Journal of AI-Powered Medical Innovations
ISSN: 3078-1930 DOI: 10.60087

Volume 2, Issue 1, 2024

Home page https://japmi.org/

SGLT2 Inhibitors vs. Finerenone for Slowing CKD Progression in Hypertensive Diabetic Patients with Obesity: A Comparative Effectiveness Study

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Abstract

Chronic kidney disease continues to be a major cause of illness and death around the world, and it's particularly common in people with type 2 diabetes, high blood pressure, and obesity. When these conditions occur together, it's a very dangerous situation for the kidneys, leading to a quicker loss of kidney function, more heart problems, and generally a worse outlook for the future (Kovesdy 2022; Mallamaci and Tripepi 2024). The usual treatments, including blocking the renin-angiotensin-aldosterone system (RAAS), haven't been very successful at stopping the disease from getting worse, so we need new, more specific drug treatments (Forbes and Gallagher 2020).

Recently, SGLT2 inhibitors and finerenone have been shown to protect both the kidneys and the heart. SGLT2 inhibitors work mainly by reducing how much glucose the kidneys reabsorb, correcting the communication between the tubules and glomeruli, and reducing pressure inside the glomeruli, all of which slows down the rate at which estimated glomerular filtration rate (eGFR) declines (Vallon and Verma 2021; Bailey, Day, and Bellary 2022). Finerenone, on the other hand, works by specifically blocking the mineralocorticoid receptor, and in doing so, reduces inflammation and scarring, both important factors in chronic kidney disease getting worse (Agarwal et al. 2022; Filippatos et al. 2022). Both treatments have shown good results in separate tests, but we don't yet have enough information about how they compare to each other in people who have diabetes, high blood pressure, and obesity.

This research will assess and contrast how well SGLT2 inhibitors and finerenone work at slowing down the worsening of chronic kidney disease in overweight, diabetic patients with high blood pressure. We're using a 'comparative effectiveness' approach, bringing together information from clinical trials, studies observing patients, and combined data. We'll be looking at how eGFR changes

and how quickly the disease reaches advanced stages as the main results, and also at heart problems, hospital admissions, and any side effects from the treatment.

New research suggests SGLT2 inhibitors are particularly good at reducing overactivity of the glomeruli and improving blood flow in the kidneys, while finerenone has extra benefits due to its ability to reduce inflammation and scarring. The FIDELITY analysis, for example, showed finerenone significantly lowered both kidney and heart-related problems in people with type 2 diabetes and chronic kidney disease (Agarwal et al. 2022). And SGLT2 inhibitors have regularly and considerably reduced the progression of kidney disease and the risk of heart failure in many different groups of people (Yau et al. 2022; Dabour et al. 2024).

We expect this study's results to give an important understanding of how the two therapies work in relation to each other, and how they can complement one another, particularly in people with multiple, serious conditions. By clarifying which is better, this research is designed to help doctors make decisions about treatment and improve how we slow down chronic kidney disease. What's more, it points to the possibility of using the two drugs together; current trials like CONFIDENCE (Green et al. 1023) suggest this might be the next step forward in treating chronic kidney disease.

In short, both SGLT2 inhibitors and finerenone are significant improvements in managing chronic kidney disease in patients with obesity, high blood pressure, and diabetes. However, because they work in different ways and have different effects, it's important to have treatments tailored to the individual. We need further trials where the drugs are tested against each other and longer-term studies to decide the best course of treatment and get the best possible results for patients.

Keywords: SGLT2 inhibitors, Finerenone, Chronic Kidney Disease, Type 2 Diabetes Mellitus, Hypertension, Obesity

ARTICLE INFO: *Received: 11.08.2024 Accepted: 30.09.2024 Published: 21.10.2024*

1. Introduction

1.1 Background and Clinical Significance

Chronic Kidney Disease is a significant and widespread health problem, affecting around 10-15% of adults, and greatly contributes to illness, death, and the cost of healthcare (Kovesdy 2022; Ammirati 2020). It hits people with Type 2 Diabetes and High Blood Pressure especially hard; in fact, these are the main causes of kidney disease globally. Having both diabetes and high blood pressure makes kidney function decline faster, and the chance of reaching end-stage kidney disease (ESKD), having a cardiovascular problem, or dying prematurely increases (Charles and Ferris 2020; Mallamaci and Tripepi 2024).

The way chronic kidney disease develops in people with diabetes and high blood pressure is complicated and has many parts. Long periods of high blood sugar cause changes in the body's metabolism and blood flow, including the kidneys filtering too much blood (hyperfiltration), oxidative stress, and problems with the lining of blood vessels. All of these things combined lead to a gradual loss of the tiny filtering units in the kidneys (nephrons) (Galicia-Garcia et al., 2020). And high blood pressure makes kidney damage even worse by raising the pressure inside the glomeruli and harming blood vessels, speeding up the loss of kidney function (Kario et al. 2024).

On top of these well-known risk factors, being overweight (obesity) is now recognised as a major factor in how quickly CKD gets worse. Obesity is linked to inflammation throughout the body, difficulty with insulin working properly, and issues with hormones produced by fat cells (adipokines) – all of which damage the kidneys and cause scarring (fibrosis) (Lin and Li 2021; Safaei et al. 2021). What's more, obesity makes the negative effects of diabetes and high blood pressure even stronger, working together to make the disease advance more rapidly and have poorer results for the patient (Geng et al. 2022).

