

CONSENSUS DOCUMENT

Comprehensive approach to people with type 2 diabetes. Diabetes Knowledge Area of the Spanish Society of Endocrinology and Nutrition



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KEYWORDS

Type 2 diabetes;
Evidence-based
medicine;
Comprehensive
approach

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Abstract:

Objective: To provide practical recommendations for the comprehensive approach of people with type 2 diabetes according to evidence-based medicine.

Participants: Members of the Diabetes Knowledge Area of the Spanish Society of Endocrinology and Nutrition.

Methods: The recommendations were formulated according to the degrees of evidence of the Standards of Medical Care in Diabetes—2022. After reviewing the available evidence and formulating recommendations by the authors of each section, several rounds of comments were developed incorporating the contributions and voting on controversial points. Finally, the final document was sent to the rest of the members of the area for review and incorporation of contributions, to finally carry out the same process with the members of the Spanish Society of Endocrinology and Nutrition Board of Directors.

Conclusions: The document establishes practical recommendations based on the latest available evidence for the management of people with type 2 diabetes.

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PALABRAS CLAVE

Diabetes tipo 2;
Medicina basada en la
evidencia;
Abordaje integral

Abordaje integral de las personas con diabetes tipo 2. Área de Conocimiento de Diabetes de la Sociedad Española de Endocrinología y Nutrición

Resumen

Objetivo: Proporcionar recomendaciones prácticas para el abordaje integral de las personas con diabetes tipo 2 según la medicina basada en la evidencia.

Participantes: Miembros del Área de Conocimiento de Diabetes de la Sociedad Española de Endocrinología y Nutrición.

Métodos: Las recomendaciones se formularon según los grados de evidencia de los Standards of Medical Care in Diabetes—2022. Tras la revisión de la evidencia disponible y la formulación de recomendaciones por los autores de cada apartado, se desarrollaron varias rondas de comentarios con incorporación de las aportaciones y votación de los puntos controvertidos. Por último, el documento final se remitió al resto de los miembros del área para revisión e incorporación de aportaciones, para, finalmente, realizar el mismo proceso con los miembros de la Junta Directiva de la Sociedad Española de Endocrinología y Nutrición.

Conclusiones: El documento establece unas recomendaciones prácticas basadas en la última evidencia disponible para el manejo de las personas con diabetes tipo 2.

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Introduction

In 2018, the Diabetes Working Group of the Sociedad Española de Endocrinología y Nutrición [Spanish Society of Endocrinology and Nutrition] (SEEN) drafted a document on a comprehensive approach to type 2 diabetes (DM2), which compiled the evidence available at the time. Although some specific updates were made to the document based on the publication of new studies, the SEEN Diabetes Knowledge Area suggested that there were substantial changes, not only in terms of new evidence on anti-diabetic therapies, but also in terms of the comprehensive approach to people with

DM2. Therefore, a comprehensive update of the document was proposed.

Method

The recommendations were formulated according to the degrees of evidence of the Standards of Medical Care in Diabetes—2022.¹ Following the review of the available evidence and the formulation of recommendations by the authors of each section, there were several rounds of comments, incorporating the contributions and voting on controversial points. The final document was sent to the

other members of the area for review and incorporation of the contributions made, and then the same process was carried out with the members of the SEEN Board of Directors.

The following is a summary of the main changes in the document: Comprehensive Approach to People with Type 2 Diabetes, 2022, available at: <https://www.seen.es/portal/documentos/texto-completo-abordaje-integral-dm2-2022>.

Guide to recommendations

This section covers the main points of comprehensive management of people with DM2 in terms of treatment selection and the detection of complications associated with diabetes, in an attempt to advance the concept of personalised medicine.

