new risk prediction equations. Kidney Int Rep. 2024;9(9):2608–18.

22. Marassi M, Fadini GP. The cardio-renal-metabolic connection: a review of the evidence. Cardiovasc Diabetol. 2023;31(22):195.

23. American Diabetes Association Professional Practice Committee. 10. Cardiovascular disease and risk management: standards of care in diabetes—2024. Diabetes Care. 2023;47(Supplement_1):S179–218.

24. Marx N, Federici M, Schütt K, Müller-Wieland D, Ajjan RA, Antunes MJ, et al. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. Eur Heart J. 2023;44(39):4043–140.

25. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) | Diabetes Care | American Diabetes Association [Internet]. https://diabetesjournals.org/care/article/45/11/2753/147671/Management-of-Hyperglycemia-in-Type-2-Diabetes. Accessed 17 Dec 2024.

26. de Boer IH, Khunti K, Sadusky T, Tuttle KR, Neumiller JJ, Rhee CM, et al. Diabetes management in Chronic Kidney Disease: a consensus report by the American Diabetes Association (ADA) and kidney disease: improving global outcomes (KDIGO). Diabetes Care. 2022;45(12):3075–90.

27. Zhou L, Li W. Effectiveness and safety of finerenone in Chinese CKD patients without diabetes: a retrospective, real-world study. Int Urol Nephrol. 2024;56(12):3877–85.

28. Heerspink HJL, Agarwal R, Bakris GL, Cherney DZI, Lam CSP, Neuen BL, et al. Design and baseline characteristics of the Finerenone, in addition to standard of care, on the progression of kidney disease in patients with Non-Diabetic Chronic Kidney Disease (FIND-CKD) randomized trial. Nephrol Dial Transplant. 2024;gfae132.

29. Theodorakis N, Nikolaou M. Integrated management of cardiovascular–renal–hepatic–metabolic syndrome: expanding roles of SGLT2is, GLP-1RAs, and GIP/GLP-1RAs. Biomedicines. 2025;13(1):135.

30. Perkovic V, Tuttle KR, Rossing P, Mahaffey KW, Mann JFE, Bakris G, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. N Engl J Med. 2024;391(2):109–21.

31. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. N Engl J Med. 2023;389(24):2221–32.

32. TCTMD.com [Internet]. 2024. SOUL: Oral Semaglutide Cuts CV Events in Diabetic Patients. https://www.tctmd.com/news/soul-oral-semaglutide-cuts-cv-events-diabetic-patients. Accessed 29 Jan 2025.

33. Várkonyi TT, Pósa A, Pávó N, Pavo I. Perspectives on weight control in diabetes—Tirzepatide. Diabetes Res Clin Pract. 2023;1(202): 110770.

34. Packer M, Zile MR, Kramer CM, Baum SJ, Litwin SE, Menon V, et al. Tirzepatide for heart failure with preserved ejection fraction and obesity. N Engl J Med [Internet]. 2025. https://doi.org/10.1056/NEJMoa2410027.

35. Loomba R, Hartman ML, Lawitz EJ, Vuppalanchi R, Boursier J, Bugianesi E, et al. Tirzepatide for metabolic dysfunction-associated steatohepatitis with liver fibrosis. N Engl J Med. 2024;391(4):299–310.

36. U.S FDA. FDA. FDA; 2024. FDA Approves First Medication for Obstructive Sleep Apnea. https://www.fda.gov/news-events/press-announcements/fda-approves-first-medication-obstructive-sleep-apnea. Accessed 21 Jan 2025.

37. Malhotra A, Grunstein RR, Fietze I, Weaver TE, Redline S, Azarbarzin A, et al. Tirzepatide for the treatment of obstructive sleep apnea and obesity. N Engl J Med. 2024;391(13):1193–205.

38. Yau K, Dharia A, Alrowiyti I, Cherney DZI. Prescribing SGLT2 inhibitors in patients with CKD: expanding indications and practical considerations. Kidney Int Rep. 2022;7(7):1463–76.

