

Clinical Practice Guideline

# Shared Decision Making, Diagnostic Evaluation, and Pharmacotherapy in Type 2 Diabetes

National Disease Management Guideline

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## Summary

**Background:** Type 2 diabetes is one of the most important widespread diseases worldwide. In Germany, nearly one in five persons over age 65 has type 2 diabetes. The German National Disease Management Guideline for Type 2 Diabetes (NDMG; in German: Nationale Versorgungsleitlinie, NVL) contains updated recommendations for the diagnostic evaluation and pharmacotherapy of this disease as well as information about specific groups of people for whom early detection may be useful.

**Methods:** The guideline has been updated, chapter by chapter, since 2018. Its recommendations are based on systematically searched and evaluated scientific evidence, the clinical expertise of a multidisciplinary panel of experts, and patient perspectives.

**Results:** The new chapter on shared decision making includes a description of a structured approach that can be used when individual treatment goals have not been achieved. The diagnosis of diabetes newly requires at least two abnormally elevated laboratory values: e.g., fasting plasma glucose  $\geq 126$  mg/dL ( $\geq 7.0$  mmol/L), HbA1c  $\geq 6.5\%$  ( $\geq 48$  mmol/mol) and/or casual plasma glucose  $\geq 200$  mg/dL ( $\geq 11.1$  mmol/L). Cardiovascular and renal risks are to be considered in the choice of drug. Studies have shown that, in persons with cardiovascular disease, treatment with GLP-1 receptor agonists (GLP-1, glucagon-like peptide-1) or SGLT2 inhibitors (SGLT2, sodium-glucose co-transporter-2) was less likely than the comparison intervention to lead to certain patient-relevant endpoints, including all-cause mortality (OR = 0.88 and 0.84, respectively), hospitalization for heart failure (SGLT2 inhibitors: OR = 0.65), and worsening of renal function (OR = 0.61 and 0.59, respectively).

**Conclusion:** Current evidence continues to support the recommendations on pharmacotherapy of the 2021 guideline. The Guideline Group did not find evidence of adequate certainty to inform recommendations about the screening of persons at risk, HbA1c target values, or screening for sequelae and comorbidities. Better evidence on these matters would be desirable.

## Cite this as:

Brockamp C, Landgraf R, Müller UA, Müller-Wieland D, Petrak F, Uebel T, on behalf of the National Disease Management Guideline Group: Clinical practice guideline: Shared decision making, diagnostic evaluation, and pharmacotherapy in type 2 diabetes. National Disease Management Guideline.

Dtsch Arztebl Int 2023; 120: 804–10. DOI: 10.3238/arztebl.m2023.0219

In Germany, nearly one in five persons over the age of 65 reports known diabetes (1). One of the central aims of the German National Disease Management Guideline for Type 2 Diabetes (NDMG; in German: *Nationale Versorgungsleitlinie*, NVL) is to improve the care of people with type 2 diabetes through up-to-date, scientifically based recommendations on diagnosis, treatment, and rehabilitation (2).

The NDMG meets all the requirements placed on an S3 guideline, according to the specifications of the Association of the Scientific Medical Societies in

Germany (*Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften*, AWMF) (3). These include a multidisciplinary panel (34 scientific societies and institutions as well as three patient organizations, *eTable 1*), a transparent approach to handle conflicts of interest, a systematic search and evaluation of the evidence taking GRADE criteria into consideration (search period: unrestricted up to the end of 2022) (4, 5) as well as a structured, formal consensus-finding process. The formulation and grading of the recommendations also take into account

clinical and practical care considerations as well as aspects introduced by patient representatives (6). Draft versions of the chapters could be commented on publicly; the comments received were discussed by the guideline group and led to adjustments in the final version. Detailed information on methodology can be found in the corresponding guideline report (7, 8). Chapters that are not yet included in the current version (2), for example, the chapters on non-pharmacological treatment as well as on concomitant diseases and sequelae, will be prepared and published in the near term.

### A new chapter on the topic of shared decision making

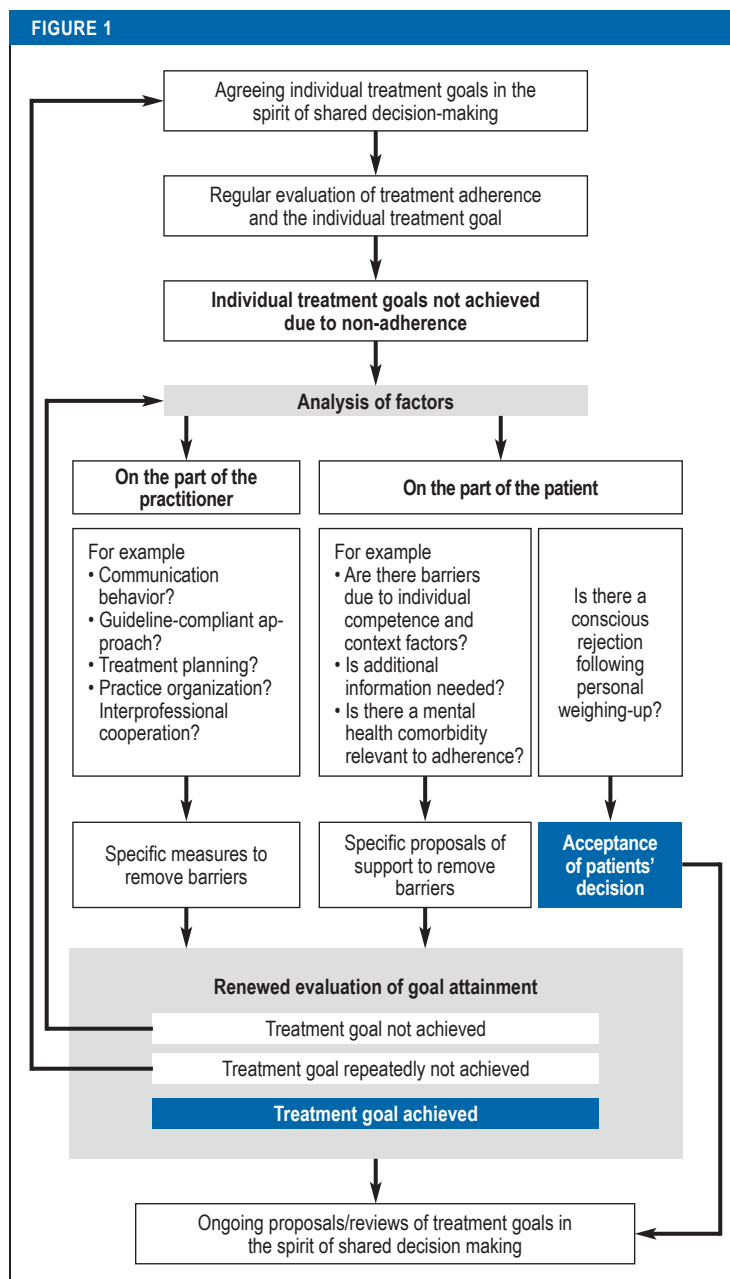
In order to highlight the importance of patient-centered communication and individual treatment planning, the guideline group has dedicated a specific chapter to this topic in the new NDMG. While it is generally undisputed that treatment should be geared towards the needs and goals of those affected, the clinical experience of the guideline group suggests that the implementation of this in everyday clinical practice is not always ensured. In order to support goal setting, the NDMG offers extensive assistance and further information on the concept of shared decision making (NDMG at [www.leitlinien.de/diabetes](http://www.leitlinien.de/diabetes)).