- Consider the initial combination therapy of choice, depending on comorbidities and glycaemic control.
- Early intensification of treatment (and reassessment every 3–6 months) until therapeutic goals are achieved.
- Individualise glycaemic control targets dynamically throughout the course of diabetes.
- Use of therapies with proven cardiorenal benefit, regardless of the degree of glycaemic control, assessing whether adjustments of other therapies are necessary.
- Intensive treatment of cardiovascular risk factors (dyslipidaemia, hypertension, smoking) together with the prevention and treatment of overweight/obesity.
- Perform systematic screening for micro- and macrovascular complications and other comorbidities associated with DM2, such as metabolic liver disease.
- The presence of high or very high cardiovascular risk, established cardiovascular disease (CVD)/heart failure (HF) or diabetic kidney disease should be determining factors for the selection of pharmacological treatment.
- Prevention and treatment of overweight and obesity should be one of the key determining factors of treatment.
- Prescribe diet and physical exercise at any time during the course of diabetes, adapting according to comorbidities. Ensure personalised therapeutic education as a pillar of comprehensive care for people with diabetes.
- Prioritise patient-centred conversation: anticipatory guidance. Inform the person with diabetes of the benefits of the therapies, as well as possible adverse events, in order to improve adherence.
- Consider de-intensifying treatment if frailty is present, maintaining drugs with cardiorenal benefit on a case-by-case basis.

Metabolic control objectives

The overall glycaemic control target, $HbA_{1c} < 7\%$, should be adapted during the course of diabetes, individualising and avoiding episodes of hypoglycaemia. A more stringent HbA_{1c} target of $< 6.5\%$ can be achieved in people without frailty and on antidiabetic therapies without risk of hypoglycaemia. In contrast, in the presence of frailty and other comorbidities, in case of high hypoglycaemic risk or the presence of inadvertent hypoglycaemia, a less stringent glycaemic control target may be appropriate ($HbA_{1c} 8\%–8.5\%$).

In addition, control targets are included depending on the continuous monitoring record or flash glucose, adapted according to each clinical situation.²

Prescription of physical exercise

The prescription of physical exercise is a highly relevant aspect in people with DM2. Physical exercise should be prescribed and monitored at each visit. The minimum recommendation is 150 min/week, distributed over at least three days a week, and combining aerobic and strength exercise, subsequently increasing the frequency, duration and intensity of the exercise, according to the sequence, frequency, duration and intensity (Fig. 1).

Prior assessment is recommended in patients with CVD, risk factors and/or microvascular complications. In addition to prescribing exercise, it is necessary to assess whether treatment adjustments (insulin and secretagogues) are necessary, ensuring sufficient knowledge for the detection and treatment of hypoglycaemia. In addition, if there are chronic micro- or macrovascular complications, some exercises are advisable and others should be avoided.

To supplement this information, reference is made to the RECORD³ Guide: clinical recommendations for the practice of sport in people with diabetes mellitus, produced by the diabetes area and available on the SEEN website.

Nutritional therapy

The first step should be to assess the body mass index. Other optional techniques are bioimpedance body composition assessment and morphofunctional assessment with bioimpedance, muscle ultrasound and muscle function testing. In addition to the Mediterranean diet, there are other dietary approaches that have shown benefit in DM2, such as low-carbohydrate diets and vegetarian or vegan diets⁴ (Fig. 1).

It also includes updated recommendations for the different food groups, indicating which ones are advisable and which ones should be avoided or limited.⁴

Selection of drugs in type 2 diabetes mellitus

Two situations are identified: moderate cardiovascular risk (age < 50 years and diabetes duration < 10 years, without other cardiovascular risk factors [CVRF]) and high or very high CV risk, depending on the presence of CV and/or renal involvement⁵ (Fig. 2).

In both situations, it is advisable to select treatment that includes metformin in combination with other anti-diabetic therapies that have demonstrated benefit in CVD, HF or diabetic kidney disease (GLP-1 receptor agonists [GLP-1 RA], SGLT2 inhibitors [SGLT2i]), while ensuring adequate glycaemic and weight control.⁶ Dual therapy is considered at baseline according to risk, intensifying early until targets are achieved.

The different therapies are prioritised according to the main treatment goal (glycaemic control, weight, prevention and treatment of CVD-HF-diabetic kidney disease) and the evidence demonstrated for each goal is specified.

