

Impact of dapagliflozin on renal function and serum uric acid: An updated meta-analysis

YU FENG*
YANGSONG TAO
DENG RONG
XUEHONG RI
DI PAN
JINGRU YANG
LIYUAN YUAN

*Department of Nephrology
China Aerospace Science and
Industry Corporation
731 Hospital, Beijing, 100074, China*

License



© 2026 Feng *et al.*

This article is distributed
under the terms of the license
Creative Commons Attribution-
NonCommercial-NoDerivatives
4.0 International License

Accepted October 9, 2026
Published online October 10, 2026

ABSTRACT

This study aimed to investigate the effects of dapagliflozin on renal function indicators and serum uric acid concentration in human patients. A systematic search was conducted in PubMed, Embase, Cochrane Library, and Web of Science databases. Qualified randomized controlled trials (RCTs) related to dapagliflozin treatment were screened, subjected to quality assessment, and data extraction and analysis, using Review Manager 5.3. A total of 19 RCTs were finally included. Regarding serum uric acid levels, dapagliflozin significantly reduced serum uric acid levels [weighted mean difference by -11.4% , 95% confidence interval (CI) = -14.5% to -8.4% , $p < 0.0001$]. Compared with the control group, the treatment group showed no significant change in serum creatinine levels (Scr) ($+0.6\%$, 95% CI = -0.6% to 1.8% , $p = 0.294$), estimated glomerular filtration rate (eGFR) (0.1% , 95% CI = -1.7% to 2.0% , $p = 0.863$), or cystatin-C (Cys-C) levels (4.2% , 95% CI = -0.4% to 8.8% , $p = 0.061$). Regarding renal outcomes, dapagliflozin showed no significant effect in the urine albumin-to-creatinine ratio (-33.1% , 95% CI = -115.7 to 49.4% , $p = 0.226$). Dapagliflozin reduced serum uric acid levels and exhibited good safety with respect to the stability of renal function parameters.

Keywords: sodium-glucose transporter 2 inhibitors, dapagliflozin, uric acid, renal function, meta-analysis

INTRODUCTION

Hyperuricemia (HUA) is a metabolic disorder caused by purine metabolism disorder. As a medical condition characterized by elevated serum uric acid levels, its prevalence varies substantially across different geographic regions. Studies estimate that approximately $15\text{--}25\%$ of the general population is affected by this condition. Previous studies have confirmed that HUA is associated with an increased risk of gout, chronic kidney disease (CKD), hypertension, and cardiovascular diseases, thereby imposing a substantial disease burden on patients (1, 2). As a risk factor for CKD progression, HUA also predicts increased all-cause mortality in CKD patients (3). Extensive research indicates that lowering serum uric acid levels has a positive impact on renal injury (4). Notably, over 40% of

* Correspondence; e-mail: YU_FengHemo@hotmail.com

diabetic patients may also develop CKD (4). Accumulating evidence suggests that uric acid may contribute to the pathogenesis of diabetic nephropathy. In the Joslin Kidney Study which evaluated predictors of GFR decline in 355 non-proteinuric patients with type 1 diabetes, elevated serum uric acid was independently associated with a significantly increased risk of GFR loss, with a relative risk of 1.5 (95 % CI 1.3–1.9; $p = 0.002$) per 1 mg per 100 mL increment in serum uric acid (5). Patients with type 2 diabetes and HUA exhibit accelerated CKD progression and elevated risk of adverse cardiovascular events, substantially increasing the risk of polypharmacy (6). However specific recommendations for medication safety management in this patient group remain limited. Current guidelines recommend dapagliflozin as therapeutic option for impaired renal function (7). However, an increase in serum creatinine levels has been observed in patients treated with dapagliflozin (8). Concerns still persist regarding the potential of dapagliflozin to improve renal outcomes in patients; although its effect on serum uric acid is supported by data from diabetic patients, its impact on serum uric acid and renal outcomes in broader patient populations remains unclear (9). In order to address this research gap, we conducted a meta-analysis of clinical study data. This study aimed to investigate the potential mechanisms of dapagliflozin in controlling uric acid levels and improving renal function as well as to identify the patient populations most suitable for treatment with dapagliflozin.

DATA SOURCES AND METHODS

This meta-analysis evaluated the effect of dapagliflozin compared with placebo or active controls on uric acid control and renal outcomes in patients. Randomized controlled trials (RCTs) of dapagliflozin (with or without other medications) as the intervention for renal outcomes and serum uric acid indicators in any population and age group were eligible for inclusion. Studies that lacked a control group or contained incomplete/erroneous data were excluded; non-RCT type studies such as prospective studies, case reports, conference papers, case-control, cohort studies, cross-sectional designs, and animal or cell experiments were also excluded.

We searched four databases Embase, PubMed, Cochrane Library, and Web of Science, yielding an initial pool of 488 publications. After screening, 19 RCTs were included. We included RCTs that reported the following outcomes measures: serum uric acid, Scr, estimated glomerular filtration rate (eGFR), cystatin C (Cys-C), urine albumin-to-creatinine ratio (UACR). Only English publications were included.

Literature quality assessment

All retrieved articles were subjected to blinded title and abstract screening that was independently conducted by two researchers. Full texts of all potentially eligible studies were rigorously evaluated against a predefined set of inclusion and exclusion criteria. Study characteristics and outcome data were extracted independently by two reviewers from all studies meeting the inclusion criteria. Any discrepancies were adjudicated through mutual consensus or, whenever necessary, by consultation with a third reviewer, who carefully reviewed the finally selected trials. Literature screening was performed independently using EndNote X9 software (Clarivate Analytics, USA).

The methodological quality of the included RCTs was assessed using the Cochrane Handbook for Systematic Reviews of Interventions (Cochrane Handbook) (10). Multiple bias-related domains were evaluated, including random sequence generation, blinding of participants and personnel, allocation concealment, blinding of outcome assessment and of outcome data, selective reporting, and other potential sources of bias. Based on the assessment, the risk of bias was categorized into three levels: high, low and unclear risk. The following core domains were applied in the risk-of-bias assessment of eligible RCTs: random sequence generation (selection bias), allocation concealment (selection bias), blinding (performance bias and detection bias), incomplete outcome data (attrition bias), and selective reporting (reporting bias). Fig. S1 graphically summarizes the overall risk of bias.

Data extraction

A set of core information was extracted from each included study: first author name, publication year, participant nationality, intervention protocols for both experimental and control groups, sample size and study duration. Mean difference (MD) with standard deviation (SD) was used to express continuous outcomes, while OR with 95 % confidence interval (CI) was used to express binary applied outcomes.