### Individual HbA1c target values and a new target corridor

For HbA1c target values, the new guideline describes a target corridor of 6.5–8.5% (48–69 mmol/mol Hb) and specifies aspects that should be taken into consideration when setting individualized treatment targets (↑↑ = strong recommendation) (*eFigure*). Compared to the 2014 NDMG, the corridor in the upper range has been extended to 8.5%. The recommendation is based not only on the clinical experience of the guideline group but also on a rapid report published by the German Institute for Quality and Efficiency in Health Care (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen*, IQWiG) on the benefits of near-normal blood glucose lowering in type 2 diabetes (9). The studies analyzed do not permit any clear cut-off value to be derived. There is evidence that lowering blood glucose to near-normal levels has only minor benefits compared to less strict blood glucose control in the form of a possibly slightly reduced rate of non-fatal myocardial infarction (approximately one fewer per 100 individuals treated) but, at the same time, a significantly increased rate of hypoglycemia (approximately eight more per 100 individuals treated). However, the certainty of the evidence was low (risk of bias, indirectness, and heterogeneous definitions of strict versus less strict glucose control) (9).

### Dealing with unachieved treatment goals

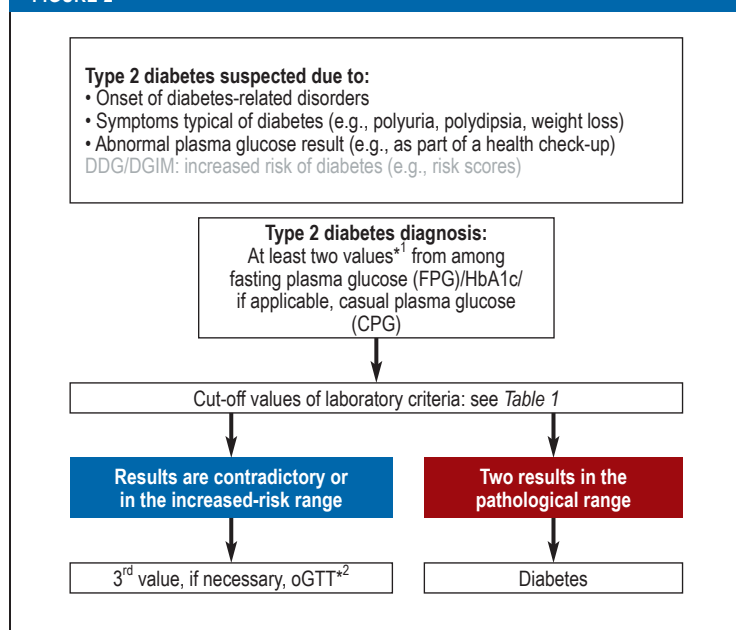
In the new NDMG, the guideline group has placed emphasis on non-adherence to agreed treatment goals, since experience has shown that this frequently occurs



**Approach in the case of non-adherence**, modified from Petrak et al. 2019 (10) and (2). For detailed information and explanatory notes, as well as examples of barriers and possible solution approaches, see NDMG ([www.leitlinien.de/diabetes](http://www.leitlinien.de/diabetes)).

in practice and can lead to potentially inadequate treatment regimens. If individual treatment goals are not achieved, the NDMG recommends a structured analysis of possible factors (↑↑) before treatment is adjusted. These include not only factors on the side of the patients but also factors on the side of the practitioners (*Figure 1*). The NDMG provides users with a detailed list of possible barriers and solution approaches. If the identified barriers cannot be removed, the individual treatment goal has to be adjusted—where necessary, also in the form of a treatment de-escalation.

FIGURE 2



#### Diagnostic algorithm (2)

\*1 HbA1c values are only informative if there is sufficient certainty that no confounding factors or influencing factors are present (for more information, see NDMG). CPG can only be used to confirm the diagnosis of diabetes if the result is clearly within the pathological range.

\*2 The German College of General Practitioners and Family Physicians (*Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin, DEGAM*), the Drug Commission of the German Medical Association (*Arzneimittelkommission der deutschen Ärzteschaft, AkdÄ*), the German Society of Wound Healing and Wound Treatment (*Deutsche Gesellschaft für Wundheilung und Wundbehandlung, DGfW*), and the German Society of Nursing Science (*Deutsche Gesellschaft für Pflegewissenschaft, DGP*) do not consider the oral glucose tolerance test (oGTT) to be of value in the primary care setting, see also *eTable 3*.

DDG, *Deutsche Diabetes Gesellschaft* (German Diabetes Association); DGIM, *Deutsche Gesellschaft für Innere Medizin* (German Society of Internal Medicine); HbA1c, hemoglobin A1c

TABLE 1

#### Laboratory criteria (modified from [18]) (2)

|         | No diabetes                     | Increased risk of diabetes                   | Diabetes                       |
|---------|---------------------------------|----------------------------------------------|--------------------------------|
| FPG     | < 100 mg/dL*1<br>(< 5.6 mmol/L) | 100–125 mg/dL*1<br>(5.6–6.9 mmol/L)          | ≥ 126 mg/dL<br>(≥ 7.0 mmol/L)  |
| HbA1c*2 | < 5.7%<br>(< 39 mmol/mol)       | 5.7 up to < 6.5%<br>(39 up to < 48 mmol/mol) | ≥ 6.5%<br>(≥ 48 mmol/mol)      |
| CPG     |                                 |                                              | ≥ 200 mg/dL<br>(≥ 11.1 mmol/L) |

