

Treating Asthma and COPD – A Systematic Review

Summary and conclusions

Introduction

Somewhat over one million people in Sweden suffer from asthma or chronic obstructive pulmonary disease (COPD). These two diseases greatly reduce the quality of life, and together they account for approximately 2300 deaths annually in Sweden.

Asthma

Asthma is a chronic inflammatory disease of the bronchial airways that leads to periods of reduced airflow and respiratory distress. The disease, particularly allergic asthma, has increased in Sweden and other Western countries in recent decades. The increase is most notable among children and adolescents. Approximately 6% to 8% of all Swedish school children are estimated to have asthma. The disease is equally common among adults. Approximately 700 000 people in Sweden suffer from asthma. Hospital admissions due to asthma have, nevertheless, declined by two thirds since 1987. Somewhat over 250 people died from asthma in 1997.

The basic reasons why certain individuals develop asthma and why asthma is increasing remains unknown despite intensive research. There is a strong association between asthma and respiratory tract allergies, eg, to cats or dust mites. Common symptoms are sudden respiratory distress - particularly in cold air, during respiratory tract infections, and during stress - "wheezy chest", and nocturnal coughing. Most people are free of symptoms between the attacks, but are always at greater risk for a new attack when any of the triggering factors are present. Some people are affected by repeated severe asthma attacks that can be life threatening. With the help of new medications, many people with asthma can now live nearly normal lives, and hospital admissions and mortality due to asthma have become uncommon. Having a chronic disease such as asthma, however, still places a major burden on the family and the individual - both in school, at work, and during recreational time.

COPD (Chronic Obstructive Pulmonary Disease)

The dominant cause of COPD is tobacco smoking. Although asthma has been known for thousands of years, chronic obstructive pulmonary disease represents a new disease concept. Airway obstructions, ie, reduced airflow in the respiratory tract, is common to the obstructive respiratory diseases of asthma and COPD. In asthma, pulmonary function usually returns to normal between attacks. In COPD, however, the airway obstructions are chronic and lead to a progressive reduction in breathing ability. The concept of COPD includes long-term coughing with increased mucous production (chronic bronchitis) and destruction of the smallest airways and the pulmonary alveoli (emphysema).

The continual respiratory distress in advanced COPD creates anxiety, substantially reduces the quality of life, and often leads to social isolation for the patient. The association with smoking causes many to perceive the disease as self-induced and a social stigma. Acute deterioration that leads to emergency room visits and hospital admissions are common. In males with COPD, the number of hospital admissions has remained unchanged over the past decade, but has doubled for women.

Late stages of the disease are accompanied by reduced oxygenation and respiratory failure which often leads to death. Since the late 1980s, mortality has nearly doubled. The number of women who die due to COPD has increased and reached 800 in 1997. The same year, 1250 men died due to COPD.

The gradual increase in the disease in Sweden reflects smoking habits following the Second World War, when smoking became a serious problem among women. When the disease appears - often as chronic "smokers cough" and severe shortness of breath, usually after 30 to 50 years of smoking - patients with COPD have already lost half or more of their breathing capacity. Earlier it was thought that only a minority of smokers were affected by COPD, but recent Swedish studies show that in smokers who reach higher ages, nearly one half develop COPD. From 50 years of age and upward, approximately 8% of the population has COPD, corresponding to 400 000 Swedish people. Only about 40% of these are known by diagnosis. Despite the major suffering involved in COPD for those affected, and despite the rapidly increasing cost of hospitalization, primary care visits, and drugs, the disease has not received major attention.

Socioeconomic costs of asthma and COPD

In 1991, the direct healthcare costs for asthma and COPD in Sweden were nearly equal, each costing approximately 1.1 billion SEK per year. Added were the indirect costs, ie, production loss due to sick leave, early retirement, and premature death, at an annual cost of 1.9 billion SEK for asthma and 1.7 billion SEK for COPD. Thus, the total socioeconomic costs for asthma and COPD totaled approximately 6 billion SEK.

Currently (year 2000), the total socioeconomic costs for asthma and COPD are approximately 7 billion SEK. The costs for drugs and outpatient services have increased for both asthma and COPD since 1991 while the costs for inpatient short-term acute hospital care have declined for asthma but increased for COPD.

