

IQWiG Reports - Commission No. V09-02

# **Treatment of obesity in patients with type 2 diabetes mellitus - Guideline synopsis and supplementary search for and assessment of systematic reviews<sup>1</sup>**

## **Executive Summary**

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<sup>1</sup> Translation of the executive summary of the final report “Behandlung der Adipositas bei Patientinnen und Patienten mit Diabetes mellitus Typ 2 – Leitliniensynopse und ergänzende Recherche und Bewertung systematischer Übersichtsarbeiten” (Version 1.0; Status: 14.05.2012). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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This report was prepared in collaboration with external experts. According to § 139b (3) No. 2 of Social Code Book (SGB) V, Statutory Health Insurance, external experts who are involved in the Institute's research commissions must disclose "all connections to interest groups and contract organizations, particularly in the pharmaceutical and medical devices industries, including details on the type and amount of any remuneration received." The Institute received the completed form "Disclosure of conflicts of interest" from each external expert. The information provided was reviewed by a Committee of the Institute specifically established to assess conflicts of interests. The information on conflicts of interest provided by the external experts and external reviewers is presented in Appendix F of the full report. No conflicts of interest were detected that could endanger professional independence with regard to the work on the present commission.

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**External review of the preliminary report:**

- Manfred J. Müller, Institute for Human Nutrition and Food Science, Christian-Albrechts-University of Kiel

IQWiG thanks the external reviewer for his comments on the preliminary report. However, the external reviewer was not involved in the preparation of the final report. Individual sections and conclusions in the final report therefore do not necessarily reflect his opinion.

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<sup>2</sup> Due to legal data protection regulations, employees have the right not to be named.

## **Background**

On 2.12 2009, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to undertake a literature search for (clinical practice) guidelines on the treatment of obesity in patients with type 2 diabetes mellitus (“type 2 diabetes”), together with a supplementary search for and assessment of high-quality systematic reviews of the effects of obesity treatment in patients with type 2 diabetes on patient-relevant outcomes.

## **Research question**

The aim of the present investigation was to compile fundamental information about the treatment of obesity in patients with type 2 diabetes.

The investigation was divided into 2 areas:

- systematic literature search, selection and methodological assessment of current guidelines on the subject of type 2 diabetes and obesity that are applicable to the German health care system, and extraction of the recommendations from the guidelines on the treatment of obesity in patients with type 2 diabetes,
- systematic literature search and assessment of systematic reviews on the treatment of obesity in patients with type 2 diabetes with respect to patient-relevant outcomes, with the aim of supplementing the recommendations of the guideline synopsis on the basis of high-quality systematic reviews.

The purpose of this supplementation by the results of such reviews was to assess the evidence on which the guideline recommendations were based (e.g. with regard to the identified literature, the allocation of the level of evidence (LoE), and the textual account of the evidence in the guideline recommendations).

It was not the aim of the investigation to issue recommendations in the sense of a benefit assessment by IQWiG.

## **Methods**

### ***Guidelines***

A systematic literature search for diabetes and obesity guidelines via the guideline databases of the German Association of Scientific Medical Societies (AWMF), the Guidelines International Network (G-I-N) and the National Guideline Clearinghouse (NGC), as well as the search on the websites of multidisciplinary and specialist guideline providers were undertaken on the Internet. In addition, a systemic literature search was conducted in the bibliographical databases MEDLINE and EMBASE. The literature search covered the period from 2005 to September 2011. A further inclusion criterion, alongside the languages of German, English and French, was the country in which the guidelines were compiled. According to the commission, only guidelines that were applicable to the German health care

system were to be searched for and selected. The applicability of guidelines to the German health care system was judged using the division of states of the World Health Organization (WHO) report on world health of 2003. The documented evidence base of a guideline was a further important inclusion criterion. "Evidence-based guidelines" were regarded in the following report to refer to guidelines whose recommendations were provided with a LoE and/or Grade of Recommendation [GoR] and were linked to the references of the primary and/or secondary literature on which they are based.

The methodology of the included guidelines was assessed using the Appraisal of Guidelines for Research & Evaluation (AGREE) tool.

