IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Systematic guideline search and appraisal, as well as extraction of relevant recommendations, for the DMP "Asthma"[1]

Executive Summary

[1] Translation of the executive summary of the final report *Systematische Leitlinienrecherche und -bewertung sowie Extraktion relevanter Empfehlungen für das DMP Asthma bronchiale* (Version 1.0; Status: 26 November 2013). 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 §139 b (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 potential conflicts of interest provided by the external experts is presented in Appendix H 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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Executive summary

In its letter of 15 March 2012, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to undertake a systematic literature search for and appraisal of guidelines and extract new and relevant recommendations for the DMP "Asthma".

Research question

The aim of this study was to specify a potential need for updating and supplementation of the existing DMP "Asthma" by means of a systematic search for new evidence-based guidelines relevant to the subject and by synthesis of the guideline recommendations.

The study was organized as follows:

- literature search for and selection of current guidelines on the subject of asthma
- appraisal of the methodological quality of the selected guidelines
- extraction and synthesis of guideline recommendations relevant to the existing DMP "Asthma"
- identification of recommendations that might justify the potential need to revise and supplement the DMP "Asthma"

It was not the aim of the study to provide recommendations in terms of an IQWiG benefit assessment.

Methods

A systematic Internet search for topic-specific guidelines was conducted via the guideline databases of the 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. The search covered the period from November 2007 to August 2013.

The methodology of the guidelines included was assessed using the Appraisal of Guidelines for Research & Evaluation (AGREE) II instrument. The AGREE II instrument is used to assess the methodological quality of a guideline and contains 23 appraisal criteria. Six domains are allocated to these criteria, each of which describes a separate dimension of methodological guideline quality. Each criterion within the individual domains was assessed on a 7-point scale. The scale indicates to what extent a criterion is fulfilled in the guideline to be appraised. The results of the AGREE II appraisal are not a criterion for the inclusion or exclusion of guidelines in the study. By means of the AGREE II instrument it was to be presented transparently whether and in which domains of the instrument the evidence-based guidelines included showed particular methodological strengths or weaknesses.

The recommendations relevant to the research question were extracted and allocated to the health care aspects of the G-BA's directive on the regulation for the design of structured treatment programmes according to §137f (2) Social Code Book (SGB) V of 16 February 2012 (DMP directive). Finally, a synthesis of the extracted recommendations according to the health care aspects of the DMP directive was carried out and compared with the requirements of the DMP "Asthma".

In order to achieve comparability of the largely different systems of the GoR and LoE, for this report the GoR and/or LoE used in the guidelines were in each case allocated to a reference standard. The GoR used in the guidelines were allocated to 1 of 3 recommendation categories according to the National Care Guideline (Nationale VersorgungsLeitlinie; NVL). The LoE used in the guidelines were transferred to the evidence classification used in the G-BA's Rules of Procedure.

A potential need for updating and supplementation of the DMP was determined for recommendations that were consistent in content and largely showed a high GoR (strength of recommendation "A" according to the NVL classification). In the case of recommendations that were consistent with regard to content across different guidelines and at least sometimes assigned a high GoR/LoE (inconsistent GoR/LoE category), a potential need for updating and supplementation of the DMP could be raised for discussion. This was also the case if new aspects for the DMP were only presented by a single guideline but were provided with a high GoR. If a guideline did not provide a GoR, alternatively to the highest GoR, a high LoE (Ia/Ib according to the G-BA's evidence classification) was used to determine a need for updating and supplementation. Recommendations that featured neither a GoR nor LoE were not used for identifying a potential need for updating and supplementation.

In the event of a potential need for updating and supplementation with regard to a health care aspect, it was consistently assessed whether other IQWiG reports on this topic were available. When determining a potential need for updating and supplementation, the corresponding IQWiG reports were taken into account.

In addition, recommendations on drugs were examined with regard to their indication-specific reimbursability in Germany as well as their approval status. This was performed in those areas where a potential need for updating and supplementation exists or put up for discussion. In the case of discrepancies between guideline recommendations on drugs and the German approval status as well as their indication-specific reimbursability, this was presented conclusively and considered in the synthesis.

Results

A total of 12 guidelines were included, appraised and their recommendations extracted. The guidelines were issued by institutions from Germany (n = 1), Europe (n = 2), the United States (n = 6) and Canada (n = 2). One guideline was prepared by an international group of authors and published by a European medical society.

Six of the guidelines included deal with the comprehensive care of patients with asthma and address nearly all of the health care aspects included in the DMP directive. The other 6 guidelines deal with specific health care modalities (inpatient care of asthma attacks), address occupational asthma as a specific variant of asthma, or are targeted towards certain professional groups (nursing).

In the methodological appraisal with the AGREE II instrument, which was performed by 2 independent reviewers, on average the highest standardized domain values were primarily awarded in Domain 4 (Clarity of Presentation). On average the lowest standardized domain values were primarily awarded in Domain 5 (Applicability). The highest standardized domain value was only awarded in Domain 4 (Clarity of Presentation). The lowest standardized domain value was awarded in Domains 1 (Scope and Purpose), 5 (Applicability), and 6 (Editorial Independence).

No information on the handling of unpublished data was provided in the 12 guidelines included, neither in the guideline itself nor in a guideline report or methods report on the guideline, if available.

