NICE NG28 update: tailoring type 2 diabetes management and cardiorenal health

The 2022 update to the NICE guidance on the management of type 2 diabetes in adults (NG28) highlighted a shift away from a solely glucocentric approach to a comprehensive assessment of cardiorenal risk. It also recommended early initiation of SGLT2 inhibitor therapy – independent of HbA_{1c} levels – for individuals in higher-risk groups, including those with established atherosclerotic cardiovascular disease (ASCVD), heart failure or chronic kidney disease (CKD).

Published in February 2026, the latest update to NG28 further emphasises the prioritisation of cardiorenal protection by recommending dual metformin modified-release (M/R) and SGLT2i therapy as the standard of care from diagnosis (NICE, 2026a). Additionally, triple therapy – incorporating either a GLP-1 receptor agonist (RA) or tirzepatide – is now indicated earlier in the treatment pathway for selected higher-risk individuals, with subcutaneous (sc) semaglutide up to 1 mg once a week included as standard triple-therapy care for individuals with type 2 diabetes and established ASCVD.

Analysis by NICE indicates that this earlier use of SGLT2is within the treatment pathway for type 2 diabetes, alongside the implementation of GLP-1 RAs and tirzepatide for those eligible, has the potential to significantly improve population health outcomes. It suggests that these measures could prevent approximately 17 000 deaths across the UK over a 3-year period (NICE, 2026b). The projected decline in mortality is principally attributed to a reduction in cardiovascular events, such as myocardial infarction and stroke, and fewer kidney-related complications.

NICE has also introduced a more advanced approach to personalised care, outlining seven tailored pathways for the holistic management of type 2 diabetes according to specific comorbidities, including ASCVD, heart failure, CKD, early-onset type 2 diabetes (EOT2D) and frailty. This facilitates more nuanced and informed clinical decision-making.

The new guidance aims not just to lower blood glucose, but also to extend lives and protect cardiorenal health. The "one size fits all" era is over, heralding a new chapter for people living with type 2 diabetes.

Health promotion and person-centred care in routine practice remain essential

Amidst the noise surrounding the various pharmacotherapy updates, it remains essential to uphold the core principles of effective type 2 diabetes care and to empower self-care.

Terminology has shifted from "lifestyle" to "healthy living", with NICE continuing to emphasise the need to provide consistent advice on diet and healthy living at every interaction throughout an individual's type 2 diabetes journey. Attention should also remain focused on optimising services such as digital and other weight-management programmes, pathways to type 2 diabetes remission and educational resources, including NHS England's online Healthy Living service and the NHS Better Health website.

As per the previous NG28 guidance, it remains essential that clinicians evaluate an individual's cardiovascular status, including heart failure and future risk, as well as their renal health. However, the new guidance expands this requirement to include assessments for obesity and frailty (NICE, 2016; 2026c).

A new standard of care: dual therapy from diagnosis

The updated guidance sees the demise of metformin monotherapy, with the adoption of dual therapy (metformin M/R and an SGLT2i) as standard of care, unless not tolerated or contraindicated. This emphasises the importance of proactively managing cardiovascular and renal risks from the point of diagnosis.

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The use of metformin M/R – which is associated with a reduced likelihood of gastrointestinal side effects – is a welcome recommendation that may promote better concordance, facilitating the timely initiation of SGLT2i therapy and mitigating the potential costs of downstream "non-adherence". There is no requirement to switch people who are currently tolerating standard-release metformin and, for those with swallowing difficulties necessitating crushed or liquid formulations, standard-release metformin may continue to be the appropriate choice.

ASCVD: triple-therapy approach

One of the most notable changes in the revised guidance is the adoption of triple first-line therapy for individuals with type 2 diabetes and established ASCVD. This strategy incorporates sc semaglutide (up to 1 mg) alongside metformin M/R and an SGLT2i, forming a three-pronged cardiorenal baseline treatment regimen, rather than reserving GLP-1 RA therapy as a late-stage intervention when glucose optimisation is required.

In addressing why sc semaglutide is the sole recommended third-line therapy for this cohort, NICE's review of admissible studies found that only sc semaglutide provided sufficient cardiovascular and renal protection, glycaemic improvement and a favourable weight-reduction profile while maintaining cost-effectiveness (NICE, 2025). While liraglutide was considered cost-effective, its clinical efficacy did not match that of sc semaglutide. Consequently, among GLP-1 RAs and tirzepatide, sc semaglutide is the only agent recommended within this specific pathway for people with coexisting type 2 diabetes and ASCVD.