Aim

The aim of this study is to systematically and critically review the scientific base for the various types of treatment for asthma (both in children and adults) and COPD. Assessment of primary prevention is not included. The cost-effectiveness of treatment is addressed.

Methods

Selecting outcome measures

Opinions vary on how to best assess the effects of different treatments for asthma and COPD. Traditionally, various physiological pulmonary measurements of airflow or breathing capacity have dominated as outcome measures in treatment research in the field. The basis for this reasoning has been that if a treatment improves airflow in the lungs it must benefit the patient. It has taken many years to gain acceptance for the idea that the purpose of treatment is not limited to improving airflow. Patients do not suffer from the reduced airflow, but from its impact on daily life, eg, the breathing distress and anxiety that accompanies reduced pulmonary function or the periods of deterioration that require acute care. Impaired pulmonary function is, however, not unimportant for patients with asthma or COPD, but there is a weak association between pulmonary function and how patients experience their disease and its impact. The following four primary outcome measures, which are important for individuals with asthma or COPD, have been used in the report (not in rank order):

- Mortality from asthma or COPD
- Need for increased medication, emergency visits or hospital admission
- Health-related quality of life
- Symptoms

Literature search and review

This report is based on a systematic and critical analysis of results from studies that have been published in the international scientific literature. During the course of the project, the Cochrane Collaboration has also published several reviews in this field, some of which are included in the report. The literature search in MEDLINE and other databases includes studies published through June 1999, with inclusion of some later studies.

For inclusion in this review, the studies must be of high quality, ie, they should:

- Be randomized and controlled or be a quality-controlled, systematic review of such studies
- Report on at least one of the four primary outcome measures
- Use a treatment period of at least 3 months

Using the above criteria, many studies were excluded from the review. No documentation of high quality could be found in some therapeutic areas. In such cases, the review included studies which did not report on any of the primary outcome measures, used shorter treatment times, or had other deficiencies in study design. Such studies are of lower quality and provide a weak basis for conclusions. Studies of treatment for acute exacerbation have been included in the review, although only data for pulmonary function were included and followup times were short. As regards drug studies, only studies that included drugs approved in Sweden were reviewed. In the treatment studies for asthma, the gender distribution among patients is similar while the COPD studies are highly dominated by men. Gender-specific analyses of treatment results are almost completely lacking.

Synthesis and grading conclusions

Approximately 350 studies met the basic standards for scientific quality. These studies were reviewed, assessed, and considered as a basis for conclusions according to the following four-grade scale:

Grade 1 - Strong support (for conclusions)

Grade 2 - Moderate support

Grade 3 - Weak support

Grade 4 - Little support, including consensus among experts or no support.

Although the grading of conclusions cannot be interpreted as the absolute truth, Grade 1 conclusions should provide more concrete evidence than Grade 3 or Grade 4. It is important to note that a conclusion at Grade 4 does not necessarily mean that a particular treatment is ineffective. It only means that the scientific basis for assessment is insufficient. On the other hand, conclusions concerning the lack of effects may be ranked as grade 1, 2, or 3.

Results of the literature review

Preventive interventions

Since the reasons underlying why some people develop asthma are yet unknown, there is no effective primary prevention. Many attempts to stop the development of asthma by intervening on known or suspected risk factors, mainly allergies, have been carried out, but without convincing results. A review of primary prevention is, however, beyond the scope of the group's work.

The most important interventions in the primary prevention of COPD are to prevent the debut of smoking and to facilitate smoking cessation. Unfortunately, we do not have effective strategies for achieving these goals. An SBU report on smoking cessation in 1998 described the state of current knowledge. The report also emphasized the importance of brief counseling when smokers come into contact with the health and dental services, and that the use of nicotine replacement agents increases the percentage who successfully stop smoking.

