



Bridging the gap in early cardio-renal risk prevention in type 2 diabetes: evidence, guidelines, and real-world insights from the PRECARE NO LiMITS initiative

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Abstract

Type 2 diabetes (T2D) is associated with a substantial burden of cardiovascular and renal complications. Although current evidence supports early implementation of organ-protective strategies, therapeutic inertia and uncertainty regarding guideline implementation may delay treatment intensification. The goal of this review is to discuss the rationale for early cardiorenal protection in T2D and to explore real-world perspectives on the use of SGLT2 inhibitors and GLP-1 receptor agonists through insights from the PRECARE NO LiMITS initiative. This narrative review integrates current evidence with exploratory findings from the PRECARE NO LiMITS project, a multicentre educational initiative involving diabetologists from ten diabetes centres in Lombardy, Italy. The initiative included two descriptive clinician survey rounds, conducted at baseline (T0) and after six months (T1), together with moderated expert discussions. At T1, a higher proportion of respondents reported considering SGLT2 inhibitor initiation in a greater proportion of patients with early cardiorenal risk markers, including albuminuria and mildly reduced eGFR, even in the absence of established cardiovascular or renal disease. Survey responses also suggested greater consideration of risk-based treatment strategies extending beyond glycaemic control alone. Persistent perceived barriers included reliance on HbA1c as a primary driver of treatment intensification, uncertainty regarding the timing and implementation of organ-protective therapies, and concerns related to treatment complexity and access. Given the descriptive nature of the survey, differences between T0 and T1 should be interpreted as exploratory. Overall, these exploratory observations, considered alongside current evidence and guideline recommendations, highlight the potential value of a proactive approach to T2D management focused on early identification of cardiorenal risk and appropriate consideration of organ-protective therapies. Educational initiatives, multidisciplinary collaboration, and improved translation of guideline recommendations into routine clinical practice may help address therapeutic inertia and facilitate timely, individualised treatment decisions.

Keywords Type 2 diabetes · Early intervention · Cardiorenal protection · SGLT2 inhibitors · Therapeutic inertia

Introduction

Type 2 diabetes (T2D) represents a growing clinical and epidemiological challenge worldwide and in Italy, with an estimated adult prevalence of 6%. Often asymptomatic

in its early stages, the disease is frequently diagnosed late and suboptimally managed, contributing to a high burden of cardiovascular (CV) and renal complications, hospitalizations, and healthcare costs [1–3]. Most patients do not die from hyperglycemia per se, but from systemic

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consequences of prolonged metabolic and vascular dysfunction. A shift from glycemic control alone to comprehensive, organ-protective strategies is therefore essential [2, 3]. Seminal studies, including UKPDS and its long-term follow-ups, have demonstrated a “legacy effect,” whereby early glycemic control yields durable reductions in micro- and macrovascular events [4–8]. Benefits persist even if glycemic control later deteriorates, underscoring the importance of timely intervention – ideally at or soon after diagnosis. Yet, early intervention remains uncommon, and many patients progress before treatment is intensified [7, 9]. Although major guidelines (ADA, ESC, KDIGO, SID-AMD) increasingly advocate for organ protection, recommendations are often clearest for patients with established comorbidities [10–13]. This creates a grey area in early T2D, where evidence supports intervention, but guidance may appear conservative or unclear. Despite mounting data supporting the efficacy of SGLT2 inhibitors (SGLT2i) and GLP-1RA even in early-stage T2D, these agents are often introduced only after complications emerge [14–16]. Early markers such as microalbuminuria, mildly reduced eGFR, and elevated LDL-C signal vascular and renal risk, but are frequently under-recognized [17–19]. Acting on these indicators before clinical deterioration may prevent irreversible damage. Nonetheless, uptake of early interventions remains limited, hindered by concerns over cost, tolerability, and treatment complexity, and by overreliance on HbA1c as the primary treatment driver [20–23]. This underscores the need for a more holistic, risk-based approach to care. The PRECARE – NO LiMITS project explored how clinicians perceive and respond to early risk indicators in everyday practice. Through a multicentre survey across diabetes centers in Lombardy, the initiative assessed real-world prescribing behaviors and evolving attitudes toward early intensification. It offers pragmatic insights into the barriers, opportunities, and feasibility of implementing proactive care models. This review synthesizes current evidence and expert perspectives from the PRECARE – NO LiMITS initiative. Its objectives are:

- To highlight the rationale for early cardio-renal protection in T2D, even in the absence of comorbidities;
- To describe real-world prescriptive trends across multiple centers;
- To provide practical strategies for overcoming therapeutic inertia.