\*1 The German College of General Practitioners and Family Physicians (*Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin, DEGAM*), the Drug Commission of the German Medical Association (*Arzneimittelkommission der deutschen Ärzteschaft, AkdÄ*), the German Society of Wound Healing and Wound Treatment (*Deutsche Gesellschaft für Wundheilung und Wundbehandlung, DGfW*), and the German Society of Nursing Science (*Deutsche Gesellschaft für Pflegewissenschaft, DGP*) concur with the WHO cut-off values for FPG: no diabetes < 110 mg/dL (< 6.1 mmol/L), increased risk of diabetes 110–125 mg/dL (6.1–6.9 mmol/L) (19, 20)

\*2 For particular features/influencing factors (e.g., age) see NDMG

HbA1c, hemoglobin A1c; CPG, casual plasma glucose; FPG, fasting plasma glucose

## Diabetes screening in the case of increased diabetes risk

The NDMG recommends that people at increased risk of diabetes should be offered screening for the presence of diabetes (↑↑). Although it is not possible on the basis of the available evidence to adequately assess the direct benefit of screening high-risk patients and the associated early initiation of treatment with regard to patient-relevant outcomes (11, 12), this appears plausible, at least indirectly, on the basis of evidence on the benefit of non-pharmacological and pharmacological treatments (13). Offering patients with risk factors for a potentially controllable disease a screening examination that opens up the option for action is also consistent with the principle of patient autonomy. Important onset-promoting and associated factors of type 2 diabetes in the assessment of diabetes risk include older age, family history as well as metabolic and vascular factors.

## Laboratory values in the range of increased diabetes risk

Recent review articles support the recommendation of the NDMG to advise lifestyle-modifying measures in the case of laboratory values in the range of increased diabetes risk (↑↑). Individuals with laboratory values in the cut-off ranges indicated in (*eTable 2*) were at increased risk of developing diabetes in studies (14). If fasting plasma glucose was in the range of 5.6–6.9 mmol/L or 100–125 mg/dL, the risk was more than four times higher compared to values in the normal range (hazard ratio [HR] 4.32; 95% confidence interval [2.61; 7.12], eight studies, 9017 participants, follow-up of 4–22 years, low certainty of evidence). The cumulative incidence of diabetes rose with increasing observation time and was 17% [6; 32%] at 3 years, 22% [15; 31%] at 6 years, and 38% [10; 70%] at 9 years (overall moderate certainty of evidence) (14). A Cochrane review yields evidence that lifestyle-modifying measures (nutrition therapy and physical activity) are associated with a lower incidence of diabetes. Fewer people in the intervention group developed diabetes compared to the control group (315/2122, 14.8% versus 614/2389, 25.7%; RR 0.57 [0.50; 0.64],  $I^2 = 6.11\%$ , 11 studies,  $n = 4511$ , moderate certainty of evidence) (13).

## A new diagnostic algorithm—uncertainties of diagnostic parameters

The revised chapter on diagnostic evaluation in the guideline addresses, more closely than previous NDMGs, the limitations and uncertainties of the laboratory parameters used. The new diagnostic algorithm requires two laboratory values in the pathological range for the diagnosis of diabetes to be made (*Figure 2, Table 1*). The combination of different measurement methods is able to compensate for the limitations of the individual methods (*eTable 3*), thereby reducing the risk of over- and underdiagnosis. Since the diagnostic parameters only allow a statement to be made on the current point in time, the updated NDMG recommends

Detailed information and explanatory notes, as well as examples of barriers and possible solution approaches, can be found in the NDMG ([www.leitlinien.de/diabetes](http://www.leitlinien.de/diabetes)).

reviewing the diagnosis in the further course, particularly in the case of results close to the cut-off values. (↑↑).

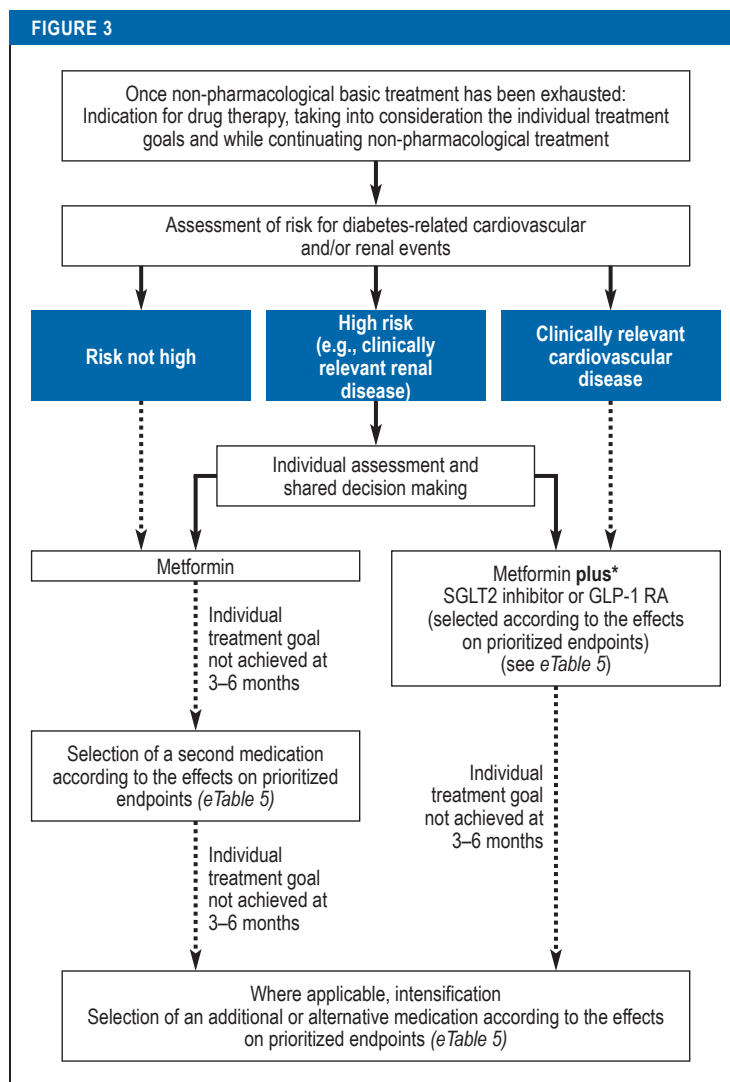
Also new in the NDMG is the explicit recommendation to take the “minimal difference” into account in addition to the limits of the respective test procedures when interpreting test results (↑↑). The minimal difference gives specific concentrations in absolute values from which a measured value differs from a cut-off value with a confidence interval of 95% and should be reported by the relevant laboratory (see NDMG for further information).

