

Original article

Multidisciplinary Delphi study on residual risk in patients with chronic kidney disease and type 2 diabetes mellitus

*Estudio Delphi multidisciplinar sobre riesgo residual en pacientes con enfermedad renal crónica y diabetes mellitus tipo 2*Alberto Ortiz^{a,*}, Ana Cebrián^b, Alfonso Soto^c, Andrés Reyes^d, Jose Luis Górriz^e^a Departamento de Nefrología e Hipertensión Arterial, IIS-Fundación Jiménez Díaz UAM, Madrid, Spain^b Medicina de Familia, Centro de Salud Casco Antiguo Cartagena, Grupo de Investigación en Atención Primaria, Instituto de Investigación Biomédica de Murcia (IMIB), 30201 Cartagena, Murcia, Spain^c Adjunto en el servicio de Endocrinología y Nutrición del Hospital Universitario de A Coruña, Spain^d Medical Advisor, Bayer^e Servicio de Nefrología, Hospital Universitario Clínico de Valencia, Instituto de Investigación Sanitaria (INCLIVA), Universitat de València, Valencia, Spain

ARTICLE INFO

Keywords:

Residual risk

Chronic kidney disease

Type 2 diabetes

Delphi consensus

ABSTRACT

Background and objective: Currently, patients with chronic kidney disease (CKD) and type-2 diabetes mellitus (T2DM) present a persistent residual renal and cardiovascular (CV) risk despite receiving standard treatment. Therefore, the aim was to assess the degree of multidisciplinary consensus on the persistent residual risk in these patients and its possible therapeutic approach.

Materials and Methods: A Scientific Committee of 4 experts accustomed to the management of CKD and T2DM proposed the content of a Delphi questionnaire and the profile of panelists and validated the final questionnaire. A panel composed of 60 specialists in Nephrology (n = 20), Endocrinology (n = 20) and Primary Care (n = 20) completed the questionnaire specifically designed for the study, which contained 76 statements generated after a targeted literature review, to which 2 more statements were added for the second round. Using Delphi methodology adapted between May and June 2024, the panel assessed the statements included in the questionnaire in 2 rounds. Each statement was to be rated on an ordinal Likert-type scale from 1 to 9 points.

Results: A response was obtained from 60 specialists in the 2 rounds of the study. Seventy-two percent of the panelists had more than 15 years of experience, 70.0% followed more than 25 patients with CKD and T2DM monthly, and all belonged to a scientific society. In the first Delphi round, the defined level of agreement was reached for 43 statements and in the second round for 10 additional statements [53/78 (68%) consensus statements]. The section with consensus on the largest number of statements was residual risk (86.4%). In this block, the predefined level of agreement was reached in aspects such as elevated risk of renal complications (median; interquartile range: 9 [8–9]), CV (9 [8–9]) or premature death (9 [8–9]) despite receiving standard treatment, the complementary action of different drugs with different mechanism of action (9 [9–9]), the simultaneous establishment of 3 pillars of treatment [renin-angiotensin system blockade + SGLT2 inhibitors (iSGLT2) + Non-steroidal Mineralocorticoid Receptor Antagonists (mRNAs)] (8 [7–9]), the progress made by iSGLT2 (9 [9–9]) and ARMn (8 [7–9]) in renal and CV protection, and the need to avoid therapeutic inertia (9 [8–9]), use treatments early and intensively (9 [8–9]) and coordination between levels of care (9 [9–9]).

Conclusions: Multidisciplinary consensus was obtained that patients with T2DM and CKD present a high residual risk of disease progression, premature death, renal and CV complications. The simultaneous implementation of the 3 pillars of treatment, the avoidance of therapeutic inertia, and coordination between levels of care are considered relevant measures to contribute to reducing the residual risk in these patients.

* Corresponding author.

E-mail address: aortiz@fjd.es (A. Ortiz).<https://doi.org/10.1016/j.nefro.2025.501338>

Received 30 January 2025; Accepted 4 April 2025

Available online 12 September 2025

2013-2514/© 2025 Sociedad Española de Nefrología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

RESUMEN

Palabras clave:

Riesgo residual
Enfermedad renal crónica
Diabetes tipo 2
Consenso Delphi

Antecedentes y objetivo: Actualmente las personas que padecen Enfermedad Renal Crónica (ERC) y Diabetes Mellitus tipo-2 (DMT2) presentan un riesgo residual renal y cardiovascular (CV) persistente a pesar de recibir el estándar de tratamiento. Por ello, el objetivo fue evaluar el grado de consenso multidisciplinar sobre el riesgo residual persistente en estos pacientes y su posible abordaje terapéutico.

Materiales y métodos: Un Comité Científico de 4 expertos habituados al manejo de la ERC y DMT2 propuso el contenido de un cuestionario Delphi y el perfil de panelistas y validó el cuestionario final. Un panel compuesto por 60 especialistas en Nefrología (n = 20), Endocrinología (n = 20) y Atención Primaria (n = 20) completó el cuestionario diseñado específicamente para el estudio, que contenía 76 afirmaciones generadas tras una revisión dirigida de la literatura, a las que se añadieron 2 afirmaciones más para la segunda ronda. Utilizando metodología Delphi adaptada entre mayo y junio de 2024, el panel valoró en 2 rondas las afirmaciones incluidas en el cuestionario. Cada afirmación debía valorarse en una escala ordinal de tipo Likert de 1 a 9 puntos.