Ultimately, the goal is to foster a more proactive, integrated model of care aligned with the current evidence base and future direction of T2D management.

Methods

Study objective and design

The PRECARE – NO LiMITS initiative was conceived as a collaborative, multicentre educational project aimed at examining clinicians’ approaches to early cardiorenal risk identification and the use of organ-protective therapies in patients with T2D without established cardiovascular or renal disease. The initiative was not designed as an interventional clinical study, a formal observational cohort study, a Delphi exercise, or a consensus-development process. Rather, it combined two descriptive clinician survey rounds with moderated expert discussions to explore prescribing attitudes, perceived barriers to early therapeutic intensification, and practical considerations arising in routine specialist diabetes care. The narrative review and the PRECARE initiative represented distinct but complementary components of the present manuscript. The narrative review was used to contextualise current evidence and guideline recommendations for cardiorenal protection in T2D, whereas the PRECARE component provided exploratory, self-reported perspectives from practising diabetologists. Findings from the survey and expert discussions were therefore interpreted descriptively and were not intended to establish treatment effectiveness or causal changes in prescribing behaviour. The initiative involved ten specialist diabetes care centers across the Lombardy region of Italy (see Supplementary Material 1). Overall, 48 diabetologists completed the baseline survey (T0), and 44 completed the follow-up survey (T1). Participating clinicians engaged in two structured survey rounds – T0 (baseline) and T1 (follow-up) – as well as in moderated expert discussions. These sessions served both to contextualize the survey findings and to stimulate the exchange of clinical experiences and perspectives. The T0 survey captured self-reported prescribing approaches, perceived barriers to early intervention, and factors influencing the consideration of SGLT2i and GLP-1RA in patients without established cardiovascular or renal disease. The T1 survey was conducted after 6 months using the same questionnaire to provide a second descriptive assessment of these domains. The survey included both multiple-choice questions addressing several aspects of routine clinical decision-making (Supplementary Material 2). Core areas of inquiry included:

- Timing and clinical circumstances associated with SGLT2i or GLP-1RA initiation;
- Clinical criteria considered when initiating these therapies, including HbA1c, albuminuria, eGFR, blood pressure, LDL-C, obesity, age, and diabetes duration;

- Perceived factors contributing to therapeutic inertia and delayed initiation of SGLT2i or GLP-1RA;
- Organisational and administrative barriers to early treatment initiation; and
- Strategies perceived as potentially facilitating earlier implementation of these therapies in clinical practice.

Responses were analyzed descriptively. Results from T0 and T1 are presented as separate survey rounds, and no formal statistical comparisons were performed. Individual-level responses could not be reliably linked between T0 and T1; therefore, paired analyses were not possible, and differences between the two survey rounds should be interpreted as exploratory rather than as within-clinician longitudinal changes. No predefined therapeutic intervention or formal training programme was implemented between T0 and T1. Moderated expert discussions were conducted as part of the educational initiative; however, given the absence of a control group, paired individual-level data, and objective prescribing outcomes, the study design does not allow causal attribution of differences between survey rounds to these discussions or to any other specific factor.

Literature search strategy

A non-systematic narrative literature search was conducted using PubMed/MEDLINE to contextualise current evidence and guideline recommendations regarding early cardiorenal protection in T2D. English-language publications from January 2015 to August 2026 were considered. The literature search was updated during manuscript revision, with the final search performed in August 2026. Search terms included combinations of “type 2 diabetes”, “cardiorenal risk”, “cardiovascular risk”, “chronic kidney disease”, “organ protection”, “SGLT2 inhibitor”, “sodium-glucose cotransporter-2 inhibitor”, “GLP-1 receptor agonist”, “therapeutic inertia”, “early treatment”, and “treatment intensification”. Publications were considered relevant if they addressed cardiorenal risk assessment or prevention in adults with T2D; cardiovascular or renal outcomes associated with SGLT2 inhibitors or GLP-1 receptor agonists; timing of treatment initiation; therapeutic inertia; or contemporary recommendations for cardiorenal risk management. Priority was given to international and national clinical practice guidelines, major randomized cardiovascular and renal outcome trials, meta-analyses, and relevant observational or real-world studies. Additional publications were identified from the reference lists of selected articles and guideline documents. Study selection was based on relevance to the predefined narrative topics and was performed through review of titles, abstracts, and,

where appropriate, full texts. Because this was a narrative rather than a systematic review, no formal PRISMA-based study-selection process, risk-of-bias assessment, or evidence-grading framework was applied. The literature synthesis was intended to provide clinical and guideline context for the PRECARE NO LiMITS initiative rather than a comprehensive systematic assessment of all available evidence.