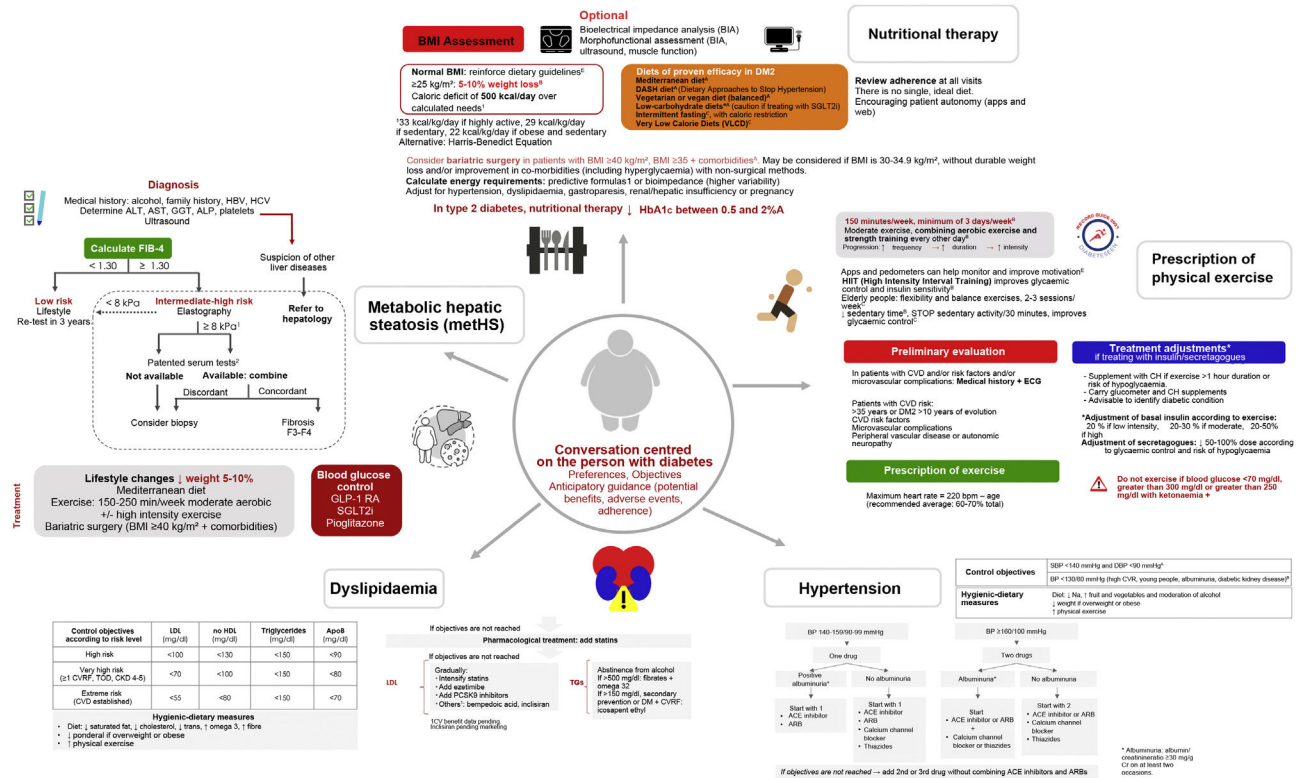


Figure 1 Comprehensive approach to people with type 2 diabetes mellitus (DM2): nutritional therapy, physical activity, hypertension, dyslipidaemia and metabolic hepatic steatosis.

ELF: Enhanced Liver Fibrosis; N/E: not evaluated.

¹If the result is compatible with F3–F4, consider serum tests for metabolic hepatic steatosis.

²Cut-off points: ELF™ 9.8 (NAFLD/ALD); FibroMeter 0.45 (NAFLD), Fibrotest 0.48 (NAFLD).

