

Genitourinary Infections Associated with SGLT2 Inhibitors: A Narrative Review

Almoutaz Alkhier Ahmed *

A/Professor - Family Medicine- MBRU, SSR family medicine -Nad Alhamar Health Center. DAHC

FRCGP [int], MSc Diabetes, MSc endocrinology, Senior fellow of IDF, MPH, FESC, FASLM, Dip IBLM, ELMC, Pg Cer medical education.

Abstract

Background: Sodium-glucose cotransporter-2 inhibitors (SGLT2i) are widely used in type 2 diabetes mellitus, chronic kidney disease, and heart failure because of their established cardiovascular and renal benefits. However, SGLT2-mediated glycosuria has raised concerns about genitourinary infections, particularly urinary tract infections (UTIs) and genital mycotic infections.

Objective: To summarize current evidence regarding the association between SGLT2i therapy and genitourinary infections, including risk factors, clinical outcomes, and management strategies.

Methods: Evidence from randomized controlled trials, observational studies, systematic reviews, and meta-analyses was reviewed to evaluate the incidence and severity of UTIs and genital mycotic infections associated with SGLT2i therapy.

Results: Available evidence indicates that SGLT2is do not consistently increase the overall risk of UTIs compared with placebo or other glucose-lowering therapies. Serious urinary infections, including pyelonephritis and urosepsis, are uncommon and have not demonstrated a consistent association with SGLT2i use. In contrast, genital mycotic infections are consistently more frequent among SGLT2i-treated patients, suggesting that glycosuria promotes *Candida* growth. Women and individuals with previous genital infections appear to be at increased risk. Most infections are mild to moderate, respond to conventional antifungal therapy, and rarely require permanent discontinuation of therapy. Patient-related factors, including female sex, older age, previous recurrent UTIs, poor glycemic control, and underlying urinary tract abnormalities, may influence susceptibility to infection.

Conclusion: SGLT2i therapy is associated with a well-established increased risk of genital mycotic infections but does not appear to substantially increase the risk of clinically significant UTIs or severe urinary infections. Given their substantial cardiovascular and renal benefits, SGLT2i should generally not be discontinued solely because of concerns about infection. Appropriate patient selection, education regarding genital hygiene and infection symptoms, early diagnosis, and prompt treatment are important for limiting adverse events while continuing the substantial cardiorenal benefits of SGLT2i therapy.

Keywords: SGLT2 inhibitors; urinary tract infection; diabetes mellitus; pyelonephritis; genital mycotic infections; urosepsis.

Introduction

SGLT2 inhibitors are now a key part of the treatment of heart and metabolic conditions [1]. Drugs like dapagliflozin, empagliflozin, canagliflozin, and ertugliflozin were first made to help lower blood glucose in people with type 2 diabetes. But large-scale studies on heart and kidney health have shown that these drugs can do much more than control blood sugar. They can help slow the progression of kidney disease [2] and prevent heart problems [3]. Because of this, current guidelines for kidney health recommend using Sodium Glucose Cotransport 2 inhibitors (SGLT2is) in patients with chronic kidney disease, even if they do not have diabetes [4]. This is because these drugs can help reduce the risk of kidney disease getting worse and can also lower the risk of heart problems [4]. Even with all its benefits, a genitourinary tract infection is a major concern for health care provider [5]. Patients use SGLT2 inhibitors excreted more glucose in their urine, and at first, people were worried that this could make it easier for bacteria to grow in the urinary tract. This makes sense because glucose can help microbes grow, and some studies have shown that glucose in the urine might make certain types of *E. coli* more aggressive [6].

It is important to distinguish between urinary tract infections and genital yeast infections (Table 1). Genital yeast infections are clearly more common among people taking SGLT2 inhibitors, but the link between these medications and bacterial urinary tract infections is less

clear. Making this distinction is important for doctors when deciding which medications to prescribe, how to counsel their patients, and whether to stop treatment after a patient has a urinary tract infection. This information can help guide these decisions and ensure the best optimal care for patients.

Pharmacological basis and potential mechanisms [7]:

SGLT2 is mainly found in the part of the kidney that filters waste and excess fluid from the blood. It helps the body reabsorb glucose and sodium. When this process is blocked by medication, the kidney cannot reabsorb as much glucose and sodium, so more of them are excreted in the urine (Figure 1). This can lead to a few things: urine may contain a lot of glucose, and people may produce more urine than usual. High glucose levels in the urine can be problematic because they provide bacteria and fungi with a food source, which may cause infections.

There are a few reasons why some people might be more likely to get urinary tract infections (UTIs) [6,8,9]. One reason is that high sugar levels in the urine can provide bacteria with the nutrients they need to grow [6]. Studies have shown that adding glucose to urine can enhance bacterial growth and that high urine glucose can make certain types of *E. coli* more virulent [6]. Another reason is that high glucose in the urine can disturb the balance of bacteria in the genital area [8,9]. This can make it easier for bad bacteria to grow and cause infec-

*Corresponding Author: *Almoutaz Alkhier Ahmed, A/Professor -MBRU, SSR family medicine -Nad Alhamar Health Center. DAHC

Citation: Almoutaz Alkhier Ahmed*, Genitourinary Infections Associated with SGLT2 Inhibitors: A Narrative Review . Jour of Clin & Med Case Rep, Imag 2026; 7(2): 1266.

tions. Finally, having to urinate more regularly due to excess glucose in the urine can alter how the urinary tract functions [8,9]. While it's possible that urinating more often could help flush out bacteria, it is not clear if this helps prevent UTIs. The connection between glycosuria and infection is complicated. Having diabetes already puts you at a higher risk of getting infections due to high blood glucose, a weaker immune system, nerve damage, bladder problems, and other health issues [10]. So, it is not right to say that UTIs are only caused by glycosuria that is brought on by medication, we should remember that SGLT2 inhibitors help control blood sugar levels, which could possibly lower the chance of infections over time. This means that while glycosuria might increase the risk of UTIs, the overall effect of these medications on infection risk is still unclear.