PRECARE survey methodology

The PRECARE NO LiMITS survey involved specialist diabetologists from ten diabetes care centers across Lombardy, Italy, participating in a regional multicenter network coordinated by Prof. Paolo Fiorina. Participating centers included specialist diabetes services located across the provinces of Milan, Bergamo, Brescia, and Pavia (Supplementary Material 1). Centre and clinician participation was not based on probability sampling, and the participating sample was not intended to be representative of all diabetes centers or diabetologists practicing in Lombardy or Italy. Overall, 48 clinicians completed the T0 survey and 44 participated in the T1 survey. The total number of clinicians invited to each survey round could not be reliably reconstructed from the available records; therefore, a formal response rate could not be calculated.

The questionnaire was developed specifically for the PRECARE NO LiMITS initiative and was not formally validated. It was designed to explore clinicians’ self-reported prescribing approaches and factors influencing the initiation of SGLT2 inhibitors and GLP-1 receptor agonists in routine specialist diabetes care. It included questions addressing clinical triggers for treatment initiation, perceived barriers to early treatment intensification, organizational and administrative barriers, and strategies considered potentially useful for facilitating earlier implementation. The complete questionnaire is provided in Supplementary Material 2. Survey responses were analysed descriptively. Results from T0 and T1 were treated as separate survey rounds, and no formal statistical comparisons were performed. Individual-level survey responses could not be reliably linked between T0 and T1; therefore, paired analyses were not possible. Results are reported using absolute numbers, item-specific denominators, and percentages. Item-level non-response was handled using available-case analysis, with no imputation of missing responses. Differences between the two survey rounds were interpreted as exploratory and were not considered evidence of within-clinician longitudinal changes. Detailed demographic characteristics and years of clinical experience of participating

clinicians were not systematically collected. PRECARE NO LiMITS involved healthcare professionals only and did not involve patient recruitment, collection of individual-level patient data, or protocol-driven modification of patient care. PRECARE NO LiMITS was conducted as an educational initiative involving healthcare professionals only, without patient recruitment, collection of individual-level patient data, or protocol-driven modifications of patient care; accordingly, it was not submitted for formal ethics committee review.

Participant profile

The participating experts were diabetologists actively involved in the longitudinal care of patients with T2D. The selection of centers ensured heterogeneity in terms of clinical volume and institutional affiliations (hospital-based vs outpatient settings). All clinicians had experience in managing patients across the full spectrum of disease severity and comorbidity profiles, from newly diagnosed individuals to those with complex multi-organ involvement.

Results

Early intervention: evidence from international guidelines

This project was informed by a growing body of literature and evolving clinical guidelines that increasingly emphasize the importance of early risk identification and intervention in T2D. International recommendations, from the American Diabetes Association (ADA), the European Society of Cardiology (ESC), and the Kidney Disease: Improving Global Outcomes (KDIGO) consortium, as well as national guidance from the Italian Società Italiana di Diabetologia (SID) and Associazione Medici Diabetologi (AMD), have progressively expanded the focus from glycemic control alone to broader organ protection goals. These documents advocate for a shift in treatment paradigms, recommending the use of agents such as SGLT2i and GLP-1RA not only in patients with established CV or renal disease but also, more recently, in those with early markers of risk (e.g., albuminuria, reduced eGFR, elevated LDL-C or blood pressure), even when glycemic control is adequate. Table 1 provides a comparative summary of the key recommendations across major international and national guidelines, highlighting areas of consensus and divergence regarding early intervention strategies in T2D. This framework served as a conceptual foundation for the survey tool and expert reflections developed within the PRECARE initiative.

Key findings from the survey: shifting towards earlier initiation of cardio-renal protective therapies

As summarized in Table 1, major guidelines converge on the need for earlier intervention based on cardio-renal risk markers. Against this backdrop, the survey explored how these principles are applied in real-world clinical decision-making. A total of 48 diabetologists completed the baseline survey (T0), and 44 participated in the follow-up survey (T1).