Chi² test and I² statistic, recommended by the Cochrane risk-of-bias tool, were utilized to evaluate inter-study heterogeneity, and a random-effects framework was employed for performing the meta-analysis. To verify the stability of the results, a sensitivity analysis was performed by sequentially removing one study at a time.

The presence of heterogeneity was examined using the above statistical tests. The I² statistic and Cochrane Q test were used to assess heterogeneity. High inter-study heterogeneity was defined as $p < 0.1$ or $I^2 > 50\%$. When significant heterogeneity was present ($I^2 > 50\%$ or $p < 0.1$), a random-effects model using restricted maximum likelihood estimation was applied for the meta-analysis; otherwise, a fixed-effect model was used. Statistical significance was defined as $p < 0.05$, and all analyses were completed using the Stata version 16 (StataCorp LLC, USA).

To assess small-study effects, we employed Egger's linear regression tests. Specifically, Egger's test quantifies funnel plot asymmetry by modelling standardized effect estimates as a function of precision (inverse standard error). These formal bias assessments were restricted to meta-analyses comprising eight or more studies. All statistical analyses were performed using Stata version 16 (StataCorp LLC). A two-tailed test was applied, p -value < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The initial electronic search yielded 488 papers in total. After removing 161 duplicate records, 327 articles were screened for eligibility, of which 19 were included in the meta-analysis. Fig. 1 summarizes the complete workflow of study selection, assessment and data analysis. Baseline characteristics of the 19 included trials are presented in Table I.

Of these, 18 studies (11–28) reported changes in serum uric acid (SUA) levels from baseline to post-dapagliflozin treatment, while the study by Kohan *et al.* (29) did not report SUA but provided data on estimated glomerular filtration rate (eGFR).

Table I. Summary of study characteristics

Intervention	Control	No. of patients (dapagliflozin/ control)	Dura- tion (weeks)	Outcome	Country/region	Ref.
Dapagliflozin 10 mg per day + OADs	PBO + OADs	145/148	24	SUA, eGFR, Scr	Multinational (Australia, Canada, Japan, South Korea, Mexico, South Africa, Spain, Taiwan, USA)	11
Dapagliflozin 10 mg per day + MET > 1.5 g/day ^a	PBO + MET > 1.5 g per day ^a	95/73	102	SUA, eGFR, Scr	Multinational (Argentina, Brazil, Canada, Mexico, USA)	12
Dapagliflozin 10 mg per day + OADs (insulin) ^b	PBO + OADs (insulin) ^b	139/133	24	SUA, eGFR	China, South Korea, Singapore	13
Dapagliflozin 10 mg per day + MET	PBO + MET	113/112	24	SUA, eGFR, Scr	China, South Korea, Taiwan, India	14
Dapagliflozin 10 mg per day + OADs	OADs	36/38	24	SUA, Scr, UACR	Japan	15
Dapagliflozin 10 mg per day + MET	PBO + MET	70/75	24	SUA, Scr, Cystatin C	USA	16
Dapagliflozin 10 mg per day	MET 1.5 g per day	30/30	12	SUA, UACR	China	17
Dapagliflozin 10 mg per day + MET	PBO + MET	209/209	24	SUA, Scr	Multinational (North America, Latin America, Europe, Asia)	18
Dapagliflozin 10 mg per day + glimepiride 4 mg per day	PBO + glimepiride 4 mg per day	151/146	24	SUA, eGFR, Scr	Multinational (Poland, Korea, Germany, Sweden, USA)	19
Dapagliflozin 10 mg per day	PBO	135/137	24	SUA, Scr, Cystatin C	Canada, Argentina, Mexico, Brazil	20

Intervention	Control	No. of patients (dapagliflozin/ control)	Dura- tion (weeks)	Outcome	Country/region	Ref.
Dapagliflozin 10 mg per day + OADs	PBO + OADs	28/29	12	UACR	Thailand	21
Dapagliflozin 5 mg per day + MET 0.75 g per day	MET 1.5 g per day	37/37	16	SUA	Japan	22
Dapagliflozin 10 mg per day	PBO	25/24	6	SUA	Finland, Sweden	23
Dapagliflozin 10 mg per day + OADs (insulin) ^b	PBO + OADs (insulin) ^b	29/30	3 days	SUA	China	24
Dapagliflozin 10 mg per day + pioglitazone ≥ 30 mg per day	PBO + pioglitazone ≥ 30 mg per day	140/139	24	SUA, Scr	Multinational (Argentina, Canada, India, Mexico, Peru, Philippines, Taiwan, USA)	25
Dapagliflozin 10 mg per day	Sitagliptin 100 mg	168/163	24	SUA, eGFR	Japan	26
Dapagliflozin 10 mg per day + OADs (insulin) ^b	OADs (insulin) ^b	196/197	48	SUA, eGFR, Scr, UACR, Cystatin C	Europe, North America	27
Dapagliflozin 10 mg per day + MET	PBO	40/44	12	SUA, Scr	USA, Canada, Mexico, Puerto Rico	28
Dapagliflozin 10 mg per day + MET	PBO + MET	85/84	104	eGFR	Multinational (USA, Argentina, Canada, India, Mexico, Peru, Italy, Australia, France, Spain, Denmark, Puerto Rico, Singapore)	29

PBO – placebo; MET – metformin; OAD – oral antidiabetic drug; Scr – serum creatinine; SUA – serum uric acid; eGFR – estimated glomerular filtration rate; UACR – urine albumin-to-creatinine ratio; ^a Metformin (≥ 1,500 mg per day);