The guideline group draws attention to the fact that the interpretation of the HbA1c value is complicated by numerous interferences and influencing factors, and refers at various points to the diabetes-independent increase in HbA1c with age. The reference range (2.5<sup>th</sup>–97.5<sup>th</sup> percentiles) for HbA1c values in two large German collectives of non-diabetic adults was 4.6–5.9% (27–41 mmol/mol Hb) and 4.0–6.0% (20–42 mmol/mol Hb), respectively, and for persons aged ≥ 60 years 5.0–6.4% (31–46 mmol/mol Hb) and 4.4–6.6% (25–49 mmol/mol Hb), respectively ([15, 16] cited from [17]). In the opinion of the guideline group, the HbA1c level carries less weight as a diagnostic criterion in individuals ≥ 60 years. Particularly in this age group, results close to the diagnostic cut-off value of 6.5% (6.5–7.0%) are of limited significance to confirm the diagnosis.

### Screening for sequela and comorbidities

The recommendations in the previous NDMG on screening intervals have largely been confirmed (eTable 4). What is new, however, is that screening for diabetic neuropathy is no longer recommended annually for everyone with type 2 diabetes, but instead every 1–2 years in a risk-adjusted manner (↑↑). A prospective cohort study of participants with diabetes detected in screening calculated a cumulative incidence of 10% (n = 78) over 13 years and a corresponding incidence of 0.7% per year (seven cases/1000 patient-years) (21). If there is no increased risk according to the patient-specific risk assessment, a screening interval of 2 years is justifiable in the experience of the guideline group, particularly at the general practitioner level of care and according to the data in the present study.

The recommended neurological screening program to detect diabetic sensorimotor neuropathy has been simplified. In contrast to earlier versions that required testing of the Achilles tendon reflexes, vibration perception according to Rydel-Seiffer, and pressure and touch sensation with the 10-g monofilament, the new NDMG recommends a minimal program consisting of at least one large-fiber test (testing of vibration and pressure and/or touch perception) and one small-fiber test (pain or temperature sensation testing). Which tests are carried out is a decision for the examiners according to their experience and based on the testing instruments at their disposal. With regard to testing the Achilles tendon reflex, the guideline group, based



### Pharmacological treatment of type 2 diabetes (2)

\* For an HbA1c of ≤ 7% (53 mmol/mol), there are no data on the efficacy of combination therapy in individuals with type 2 diabetes without heart failure.

Dotted arrows = review of the treatment strategy and treatment goal in shared decision making. The algorithm does not relate to patients with severe metabolic decompensation or emergency situations. Current summaries of product characteristics need to be taken into consideration.

For information on the integrative risk assessment (cardiovascular risk factors), see NDMG ([www.leitlinien.de/diabetes](http://www.leitlinien.de/diabetes))

GLP-1 RA, glucagon-like peptide-1 receptor agonists; SGLT2, sodium-glucose co-transporter-2

on their clinical experience, sees no value in this required minimal program due to its high variability and low reliability.

### Choice of treatment according to the cardiovascular risk profile

The basis of treatment for type 2 diabetes remains a non-pharmacological approach. If this alone is insufficient to achieve the individual treatment goals and pharmacological treatment of glucose metabolism is indicated, the algorithm for pharmacological treatment of

TABLE 2

**Effects of treatment with GLP-1 RA and SGLT2 inhibitors in individuals with cardiovascular diseases**

| Endpoint/drugs                                                     | Expected absolute effects [95% CI] |                   | Relative effects [95% CI] | GRADE*   |
|--------------------------------------------------------------------|------------------------------------|-------------------|---------------------------|----------|
|                                                                    | Risk with placebo                  | Risk with drug    |                           |          |
| All-cause mortality                                                |                                    |                   |                           |          |
| GLP-1 RA (seven RCTs, n = 46 393, follow-up: 0.5–3.8 years)        | 68/1000                            | 60/1000 [57; 65]  | OR 0.88 [0.82; 0.95]      | High     |
| SGLT2 inhibitors (two RCTs, n = 24 962, follow-up: 0.8–3.5 years)  | 113/1000                           | 96/1000 [86; 109] | OR 0.84 [0.74; 0.96]      | Moderate |
| Hospitalization due to heart failure                               |                                    |                   |                           |          |
| GLP-1 RA (six RCTs, n = 36 930, follow-up: 0.5–3.8 years)          | 40/1000                            | 38/1000 [34; 42]  | OR 0.95 [0.85; 1.06]      | High     |
| SGLT2 inhibitors (five RCTs, n = 24 962, follow-up: 0.8–3.5 years) | 116/1000                           | 78/1000 [72; 85]  | OR 0.65 [0.59; 0.71]      | High     |
| Worsening renal function (safety endpoint)                         |                                    |                   |                           |          |
| GLP-1 RA (one RCT, n = 3297, median follow-up 2.1 years)           | 61/1000                            | 38/1000 [28; 51]  | OR 0.61 [0.44; 0.84]      | Low      |
| SGLT2 inhibitors (two RCTs, n = 8474, follow-up: 1.3–1.5 years)    | 23/1000                            | 14/1000 [10; 19]  | OR 0.59 [0.43; 0.82]      | Moderate |

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\*Quality of evidence according to GRADE, assessed by the review authors (23)

Follow-up, given as follow-up range; GLP-1 RA, glucagon-like peptide-1 receptor agonists; n, number of study participants; OR, odds ratio; RCT, randomized controlled trial; SGLT2, sodium-glucose co-transporter-2

type 2 diabetes (Figure 3) should be applied (↑↑). An important new feature compared to the algorithm of the NDMG Treatment of Type 2 Diabetes (*Therapie des Typ-2-Diabetes*) from 2014 (22) is the selection of drugs on the basis of a risk assessment for diabetes-related cardiovascular and/or renal events. If the risk is not high, the algorithm stipulates, as before, monotherapy with metformin as the first step. If the patient has a clinically relevant cardiovascular disease, they should be offered a combination of metformin with an SGLT2 inhibitor (SGLT2, sodium-glucose co-transporter-2) or a GLP-1 receptor agonist (GLP-1, glucagon-like peptide-1).

A recent systematic review of high methodological quality examined the benefits of SGLT2 inhibitors, GLP-1 receptor agonists, and dipeptidyl peptidase-4 (DPP-4) inhibitors in individuals with cardiovascular disease. The respective treatment and the comparison intervention (placebo) were given in addition to standard treatment. Treatment with GLP-1 RA and SGLT2 inhibitors resulted in fewer patient-relevant long-term endpoints than did the comparison intervention (Table 2) (23).

