

IQWiG Reports – Commission No. V09-04

**Systematic guideline search
and appraisal, as well as
extraction of new and relevant
recommendations, for the
DMP “diabetes mellitus type 2”¹**

Executive Summary

¹ Translation of the executive summary of the final report “Systematische Leitlinienrecherche und -bewertung sowie Extraktion neuer und relevanter Empfehlungen für das DMP Diabetes mellitus Typ 2” (Version 1.0; Status: 07.11.2011). 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 G of the full report. No conflicts of interest were detected that could endanger professional independence with regard to the work on the present commission.

External review of the preliminary report:

- Michael Roden, German Diabetes Centre, Institute for Clinical Diabetology, Düsseldorf

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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Executive summary

Background

The Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct a literature search for clinical practice guidelines on diabetes mellitus type 2 (resolution of 17.12.2009). The recommendations extracted from evidence-based guidelines were consequently to serve the legally specified regular update of the disease management programme (DMP).

Research questions

The aim of this study was to specify a potential need for updating and supplementation of the existing DMP “diabetes mellitus type 2” by systematically searching for new, topic-relevant, evidence-based guidelines and by synthesizing the guideline recommendations.

The study was organized according to the following working steps:

- Literature search for and selection of current guidelines on diabetes mellitus type 2
- Appraisal of the methodological quality of selected guidelines
- Extraction and synthesis of guideline recommendations relevant to the existing DMP “diabetes mellitus type 2”
- Identification of recommendations justifying a potential need for revision of the DMP

Methods

An Internet search for topic-specific guidelines was conducted 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 by searching the websites of multidisciplinary and specialist guideline providers. In addition, a search was conducted in the bibliographic databases MEDLINE and EMBASE. The publication period started in 2005. The period up to March / April 2011 was covered. Besides the languages German, English and French, a further inclusion criterion was the country in which the guidelines had been developed. According to the commission, only guidelines transferable to the German health care system were to be searched for and selected. The classification of nations from the World Health Report 2003, published by the World Health Organization (WHO), was used to operationalize the transferability of guidelines to the German health care system. The documentation of the evidence base of a guideline was a further important inclusion criterion. In the following report, “evidence-based” guidelines are understood to be guidelines whose recommendations are allocated as a matter of principle to a level of evidence (LoE) and/or grade of recommendation (GoR), and are linked to citations of the underlying primary and secondary literature.

The guidelines included were appraised methodologically by means of the Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument.

The recommendations relevant to the research questions were extracted and allocated to the health care aspects noted in Appendix 1 of the 20th Risk Adjustment Scheme Amendment Act (RAS-AA) of 23.06.2009. Finally the extracted recommendations were synthesized according to the items of Appendix 1 of the RAS-AA and compared with the requirements of the DMP “diabetes mellitus type 2”.

The procedure for identifying a potential need for updating and supplementation was as follows: A potential need for updating and supplementation was determined for recommendations that were consistent in content and largely showed a high grade of recommendation or level of evidence. A potential need for updating and supplementation was to be discussed for recommendations that were consistent in content in various guidelines and showed, at least in part, a high grade of recommendation or level of evidence. A potential need for updating and supplementation was also to be discussed in the event that new aspects for the DMP were presented in only a single guideline but were identified as having a high grade of recommendation or level of evidence. In this context, the two highest grades of recommendation were considered for all guidelines with their different grading systems.

In the event of a potential need for updating and supplementation with regard to an item of Appendix 1 of the RAS-AA, it was assessed whether further IQWiG reports on this topic were available. When a potential need for updating and supplementation was determined, the corresponding IQWiG reports were taken into account.

In addition, the indication-specific reimbursability of the drugs in Germany was also considered.

Results

A total of 35 evidence-based guidelines were included and appraised and their recommendations extracted. The included guidelines were issued by institutions in Germany (n = 6), Europe (n = 3), the USA (n = 13), Canada (n = 4), Australia (n = 7), as well as international institutions (n = 2).