The recommendations relevant to the research question on dietary treatment, exercise, behavioural therapy, drug treatment and surgery in patients with obesity and type 2 diabetes were extracted and shown in a guideline synopsis.

### ***Systematic reviews***

In addition, a search for relevant systematic reviews was performed in the databases MEDLINE, EMBASE and the Cochrane Database of Systematic Reviews (Cochrane Reviews), the Database of Abstracts of Reviews of Effects (Other Reviews) and the Health Technology Assessment Database (Technology Assessments). The literature search covered the period up to 28.09.2011.

Systematic reviews published in German, English or French, based on randomized controlled trials (RCTs) with a minimum duration of 24 weeks in adult patients with type 2 diabetes and concurrent obesity, were included.

The interventions to be examined in these studies were dietary treatment, exercise, behavioural therapy, drug treatment or surgical treatment for obesity (or combinations thereof). The comparator intervention was any other of the above-named interventions (or combinations), the lack of a corresponding intervention in the control group or one of the named interventions used less frequently or at lower intensity.

Pre-defined outcome measures that enable an assessment of the following patient-relevant outcomes were used for the investigation: all-cause mortality, cardiac morbidity and mortality, cerebral morbidity and mortality, vascular-related non-cardiac and non-cerebral morbidity and mortality, blindness or its precursor states, end-stage renal failure with the need for dialysis, amputation (major and minor), hyperosmolar or ketoacidotic coma, symptoms caused by chronic hyperglycaemia, hypoglycaemia, especially severe hypoglycaemia, adverse events of the interventions, health-related quality of life and diabetes remission.

The methodological quality of the systematic reviews was assessed using the quality index of Oxman and Guyatt. Reviews were included that had been awarded at least 5 out of a possible 7 points by 2 independent reviewers.

The results of the systematic reviews included in the investigation and the evidence on which the systematic reviews were based were presented.

### ***Comparative analysis***

The extracted results of the systematic reviews were to be compared with the guideline recommendations relevant to the subject, in order to identify agreements and differences between the guideline recommendations and the systematic reviews. Reasons for possible differences were also to be identified.

## **Results**

### ***Guidelines***

A total of 20 evidence-based guidelines (11 obesity and 9 diabetes guidelines) were assessed and their recommendations extracted. The number of diabetes and obesity guidelines is far higher, but only these 20 contained recommendations for the target group of patients with type 2 diabetes and obesity relevant for this report.

The obesity guidelines included were issued by institutions in Germany (n = 1), France (n = 1), Great Britain (n = 3), Canada (n = 1), New Zealand (n = 1) and the USA (n = 3), as well as by international societies (n = 3); the included diabetes guidelines were issued by institutions in France (n = 1), Great Britain (n = 2), Canada (n = 2) and the USA (n = 2).

In the methodological assessment using the AGREE tool by 2 assessors independent of each other, most of the guidelines in Domain 1 (Scope and Purpose) and Domain 4 (Clarity and Presentation) achieved medium and high standardized domain scores, whereas in Domains 2 (Stakeholder Involvement), 5 (Applicability) and 6 (Editorial Independence) lower domain scores were awarded.

Eight of the 20 included guidelines basically recommended a weight reduction in patients with type 2 diabetes and obesity, because this can be associated with an improvement in type 2 diabetes or an improvement in or a reduction in risk for comorbidities such as coronary heart disease (CHD), osteoarthritis or increased blood pressure. However, the GoR and/or LoE associated with this recommended weight reduction varied between the guidelines (i.e. sometimes higher and sometimes lower).

According to 5 guidelines, the weight reduction should be supported by dietary therapy.<sup>3</sup> Three of the included guidelines also contained special recommendations concerning specific diets. These recommendations were provided without, or with non-uniform, GoR and/or LoE.

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<sup>3</sup> The guidelines use different terms in respect of dietary therapy/advice. The terms are not defined in the guidelines. Because of better readability, the term “dietary therapy” is used in this report.

Exercise therapy was recommended for weight reduction by 7 of the 20 guidelines explicitly for overweight and obese patients with type 2 diabetes. These recommendations were provided without, or with non-uniform, GoR and/or LoE.