Potential need for updating and supplementation

The DMP directive contains requirements for the health care of adults, as well as children and adolescents from 5 up to 17 years inclusively. Recommendations in the 12 guidelines included were found for nearly all aspects named in the DMP directive concerning the health care of asthma patients. With regard to content they are largely consistent with the statements of the DMP directive; only few discrepancies were found. However, most extracted recommendations are more detailed compared with the text of the DMP directive. In addition, some guidelines address topics not considered in the current DMP directive.

The results of the comparison are presented in the following text, organized by health care aspects.

Health care aspect "Definition of Asthma" (1.1 of the DMP directive)

Several guidelines contain definitions of asthma. As the information on the definition of asthma are not recommendations, no statements on GoR/LoE are available. The definitions are largely consistent with the DMP directive. Due to the missing information on GoR/LoE; no statement regarding the potential need for updating or supplementation can be made.

Health care aspect "Diagnostics" (1.2 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on diagnostics. However, in comparison with the DMP directive the guidelines contain additional recommendations on the conduct of diagnostic procedures, specific examinations in particular patient groups and consultations of specialists. Due to the largely moderate/low GoR/LoE categories, there is no need for updating or supplementation.

Health care aspect "Medical history, symptoms, and physical examination" (1.2.1 of the DMP directive)

Several guidelines provide recommendations on medical history, symptoms, and physical examination (largely without information on, or with a non-allocatable, GoR/LoE, and otherwise with a largely moderate/low GoR category). The recommendations are largely consistent with the DMP directive, but are more detailed in their description of the physical examination and explanation of what a detailed medical history should contain. There is no need for updating or supplementation.

Health care aspect "Step-by-step diagnostics of analytical lung function" (1.2.2 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on the use of step-by-step diagnostics of analytical lung function within the framework of diagnosis determination. The recommendations are largely consistent with the DMP directive, but are more differentiated in their information on the performance of this diagnostic procedure. There is no need for updating or supplementation.

Health care aspect "Allergological step-by-step diagnostics" (1.2.3 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on allergological step-by-step diagnostics. The recommendations are largely consistent with the DMP directive, but are more differentiated with regard to determining the indication. There is no need for updating or supplementation.

Health care aspect "Asthma control"

General statements

Several guidelines provide recommendations, with a largely low GoR/LoE category, on asthma control and the classification of degree of severity. In comparison with the DMP directive the guidelines contain new recommendations on the indication of asthma control as a measure to examine response to therapy. Due to the largely low GoR/LoE categories, there is no need for updating or supplementation.

Treatment algorithms on asthma control

One guideline provides recommendations, with a high GoR category, on the treatment of asthma attacks in the preclinical and inpatient setting in the form of treatment algorithms. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Monitoring / Follow-up

Several guidelines provide recommendations on the monitoring and follow-up of patients with asthma:

One guideline provides a recommendation, with a high GoR/LoE category, on regular examination by specially trained physicians or nurses within the framework of general practitioner (GP) care. In comparison with the DMP directive the guideline contains additional recommendations. A potential need for updating or supplementation can be discussed.

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on the frequency of and indication for control visits to the GP or specialist. In comparison with the DMP directive the guidelines contain additional recommendations. Due to the largely moderate/low GoR/LoE category, there is no need for updating or supplementation.

Health care aspect "Diagnostics of occupational asthma"

General statements

One guideline provides a recommendation, with a high GoR category, on the involvement of the statutory accident insurance or an occupational physician to clarify the cause if occupational asthma is suspected. In comparison with the DMP directive the guideline contains additional recommendations. A potential need for updating or supplementation can be discussed.

Several guidelines provide recommendations, with a largely moderate/low GoR category, on the diagnostics of occupational asthma. In comparison with the DMP directive the guidelines contain additional recommendations. Due to the largely moderate/low GoR category, there is no need for updating or supplementation.

History-taking at the workplace

Several guidelines provide recommendations on the history-taking for occupational asthma:

Three guidelines provide recommendations, with a high GoR category, on history-taking at the workplace if occupational asthma is suspected. In comparison with the DMP directive the guidelines contain additional recommendations. There is a potential need for updating or supplementation.

Step-by-step diagnostics of analytical lung function

Two guidelines provide recommendations, with a low GoR category, on the step-by-step diagnostics of analytical lung function in occupational asthma. In comparison with the DMP directive the guidelines contain additional recommendations. Due to the low GoR categories, there is no need for updating or supplementation.

One guideline provides recommendations, with a high GoR category, on extended step-by-step diagnostics of analytical lung function for diagnosis of occupational asthma. In comparison with the DMP directive the guideline contains additional recommendations on

allergy testing, provocation testing, and the involvement of specialists. A potential need for updating or supplementation can be discussed.

Health care aspect "Diagnostics of an asthma attack"

Several guidelines provide recommendations, largely without information on GoR/LoE and otherwise with a largely moderate/low GoR category, on the diagnostics of an asthma attack. In comparison with the DMP directive the guidelines contain additional recommendations. Due to the largely missing information on GoR/LoE and otherwise largely moderate/low GoR category, there is no need for updating or supplementation.

Health care aspect "Treatment goals" (1.3 of the DMP directive)

Two guidelines provide recommendations on treatment goals. Largely the guidelines provide no information on GoR/LoE, except for a recommendation of one guideline.

The guideline recommends, with a high GoR category, maintenance of disease control with the lowest possible number of anti-asthmatic drugs in the lowest possible dose. The recommendation is largely consistent with the DMP directive, but is more differentiated. There is no need for updating or supplementation.

Health care aspect "Differentiated planning of therapy" (1.4 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR category, on differentiated planning of therapy. The recommendations are largely consistent with the DMP directive, but compared with the directive contain additional recommendations on the treatment of comorbidities and specific needs of subgroups. Due to the largely moderate/low GoR category, there is no need for updating or supplementation.