39. Finerenone | Drugs | BNF content published by NICE [Internet]. https://bnf.nice.org.uk/drugs/finerenone/. Accessed 17 Dec 2024.

40. Bakris GL, Agarwal R, Anker SD, Pitt B, Ruilope LM, Rossing P, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. N Engl J Med. 2020;383(23):2219–29.

41. Pitt B, Filippatos G, Agarwal R, Anker SD, Bakris GL, Rossing P, et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. N Engl J Med. 2021;385(24):2252–63.

42. Solomon SD, McMurray JJV, Vaduganathan M, Claggett B, Jhund PS, Desai AS, et al. Finerenone in heart failure with mildly reduced or preserved ejection fraction. N Engl J Med. 2024;391(16):1475–85.

43. Green JB, Mottl AK, Bakris G, Heerspink HJL, Mann JFE, McGill JB, et al. Design of the COmbinatioN effect of FInerenone anD EmpagliflOziN in participants with chronic kidney disease and type 2 diabetes using a UACR Endpoint study (CONFIDENCE). Nephrol Dial Transplant. 2022;38(4):894–903.

44. Heerspink HJL, Birkenfeld AL, Cherney DZI, Colhoun HM, Ji L, Mathieu C, et al. Rationale and design of a randomised phase III registration trial investigating finerenone in participants with type 1 diabetes and chronic kidney disease: The FINE-ONE trial. Diabetes Res Clin Pract. 2023;204: 110908.

45. Gorgojo-Martínez JJ, Mezquita-Raya P, Carretero-Gómez J, Castro A, Cebrián-Cuenca A, de Torres-Sánchez A, et al. Clinical recommendations to manage gastrointestinal adverse events in patients treated with Glp-1 receptor agonists: a multidisciplinary expert consensus. J Clin Med. 2022;12(1):145.

46. Chauhan S, Diaz V, Ogbu IR, Sanchez JRP, Manov AE, Shah P. empagliflozin-associated euglycemic diabetic ketoacidosis masked by urinary tract infection. Cureus. 2024;16(8):e66408.

47. Agarwal R, Joseph A, Anker SD, Filippatos G, Rossing P, Ruilope LM, et al. Hyperkalemia risk with finerenone: results from the FIDELIO-DKD trial. J Am Soc Nephrol JASN. 2022;33(1):225–37.

48. Lingvay I, Sumithran P, Cohen RV, le Roux CW. Obesity management as a primary treatment goal for type 2 diabetes: time to reframe the conversation. Lancet Lond Engl. 2022;399(10322):394–405.

49. Jakubowska A, le Roux CW, Viljoen A. The road towards triple agonists: glucagon-like peptide 1, glucose-dependent insulinotropic polypeptide and

glucagon receptor—an update. Endocrinol Metab. 2024;39(1):12–22.

50. Abdel-Magid AF. Lysophosphatidic acid receptor 1 antagonists for the treatment of fibrosis. ACS Med Chem Lett. 2019;10(10):1378–9.

51. Knerr PJ, Mowery SA, Douros JD, Premdjee B, Hjøllund KR, He Y, et al. Next generation GLP-1/GIP/glucagon triple agonists normalize body weight in obese mice. Mol Metab. 2022;7(63): 101533.

52. Alfaris N, Waldrop S, Johnson V, Boaventura B, Kendrick K, Stanford FC. GLP-1 single, dual, and triple receptor agonists for treating type 2 diabetes and obesity: a narrative review. eClinicalMedicine [Internet]. 2024 Sep 1;75. https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(24)00361-4/fulltext. Accessed 17 Dec 2024.

53. Rosenstock J, Frias J, Jastreboff AM, Du Y, Lou J, Gurbuz S, et al. Retatrutide, a GIP, GLP-1 and glucagon receptor agonist, for people with type 2 diabetes: a randomised, double-blind, placebo and active-controlled, parallel-group, phase 2 trial conducted in the USA. Lancet Lond Engl. 2023;402(10401):529–44.