Table 1: Clinical differentiation between UTI and genital yeast infection.

Feature	Urinary tract infection (UTI)	Genital yeast infection (GMI)
Anatomical site	Urethra, bladder or kidneys	Vulva, vagina, glans penis or foreskin
Common organisms	Mainly bacteria, particularly <i>Escherichia coli</i>	Mainly <i>Candida albicans</i>
Underlying mechanism	Bacterial infection of the urinary tract	<i>Candida</i> overgrowth in the genital region
Typical symptoms	Dysuria, urinary frequency, urgency, suprapubic pain	Genital itching, redness, irritation, burning
Discharge	Usually, absent	Thick white vaginal discharge may occur
Dysuria	Common, often with urgency and frequency	May occur due to external genital inflammation
Fever	Possible, particularly with pyelonephritis	Unusual in uncomplicated infection
Flank pain	May occur with upper UTI	Not typical
Diagnosis	Urinalysis and urine culture when indicated	Usually clinical; microscopy or fungal testing when indicated
Treatment	Appropriate antibiotics	Topical or oral antifungal treatment
Complications	Pyelonephritis, urosepsis	Recurrent vulvovaginal candidiasis or balanitis
Association with SGLT2is	Overall risk increase is small or inconsistent	Consistently increased risk
SGLT2i discontinuation	Usually unnecessary for uncomplicated UTI	Usually unnecessary for mild, uncomplicated GMI

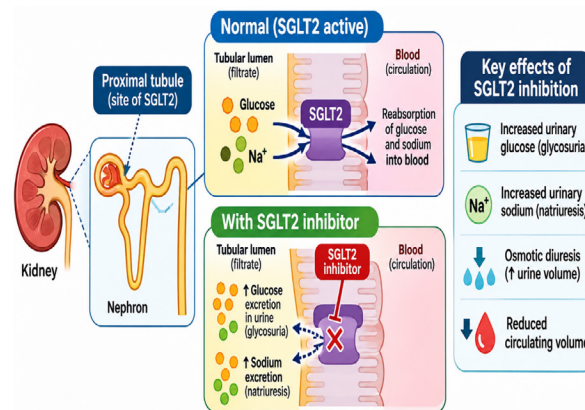


Figure 1: Pharmacological basis and potential mechanism of SGLT2is.

Evidence from randomized controlled trials has given us a better understanding of how SGLT2 inhibitors affect the risk of getting a urinary tract infection (UTI). A large systematic review and network meta-analysis examined eight different SGLT2 inhibitors in over 60,082 people, including 4,348 cases of UTIs [11]. Most of the time, the studies didn't find a significant increase in UTI risk [11]. But there was one exception: when people took a high dose of dapagliflozin (10 mg or more), they were more likely to get a UTI compared to those who took a placebo or some other medications [11]. Another systematic review and meta-analysis of randomized controlled trials [12] found that SGLT2 inhibitors were not associated with increased UTIs compared with placebo (RR 1.03, 95% CI 0.96–1.11) or active comparators (RR 1.08, 95% CI 0.93–1.25). In contrast, genital infections were substantially increased, with a pooled RR of approximately 3.4 compared with placebo [12].

These findings show the important difference between genital mycotic infections and bacterial UTIs. The DECLARE-TIMI 58 trial [13], involving approximately 17,160 patients with T2DM, provides particularly important long-term evidence for dapagliflozin. UTI incidence was similar between dapagliflozin and placebo groups, while genital infections were more frequent with dapagliflozin [13]. Importantly, UTI-related discontinuation was uncommon [13]. Studies on empagliflozin; EMPA-REG OUTCOME [14], EMPEROR-Reduced [15], EMPEROR-Preserved [16], and EMPA-KIDNEY [17] which included over 10,000 people who took empagliflozin have shown that it does not seem to significantly increase the risk of getting a urinary tract infection, or UTI for short. Moreover, serious UTIs and other related infections, like pyelonephritis or urosepsis, were also similar in both groups [14–17]. This suggests that empagliflozin may not have a major impact on the risk of getting these types of infections. Data from renal outcome trials [14] are similarly reassuring. In patients with diabetic kidney disease, empagliflozin was associated with similar rates of overall UTI, complicated UTI, and pyelonephritis compared with placebo [14].

Meta-analyses as well as observational evidence:

Studies on SGLT2 inhibitors have had mixed results when it comes to the risk of urinary tract infections (UTIs). Some randomized trials have not found a significant increase in UTIs, but other observational studies have had more varied findings. This might be because the people taking SGLT2 inhibitors are often quite different from those who are not taking them, they may have had diabetes for longer, or have other health issues like kidney disease, heart problems, or obesity, which can all affect their risk of getting an infection [8,9]. A new study by Aboukaoud, Morhi and Osher [18] looked at people with type 2 diabetes and found something interesting. The study, which included over 679,617 people with type 2 diabetes, found that those taking SGLT2 inhibitors had a lower risk of severe UTIs compared to those taking other medications; with SGLT2is OR = 0.73, 95% CI =

0.60-0.88 and with Dipeptidyl peptidase-4 inhibitors (DPP4i) OR = 0.48, 95% CI = 0.43-0.54 [18]. Specifically, the risk was lower than in people taking DPP-4 inhibitors, but there was no significant difference compared with that in people taking glucagon-like peptide-1 (GLP-1) receptor agonists with OR = 0.94, 95% CI = 0.78-1.14 [18].