^b Stratified by insulin alone or insulin + OADs

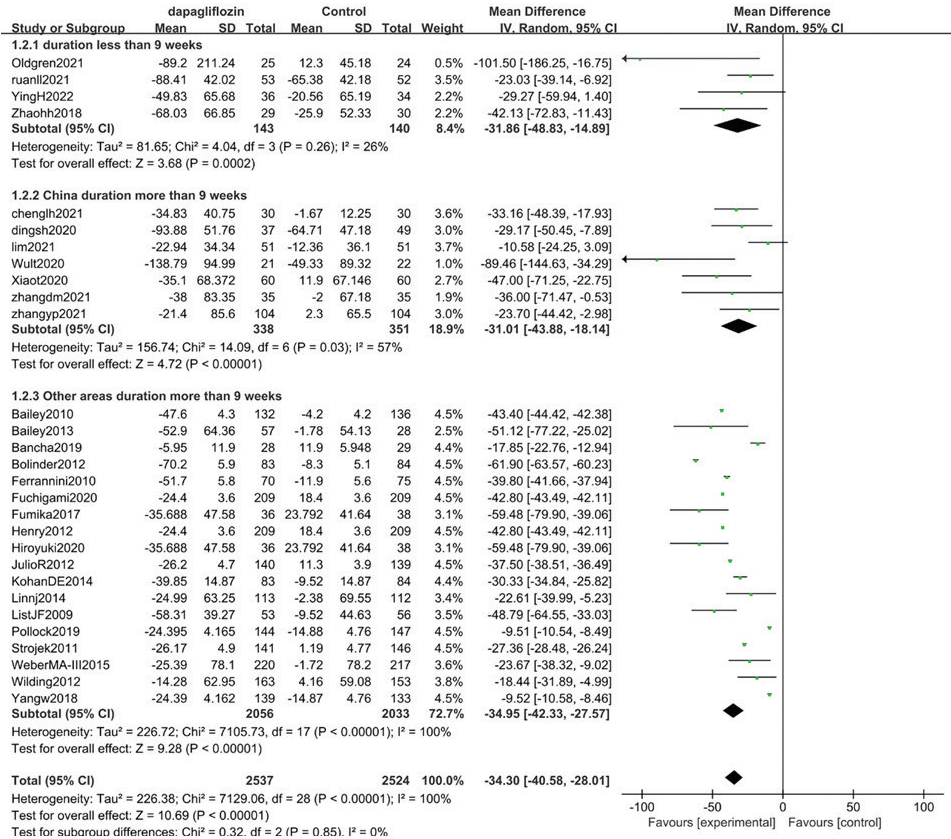


Fig. 1. Flowchart illustrating the process of literature selection.

The meta-analysis showed that dapagliflozin treatment was associated with significantly reduced serum uric acid concentration (−11.4 %, 95 % confidence interval CI = −14.5 to −8.4 %, $p < 0.0001$) (Fig. 2). Given the significant inter-study heterogeneity ($I^2 = 76.8$ %), a random-effects model was applied. Sensitivity analysis confirmed that no single variable disproportionately influenced the overall results, validating the robustness of conclusions derived from the random-effects model.

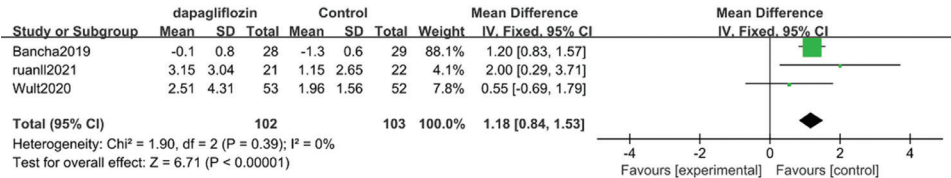


Fig. 2. Forest plot comparing uric acid (UA) concentrations between the control and dapagliflozin groups.

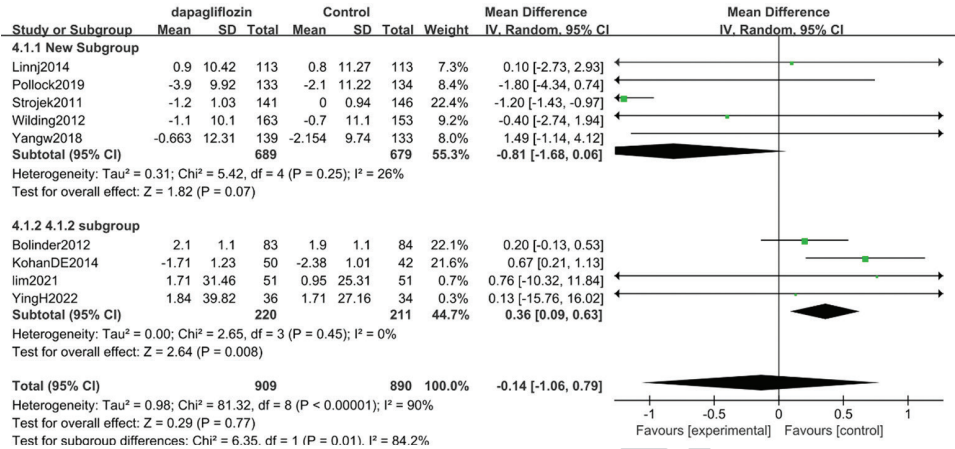


Fig. 3. Forest plot depicting variations in estimated glomerular filtration rate (eGFR) following dapagliflozin treatment relative to control condition.

Six studies reported changes in eGFR (14, 19, 21, 26, 27, 29) but no statistically significant difference in eGFR change was observed between the dapagliflozin groups and the control groups (0.1 %, 95 % CI = -1.7 to 2.0 %, $p = 0.863$) (Fig. 3).

Ten studies reported changes in serum creatinine level (Scr) (12, 14–16, 18–20, 25, 27, 28). Significant heterogeneity supported the use of a random-effects model in the meta-analysis. Changes in Scr were observed between the dapagliflozin and control groups, with no statistically significant difference (+0.6 %, 95 % CI = -0.6 to 1.8 %, $p = 0.294$) (Fig. 4).

Three studies reported changes in cystatin C levels (16, 20, 27) with no statistically significant difference between the dapagliflozin and control groups (4.2 %, 95 % CI = -0.4 to 8.8 %, $p = 0.061$) (Fig. 5).

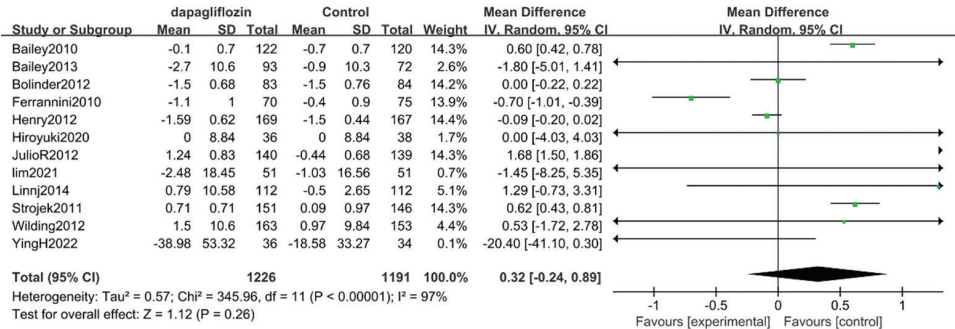


Fig. 4. Forest plot illustrating alterations in serum creatinine (Scr) levels in the dapagliflozin and control groups.

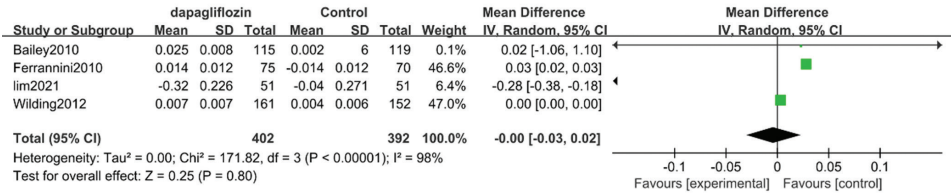


Fig. 5. Forest plot displaying changes in cystatin C (Cys-C) levels in the dapagliflozin and control groups.