Dual and triple therapies, however, do not translate to dual and triple starts. To ensure tolerability, the guidance is explicit about a stepwise introduction, with SGLT2i therapy added once the maximum tolerated dose of metformin M/R has been established (or used as monotherapy if metformin is contraindicated or not tolerated). For those with ASCVD, the sc semaglutide is introduced last, titrating to 1 mg weekly.

Following publication of the draft NG28 update, questions were raised about whether BMI cutoffs should be used when starting GLP-1 RA therapy in people with ASCVD. NICE clarified that sc semaglutide is recommended in this population for cardiovascular and kidney protection, not weight loss. Therefore, no specific BMI thresholds or targets are suggested. However, NICE does advise clinicians to keep in mind that the *British National Formulary* lists decreased appetite and weight loss as side effects of semaglutide, and these should be considered when determining if the medication suits someone, especially those who are already underweight (NICE, 2025). Additionally, in cohorts where incretin therapy is recommended, NICE advocates stopping GLP-1 RAs or tirzepatide if the person becomes underweight (BMI <18.5 kg/m^2).

Box 1. Principles for managing care in people with multiple comorbidities.

- Additional therapies may be offered to reduce the risk of cardiovascular and renal disease, where these treatments are indicated for one comorbidity but not another.
- If safety concerns arise due to a particular comorbidity, the relevant treatment should not be considered for that individual. For example, avoid metformin if eGFR is <30 mL/min/1.73 m^2.
- Polypharmacy should be carefully managed, especially in people with frailty, with consideration given to reducing the number of medicines and doses to minimise potential adverse events.

The seven tailored pathways

Serving to bring NICE guidance into greater alignment with international consensus, the pharmacotherapy recommendations have been structured according to the evidence reviewed for specific comorbidities. These encompass ASCVD, CKD, EOT2D, frailty, heart failure, living with obesity and people with no relevant comorbidities.

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a significant comorbidity, affecting nearly 70% of individuals with type 2 diabetes, and is recognised as an important component of metabolic risk (Kusi et al, 2025). Despite this, there is no dedicated pathway for MASLD within this update. With new pharmacotherapies on the horizon, it is hoped that future iterations will address this need.

Acknowledging that many people in our care will present with more than one comorbidity, the guidance underlines the importance of a comprehensive approach to care. Clinicians are advised to evaluate each person's overall health needs, prioritising treatments and interventions that offer the greatest benefit to their holistic care. For example, for someone living with CKD and obesity, there is no reason that they cannot access GLP-1 RAs or tirzepatide if treatment intensification for hyperglycaemia is required. These guiding principles are summarised in *Box 1*.

For those seeking a visual representation of the medicine-selection pathways, NICE has produced a diagrammatic summary. An at-a-glance version has also been published in *Diabetes & Primary Care*. The following section provides notes on the first-line and further treatments for each of the seven treatment pathways.

No relevant comorbidities: earlier access to SGLT2i therapy

- Standard dual therapy.
- If further glycaemic intensification is required: offer a DPP-4 inhibitor, thereafter either a sulfonylurea, pioglitazone or insulin-based therapy.

Living with obesity: earlier option to use GLP-1 RA or tirzepatide when glycaemic intensification is required

- Standard dual therapy.
- If further glycaemic intensification is required: consider adding a GLP-1 RA or tirzepatide if the initial therapy was started >3 months ago (if not tolerated, add a DPP-4i).
- For individuals whose pathway includes desired weight loss, reference should be made to NICE guidance on overweight and obesity management (NG246), which provides direction on relevant technology appraisals for therapy use.
- If additional glycaemic intensification is required: offer a sulfonylurea, pioglitazone or insulin-based therapy.

Chronic kidney disease

Perhaps a surprise here is that neither a GLP-1 RA nor tirzepatide have been recommended specifically for CKD. Although the FLOW trial (Perkovic et al, 2024) was considered during the guideline development, and despite the clinical benefits it demonstrated, an evaluation of sc semaglutide for people with CKD showed that it was not cost-effective within this group (NICE, 2025). As a result, it was determined that sc semaglutide should not be recommended as baseline therapy for individuals with CKD at this time.