Resultados: Se obtuvo respuesta de 60 especialistas en las 2 rondas del estudio. El 72% de los panelistas contaban con más de 15 años de experiencia, el 70,0% seguían a más de 25 pacientes con ERC y DMT2 mensualmente y todos pertenecían a alguna Sociedad Científica. En la primera ronda Delphi se alcanzó el nivel de acuerdo definido para 43 afirmaciones y en la segunda ronda en 10 afirmaciones adicionales [53/78 (68%) afirmaciones consensuadas]. La sección con consenso en un mayor número de afirmaciones fue la de riesgo residual (86,4%). En este bloque se alcanzó el nivel predefinido de acuerdo en aspectos como el riesgo elevado de complicaciones renales (mediana; rango intercuartílico: 9 [8–9]), CV (9 [8–9]) o de muerte prematura (9 [8–9]) a pesar de recibir tratamiento estándar, la acción complementaria de diferentes fármacos con distinto mecanismo de acción (9 [9–9]), la instauración simultánea de 3 pilares de tratamiento [bloqueo del sistema renina-angiotensina + inhibidores de SGLT2 (iSGLT2) + Antagonistas no esteroideos del Receptor Mineralocorticoide (ARMns)] (8 [7–9]), el avance que han supuesto iSGLT2 (9 [9–9]) y ARMn (8 [7–9]) en protección renal y CV, y la necesidad de evitar la inercia terapéutica (9 [8–9]), utilizar los tratamientos de forma temprana e intensiva (9 [8–9]) y coordinación entre niveles asistenciales (9 [9–9]).

Conclusiones: Se obtuvo consenso multidisciplinar en que los pacientes con DMT2 y ERC presentan un riesgo residual elevado de progresión de la enfermedad, muerte prematura, complicaciones renales y CV. La instauración simultánea de los 3 pilares de tratamiento, evitar la inercia terapéutica y la coordinación entre niveles asistenciales son medidas consideradas relevantes para contribuir a reducir el riesgo residual en estos pacientes.

Introduction

Chronic kidney disease (CKD) is defined as the presence of alterations in kidney structure or function that negatively impact health for more than 3 months. The combination of glomerular filtration rate (GFR) and albuminuria allows for risk stratification of various adverse outcomes, including progression to kidney failure requiring kidney replacement therapy and premature death from cardiovascular (CV) and non-CV causes.^{1–4} In fact, the increased risk of premature death is the main consequence of CKD and is not corrected by dialysis or transplantation. These factors are associated with a loss of life expectancy of up to 44 years as compared to the general population.⁵ Consequently, CKD is expected to become the third leading cause of death in Spain before 2050, this is largely due to the aging of the population.⁶ Type 2 diabetes mellitus (T2DM) is a significant risk factor for the development of CKD which affects one-third of patients with T2DM.⁷ Multiple factors contribute to the pathogenesis of CKD, primarily metabolic, hemodynamic, and inflammatory/fibrotic alterations.^{1,8–10}

In Spain, the prevalence of T2DM has been estimated at 7.8% in the adult population, increasing to 13.8% when undiagnosed patients are included.¹¹ Among adults with T2DM, a 33.8% have CKD, and 21.2% have albuminuria (category A2–A3).⁷

Despite the current treatments, many patients with T2DM develop severe forms of CKD and maintain a high residual risk of CV death and disease progression, even despite receiving renin-angiotensin system (RAS) inhibitors and sodium-glucose cotransporter 2 (SGLT2i) inhibitors.^{8,12,13} This may be influenced by poor glycemic control, blood pressure, and patient lifestyle.¹⁴ Furthermore, the absolute residual risk is increased with higher albuminuria or lower baseline GFR.¹⁵ The dynamic nature of the residual risk depends on disease duration and the effectiveness of therapeutic interventions. It is crucial to consider in clinical trials factors such as disease duration, glycemic control, blood pressure, proteinuria, and renal function to

adequately identify and manage residual risk in patients with CKD and T2DM.¹⁶ The pharmacological approach to residual risk is based on a comprehensive approach based on pharmacological control of glucose, lipids, and hypertension, as well as inflammation and fibrosis. Clinical guidelines suggest the use of SGLT2 inhibitors, glucagon-like peptide-1 receptor agonists (GLP-1 RA), aldosterone-reducing enzyme inhibitors (RAAS) with angiotensin-converting enzyme inhibitors (ACE inhibitors), or angiotensin II receptor blockers (ARBs^{1,17,18}). Furthermore, nonsteroidal mineralocorticoid receptor antagonists (nsMRAs) have demonstrated benefits in renal and cardiovascular protection,¹⁹ and are recommended by clinical practice guidelines such as the Kidney Disease Improving Global Outcomes (KDIGO), the American Diabetes Association (ADA), and the European Society of Cardiology guidelines.^{4,17,20–22}

However, currently no consensus definition of residual risk has been established in patients with CKD and T2DM. In this sense, there are still areas of residual risk associated with CKD that remain unknown, such as the interaction of genetic factors with the environment, the complete molecular mechanisms, and the long-term effectiveness of new treatments.