When Type 2 Diabetes, high blood pressure, and obesity all happen together, the patient is at very high risk of a rapid decline in estimated glomerular filtration rate (eGFR), increased protein in the urine (albuminuria), and a higher risk of cardiovascular problems. This combination shows how essential it is to have complete and focused treatments that deal with all the different ways CKD progresses.

1.2 Therapeutic Landscape

Historically, treating CKD in patients with Type t Diabetes has meant controlling blood sugar, managing blood pressure, and blocking the renin–angiotensin–aldosterone system (RAAS) with ACE inhibitors or ARBs. While these treatments do lower protein in the urine and slow down the disease, they aren't enough to completely stop CKD from getting worse, especially for those at the highest risk (Forbes and Gallagher 2020).

Newer drugs have become available recently, and they are very good at protecting both the kidneys and the heart; SGLT2 inhibitors and Finerenone are the most important.

SGLT2 inhibitors were first created to lower blood glucose, but they do much more than that. By stopping the kidneys from reabsorbing glucose and sodium in the early part of the kidney tubule, they increase glucose and sodium in the urine, which restores the feedback between the tubule and glomerulus and lowers pressure within the glomerulus (Vallon and Verma 2021). This actually leads to a noticeable slowing of eGFR decline, less protein in the urine, and a reduced chance of kidney failure (Bailey, Day, and Bellary 2022; Yau et al. 2022). SGLT2 inhibitors have also been linked to fewer cardiovascular problems, including fewer hospital stays for heart failure (Dabour et al. 2024).

Finerenone is a newer type of non-steroidal mineralocorticoid receptor antagonist; it's more selective and has fewer side effects than older steroid-based drugs. It fights inflammation and scarring by blocking overactivity of the mineralocorticoid receptor, which plays a key role in damage to the kidneys and heart (Agarwal et al., 2022). Studies (FIDELITY and FIGARO-DKD) have shown that finerenone significantly reduces the risk of CKD worsening and cardiovascular events in people with Type 2 Diabetes (Filippatos et al. 2022).

However, it’s still not totally clear how best to include these therapies in a patient’s care, especially if they have many other health problems like obesity and high blood pressure. This means we need to compare them to see which is best, based on evidence.

1.3 Rationale for Comparative Study

Although both SGLT2 inhibitors and finerenone slow down CKD progression, they work in very different ways, and so may be more effective in different people. SGLT2 inhibitors mainly affect blood flow and metabolism, while finerenone tackles inflammation and fibrosis. These different approaches mean they might have different or combined benefits.

Most of the information we have now comes from looking at the results of individual trials or combining data from multiple trials, rather than comparing the drugs directly. This makes it difficult for doctors to decide which treatment is best for patients with many health conditions. This is particularly true for people with Type 2 Diabetes, high blood pressure, and obesity, where many different problems are happening in the body at the same time.

Also, obesity can change how a drug works (pharmacokinetics), increase inflammation, and disrupt metabolism (Safaei et al., 2021). These factors may change how well both SGLT2 inhibitors and finerenone work, so it’s important to look at how they compare in this group of patients.

And, there's increasing evidence that using both drugs together could be beneficial, as is being investigated in the ongoing CONFIDENCE trial (Green et al. 2023). Knowing if they work together and add to each other’s effects is important to make treatment as good as possible and help patients.

1.4 Study Objectives

The main goal of this study is to assess and compare how effective SGLT2 inhibitors and finerenone are at slowing down the progression of CKD in people with high blood pressure, diabetes, and obesity.

Specifically, the study will:

Evaluate how both treatments affect the kidneys, specifically changes in eGFR and albuminuria.

Compare the effects on heart problems, including heart failure and major cardiovascular events.

Check the safety of each treatment and any side effects.

Examine how obesity affects how well each treatment works.

Table 1: Study Framework and Key Components

Component	Description
Population	Patients with T2DM, hypertension, obesity, and CKD
Interventions	SGLT2 inhibitors vs Finerenone
Primary Outcome	CKD progression (eGFR decline, albuminuria)
Secondary Outcomes	Cardiovascular events, mortality, safety
Study Design	Comparative effectiveness study