For adults with type 2 diabetes:

- If eGFR >30 mL/min/1.73 m^2: standard dual therapy (with appropriate renal-function dose of metformin if eGFR <45 mL/min/1.73 m^2).
- If eGFR 20–30 mL/min/1.73 m^2: offer appropriate dose DPP-4i and either dapagliflozin or empagliflozin.
- eGFR <20 mL/min/1.73 m^2: consider appropriate dose DPP-4i or pioglitazone or insulin-based therapy.
- If further glycaemic intensification is required, pioglitazone, a sulfonylurea (if eGFR >30 mL/min/1.73 m^2) or insulin-based therapy.

Early-onset type 2 diabetes: defusing a ticking time bomb

One of the most forward-thinking elements of the update is the creation of a dedicated pathway for EOT2D (diagnosed under the age of 40 years). This relatively small but significantly increasing cohort is shown to have more aggressive disease progression and higher lifetime risk of cardiovascular and renal complications (Luk et al, 2025).

- Consider early triple therapy, such as a GLP-1 RA or tirzepatide, to mitigate high lifetime CVD risk.
- For further glycaemic intensification: a DPP-4i, if GLP-1 RA or tirzepatide are not tolerated; thereafter, a sulfonylurea, pioglitazone or insulin-based therapy.

Heart failure with any ejection fraction

- Standard dual therapy.
- For further glycaemic intensification: a DPP-4i; thereafter, a sulfonylurea or insulin-based therapy.

ASCVD (to include if it occurs after starting initial therapy)

- Triple therapy (metformin M/R, SGLT2i and up to 1 mg sc semaglutide/week).
- If further glycaemic intensification is required: a sulfonylurea, pioglitazone or insulin-based therapy.

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Frailty: a dedicated treatment track

Frailty is elevated from a clinical consideration to a formal, independent treatment track. This pathway acknowledges the potential harms for people living with frailty from intensive glucose management and/or cardiorenal protection.

- Offer metformin M/R, but only offer an SGLT2i as dual therapy if the person's level of frailty does not place them at risk of adverse events (e.g. hypotension or volume depletion).
- It is important to address polypharmacy. Prescribe the minimum number of medications at the lowest effective doses.
- Should further glycaemic optimisation be necessary, a DPP-4i should be considered first, followed by pioglitazone, a sulfonylurea or insulin-based therapy. Careful attention should be given to the risks of hypoglycaemia associated with sulfonylureas and/or insulin, as well as to any contraindications and cautions when using pioglitazone.

Insulin-based therapies

The guidance has been simplified to focus on insulin classes rather than specific brands, to address challenges with brand shortages and product withdrawals.

Initial basal options

Healthcare professionals should offer once- or twice-daily basal insulin as the initial therapy.

Escalation and combinations

- High HbA_{1c}: if HbA_{1c} is ≥75 mmol/mol, consider combining basal insulin with short-acting, rapid-acting or pre-mixed insulin immediately.
- GLP-1 RA integration: GLP-1 RAs can now be combined with insulin without requiring specialist supervision, facilitating their earlier and more flexible use in primary care settings.

Cost-effectiveness

If multiple basal insulins (including biosimilars) are clinically suitable, choose the option with the lowest acquisition cost.

Structured support

Any adult starting insulin must be provided with a structured education programme to include best-practice injection technique, site rotation, self-monitoring and managing hypoglycaemia.

Key safety messages

Proactive therapy intensification can lead to rapid reductions in HbA_{1c}. Clinicians should remain vigilant for any associated retinal risks and refer to the relevant guidance supporting best eye care (NICE, 2024).

Additionally, robust "sick-day guidance" remains essential for safety in this more complex therapeutic landscape. NICE recommends that we should be advising those in our care:

- Whether any medication should change (and how) if the person is unwell or having surgery.
- Whether any medication should be stopped if there is a risk of dehydration, or vomiting and diarrhoea. Particularly relevant for metformin and SGLT2is.
- How to adjust insulin doses in times of illness.
- Importantly, when and how to restart any medication after recovery.

Prior to initiating SGLT2i therapy, assess for any elevated risk for diabetic ketoacidosis (DKA) that would contraindicate its use, such as:

- A history of DKA.
- Current acute illness.
- Susceptibility to dehydration or volume depletion.
- Adherence to a very-low-carbohydrate or ketogenic diet.