The analyzed studies showed no statistically significant benefit for DPP-4 inhibitors with regard to cardiovascular and all-cause mortality, myocardial infarctions (high certainty of the evidence in each case) and hospitalizations due to heart failure (moderate certainty of evidence) (23). In 2023, the guideline group saw no reason to modify the algorithm first published in 2021 based on the newly available evidence (Figure 3).

In the case of patients with several risk factors for a renal or cardiovascular event, there are reasons for metformin monotherapy, but also for an immediate combination therapy. Since it is not clear who benefits most from which treatment option, a critical case-by-case assessment and shared decision making based on the available data are recommended.

### Individual selection of drugs

If monotherapy with metformin in people with diabetes who are not at high risk of cardiovascular and/or renal events is not sufficient to achieve the individual treatment goals within 3–6 months, the algorithm recommends selecting a second drug depending on individual patient factors and the impact on prioritized endpoints (Figure 3, eTable 5).

A recently published RCT that investigated the choice of drugs in combination with metformin was taken into consideration for the current version of the NDMG (2, 24, 25). The benefits of various drugs in addition to metformin were investigated in 5047 individuals with a less than 10-year history of diabetes. The primary endpoint was an HbA1c of  $\geq 7.0\%$  or 53 mmol/mol. Cardiovascular endpoints and mortality were considered as pre-specified secondary endpoints (average follow-up of 5 years).

The drugs tested (insulin glargine, glimepiride, liraglutide, and sitagliptin) lowered HbA1c values in a similar way but with different side-effect profiles. At 4 years, the average HbA1c value in the groups was 7.1% (liraglutide and glargine), 7.2% (sitagliptin), and 7.3% (glimepiride) (25). In terms of clinical

endpoints, there were advantages for treatment with liraglutide. In the liraglutide group, 21 deaths per 1000 participants were reported, whereas 30–34 deaths were reported in the other drug groups. Cardiovascular deaths (7/1000 versus 13–17/1000 participants), cardiovascular disease (66/1000 versus 86–96/1000), and hospitalizations due to heart failure (11/1000 versus 20–24/1000) were also less frequent in the liraglutide group (24). SGLT2 inhibitors were not subject to this study.

When choosing the second drug after metformin monotherapy, several factors play a role for the guideline group. These include not only the effect on clinical endpoints but also the side-effect profile, treatment goals, and patient-specific factors. Therefore, based on the available evidence, the guideline group retains the recommendation regarding individual drug selection as shown in *Figure 3* and *eTable 5*.

## Implementation and patient materials

All materials in the NDMG for type 2 diabetes are available for free at [www.leitlinien.de/diabetes](http://www.leitlinien.de/diabetes) and [www.awmf.org](http://www.awmf.org). The long version of the NDMG is available both as a PDF download and in html format for use on mobile devices. The short version summarizes all recommendations, algorithms, and important tables. Decision making aids and patient information in plain language have been developed for prioritized clinical situations. The same applies to the patient guideline (currently in preparation).

## Acknowledgments

The authors would like to thank all mandate holders involved in the NDMG for Type 2 Diabetes (*eTable 1*).

## Conflict of interest statement

CB is a research scientist in the NDMG program, which is funded by the National Association of Statutory Health Insurance Physicians (Kassenärztliche Bundesvereinigung, KBV) and the German Medical Association (Bundesärztekammer, BÄK).

RL has received contributions from AstraZeneca, Lilly Deutschland, and Novo Nordisk for presentations and educational events; he is also a member of the Advisory Board of Lilly and Novo Nordisk.

UAM carries out unpaid work as a full member of the AkdÄ.

DMW has received consultancy fees from Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Daiichi-Sankyo, EvivaMed, Lilly, MSD, Novartis, Novo Nordisk, Sanofi, and sobi. He has accepted honoraria for lectures, presentations, manuscript preparation, and further training events from Amarin, AstraZeneca, Bayer, Boehringer Ingelheim, Daiichi-Sankyo, MSD, Novo Nordisk, and Sanofi. He is spokesperson of the committee on "Digitalization of the German Diabetes Association" (*Deutsche Diabetes Gesellschaft*, DDG), the panel for "Quality Assurance, Training and Continuing Education" of the DDG, the "Patient Care Structure" committee of the German Society of Internal Medicine (*Deutsche Gesellschaft für Innere Medizin*, DGIM), a board member of the Society for the Prevention of Cardiovascular Diseases in German-speaking countries (*DACH-Gesellschaft Prävention von Herz-Kreislauf-Erkrankungen*), and spokesperson for the joint "Cardio-Hormone Diabetes" committee of the German Cardiac Society (*Deutsche Gesellschaft für Kardiologie*, DGK), DDG, and the German Society of Endocrinology (*Deutsche Gesellschaft für Endokrinologie*, DGE).

FP received reimbursement of expenses for travel to the inaugural meeting for the NDMG on diabetes.

TU is a special representative and spokesperson for the Diabetes Working Group of the German College of General Practitioners and Family Physicians (*Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin*, DEGAM). As an external expert to the German Federal Joint Committee (*Gemeinsamer Bundesausschuss*, G-BA), he receives compensation and, where appropriate, reimbursement of travel expenses when unable to practice as a result of this activity.

Manuscript received on 27 July 2023, revised version accepted on 27 September 2023.

Clinical guidelines in the *Deutsche Ärzteblatt*, as in numerous other specialist journals, are not subject to a peer review procedure, since S3 guidelines represent texts that have already been evaluated, discussed, and broadly agreed upon multiple times by experts (peers).

Translated from the original German by Christine Rye.