54. Coskun T, Urva S, Roell WC, Qu H, Loghin C, Moyers JS, et al. LY3437943, a novel triple glucagon, GIP, and GLP-1 receptor agonist for glycemic control and weight loss: from discovery to clinical proof of concept. Cell Metab. 2022;34(9):1234-1247.e9.

55. Raja AA, Wakimoto H, DeLaughter DM, Reichart D, Gorham J, Conner DA, et al. Ablation of lysophosphatidic acid receptor 1 attenuates hypertrophic cardiomyopathy in a mouse model. Proc Natl Acad Sci USA. 2022;119(28): e2204174119.

56. Naruse T, Otake H, Takahashi T. Effects of a lysophosphatidic acid receptor 1 antagonist on hypertensive renal injury in Dahl-Iwai salt-sensitive rats. J Pharmacol Sci. 2022;149(4):179–88.

57. Swaney J, Chapman C, Correa L, Stebbins K, Bundey R, Prodanovich P, et al. A novel, orally active LPA1 receptor antagonist inhibits lung fibrosis in the mouse bleomycin model. Br J Pharmacol. 2010;160(7):1699–713.

58. Decato BE, Leeming DJ, Sand JMB, Fischer A, Du S, Palmer SM, et al. LPA1 antagonist BMS-986020 changes collagen dynamics and exerts antifibrotic effects in vitro and in patients with idiopathic pulmonary fibrosis. Respir Res. 2022;23(1):61.

59. Ito S, Kashihara N, Shikata K, Nangaku M, Wada T, Okuda Y, et al. Esaxerenone (CS-3150) in Patients with Type 2 Diabetes and Microalbuminuria (ESAX-DN). Clin J Am Soc Nephrol CJASN. 2020;15(12):1715–27.

60. AstraZeneca. A Phase III, Randomised, Double-blind Study to Evaluate the Effect of Balcinrenone /Dapagliflozin, Compared With Dapagliflozin, on the Risk of Heart Failure Events and Cardiovascular Death in Patients With Heart Failure and Impaired Kidney Function [Internet]. clinicaltrials.gov; 2024 Dec. Report No.: NCT06307652. https://clinicaltrials.gov/study/NCT06307652. Accessed 21 Jan 2025.

61. AstraZeneca. A Phase IIb, Multicenter, Randomised, Double-Blind, Dose-finding Study to Evaluate the Efficacy, Safety and Tolerability of Balcinrenone in Combination With Dapagliflozin Compared With Dapagliflozin in Patients With Chronic Kidney Disease and Albuminuria [Internet]. clinicaltrials.gov; 2025 Jan. Report No.: NCT06350123. https://clinicaltrials.gov/study/NCT06350123. Accessed 21 Jan 2025.

62. Sun W, Sanderson P, Zheng W. Drug combination therapy increases successful drug repositioning. Drug Discov Today. 2016;21(7):1189–95.

63. Heerspink HJL, Kiyosue A, Wheeler DC, Lin M, Wijkmark E, Carlson G, et al. Zibotentan in combination with dapagliflozin compared with dapagliflozin in patients with chronic kidney disease (ZENITH-CKD): a multicentre, randomised, active-controlled, phase 2b, clinical trial. Lancet. 2023;402(10416):2004–17.

64. CDEK. EASi-KIDNEY™ (The Studies of Heart & Kidney Protection With BI 690517 in Combination With Empagliflozin) [Internet]. https://cdek.pharmacy.purdue.edu/trial/NCT06531824/. Accessed 21 Jan 2025.

65. Tacke F, Horn P, Wong VWS, Ratziu V, Bugianesi E, Francque S, et al. EASL–EASD–EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol. 2024;81(3):492–542.

66. Miao L, Targher G, Byrne CD, Cao YY, Zheng MH. Current status and future trends of the global burden of MASLD. Trends Endocrinol Metab. 2024;35(8):697–707.

67. Zheng H, Sechi LA, Navarese EP, Casu G, Vidili G. Metabolic dysfunction-associated steatotic liver disease and cardiovascular risk: a comprehensive review. Cardiovasc Diabetol. 2024;23(1):346.