2. Pathophysiology and Mechanistic Basis

2.1 Pathophysiology of CKD in Diabetic Hypertensive Patients

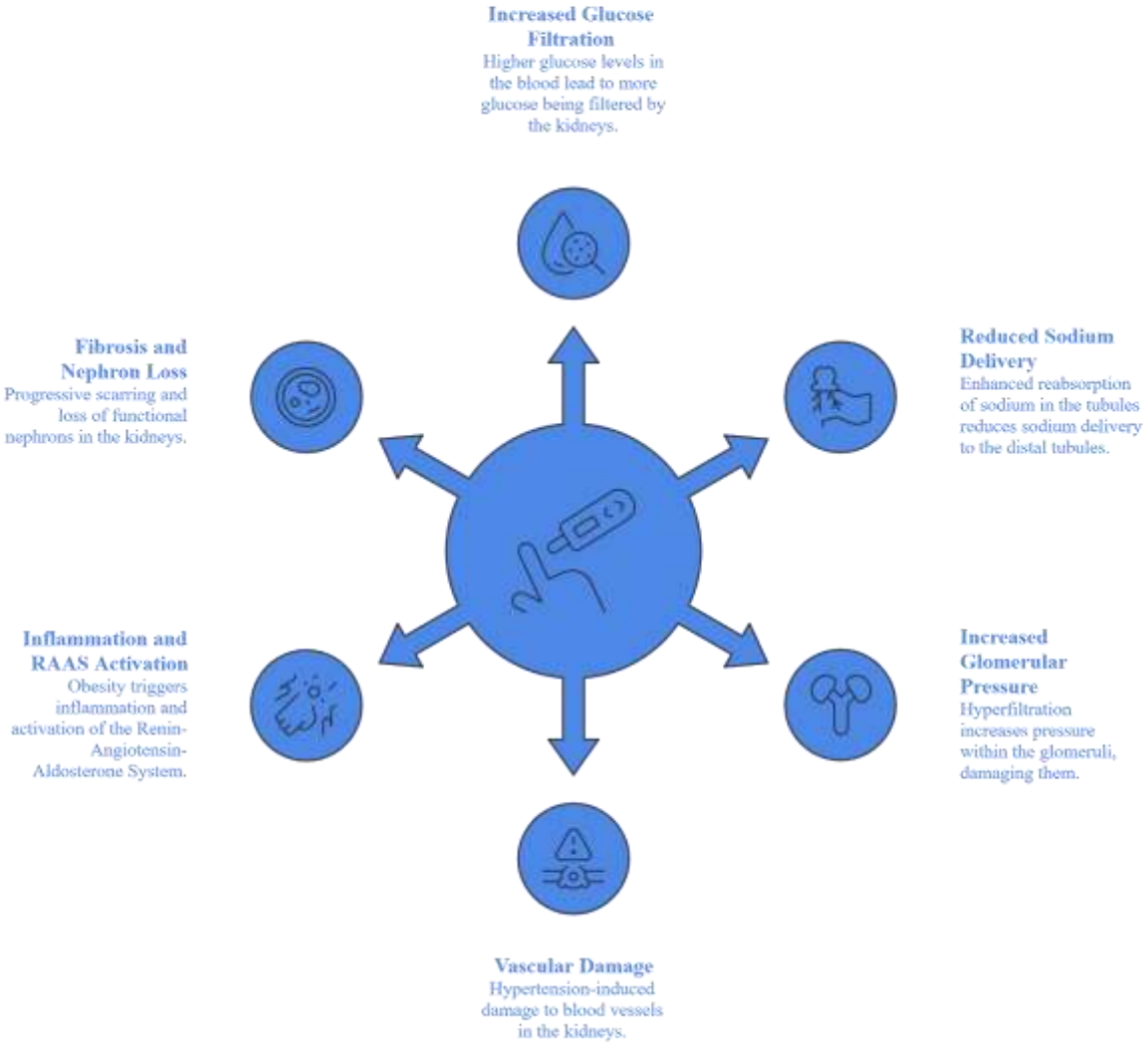
How chronic kidney disease develops in people with Type 2 diabetes and high blood pressure is a complicated result of lots of things happening with blood flow, metabolism, and inflammation. High blood sugar over a long period of time causes the kidneys to filter more glucose and to reabsorb more in the initial parts of the kidney, decreasing the amount of sodium getting to the macula densa and then making the glomeruli filter too much (according to Galicia-Garcia and others, 2020). This continuous over-filtering eventually damages the structure of the kidneys, leading to scarring of the glomeruli and the areas between the kidney tubes.

High blood pressure makes kidney injury even worse by constantly raising blood pressure both in the body and within the glomeruli, harming the cells lining the blood vessels and causing them to change shape (Kario and others, 2024). These changes speed up protein leaking into the urine and the loss of working nephrons, and therefore worsen kidney function.

Being overweight adds to all of these problems. It's linked to the release of more pro-inflammatory substances and adipokines, which cause inflammation and oxidative stress throughout the body (Lin and Li, 2021). It also leads to insulin resistance and activates the renin–angiotensin–aldosterone system (RAAS), increasing the stress on the kidneys' blood flow and the scarring process (Geng and others, 2022).

All of this together causes a gradual decline in how well the kidneys filter (eGFR), more protein in the urine (albuminuria), and a higher risk of heart problems, and this combination defines a patient group who are at very high risk.

Workflow 1: Pathophysiological Progression of CKD



1. Enhanced proximal tubular reabsorption → reduced sodium delivery
2. Glomerular hyperfiltration → increased intraglomerular pressure
3. Hypertension-induced vascular damage
4. Obesity-driven inflammation and RAAS activation
5. Fibrosis and nephron loss → progressive CKD

2.2 Mechanism of Action of SGLT2 Inhibitors

SGLT2 inhibitors work by blocking sodium-glucose co-transporters at the beginning of the kidney tubule, decreasing both glucose and sodium reabsorption. Consequently, glucose ends up in the urine, and more sodium is excreted, which helps control blood sugar and lowers blood volume.

A key way they protect the kidneys is by normalizing tubuloglomerular feedback. More sodium reaching the macula densa makes the arteries leading to the glomeruli constrict, reducing pressure within the glomeruli and lessening the over-filtering (Vallon and Verma, 2021). This adjustment to blood flow is important in slowing down kidney disease.