Behavioural therapy to accompany the dietary and exercise treatment was recommended by 4 of the included guidelines, with non-uniform GoR and/or LoE.

Eight of the included guidelines named drug therapy as a possible option in the treatment of obesity in patients with type 2 diabetes. According to 3 guidelines, this should always be used concomitantly with diets, exercise and behavioural therapy and should only be continued if a weight reduction can be shown after 3 months. These recommendations were provided with a non-uniform GoR and/or LoE.

According to 3 guidelines, drug treatment can be initiated in patients with type 2 diabetes and a BMI of  $\geq 27$  kg/m<sup>2</sup>. Another guideline recommended drug treatment in patients with type 2 diabetes and a BMI of  $\geq 28$  kg/m<sup>2</sup>. These recommendations were also provided with non-uniform GoR and/or LoE. Four guidelines named no specific BMI above which drug treatment is recommended.

If conservative treatment such as dietary and exercise therapy or drug treatment had been unsuccessful in achieving a weight loss, 14 of the 20 included guidelines named a bariatric procedure as a therapeutic option in the case of a BMI of  $\geq 35$  kg/m<sup>2</sup> and existing type 2 diabetes. These recommendations were provided with a non-uniform GoR and/or LoE.

Two guidelines - again with a non-uniform GoR and/or LoE - recommended pregnant women who were overweight or obese and suffering from type 2 diabetes to reduce their weight.

### ***Systematic reviews***

A total of 4 high-quality systematic reviews by 2 groups of authors were included in the report.

However, the systematic reviews contained no aggregated results from RCTs in obese patients with type 2 diabetes concerning relevant outcomes. Results on relevant outcomes were available in these systematic reviews only for individual RCTs (4 RCTs for drug therapies and 1 RCT for surgical treatment) concerning adverse events, complications of the intervention and the outcome “diabetes remission”.

Under treatment with orlistat, gastrointestinal symptoms occurred in more patients than in the study participants of the control groups.

After the surgical procedure to treat obesity (gastric band), adverse events occurred equally often as in patients who had not undergone this procedure.

Diabetes remission was achieved through the surgical procedure in significantly more patients than was the case in those treated conservatively.

### ***Comparative analysis***

Since no robust aggregated results on the research question of this report could be identified in the systematic reviews, the originally planned comparative analysis of the recommendations from guidelines and the results of systematic reviews could not be performed.

On the basis of the results of individual RCTs in the systematic reviews, only a reference to the rate of adverse events of orlistat can be added to the results of the guideline synopsis.

### **Conclusions**

Obesity and diabetes guidelines for patients with obesity and type 2 diabetes essentially recommended a weight reduction and, for the treatment of obesity in particular, diet, exercise and behavioural therapy. A few guidelines also named drug treatment in the case of a BMI  $\geq 27$  kg/m<sup>2</sup> or  $\geq 28$  kg/m<sup>2</sup> and surgery as a therapeutic option for a BMI  $\geq 35$  kg/m<sup>2</sup>. The guideline recommendations were provided with a non-uniform or absent GoR and/or LoE.

No systematic reviews on the treatment of obesity in patients with type 2 diabetes were available that contained aggregated results on patient-relevant outcomes relevant to this report. The included systematic reviews provided few individual results relevant for this report from RCTs. These enable possible conclusions regarding an increased rate of adverse events for the drug treatment with orlistat and an increased rate of diabetes remission after surgical treatment. However, a more detailed examination and assessment of the individual results from RCTs reported in the systematic reviews at study level did not take place.

Due to the lack of evidence from systematic reviews, a comparison of the evidence on which the guideline recommendations are based and systematic reviews was not possible (e.g. in respect of the identified literature, the allocation of the level of evidence (LoE) and the textual account of the evidence in the guideline recommendations).

**Keywords:** Weight Loss, Diet Therapy, Exercise Therapy, Behaviour Therapy, Drug Therapy, Surgical Procedures – Operative, Diabetes Mellitus – Type 2, Obesity, Methodological Guideline Evaluation, Disease Management Programme, Systematic Review

*The full report (German version) is published under [www.iqwig.de](http://www.iqwig.de)*