This is good news, as severe UTIs can be a real problem for people with type 2 diabetes. The study's data [18] suggest that SGLT2 inhibitors might be a good choice for people with type 2 diabetes who are at risk of getting UTIs [18]. Research suggests that there is not a strong link between SGLT2 inhibitors and severe bacterial urinary tract infections (UTIs). However, some newer studies indicate a small increase in the overall risk of getting a UTI. A recent review of SGLT2 inhibitors in people with chronic kidney disease (CKD) found that the risk of getting a UTI was about 1.08 times higher compared to those who didn't take the medication [19]. But it is worth noting that the risk of serious UTIs wasn't significantly higher [19]. This information is important for people taking SGLT2 inhibitors, as it can help them understand the possible risks and benefits of their medication. So far, what we know suggests there might not be a considerable increase in simple urinary tract infections, or, if there is, it is likely to be small. On the other hand, we have much stronger evidence pointing to a higher risk of genital yeast infections.

A study [20] that examined 52 randomized trials involving 36,689 patients found similar results. It showed that dapagliflozin, canagliflozin, and empagliflozin increased the risk of genital infections a lot. However, the evidence for urinary tract infections (UTIs) was not as strong; 3.21 (95% CI 2.08-4.93) for dapagliflozin 2.5 mg to 5.23 (95% CI 3.86-7.09) for canagliflozin 300 mg, only one dose of dapagliflozin, 10 mg, was associated with a statistically significant increase in UTIs compared with placebo (4.7% vs 3.5%) [20]. This suggests that any possible link between the dose and the effect might be small and depend on the specific medication used. The Evidence from randomized studies point to a point that matters in a clinical setting [12], SGLT2 inhibition produce glycosuria with substantial increase in genital mycotic infections, whereas: SGLT2 inhibition produce glycosuria with little or no clinically significant increase in bacterial UTI. This distinction should be emphasized in clinical practice because dysuria, genital irritation, and urinary frequency can occur with either condition or may lead to inappropriate discontinuation of an otherwise beneficial SGLT2 inhibitor.

Interpretation for Clinical Practice:

The cumulative evidence from EMPA-REG OUTCOME [14], CANVAS [21], DECLARE-TIMI 58 [13], CREDENCE [22], DAPA-HF [23], DAPA-CKD [24], EMPEROR-Reduced [15], EMPEROR-Preserved [16], DELIVER [25], and EMPA-KIDNEY [17] indicates that concern about UTI should not generally prevent initiation of SGLT2 inhibitors in appropriate patients. When it comes to the side effects of certain medications, one thing stands out: genital mycotic infections are a bigger concern than bacterial urinary tract infections (UTIs). The doctor should look at how severe the infection is, whether it keeps coming back, how well their kidneys are working, whether they are getting enough fluids, and whether there are any problems with their urinary tract. If the infection is bad, or if they have a more serious condition like a kidney infection, blood poisoning, are very dehydrated, or have another acute illness, the doctor might stop the medicine for a little while.

the first place, educate them on what to watch for, and ensure they can distinguish a genital infection from a bacterial UTI. They should also keep a close eye on patients who get UTIs often or have severe ones. Overall, the evidence from these trials suggests that the benefits of SGLT2 inhibitors outweigh the risks for people with diabetes, heart failure, and chronic kidney disease, critical appraisal of the major SGLT2 inhibitor trials for UTI outcomes. When looking at the big picture of heart and kidney health, many studies help us understand whether a class of medicines called SGLT2 inhibitors can increase the risk of urinary tract infections. But we must carefully consider the results because these studies were not specifically designed to look at urinary tract infections, and they defined these infections in different ways. Most of these studies were also not large enough to detect rare but serious infections like pyelonephritis or urosepsis. Overall, it seems these medicines do not significantly increase the risk of serious urinary tract infections, although they may slightly increase the risk of less severe infections.

Critical appraisal of key studies:

1. Urinary tract infections: Evidence from major trials

The EMPA-REG OUTCOME trial [14] enrolled 7,020 patients with type 2 diabetes mellitus (T2DM) and established cardiovascular disease. Empagliflozin was not linked to a clinically significant increase in reported urinary tract infections (UTIs) compared with placebo. However, infections were assessed as adverse events rather than as predefined primary outcomes. Therefore, while the trial offers reassurance regarding common UTIs, it provides limited certainty about rare complications such as pyelonephritis and urosepsis. The CANVAS Program [21], which included over 10,000 patients with T2DM at elevated cardiovascular risk, also demonstrated no clinically significant increase in UTIs with canagliflozin. However, infection ascertainment primarily relied on adverse event reporting, potentially introducing variability in diagnostic accuracy and limiting conclusions regarding recurrent or culture-confirmed infections.

The DECLARE-TIMI 58 trial [13], which included approximately 17,000 participants, provided additional evidence regarding dapagliflozin. UTI rates were similar between dapagliflozin and placebo, with no clear increase in serious infections such as pyelonephritis or urosepsis. The large sample size and extended follow-up strengthen these findings. However, small increases in uncomplicated UTIs cannot be excluded, as some pooled analyses suggest a potential dapagliflozin-specific risk.

2. Urinary infections in chronic kidney disease

The CREDENCE trial [22] enrolled 4,401 patients with T2DM and established diabetic kidney disease. The incidence of UTIs was approximately 48.3 events per 1,000 patient-years with canagliflozin and 45.1 events per 1,000 patient-years with placebo, corresponding to a hazard ratio (HR) of 1.08 (95% CI 0.90–1.29). Although the point estimate indicated a numerical increase, the confidence interval included 1.0, signifying no statistically significant difference. DAPA-CKD [24] extended the evidence to patients with CKD, including individuals without diabetes. Dapagliflozin did not substantially increase reported UTIs. Nevertheless, infections were secondary safety outcomes, and the study was not specifically powered to identify small differences in uncomplicated infections.