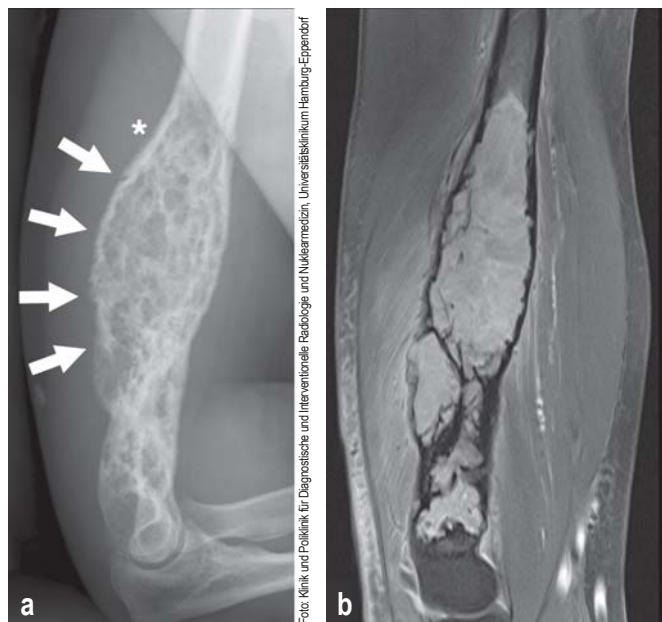
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- Cite this as**  
Brockamp C, Landgraf R, Müller UA, Müller-Wieland D, Petrak F, Uebel T, on behalf of the National Disease Management Guideline Group: Clinical practice guideline: Shared decision making, diagnostic evaluation, and pharmacotherapy in type 2 diabetes. *National Disease Management Guideline. Dtsch Arztebl Int* 2023; 120: 804–10. DOI: 10.3238/arztebl.m2023.0219
- **Supplementary material**  
**eTables, eFigures:**  
[www.aerzteblatt-international.de/m2023.0219](http://www.aerzteblatt-international.de/m2023.0219)

## CLINICAL SNAPSHOT

### Atraumatic Pain as First Symptom of Solitary Plasmacytoma



**Figure:**

- a) Radiograph of the right upper arm (lateral projection): a diametaphyseal lytic lesion with cortical destruction (arrows) and interrupted periosteal reaction (asterisk).
- b) Magnetic resonance tomography (T1 TSE with fat saturation after administration of contrast medium) in the sagittal plane: a macrolobulated lesion with homogeneous internal structure and distinct contrast enhancement.

A 50-year-old woman attended our orthopedic department with a 3-month history of painful swelling of the right upper arm. Radiography (a) identified an area of marked humeral osteolysis, which on magnetic resonance imaging (b) showed distinct contrast enhancement. The lesion was homogeneous in structure, so the possible diagnoses were a metastasis, lymphoma, or plasmacytoma. Histological analysis demonstrated a lambda-type plasmacytic myeloma. No further manifestations were detected on whole-body computed tomography, so the diagnosis was solitary plasmacytoma of bone (SPB). The incidence of SPB is 0.15/100 000. Its prognosis is more favorable than that of multiple myeloma, which, however, develops in 50–60% of cases of SPB. SPB is highly sensitive to radiotherapy, which was

performed with curative intent in our patient (50.0 Gy in 25 × 2.0 Gy). At the conclusion of this treatment the situation was stable and the clinical picture had improved, so partial loading of 2 kg was permitted and it was decided not yet to carry out surgical stabilization.

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**Conflict of interest statement:** The authors declare that no conflict of interest exists.

Translated from the original German by David Roseveare.

**Cite this as:** Götz S, Priemel M, Köhler D: Atraumatic pain as first symptom of solitary plasmacytoma. *Dtsch Arztebl Int* 2023; 120: 810. DOI: 10.3238/arztebl.m2023.0092

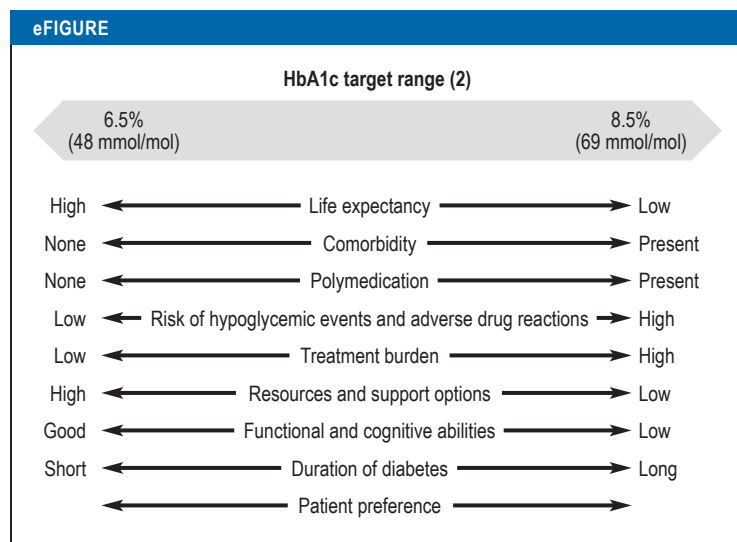
Supplementary material to:

# Clinical Practice Guideline: Shared Decision Making, Diagnostic Evaluation, and Pharmacotherapy in Type 2 Diabetes

National Disease Management Guideline

by Christina Brockamp, Rüdiger Landgraf, Ulrich Alfons Müller, Dirk Müller-Wieland, Frank Petrak, and Til Uebel, on behalf of the National Disease Management Guideline Group

Dtsch Arztebl Int 2023; 120: 804–10. DOI: 10.3238/arztebl.m2023.0219



Regarding limitations in the reliability of the HbA1c value (e.g., physiological rise as a result of older age), see NDMG ([www.leitlinien.de/diabetes](http://www.leitlinien.de/diabetes))

HbA1c, hemoglobin A1c

eTABLE 1

**Authors of the NDMG for type 2 diabetes, version 3.0 (2023) (2) – Collaborators**

| Author                                                                                                                                                                                                               | Scientific society/organization                                                                                                                                                                                                |
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|                                                                                                                                                                                                                                                                        |                                                                                                                                                                            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
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| <b>Methodological guidance, coordination, and moderation</b>                                                                                                                                                                                                           |                                                                                                                                                                            |
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eTABLE 2

**Laboratory values in the range of increased diabetes risk (2)**

Laboratory values in the range of increased risk for the development of diabetes (modified from [18])

|                                                                             |                                                                                                           |
|-----------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| Impaired fasting plasma glucose (IFG)                                       | 100–125 mg/dL or 5.6–6.9 mmol/L* <sup>1</sup>                                                             |
| HbA1c value                                                                 | 5.7 to < 6.5 % or 39 to < 48 mmol/mol* <sup>2</sup>                                                       |
| Impaired glucose tolerance (IGT) (in the oral glucose tolerance test, 75 g) | FPG: < 126 mg/dL or < 7.0 mmol/L<br>2-hour plasma glucose: 140–199 mg/dL or 7.8–11.0 mmol/L* <sup>1</sup> |

