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Systematic guideline search and appraisal, as well as extraction of new and relevant recommendations, for the DMP "Coronary heart disease"[1]

Executive Summary

[1] Translation of the executive summary of the final report V09-05 "Systematische Leitlinienrecherche und -bewertung sowie Extraktion neuer und relevanter Empfehlungen für das DMP KHK" (Version 1.0; Status:.13.12.2010). V09-05 is an update of final report V06-03 (Version 1.0, 28.02.2008). 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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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 (CPGs) on coronary heart disease (CHD) (resolution 17.12.2009). The recommendations extracted from evidence-based CPGs were consequently to serve the legally specified regular update of the disease management programme (DMP) for CHD.

Research questions

The aim of this study was to specify a potential need for updating and supplementation of the existing DMP-CHD by means of a systematic search for new, topic-relevant evidence-based CPGs and by means of a synthesis of the CPG recommendations.

The study was organized according to the following working steps:

- Literature search for and selection of current CPGs on CHD
- Appraisal of the methodological quality of selected CPGs
- Extraction and synthesis of CPG recommendations relevant to the existing DMP-CHD[2]
- Labelling of recommendations justifying a potential need for revision of the DMP

Methods

A search for topic-specific CPGs on the Internet was conducted via the CPG databases of the Association of the Scientific Medical Societies,[3] the Guidelines International Network (G-I-N), and the National Guideline Clearinghouse (NGC), as well as via a search of websites of multidisciplinary and specialist CPG providers. In addition, a search in the bibliographic databases MEDLINE and EMBASE was performed. The publication period was limited to CPGs published after June 2007, as the IQWiG commission V06-03, which addressed the same research questions, had already covered the publication period between 2002 and June 2007. The present study follows the previous commission and covers the period up to September 2010. Besides the languages German, English and French, a further inclusion criterion was the country in which the CPGs had been developed. According to the commission, only CPGs 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 CPGs to the German health care system. The documentation of the evidence base of a CPG was a further important inclusion criterion. In the following report, “evidence-based” CPGs

[2] The recommendations extracted from the guidelines are to be understood as citations whose underlying evidence was not as such reassessed.
[3] Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, AWMF

are understood to be CPGs whose recommendations are a) based on a systematic literature search, b) allocated as a matter of principle to a Level of Evidence (LoE) and/or Grade of Recommendation (GoR), and c) linked to citations of the underlying primary and secondary literature.

The CPGs 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 5 of the 20th Risk Adjustment Scheme Amendment Act[4] (RAS-AA) of 23.06.2009. Finally the extracted recommendations were synthesized according to the items of Appendix 5 of the RAS-AA and compared with the requirements of the DMP-CHD.

Results

A total of 14 evidence-based CPGs were included, appraised and their recommendations extracted. The CPGs included were published by institutions from Germany (n = 1), the rest of Europe (n = 3), the United States (n = 9) and Canada (n = 1).

Only 1 of 14 of the CPGs included addressed all health care aspects of chronic or stable CHD. Seven of the CPGs included focused on the partial aspects diagnosis, primary and secondary prevention, as well as interventional treatment or rehabilitation of CHD. In 6 of the CPGs included, recommendations were provided on the partial aspects diagnosis of acute coronary syndrome (ACS) and long-term treatment after myocardial infarction (MI). A further CPG addressed the diagnosis and treatment of depression after an MI.

In the methodological appraisal with the AGREE instrument, which was in each case conducted by 2 assessors independently of each other, most CPGs achieved average and high standardized domain scores in domain 1 (scope and purpose), 3 (rigour of development), 4 (clarity and presentation), and 6 (editorial independence), whereas in domain 2 (stakeholder involvement) and 5 (applicability) the domain scores awarded tended to be low.

For all CPGs included, those recommendations were identified and extracted whose content could be allocated to one of the health care aspects of the items 1.1 to 1.7 and 4.2 of Appendix 5 of the RAS-AA. The CPGs included addressed some health care aspects in more detail than is the case in Appendix 5 of the RAS-AA.

Non-drug therapy and general measures

Appendix 5 of the RAS-AA does not include requirements for the control of arterial hypertension and diabetes mellitus. In the RAS-AA there is less emphasis on the treatment of

[4] Risikostrukturausgleichs-Änderungsverordnung, RSA-ÄndV

arterial hypertension as one of the underlying diseases of CHD than in international CPGs. This could result in a potential need for updating or supplementation.

Regarding the prognostic factor “excess weight,” neither the body mass index (BMI) nor the waist circumference are mentioned as appropriate recording methods in the RAS-AA; however, the recording of these measures is recommended by international CPGs. Nutrition advice is presented in more detail in the recommendations of international CPGs than in the requirements of Appendix 5 of the RAS-AA. Target values for cholesterol and triglyceride levels are stated in CPG recommendations; these are not found in Appendix 5 of the RAS-AA. This could result in a potential need for updating or supplementation.