Given the uncertainty surrounding residual risk in patients with CKD and T2DM, the objective of this study was to evaluate the degree of multidisciplinary consensus on the persistent residual risk, from the perspectives of nephrology, endocrinology, and family medicine, despite standard treatment in Spain of these patients and its possible therapeutic approach.

Methods

Study design

The study was conducted using the Delphi methodology adapted in two rounds, aiming to reach consensus on the management of

residual risk that persists in patients with CKD and T2DM. The Delphi method is a social research technique that aims to obtain a reliable opinion from a group of experts.^{23,24} This research method is characterized by an iterative process in which panelists must be consulted at least twice on the same issue, allowing them to re-issue their opinions once they receive the opinions of the other panelists. Responses are kept anonymous, and panelists do not coincide in time or physically, avoiding influence from others. Information exchange is carried out through the study's scientific committee, which decides what information is provided to the panelists.^{23,24} The decision to establish two rounds is based on existing literature which shows that two rounds can be sufficient to reach consensus among experts.

The study was conducted in Spain between February and June 2024. Ethics committee approval was not required because patient data was not used.

A scientific committee constituted by four experts with experience in the management of CKD and T2DM (two nephrologists, one endocrinologist, and one family physician) designed the content of the Delphi questionnaire, validated it, and determined the panelist profile.

An external company, IQVIA, was involved in the development of the study from the design through the field phase and analysis of results.

Study questionnaire

The questionnaire was designed based on a focused literature search conducted in PubMed and non-conventional sources of information, such as research reports and technical documents; the idea was to identify aspects relevant to the study. Based on this information, the questionnaire was developed, containing 76 statements, to which two additional statements were added for the second round (78 statements in total).

Each statement had to be rated on a Likert-type ordinal scale of 1–9 points, with 1 generally representing completely disagreement and 9 completely agreement. The statements were organized into three sections: (a) clinical management (33 statements); (b) therapeutic strategy (23 statements); and (c) residual risk (22 statements). The questionnaire was programmed using Google Forms.

The Delphi questionnaire is available in Appendix B (supplementary material), including the results for the different rounds.

Selection of the expert panel

The Delphi study's scientific committee defined the profile of the panelists and collaborated in the selection of potential participants. This selection was based on experience with this type of patients and membership in scientific societies. The expert panel consisted of 60 professionals involved in the management of CKD and T2DM in Spain, with the following distribution: 20 experts in nephrology, 20 in

endocrinology, and 20 in family medicine. The Delphi study was double-blinded for panelists.

The eligibility criteria for participating in the study as a panelist and completing the questionnaire were: (1) at least 5 years of experience managing patients with CKD and T2DM; (2) visiting every month at least 20 patients in nephrology and at least 10 patients in endocrinology and family medicine with CKD and T2DM; (3) currently working with patients in the corresponding national health department; (4) availability to participate throughout in the duration of the study (May and June); (5) membership in a scientific society or association.

An invitation was sent out describing the study objective and the Delphi process. After agreeing to participate, the experts received a link to access the Delphi questionnaire, with the option to withdraw at any time.

Delphi rounds

The first round took place in from 10 to 21 of May 2024; and the second round was held from June 7 to 17 of June 2024, with three reminders sent to panelists to encourage participation. The questionnaire was answered virtually and anonymously, based on the panelists' knowledge and experience.

After analyzing the data from the first round, the items that reached consensus were eliminated. The updated Delphi questionnaire and a summary of the first-round results were sent only to those that responded the first Delphi round, allowing them to modify their responses according to the overall judgment of the expert panel.

The scientific committee reviewed the results of rounds 1 and 2 of the Delphi study in different virtual meetings after their completion (Fig. 1).

Data analysis

For statistical analysis, the median and interquartile range were calculated to assess the degree of consensus using Microsoft Excel. It was considered that, to achieve consensus, the median score and interquartile range should be within the same range on the scale: 1–3, 4–6, or 7–9.

Results

A 100% response rate was obtained from the 60 specialists in the two rounds of the Delphi study. A 72% of the panelists had more than 15 years of work experience, 70.0% saw more than 25 patients with CKD associated with T2DM monthly, and all belonged to a scientific society (Appendix B, Table S1 of the supplementary material).

In the first round of Delphi, the defined level of agreement was reached for 43 statements out of the 76 statements initially included (56.6%). The consensus-based statements were excluded from the next round, but two new statements were added and another one was

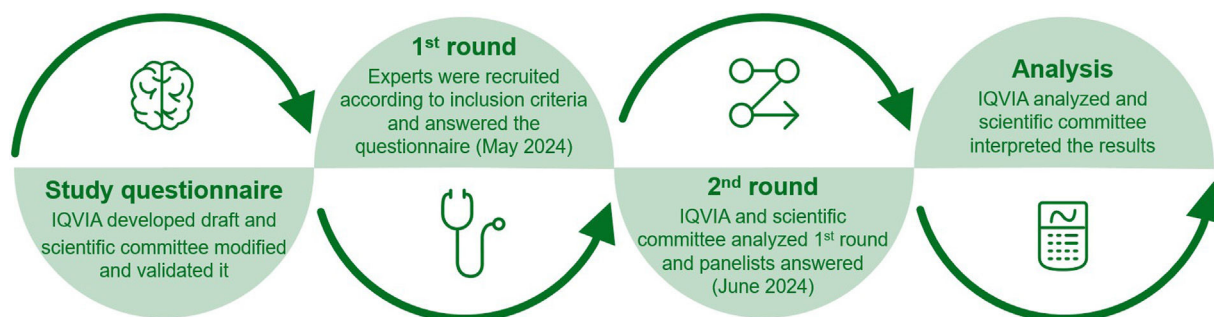


Figure 1. Methodology of Delphi study adapted in 2 rounds.