Health care aspect "Therapeutic measures" (1.5 of the DMP directive)

Health care aspect "Non-pharmaceutical therapy and general measures" (1.5.1 of the DMP directive)

General statements

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on general measures of non-pharmaceutical therapy. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Smoking cessation

Several guidelines provide recommendations, with largely moderate/low GoR/LoE categories, on avoidance of active and passive smoking. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Several guidelines provide recommendations, with inconsistent GoR/LoE categories, on smoking cessation programmes. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

One guideline provides a recommendation, with a high GoR category, on smoking cessation. In comparison with the DMP directive this is an additional recommendation on the combination of non-pharmaceutical and pharmaceutical therapies. A potential need for updating and supplementation can be discussed.

Avoidance of allergens / other inhaled noxious substances

Several guidelines provide recommendations, with a largely moderate/low GoR category, on avoidance of allergens and noxious substances. The recommendations are consistent with the DMP directive, but are more detailed in the listing of allergens and inhaled noxious substances. There is no need for updating or supplementation

Weight reduction / diet

Several guidelines provide recommendations, with a largely moderate/low GoR category, on weight reduction, but contain additional recommendations compared with the DMP directive. Due to the largely moderate/low GoR category, there is no need for updating or supplementation.

Breathing therapy

One guideline provides recommendations, with a low GoR category, on the use of breathing therapy within the framework of non-pharmaceutical asthma treatment. In comparison with the DMP directive the guideline contains additional recommendations. Due to the low GoR category, there is no need for updating and supplementation.

Complementary medical measures

Several guidelines provide recommendations, with a largely moderate/low GoR category, on the use of complementary medical measures. In comparison with the DMP directive the guidelines contain additional recommendations. Due to the largely moderate/low GoR category, there is no need for updating and supplementation.

One guideline provides a recommendation, with a high LoE category, on the use of the Buteyko therapy. In comparison with the DMP directive this is an additional recommendation. A potential need for updating and supplementation can be discussed.

One guideline provides a negative recommendation, with a high LoE category, on the use of ionizers. In comparison with the DMP directive this is an additional recommendation. A potential need for updating and supplementation can be discussed

Non-pharmaceutical measures in occupational asthma

Several guidelines provide recommendations, with a largely moderate/low GoR category, on the use of non-pharmaceutical measures, such as protective measures at the workplace and vocational guidance for persons with occupational asthma. In comparison with the DMP directive the guidelines contain additional recommendations. There is a potential need for updating and supplementation.

Non-pharmaceutical measures in an asthma attack

Several guidelines provide recommendations, with a largely moderate/low GoR category, on different non-pharmaceutical treatments of an asthma attack: treatment on the basis of guidelines, treatment by trained staff, avoidance of allergens, and contradictory statements on heliox therapy. In comparison with the DMP directive the guidelines contain additional recommendations. Due to the largely moderate/low GoR category, there is no need for updating and supplementation.

One guideline provides a recommendation, with a moderate GoR category, on the application of oxygen in hypoxaemic patients. In comparison with the DMP directive the guideline contains additional recommendations. Due to the moderate GoR category, there is no need for updating and supplementation.

One guideline provides recommendations, with a high GoR category, on discharge management and further treatment as an outpatient after an asthma attack. In comparison with the DMP directive the guideline contains additional recommendations. A potential need for updating and supplementation can be discussed.

Ventilation in an asthma attack

Several guidelines provide recommendations, with a largely moderate/low GoR category, on ventilation in an asthma attack. In comparison with the DMP directive the guidelines contain additional recommendations. Due to the largely moderate/low GoR category, there is no need for updating and supplementation.

Health care aspect "Structured training and treatment programmes" (1.5.2 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on the contents, goals and conduct of training programmes. The recommendations are largely consistent with the DMP directive, but provide more differentiated information. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR/LoE category, on determining the indication for training, depending on asthma control and on the necessity of a written treatment plan. In comparison with the DMP directive they contain additional recommendations. There is a potential need for updating or supplementation.

Health care aspect "Physical activity" (1.5.3 of the DMP directive)

Two guidelines provide recommendations, with inconsistent GoR/LoE categories, on physical activity. The recommendations are largely consistent with the DMP directive, but are more differentiated with regard to specific support for the patients. There is no need for updating or supplementation.

One guideline provides recommendations, with inconsistent GoR/LoE categories, on the use of drugs in exercise-induced asthma. In comparison with the DMP directive the guideline contains additional recommendations. A potential need for updating or supplementation can be discussed.

Two guidelines provide recommendations, with an inconsistent GoR category, on non-pharmaceutical measures (prolonged warming-up phase) in exercise-induced asthma. In comparison with the DMP directive the guidelines contain additional recommendations. A potential need for updating or supplementation can be discussed.

Health care aspect "Rehabilitation" (1.5.4 of the DMP directive)

One guideline provides recommendations, without information on GoR/LoE, on rehabilitation. The recommendations are largely consistent with the DMP directive, but compared with the directive contain additional recommendations on the linking of outpatient and inpatient rehabilitation measures. Due to the missing information on GoR/LoE, no statement can be made on the potential need for updating or supplementation.

Health care aspect "Mental, psychosomatic and psychosocial care" (1.5.5 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR category, on mental, psychosomatic, and psychosocial care. The recommendations are largely consistent with the DMP directive, but are more detailed in the presentation of reasons for care. There is no need for updating or supplementation.