Descriptive comparison of survey responses at T0 and T1 showed differences in clinicians' reported consideration of cardiorenal-protective therapies in patients with T2D, including those without established cardiovascular or renal disease. Given the descriptive survey design and the inability to link individual responses across survey rounds, these differences should be interpreted as exploratory and not as evidence of longitudinal changes in individual prescribing behavior. Detailed descriptive results, including absolute numbers, item-specific denominators, percentages, and 95% confidence intervals, are provided in Supplementary Table 3. At T0, while clinicians acknowledged the efficacy of SGLT2i and GLP-1RA, their use was largely confined to patients with overt CVD, CKD, or other advanced complications. There was evident caution regarding the initiation of these agents in patients at earlier disease stages, primarily due to concerns about side effects, patient adherence, and lack of strong guideline endorsement for low-risk profiles. By T1, survey responses suggested a shift towards earlier initiation of SGLT2 inhibitors in patients without established cardiovascular or renal disease, particularly when early cardiorenal risk markers such as albuminuria, mildly reduced eGFR, elevated LDL-C, or borderline hypertension were present. Overall, clinicians appeared more inclined to adopt a risk-based therapeutic approach extending beyond glyce-mic control alone. The primary limiting factors to SGLT2i and GLP-1RA administration remained related to perceived complexity of use, cost/access barriers, and weight management being considered a secondary priority in patients without obesity. Although HbA1c remained a major determinant of treatment intensification, survey responses suggested a progressive shift towards the consideration of additional cardiorenal risk markers (Fig. 1).

Prescriptive trends and use of cardio-renal protective therapies

At T1, a higher proportion of respondents reported considering earlier initiation of cardiorenal-protective therapies compared with T0 respondents. A higher proportion of T1 respondents reported considering a proactive, risk-based

Table 1 Practical framework for individualized cardiorenal risk assessment and therapeutic consideration in T2D

Clinical scenario	Main therapeutic focus	Therapeutic consideration	Practical considerations	Supporting source
T2D without established CVD or CKD	Comprehensive risk assessment and individualized metabolic management	Individualize glucose-lowering therapy according to glycaemic, weight, and cardiorenal risk profile	Consider SGLT2i or GLP-1RA when supported by the individual risk profile and current guideline recommendations; consider expected benefit, adverse effects, preferences, access, and cost	[10, 13]
CKD / reduced eGFR	Kidney and cardiovascular protection	Consider SGLT2i with demonstrated kidney benefit; GLP-1RA may also be considered according to individual clinical characteristics	Consider eGFR, albuminuria, glycaemic needs, tolerability, and concomitant therapy	[10, 12]
CKD with albuminuria	Reduction of CKD progression and cardiovascular risk	SGLT2i with demonstrated benefit; consider non-steroidal MRA in eligible patients	Optimize RAAS blockade when indicated and tolerated; individualize according to eGFR and albuminuria	[10, 12]
Established ASCVD or multiple ASCVD risk factors	Cardiovascular risk reduction	GLP-1RA and/or SGLT2i with demonstrated cardiovascular benefit	Selection should reflect individual cardiovascular, kidney, metabolic, tolerability, and treatment-burden considerations	[10, 11]
Prior cardiovascular event	Secondary cardiovascular prevention	Consider GLP-1RA and/or SGLT2i with demonstrated cardiovascular benefit	Combined therapy may be considered in selected patients when clinically appropriate; routine combination therapy is not implied	[10]
Heart failure	Reduction of HF events and cardiorenal risk	SGLT2i with demonstrated HF benefit	Consider renal function, volume status, tolerability, and concomitant HF therapy	[10, 11]
Progressive/advanced CKD	Kidney protection and slowing disease progression	Consider SGLT2i when guideline eligibility criteria are met; consider nonsteroidal MRA in eligible patients	Individualize according to eGFR, albuminuria, potassium, concomitant therapy, and tolerability	[10, 12]
Older adults / frailty	Individualized goals, safety, and minimization of treatment burden	Prefer therapies with low hypoglycaemia risk; individualize pharmacological treatment	Consider frailty, cognitive and functional status, comorbidities, renal function, polypharmacy, adverse effects, life expectancy, and patient preferences	[10]

This framework summarizes guideline-supported considerations for individualized clinical decision-making and should not be interpreted as a prescriptive treatment algorithm. Therapeutic decisions should be based on current guideline recommendations and individualized according to absolute cardiorenal and metabolic risk, expected absolute benefit, comorbidities, potential adverse effects and treatment tolerability, treatment burden, patient preferences, accessibility, and cost