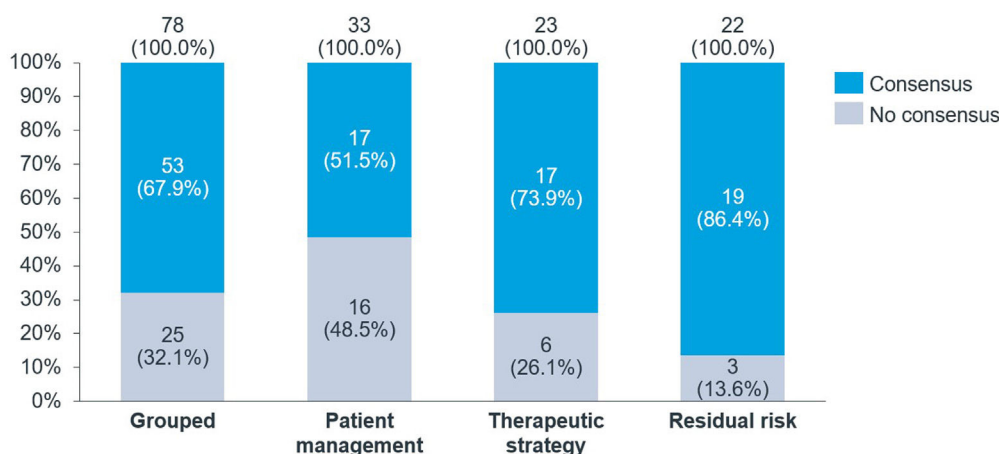


Figure 2. Results of Delphi study grouped and per sections.

reformulated. In the second round, the defined level of agreement was reached for 10 statements out of a total of 35 statements (28.6%). Overall, after the two rounds, the defined level of agreement was reached for 53 of the 78 statements included in the questionnaire (67.9%).

The section with the highest number of consensus statements was the residual risk section (86.4%), followed by the section of therapeutic strategy (73.9%), and the therapeutic management section (51.5%) (Fig. 2, Appendix B, Table S1 of the supplementary material). The statements and results (median, 25th percentile, and 75th percentile) from the first and second rounds are presented in Appendix B, Table S2 of the supplementary material.

Patient management

Regarding the clinical practice guidelines that should be used as references, consensus was reached that the KDIGO guidelines (8 [8–9]), the ADA (8 [7–9]), and the consensus document of the 10 scientific societies (8 [7–9]) should be the primary reference documents.

No consensus was reached on the barriers limiting the application of the guidelines in clinical practice, such as time restrictions, lack of training, and variability in access to diagnostic tests.

Likewise, there was consensus that primary care physicians, endocrinologists, and nephrologists should be familiar with and apply the KDIGO classification for risk stratification of CKD-related adverse events, such as premature death, CKD progression, acute kidney injury, and cardiovascular events such as stroke, myocardial infarction, and atrial fibrillation (9 [8–9]), and there was disagreement on that only nephrologists should be familiar with and apply the KDIGO classification (1 [1–3]).

Regarding the diagnosis of diseases, there was consensus that T2DM is primarily diagnosed in family medicine (8 [7, 75–9]). However, there was no consensus regarding CKD screening and detection levels. Regarding statements about the level of monitoring of CV risk, CKD, and other complications and their management, there was a consensus in the intermediate range of 4–6 on the Likert scale, indicating a lack of knowledge about these aspects.

Therapeutic strategy

Consensus was reached among panelists on most treatment goals. The statement with the highest level of agreement was on lifestyle recommendations, in agreement with the patient (9 [9–9]).

Regarding pharmacological treatments, there was no consensus that the majority of patients who would benefit from treatment were

receiving such a treatment routinely, regardless of the type of treatment.

Residual risk

The key factors for addressing residual risk that were agreed upon by the panelists are summarized in Table 1 (for more information, see the supplementary material).

Consensus was reached that the concurrence of CKD and T2DM reduces life expectancy more than expected from the independent effect of each disease (9 [8–9]). It was also agreed that, in patients with CKD category G3, albuminuria influences the risk of premature death more than GFR (7 [7–8]).

The panelists agreed that patients with T2DM and CKD have a high residual risk of disease progression or renal complications (9 [8–9]), CV complications (9 [8–9]), and premature death (9 [8–9]), despite standard treatment.