Regarding general measures, beyond nicotine replacement therapy, Appendix 5 of the RAS-AA contains no recommendations on the use of additional drugs in the treatment of the prognostic factor “smoking”. In addition it is recommended in CPGs to reduce exposure to smoke. This could result in a potential need for updating or supplementation.

CPGs provide specific recommendations on the duration, type and intensity of physical activity. They thus go beyond the requirements of Appendix 5 of the RAS-AA, which could result in a potential need for updating or supplementation.

Influenza vaccination for CHD patients is not part of Appendix 5 of the RAS-AA, but is consistently recommended by international CPGs; this could result in a potential need for supplementation.

The prognostic factors comorbidities, weight, nutrition, and smoking, as well as vaccinations, are usually addressed separately in international CPGs. For prognostic factors, therapeutic goals are sometimes named and non-drug and drug interventions recommended for their modification.

Drug therapy

The CPG recommendations on the use of beta blockers, calcium antagonists and statins are by and large consistent with the requirements of Appendix 5 of the RAS-AA; this does not result in a potential need for updating or supplementation.

In addition, there are 6 areas of drug therapy in which the recommendations of the CPGs included deviate from the requirements of Appendix 5 of the RAS-AA.

With regard to the use of long- and short-acting nitrates, the CPG recommendations are more differentiated than Appendix 5 of the RAS-AA. Short-acting nitrates are recommended for the treatment of angina pectoris attacks (GoR I, LoE C). This could result in a potential need for updating or supplementation.

In addition, beyond the use of statins, the CPGs provide recommendations on fibrates, niacin and omega-3 fatty acids (GoR IIa, IIb; LoE B, C). Due to the low grades of recommendation there is no potential need for updating or supplementation.

The recommendations on the use of angiotensin-converting enzyme (ACE) inhibitors for all patients in the early phase after MI are by and large consistent with Appendix 5 of the RAS-AA. In addition, in contrast to the requirements of Appendix 5 of the RAS-AA, the administration of ACE inhibitors is recommended in 5 CPGs as a long-term treatment and independent of a left-ventricular dysfunction or other existing comorbidities (consistent classification in GoR IIa, LoE A, B). The recommendations of the included CPGs on the medical indication for the use of ACE inhibitors in patients with CHD who have a low risk for secondary events go beyond the requirements of Appendix 5 of the RAS-AA. This also applies to the duration of treatment in patients who experienced an MI. This could result in a potential need for updating or supplementation.

The recommendations on the use of AT1-receptor antagonists are by and large consistent with the requirements of Appendix 5 of the RAS-AA; this does not result in a potential need for updating or supplementation. In addition to these requirements, 3 CPGs of the American College of Cardiology / American Heart Association recommend a combination of ACE inhibitors and AT1-receptor antagonists if symptoms remain persistent under monotherapy (GoR IIb, LoE B). Due to the low grades of recommendation there is no potential need for updating or supplementation.

Aldosterone antagonists are not represented in Appendix 5 of the RAS-AA. In contrast, the CPGs included recommend the use of aldosterone antagonists with the highest grade of recommendation for patients after an MI who have no relevant limitation of kidney function or hyperkalaemia, have already been treated with ACE inhibitors or beta blockers, have an LVEF $\leq$ 40 %, as well as suffer either from heart failure or diabetes mellitus. This could result in a potential need for updating or supplementation.

The CPGs included define indications and contraindications for the use of further platelet aggregation inhibitors beyond acetylsalicylic acid (ASA); these inhibitors are not named in Appendix 5 of the RAS-AA. Clopidogrel is recommended as a substitute if ASA is either not tolerated or contraindicated (GoR I and Ib, LoE A, B); this does not result in a potential need for updating or supplementation.

If neither drug can be tolerated, oral anticoagulants are recommended (GoR IIa and IIb, LoE B). These drugs are not named in the requirements of Appendix 5 of the RAS-AA; in some CPGs, the medical indications for their use in patients with CHD showing an increased risk of thromboembolic events are precisely defined. This could result in a potential need for updating or supplementation.

The recommendations on the dual use of platelet aggregation inhibitors in patients who experienced an ACS are by and large consistent with the requirements of Appendix 5 of the RAS-AA. ACS is not differentiated in Appendix 5 of the RAS-AA; this would be of particular relevance for MI with or without an ST-segment elevation. In patients who experienced an MI, independent of the type of revascularization, some CPGs specify the duration of combination therapy with ASA and clopidogrel and recommend treatment for up to 12 months (GoR I, LoE A for non-STEMI[5] and GoR IIa, LoE C for STEMI). In consequence, for patients with a non-STEMI, this could result in a potential need for updating or supplementation with regard to treatment duration. For patients with a STEMI the grades of recommendation are lower and the CPG recommendations are in contrast to the results of the IQWiG report A04-01B on the benefit assessment of clopidogrel plus ASA in patients with ACS. In addition, clopidogrel and ASA combination therapy in patients who received a stent after a STEMI is not approved in Germany.