Three studies reported changes in the UACR (17, 21, 27). Still, dapagliflozin treatment resulted in no significant reduction in UACR compared with the control condition (-33.1% , 95% CI = -115.7 to 49.4% , $p = 0.226$). Two trials reported outcomes related to urinary protein excretion (11, 27). Due to discrepancies in the analyte evaluated, the effect metric employed, the units of measurement utilized, the duration of treatment, and the baseline proteinuria status, quantitative pooling was deemed inappropriate. Consequently, a narrative synthesis was performed in accordance with the SWiM guideline, employing direction of effect for the calculation of votes. The results of both trials demonstrated a clear preference for dapagliflozin over placebo, with this observation being consistent across all four studies. In the DELIGHT trial (11), conducted in patients with type 2 diabetes and moderate-to-severe CKD receiving renin-angiotensin system blockade, dapagliflozin 10 mg daily significantly reduced 24-hour urinary albumin excretion at week 24 *versus* placebo (-19.9% , 95% CI -35.6 to -0.3% ; $p = 0.047$), with a greater reduction for dapagliflozin plus saxagliptin (-39.7% ; $p < 0.0001$). In Wilding *et al.* report (27), patients treated with insulin and exhibiting near-normal baseline proteinuria experienced an increase in urinary albumin under placebo ($+4.7\text{ mg L}^{-1}$) but a decline in all dapagliflozin groups (-17.8 to -34.3 mg L^{-1}) at week 48. These endpoints were reported descriptively without formal testing. Publication bias was assessed by funnel plot and Egger's test. No evidence of significant publication bias was detected by Egger's test ($p = 0.42$), consistent with the visual symmetry observed in the funnel plot (Fig. S2). If considered as a whole, and despite the exclusion of a quantitative synthesis, the consistent direction of the effect suggests that dapagliflozin reduces urinary protein and albumin excretion in patients with established CKD and albuminuria, and to a large extent independent of glycemic and blood pressure lowering.

Therapeutic and clinical relevance

HUA, as an important metabolic disorder, poses a serious threat to global public health, with its prevalence showing a continuous upward trend worldwide. This disease exhibits a significantly higher incidence among patients diagnosed with CKD (30). Extensive research has confirmed a strong relationship between HUA and various metabolic disorders, including kidney disease, diabetes and cardiovascular diseases (31). The relationship between renal function and uric acid excretion is bidirectional: impaired renal function leads to reduced uric acid excretion and secondary HUA, while elevated uric acid levels actively promote the progression of diabetes. This is reflected in the complex correlation between HbA1c and serum uric acid levels (32). Furthermore, elevated uric

acid levels promote cardiovascular morbidity through multiple mechanisms, including activation of the renin-angiotensin system, oxidative stress induction and endothelial dysfunction (33). Another critical aspect of HUA is its role in accelerating CKD and increasing the risk of renal function deterioration. Evidence indicates that HUA significantly exacerbates renal damage through various pathological pathways, including induction of glomerular hypertension, renal hypertrophy and eventual sclerosis (34). In the current clinical context, characterized by frequent multimorbidity, developing a comprehensive therapeutic approach capable of simultaneously addressing HUA and its associated comorbidities is crucial. Further, implementing personalized uric acid management strategies hold crucial clinical significance for breaking the vicious cycle of metabolic disease.

SGLT-2 inhibitors, a recently developed class of oral glucose-lowering agents, have attracted considerable attention due to their unique mechanism of action (34). The pharmacological actions of these drugs involve lowering the threshold for glucose reabsorption and inhibiting glucose uptake within the renal tubules. Consequently, these drugs promote urinary glucose excretion (35).

Current clinical guidelines present a notable paradox. While the 2024 KDIGO CKD (36), 2020 ACR (37), and EULAR gout guidelines (38) all conditionally recommend against initiating urate-lowering therapy (ULT) for CKD and asymptomatic HUA, accumulating evidence from clinical trials that controlled for serum uric acid levels showed renoprotective benefits (39). We argue that this discrepancy between guideline recommendations and clinical evidence does not stem from conflicting data, but rather from fundamental disagreements surrounding the definition of the "asymptomatic." Current guidelines narrowly define "asymptomatic" as the absence of prior gout flares or subcutaneous tophi (38), establishing this as the sole symptom-based threshold for ULT initiation. However, from a pathophysiological perspective, the clinical spectrum of urate crystal deposition disease extends far beyond joint inflammation. Nephrolithiasis, urate nephropathy, and subsequent declines in eGFR, proteinuria, and elevated Scr are all direct consequences of monosodium urate crystal deposition in renal tissue (40). Categorizing a patient with confirmed CKD and clear signs of renal injury as "asymptomatic" solely because they do not have gout – thereby failing to meeting the criteria for ULT – ignores the fact that urate crystal deposition disease affects the whole body. This leads to a significant gap between guideline-directed practice and actual pathophysiology.

Dapagliflozin offers a pragmatic solution to this therapeutic stalemate. Unlike conventional ULT agents, dapagliflozin indirectly promotes uric acid excretion by enhancing urinary glucose excretion, thereby inducing a compensatory increase in proximal tubular secretion. Since dapagliflozin is already approved for the treatment of CKD or diabetes, its prescription is not directly influenced by the controversy over whether asymptomatic HUA patients should initiate ULT. Therefore, clinicians may prescribe this drug based on solid evidence for glycemic control and cardiorenal protection, while simultaneously obtaining the additional benefit of serum uric acid lowering and renal protection (31). Thus, dapagliflozin may serve as a pragmatic bridge between metabolic intervention and renoprotection, offering a therapeutic alternative for HUA in patients with CKD that transcends the conventional ULT framework.