Regarding pharmacological strategies, there was also consensus on the need to simultaneously implement RAAS blockade, SGLT2 inhibitors, and nsMRAs (8 [7–9]) and to apply nephroprotective treatments early and intensively (9 [8–9]). It was also agreed that residual risk can be reduced by using nephroprotective and cardioprotective drugs with complementary mechanisms of action (9 [9–9]). It was also agreed that SGLT2 inhibitors and nsMRAs represented a significant progress (9 [9–9] and 8 [7–9], respectively) and could have complementary effects (9 [8–9]).

Regarding non-pharmacological strategies, it was agreed that patients with residual renal risk need more frequent monitoring of the urine albumin/creatinine ratio and estimated glomerular filtration rate to evaluate the effect of treatments (8 [7–9]), as well as the recommendation to avoid smoking.

Therapeutic inactivity should be avoided; by monitoring glomerular filtration rate and albuminuria should be monitored least once a year, regardless of treatment (9 [8–9]). Improved coordination between levels of care (9 [9–9]) and the use of bidirectional communication systems (9 [8–9]) were other key strategies to mitigate residual risk.

No consensus was reached regarding the assessment of CV risk in routine clinical practice (6 [5–7]), the risk of kidney failure versus CV death in patients with CKD category G3 (3 [2–4]), and the importance of calculating the plasma phosphorus-to-protein ratio (6 [5–7]).

Discussion

This study gathers the experience-based opinions of various specialists, including nephrologists, endocrinologists, and family

Table 1

Key factors to address residual risk agreed upon by panelists.

Burden of disease in patients with CKD and T2DM	
1	When T2DM and CKD concur, the effect on life expectancy is greater than expected due to the independent effect of both pathologies.
2	In patients with category G3 CKD, albuminuria has a greater influence than glomerular filtration rate on the risk of premature death.
Existence of residual risk in patients with CKD and T2DM	
3	Despite treatment, patients with T2DM and CKD may continue to be at high risk of disease progression or kidney complications.
4	Despite treatment, patients with T2DM and CKD may continue to be at high risk of cardiovascular (CV) complications.
5	Despite treatment, patients with T2DM and CKD may continue to be at high risk of premature death.
6	This high risk of premature death is not completely corrected by dialysis or transplantation: the life expectancy of these patients is reduced by up to 40 and 15 years, respectively, compared to the general population.
Pharmacological strategies	
7	Management of the residual risk of renal and CV complications in patients already receiving standard of care can be improved by the use of nephroprotective and cardioprotective drugs with complementary mechanisms of action.
8	Reducing the residual risk of renal complications, CV and premature death can be achieved by using treatments that have an additional effect on patients who are already receiving standard treatment.
9	The establishment of the 3 pillars of treatment simultaneously (ACEi/ ARAII + iSGLT2 + NSMRAs) is the optimal strategy to address residual risk as opposed to sequential treatment.
10	The iSGLT2 have advanced the renal and CV protection of patients with T2DM and CKD already treated with RAS inhibitors.
11	Non-steroidal MRAs have advanced the renal and CV protection of patients with T2DM and CKD already treated with RAS and independent of the benefit obtained with SGLT2 inhibitors.
12	Given the different mechanisms of action of SGLT2 inhibitors and nonsteroidal MRAs, they may have complementary action.
13	To mitigate the residual risk of patients who are already receiving standard treatment, it is essential to apply nephroprotective treatments early and intensively.
Non-pharmacological strategies	
14	Patients with renal residual risk require more frequent monitoring of urine albumin/creatinine ratio and estimated glomerular filtration rate to assess the effect of the treatments applied.
15	However, if the estimated glomerular filtration rate is low and albuminuria is high (red boxes on the KDIGO heatmap), the CV risk is already very high and it is not necessary to use SCORE2.
16	To mitigate residual risk, therapeutic inertia should be avoided by monitoring eGFR and albuminuria at least once a year, regardless of treatment.
17	Coordination between levels of care would also reduce the residual risk of patients who are already receiving standard treatment by implementing an optimal approach to patients with T2DM and CKD.
18	Two-way communication systems between specialties and levels of care, such as teleconsultation, would facilitate the prescription of nephroprotective treatments early.
19	Smoking is a key factor in mitigating the residual risk of patients who are already receiving standard treatment.

ACEi: angiotensin-converting enzyme inhibitors; ARAII: angiotensin II receptor antagonists; CV: cardiovascular; DM: diabetes mellitus; T2DM: type 2 diabetes mellitus; CKD: chronic kidney disease; GFR: glomerular filtration rate; MR: mineralocorticoid receptor; NSMRA: non-steroidal mineralocorticoid receptor antagonists; RAS: renin-angiotensin system; SGLT2: sodium-glucose cotransporter 2 inhibitors.

physicians, providing diverse perspectives on residual risk and its management in patients with CKD and T2DM.

The results of the Delphi study indicated that patients with CKD associated with T2DM have a high residual risk of disease progression, renal and cardiovascular complications, and premature death. Furthermore, the panelists considered that this residual risk persists despite current therapeutic interventions and underscored the urgent need for more effective approaches.