The EMPA-KIDNEY trial [17] provided relevant evidence in a broader CKD population, both with and without diabetes. The incidence of serious UTIs was approximately 0.81 events per 100 person-years with empagliflozin and 0.84 events per 100 person-years with placebo. These findings are reassuring regarding serious urinary infections, although the relatively low event rates limit the precision of estimates

So, what does this mean for doctors and patients? The main takeaway from these trials is that SGLT2 inhibitors shouldn't be avoided solely because of the risk of urinary tract infections (UTIs). Instead, doctors should identify which patients are more likely to develop UTIs in

for uncommon complications.

3. Evidence from heart failure trials

The EMPEROR-Reduced [15] and EMPEROR-Preserved [16] trials evaluated empagliflozin in patients with heart failure across various ejection fraction categories, including those without diabetes. Neither trial demonstrated a clinically significant increase in UTIs.

Similarly, the DELIVER trial [25], which included 6,263 patients with mildly reduced or preserved ejection fraction, found no significant signal for serious urinary infections with dapagliflozin.

These studies expand the safety evidence to populations beyond those with diabetes. However, infection outcomes were not primary endpoints, and patients with recurrent or complicated infections may have been underrepresented.

4. Genital mycotic infections: An important evidence distinction

In contrast to bacterial UTIs, genital mycotic infections are a well-recognized adverse effect of SGLT2 inhibitors. Glucose-rich genital environments can facilitate fungal proliferation, particularly of *Candida* species. However, the provided trials summaries primarily report UTI outcomes and do not include trial-specific genital mycotic infection (GMI) incidence, relative risks, or confidence intervals. As a result, the available material does not support reliable quantitative comparisons of genital infection risk across these landmark trials. This distinction is clinically important. The absence of a substantial increase in bacterial UTIs should not be interpreted as evidence that SGLT2 inhibitors are without genital infection risk. Health care providers need to evaluate and report genital mycotic infections and bacterial UTIs separately.

5. Pooled evidence and critical interpretation

A synthesis of 13 large randomized SGLT2 inhibitor trials [26] identified a small increase in overall UTI risk (RR 1.08, 95% CI 1.02–1.15), but no statistically significant increase in serious UTIs (RR 1.07, 95% CI 0.90–1.27). These findings highlight several methodological considerations. First, UTIs were generally recorded as adverse events rather than systematically confirmed through urine cultures. Second, infection definitions and surveillance methods varied between trials. Third, serious infections were relatively uncommon, reducing statistical power. Finally, patients with recurrent UTIs, advanced comorbidities, or clinical instability may have been underrepresented.

In Conclusion, evidence from landmark randomized controlled trials (RCTs) indicates that SGLT2 inhibitors are not associated with a substantial or consistent increase in serious urinary tract infections, although a possible small increase in overall UTI incidence cannot be excluded. These findings are broadly reassuring across diabetes, heart failure, and CKD populations. In contrast, genital mycotic infections remain an established safety concern, although the provided summaries do not allow for a clear assessment. Clinical practice should therefore distinguish uncomplicated bacterial UTIs from serious urinary infections and genital mycotic infections, while incorporating individualized risk assessment, patient education, and early recognition of infection symptoms. Early recognition of infection symptoms.

Limitations:

UTI was generally a secondary safety outcome. This is a major limitation of the trials. They mainly focused on how the treatment affected the heart, blood vessels, and kidneys. They weren't really designed to see if it caused urinary tract infections, or UTIs. So, just because the results didn't show a statistically significant link doesn't mean there's no risk of UTIs. In other words, the trials might not have been able to detect a potential problem with UTIs, even if one exists. This is some-

thing to keep in mind when interpreting the results.

Heterogeneous definitions of UTI. When looking at the results of various studies on urinary tract infections (UTIs), it's clear that there's no single definition everyone agrees on. Some studies examined simple cases of cystitis, while others focused on more serious cases requiring hospitalization, such as pyelonephritis or urosepsis. Because of these differences, it's not a good idea to directly compare the number of UTI cases between studies. The way that researchers reported problems with UTIs also varied, which adds to the challenge of comparing results.

Limited power for severe UTI: Severe urinary tract infections, such as pyelonephritis and urosepsis, don't occur very often. In fact, when researchers have reviewed cardiovascular outcome trials, they've found that severe UTIs occur in fewer than 2% of cases. This makes it tough for individual trials to detect small differences in relative risk. As a result, it's hard to get a clear picture of how often severe UTIs happen and what factors might contribute to them. Exclusion of high-risk patients: Lots of clinical trials didn't include people with bad kidney problems, unstable health issues, or other things that may cause infections. So, the results of these trials might not show the whole picture when it comes to the risks for people who get urinary tract infections over and over, have blockages in their urinary tract, use catheters all the time, have nerve problems that affect their bladder, or have other abnormalities in their urinary system. This means we might not know the full extent of the risks for these people.

Limited microbiological confirmation. Typically, reports on clinical trials don't provide detailed information about urinary tract infections confirmed by culture. This is a problem because things like painful urination, needing to go to the bathroom often, yeast infections, and having too much sugar in the urine can all cause symptoms that seem like a UTI, even if there's no bacterial infection present. Insufficient information on recurrent UTIs. Many studies focus on the total number of side effects, rather than how many patients actually experience repeated infections. As a result, there's limited evidence on whether SGLT2 inhibitors are safe for patients who repeatedly develop urinary tract infections. This makes it hard to know for sure if these medications should be avoided in people with a history of recurrent UTIs.