T2D Type 2 Diabetes; *HbA1c* Hemoglobin A1c; CVD cardiovascular disease; SGLT2i Sodium–Glucose Cotransporter-2 Inhibitors; GLP-1 RA Glucagon-Like Peptide-1 Receptor Agonists; RAAS renin–angiotensin–aldosterone system; ASCVD atherosclerotic cardiovascular disease; HF heart failure; CKD chronic kidney disease; eGFR estimated glomerular filtration rate; MRA Mineralocorticoid Receptor Antagonist

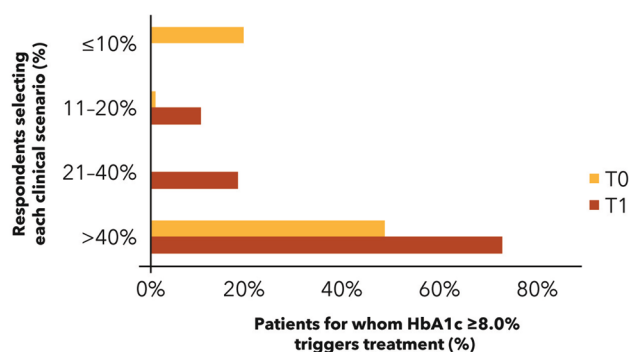
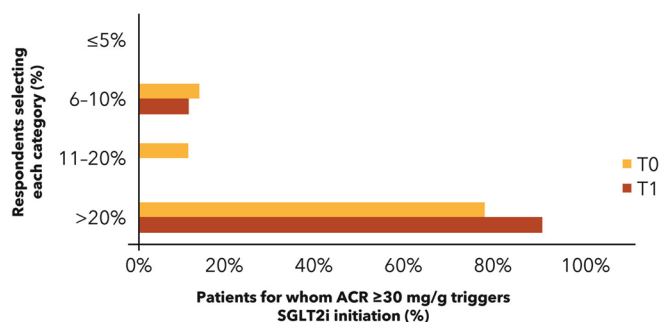


Fig. 1 HbA1c-driven initiation of SGLT2 inhibitors or GLP-1 receptor agonists in patients with type 2 diabetes without established cardiovascular or renal disease. Distribution of clinician responses at baseline (T0) and follow-up (T1) regarding the HbA1c threshold prompting the addition of an SGLT2 inhibitor (SGLT2i) or a GLP-1 receptor agonist (GLP-1RA) in patients with type 2 diabetes treated with metformin alone and without documented cardiovascular or renal comorbidities. The results indicate a shift towards earlier treatment intensification and a reduced reliance on HbA1c as the sole determinant of therapeutic decision-making. Data are expressed as percentage of respondents. Forty-eight respondents at T0 and forty-four at T1. *HbA1c* glycated haemoglobin; *SGLT2i* sodium–glucose cotransporter-2 inhibitor; *GLP-1RA* glucagon-like peptide-1 receptor agonist

approach, using clinical markers such as albumin-to-creatinine ratio (ACR), eGFR, blood pressure, and LDL-C to guide therapeutic decisions. This descriptive difference suggests greater consideration of cardiorenal risk factors among T1 respondents; however, it should not be interpreted as evidence of a longitudinal change in individual clinicians' prescribing behavior. This trend was particularly evident for renal risk markers. Compared with baseline, a higher proportion of clinicians reported initiating SGLT2i in response to albuminuria (ACR ≥ 30 mg/g) or mildly impaired renal function (eGFR < 60 mL/min/1.73 m²), even in the absence of documented CKD (Fig. 2). Notably, the use of SGLT2i was increasingly reported in the following patient categories:



- Patients without established cardiovascular or renal disease presenting early renal risk markers (ACR > 30 mg/g and/or mildly reduced eGFR);
- Patients with moderate disease duration and early signs of cardiometabolic risk;
- Elderly and frail patients, where clinicians favored SGLT2i due to their low risk of hypoglycemia and simple dosing regimens.

GLP-1RA use was predominantly maintained in patients with obesity, established atherosclerotic cardiovascular disease (ASCVD), or a prior CV event.

Main barriers to early intervention identified by clinicians

Across the two survey rounds, respondents reported several perceived barriers to early therapeutic intensification. These included:

- Therapeutic inertia: many clinicians acknowledged a persistent tendency to delay therapy intensification until glycemic targets are not met or comorbidities are diagnosed, often due to ingrained habits or institutional pressures.
- Uncertainty regarding guideline implementation: some respondents noted that national and international guidelines remain conservative in recommending early use of SGLT2i or GLP-1RA in patients without established complications, creating hesitation in lower-risk scenarios.
- Administrative and reimbursement hurdles: limited access to newer therapies, particularly in primary care or outside specialist settings, was cited as a barrier to broader implementation.