Two of the 35 included guidelines deal with almost all aspects of the care of diabetes mellitus type 2. 21 guidelines deal with partial aspects of the therapy of diabetes mellitus type 2 – including basic therapy, therapy to reduce blood glucose and the treatment of hyperglycaemic or hypoglycaemic metabolic decompensation. 26 guidelines contain recommendations on macrovascular and microvascular concomitant diseases and late complications. 18 of the 35 included guidelines deal with psychological, psychosomatic and psychosocial impairment, as well as training programme for insured persons. 2 of the 6 German guidelines contain recommendations on cooperation with healthcare sectors.

The methodological appraisal was performed by 2 independent reviewers using the AGREE instrument. Most guidelines achieved intermediate or high standardized domain values in Domain 1 (Scope and Purpose) and in Domain 4 (Clarity of Presentation). The standardized

domain values in the other domains were rather low. The lowest possible value (0) was not awarded in Domain 3 (Rigour of Development).

Eight of the 35 recommendations included in the study (NVL-Fuß [foot] 2010, NVL-Netzhaut [retina] 2010, AAN 2011, NHMRC PE 2009, NHMRC 2008, KDOQI 2007, RNAO 2007, RNAO 2005) contain information about how the authors of the guidelines dealt with unpublished data. The guidelines contain virtually no indication as to how the unpublished data were used in the formulation of recommendations.

Potential need for updating and supplementation

The included guidelines deal with some aspects of care in more detail than is the case in Appendix 1 of the RAS-AA. Nevertheless, the included guidelines do not deal with all relevant aspects of the medical care of diabetes mellitus type 2. The recommendations of the guidelines essentially agree with the requirements in Appendix 1 of the RAS-AA. There are however deviations from the recommendations of the guidelines in some areas of Appendix 1. Firstly, those items or sub-items are described for which a potential need for updating and supplementation was identified. This is followed by items or sub-items for which a potential need for updating and supplementation can be discussed. Areas are then presented for which there are no deviations between Appendix 1 of the RAS-AA and the guidelines. Items for which no guideline recommendations could be identified are named last. No statement can be made on the potential need for updating and supplementation of these items.

A potential need for updating and supplementation was identified for the following items or sub-items:

Item 1.4.3 Physical activities

Several guidelines provide recommendations on physical activity – mostly with high GoR or LoE. However, these guidelines contain additional recommendations to those in RAS-AA. There is a potential need for updating and supplementation with respect to the type and duration of physical activity.

With respect to the increase in physical activity, IQWiG will soon publish rapid report A05-06A: “Benefit assessment of non-drug treatment strategies in patients with diabetes mellitus type 2: increase of physical activity”.

Item 1.7.1.1 Antihypertensive therapy

Sub-item therapeutic goals

Several guidelines provide recommendations for target blood pressure values below the target blood pressure values given in Appendix 1 of the RAS-AA. These recommendations mostly have high GoR or LoE. There is thus a potential need for updating and supplementation.

With respect to the long-term reduction in blood pressure to the lower normotonic range in patients with diabetes mellitus, IQWiG will soon publish rapid report A05-10: “Benefit

assessment of long-term lowering of blood pressure to levels in the lower normal range in patients with diabetes mellitus.”

Item 1.7.1.2 Statin therapy

Several guidelines provide recommendations on stain therapy – mostly with high GoR or LoE. However, the guidelines contain additional recommendations in comparison to the RAS-AA. Several guidelines provide recommendations on target blood lipid values and on therapy with fibrates in cases of statin intolerance. Most of these recommendations have high GoR. The latter two items are not given in Appendix 1. There is a potential need for updating and supplementation with respect to blood lipid target values and fibrates.