As a novelty, the importance of a conversation centred on the person with diabetes is established, considering their preferences and setting agreed treatment goals. In addition, it is advisable to provide information on both the expected benefits of antidiabetic treatment and the potential adverse effects, in order to try to improve adherence.

In selecting antidiabetic therapies in DM2, it is recommended that metformin, GLP-1 RA and SGLT2i be prioritised. If using GLP-1 RA, the dose should be optimised to achieve the greatest clinical benefit.⁶

Renal function, measured by eGFR, determines the eligibility for different antidiabetic therapies and may condition a dose adjustment, as indicated in the document (Fig. 2).

Evidence on CVD, mortality and diabetic kidney disease from diabetes therapies

Different antidiabetic therapies have demonstrated benefits on major adverse CV events, CV and all-cause mortality, hospitalisation due to HF, stroke and major adverse renal events.⁶

The available evidence on the different targets is compiled in the 2022 version of the document, and it is recommended to use the therapies within each pharmacological group that have demonstrated CV or renal benefit

(GLP-1 RA, SGLT2i), or that have at least completed a CV safety study with a neutral result (sitagliptin, linagliptin).

DM2 treatment in hospitalised patients

This chapter is a new addition in the 2022 version of the document. In addition to insulin treatment during hospitalisation, there is the possibility of a comprehensive multidisciplinary approach in ENDOCARE units (ENDO: Endocrinology and Nutrition; CA: Cardiology; RE: Nephrology), using GLP-1 RA and SGLT2i not only on hospital discharge, but also as part of the management of the hospitalised DM2 patient.

Hospitalisation of a person with DM2 is an excellent opportunity to improve not only antidiabetic and CVRF treatment, but also to positively influence the subsequent evolution by associating disease-modifying therapies, to make a comprehensive assessment of the different comorbidities and, ideally, to improve treatment adherence. Multidisciplinary inpatient care would allow for optimisation of treatment, and at the same time, would ideally improve transition to discharge, coordination of the different specialists involved in the care of people with DM2 and variability in treatment.

Diabetes is present in approximately 30% of hospitalised patients, and almost all of these patients have very high cardiovascular risk or established atherosclerotic disease.