Real-world evidence has raised concerns regarding the efficacy of dapagliflozin in reducing UACR (41), and the initial eGFR decline observed during treatment initiation has

further tempered clinician enthusiasm for its use (42). Indeed, real-world prescribing of SGLT2 inhibitors in non-diabetic chronic kidney disease (ND-CKD) remains suboptimal; this therapeutic inertia reflects an interplay of clinician-level barriers, socio-economic disparities, and healthcare system constraints (7). A global prospective study of approximately 15,000 patients with diabetes across 37 countries demonstrated that ND-CKD was associated with a 27 % reduction in SGLT2i prescribing (43). In this context, we conducted the present meta-analysis to quantify the urate-lowering and renoprotective effects of dapagliflozin, thereby strengthening the evidence base to inform clinical practice. It is evident that the present article is deficient in its demonstration of the beneficial effects of dapagliflozin in relation to UACR. Notably, Pollock *et al.* (11) (patients with average eGFR 49 mL min⁻¹ per 1.73 m²), Kohan *et al.* (29) (patients with average eGFR = 44.2 mL min⁻¹ per 1.73 m²), Huang *et al.* (44) (patients with average Scr of 143.08 µmol L⁻¹) enrolled predominantly CKD populations. Analyses of these studies demonstrated that dapagliflozin effectively reduced UACR (WMD: -39.67 mg g⁻¹, 95 % CI = -70.14 to -9.19, *p* = 0.01) without resulting in a precipitous decline in eGFR, providing further confidence for its use in CKD populations. Of note, while dapagliflozin reduced proteinuria, it did not have a significantly adverse impact on renal function, as evidenced by the eGFR. Hence, dapagliflozin provides renoprotection without imposing additional renal burden. Conversely, the sustained and stable trajectory of renal function in patient suggests potential long-term reno-

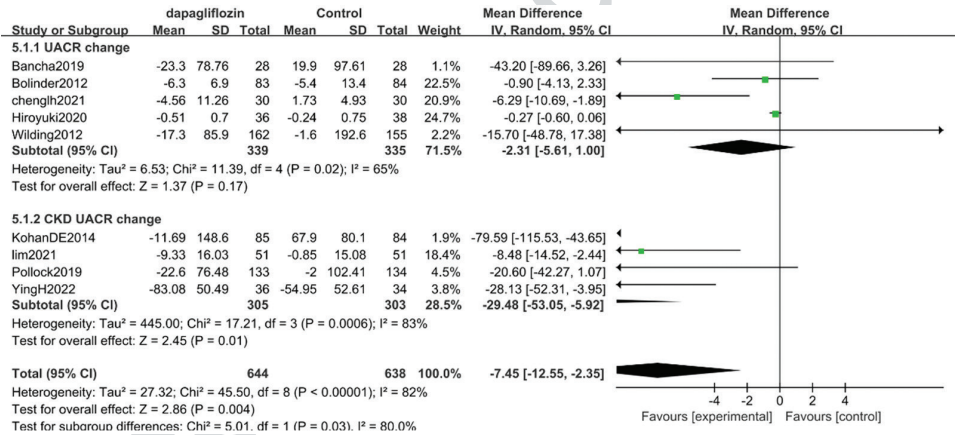


Fig. 6. Forest plot showing changes in urine albumin-to-creatinine ratio (UACR) in the dapagliflozin and control groups.

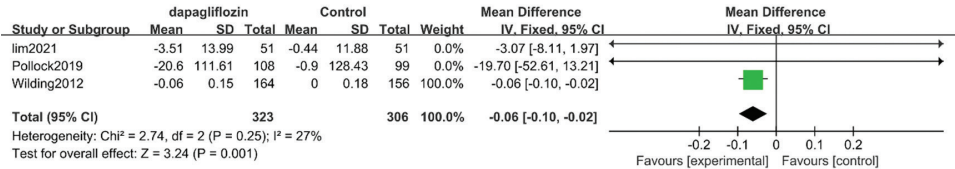


Fig. 7. Forest plot showing outcomes measures in the dapagliflozin and control groups.

protective benefits. As demonstrated in preceding studies, a slight decline in eGFR can be observed during the early stages of initiating dapagliflozin therapy (45). This is followed by a longer period of renal function maintenance. This early eGFR decline may reflect hemodynamic adaptation and a protective mechanism (46).

Clinical implications

This meta-analysis demonstrated that dapagliflozin significantly reduces serum uric acid levels while concomitantly lowering proteinuria, as reflected by decreased UTP and UACR. Notably, conventional markers of renal function – Scr and eGFR – remained stable throughout treatment with dapagliflozin, underscoring its favourable renal safety profile. Collectively, these findings indicate that dapagliflozin offers dual metabolic and renoprotective benefits, supporting its potential as a therapeutic option for patients with chronic kidney disease and hyperuricemia, irrespective of conventional urate-lowering therapy paradigms.

Limitations of the study

Firstly, the follow-up periods of the included studies were mainly concentrated between 24 and 52 weeks, resulting in a lack of long-term data to assess the impact of dapagliflozin on hard endpoints, such as end-stage renal disease or cardiovascular events. Secondly, there is a paucity of research reporting on urinary protein excretion; further research is needed to investigate their renal protective functions. Third, differences in dosing regimens and patient characteristics (*e.g.*, baseline renal function) across studies may have introduced heterogeneity. In conclusion, the lack of subgroup analyses in non-diabetic populations limits the generalizability of the conclusions.

CONCLUSIONS

In summary, dapagliflozin effectively lowers serum uric acid levels by promoting uric acid excretion, reduces urinary protein excretion, and demonstrates good safety under conditions with stable renal function. These findings further consolidate our confidence in treating patients with diabetes and CKD accompanied by HUA with dapagliflozin, providing important evidence for its clinical application. Future research should focus on the efficacy of dapagliflozin in different populations (*e.g.*, various CKD stages), explore its synergistic effects with other urate lowering drugs, and verify its long-term impact on hard endpoints through extended follow-up.

Abbreviations, acronyms, symbols. – CKD – chronic kidney disease, Cys-C – cystatin C, eGFR – estimated glomerular filtration rate, GFR – glomerular filtration rate, HUA – hyperuricemia, MD – mean difference, ND-CKD – non-diabetic chronic kidney disease, RCTs – randomized controlled trials, Scr – serum creatinine levels, SUA – serum uric acid, UACR – urine albumin-to-creatinine ratio, ULT – urate-lowering therapy.

Availability of data and materials. – The datasets used and/or analysed during the current study were publicly available from the PubMed, Embase, Cochrane Library, Web of Science databases. This meta-analysis is registered in PROSPERO under registration number CRD42022325174.

Acknowledgements. – Thanks for the support from the Intramural Research Project of China Aerospace Science and Industry Corporation, 731 Hospital.

Conflict of interests – The authors declare no conflict of interests.

Funding. – This work was funded by the Intramural Research Project of China Aerospace Science and Industry Corporation, 731 Hospital (NO. 2022-QSYN-06).

Author's contribution. – Conceptualization, Y.F. and Y.T.; methodology, Y.F.; software, D.R.; validation, X.R., D.P., and J.Y.; formal analysis, L.Y.; investigation, Y.F.; resources, Y.T.; data curation, D.R.; writing, original draft preparation, Y.F.; writing, review and editing, Y.S.; supervision, X.H.; project administration, D.P.; funding acquisition, Y.F. All authors have read and agreed to the published version of the manuscript.