Item 1.7.2.2 Nephropathy in diabetes mellitus type 2

Several guidelines provide recommendations on nephropathy in diabetes mellitus, mostly with high GoR or LoE. However, the guidelines contain additional recommendations in comparison to Appendix 1 of the RAS-AA. In contrast to Appendix 1 of the RAS-AA, several guidelines provide reference values for the glomerular filtration rate (GFR) with respect to referral to a specialist physician, as well as criteria for diagnosis of chronic renal failure. There is thus a potential need for updating and supplementation with respect to the reference values for GFR and the criteria for the diagnosis of chronic renal failure.

Item 1.7.2.4 Diabetic neuropathy

Several guidelines provide recommendations on the treatment of painful diabetic polyneuropathy, mostly with high GoR. In comparison to the RAS-AA, 3 guidelines contain additional recommendations on the treatment of painful polyneuropathy with various drugs.

Three guidelines provide recommendations on the use of opiates for the treatment of painful polyneuropathy – with high GoR. There is thus a potential need for updating and supplementation with respect to the treatment of painful polyneuropathy with opiates.

In addition, 2 guidelines provide recommendations on the topical use of isosorbide dinitrate for the treatment of painful polyneuropathy. There is thus a potential need for updating and supplementation in this respect.

Item 1.7.2.5 The diabetic foot syndrome

Several guidelines provide recommendations on the diabetic foot syndrome – mostly with high GoR or LoE. The recommendations essentially agree with Appendix 1 of the RAS-AA, although the guidelines contain additional recommendations. Three guidelines provide recommendations on controlling the vascular status using the ankle-brachial index. These recommendations are mostly of high GoR or LoE. There is thus a potential need for updating and supplementation.

Items for which a potential need for updating and supplementation can be discussed:***Item 1.7.1.1 Antihypertensive therapy****Drug treatment for hypertension*

Two guidelines provide recommendations on antihypertensive therapy with beta-blockers – mostly with high GoR. However, the guidelines contain additional recommendations in comparison to the RAS-AA. One guideline – with the highest GoR – advises against the use of a beta-blocker or an alpha-blocker as first-line drug treatment for hypertension. Alpha-blockers are not mentioned in Appendix 1. A potential need for updating and supplementation can be discussed with respect to the negative recommendation on alpha-blockers and beta-blockers as first-line therapy.

Several guidelines provide recommendations on antihypertensive therapy with ACE inhibitors or AT₁ receptor antagonists. Most of these recommendations are of high GoR or LoE. However, the guidelines contain additional recommendations in comparison to the RAS-AA. One guideline recommends with high GoR either an AT₁ receptor antagonist or an ACE inhibitor as first-line drug therapy for hypertensive diabetics – without explicitly mentioning diabetic nephropathy. One other guideline recommends with high GoR either an AT₁ receptor antagonist or an ACE inhibitor as equivalent treatments in these patients. Once again, nephropathy is not explicitly mentioned. A potential need for updating and supplementation can be discussed, both for the use of AT₁ receptor antagonist or an ACE inhibitor as first-line therapy, or their use as equivalent treatment.

Item 1.7.2.4 Diabetic nephropathy

One guideline recommends with high GoR the topical use of capsaicin spray for the treatment of painful diabetic polyneuropathy. A potential need for updating and supplementation can therefore be discussed.

There is no need for updating or supplementation for the following items:

- Item 1.2 Diagnostic testing (initial diagnosis)
- Item 1.3.1 Therapeutic goals
- Item 1.3.2 Differentiated therapeutic planning
- Item 1.4 Basic therapy – general measures
- Item 1.4.1 Nutritional advice
- Item 1.4.2 Abstinence from tobacco
- Item 1.4.4 Metabolic self-control
- Item 1.5 Therapy to reduce blood glucose
- Item 1.6 Treatment of hyperglycaemic and hypoglycaemic metabolic decompensation
- Item 1.7.1 Macroangiopathy