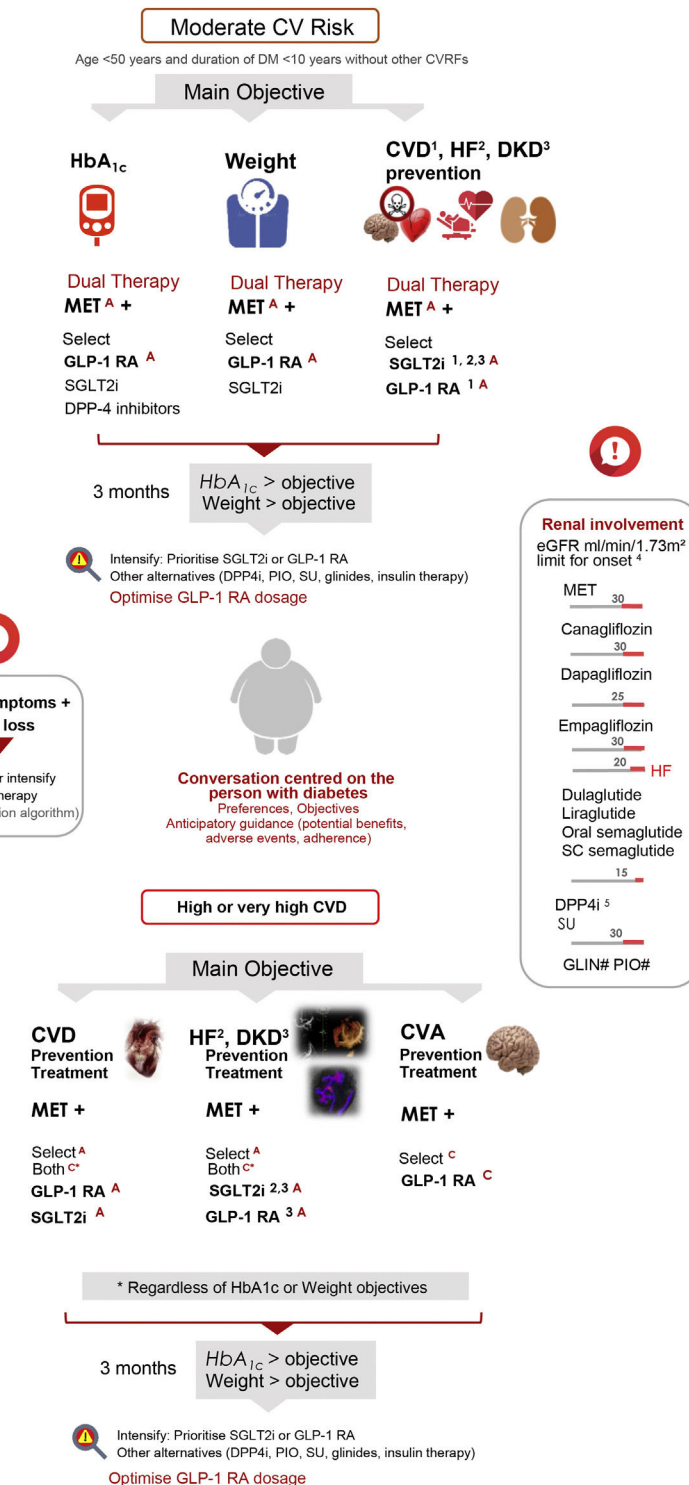


Figure 2 Drug selection in type 2 diabetes mellitus. Initial treatment or with previous therapy (OAD, GLP-1 RA, insulin). Drugs indicated in order of priority. GLP-1 RA in Spain funding limited to BMI ≥ 30 kg/m². Avoid sudden drops in HbA_{1c} in patients with advanced retinopathy.

CVD: cardiovascular disease; CVRF: cardiovascular risk factors; DKD: diabetic kidney disease; DM: diabetes mellitus; GLP-1 RA: GLP1 receptor agonists; HF: heart failure; MET: metformin; OAD: oral antidiabetics; PIO: pioglitazone; SGLT2i: sodium-glucose cotransporter 2 inhibitors; SU: sulfonylureas.

Benefit demonstrated in ¹CVD, ²HF, ³DKD, with the indicated therapeutic groups.

⁴If eGFR <60, CANA 100 mg, EMPA 10 mg, maintain SGLT2i and GLP-1 RA until haemodialysis.

⁵Dose adjustment in CKD except for linagliptin.

No dose adjustment required; in advanced CKD, monitor repaglinide dose (hypoglycaemia).

approach. The possibility of evaluating forthcoming new lipid-lowering therapies, such as bempedoic acid and inclisiran, which have yet to demonstrate their efficacy on cardiovascular morbidity and mortality, is included (Fig. 1).

Abstinence from alcohol is recommended for the treatment of hypertriglyceridaemia. If triglyceride concentrations are greater than 500 mg/dl, treatment with fibrates and omega-3s is indicated, although high doses of omega-3s are needed and CV benefit has only been demonstrated with icosapent ethyl, which will be available soon. If triglyceride concentrations are >150 mg/dl, secondary prevention or for diabetes + CVRF, icosapent ethyl is advised.

Safety profile

Information on the adverse effects of anti-diabetic therapies is compiled according to the latest information in the summaries of product characteristics. Precautions regarding the use of metformin and SGLT2i during hospitalisation and prior to scheduled surgery are included.

The importance of informing the person with diabetes of the potential adverse effects of GLP-1 RA and SGLT2i and measures to reduce these adverse effects is included, as a measure to promote treatment adherence and consistency.

Metabolic hepatic steatosis

The diagnostic approach to metabolic liver disease is based on the calculation of FIB-4 (pathological if value ≥ 1.3); depending on the estimated risk (intermediate-high), elastography is recommended. If the elastography value is ≥ 8 kPa and the result is compatible with F3–F4, serum tests in combination with other patented serum tests, if available (ELFTM, FibroMeter, Fibrotest) should be considered, as they will help to define the degree of fibrosis. If these tests are not available or the results are not consistent, a liver biopsy should be considered⁸ (Fig. 1).