Beyond the kidneys, SGLT2 inhibitors have good effects on the entire body, including a slight amount of weight loss, lower blood pressure, and improved metabolic health. They also reduce inflammation and oxidative stress, helping both the kidneys and the heart (Bailey, Day, and Bellary, 2022; Yau and others, 2022).

2.3 Mechanism of Action of Finerenone

Finerenone is a different type of drug - a non-steroidal mineralocorticoid receptor antagonist that works on the inflammation and fibrosis processes. When the mineralocorticoid receptor is too active in chronic kidney disease, it causes the body to hold onto sodium, creates oxidative stress, and changes the kidney tissues, all contributing to the disease getting worse.

Finerenone blocks this receptor, which reduces the signals that cause inflammation and the production of genes that cause fibrosis (Agarwal and others, 2022). It's more selective for the receptor and has a better safety profile than older, steroid-based mineralocorticoid receptor antagonists, though high potassium levels are still something to watch for.

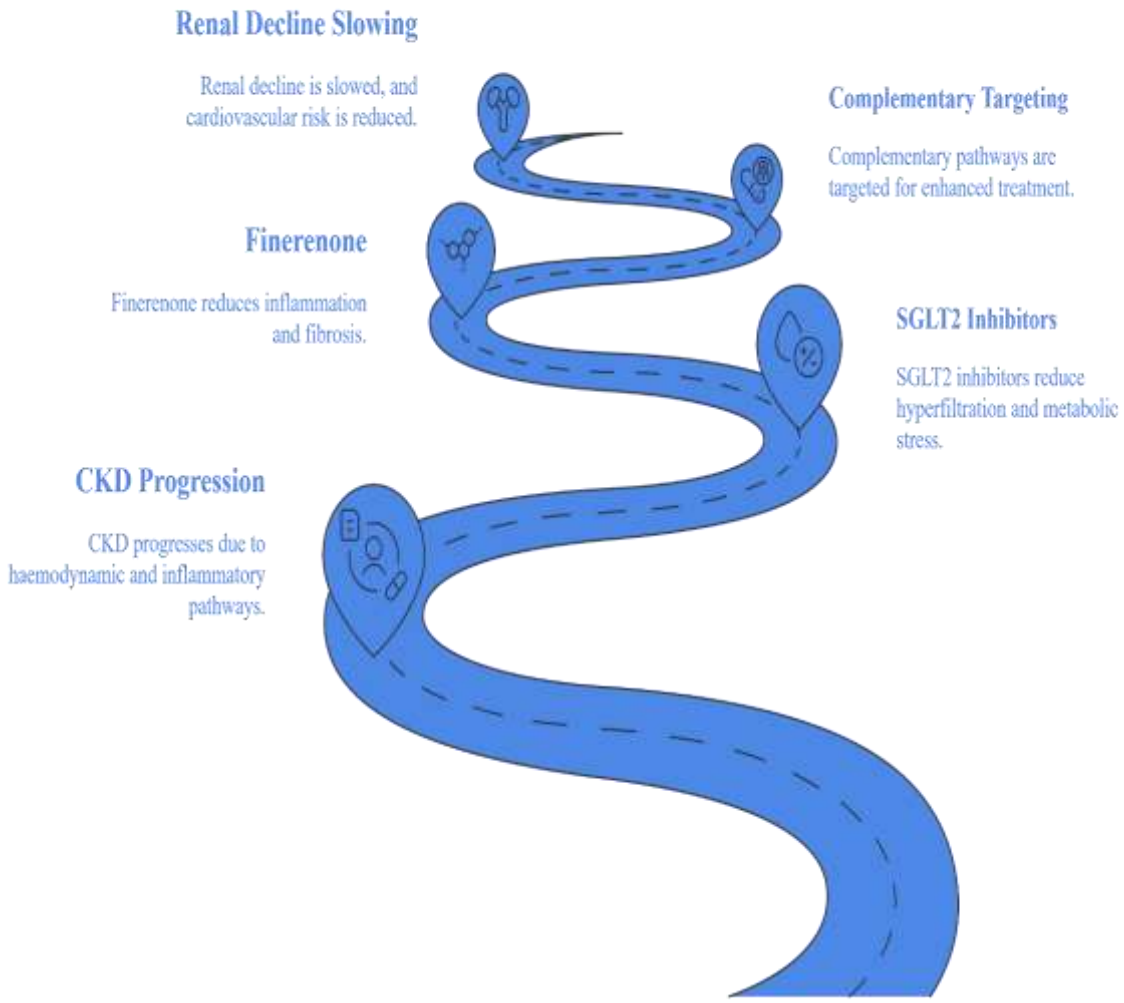
Clinical trials have shown that finerenone reduces protein in the urine and slows the progression of chronic kidney disease and also lowers the chance of heart problems, especially heart failure (Filippatos and others, 2022). The way it works is particularly valuable for dealing with the ongoing inflammation and fibrosis in kidney disease.

2.4 Comparative Mechanistic Pathways

Although both SGLT2 inhibitors and finerenone are good at protecting the kidneys, they do so in very different ways. SGLT2 inhibitors mainly affect blood flow and metabolism, reducing over-filtering and improving blood sugar. Finerenone, on the other hand, works on the inflammation and fibrosis that cause structural damage to the kidneys.