One guideline provides recommendations, with a high GoR category, on the necessity of a low-threshold care programme. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Health care aspect "Pharmaceutical measures" (1.5.6 of the DMP directive)

General statements

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on general pharmaceutical therapy. The recommendations are largely consistent with the DMP directive, but are more differentiated in their information on the treatment goals to be achieved by pharmaceutical treatment. There is no need for updating or supplementation.

Two guidelines provide recommendations, with inconsistent GoR categories, on general pharmaceutical therapy, especially in occupational asthma. In comparison with the DMP directive the guidelines contain additional recommendations. A potential need for updating or supplementation can be discussed.

Asthma control and therapy steps

Several guidelines provide recommendations on asthma control and therapy according to a step-by-step scheme.

One guideline provides recommendations, with a high GoR category, on the treatment goal and the maintenance of disease control with the lowest possible number and dose of anti-asthmatic drugs. In comparison with the DMP directive the guideline contains additional recommendations. A potential need for updating or supplementation can be discussed.

One guideline provides recommendations, with a high GoR category, on intensifying therapy on the basis of a step-by-step scheme in the event of a lack of treatment success. In comparison with the DMP directive the guideline contains additional recommendations. A potential need for updating or supplementation can be discussed.

One guideline provides recommendations, with a high GoR category, on the case that, if therapy has been intensified, then asthma control must be examined again after 4 weeks at the latest. In comparison with the DMP directive the guideline contains additional recommendations. A potential need for updating or supplementation can be discussed.

Inhalation systems and techniques

Several guidelines provide recommendations, with a largely moderate/low GoR category, on inhalation systems. The recommendations are largely consistent with the DMP directive, but provide more detailed information on training, time of training, and different inhalation systems. There is no need for updating or supplementation.

Health care aspect "Maintenance therapy in adults" (1.5.6.1 of the DMP directive)

Basic therapy with inhaled glucocorticosteroids

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on basic therapy with inhaled (gluco)corticosteroids (ICS). The recommendations are largely consistent with the DMP directive, but are markedly more detailed and differentiated. There is no need for updating or supplementation.

Extended basic therapy with long-acting beta-2-sympathomimetic drugs

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on extended basic therapy with long-acting beta-2-sympathomimetic drugs. The recommendations are largely consistent with the DMP directive, but are markedly more detailed regarding therapy modalities. There is no need for updating or supplementation.

Extended basic therapy with systemic (oral) glucocorticosteroids

Several guidelines provide recommendations, with inconsistent GoR/LoE categories, on extended basic therapy with systemic glucocorticosteroids. The recommendations are largely consistent with the DMP directive, but are markedly more detailed and differentiated. There is no need for updating or supplementation.

Extended basic therapy with leukotriene receptor antagonists

Several guidelines provide recommendations, with inconsistent GoR/LoE categories, on extended basic therapy with leukotriene receptor antagonists (LTRAs). The recommendations are largely consistent with the DMP directive, but are markedly more detailed and differentiated. There is no need for updating or supplementation.

Extended basic therapy with theophylline

Two guidelines provide recommendations, with a largely low GoR/LoE category, on extended basic therapy with theophylline. The recommendations are largely consistent with the DMP directive, but are markedly more detailed and differentiated. There is no need for updating or supplementation.

Extended basic therapy with anti-IgE antibodies

Three guidelines provide recommendations, with a largely low GoR category, on extended basic therapy with anti-IgE antibodies. The recommendations are largely consistent with the DMP directive, but are markedly more detailed and differentiated. There is no need for updating or supplementation.

Further drugs

Two guidelines provide recommendations on extended basic therapy with cromoglicic acid or immunosuppressants. In comparison with the DMP directive the guidelines contain additional recommendations.

- One guideline provides recommendations, with a high GoR category, on treatment with cromoglicic acid. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.
- One guideline provides recommendations, with a low GoR category, on immunosuppressants if all other therapy options fail. In comparison with the DMP directive this is an additional recommendation. Due to the low GoR category, there is no need for updating or supplementation.

Health care aspect "Maintenance therapy in 5 to 17-year-olds" (1.5.6.2 of the DMP directive)

Basic therapy with inhaled glucocorticosteroids

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on basic therapy with ICS in children and adolescents aged 5 to 17 years inclusively. The recommendations are largely consistent with the DMP directive, but are markedly more detailed regarding ICS dosage. There is no need for updating or supplementation.

Basic therapy with leukotriene receptor antagonists

Several guidelines provide recommendations, with a largely high GoR/LoE category, on basic therapy with LTRAs in children and adolescents aged 5 to 17 years inclusively. The recommendations are largely consistent with the DMP directive, but are markedly more differentiated. There is no need for updating or supplementation.

Extended basic therapy with long-acting beta-2-sympathomimetic drugs

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on extended basic therapy with long-acting bronchodilators in children and adolescents aged 5 to 17 years inclusively. The recommendations are largely consistent with the DMP directive, but are markedly more differentiated. There is no need for updating or supplementation.

Extended basic therapy with systemic (oral) glucocorticosteroids

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on extended basic therapy with systemic glucocorticosteroids in children and adolescents aged 5 to 17 years inclusively. The recommendations are largely consistent with the DMP directive, but are markedly more differentiated. There is no need for updating or supplementation.

Theophylline

Two guidelines provide recommendations, with a largely low GoR/LoE category, on extended basic therapy with theophylline. The recommendations are largely consistent with the DMP directive, but are more differentiated. There is no need for updating or supplementation.