Why are genital infections more common than UTIs?

The markedly greater increase in genital mycotic infections than in bacterial UTIs is biologically plausible [27]. Urinary glucose may contaminate the perineal region, creating an environment conducive to *Candida* species [27]. This effect is clearly visible in women and in individuals with a history of genital infection [27]. A meta-analysis found that SGLT2 inhibitors increased the risk of genital infections approximately threefold compared with placebo, whereas the pooled effect on UTIs was close to neutral [12]. This difference is clinically important because patients may interpret dysuria or genital irritation as evidence of UTI when the underlying problem is vulvovaginal candidiasis.

Appropriate diagnosis should therefore distinguish cystitis from genital candidiasis (Table 1).

Evidence from randomized controlled trials

Dapagliflozin: Clinical trials consistently demonstrate a higher risk of genital infection compared to placebo. A meta-analysis of 52 randomized controlled trials [20] involving 36,689 participants reported a significantly increased incidence of genital infections, with an odds ratio of 3.21 (95% CI 2.08–4.93) for dapagliflozin 2.5 mg.

Another systematic review [31] found a relative risk of 3.22 (95% CI 1.95–5.32). Most infections were mild to moderate in severity and

responded to conventional antifungal therapy.

Canagliflozin: A 104-week, randomized, double-blind, placebo-controlled [32] involving 714 adults aged 55 to 80 years with type 2 diabetes demonstrated that canagliflozin increased the incidence of genital mycotic infections. Among women, infection rates were 23.9% with canagliflozin 100 mg, 18.7% with 300 mg, and 4.3% with placebo. For men, the rates were 5.6%, 10.9%, and 1.4%, respectively. Most infections occurred within the first six months, were classified as mild to moderate, and responded to standard antifungal therapy.

The CANVAS Program [21] and CREDENCE trial [22] identified genital infections as recognized adverse events, while severe complications remained uncommon. Empagliflozin: The EMPA-REG OUTCOME trial [14] demonstrated an increased incidence of genital infections with empagliflozin compared to placebo, in addition to significant cardiovascular benefits. Pooled randomized evidence [31] estimated a threefold increase in genital infections (RR 3.14, 95% CI 2.29–4.30). Most episodes were uncomplicated and amenable to treatment.

Evidence from cardiovascular and renal outcome trials

Major trials, such as DAPA-HF [23], DAPA-CKD [24], EMPEROR-Reduced [15], EMPEROR-Preserved [16], DELIVER [25], and EMPA-KIDNEY [17], provide additional safety data across heart failure and chronic kidney disease (CKD) populations, including individuals without diabetes. Although infection outcomes were secondary safety measures, these studies contribute to the broader body of evidence supporting genital mycotic infections as a class effect. A large network meta-analysis [33] of over 121,000 participants estimated an overall odds ratio for genital infection of 3.5 (95% CI 3.1–3.9). Another meta-analysis demonstrated increasing pooled relative risks with longer study durations: 2.10 for trials lasting 26 weeks or less, 3.26 for 26 to 52 weeks, and 4.23 for trials exceeding 52 weeks [31]. These findings indicate a greater cumulative incidence of infections with prolonged exposure, although they do not establish a progressively increasing individual risk.

Clinical implications and critical appraisal

Most SGLT2 inhibitor-associated genital infections are mild, respond to topical or oral antifungal treatment, and rarely necessitate permanent discontinuation of therapy. Patient education on genital hygiene, symptom recognition, and early intervention is essential, particularly for women and individuals with recurrent candidiasis. Although randomized trials and meta-analyses consistently demonstrate an increased risk of genital infection, variations in infection definitions, adverse event reporting, and participant selection limit the precision of comparisons between medications. Additionally, researchers generally assessed genital infections as secondary safety outcomes.

Risk factors for UTI during SGLT2 inhibitor therapy

Patients with T2DM already have multiple risk factors for UTI. These include:

- Female sex
- Advanced age
- Poor glycaemic control
- Recurrent UTI
- Autonomic neuropathy
- Urinary retention
- Bladder dysfunction
- Nephrolithiasis
- Structural urinary tract disease
- Use of urinary catheters

The risk of urogenital infection may also vary with treatment duration and patient characteristics. Recent clinical guidance identifies

women, people with obesity, and individuals treated for six months or longer as groups with increased urogenital infection risk [28].

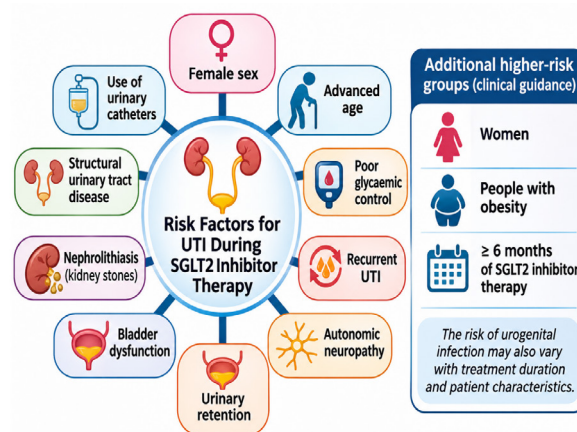


Figure 2: Risk factors for UTI during SGLT2is therapy.

Patients with recurrent or severe UTI deserve particular attention. The ADA's guidance for older adults notes that SGLT2 inhibitors may be associated with a small increase in UTI and recommends caution in people with recurrent or severe UTIs [29].