\*<sup>1</sup> WHO cut-off values: 110–125 mg/dL (6.1–6.9 mmol/L), the German College of General Practitioners and Family Physicians (*Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin*, DEGAM), the Drug Commission of the German Medical Association (*Arzneimittelkommission der deutschen Ärzteschaft*, AkdÄ), the German Society of Wound Healing and Wound Treatment (*Deutsche Gesellschaft für Wundheilung und Wundbehandlung*, DGfW), and the German Society of Nursing Science (*Deutsche Gesellschaft für Pflegewissenschaft*, DGP) support the WHO cut-off values for FPG (see also eTable 1). The DEGAM, the AkdÄ, the DGfW, and the DGP do not consider the oGTT, and thus impaired glucose tolerance, to be of value in the primary care setting

\*<sup>2</sup> For special features/influencing factors (e.g., age), see long version of the NDMG ([www.leitlinien.de/diabetes](http://www.leitlinien.de/diabetes))

HbA1c, hemoglobin A1c; oGTT, oral glucose tolerance test; FPG, fasting plasma glucose

eTABLE 3

**Laboratory parameters for the diagnosis of type 2 diabetes (2)**

| Laboratory parameter | Advantages                                                                                                                                                                                                                                                                                   | Disadvantages                                                                                                                                                                                                                                                                                                                                                                                    |
|----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| FPG                  | <ul style="list-style-type: none"> <li>– Simple to perform</li> <li>– Independent of age, hemoglobinopathy, hematological disorders, and red blood cell turnover</li> </ul>                                                                                                                  | <ul style="list-style-type: none"> <li>– Individual variation from day to day</li> <li>– Time-of-day fluctuations (therefore, test performed, e.g., between 7:00 am and 9:00 am)</li> <li>– Uncertainty regarding fasting status</li> <li>– Preanalytical pitfalls (standardized processing and suitable blood collection tubes necessary)</li> </ul>                                            |
| HbA1c                | <ul style="list-style-type: none"> <li>– Independent of time of day and fasting status</li> <li>– Independent of muscle work and site of blood collection</li> <li>– Low individual variation from day to day</li> <li>– Reflects mean plasma glucose for the previous 8–12 weeks</li> </ul> | <ul style="list-style-type: none"> <li>– Multiple interferences</li> <li>– Analytical problems (insufficiently reproducible)</li> <li>– Among other factors, dependent on age and ethnic origin</li> </ul>                                                                                                                                                                                       |
| oGTT                 | <ul style="list-style-type: none"> <li>– Reference test (26)</li> <li>– Only test for the diagnosis of impaired glucose tolerance</li> <li>– Independent of age, hemoglobinopathy, hematological disorders, and red blood cell turnover</li> </ul>                                           | <ul style="list-style-type: none"> <li>– Lower reproducibility than FPG and HbA1c</li> <li>– More complex and prone to errors</li> <li>– Intraindividual fluctuations</li> <li>– Preanalytical pitfalls (standardized processing and suitable blood collection tubes necessary)</li> </ul>                                                                                                       |
| CPG                  | <ul style="list-style-type: none"> <li>– Fasting status not required</li> <li>– Simple to perform</li> <li>– Independent of age, hemoglobinopathy, hematological disorders, and red blood cell turnover</li> </ul>                                                                           | <ul style="list-style-type: none"> <li>– Intraindividual fluctuations</li> <li>– Fluctuations depending on length of fasting status and the type and volume of previous food intake</li> <li>– Preanalytical pitfalls (standardized processing and suitable blood collection tubes necessary)</li> <li>– Not suitable for the exclusion of a diagnosis due to lack of standardization</li> </ul> |

The table is based on the clinical experience of the guideline group.

CPG, casual plasma glucose; HbA1c, hemoglobin A1c; FPG, fasting plasma glucose; oGTT, oral glucose tolerance test

eTABLE 4

**Screening intervals for hitherto absent or undetected sequelae and comorbidities in individuals with type 2 diabetes**

| Screening for                                                                                                        | Time interval                                                                                                                                                                                                                                                                                                                                                  |
|----------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Neuropathy                                                                                                           | If no neuropathy has been detected to date, every 1—2 years depending on the individual risk assessment*                                                                                                                                                                                                                                                       |
| Foot lesions                                                                                                         | If no foot lesions have been detected to date<br>– In the absence of clinical findings of diabetic sensorimotor polyneuropathy and of PAOD, at least once annually<br>– In the case of clinical finding of diabetic sensorimotor polyneuropathy and/or PAOD, every 3–6 months (see NDMG for type 2 diabetes)                                                   |
| Nephropathy in diabetes                                                                                              | If no nephropathy has been detected to date, once annually                                                                                                                                                                                                                                                                                                     |
| Nephropathy in diabetes                                                                                              | If no diabetic retinal changes have been detected to date, then risk-adapted:<br>– In the case of low risk (= no ophthalmological risk and no general risk), every 2 years<br>– For all other risk constellations, annually.<br>If the general risk factors are not known, then assume an unfavorable general risk profile.<br>(see NDMG for type 2 diabetes*) |
| Depressive disorders and other mental health comorbidities (e.g., eating or anxiety disorders, cognitive impairment) | Once annually or as required<br>If screening is positive, a comprehensive diagnostic evaluation should be carried out.                                                                                                                                                                                                                                         |
| Risk assessment                                                                                                      | Time interval                                                                                                                                                                                                                                                                                                                                                  |
| Assessment of cardiovascular risk (e.g., CHD, heart failure, atrial fibrillation)                                    | Once annually or as required                                                                                                                                                                                                                                                                                                                                   |

\*For an individual risk assessment in relation to neuropathy, foot lesions, and retinopathy, see further information in the NDMG for type 2 diabetes ([www.leitlinien.de/diabetes](http://www.leitlinien.de/diabetes))