REFERENCES

1. C. Zeng, J. Wei, T. Yang, H. Li, W. F. Xiao, W. Luo, S. G. Gao, Y. S. Li, Y. L. Xiong and G. H. Lei, Higher blood hematocrit predicts hyperuricemia: A prospective study of 62897 person-years of follow-up, *Sci. Rep.* **5** (2015) Article ID 13765 (11 pages); <https://doi.org/10.1038/srep13765>
2. N. Dawood, A. Mian Sajjad, H. Shahzad, R. Sundus, S. Anam and K. Sibgha, Hyperuricemia as an independent risk factor for acute coronary syndrome in patients without metabolic syndrome, *Pak. Postgrad. Med. J.* **36** (2025) 37–41; <https://doi.org/10.51642/ppmj.v36i01.727>
3. X. Li, J. Sun, Q. Bu, B. Zhou, L. Li, X. Man, L. Zhao, Y. Xu and H. Luan, Association between serum uric acid levels and clinical outcomes in patients with acute kidney injury, *Renal Fail.* **45** (2023) Article ID 2169617 (9 pages); <https://doi.org/10.1080/0886022x.2023.2169617>
4. Z. Zhang, F. Zhang, Y. Bai, J. Li and Y. Zhong, Association of finerenone with prognosis and safety in diabetic kidney disease patients: An updated meta-analysis based on four RCTs, *Front. Med.* **12** (2025) Article ID 1594202 (10 pages); <https://doi.org/10.3389/fmed.2025.1594202>
5. S. S. Khan and S. E. Quaggin, Therapies on the horizon for diabetic kidney disease, *Curr. Diab. Rep.* **15** (2015) Article ID 111 (13 pages); <https://doi.org/10.1007/s11892-015-0685-3>
6. Y. Zhang, P. Xie, Y. Li, Z. Chen and A. Shi, Mechanistic evaluation of the inhibitory effect of four SGLT-2 inhibitors on SGLT 1 and SGLT 2 using physiologically based pharmacokinetic (PBPK) modeling approaches, *Front. Pharmacol.* **14** (2023) Article ID 1142003 (18 pages); <https://doi.org/10.3389/fphar.2023.1142003>
7. R. Minutolo, S. Borrelli, A. Ambrosini, L. Amoroso, F. Aucella, V. Batini, Y. Battaglia, L. Bregoli, V. Cantaluppi, G. Cianciolo, P. Conti, P. Fabbrini, C. Giammarresi, E. Imbalzano, S. La Rosa, M. Marengo, V. Montinaro, D. Musone, M. Napoli, F. Nappi, C. Pluvio, D. Santoro, R. Scarpioni, F. Sopranzi, T. Tullio and L. De Nicola, Efficacy and safety of dapagliflozin in patients with CKD: Real-world experience in 93 Italian renal clinics, *Clin. Kidney J.* **18**(1) (2025) Article ID sfac396 (9 pages); <https://doi.org/10.1093/ckj/sfae396>
8. Z. Zhang, H. J. L. Heerspink, G. M. Chertow, R. Correa-Rotter, A. Gasparrini, N. Jongs, A. M. Langkilde, J. J. V. McMurray, M. N. Mistry, P. Rossing, R. D. Toto, P. Vart, D. Nitsch, D. C. Wheeler and B. Caplin, Ambient heat exposure and kidney function in patients with chronic kidney disease: A post-hoc analysis of the DAPA-CKD trial, *Lancet Planet. Health* **8**(4) (2024) E225–E233; [https://doi.org/10.1016/s2542-5196\(24\)00026-3](https://doi.org/10.1016/s2542-5196(24)00026-3)
9. D. Z. I. Cherney, C. C. J. Dekkers, S. J. Barbour, D. Cattran, A. H. Abdul Gafor, P. J. Greasley, G. D. Laverman, S. K. Lim, G. L. Di Tanna, H. N. Reich, M. G. Vervloet, M. G. Wong, R. T. Gansevoort and H. J. L. Heerspink, Effects of the SGLT2 inhibitor dapagliflozin on proteinuria in non-diabetic patients with chronic kidney disease (DIAMOND): A randomised, double-blind, crossover trial, *Lancet Diabetes Endocrinol.* **8** (2020) 582–593; [https://doi.org/10.1016/s2213-8587\(20\)30162-5](https://doi.org/10.1016/s2213-8587(20)30162-5)

10. J. P. T. Higgins, J. Thomas, J. Chandler, M. Cumpston, T. Li, M. J. Page and V. A. Welch (Eds.), *Cochrane Handbook for Systematic Reviews of Interventions – version 6.3* (updated February 2022), Cochrane, 2022.
11. C. Pollock, B. Stefánsson, D. Reyner, P. Rossing, C. D. Sjöström, D. C. Wheeler, A. M. Langkilde and H. J. L. Heerspink, Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin and effect of dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease (DELIGHT): A randomised, double-blind, placebo-controlled trial, *Lancet Diabetes Endocrinol.* **7** (2019) 429–441; [https://doi.org/10.1016/s2213-8587\(19\)30086-5](https://doi.org/10.1016/s2213-8587(19)30086-5)
12. C. J. Bailey, J. L. Gross, D. Hennicken, N. Iqbal, T. A. Mansfield and J. F. List, Dapagliflozin add-on to metformin in type 2 diabetes inadequately controlled with metformin: A randomized, double-blind, placebo-controlled 102-week trial, *BMC Med.* **11** (2013) Article ID 43 (10 pages); <https://doi.org/10.1186/1741-7015-11-43>
13. W. Yang, J. Ma, Y. Li, Y. Li, Z. Zhou, J. H. Kim, J. Zhao and A. Ptaszynska, Dapagliflozin as add-on therapy in Asian patients with type 2 diabetes inadequately controlled on insulin with or without oral antihyperglycemic drugs: A randomized controlled trial, *J. Diabetes* **10** (2018) 589–599; <https://doi.org/10.1111/1753-0407.12634>
14. L. Ji, J. Ma, H. Li, T. A. Mansfield, C. L. T'Joën C, N. Iqbal, A. Ptaszynska and J. F. List, Dapagliflozin as monotherapy in drug-naïve Asian patients with type 2 diabetes mellitus: A randomized, blinded, prospective phase III study, *Clin. Ther.* **36**(1) (2014) P84-100.E9; <https://doi.org/10.1016/j.clinthera.2013.11.002>
15. H. Kayano, S. Koba, T. Hirano, T. Matsui, H. Fukuoka, H. Tsujita, S. Tsukamoto, T. Hayashi, T. Toshida, N. Watanabe, Y. Hamazaki, E. Geshi, M. Murakami, K. Aihara, K. Kaneko, H. Yamada, Y. Kobayashi and T. Shinke, Dapagliflozin influences ventricular hemodynamics and exercise-induced pulmonary hypertension in type 2 diabetes patients – a randomized controlled trial, *Circ. J.* **84** (2020) 1807–1817; <https://doi.org/10.1253/circj.cj-20-0341>
16. E. Ferrannini, S. J. Ramos, A. Salsali, W. Tang and J. F. List, Dapagliflozin monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: A randomized, double-blind, placebo-controlled, phase 3 trial, *Diabetes Care* **33** (2010) 2217–2224; <https://doi.org/10.2337/dc10-0612>
17. C. L. Hu, Y. C. Wang, Y. Xi and X. M. Yao, Dapagliflozin therapy curative effect observation on nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus, *Indian J. Pharm. Sci.* **82** (2020) 122–129; <https://doi.org/10.36468/pharmaceutical-sciences.spl.155>
18. R. R. Henry, A. V. Murray, M. H. Marmolejo, D. Hennicken, A. Ptaszynska and J. F. List, Dapagliflozin, metformin XR, or both: Initial pharmacotherapy for type 2 diabetes, a randomised controlled trial, *Int. J. Clin. Pract.* **66** (2012) 446–456; <https://doi.org/10.1111/j.1742-1241.2012.02911.x>
19. K. Strojek, K. H. Yoon, V. Hrubá, M. Elze, A. M. Langkilde and S. Parikh, Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with glimepiride: A randomized, 24-week, double-blind, placebo-controlled trial, *Diabetes Obes. Metab.* **13** (2011) 928–938; <https://doi.org/10.1111/j.1463-1326.2011.01434.x>
20. C. J. Bailey, J. L. Gross, A. Pieters, A. Bastien and J. F. List, Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with metformin: A randomised, double-blind, placebo-controlled trial, *Lancet* **375** (2010) 2223–2233; [https://doi.org/10.1016/s0140-6736\(10\)60407-2](https://doi.org/10.1016/s0140-6736(10)60407-2)
21. B. Satirapoj, P. Korkiatpitak and O. Supasyndh, Effect of sodium-glucose cotransporter 2 inhibitor on proximal tubular function and injury in patients with type 2 diabetes: A randomized controlled trial, *Clin. Kidney J.* **12** (2019) 326–332; <https://doi.org/10.1093/ckj/sfy122>
22. F. Shigiyama, N. Kumashiro, M. Miyagi, K. Ikehara, E. Kanda, H. Uchino and T. Hirose, Effectiveness of dapagliflozin on vascular endothelial function and glycemic control in patients with early-