Severe UTI, pyelonephritis and urosepsis

One of the major concerns following early regulatory reports was whether SGLT2 inhibitors could cause serious ascending urinary infection. The FDA previously added warnings concerning serious UTIs, including cases of pyelonephritis and urosepsis [34]. Subsequent evidence has substantially reduced concern about a major excess risk. DECLARE-TIMI 58 [13] demonstrated balanced rates of UTI, pyelonephritis, and urosepsis between dapagliflozin and placebo. Similarly, long-term pooled empagliflozin trials showed comparable serious UTI and serious pyelonephritis/urosepsis rates. KDIGO 2024 consequently concluded that the vast majority of UTIs in patients taking SGLT2 inhibitors are not attributable to SGLT2 inhibition and found no overall increased risk of UTI in the evidence base supporting their use in CKD [30].

Clinical management of UTI in patients receiving SGLT2 inhibitors

The occurrence of an uncomplicated UTI should not automatically result in permanent discontinuation of an SGLT2 inhibitor. Treatment should generally follow standard principles for UTI diagnosis and antimicrobial management, considering local resistance patterns, patient characteristics, renal function, and the distinction between uncomplicated cystitis and complicated infection (Figure 3).

Temporary interruption may be considered in patients with severe systemic infection, pyelonephritis, urosepsis, significant dehydration, or other acute illness, particularly when oral intake is compromised [26]. The decision should balance infection severity against the substantial cardiovascular and renal benefits of continued SGLT2 inhibition (Figure 3).

Recurrent UTI requires a more individualized approach (Figure 3). Clinicians should assess for predisposing factors such as urinary retention, stones, structural abnormalities, catheter use, uncontrolled diabetes, and recurrent genital infection [26]. In selected patients with frequent severe infections despite appropriate management, discontinuation or switching therapy may be appropriate [26].

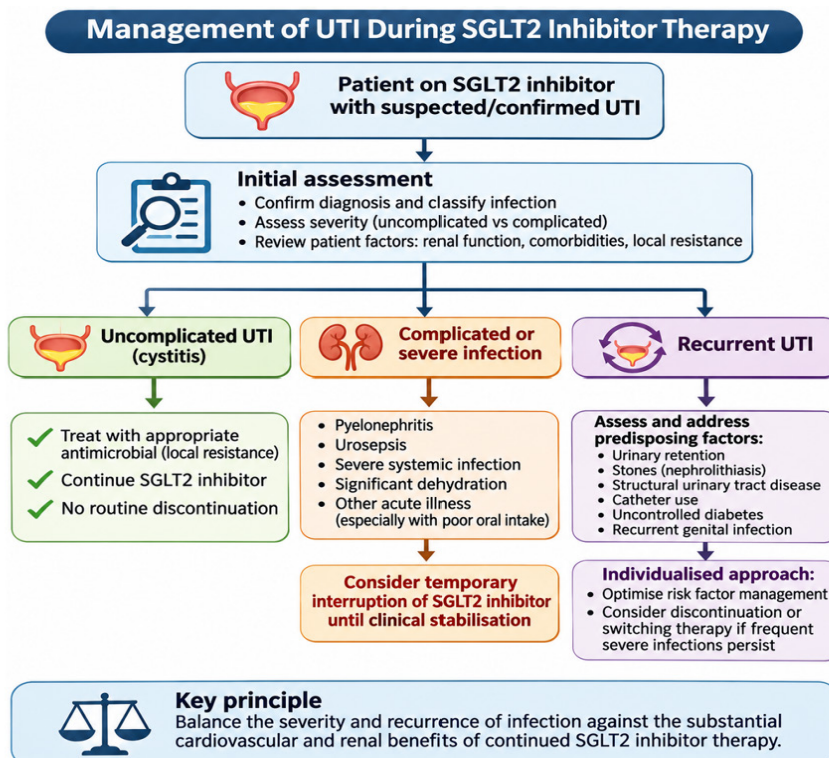


Figure 3: Management of UTI during SGLT2is therapy.

Management of Genital Mycotic Infections During SGLT2 Inhibitor Therapy

Genital mycotic infections associated with sodium–glucose cotransporter-2 inhibitors (SGLT2is) are generally mild to moderate and respond effectively to conventional antifungal therapy (Figure 4). Treat uncomplicated vulvovaginal candidiasis or candidal balanitis with topical azole antifungals or oral fluconazole, where appropriate [5]. Routine discontinuation of SGLT2is is not recommended because infections are usually manageable and treatment provides substantial cardiovascular and renal benefits [5].

Preventive measures include:

- Genital hygiene

- Glycaemic optimization,
- Avoiding local irritants
- Patient education on early symptom recognition

Recurrent infections need microbiological confirmation, identification of *Candida* species, and assessment of predisposing factors, including poor glycaemic control, previous infections, and immunosuppression [5]. Consider extended antifungal treatment or maintenance therapy for recurrent vulvovaginal candidiasis. Severe, persistent, or frequently recurrent infections require individualized assessment, including consideration of alternative glucose-lowering therapies. Temporary interruption is appropriate during severe systemic illness, while permanent discontinuation should generally be reserved for selected refractory cases.