68. Burra P, Becchetti C, Germani G. NAFLD and liver transplantation: Disease burden, current

management and future challenges. JHEP Rep. 2020;2(6): 100192.

69. Mouton AJ, Li X, Hall ME, Hall JE. Obesity, hypertension, and cardiac dysfunction. Circ Res. 2020;126(6):789–806.

70. Packer M. HFpEF is the substrate for stroke in obesity and diabetes independent of atrial fibrillation. JACC Heart Fail. 2020;8(1):35–42.

71. Lai W, Zhao X, Yu S, Mai Z, Zhou Y, Huang Z, et al. Chronic kidney disease increases risk of incident HFrEF following percutaneous coronary intervention. Front Cardiovasc Med. 2022;1(9): 856602.

72. Vijay K, Neuen BL, Lerma EV. Heart failure in patients with diabetes and chronic kidney disease: challenges and opportunities. Cardiorenal Med. 2021;12(1):1–10.

73. Overview | Chronic heart failure in adults: diagnosis and management | Guidance | NICE [Internet]. NICE; 2018. https://www.nice.org.uk/guidance/ng106. Accessed 17 Dec 2024.

74. D'Amario D, Rodolico D, Delvinioti A, Laborante R, Iacomini C, Masciocchi C, et al. Eligibility for the 4 pharmacological pillars in heart failure with reduced ejection fraction at discharge. J Am Heart Assoc. 2023;12(13): e029071.

75. Straw S, McGinlay M, Witte KK. Four pillars of heart failure: contemporary pharmacological therapy for heart failure with reduced ejection fraction. Open Heart. 2021;8(1): e001585.

76. BrJCardiol. Foundational drugs for HFrEF: the growing evidence for a rapid sequencing strategy [Internet]. https://bjcardio.co.uk/2022/01/foundational-drugs-for-hfref-the-growing-evidence-for-a-rapid-sequencing-strategy/. Accessed 30 Jan 2025.

77. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular disease in chronic kidney disease. Circulation. 2021;143(11):1157–72.

78. Krisanapan P, Sanpawithayakul K, Pattharanitima P, Thongprayoon C, Miao J, Mao MA, et al. Safety and efficacy of GLP-1 receptor agonists in type 2 diabetes mellitus with advanced and end-stage kidney disease: a systematic review and meta-analysis. Diseases. 2024;12(1):14.

79. Gansevoort R. A randomized controlled clinical trial to assess the effect of dapagliflozin on renal and cardiovascular outcomes in patients with severe chronic kidney disease [Internet]. clinicaltrials.gov; 2024 May. Report No.: NCT05374291. https://clinicaltrials.gov/study/NCT05374291. Accessed 21 Jan 2025.

80. Rossignol P. Spironolactone failed to reduce major adverse cardiac effects in patients with CKD on haemodialysis [Internet]. Medical Conferences. 2023. https://conferences.medicom-publishers.com/specialisation/nephrology/asn-2023/spironolactone-failed-to-reduce-major-adverse-cardiac-effects-in-patients-with-ckd-on-haemodialysis-2/. Accessed 27 Mar 2025.

81. Barton C, Sturge G, Harker R. The UK's changing population. 2024 Jul 16. https://commonslibrary.parliament.uk/the-uks-changing-population/. Accessed 17 Dec 2024.

82. Ijaz N, Buta B, Xue QL, Mohess DT, Bushan A, Tran H, et al. Interventions for frailty among older adults with cardiovascular disease: JACC state-of-the-art review. J Am Coll Cardiol. 2022;79(5):482–503.

83. Strain WD, Down S, Brown P, Puttanna A, Sinclair A. Diabetes and frailty: an expert consensus statement on the management of older adults with type 2 diabetes. Diabetes Ther. 2021;12(5):1227–47.

84. Clegg A, Young J. The frailty syndrome. Clin Med. 2011;11(1):72–5.

85. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes—ClinicalKey [Internet]. https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S0895435612000844. Accessed 29 Jan 2025.