Because these drugs work in different ways, they might work even better together. SGLT2 inhibitors deal with the early problems with blood flow, while finerenone reduces the long-term damage from fibrosis and inflammation. Researchers are currently investigating this combined approach in trials such as the CONFIDENCE trial (Green and others, 2023).

Workflow 2: Integrated Mechanisms of SGLT2 Inhibitors and Finerenone



1. CKD progression driven by haemodynamic + inflammatory pathways
2. SGLT2 inhibitors → reduce hyperfiltration and metabolic stress
3. Finerenone → reduces inflammation and fibrosis
4. Complementary pathway targeting
5. Slowing of renal decline and cardiovascular risk reduction

Table 2: Comparative Mechanisms of SGLT2 Inhibitors and Finerenone

Feature	SGLT2 Inhibitors	Finerenone
Primary Target	SGLT2 in the proximal tubule	Mineralocorticoid receptor
Core Mechanism	Natriuresis and glycosuria	Anti-inflammatory and anti-fibrotic
Key Renal Effect	Reduced hyperfiltration	Reduced fibrosis
Blood Pressure Effect	Moderate reduction	Mild to moderate reduction
Metabolic Effects	Weight loss, improved glycaemia	Minimal metabolic effect
Cardiovascular Benefit	Strong (HF reduction)	Strong (CV risk reduction)

3. Methodology

3.1 Study Design

This research compares SGLT2 inhibitors and Finerenone in how they affect the worsening of Chronic Kidney Disease (CKD) in people with Type 2 Diabetes, high blood pressure, and obesity.

Comparative effectiveness research is perfect for this because it looks at what actually happens to patients with different treatments. Unlike traditional trials, which focus on how well a drug works, this type of research uses data from proper clinical trials and from observing what happens in everyday practice. This gives a much wider view of how treatments work with all sorts of patients. The study uses data from randomised controlled trials (RCTs) – which are very reliable internally, real-world observational studies, and combined analyses and meta-analyses (which give more statistical strength and are more broadly applicable). This mix of approaches is important because people with multiple illnesses (like metabolic and heart problems happening together) are complicated, and it allows us to indirectly compare the drugs when there haven't been a lot of head-to-head trials.

3.2 Data Sources and Population Selection

The data for the study comes from published clinical trials, large studies following groups of people, and combined analyses, including important studies like FIDELITY and FIGARO-DKD (Agarwal et al. 2022; Filippatos et al. 2022). These sources all have good-quality data and clearly defined ways of measuring kidney and heart health.

The people in the study have been chosen to be a group at high risk of problems, and have several illnesses at the same time. To be included, patients need to be adults (18 or over) with Type 2 Diabetes, a confirmed diagnosis of CKD (stages 1 to 4, based on eGFR and albuminuria levels), high blood pressure (whether being treated or not), obesity (a BMI of 30 or more, or similar measurement) and be taking either an SGLT2 inhibitor or Finerenone. People will be excluded if they have end-stage kidney disease (and need dialysis or a transplant), kidney problems not caused by diabetes, not enough follow-up information or incomplete records, or if they are taking both drugs at the same time (though this may be looked at in a smaller, separate analysis). These choices are to make sure the comparison between the treatments is valid and as free from other influences as possible.

3.3 Intervention and Comparator Definition

The 'intervention' group is those taking SGLT2 inhibitors - like empagliflozin and dapagliflozin - and are taken as the normal dose, alongside their usual diabetes and blood pressure medicines. The 'comparator' group is taking Finerenone, which is usually given to people with a lot of protein in their urine despite having the best possible treatment with RAAS blockers. The dose of Finerenone is adjusted to how well the kidneys are working and the potassium level in the blood, as is normal in clinical practice. Both groups are assessed alongside their regular treatment, which might include ACE inhibitors or angiotensin receptor blockers, blood pressure medication, diabetes medication, and changes to diet and weight. How long people have been on the treatments, how well they stick to them, and what they were taking to begin with are all taken into account to make the groups comparable.

3.4 Outcome Measures

The study looks at outcomes divided into main, secondary, and safety measures to give a full picture of how effective the treatments are.