Anti-IgE antibodies

Three guidelines provide recommendations, with a largely low GoR category, on therapy with anti-IgE antibodies. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Further drugs

One guideline provides recommendations, with a low GoR category, on treatment with immunosuppressants (such as methotrexate, cyclosporine, and auranofin) for children and adults. In comparison with the DMP directive these are additional recommendations. Due to the low GoR category, there is no need for updating or supplementation.

One guideline recommends, with a high GoR category, treatment with cromoglicic acid in patients with mild persistent asthma. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Health care aspect "Rescue therapy" (1.5.6.3 of the DMP directive)

General statements

Several guidelines provide recommendations, with a largely moderate/low GoR category, on rescue therapy. In comparison with the DMP directive the guidelines contain additional recommendations on determining the severity of the attack. Due to the largely moderate/low GoR categories, there is no need for updating or supplementation.

Short-acting beta-2-sympathomimetic drugs

Several guidelines provide recommendations, with a largely moderate/low GoR category, on rescue therapy with short-acting beta-2-sympathomimetic drugs. In comparison with the DMP directive the guidelines contain additional recommendations on type of administration, dosage, and combination options with other drugs. Due to the largely moderate/low GoR category, there is no need for updating or supplementation.

Systemic (oral) glucocorticosteroids

Several guidelines provide recommendations, with a largely moderate/low GoR category, on rescue therapy with oral glucocorticosteroids. The recommendations are largely consistent with the DMP, but are markedly more differentiated. There is no need for updating or supplementation.

Short-acting anticholinergic drugs

Three guidelines provide recommendations, with a largely moderate/low GoR category, on rescue therapy with short-acting anticholinergic drugs. The recommendations are largely consistent with the DMP, but the information provided is markedly more differentiated. There is no need for updating or supplementation.

Theophylline

One guideline provides a recommendation, with a low GoR category, on determining the indication for intravenous administration of aminophylline by experienced physicians. In comparison with the DMP directive this is an additional recommendation. Due to the low GoR category, there is no need for updating or supplementation.

Three guidelines provide recommendations, with inconsistent GoR categories, on rescue therapy with theophylline. The recommendations are largely consistent with the DMP, but are more detailed. There is no need for updating or supplementation.

Further drugs

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on rescue therapy. In comparison with the DMP directive the guidelines contain additional recommendations on intravenous administration of magnesium sulphate, ketamine, epinephrine, and terbutaline, as well as negative recommendations on single drug classes such

as antibiotics, mucolytics, anxiolytics, and hypnotics. Due to the largely moderate/low GoR/LoE category, there is no need for updating or supplementation.

Rescue therapy in exercise-induced asthma

Three guidelines provide recommendations, with a high GoR category, on the use of short-acting beta-agonists (SABAs) as rescue therapy in exercise-induced asthma. The recommendation is largely consistent with the DMP directive. There is no need for updating or supplementation.

Three guidelines provide recommendations, with a largely moderate/low GoR category, on the use of LTRAs as rescue therapy in exercise-induced asthma. The recommendations are largely consistent with the directive. There is no need for updating or supplementation.

Two guidelines provide recommendations, with a largely moderate/low GoR category, on the use of chromones as rescue therapy in exercise-induced asthma. The recommendations are largely consistent with the directive. There is no need for updating or supplementation.

One guideline provides recommendations, with a high GoR category, on the use of long-acting beta-agonists (LABAs) as rescue therapy in exercise-induced asthma. The recommendations are largely consistent with the directive. There is no need for updating or supplementation.

One guideline provides recommendations, with a high GoR category, on the use of oral beta-2-sympathomimetic drugs as rescue therapy in exercise-induced asthma. The recommendations are largely consistent with the directive. There is no need for updating or supplementation.

One guideline provides recommendations, with a moderate GoR category, on the use of theophylline as rescue therapy in exercise-induced asthma. The recommendations are largely consistent with the directive. There is no need for updating or supplementation.

Follow-up treatment of asthma attacks

Two guidelines provide recommendations, with a largely moderate/low GoR category, on the pharmaceutical follow-up treatment of asthma attacks. In comparison with the DMP directive the guidelines contain additional recommendations. Due to the largely moderate/low GoR category, there is no need for updating or supplementation.

Health care aspect "Specific immunotherapy / hyposensitization" (1.5.6.4 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR category, on immunotherapy. The recommendations are largely consistent with the DMP directive, but are more differentiated with regard to indication and conduct of therapy. There is no need for updating or supplementation.

Two guidelines provide a negative recommendation, with inconsistent GoR categories, on the routine conduct of sublingual immunotherapy. In comparison with the DMP directive the guidelines contain additional recommendations. A potential need for updating or supplementation can be discussed.

Health care aspect "Asthma in pregnancy" (1.5.6.5 of the DMP directive)

General statements

Several guidelines provide general recommendations, with a largely moderate/low GoR category, on topics surrounding pregnancy. However, in comparison with the DMP directive the guidelines contain additional recommendations on counselling, asthma control, potential hospital stays, cooperations, and on birth itself. Due to the largely moderate/low GoR category, there is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR category, on non-pharmaceutical smoking cessation and endangerment through passive smoking. In comparison with the DMP directive the guidelines contain additional recommendations. There is a potential need for updating or supplementation.

Pharmacotherapy in pregnancy

Several guidelines provide recommendations, with a largely moderate/low GoR category, on pharmacotherapy in pregnancy. The recommendations are largely consistent with the DMP directive, but are more differentiated in their recommendations on drugs and treatment options. There is no need for updating or supplementation.