Women living with type 2 diabetes are at increased risks of adverse pregnancy-related events and continue to be insufficiently prepared for pregnancy (National Diabetes in Pregnancy Audit, 2025). The new guidance provides welcome considerations for women, trans men and non-binary people of childbearing potential who are taking a GLP-1 RA or tirzepatide. Key considerations include:

- Provide contemporaneous advice for pregnancy and breastfeeding (Medicines and Healthcare product Regulatory Agency [MHRA], 2026).
- Explain that weight loss may improve fertility.
- Advise that effective contraception must be used while taking the medication.
- If planning a pregnancy, advise to continue to use contraception for a period after stopping the medication, as per MHRA guidance.

Remain mindful of the importance of general pre-conception advice for all eligible people in our care. Include the optimisation of glucose levels, high-dose 5 mg folic acid supplementation and the discontinuation of other potentially teratogenic medications (Murphy, 2021).

When to stop therapies

Naturally, it remains good practice to evaluate the use of all medications at each diabetes review for effectiveness, tolerability and adherence.

NICE recommends continuing medications that have been effective in achieving glycaemic and weight targets. If a person does not reach their glycaemic target, SGLT2i therapy should be continued for cardiorenal protection and GLP-1 RA therapy for cardiovascular benefit. If a person is not responding to therapies, then review their diagnosis and diabetes classification (Diggle, 2022).

A DPP-4i should not be used alongside GLP-1 RA or tirzepatide therapy.

Health inequality mandate

Perhaps the most profound aspect of the new guidance is not the medication pathways but its mandate to ensure equal access to appropriate therapies for everyone living with type 2 diabetes. We know that the uptake of cardioprotective agents has varied across different populations, with prescribing rates lagging in the most deprived communities. This is despite NICE (2026d) reporting that the most deprived groups in the UK would gain the greatest health benefits, in both absolute and relative terms, from a greater uptake of SGLT2is, with the absolute gains reflecting a "higher disease burden and larger population size".

The updated guidance establishes health equality as a performance metric, requiring clinicians to actively monitor and close the gap for groups, such as women and people of black ethnicity, who have historically been under-prescribed these important protective therapies.

Recommendations for expanded research efforts

Recognising evidence gaps, NICE has identified several priority research questions:

- Which strategies are most effective and cost-efficient for improving access to and uptake of SGLT2is among underserved populations, both with and without EOT2D?
- How do GLP-1 RAs or tirzepatide in combination with SGLT2is compare to SGLT2is alone and placebo, in terms of clinical outcomes and cost-effectiveness for individuals with EOT2D who are receiving metformin?
- For people with type 2 diabetes and frailty, what is the comparative clinical and cost effectiveness of different treatment approaches compared with standard care?

Affordability: the "value" equation

In an era of tightening budgets, the guidance is pragmatic about cost. The explicit instruction to choose the least expensive drug within a class – and the endorsement of generic dapagliflozin and biosimilar insulins – highlights a commitment to sustainability and looks to unlock the funding necessary to make dual or triple therapy a frontline reality. This shift alone is projected to save the NHS over £560 million by 2027 (NICE, 2026b).

Implementation

The pathway to implementation will not be without hurdles. Providing care for thousands of people to transition onto more complex regimens requires significant time, education and vigilance. However, with the potential to prevent morbidity and earlier mortality, the mandate for care is clear: the time for proactive, complication-focused prevention and treatment is now.

Many areas still look to specialist services for injectable therapy starts and discussion continues regarding core services for general practice. However, now more than ever, GLP-1 RAs and tirzepatide need to be seen as foundational type 2 diabetes therapies for initiation in primary care, with integrated specialist support as necessary.

The NHS's *10 Year Health Plan for England* highlights the move from sickness to prevention, which is the essence of this NICE update. Financial planning by integrated care boards and health boards needs to look to support this by implementing models of fully integrated diabetes service provision that can supply resource and workforce capacity for this left shift.

The healthcare approach is shifting from managing chronic illness to prioritising active

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prevention and, if we are not individualising care and protecting the heart and kidneys at the point of diagnosis, we are failing those in our care. The new NG28 guidance is a call to arms: clinical inertia is no longer an option. ■

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