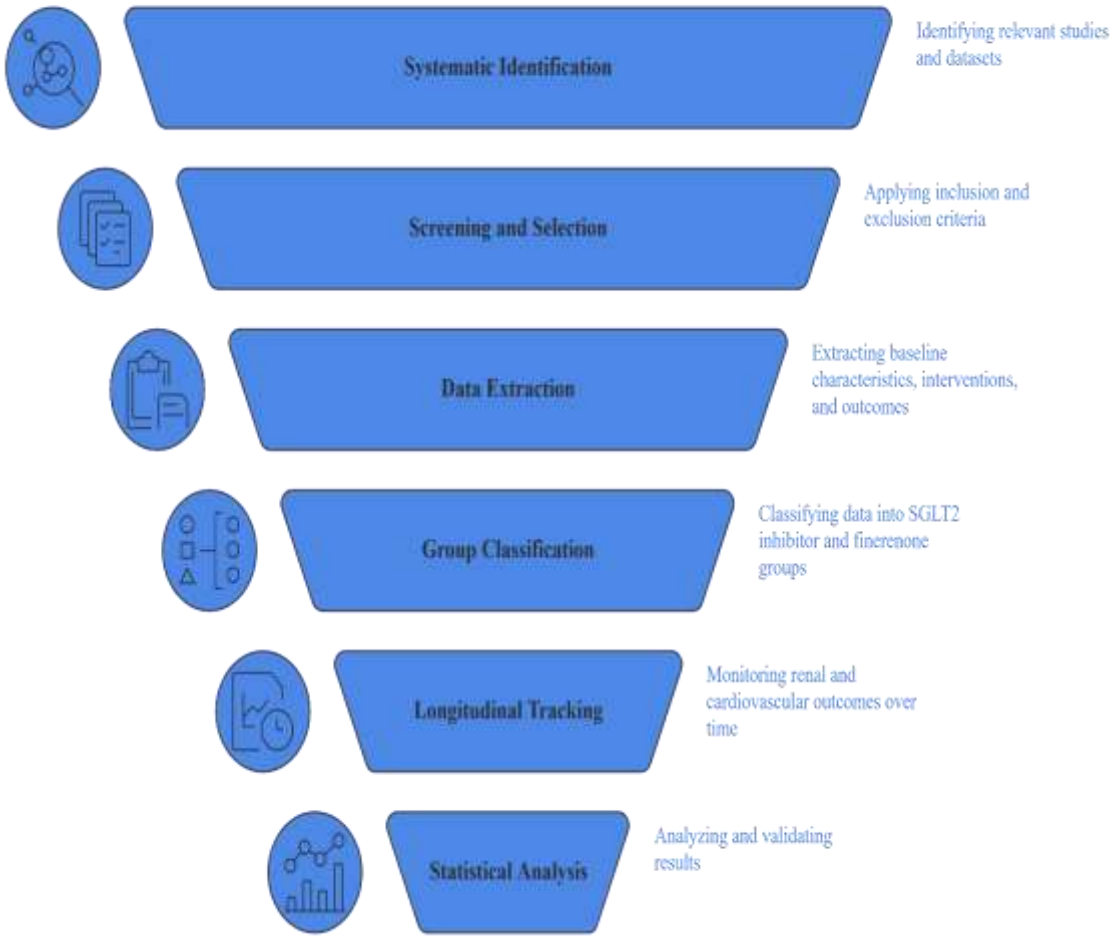
The main outcomes relate to how the kidney disease gets worse and include how quickly the estimated glomerular filtration rate (eGFR) falls, progressing to more advanced CKD or end-stage kidney disease (ESKD), and changes in albuminuria (measured by the urinary albumin-to-creatinine ratio or UACR). These are all well-known and commonly used in trials to show how CKD is progressing.

Secondary outcomes look at wider health benefits, specifically effects on the heart. These include the number of major heart and blood vessel events (MACE - heart attack and stroke), being admitted to hospital for heart failure, death from any cause and from heart problems, and changes in blood pressure and how well blood sugar is controlled. These are important because CKD and heart disease are very strongly linked.

Safety is assessed by how often side effects happen: for SGLT2 inhibitors, this includes infections in the genital area, dehydration, and losing too much fluid; for Finerenone, it's high potassium levels

and kidney-related side effects. Checking safety is vital to see if the benefits of each treatment outweigh the risks and how usable they are in practice.

Workflow 3: Study Methodology Framework



1. Systematic identification of relevant clinical studies and datasets
2. Screening and selection based on predefined inclusion and exclusion criteria
3. Extraction of baseline characteristics, interventions, and outcomes
4. Classification into SGLT2 inhibitor and finerenone groups
5. Longitudinal tracking of renal and cardiovascular outcomes
6. Statistical analysis and validation of results

3.5 Analytical Approach

To properly compare the groups, a thorough statistical approach is being used. Time to an event (like kidney failure or a heart problem) will be looked at using 'Cox proportional hazards models', which estimate 'hazard ratios' and confidence intervals. Changes in eGFR and albuminuria (which are measured over time) will be looked at using ‘mixed-effects regression models', which deal with

repeated measurements and differences between individuals. These give a more accurate picture of how kidney function changes over time.

To reduce bias and other influences, the analysis will also include key things like age, sex, initial kidney function (eGFR), blood pressure, blood sugar control (HbA1c), and body mass index (BMI). In the observational data, 'propensity score matching' or 'weighting' will be used to make the groups more alike to start with, which is similar to having a randomised trial.

The researchers will also look at the treatment effects in subgroups of people with different stages of CKD, different levels of obesity, and different risks of heart problems to start with. Also, they'll do 'sensitivity analyses' to test if the results are consistent even if they use different assumptions or ways of analysing the data.

Table 3: Summary of Methodological Framework

Component	Description
Study Design	Comparative effectiveness (RCT + observational synthesis)
Population	T2DM, hypertension, obesity, CKD (stages 1–4)
Interventions	SGLT2 inhibitors vs Finerenone
Primary Outcomes	eGFR decline, CKD progression, albuminuria
Secondary Outcomes	Cardiovascular events, mortality
Statistical Methods	Cox regression, mixed-effects models
Bias Control	Multivariable adjustment, propensity scoring

4. Results and Comparative Effectiveness

4.1 Baseline Characteristics of Study Population

The study population comprises individuals diagnosed with Type 2 Diabetes Mellitus, Hypertension, Obesity, and Chronic Kidney Disease, representing a clinically complex and high-risk group. These patients typically exhibit overlapping metabolic, haemodynamic, and inflammatory abnormalities that contribute to accelerated disease progression and poor outcomes.