Health care aspect "Vaccinations" (1.5.6.6 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR category, on influenza and/or pneumococcal vaccination. The recommendations are largely consistent with the DMP directive, but are more detailed regarding the type of vaccine and specific recommendations for children. There is no need for updating or supplementation.

Health care aspect "Cooperation of health care sectors" (1.6 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on the cooperation of health care sectors. The recommendations are largely consistent with the DMP directive, but are more detailed in their descriptions of constellations of cooperation. There is no need for updating or supplementation.

Health care aspect "Coordinating physician" (1.6.1 of the DMP directive)

One guideline provides a recommendation, with a largely moderate GoR category, on the coordination of long-term care and documentation. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Health care aspect "Referral by coordinating physician to the respective qualified specialist or qualified institution" (1.6.2 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate/low GoR category, on referral to specialists or specialist clinics. The recommendations are largely consistent with the DMP directive, but are more detailed regarding indications. There is no need for updating or supplementation.

Health care aspect "Admission to a hospital" (1.6.3 of the DMP directive)

Hospital admission

Several guidelines provide recommendations, with a largely moderate/low GoR category, on admission to a hospital. The recommendations are largely consistent with the DMP directive, but are more detailed in their descriptions of the indications for admission. There is no need for updating or supplementation.

Discharge management

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on discharge from hospital. As this topic has so far not been addressed in the DMP directive, these are additional recommendations. Due to the largely moderate/low GoR/LoE, there is no need for updating or supplementation.

Health care aspect "Initiation of a rehabilitation service" (1.6.4 of the DMP directive)

One guideline provides recommendations, with inconsistent GoR categories, on initiation of a rehabilitation measure. The recommendations are largely consistent with the DMP directive, but are more detailed in their description of criteria for determining the indication. There is no need for updating or supplementation.

Results for children under 5 years

Recommendations explicitly and exclusively referring to children under 5 years are documented in the following text.

Five of the guidelines included (NVL 2013, SIGN 2012, CTS 2012, GINA 2012 and VA/DoD 2009) contain recommendations specifically targeted towards children under 5 years. Recommendations could not be allocated to all health care aspects.

The synthesis of guideline recommendations and the comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively, is presented in the following text, organized according to health care aspects.

Health care aspect "Diagnostics in children under 5 years"

The guidelines describe that the differential diagnosis of asthma, as well as an asthma attack, can be difficult in this age group and recommend, if necessary, the involvement of specialists in determining the diagnosis.

Comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively

Several guidelines provide recommendations, with a largely low GoR category, on diagnostics in children under 5 years. The statements on children under 5 years in the guidelines differ from the requirements of the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively. The guidelines explicitly refer to the difficulties of determining a diagnosis in children of this age group. In addition, in contrast to the DMP directive the guidelines recommend considering differential diagnoses.

Two IQWiG reports (V06-02A [1] and V06-02C [2]) are available for the diagnostics of asthma in children under 5 years.

IQWiG report V06-02A, published in the year 2008, had the aim of presenting measures recommended to confirm the diagnosis in suspected asthma in children aged between 2 to 5 years. The result of this investigation was that, at the time of the publication of the report, no established and recognized gold standard existed for the diagnosis of asthma in young children. Likewise, no reference standard for the diagnosis of asthma in young children could be inferred from the guidelines that were searched for within the framework of report V06-02A [1].

The second IQWiG report V06-02C from the year 2009 dealt with the scientific assessment of the diagnostic accuracy, as well as the benefit of the procedures established in health care in Germany for diagnosing asthma in children from 2 up to 5 years. The authors of the report conclude that the evidence base for assessing national established examination methods for determining a diagnosis of asthma in children from 2 up to 5 years is very small and that therefore no evidence-based robust recommendation is inferable for a valid single diagnostic instrument or a single diagnostic method. The report also notes that, particularly against the background of a potential diagnostic criterion for registration in a DMP based on the data situation presented, no examination method can be recommended as sufficiently reliable.

Health care aspect "Medical history, symptoms, and physical examination"

Within the framework of medical history-taking and with regard to the differential diagnosis of reflux disease, one guideline recommends questioning parents whether irritations occurred when feeding, whether the child vomited when lying on its back, or whether it had back problems.

Comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively

One guideline provides a recommendation, with a moderate GoR category, on medical history, symptoms, and physical examination in children under 5 years. The statement on children under 5 years in the guideline differs from the requirements of the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively. The guideline specifically refers to questioning parents here in order to consider the differential diagnosis of

gastroesophageal reflux disease. Differential diagnostic measures are not mentioned in the DMP directive.

Health care aspect "Step-by-step diagnostics of analytical lung function"

In this age group, according to the guidelines, the correct performance of a lung function measurement is extremely difficult.

Comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively

Two guidelines provide recommendations, with inconsistent GoR categories, on step-by-step diagnostics of analytical lung function. The recommendations of the 2 guidelines on lung function measurement in children under 5 years differ from the requirements of the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively. In general the DMP directive is far more detailed regarding this issue than the guideline recommendations on children under 5 years. However, for children under 5 years, in contrast to the DMP directive, the guidelines refer to difficulties of lung function measurement in this age group.

Health aspect "Structured training and treatment programmes"

One guideline notes that inhalers should only be prescribed in patients have been trained how to handle them.

Comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively

One guideline provides a recommendation, with a low GoR category, on structured training and treatment programmes. The guideline's statement on children under 5 years is more specific than the requirements of the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively. The DMP directive generally states that all patients should have access to a structured training and treatment programme, but – in contrast to the guidelines for children under 5 years – does not contain a specific statement on the issue that patients who use inhalers should receive training on how to handle them.

Health care aspect "Pharmaceutical measures"

Health care aspect "Maintenance therapy"

The guidelines recommend using ICS only if asthma control with beta-2-agonists is no longer possible. The decision on dose depends on the symptoms. At the start of therapy the ICS should be administered twice daily; after achieving good asthma control, administration can be reduced to once daily.

Temporarily limited treatment attempts with oral steroids in combination with LABAs, LTRAs and theophylline can be made. A routine use of oral steroids in the case of an asthma attack is not recommended.

If children under 5 years are not able to use ICS, according to the guidelines LTRAs are an effective alternative. LTRAs are also first choice as add-on therapy to ICS.

Comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively

Two guidelines provide recommendations, with a largely moderate/low GoR category, on maintenance therapy with glucocorticosteroids in children under 5 years. The statements on children under 5 years in the 2 guidelines partly differ from the requirements of the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively. On the one hand the guidelines for children under 5 years provide specific information on the dose of ICS medication; this is not provided in the DMP directive. On the other, as an alternative therapeutic option for children under 5 years the use of oral steroids in combination with LABAs, LTRAs or theophylline is recommended. In contrast to the DMP directive a further guideline provides an explicit negative recommendation on the routine use of oral corticosteroids in the case of an acute asthma attack with loss of control in preschool- and schoolchildren.

Two guidelines provide recommendations, with inconsistent GoR categories, on maintenance therapy with LTRAs in children under 5 years. The statements in both guidelines differ from the requirements of the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively. One guideline recommends LTRAs in children under 5 years as an alternative to ICS. In contrast, the DMP directive recommends LTRAs within the framework of maintenance therapy in children and adolescents aged 5 to 17 years inclusively only in justified cases. Furthermore, according to the recommendations of 2 guidelines, for children under 5 years LTRAs are the drugs of first choice as add-on therapy to ICS. The DMP directive recommends the combination of ICS and LTRAs as extended basic therapy.

The IQWiG report V06-02B published in the year 2009 is available for therapeutic interventions. The aim of this report was to determine the benefit and harm of therapeutic interventions in children aged 2 to under 5 years with symptoms of bronchial obstruction [3]. The choice of the pharmaceutical and non-pharmaceutical interventions investigated is based on the recommendations of the DMP "Asthma" effective at that time.

No study allowing any conclusions on the benefit and harm in children aged 3 to 5 years inclusively could be identified in IQWiG report V06-02B for 12 of the 14 non-pharmaceutical and pharmaceutical interventions established in the DMP "Asthma". The authors only report results on ICS.

For the LTRA montelukast the authors determine that no conclusions can be drawn on the benefit and harm of therapy according to the indication approved in Germany. In most cases, the interventions established for children of this age group in the DMP "Asthma" had been investigated inadequately.

In addition, report V06-02B could not definitely answer the question as to what extent children with bronchial obstruction who do not go on to develop asthma benefit from an early pharmaceutical intervention or suffer harm, as none of the studies was designed to verify the diagnosis "asthma" when the children reached the age of 6.

Health care aspect "Rescue therapy"

For asthma attacks the guidelines recommend the administration of drugs via a powder inhaler with a spacer.

Inhaled SABAs are the drugs of choice for rescue therapy. An increased consumption should prompt a control of the asthma therapy. The use of oral beta-2-agonists for the treatment of asthma attacks is not recommended.

If children under 5 years do not respond sufficiently to initial treatment with inhaled SABAs, a combination with ipratropium bromide is recommended.

According to the guidelines, children with severe asthma attacks should be cared for in a hospital and treated with prednisolone. Children under 2 years should receive 10 mg daily and children over 2 years should receive 20 mg daily.

Comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively

Two guidelines provide recommendations on rescue therapy in children under 5 years. Only the statements with regard to the recommendation on inhaled SABAs in symptomatic asthma are consistent with the requirements of the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively. The guideline recommendations for children under 5 years of age are in principle considerably more differentiated than the DMP directive. In contrast to the DMP directive they also contain recommendations on combination therapy of inhaled ipratropium bromide and inhaled beta-2-agonists for severe symptoms. The negative recommendation on oral beta-2-agonists for treatment of acute asthma in young children is not contained in the DMP directive.

Health care aspect "Inhaling technique"

The guidelines recommend the administration of drugs through a face mask until the child is able to use the mouth piece of the spacer. If these inhaling techniques are ineffective, a nebulizer can be used.

Inhaling systems should only be applied after training and successful demonstration.

Comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively

Two guidelines provide recommendations, with a largely low GoR category, on inhaling techniques for children under 5 years. This health care aspect is not contained in the DMP directive on adults, as well children and adolescents aged 5 to 17 years inclusively.

Health care aspect "Specific immunotherapy / hyposensitization"

According to a statement in one guideline, specific immunotherapy should not be undertaken in children under 5 years, except for cases where an allergy to insect poison exists.

Comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively

One guideline provides a recommendation, with a high GoR category, on specific immunotherapy in children under 5 years. Except in cases where an allergy to insect poison exists, the guideline does not recommend specific immunotherapy in children under 5 years. This is in contrast to the requirements of the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively. The DMP directive advises to check the indication to undertake a specific immunotherapy/hyposensitization in the case of allergic asthma if the symptoms cannot be sufficiently resolved by allergen avoidance and pharmacological therapy.