- stage type 2 diabetes mellitus: DEFENCE study, *Cardiovasc. Diabetol.* **16** (2017) Article ID 84 (12 pages); <https://doi.org/10.1186/s12933-017-0564-0>
23. J. Oldgren, S. Laurila, A. Åkerblom, A. Latva-Rasku, E. Rebelos, H. Isackson, M. Saarenhovi, O. Eriksson, K. Heurling, E. Johansson, U. Wilderäng, C. Karlsson, R. Esterline, E. Ferrannini, J. Oscarsson and P. Nuutila, Effects of 6 weeks of treatment with dapagliflozin, a sodium-glucose cotransporter-2 inhibitor, on myocardial function and metabolism in patients with type 2 diabetes: A randomized, placebo-controlled, exploratory study, *Diabetes Obes. Metab.* **23** (2021) 1505–1517; <https://doi.org/10.1111/dom.14363>
24. Z. Hao, X. Huang, H. Shao and F. Tian, Effects of dapagliflozin on serum uric acid levels in hospitalized type 2 diabetic patients with inadequate glycemic control: A randomized controlled trial, *Ther. Clin. Risk Manag.* **2018**(14) (2018) 2407–2413; <https://doi.org/10.2147/tcrm.s186347>
25. J. Rosenstock, M. Vico, L. Wei, A. Salsali and J. F. List, Effects of dapagliflozin, an SGLT2 inhibitor, on HbA1c, body weight, and hypoglycemia risk in patients with type 2 diabetes inadequately controlled on pioglitazone monotherapy, *Diabetes Care* **35** (2012) 1473–1478; <https://doi.org/10.2337/dc11-1693>
26. A. Fuchigami, F. Shigiyama, T. Kitazawa, Y. Okada, T. Ichijo, M. Higa, T. Hiyoshi, I. Inoue, K. Iso, H. Yoshii, T. Hirose and N. Kumashiro, Efficacy of dapagliflozin versus sitagliptin on cardiometabolic risk factors in Japanese patients with type 2 diabetes: A prospective, randomized study (DIVERSITY-CVR), *Cardiovasc. Diabetol.* **19** (2020) Article ID 1 (11 pages); <https://doi.org/10.1186/s12933-019-0977-z>
27. J. P. H. Wilding, V. Woo, N. G. Soler, A. P. Pahor, J. Sugg, K. Rohwedder and S. Parikh, Long-term efficacy of dapagliflozin in patients with type 2 diabetes mellitus receiving high doses of insulin: A randomized trial, *Ann. Intern. Med.* **156** (2012) 405–415; <https://doi.org/10.7326/0003-4819-156-6-201203200-00003>
28. J. F. List, V. Woo, E. Morales, W. Tang and F. T. Fiedorek, Sodium-glucose cotransport inhibition with dapagliflozin in type 2 diabetes, *Diabetes Care* **32**(4) (2009) 650–657; <https://doi.org/10.2337/dc08-1863>
29. D. E. Kohan, P. Fioretto, W. Tang and J. F. List, Long-term study of patients with type 2 diabetes and moderate renal impairment shows that dapagliflozin reduces weight and blood pressure but does not improve glycemic control, *Kidney Int.* **85** (2014) 962–971; <https://doi.org/10.1038/ki.2013.356>
30. H. Li, L. Shi, X. Chen and M. Wang, Association between dietary intake of flavonoids and hyperuricemia: A cross-sectional study, *BMC Public Health* **23** (2023) Article ID 1227 (10 pages); <https://doi.org/10.1186/s12889-023-16134-4>
31. H. Wang, X. Zhao, X. Wang, Y. Gong, S. Li, Y. Gu, B. He and J. Wang, Investigation of the role and mechanism of dapagliflozin in mitigating renal injury in rats afflicted with diabetic kidney disease, *Biochem. Pharmacol.* **233** (2025) Article ID 116795 (12 pages); <https://doi.org/10.1016/j.bcp.2025.116795>
32. X. Xia, H. Niu, C. Xu, X. Liu, G. Zhang and J. Ling, Revisiting the metabolic crosstalk between type 2 diabetes and hyperuricemia: Pathophysiological insights and therapeutic perspectives, *Biochim. Biophys. Acta – Mol. Basis Dis.* **1872**(2) (2026) Article ID 168102 (11 pages); <https://doi.org/10.1016/j.bbdis.2025.168102>
33. A. Shubietah, A. Awashra, F. Milhem, M. Ghannam, M. Hattab, I. Rajab, H. Neiroukh, M. Zahdeh, A. Nouri, A. Assaassa, K. Nair, A. Sahni and A. Abu Rmilah, Hyperuricemia and cardiovascular risk: Insights and implications, *Crit. Pathw. Cardiol.* **24**(3) (2025) e0388; <https://doi.org/10.1097/hpc.0000000000000388>
34. P. Sánchez-Brales, M. Marques Vidas, P. López-Sánchez, M. V. López-Illázquez, L. Martín-Testillano, A. Vedat-Ali and J. Portolés, The uricosuric effect of SGLT2 inhibitors is maintained in the long term in patients with chronic kidney disease and type 2 diabetes mellitus, *J. Clin. Med.* **13** (2024) Article ID 1360 (10 pages); <https://doi.org/10.3390/jcm13051360>
35. B. Chen, J. Guo, H. Ye, X. Wang and Y. Feng, Role and molecular mechanisms of SGLT2 inhibitors in pathological cardiac remodeling (Review), *Mol. Med. Rep.* **29** (2024) Article ID 73 (18 pages); <https://doi.org/10.3892/mmr.2024.13197>