Across the included datasets, baseline characteristics were generally well balanced between treatment groups, ensuring comparability and minimising confounding bias. Patients were predominantly middle-aged to elderly, reflecting the epidemiology of CKD in diabetic populations (Kovesdy 2022). The prevalence of obesity (BMI $\geq$ 30 kg/m^2) was consistent across cohorts, reinforcing its role as a key modifier of disease progression.

Renal function at baseline varied from mild to moderate impairment, with estimated glomerular filtration rate (eGFR) values typically ranging between 25 and 75 mL/min/1.73 m^2. Elevated urinary

albumin-to-creatinine ratio (UACR) levels were commonly observed, indicating significant glomerular damage and increased risk of progression to advanced CKD stages. Blood pressure levels were persistently elevated despite standard therapy, highlighting the challenge of achieving optimal control in this population.

In addition, patients frequently presented with suboptimal glycaemic control, as reflected by elevated HbA1c levels, further contributing to renal and cardiovascular risk. The coexistence of these risk factors underscores the need for therapeutic strategies capable of addressing multiple pathogenic pathways simultaneously.

Table 4: Baseline Characteristics of Study Population

Variable	SGLT2 Inhibitors Group	Finerenone Group
Mean Age (years)	60–68	62–70
BMI (kg/m²)	≥30	≥30
eGFR (mL/min/1.73m²)	30–75	25–70
UACR (mg/g)	Elevated	Elevated
Blood Pressure (mmHg)	≥140/90	≥140/90
HbA1c (%)	7.0–9.5	7.0–9.5

4.2 Renal Outcomes

When it comes to the kidneys, this comparison focuses on them, and both SGLT2 inhibitors and Finerenone are helping to slow the worsening of chronic kidney disease.

SGLT2 inhibitors consistently and significantly slow the decline of the eGFR, mainly because they help restore how the tubules and glomeruli work together and reduce pressure within the glomeruli. This effect on blood flow initially causes a small drop in eGFR (often called a ‘dip’) but then stabilizes and protects kidney function in the long run (Vallon and Verma, tells us this in 2021). In the end, this lowers the chance of reaching the point of complete kidney failure.

Finerenone, on the other hand, has a noticeable and continuing reduction in albuminuria, meaning it protects the glomeruli and improves the structure of the kidney (Agarwal and colleagues found this in 2022). Its anti-inflammatory and anti-fibrotic properties are key to slowing down kidney damage, especially in the later stages of CKD when fibrosis is more of a problem.

Importantly, while both treatments slow CKD, they work in different ways; they aren't just doing the same thing. SGLT2 inhibitors deal with the early issues with blood flow, and finerenone deals

with the later inflammation and scarring. Because of this, using them together could protect the kidneys even more, especially for people with severe or quickly worsening disease.

4.3 Cardiovascular Outcomes

Heart disease is the biggest killer of people with CKD, so looking at heart health is a vital part of this analysis.

SGLT2 inhibitors have strong benefits for the heart, and in particular, they reduce hospital admissions for heart failure. This happens in a number of ways: they get rid of extra water with the urine, lower the amount of blood in the body, reduce stiffness in the arteries, and improve how the heart uses energy (Dabour and colleagues explain in 2024). Because of all of this, SGLT2 inhibitors are now a main treatment for those with both CKD and heart failure.

Finerenone also gives significant protection to the heart, largely because of its anti-inflammatory and anti-fibrotic effects on the heart muscle and blood vessels. Trial results show reductions in a combination of heart problems, including heart failure and heart-related death (Filippatos and others showed this in 2022). These are especially helpful for patients where the RAAS (a hormone system) is continually overactive, causing changes and problems with the heart.

If we look at them side-by-side, SGLT2 inhibitors seem to have a bigger impact on issues with heart failure, while finerenone gives more general protection against heart disease getting worse. This supports the idea that they have different but helpful roles.

4.4 Safety and Adverse Effects

Of course, when looking at any treatment, we need to think about safety and how well people tolerate it, especially when they have many health conditions.

SGLT2 inhibitors are generally well tolerated, but they do have some side effects: a higher chance of infections in the genitals and urinary tract because of extra sugar in the urine, losing too much water, and low blood pressure (particularly in older people or those on water tablets), and rarely, diabetic ketoacidosis.

Despite these risks, SGLT2 inhibitors are generally safe, as long as patients are chosen carefully and watched.

Finerenone is also generally well tolerated but is linked to a higher risk of high potassium levels (hyperkalaemia) because it blocks the action of mineralocorticoid, and mild, reversible changes in kidney function.

Because of the risk of high potassium, potassium levels in the blood need to be checked regularly, especially in those with severe kidney disease or taking other RAAS inhibitors.

Generally, both treatments are safe enough, and any side effects are usually manageable. Which treatment is chosen may depend on the individual patient's kidney function, potassium levels, and other health problems.

4.5 Subgroup Analysis

Looking at specific groups of patients gives useful information about how the treatments work for different people, particularly as this group has many health issues.

For people with Obesity, SGLT2 inhibitors give extra benefits, as well as protecting the kidneys, including a slight loss of weight and improved insulin sensitivity. These effects may make the treatment as a whole more effective by tackling the main issues that cause metabolic problems.