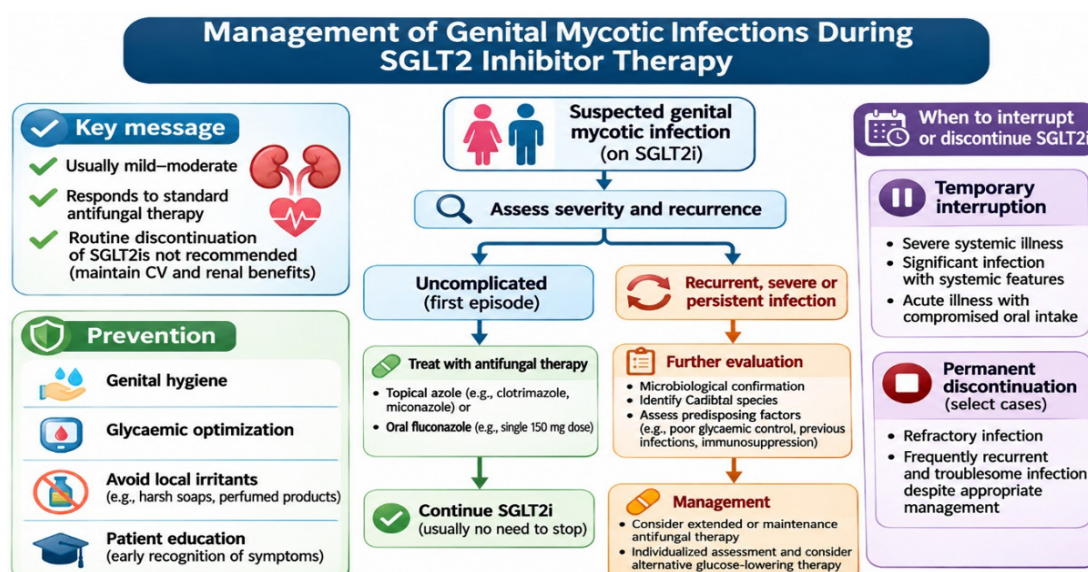


Figure 4: Management of Genital Mycotic infection during SGLT2is therapy.

Prevention and patient education

Patient education is central to reducing genitourinary complications.

Patients should understand the difference between genital infection and UTI and should seek medical assessment when symptoms develop [5]. Good perineal hygiene, adequate fluid intake, avoidance of unnecessary urinary retention, and appropriate diabetes management are reasonable preventive measures [5].

Patients should be educated about symptoms of cystitis, including dysuria, urinary frequency, urgency, suprapubic discomfort, and haematuria [5]. Fever, flank pain, nausea, vomiting, rigors, or systemic deterioration should raise concern for pyelonephritis or systemic infection and require prompt assessment. Routine urine cultures or prophylactic antibiotics are not justified solely because a patient is receiving an SGLT2 inhibitor [5]. Similarly, asymptomatic glycosuria is an expected pharmacological effect and should not be interpreted as evidence of UTI.

Conclusion

SGLT2 inhibitors cause pharmacological glycosuria, providing a biologically plausible mechanism for increased genitourinary infection. However, the clinical evidence demonstrates an important distinction between genital mycotic infection and bacterial UTI. Genital mycotic infection is the most consistent infectious adverse effect of SGLT2 inhibitors. Evidence from major trials and meta-analyses demonstrates approximately a three- to fourfold increase in relative risk [31], with canagliflozin, dapagliflozin and empagliflozin all demonstrating this association. Women are particularly susceptible, and infections are most common early after treatment initiation. Fortunately, most episodes are mild or moderate, respond to conventional antifungal therapy, and rarely require permanent discontinuation of treatment. Thus, genital candidiasis should be regarded as an important but generally manageable safety consideration, rather than a major limitation on the substantial cardiovascular, heart failure, and renal benefits of SGLT2 inhibitors.

SGLT2 inhibitors should therefore generally be continued in appropriate patients because their cardiovascular, heart failure, and renal benefits are notable. Clinicians should apply increased caution in individuals with recurrent or severe UTIs and should temporarily interrupt treatment when clinically appropriate during severe acute illness. Patient education, early recognition of urinary and genital symptoms, appropriate antimicrobial treatment, and individualized risk assessment remain the foundation of safe SGLT2 inhibitor use.

Table. Key Messages

1. SGLT2 inhibitors induce glycosuria, giving a theoretical basis for increased genitourinary infections.
2. Genital mycotic infections are clearly increased, whereas the association with bacterial UTI is much weaker.
3. Large, randomized trials generally show no clinically significant increase in UTI, pyelonephritis, or urosepsis.
4. Some recent evidence suggests a small increase in uncomplicated UTI, particularly in susceptible patients.
5. Women, older adults, patients with obesity, and those with recurrent or severe UTI may require closer monitoring.
6. An uncomplicated UTI does not automatically require permanent discontinuation of an SGLT2 inhibitor.
7. Severe infection, pyelonephritis, urosepsis, dehydration, or acute illness may justify temporary treatment interruption.
8. The cardiovascular and renal benefits of SGLT2 inhibitors generally outweigh their relatively small potential risk of UTIs.