In people with DM2 and metabolic hepatic steatosis, it is important to assess CV risk and the presence of renal involvement, given the coexistence of these conditions.

The main pillar of treatment is lifestyle change and following a Mediterranean diet to achieve a weight loss of 5%–10%. GLP-1 RA (semaglutide, liraglutide), SGLT2i and pioglitazone are recommended as anti-diabetic therapies. These three therapies have been shown to reduce steatosis, GLP-1 RA and pioglitazone reduce inflammation, and pioglitazone has been shown to reduce fibrosis, although the evidence is limited.

Given the association between metabolic hepatic steatosis, CVD and renal disease, strict blood pressure control (ARBs have preliminary data of hepatic benefit) and intensive lipid-lowering therapy are also advised.

Comprehensive approach in the elderly patient

In people with DM2 and advanced age, it is advisable to assess for frailty (FRAIL scale). In individuals with good functional status, the principles of treatment selection are the same as those recommended in the section on selection of antidiabetic treatment. An annual geriatric assessment

using the Pfeiffer test and the Yesavage scale is recommended, and family support should be assessed at each visit. Avoidance of hypoglycaemic episodes should be a priority, as well as proper treatment of CVRFs (hypertension and dyslipidaemia) and systematic assessment of chronic complications.⁹

In elderly people with DM2 and frailty, the glycaemic control target may be less stringent and it is advisable to consider treatment withdrawal if HbA_{1c} is below target, while maintaining therapies with CV and renal benefit on an individualised basis. Consideration will be given to treatment with weekly GLP-1 RA, ensuring adapted nutritional and physical activity therapy, and with iSGT2 and DPP4i because of the low risk of hypoglycaemia.

Diabetes and pregnancy

Gestational diabetes (GD) is diabetes that is diagnosed for the first time during pregnancy, although other types of diabetes (DM2, type 1 diabetes, MODY) may manifest for the first time during pregnancy. GD entails increased morbidity in the mother/foetus and neonate, increased CV risk in the mother, and increased risk of DM2 in the mother and child. Therefore, proper postpartum reassessment and multidisciplinary collaboration (endocrinology, family and community medicine, nursing/education, midwifery, nutrition, obstetrics, paediatrics) is essential.

In women at risk of GD, the following measures are recommended before pregnancy: smoking cessation, weight and blood pressure control, lifestyle measures and optimisation of maternal weight. In addition, basal blood glucose, HbA_{1c} and TSH should be determined and iodine and folic acid supplementation should be initiated.

Diagnostic screening is recommended in the first trimester in women at high risk of GD and at 24 weeks, on a universal basis. The initial treatment consists of lifestyle measures, which achieve adequate control in 80% of cases. If medical treatment is necessary, only insulin therapy (basal insulins: detemir, glargine U100/U300, degludec; rapid acting insulin analogues) is advised, as other drugs are not authorised.¹⁰

Postpartum assessment is essential because GD poses a high risk for developing DM2, and periodic reassessment (every 1–3 years) is necessary if the postpartum oral glucose tolerance test is normal. Reclassification will preferably be done with a 75 g oral glucose tolerance test (4–12 weeks postpartum), using standard diagnostic criteria. Alternatively, HbA_{1c} and basal glycaemia can be measured.¹⁰

In women without diabetes, lifestyle measures, weight control and smoking cessation are advised, and metformin should be considered if there is abnormal glucose tolerance and other CVRFs. If the diagnosis is DM2, treatment will be carried out in a comprehensive approach. If another type of diabetes is suspected, the patient will be referred to endocrinology for assessment.

Conclusion

The document sets out practical recommendations based on the latest available evidence for the management of people with DM2.

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Conflicts of interest

The authors declare that they have no conflicts of interest related to this publication.

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