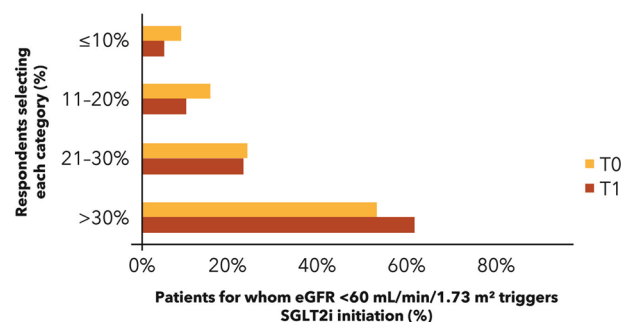


Fig. 2 Impact of early renal risk markers on SGLT2 inhibitor initiation in patients with type 2 diabetes without established chronic kidney disease. Clinician responses at baseline (T0) and follow-up (T1) regarding initiation of SGLT2 inhibitors in patients with type 2 diabetes receiving metformin alone after identification of albuminuria (ACR ≥ 30 mg/g) or mildly reduced renal function (eGFR < 60 mL/min/1.73 m²), in the absence of a documented diagnosis of chronic kidney dis-

ease or ongoing nephroprotective therapy. Survey findings demonstrate increased consideration of early renal risk markers as triggers for treatment initiation over time. Data are expressed as percentages of respondents. T0: 48 respondents; T1: 44 respondents. *ACR* albumin-to-creatinine ratio; *eGFR* estimated glomerular filtration rate; *SGLT2i* sodium–glucose cotransporter-2 inhibitor

- Patient-related factors: concerns over patient acceptance, polypharmacy, and perceived side effects – especially genital infections (for SGLT2i) and gastrointestinal symptoms (for GLP-1 RA) – also influenced prescribing behavior.

Overall, the survey findings point to a dynamic and evolving clinical attitude, where greater awareness of early risk indicators and the potential for cardio-renal protection is beginning to translate into earlier, more confident therapeutic decisions. These results support the notion that even a short interval of targeted clinical reflection, supported by updated evidence and peer dialogue, can produce meaningful shifts in real-world practice.

Expert insights and proposed strategies

The PRECARE – NO LiMITS initiative combined structured survey findings with moderated expert discussions to explore how early cardiorenal protection is being implemented in routine diabetes care. During the expert discussion sessions, participants highlighted a persistent gap between awareness of early cardiorenal risk markers and their systematic translation into routine prescribing practice.

At baseline (T0), clinicians acknowledged the importance of early risk indicators, such as albuminuria, reduced eGFR, LDL-C, and elevated blood pressure, but were not consistently acting upon them. SGLT2i and GLP-1RA were still largely prescribed reactively, once complications had already emerged. Over the T1 period, however, many participants reported a willingness to initiate therapy earlier, even in patients without overt CV or renal disease. This shift was attributed to structured peer discussions, literature updates, and clinical comparisons facilitated during the project. These insights align with emerging evidence. Educational interventions have been shown to reduce therapeutic inertia by improving clinician familiarity with early markers and newer drug classes [24, 25]. Ampudia-Blasco et al. [26] demonstrated that case-based learning can directly influence prescribing behaviors, particularly in primary care. Rossing [27] further highlighted the critical importance of recognizing early cardiorenal risk indicators before disease manifests. Ultimately, delaying treatment until HbA1c thresholds are crossed or comorbidities appear undermine the opportunity to deliver maximal long-term benefit. The PRECARE findings confirm that overcoming inertia requires more than clinical knowledge – it requires systems of support, peer engagement, and a cultural shift in the management of T2D.

Discussion

The clinical landscape of T2D is evolving. Management strategies are shifting from a historical focus on glycemic control and complication-driven care to a more proactive approach centered on early organ protection. Seminal trials such as UKPDS and long-term analyses thereof have highlighted the “legacy effect,” showing that early glycemic control can have lasting benefits in reducing micro- and macrovascular complications—even after intensification is withdrawn [5, 28]. More recently, agents such as SGLT2i and GLP-1 RA have demonstrated significant CV and renal benefits, even in patients without overt complications [15, 16, 29].