It was found that there are numerous studies published showing that, despite receiving standard treatment, many patients with CKD

associated with T2DM continue to be at high risk of complications, highlighting the importance of more comprehensive and personalized approaches. However, identifying and managing residual risk is complex and requires ongoing assessment and a personalized approach to the treatment. This involves not only controlling traditional risk factors but also considering other factors that may contribute to disease progression.²⁵

Given this challenge, the panel considered that residual risk management must be comprehensive and dynamic to adequately address the needs of these patients. Strategies to address residual risk in patients with T2DM and CKD, supported by the Delphi study consensus, include the simultaneous, early, and intensive implementation of the three pillars of treatment: RAAS inhibitors, SGLT2 inhibitors, and nsMRAs. These drugs, with complementary mechanisms of action, offer significant benefits in managing residual risk for these patients.

It should be taken into consideration that first, the use of RAASi have been shown to reduce renal progression in both diabetics^{26,27} and non-diabetics,²⁸ but only modestly, leaving much residual risk to be resolved. Second, SGLT2i improves glycemic control, reduce intraglomerular pressure and proteinuria, and offer benefits of cardiovascular disease and heart failure. However, 10% or more of patients with CKD treated with SGLT2i and RAASi experienced disease progression during a relatively short follow-up of 2–3 years.^{29,30} Blood pressure levels are higher in patients with more advanced CKD, up to 15% in those patients with higher albuminuria. These treatments do not directly target inflammation, oxidative stress, and fibrosis pathways, so additional therapeutic options are needed to block these pathogenic mechanisms.³¹ Third, nsMRAs significantly reduce proteinuria and slow the progression of CKD, thus improving kidney function and reducing CV risk in a complementary manner to the two axes mentioned above.^{8,32} Furthermore, the triple combination was safer than dual combinations.³³ Therefore, the combination of these treatments addresses multiple pathogenetic pathways of CKD and T2DM, providing a robust and multidimensional therapeutic strategy.

The international clinical practice guidelines that were considered reference guidelines by the panelists' consensus, namely the KDIGO and ADA guidelines,^{17,20} also reinforce this approach by covering all three treatment pillars. The therapeutic algorithms of Spanish scientific societies, including the consensus document by García-Maset et al.¹ in 2022, recommend a holistic approach to the disease, although at the time of publication, finerenone was not yet marketed. In other diabetes and CKD guidelines, such as the one from the redGDPS foundation, prepared in 2023, the approach of the 3 pathways is recommended in a manner aligned with the KDIGO and ADA guidelines,³⁴ as well as the guidelines for the management of patients with CKD and DM published by the Spanish Society of Nephrology and the Spanish Diabetic Nephropathy Study Group (GEENDIAB).²²

However, it is important to note that the panelists were unable to reach a consensus, or only did so with intermediate scores (between 4 and 6 on the scale), regarding statements about the management, follow-up, and administration of treatments for the patients in clinical practice. This highlights the ongoing need for progress in this area, as well as the need to optimise the management of these patients, given the current variability in clinical practice.

Therefore, it is essential to adopt a comprehensive, multidisciplinary approach to minimise residual risk and optimise long-term outcomes in patients with T2DM-associated CKD.

The Delphi methodology enables participants to express their views freely, independent of group leaders. However, this study has limitations inherent to the Delphi method, such as bias in the selection of experts, because the criteria for selecting panelists may not have adequately identified those with the most experience in this field. Nevertheless, the members of the scientific committee did have

extensive experience in treating patients in this field. Moreover, the use of a structured questionnaire could restrict the results of the study.

The panel also agreed on a series of non-pharmacological strategies that could be beneficial for effectively addressing residual risk, such as lifestyle modification and closer monitoring of the urine albumin-to-creatinine ratio and GFR. Furthermore, mitigating therapeutic inertia was considered essential, making advisable to establish continuous monitoring and proactive treatment adjustments to respond to disease progression and individual patient needs.

Another agreed strategy was the effective coordination of different levels of care for the comprehensive management of residual risk. Indeed, fluid communication and collaboration between primary care, specialized care, and other health services would ensure a cohesive and continuous approach to patient care, optimizing clinical outcomes.

Finally, promoting telemedicine could facilitate patient follow-up, allowing easier access to care and continuous monitoring of their health. Telemedicine in the management of CKD allows patients to access remote consultations and monitoring, facilitating health follow-up without the need for travel.³⁵ Furthermore, it would promote patient education and multidisciplinary collaboration, thereby improving the quality of care and treatment adherence.³⁵ Implementing these strategies can help mitigate residual risk and improve the quality of life of patients with CKD.

However, it is important to highlight that the panelists either failed to reach consensus or, alternatively, reached intermediate scores (4–6 on the scale) regarding statements about patient management and follow-up, as well as the administration of treatment in clinical practice. This reflects the persistent need to advance in this area and optimize the management of these patients, since currently there is great variability in their management in clinical practice.

Therefore, it is essential to adopt a comprehensive and multidisciplinary approach that minimizes residual risk and optimizes long-term outcomes in patients with CKD associated with T2DM.

The Delphi methodology allows participants to express themselves freely without the influence of group leaders. However, the study suffers from the limitations inherent to the Delphi method, such as expert selection bias, as the criteria for selecting panelists may not have adequately identified those with the most experience in this field. However, the members of the scientific committee did have extensive experience treating patients in this field. Furthermore, the use of a structured questionnaire could restrict the study's results.