References

- Committee AD (2025) cardiovascular disease and risk management: Standards of Care in Diabetes-2026. *Diabetes Care* 49(1): S216.
- (2026) chronic kidney disease and risk management: Standards of Care in Diabetes-2026." *Diabetes Care* 49(1): S246-S260.
- McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, et al. (2023) focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) with the special contribution of the Heart Failure Association (HFA) of the ESC. *European heart journal* 44(37): 3627-3639.
- Disease K, Group IG (2024) KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney international* 105(4S): S117-S14.
- Gorgojo-Martínez JJ, Górriz JL, Cebrián-Cuenca A, Castro Conde A, Velasco Arribas M (2024) Clinical recommendations for managing genitourinary adverse effects in patients treated with SGLT-2 inhibitors: a multidisciplinary expert consensus. *Journal of Clinical Medicine* 13(21): 6509.
- Islam MJ, Bagale K, John PP, Kurtz Z, Kulkarni R (2022) Glycosuria alters uropathogenic *Escherichia coli* global gene expression and virulence. *Msphere* 7(3): e00004-22.
- Vallon V (2024) State-of-the-art-review: mechanisms of action of SGLT2 inhibitors and clinical implications. *American Journal of Hypertension* 37(11): 841-852.
- Kittipibul V, Cox ZL, Chesdachai S, Fiuzat M, Lindenfeld J, Mentz RJ. (2024) Genitourinary tract infections in patients taking SGLT2 inhibitors: JACC review topic of the week. *Journal of the American College of Cardiology* 83(16): 1568-1578.
- Confederat LG, Dragostin OM, Condurache MI (2025) SGLT2 inhibitors and the risk of urogenital infections: a concise review. *Journal of Clinical Medicine* 14(6): 1960.
- Nitzan O, Elias M, Chazan B, Saliba W (2015) Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. *Diabetes, metabolic syndrome and obesity* 26: 129-136.
- Donnan JR, Grandy CA, Chibrikov E, PharmD CM, Aubrey-Bassler K, et al. (2018) Dose response of sodium glucose cotransporter-2 inhibitors in relation to urinary tract infections: a systematic review and network meta-analysis of randomized controlled trials. *CMAJ open* 6(4): E594-602.
- Puckrin R, Saltiel MP, Reynier P, Azoulay L, Yu OH, Filion KB (2018) SGLT-2 inhibitors and the risk of infections: a systematic review and meta-analysis of randomized controlled trials. *Acta diabetologica* 55(5): 503-514.
- Mosenzon O, Wiviott SD, Cahn A, Rozenberg A, Yanuv I, et al. (2019) Effects of dapagliflozin on development and progression of kidney disease in patients with type 2 diabetes: an analysis from the DECLARE-TIMI 58 randomised trial. *The lancet Diabetes & endocrinology* 7(8): 606-617.
- Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, et al. (2015) Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *New england journal of medicine* 373(22): 2117-2128.
- Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, et al. (2020) Cardiovascular and renal outcomes with empagliflozin in heart failure. *New England Journal of Medicine* 383(15): 1413-1424.
- Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, et al. (2021) Empagliflozin in heart failure with a preserved ejection fraction. *New England Journal of Medicine* 385(16): 1451-1461.
- Herrington WG, Judge PK, Grams ME, Wanner C (2026) Chronic kidney disease. *The Lancet* 407(10523): 90-104.
- Aboukaoud M, Morhi Y, Osher E (2025) Sodium-glucose co-transporter 2 inhibitors and severe urinary tract infections: real-world meta-analysis of cohort studies. *Annals of Pharmacotherapy* 59(10): 891-903.
- Sloan L (2024) SGLT2 inhibitors across the spectrum of chronic kidney disease: a narrative review. *Postgraduate Medicine* 136(8): 801-809.
- Li D, Wang T, Shen S, Fang Z, Dong Y, Tang H (2017) Urinary tract and genital infections in patients with type 2 diabetes treated with sodium-glucose co-transporter 2 inhibitors: a meta-analysis of randomized controlled trials. *Diabetes, Obesity and Metabolism* 19(3): 348-355.
- Neal B, Perkovic V, Mahaffey KW, De Zeeuw D, Fulcher G, Erond N, et al. (2017) Canagliflozin and cardiovascular and renal events in type 2 diabetes. *New England Journal of Medicine* 377(7): 644-657.
- Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJ, et al. (2019) Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *New England journal of medicine* 380(24): 2295-2306.
- McMurray JJ, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, et al. (2019) Dapagliflozin in patients with heart failure and reduced ejection fraction. *New England Journal of Medicine* 381(21): 1995-2008.
- Heerspink HJ, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, et al. (2020) Dapagliflozin in patients with chronic kidney disease. *New England Journal of Medicine* 383(15): 1436-1446.
- Solomon SD, McMurray JJ, Claggett B, de Boer RA, DeMets D, et al. (2022) Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. *New England Journal of Medicine* 387(12): 1089-1098.
- Roddick AJ, Wonnacott A, Webb D, Watt A, Watson MA, et al. (2023) UK Kidney Association clinical practice guideline: sodium-glucose co-transporter-2 (SGLT-2) inhibition in adults with kidney disease 2023 update. *BMC nephrology* 24(1):310.
- McGovern AP, Hogg M, Shields BM, Sattar NA, Holman RR, et al. (2020) Risk factors for genital infections in people initiating SGLT2 inhibitors and their impact on discontinuation. *BMJ open diabetes research & care* 8(1): e001238.
- Swanson J, Lucier K, Jean-Baptiste M, Neher JO (2026) SGLT-2 Inhibitors and Increased Risk of Urogenital Infections. *American Family Physician* 113(3): 281-282.
- Committee AD (2025) Older Adults: Standards of Care in Diabetes-2026. *Diabetes Care* 49(1): S277.
- Disease K (2024) Group IG. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney international* 105(4S): S117-314.
- Liu J, Li L, Li S, Jia P, Deng K, et al. (2017) Effects of SGLT2 inhibitors on UTIs and genital infections in type 2 diabetes mellitus: a systematic review and meta-analysis. *Scientific reports* 7(1): 2824.
- Bode B, Stenlöf K, Harris S, Sullivan D, Fung A, et al. (2015) G. Long-term efficacy and safety of canagliflozin over 104 weeks in patients aged 55–80 years with type 2 diabetes. *Diabetes, Obesity and Metabolism* 17(3): 294-303.
- Sridharan K, Sivaramakrishnan G (2024) Genito-urinary infectious adverse events related to sodium glucose cotransporter-2 inhibitors: a network meta-analysis and meta-regression. *Expert Review of Clinical Pharmacology* 17(5-6): 515-524.
- Voelker R (2016) Update on SGLT2 inhibitor warning. *JAMA*. 2016;315(3):243.