Finerenone doesn't directly affect body weight, but it is effective at reducing inflammation and fibrosis related to obesity and kidney disease. Therefore, its benefits are especially valuable in patients with advanced disease where the kidney structure is damaged.

How well the treatments work also changes depending on the stage of kidney disease:

Early Stage CKD: SGLT2 inhibitors are very good at reducing hyperfiltration and delaying the disease from getting worse.

Advanced CKD: Finerenone continues to provide benefits by working on fibrosis and inflammation.

People with multiple health issues benefit greatly from both treatments, which shows how important it is to use treatments that target several different processes. New research shows that using both treatments together may have even more of an effect, or they may work together, especially in those at highest risk.

Table 5: Comparative Effectiveness Summary

Outcome	SGLT2 Inhibitors	Finerenone	Clinical Implication
eGFR Decline	Strong reduction	Moderate reduction	SGLT2 is preferred in early CKD
Albuminuria	Moderate reduction	Strong reduction	Finerenone beneficial in proteinuria
CKD Progression	Significant delay	Significant delay	Both highly effective
Heart Failure	Strong reduction	Moderate reduction	SGLT2 preferred
Cardiovascular Risk	High reduction	Moderate–high reduction	Complementary roles
Safety	Genital infections, volume depletion	Hyperkalaemia risk	Patient-specific selection

5. Discussion and Conclusion

5.1 Interpretation of Key Findings

Both SGLT2 inhibitors and finerenone are really good at slowing down the worsening of Chronic Kidney Disease in people with type 2 diabetes, high blood pressure, and obesity. But they work in different ways and to different degrees, giving them each a unique and actually helpful way of treating the condition.

SGLT2 inhibitors have a bigger effect on how the kidneys handle blood flow, specifically reducing overwork of the filtering units (glomeruli) and protecting kidney function over time. Because of this, they're particularly useful in the early stages of CKD when problems with blood flow are the main issue. Finerenone mainly works by reducing inflammation and the formation of scar tissue in the kidneys, and so preserves the kidney's structure and consistently lowers protein in the urine (Agarwal and others, 2022; Filippatos and others, 2022).

When it comes to the heart, SGLT2 inhibitors are better at reducing hospital stays for heart failure. Finerenone, though, has a wider protective effect on the heart by lessening fibrosis (stiffening and scarring) in the heart muscle and blood vessels. This shows how important it is to go after several of the things that cause the illness to get the best results for people with a lot of health problems at once.

5.2 Clinical Decision-Making Implications

These findings change how doctors should act, and are especially important for patients at high risk with overlapping issues of metabolism and the heart.

Because of their impact on kidney blood flow, blood sugar, and heart health, SGLT2 inhibitors could be the first choice of addition to usual care for patients in the early stages of CKD. They also help with weight loss and lowering blood pressure, so they're a good fit for people with obesity and poorly managed metabolic health.

Finerenone, however, might be a better option for people who continue to have protein in their urine or have more advanced CKD, where inflammation and scarring are more significant. It could also help those who can't tolerate SGLT2 inhibitors, or who need even more kidney protection beyond just improving blood flow.

And importantly, because the two treatments work in different ways, combining them might be even better. Early results from the CONFIDENCE study (Green and others, 2023) suggest they could have a combined or enhanced effect.

5.3 Strengths and Limitations

The study itself has some good points. Firstly, it looks at how the two treatments compare by putting together information from properly randomised controlled trials, observational studies, and collections of data. This makes the results more applicable to a wider range of people and more accurately reflects how things are in the real world. Secondly, the study looked at a group of patients with multiple health conditions who aren't often included in trials. By looking at people with type 2 diabetes, high blood pressure, obesity, and CKD at the same time, it gives useful information about the difficulties of treatment in everyday situations.

However, it's important to be aware of some limitations. We don't have a lot of head-to-head randomised trials, so it's hard to say for sure which treatment is better. Also, the way studies were

done, the patients included, and what they were measuring varied between the sets of data used, which could lead to inconsistencies.

What's more, even after using statistics to adjust for it, the observational parts of the study could still be affected by other things that weren't measured. Finally, we don't have a lot of long-term information about how safe and effective combining the treatments is, and that needs further research.

5.4 Future Research Directions

Future research should aim to fill these gaps by doing well-designed, direct comparisons of SGLT2 inhibitors and finerenone in randomised trials. This would give us stronger evidence about how well they work and how safe they are compared to each other.

We also need to find out more about the long-term effects of combining them, especially for those with advanced CKD and many health problems. Understanding how to best use these therapies together is key to getting the best results for patients.

Research should also look at how things specific to the patient, like their genes, how much obesity they have and levels of inflammation, affect how well they respond to treatment. This would help us develop treatments tailored to someone's individual risk.

5.5 Conclusion

To sum up, both SGLT2 inhibitors and finerenone are major improvements in managing Chronic Kidney Disease in people with type 1 diabetes, high blood pressure, and obesity.

SGLT2 inhibitors protect the kidneys and heart by affecting blood flow and metabolism, while finerenone does more by targeting inflammation and scarring. Because they work differently, they could be used together to tackle the many factors that cause CKD to get worse.

In the end, the choice of which treatment to use should be based on the individual patient, how far along their disease is, and what their risks are. And as we learn more, a treatment plan that targets many things and is adjusted to each person is likely to be the best way to improve outcomes for those at high risk.

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