In patients with ACS who received a stent, one CPG recommends prasugrel[6] as continuous therapy for at least 12 months as an alternative to clopidogrel (GoR I, LoE B). In addition, some CPGs provide recommendations for the preparation of coronary artery bypass graft (CABG) surgery (GoR 2A for the cessation of clopidogrel therapy; GoR I, LoE C for the cessation of prasugrel therapy); these are not mentioned in the requirements of Appendix 5 of the RAS-AA. The treatment duration for prasugrel does not result in a need for updating or supplementation. The recommendations on dual platelet aggregation inhibition in patients with ACS who underwent percutaneous coronary intervention (PCI) are represented in Appendix 5 of the RAS-AA, except for the mentioning of prasugrel as an alternative to clopidogrel. There could be a need for updating or supplementation for prasugrel; however, only one CPG comments on this agent.

In the CPGs negative recommendations are given concerning the use of 3 drugs (COX-2 inhibitors, menopausal hormone therapy, dipyridamole), which are not mentioned in the requirements of Appendix 5 of the RAS-AA. This could result in a potential need for updating or supplementation for COX-2 inhibitors and menopausal hormone therapy; this does not apply to dipyridamole due its approval status.

With respect to the choice of method (PCI versus CABG), the recommendations on interventional therapy are by and large represented in Appendix 5 of the RAS-AA. For specific patient groups, the recommendations go beyond the requirements of Appendix 5 of the RAS-AA; this does not result in a potential need for updating or supplementation.

Regarding the medical indication for interventional therapy, under certain preconditions a lower grade of stenosis is recommended in the new CPG ESC 2010, both for patients with a

[5] STEMI= ST-segment elevation myocardial infarction
[6] Prasugrel is approved in Germany for a treatment period of up to a maximum of 12 months

symptomatic indication and for those with a prognostic indication (>50% in CPG vs. >70% in Appendix 5 of the RAS-AA). This could result in a potential need for updating or supplementation; in this context it needs to be considered that the recommendations originate from one CPG.

Under 4.2 “Training programmes for insured members” of Appendix 5 of the RAS-AA, the opportunity is offered to enable patients to cope better with their disease by means of training programmes. However, the content of the programmes is not defined in detail. In the CPGs it is recommended that patients with CHD should be trained to recognize dangerous situations and consult a doctor. Such advice is so far lacking in Appendix 5 of the RAS-AA. This could result in a potential need for updating or supplementation. However, in the structure of the RAS-AA this item lies outside the section “Treatment according to the current state of scientific knowledge”.

No potential need for updating or supplementation was noted for the items 1.2 “Sufficient diagnostic procedures”, 1.4. “Therapy planning on the basis of individual risk assessment”, 1.5.1.4 “Psychological, psychosomatic and psychosocial care”, 1.5.1.3 “Coronary angiography”, as well as 1.6 “Rehabilitation”.

No recommendations were available in the CPGs included for items 1.1 “Definition of coronary heart disease” and 1.3 “Therapy goals”. No recommendations were extracted for item 1.7 “Cooperation of health care levels,” as no recommendations exist in the included German CPG. In respect of these health care aspects no statements can therefore be made on any deviations of the recommendations of the included evidence-based CPGs from the requirements of Appendix 5 of the RAS-AA.

Conclusion

By comparing extracted recommendations from current evidence-based CPGs with the requirements of Appendix 5 of the RAS-AA, which forms the basis of the DMP-CHD, health care aspects can be identified for which a potential need for updating or supplementation can be discussed.

There could be a potential need for supplementation both for general measures and drug therapy, as well as for invasive interventions. The items “Nutritional advice”, “Physical activity”, “Counselling on smoking cessation” could be specified, the comorbidities arterial hypertension and diabetes mellitus could be given greater consideration, and the recommendation on influenza vaccination could be included. Regarding drug therapy for CHD, specifications and further aspects can be found in the evidence-based CPGs compared to the requirements of Appendix 5 of the RAS-AA. By and large these refer to the following drug classes: nitrates, ACE inhibitors, aldosterone antagonists, and blood clotting inhibitors (platelet aggregation inhibitors and oral anticoagulants) in consideration of the approval status. In one CPG, for the medical indication to initiate interventional therapy, a lower grade

of stenosis is stated under certain preconditions (> 50% vs. > 70% in Appendix 5 of the RAS-AA).

In the area “Training programmes for insured members” the requirements could be supplemented in respect of making patients more aware of life-threatening emergency situations.

On the basis of the evidence-based included CPGs, no statements on the need for updating and supplementation of the DMP-CHD can be made for the items “Definition of coronary heart disease”, “Therapy goals” and “Cooperation of health care levels”.

It is unclear whether the lack of consideration of unpublished data in the CPGs included results in bias of the external evidence underlying the recommendations. If this were the case, the direction and extent of bias would be not assessable on the basis of the available information.

Keywords: coronary heart disease, disease management programme, methodological appraisal of clinical practice guidelines, evidence-based clinical practice guidelines.

The full German-language report and related documents are available under www.iqwig.de