Conclusions

Multidisciplinary consensus was reached that in patients with CKD and T2DM have a high residual risk of disease progression, premature death, and renal and cardiovascular complications. Measures considered relevant to reduce residual risk in these patients, in which there is multidisciplinary consensus, include simultaneous, early, and intensive initiation of the three treatment pillars (ACE inhibitors/ARBs + SGLT2 inhibitors + nsMRAs), avoiding therapeutic inertia, and promoting coordination between the different levels of care.

Funding

This work was funded by Bayer. Bayer participated in the design, data analysis, and writing of the manuscript. The authors received no honoraria for authorship.

Declaration of competing interest

Alberto Ortiz has received grants from Sanofi and consulting fees, speaking fees, and travel support from Advicene, Alexion, Astellas,

Astrazeneca, Amicus, Amgen, Bioparto, Boehringer Ingelheim, Esteve, Fresenius Medical Care, GSK, Bayer, Sanofi-Genzyme, Sobi, Menarini, Mundipharma, Kyowa Kirin, Lilly, Freeline, Idorsia, Chiesi, Otsuka, Novo-Nordisk, Sysmex, and Vifor Fresenius Medical Care Renal Pharma and Spafarma. He is Director of the UAM-Astrazeneca Chair in Chronic Kidney Disease and Electrolytes. He holds shares in Telara Farma.

Ana Cebrián declares having received funding to conduct clinical trials from MSD and Sanofi (all at the IMIB institute); Consulting fees from AstraZeneca, Bayer, Eli Lilly, MSD, Novo Nordisk, and Sanofi; speaking fees from AstraZeneca, Bayer, Boehringer-Ingelheim, Eli Lilly, Menarini, MSD, Sanofi, and Novo Nordisk.

Alfonso Soto declares no conflicts of interest.

Andrés Reyes is an employee of Bayer.

José Luis Górriz declares having received funding to conduct clinical trials from AstraZeneca, Bayer, Boehringer-Ingelheim, and Novo Nordisk (all for the INCLIVA Research Institute); consulting fees from AstraZeneca, Bayer, Boehringer-Ingelheim, and Novo Nordisk; and speaking fees from AstraZeneca, Novo Nordisk, Bayer, Menarini, Boehringer-Ingelheim, and Eli Lilly.

Acknowledgments

The authors thank María Lloret, Daniel Callejo, and Aaron Aires, IQVIA staff, for their support in the study design, data analysis, and manuscript writing. These services were funded by Bayer.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.nefro.2025.501338>.

References

- García-Maset R, Bover J, de la Morena JS, Diezhandino MG, del Hoyo JC, San Martín JE, et al. Documento de información y consenso para la detección y manejo de la enfermedad renal crónica. *Nefrología*. 2022;42(3):233–64.
- Martínez-Castelao A, Górriz JL, Bover J, Segura-de la Morena J, Cebollada J, Escalada J, et al. Documento de consenso para la detección y manejo de la enfermedad renal crónica. *Atención Primaria*. 2014;46(9):501–19.
- Subdirección General de Calidad y Cohesión. Dirección General de Salud Pública CeIMdSSeICdSdIC. Documento Marco sobre Enfermedad Renal Crónica (ERC) dentro de la Estrategia de Abordaje a la Cronicidad en el SNS Accedido el 23/10/2021. Available from: https://www.msbs.gob.es/organizacion/sns/planCalidadSNS/pdf/Enfermedad_Renal_Cronica_2015.pdf2015.
- Stevens PE, Ahmed SB, Carrero JJ, Foster B, Francis A, Hall RK, et al. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int*. 2024;105(4):S117–314.
- Cordero L, Ortiz A. Decreased life expectancy: a health outcome not corrected by kidney replacement therapy that emphasizes the need for primary prevention of CKD. Oxford University Press; 2024: sfae053.
- Vollset SE, Ababneh HS, Abate YH, Abbafati C, Abbasgholizadeh R, Abbasian M, et al. Burden of disease scenarios for 204 countries and territories, 2022–2050: a forecasting analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024;403(10440):2204–56.
- Usó-Talamantes R, González-de-Julián S, Díaz-Carnicero J, Sauri-Ferrer I, Trillo-Mata JL, Carrasco-Pérez M, et al. Cost of type 2 diabetes patients with chronic kidney disease based on real-world data: an observational population-based study in Spain. *Int J Environ Res Public Health*. 2021;18(18):9853.
- Górriz JL, González-Juanatey JR, Facila L, Soler MJ, Valle A, Ortiz A. Finerenona: completando el abordaje del paciente con enfermedad renal y diabetes. *Nefrología*. 2022.
- de Boer IH, Khunti K, Sadusky T, Tuttle KR, Neumiller JJ, Rhee CM, et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Diabetes Care*. 2022;3075–90.
- Rayego-Mateos S, Rodríguez-Díez RR, Fernández-Fernández B, Mora-Fernández C, Marchant V, Donate-Correa J, et al. Targeting inflammation to treat diabetic kidney disease: the road to 2030. *Kidney Int*. 2023;103(2):282–96.
- Soriguer F, Goday A, Bosch-Comas A, Bordiú E, Calle-Pascual A, Carmena R, et al. Prevalence of diabetes mellitus and impaired glucose regulation in Spain: the Di@bet.es Study. *Diabetologia*. 2012;55(1):88–93.
- Ortiz A, Ferro CJ, Balafa O, Burnier M, Ekart R, Halimi JM, et al. Mineralocorticoid receptor antagonists for nephroprotection and cardioprotection in patients with diabetes mellitus and chronic kidney disease. *Nephrol Dial Transplant*. 2021.