86. Gnjidic D, Couteur DGL, Hilmer SN. Discontinuing drug treatments. BMJ. 2014;21(349): g7013.

87. Butt JH, Dewan P, Merkely B, Belohlávek J, Drożdż J, Kitakaze M, et al. Efficacy and safety of dapagliflozin according to frailty in heart failure with reduced ejection fraction: a post hoc analysis of the DAPA-HF trial. Ann Intern Med. 2022;175(6):820–30.

88. Reeves GR, Whellan DJ, Duncan P, O'Connor CM, Pastva AM, Eggebeen JD, et al. Rehabilitation therapy in older acute heart failure patients (REHAB-HF) trial: design and rationale. Am Heart J. 2017;185:130–9.

89. Goggins S. British Journal of Nursing. 2023. The importance of a comprehensive geriatric assessment for older people admitted onto a virtual ward. https://www.britishjournalofnursing.com/content/professional/the-importance-of-a-comprehensive-geriatric-assessment-for-older-people-admitted-onto-a-virtual-ward/. Accessed 31 Jan 2025.

90. Definition and diagnostic criteria of clinical obesity—ClinicalKey [Internet]. https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S2213858724003164. Accessed 30 Jan 2025.

91. National Chronic Kidney Disease Audit//National Report: Part 2 December 2017 [Internet]. https://www.lshtm.ac.uk/media/9951. Accessed 14 Dec 2023.

92. Scenario: Management | Management | Obesity | CKS | NICE [Internet]. https://cks.nice.org.uk/topics/obesity/management/management/. Accessed 17 Dec 2024.

93. NICE CG189. Obesity: identification, assessment and management. https://www.nice.org.uk/guidance/cg189. Accessed 3 Feb 2025.

94. Albury C, Strain WD, Brocq SL, Logue J, Lloyd C, Tahrani A. The importance of language in engagement between health-care professionals and people living with obesity: a joint consensus statement. Lancet Diabetes Endocrinol. 2020;8(5):447–55.

95. Let's Talk About Weight: A step-by-step guide to brief interventions with adults for health and care professionals [Internet]. https://assets.publishing.service.gov.uk/media/5b8d54d2e5274a0bd7d11928/weight_management_toolkit_Let_s_talk_about_weight.pdf. Accessed 17 Dec 2024.

96. Wang JY, Wang QW, Yang XY, Yang W, Li DR, Jin JY, et al. GLP-1 receptor agonists for the treatment of obesity: role as a promising approach. Front Endocrinol. 2023;1(14):1085799.

97. NICE NG246. Overview | Overweight and obesity management | Guidance | NICE [Internet]. NICE; 2025. https://www.nice.org.uk/guidance/ng246. Accessed 27 Mar 2025.

98. Besser REJ, Ng SM, Gregory JW, Dayan CM, Randell T, Barrett T. General population screening for childhood type 1 diabetes: is it time for a UK strategy? Arch Dis Child. 2022;107(9):790–5.

99. Statista [Internet]. Diabetes in England and Wales by type 2023/24. https://www.statista.com/statistics/386742/individuals-with-diabetes-by-type-in-england-and-wales/. Accessed 30 Jan 2025.

100. Escobar Vasco MA, Fantaye SH, Raghunathan S, Solis-Herrera C. The potential role of finerenone in patients with type 1 diabetes and chronic kidney disease. Diabetes Obes Metab. 2024;26(10):4135–46.

101. Type 1 diabetes | Treatment summaries | BNF content published by NICE [Internet]. https://bnf.nice.org.uk/treatment-summaries/type-1-diabetes/. Accessed 17 Dec 2024.

102. Taylor SI, Blau JE, Rother KI, Beitelshees AL. SGLT2 inhibitors as adjunctive therapy for type 1 diabetes: balancing benefits versus risks. Lancet Diabetes Endocrinol. 2019;7(12):949–58.

103. Kristófi R, Bodegard J, Norhammar A, Thuresson M, Nathanson D, Nyström T, et al. Cardiovascular and renal disease burden in type 1 compared with type 2 diabetes: a two-country nationwide observational study. Diabetes Care. 2021;44(5):1211–8.