Despite this, the uptake of these therapies in early disease remains suboptimal [22, 23]. Many patients may receive these agents only after cardiorenal complications have become established, potentially limiting opportunities for earlier risk reduction [30, 31]. Such delays may reflect therapeutic inertia—defined as the failure to initiate or intensify therapy when clinically indicated—and may adversely affect long-term outcomes. A growing body of literature calls for a broader, risk-based treatment model. Clinical indicators such as microalbuminuria, mildly reduced eGFR, elevated LDL-C, and blood pressure are early warning signs of vascular or renal dysfunction and can precede overt disease by years [17–19]. Recognition of these markers may provide an opportunity for earlier risk assessment and, where clinically appropriate, initiation of preventive strategies before overt cardiorenal disease develops. SGLT2i, in particular, have shown benefits in reducing heart failure hospitalization, slowing CKD progression, and lowering major adverse cardiovascular events [14, 32, 33], even among patients with preserved eGFR or no baseline CV disease. Yet, clinical decisions are often guided primarily by HbA1c, a marker that reflects glycemic control but fails to capture the full spectrum of metabolic risk. Several studies have questioned this approach, emphasizing the need for more holistic goals that include CV and renal protection, as well as quality of life [20, 21]. The current clinical landscape—despite updated guidelines, such as ADA 2025 and SID-AMD 2023, still reflects a cautious stance, with recommendations for SGLT2i and GLP-1RA often reserved for patients with established comorbidities [34, 35]. In patients with T2D without established cardiovascular or renal disease, consideration of SGLT2 inhibitors or GLP-1 receptor agonists should be individualized rather than routinely recommended. Treatment decisions should take into account the presence and magnitude of cardiorenal risk factors, glycemic and weight-management needs, comorbidities, expected absolute benefit, potential adverse effects, patient preferences, treatment burden, accessibility,

and cost, in accordance with current guideline recommendations. Across clinical scenarios, the expected benefit of organ-protective therapy should be interpreted in relation to absolute baseline cardiorenal risk and balanced against potential adverse effects, treatment burden, polypharmacy, patient preferences, accessibility, and cost through shared decision-making.

Practical approaches to overcome therapeutic inertia

Overcoming therapeutic inertia in T2D requires a multifaceted strategy addressing prescriber awareness, system-level processes, and patient-related factors. In earlier disease stages, clinicians often hesitate to initiate SGLT2i or GLP-1RA due to concerns about safety, adherence, and insufficient guideline support for low-risk profiles. Considering the exploratory PRECARE observations alongside current evidence and guideline recommendations, several potential strategies for addressing therapeutic inertia are discussed in Box 1.

- Recognizing and addressing early risk indicators. Markers such as blood pressure, LDL-C, eGFR, and ACR should be integrated into routine decision-making, even when HbA1c appears adequate. Tools like clinical decision support systems can facilitate the timely identification of patients eligible for early intervention. Recent studies confirm that such tools enhance the detection of early CKD and CVD risk, enabling appropriate treatment intensification [36]. PRECARE findings reflect similar trends.
- Promoting earlier and clinically appropriate use of SGLT2i and GLP-1RA. SGLT2i are increasingly favored for organ protection, including in older adults often subject to de-intensification. In older adults, particularly those with frailty, the expected cardiorenal benefits of SGLT2 inhibitors should be balanced against potential adverse effects, comorbidities, renal function, treatment burden, and patient preferences, in accordance with current guideline recommendations. This is supported by multiple studies and the SOLD trial on dapagliflozin [32, 37–41].
- Encouraging shared and integrated care models. Multidisciplinary pathways may facilitate coordination of care and reduce fragmentation, as supported by previous literature [42–44]. The PRECARE survey explored clinicians' reported experiences and perspectives regarding multidisciplinary collaboration but was not designed to evaluate its effect on clinical outcomes.
- Developing educational initiatives to increase prescriptive awareness and reduce inertia. Targeted educational

strategies, including discussion of real-world early-stage clinical scenarios, have been proposed as potential approaches to address therapeutic inertia and increase familiarity with risk-based treatment strategies [24–27]. Although educational exchange formed part of the PRECARE initiative, the present project was not designed to assess the effectiveness of education in modifying prescribing behaviour.