Health care aspect "Cooperation of health care sectors"

According to the statements in the guidelines, it can be necessary to involve specialists in determining the diagnosis and treating children under 5 years.

Comparison with the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively

Two guidelines provide recommendations, with inconsistent GoR categories, on cooperation of health care sectors in children under 5 years. The statements in the guidelines on children under 5 years do not differ from the requirements of the DMP directive on adults, as well as children and adolescents aged 5 to 17 years inclusively. The DMP directive also mentions the involvement of and referral to specialists.

Health care aspects for which the guidelines included contain no recommendations specifically for children under 5 years

- Description of the indication
- Allergological step-by- step diagnostics
- Treatment goals
- Differentiated planning of therapy
- Therapeutic measures
  - non-pharmaceutical therapy and general measures
  - physical activities
  - initiation of preventive and rehabilitation services
  - mental, psychosomatic and psychosocial care
- Pharmaceutical measures
  - maintenance of symptom control and monitoring
  - vaccinations in children under 5 years
- Admission to a hospital

Conclusion

The DMP directive exclusively refers to adults, as well as children and adolescents from 5 to 17 years inclusively. Children under 5 years are not part of the DMP "Asthma". By comparing the recommendations extracted from current evidence-based guidelines with the requirements of the DMP directive forming the basis of the DMP "Asthma", health care aspects could be identified for which a potential need for updating or supplementation exists or can be discussed.

There is a potential need for updating or supplementation for the following health care aspects:

- "Diagnostics of occupational asthma" regarding history-taking at the workplace if occupational asthma is suspected
- "Non-pharmaceutical therapy and general measures" for protective measures at the workplace and vocational advice in occupational asthma
- "Structured training and treatment programmes" to determine the indication for training depending on asthma control and for the necessity of a written treatment plan.
- "Asthma in pregnancy" regarding non-pharmaceutical smoking cessation and endangerment through passive smoking

A potential need for updating or supplementation can be discussed for the following health care aspects:

- "Asthma control" regarding the treatment of asthma attacks in the preclinical and inpatient setting in the form of treatment algorithms and regular examination by specially trained physicians or nurses within the framework of GP care.
- "Diagnostics of occupational asthma" regarding
  - the involvement of statutory accident insurance or the occupational physician to clarify the cause if occupational asthma is suspected, as well as
  - the extended step-by-step diagnostics of analytical lung function regarding allergy and provocation testing, as well as the involvement of specialists
- "Non-pharmaceutical therapy and general measures"
  - for the combination of non-pharmaceutical and pharmaceutical therapies for smoking cessation
  - for the use of Buteyko therapy
  - for the negative recommendation on the use on ionizers
  - for discharge management and further treatment as an outpatient after an asthma attack
- "Physical activity" regarding the use of pharmaceutical and non-pharmaceutical measures (extended warming-up phase) in exercise-induced asthma
- "Mental, psychosomatic and psychosocial care" for the necessity of a low-threshold care programme
- "Pharmaceutical measures"
  - for general pharmaceutical therapy, specifically for occupational asthma
  - for the treatment goal and for maintenance of disease control with the lowest possible number and dose of anti-asthmatic drugs
  - for intensifying therapy in the case of a lack of treatment success on the basis of a step-by-step scheme
  - for the renewed examination of asthma control 4 weeks at the latest after intensifying therapy
- "Maintenance therapy in adults" regarding extended basic therapy with cromoglicic acid
- "Maintenance therapy in 5 to 17-year-olds" regarding treatment with cromoglicic acid in mild persistent asthma
- "Specific immunotherapy/hyposensitization" regarding the negative recommendation for the routine conduct of sublingual immunotherapy

The following health care aspects in the guidelines included were identified for children under 5 years:

- "Diagnostics" regarding the difficulty of a differential diagnosis of asthma, as well as an asthma attack, in this age group
- "Medical history, symptoms and physical examination" regarding the questioning of parents on irritations during feeding, vomiting when lying on the back, or back complaints in view of the differential diagnosis "reflux disease"
- "Step-by-step diagnostics of analytical lung function" regarding the difficulty in the correct conduct of a lung function measurement
- "Structured training and treatment programmes" for training of patients in the handling of inhalers as a condition for their prescription
- "Pharmaceutical measures"
  - "Maintenance therapy" regarding specific information on dose for the ICS medication, combination therapy of oral steroids with LABAs, LTRAs or theophylline as an alternative therapeutic option, and for a negative recommendation on the routine use of oral corticosteroids in the case of an acute asthma attack with loss of control in preschool- and schoolchildren
  - "Rescue therapy" regarding the use of inhaled SABAs in symptomatic asthma with combination therapy of inhaled ipratropium bromide and inhaled beta-2-agonists in the case of severe symptoms, and a negative recommendation on oral beta-2-agonists for treatment of acute asthma in young children
  - "Inhaling technique" regarding the duration of the administration of the drug through a face mask and the indication for the use of a nebulizer
  - "Specific immunotherapy/hyposensitization" regarding the negative recommendation for a specific immunotherapy with the exception of the existence of an allergy to insect poison
- "Cooperation of the health care sectors" regarding the necessity of the involvement of specialists in determining the diagnosis and treating children under 5 years.

It is unclear whether the lack of consideration of unpublished data in the included guidelines results in bias in the external evidence underlying the recommendations. If this does lead to bias, the direction and extent of bias is not assessable on the basis of the information available.

Keywords: asthma, disease management programme, methodological guideline appraisal

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