104. Nwosu N. Obstructive sleep apnoea: important things to know. BDJ Stud. 2019;26(3):40–2.

105. Huang T, Lin BM, Stampfer MJ, Tworoger SS, Hu FB, Redline S. A population-based study of the bidirectional association between obstructive sleep apnea and type 2 diabetes in three prospective US cohorts. Diabetes Care. 2018;41(10):2111–9.

106. Liu M, Heizhati M, Li N, Lin M, Gan L, Zhu Q, et al. The relationship between obstructive sleep apnea and risk of renal impairment in patients with hypertension, a longitudinal study. Sleep Med. 2023;1(109):18–24.

107. Oscullo G, Torres G, Campos-Rodriguez F, Posadas T, Reina-González A, Sapiña-Beltrán E, et al. Resistant/refractory hypertension and sleep apnoea: current knowledge and future challenges. J Clin Med. 2019;8(11):1872.

108. Framnes SN, Arble DM. The bidirectional relationship between obstructive sleep apnea and metabolic disease. Front Endocrinol [Internet]. 2018. https://doi.org/10.3389/fendo.2018.00440/full.

109. Javaheri S, Barbe F, Campos-Rodriguez F, Dempsey JA, Khayat R, Javaheri S, et al. Sleep apnea: types, mechanisms, and clinical cardiovascular consequences. J Am Coll Cardiol. 2017;69(7):841–58.

110. Lin CH, Lurie RC, Lyons OD. Sleep apnea and chronic kidney disease: a state-of-the-art review. Chest. 2020;157(3):673–85.

111. NICE NG202. Overview | Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s | Guidance | NICE [Internet]. NICE; 2021. https://www.nice.org.uk/guidance/ng202. Accessed 21 Jan 2025.

112. Artificial Intelligence for Cardiovascular Care—Part 1: advances—ClinicalKey [Internet]. https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S0735109724067421. Accessed 17 Dec 2024.

113. Fayos De Arizón L, Viera ER, Pilco M, Perera A, De Maeztu G, Nicolau A, et al. Artificial intelligence: a new field of knowledge for nephrologists? Clin Kidney J. 2023;16(12):2314–26.

114. DeGroat W, Abdelhalim H, Peker E, Sheth N, Narayanan R, Zeeshan S, et al. Multimodal AI/ML for discovering novel biomarkers and predicting disease using multi-omics profiles of

patients with cardiovascular diseases. Sci Rep. 2024;3(14):26503.

115. Sun X, Yin Y, Yang Q, Huo T. Artificial intelligence in cardiovascular diseases: diagnostic and therapeutic perspectives. Eur J Med Res. 2023;28(1):242.

116. Chaudhuri S, Long A, Zhang H, Monaghan C, Larkin JW, Kotanko P, et al. Artificial intelligence enabled applications in kidney disease. Semin Dial. 2021;34(1):5–16.

117. Mohsen F, Al-Absi HRH, Yousri NA, El Hajj N, Shah Z. A scoping review of artificial intelligence-based methods for diabetes risk prediction. Npj Digit Med. 2023;6(1):1–15.

118. Mihan A, Pandey A, Van Spall HGC. Artificial intelligence bias in the prediction and detection of cardiovascular disease. Npj Cardiovasc Health. 2024;1(1):1–8.

119. Liang H, Zhang H, Wang J, Shao X, Wu S, Lyu S, et al. The application of artificial intelligence in atrial fibrillation patients: from detection to treatment. Rev Cardiovasc Med. 2024;25(7):257.

120. Yao L, Zhang H, Zhang M, Chen X, Zhang J, Huang J, et al. Application of artificial intelligence in renal disease. Clin EHealth. 2021;1(4):54–61.

121. Alowidi N, Ali R, Sadaqah M, Naemi FMA. Advancing kidney transplantation: a machine learning approach to enhance donor-recipient matching. Diagnostics. 2024;14(19):2119.