- With respect to vaccines against influenza and pneumococci
- With respect to the diagnostic testing and therapy of chronic CHD (reference to the DMP CHD)
- Item 1.7.1.1 Antihypertensive therapy
 - With respect to the definition and diagnosis of arterial hypertension
 - With respect to general drug treatment
 - With respect to the sub-item diuretics
- Item 1.7.1.2 Statin therapy
 - With respect to combination therapy of statins and other lipid lowering agents
- Item 1.7.1.3 Platelet aggregation inhibitors
 - With respect to primary prevention of cardiovascular events
 - With respect to secondary prevention of cardiovascular events
- Item 1.7.2 Microvascular complications
- Item 1.7.2.1 General measures
- Item 1.7.2.3 Diabetic retinopathy
- Item 1.7.2.4 Diabetic neuropathy
 - With respect to cardiac autonomic diabetic neuropathy
 - With respect to the therapy of erectile dysfunction
- Item 1.7.2.5 The diabetic foot syndrome
 - With respect to risk classification for the diabetic foot syndrome
 - With respect to vacuum-assisted closure for wound healing
- Item 1.7.3 Psychological, psychosomatic and psychosocial impairment
- Item 1.8.1 Coordinating physician
- Item 1.8.2 Referral from the coordinating physician to the qualified specialist or to the qualified facility
- Item 1.8.3 Admission to a hospital for treatment as an in-patient
- Item 1.8.4 Ordering rehabilitation treatment
- Item 4.2 Training insured persons

For some items in Appendix 1 of the RAS-AA, no recommendations could be identified in the guidelines. For this reason, no statement can be made about any potential need for updating and supplementation:

- Item 1.1 Definition of diabetes mellitus type 2
- Item 1.7.1.1 Antihypertensive therapy
 - With respect to the sub-item secondary hypertension
 - With respect to the sub-item basic therapy
 - With respect to the sub-item structured programme for hypertension treatment and training

Conclusion

As a result of the comparison between the extracted recommendations from current evidence-based guidelines and the requirements of Appendix 1 to the RAS-AA – which forms the basis for the DMP for diabetes mellitus type 2 -, aspects of health care could be identified for which there is a potential need for updating and supplementation, or for which this could be discussed.

A potential need for updating and supplementation was identified for the following items or sub-items:

- Item 1.4.3 Physical activities with respect to the type and duration of the physical activity
- Item 1.7.1.1 Antihypertensive therapy for the sub-item therapeutic goals, with respect to target blood pressure values
- Item 1.7.1.2 Statin therapy with respect to target values for blood lipids and therapy with fibrates in cases of statin intolerance
- Item 1.7.2.2 Nephropathy in diabetes mellitus type 2, with respect to the reference values for GFR and the criteria for the diagnosis of chronic renal failure
- Item 1.7.2.4 Diabetic neuropathy with respect to the treatment of painful neuropathy with opiates and with isosorbide dinitrate (topical application)
- Item 1.7.2.5 The diabetic foot syndrome with respect to controlling the vascular status using the ankle-brachial index.

A potential need for updating and supplementation can be discussed for the following items or sub-items:

- Item 1.7.1.1 Antihypertensive therapy with respect to the negative recommendation on the use of alpha-blockers and beta-blockers as first-line therapy, and with respect to antihypertensive therapy with an AT₁ receptor antagonist or an ACE inhibitor as first-line drug therapy or with respect to the equivalence of the 2 drug classes
- Item 1.7.2.4 Diabetic neuropathy with respect to the topical application of capsaicin spray for the treatment of painful diabetic polyneuropathy

It is unclear whether the lack of consideration of unpublished data in the included guidelines leads to bias in the external evidence underlying the recommendations. If this results in bias,

the direction and magnitude of this bias cannot be assessed on the basis of the available information.

Keywords: disease management; diabetes mellitus, type 2; guideline appraisal; guidelines as topic

The full report (German version) is published under www.iqwig.de