36. M. Madero, A. Levin, S. B. Ahmed, J. J. Carrero, B. Foster, A. Francis, R. K. Hall, W. G. Herrington, G. Hill, L. A. Inker, R. Kazancioğlu, E. Lamb, P. Lin, N. McIntyre, K. Morrow, G. Roberts, D. Sabanayagam, M. Shlipak, R. Shroff, N. Tangri, T. Thanachayanont, I. Ulası, G. Wong, C. W. Yang, L. Zhang, K. A. Robinson, L. M. Wilson, R. F. Wilson, B. L. Kasiske, M. Cheung, A. Earley, P. E. Stevens and E. Schaeffner, Evaluation and management of chronic kidney disease: Synopsis of the *Kidney Disease: Improving Global Outcomes 2024 Clinical Practice Guideline*, *Ann. Intern. Med.* **178** (2025) 705–713; <https://doi.org/10.7326/annals-24-01926>
37. J. D. FitzGerald, N. Dalbeth, T. Mikuls, R. Brignardello-Petersen, G. Guyatt, A. M. Abeles, A. C. Gelber, L. R. Harrold, D. Khanna, C. King, G. Levy, C. Libbey, D. Mount, M. H. Pillinger, A. Rosenthal, J. A. Singh, J. E. Sims, B. J. Smith, N. S. Wenger, S. S. Bae, A. Danve, P. P. Khanna, S. C. Kim, A. Lenert, S. Poon, A. Qasim, S. T. Sehra, T. S. K. Sharma, M. Toprover, M. Turgunbaev, L. Zeng, M. A. Zhang, A. S. Turner and T. Neogi, 2020 American College of Rheumatology guideline for the management of gout, *Arthritis Care Res.* **72** (2020) 744–760; <https://doi.org/10.1002/acr.24180>
38. P. Richette, M. Doherty, E. Pascual, V. Barskova, F. Becce, J. Castaneda, M. Coyfish, S. Guillo, T. Jansen, H. Janssens, F. Lioté, C. D. Mallen, G. Nuki, F. Perez-Ruiz, J. Pimentao, L. Punzi, A. Pywell, A. K. So, A. K. Tausche, T. Uhlig, J. Zavada, W. Zhang, F. Tubach and T. Bardin, 2018 updated European League against rheumatism evidence-based recommendations for the diagnosis of gout, *Ann. Rheum. Dis.* **79** (2020) 31–38; <https://doi.org/10.1136/annrheumdis-2019-215315>
39. C. Y. Hsu, C. Iribarren, C. E. McCulloch, J. Darbinian and A. S. Go, Risk factors for end-stage renal disease: 25-year follow-up, *Arch. Intern. Med.* **169** (2009) 342–350; <https://doi.org/10.1001/archinternmed.2008.605>
40. Y. F. Qing, J. X. Zheng, Y. P. Tang, F. Dai, Z. R. Dong and Q. B. Zhang, LncRNAs landscape in the patients of primary gout by microarray analysis, *PLoS One* **16** (2021) Article ID e0232918 (17 pages); <https://doi.org/10.1371/journal.pone.0232918>
41. K. Dahal, L. Rawal, S. Shah, M. Bhattarai, H. B. Bhattarai, A. Acharya, S. Bhandari, A. Paudel, S. Sah, R. Mehta and A. Gupta, Efficacy and outcomes of dapagliflozin in diabetic nephropathy: A systematic review and meta-analysis, *Medicine (Baltimore)* **104** (2025) Article ID e43171 (6 pages); <https://doi.org/10.1097/md.00000000000043171>
42. S. F. Fatima Gilani, S. Ali, M. Noor, K. Farhat, M. B. Siddique and M. Fatima, Effect of SGLT2 inhibitor dapagliflozin on sodium, potassium and creatinine levels in patients with acute heart failure, *J. Ayub Med. Coll. Abbottabad* **35**(4) (Suppl. 1) (2023) 715–720; <https://doi.org/10.55519/jamc-s4-11906>
43. S. V. Arnold, F. Tang, A. Cooper, H. Chen, M. B. Gomes, W. Rathmann, I. Shimomura, J. Vora, H. Watada, K. Khunti and M. Kosiborod, Global use of SGLT2 inhibitors and GLP-1 receptor agonists in type 2 diabetes. Results from DISCOVER, *BMC Endocr. Disord.* **22** (2022) Article ID 111 (7 pages); <https://doi.org/10.1186/s12902-022-01026-2>
44. Y. Huang, W. Lu and H. Lu, The clinical efficacy and safety of dapagliflozin in patients with diabetic nephropathy, *Diabetol. Metab. Syndr.* **14** (2022) Article ID 47 (6 pages); <https://doi.org/10.1186/s13098-022-00815-y>
45. R. Ogata, T. Kotaki, K. Tanaka, K. Higuchi, N. Kumano, K. Furukawa and Y. Fukumoto, Initial dip in estimated glomerular filtration rate after dapagliflozin affects renal function in chronic phase in chronic heart failure, *J. Clin. Med.* **14** (2025) Article ID 5246 (12 pages); <https://doi.org/10.3390/jcm14155246>
46. R. Kawano, T. Haze, A. Fujiwara, A. Haruna, M. Ozawa, Y. Kobayashi, S. Saka, N. Hirawa and K. Tamura, Favorable changes in the eGFR slope after dapagliflozin treatment and its association with the initial dip, *Clin. Exp. Nephrol.* **28** (2024) 1282–1289; <https://doi.org/10.1007/s10157-024-02532-4>