122. Ramalhete L, Almeida P, Ferreira R, Abade O, Teixeira C, Araújo R. Revolutionizing kidney transplantation: connecting machine learning and artificial intelligence with next-generation healthcare—from algorithms to allografts. BioMedInformatics. 2024;4(1):673–89.

123. Chan L, Nadkarni GN, Fleming F, McCullough JR, Connolly P, Mosoyan G, et al. Derivation and validation of a machine learning risk score using biomarker and electronic patient data to predict progression of diabetic kidney disease. Diabetologia. 2021;64(7):1504–15.

124. Jin X, Cai A, Xu T, Zhang X. Artificial intelligence biosensors for continuous glucose monitoring. Interdiscip Mater. 2023;2(2):290–307.

125. Muse ED, Topol EJ. Transforming the cardiometabolic disease landscape: multimodal AI-powered approaches in prevention and management. Cell Metab. 2024;36(4):670–83.

126. Bhaltadak V, Ghewade B, Yelne S. A comprehensive review on advancements in wearable technologies: revolutionizing cardiovascular medicine. Cureus. 2024;16(5):e61312.

127. Hughes A, Shandhi MMH, Master H, Dunn J, Brittain E. Wearable devices in cardiovascular medicine. Circ Res. 2023;132(5):652–70.

128. Aleppo G, Gal RL, Raghinaru D, Kruger D, Beck RW, Bergenstal RM, et al. Comprehensive telehealth model to support diabetes self-management. JAMA Netw Open. 2023;6(10): e2336876.

129. de Almeida OAE, de Lima MEF, Santos WS, Silva BLM. Telehealth strategies in the care of people with chronic kidney disease: integrative review. Rev Lat Am Enfermagem. 2024;31:e4050.

130. Ellis T, Kwon AJ, Hong MY. The effectiveness of telehealth intervention on chronic kidney disease management in adults: a systematic review. Mayo Clin Proc Digit Health. 2025;3(1): 100181.

131. Jackson TN, Sreedhara M, Bostic M, Spafford M, Popat S, Lowe Beasley K, et al. Telehealth use to address cardiovascular disease and hypertension in the united states: a systematic review and meta-analysis, 2011–2021. Telemed Rep. 2023;4(1):67–86.

132. Kobe EA, McVeigh T, Hameed I, Fudim M. Heart failure remote monitoring: a review and implementation how-to. J Clin Med. 2023;12(19):6200.

133. OpenSAFELY: About OpenSAFELY [Internet]. https://www.opensafely.org/about/. Accessed 22 Jan 2025

134. CVDPREVENT [Internet]. CVDPREVENT. https://www.cvdprevent.nhs.uk. Accessed 22 Jan 2025

135. Simeri A, Pezzi G, Arena R, Papalia G, Szili-Torok T, Greco R, et al. Artificial intelligence in chronic kidney diseases: methodology and potential applications. Int Urol Nephrol [Internet]. 2024. https://doi.org/10.1007/s11255-024-04165-8.

136. Jain SS, Elias P, Poterucha T, Randazzo M, Lopez Jimenez F, Khera R, et al. Artificial intelligence in cardiovascular care—part 2: applications. J Am Coll Cardiol. 2024;83(24):2487–96.

137. Sauerbrei A, Kerasidou A, Lucivero F, Hallowell N. The impact of artificial intelligence on the person-centred, doctor-patient relationship: some problems and solutions. BMC Med Inform Decis Mak. 2023;20(23):73.

138. GOV.UK [Internet]. Impact of AI on the regulation of medical products. https://www.gov.uk/government/publications/impact-of-ai-on-the-regulation-of-medical-products. Accessed 21 Jan 2025.

139. Takhar EA Julia Gillert, Jaspreet. Healthcare & Life Sciences Blog. 2024. MHRA launches AI Airlock to address challenges for regulating medical devices that use Artificial Intelligence. https://healthcarelifesciences.bakermckenzie.com/2024/05/10/mhra-launches-ai-airlock-to-address-challenges-for-regulating-medical-devices-that-use-artificial-intelligence/. Accessed 21 Jan 2025.