13. Giugliano D, Maiorino MI, Bellastella G, Esposito K. The residual cardiorenal risk in type 2 diabetes. *Cardiovasc Diabetol*. 2021;20(1):1–4.
14. González-Juanatey JR, Górriz JL, Ortiz A, Valle A, Soler MJ, Facila L. Cardiorenal benefits of finerenone: protecting kidney and heart. *Ann Med*. 2023;55(1):502–13.
15. Fernández-Fernández B, Sarafidis P, Soler MJ, Ortiz A. EMPA-KIDNEY: expanding the range of kidney protection by SGLT2 inhibitors. Oxford University Press; 2023 1187–98.
16. Hernández-Mijares A, Ascaso JF, Blasco M, Brea Á, Díaz Á, Mantilla T, et al. Riesgo cardiovascular residual de origen lipídico. Componentes y aspectos fisiopatológicos. *Clín Investig Arterioscler*. 2019;31(2):75–88.
17. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int*. 2022;102(5s):S1–27.
18. Blonde L, Umpierrez GE, Reddy SS, McGill JB, Berga SL, Bush M, et al. American association of clinical endocrinology clinical practice guideline: developing a diabetes mellitus comprehensive care plan-2022 update. *Endocr Pract*. 2022;28(10):923–1049.
19. Barrera-Chimal J, Girerd S, Jaisser F. Mineralocorticoid receptor antagonists and kidney diseases: pathophysiological basis. *Kidney Int*. 2019;96(2):302–19.
20. Draznin B, Aroda VR, Bakris G, Benson G, Brown FM, Freeman R, et al. 11. Chronic kidney disease and risk management: standards of medical care in diabetes-2022. *Diabetes Care*. 2022;45 Supplement 1:S175–84.
21. Comments on the 2023 ESC guidelines on cardiovascular disease in patients with diabetes. *Rev Esp Cardiol (Engl Ed)*. 2024;77(3):196–200.
22. Montero N, Oliveras L, Martínez-Castelao A, Górriz JL, Soler MJ, Fernández-Fernández B, et al. Clinical Practice Guideline for detection and management of diabetic kidney disease: a consensus report by the Spanish Society of Nephrology. *Nefrología*. 2024.
23. Toma C, Picioreanu I. The Delphi technique: methodological considerations and the need for reporting guidelines in medical journals. *Int J Public Health Res*. 2016;4(6):47–59.
24. Jünger S, Payne SA, Brine J, Radbruch L, Brearley SG. Guidance on Conducting and REporting DElphi Studies (CREDES) in palliative care: recommendations based on a methodological systematic review. *Palliative Med*. 2017;31(8):684–706.
25. Gómez-López EA, Molina DI, Castillo J. Del concepto del riesgo residual a la práctica: Historia, desarrollo, evolución del concepto y estado actual. *RIESGO RESIDUAL*. 2023;4–16.
26. Brenner BM, Cooper ME, De Zeeuw D, Keane WF, Mitch WE, Parving H-H, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med*. 2001;345(12):861–9.
27. Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med*. 2001;345(12):851–60.
28. Ruggenenti P, Perna A, Gherardi G, Gaspari F, Benini R, Remuzzi G. Renal function and requirement for dialysis in chronic nephropathy patients on long-term ramipril: REIN follow-up trial. *Lancet*. 1998;352(9136):1252–6.
29. Perkovic V, Jardine MJ, Neal B, Bompont S, Heerspink HJL, Charytan DM, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med*. 2019;380(24):2295–306.
30. Heerspink HJL, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, Hou F-F, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2020;383(15):1436–46.
31. D'Marco L, Puchades MJ, Gandía L, Forquet C, Giménez-Civera E, Panizo N, et al. Finerenone: a potential treatment for patients with chronic kidney disease and type 2 diabetes mellitus. *touchREV Endocrinol*. 2021;17(2):84–7.
32. Barrera-Chimal J, Lima-Posada I, Bakris GL, Jaisser F. Mineralocorticoid receptor antagonists in diabetic kidney disease — mechanistic and therapeutic effects. *Nat Rev Nephrol*. 2022;18(1):56–70.
33. Rossing P, Anker SD, Filippatos G, Pitt B, Ruilope LM, Birkenfeld AL, et al. Finerenone in patients with chronic kidney disease and type 2 diabetes by sodium-glucose cotransporter 2 inhibitor treatment: the FIDELITY analysis. *Diabetes Care*. 2022;45(12):2991–8.
34. Fundación redGDPS. Available from: In: Diabetes y enfermedad renal crónica; 2023, <https://www.diabetespractica.com/files/109/completo.pdf>.
35. Díaz NV. Telemedicina y Telenefrología en la enfermedad renal crónica. Available from: <https://www.nefrologiaaldia.org/es-articulo-telemedicina-y-telenefrologia-en-la-enfermedad-renal-cronica-585>.