Box 1 Practical considerations for addressing therapeutic inertia

- Considering cardiorenal risk indicators, including blood pressure, LDL-C, eGFR, and ACR, as part of comprehensive and individualized risk assessment
- Considering SGLT2 inhibitors and GLP-1 receptor agonists, when clinically appropriate and supported by current guideline recommendations, according to individual cardiorenal and metabolic risk, expected benefits and potential adverse effects, and patient preferences
- Encouraging multidisciplinary and integrated care, where appropriate, to support individualized cardiorenal risk management
- Developing educational initiatives aimed at increasing familiarity with contemporary evidence and guideline-based, risk-oriented treatment strategies

Conclusions and future directions

T2D without established cardiovascular or renal disease should not necessarily be regarded as a low-risk clinical condition, as cardiorenal risk may develop before overt complications become clinically apparent. Current evidence and guideline recommendations increasingly support comprehensive risk assessment and consideration of organ-protective strategies according to individual cardiovascular and renal risk profiles. In this context, the PRECARE NO LIMITS survey provides exploratory insights into how specialist diabetologists approach early cardiorenal risk assessment and therapeutic decision-making in routine clinical practice. Despite increasing emphasis on cardiorenal protection in contemporary guidelines, translating these recommendations into clinical practice may remain challenging, particularly in patients without established cardiovascular or renal disease. The PRECARE survey identified several perceived barriers to earlier therapeutic intensification, including reliance on glycemic parameters, uncertainty regarding the timing and implementation of organ-protective therapies, and organizational or access-related considerations. These observations should be interpreted as clinicians'

self-reported perspectives rather than as objective measures of prescribing behavior.

Descriptive differences between the T0 and T1 survey rounds indicated greater consideration of risk-based treatment approaches among T1 respondents. However, because no predefined therapeutic or educational intervention was implemented and no control group or objective prescribing data were available, these differences cannot be attributed to the moderated discussions, evidence sharing, or other components of the PRECARE initiative. Rather, these findings should be regarded as exploratory observations. Differences between survey rounds may reflect variation in respondent composition, attrition, sampling variability, secular changes in clinical practice, exposure to external scientific evidence or guideline updates, or other unmeasured factors. The relatively small sample size (48 respondents at T0 and 44 at T1), item-level non-response, and absence of formal statistical comparisons limit the precision and interpretation of the descriptive findings. In addition, because individual responses could not be linked across survey rounds, observed differences between T0 and T1 cannot be interpreted as within-clinician changes and may partly reflect attrition, differences in respondent composition, sampling variability, or other unmeasured factors. The specialist-only, regionally selected sample and the absence of detailed participant characteristics further limit the generalizability of the findings beyond the participating centers. Furthermore, the survey relied on self-reported clinician attitudes and prescribing approaches rather than validated or objective prescribing outcomes, introducing the possibility of recall and social desirability bias. Finally, the potential influence of industry support and authors' conflicts of interest on topic selection, framing, and interpretation should be acknowledged, although these factors do not alter the descriptive nature of the survey findings. Because no predefined intervention, control group, paired individual-level assessment, or objective prescribing outcome was included, no causal inference can be made regarding the effect of participation in PRECARE NO LiMITS, moderated discussions, evidence sharing, or educational exchange on clinicians' attitudes or prescribing behavior. Future studies involving larger and more diverse clinician populations, predefined implementation strategies, paired longitudinal assessments, and objective prescribing or clinical outcomes are needed to determine whether educational, organizational, or multidisciplinary approaches can effectively facilitate earlier and appropriately individualized cardiorenal risk management. Within these limitations, the PRECARE NO LiMITS initiative highlights practical questions surrounding the translation of evolving cardiorenal evidence into routine diabetes care and provides exploratory information that may inform the design of future implementation studies.

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Declarations

Conflict of interest PF has received honoraria or lecture/consultancy fees from Astra Zeneca, Boehringer, Lilly, Merk-Sharpe-Dome, Novonordisk, Sanofi. LB has received honoraria or lecture/consultancy fees from Astra Zeneca, Boehringer, Lilly, Abbott, Savio, Guidotti, Dexcom, Novonordisk and Sanofi. AR has received honoraria for speaking and/or consulting fees from Roche Diabetes Care, Abbott Diabetes Care, Sanofi srl. CB state honoraria for advisory boards from Eli Lilly, NovoNordisk, for consultant from Eli Lilly, NovoNordisk Aurora, for lectures, presentations, or educational events from AstraZeneca, Boehringer-Ingelheim, Eli Lilly, NovoNordisk, for research Support from NovoNordisk Eli Lilly, and for receipt of Medical Writing or Support for Statistical Analysis from Eli Lilly, NovoNordisk. CS declares honoraria from Astrazeneca, Novonordisk, Boehringer Ingelheim, Lilly. CT, NC, MEL, AC, AG, RG, PM state no conflict of interests.

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