CHD, coronary heart disease; PAOD, peripheral arterial occlusive disease

eTABLE 5

**A guiding and comparative consideration of the substance classes (as a supplement to the algorithm on the pharmacological treatment of type 2 diabetes) (2)**

| Drug             | All-cause mortality     | Cardiovascular endpoints                                 | Microvascular endpoints* <sup>1</sup>               | Renal endpoints | Hypo-glycemic events | HbA1c, weight          | Comments/selected precautionary statements                                                                                                                                   |
|------------------|-------------------------|----------------------------------------------------------|-----------------------------------------------------|-----------------|----------------------|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Metformin        | (↓)                     | (↓)                                                      | (0)                                                 | (0)             | ↔                    | HbA1c ↓↓<br>Weight: ↔↓ | • Risk of lactic acidosis<br>• Pause in the case of illness (sick days)                                                                                                      |
| SGLT2 inhibitors |                         |                                                          |                                                     |                 |                      |                        | • Risk of genital infections, atypical ketoacidosis, Fournier's gangrene<br>• Pause in the case of illness (sick days)<br>• Weight loss (undesirable in the case of frailty) |
| Empagliflozin    | ↓ Reduces* <sup>2</sup> | MACE: ↓ reduces<br>CV death: ↓ reduces<br>HHF: ↓ reduces | n.s.                                                | ↓ Reduces       | ↔                    | HbA1c ↓↓<br>Weight: ↓  | –                                                                                                                                                                            |
| Canagliflozin    | 0                       | MACE: ↓ reduces<br>CV death: 0<br>HHF: ↓ reduces         | n.s.: Retinopathy, neuropathy<br>Amputations 0 to ↑ | ↓ Reduces       | ↔                    | HbA1c ↓↓<br>Weight: ↓  | –                                                                                                                                                                            |
| Dapagliflozin    | 0* <sup>2</sup>         | MACE: 0<br>CV death: 0<br>HHF: ↓ reduces                 | n.s.: Retinopathy, neuropathy; amputations: 0       | ↓ Reduces       | ↔                    | HbA1c ↓↓<br>Weight: ↓  | –                                                                                                                                                                            |

| GLP-1 RA                                       |                         |                                                  |                                                 |           |      |                                             | <ul style="list-style-type: none"> <li>• Gastrointestinal side effects, gallstones</li> <li>• Most drugs need to be injected</li> <li>• Weight loss (undesirable in the case of frailty)</li> </ul> |
|------------------------------------------------|-------------------------|--------------------------------------------------|-------------------------------------------------|-----------|------|---------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Liraglutide                                    | ↓ Reduces* <sup>2</sup> | MACE: ↓ reduces<br>CV death: ↓ reduces<br>HHF: 0 | Retinopathy: 0<br>n.s.: Neuropathy, amputations | ↓ Reduces | ↔    | HbA1c: ↓↓<br>Weight: ↓                      | –                                                                                                                                                                                                   |
| Exenatide                                      | ↓ Reduces* <sup>2</sup> | MACE: 0<br>CV death: 0<br>HHF: 0                 | n.s.: Retinopathy, neuropathy<br>Amputations: 0 | n.s.      | ↔    | HbA1c: ↓↓<br>Weight: ↓                      | –                                                                                                                                                                                                   |
| Semaglutide s.c.                               | 0* <sup>2</sup>         | MACE: ↓ reduces<br>CV death: 0<br>HHF: 0         | Retinopathy: ↑<br>n.s.: Neuropathy, amputations | ↓ Reduces | ↔    | HbA1c: ↓↓<br>Weight: ↓                      | –                                                                                                                                                                                                   |
| Semaglutide oral                               | ↓ Reduces* <sup>2</sup> | MACE: 0<br>CV death: ↓ reduces<br>HHF: 0         | n.s.: Retinopathy, neuropathy, amputations      | n.s.      | n.s. | HbA1c: ↓↓<br>Weight: ↓                      | –                                                                                                                                                                                                   |
| Lixisenatide                                   | 0* <sup>2</sup>         | MACE: 0<br>CV death: 0<br>HHF: 0                 | n.s.: Retinopathy, amputations, neuropathy      | n.s.      | ↔    | HbA1c: ↓↓<br>Weight: ↓                      | –                                                                                                                                                                                                   |
| Albiglutide                                    | 0* <sup>2</sup>         | MACE: ↓ reduces<br>CV death: 0<br>HHF: n.s.      | Retinopathy: 0<br>n.s.: Neuropathy, amputations | n.s.      | ↔    | HbA1c: ↓↓<br>Weight: ↓                      | –                                                                                                                                                                                                   |
| Dulaglutide                                    | 0                       | MACE: ↓ reduces<br>CV death: 0<br>HHF: 0         | Retinopathy: 0<br>n.s.: Amputations, neuropathy | ↓ Reduces | ↔    | HbA1c: ↓↓<br>Weight: ↓                      | –                                                                                                                                                                                                   |
| Sulfonylureas                                  | (0)                     | MACE: n.s.<br>CV death: (0)<br>HHF: (0)          | (0 to ↓)                                        | (0 bis ↓) | ↑↑   | HbA1c: ↓↓<br>Weight: ↑                      | • Risk of severe prolonged hypoglycemic events                                                                                                                                                      |
| DPP-4 inhibitors                               | (0)                     | MACE: n.s.<br>CV death: (0)<br>HHF: (0)          | (0)                                             | (0)       | ↔    | HbA1c: ↓<br>Weight: ↔                       | • Risk of pancreatitis, inflammatory bowel diseases                                                                                                                                                 |
| Where applicable, from step 3 of the algorithm |                         |                                                  |                                                 |           |      |                                             |                                                                                                                                                                                                     |
| Insulin                                        | (0)                     | (0)                                              | (↓)                                             | (0)       | ↑↑   | HbA1c: ↓↓<br>(dose-dependent)<br>Weight: ↑↑ | <ul style="list-style-type: none"> <li>• Risk of hypoglycemic events, particularly at the start of treatment</li> <li>• Lipohypertrophy</li> <li>• Injections necessary</li> </ul>                  |

\*<sup>1</sup> Microvascular endpoints: retinopathy, neuropathy, amputations

\*<sup>2</sup> The study was not powered for the endpoint of all-cause mortality.

Effect data: ↓: positive effect (endpoint was less frequently reached in the studies); ↑: negative effect (endpoint was more frequently reached in the studies); 0: the endpoint was not affected; n.s.: not specified (effect sizes were not reported in the main publication, or were reported without a confidence interval); renal endpoints: for SGLT2 inhibitors and GLP-1 RA in relation to renal composite endpoints

Assumptions in parentheses () are from studies of low methodological quality, or there was insufficient evidence on which to base an assessment.

Hypoglycemic events: ↑: increased risk; ↔: low risk, n.s.: not specified (Hypoglycemic events: intervention > placebo, reported without a confidence interval)

HbA1c: ↓: decline

Weight: ↑: weight gain; ↓: weight loss

The data on renal endpoints for empagliflozin are from (27).

CV death, cardiovascular death; DPP-4 inhibitors, dipeptidyl peptidase-4 inhibitors; GLP-1 RA, glucagon-like peptide-1 receptor agonists; HbA1c, hemoglobin A1c; HHF, hospitalization for heart failure; MACE, major adverse cardiac event, generally cardiovascular death, stroke, myocardial infarction (definitions at times heterogeneous); s.c., subcutaneous