Measures for preventing or reducing symptoms or deterioration of the disease (secondary prevention) in those who already have asthma or COPD have been assessed to a surprisingly small extent. For decades, individuals with allergic asthma have received advice to reduce their exposure to allergens, eg, those allergic to cats should not own cats. The effects of such advice are inadequately assessed. Only as regards anti-mite interventions is there documentation that this measure reduces the onset of asthma symptoms in mite-allergic individuals with asthma (Grade 3). The effectiveness of using air-cleaners for asthma has not been demonstrated (Grade 1). Middle-aged individuals with moderate or severe COPD who stop smoking live on average 7 years longer than those who continue to smoke (Grade 3). Smokers with COPD who successfully stop smoking substantially reduce coughing and mucous formation, while wheezing and respiratory distress decline to a lesser extent (Grade 1). Notably, there is a

lack of evidence to show whether smoking cessation leads to recovery from asthma or a reduction in asthma symptoms (Grade 4).

Physical exercise and patient education

Asthma and COPD are common chronic diseases. Hence, a range of educational and rehabilitation programs have been developed for patients with these disorders. Asthma schools and COPD schools have become commonplace, and physical exercise has taken a prominent place in treating COPD in Sweden. Most of the reviewed studies address both education and training as concurrent interventions, and hence they are presented together in the report. The report concluded that self-care programs for asthmatic adults may have favorable effects on symptoms and care needs (Grade 1), while general information alone has no proven effect in children and adults with asthma (Grade 1).

However, it is noteworthy that the evidence is insufficient for judging the effects of self-care programs for asthma in Swedish environments (Grade 4) even though asthma schools and similar programs are recommended by many local clinical guidelines. Rehabilitation that includes physical exercise offers good effects on the quality of life, respiratory distress, and functional work capacity in patients with moderate COPD (Grade 2). However, it is unclear whether patients with advanced COPD have equally great benefits from physical exercise (Grade 4). Structured activities at community health centers (so-called asthma clinics) for patients with asthma may have some favorable effects on symptoms, emergency visits, and sick leave, but the scientific evidence is deficient (Grade 4).

Alternative therapies

In addition to the publicly financed health services, many alternative methods for treating disease are used by professional practitioners and in self-care. The borderline between conventional medical therapy and alternative medicine or complementary methods is not clearly delineated. Consequently, acupuncture, for example, is used by some physicians and physical therapists. Given the background of increasing interest in Sweden for alternative medical therapies, the working group committed substantial effort toward reviewing the alternative methods used to treat asthma and COPD. We found very few studies that met our requirements, despite our own extensive search of the literature and the use of systematic reviews by the Cochrane Collaboration. The only area where it was possible to draw reliable conclusions concerned nutritional therapy. The first is that supplements of unsaturated fatty acids (fish oil) have no effects in treating asthma (Grade 1). The second is that energy supplements in the diet for patients with COPD can increase the sense of wellbeing and reduce the degree of respiratory distress (Grade 3).

Most of the studies reviewed have included short treatment times, small and incompletely described patient data, or other deficiencies in trial design. Hence, evidence upon which to base conclusions on treatment effects is deficient or completely lacking (Grade 4). This applies to the following treatments: climate management, psychological treatment including family therapy, hypnosis and behavioral therapy, acupuncture, homeopathy, chiropractic, yoga, reflexology, massage, qi gong, relaxation, and biofeedback.

Pharmacological treatment

Beta-2 stimulants and anticholinergics

Airway dilating agents have traditionally been used to treat acute asthma attacks. Ephedrine from the leaves of the ephedra plant and “asthma cigarettes” produced from the leaves of the thorn apple were even used in Sweden well into the 1900s. Adrenaline for acute treatment was introduced around 1900. The selective beta-2 stimulants, which we continue to use widely, were introduced in the 1960s and complemented in the 1990s by long-acting beta-2 stimulants. “Asthma cigarettes” were replaced in the 1970s by a pure anticholinergic that continues to be used in treating asthma and COPD. A characteristic common to beta-2 stimulants and anticholinergics is that they mainly have a bronchodilator effect.

Acute asthma

Adrenaline has no advantages over selective beta-2 stimulants in treating acute asthma and children and adults (Grade 2). Clinical experience suggests that acute treatment with selective beta-2 stimulants has favorable effects in adults - although placebo controlled studies are lacking (Grade 4) - and probably has effects in children (Grade 3). On the other hand, beta-2 stimulants have no, or only minor, effects in the treatment of acute obstructive conditions related to viral airway infections in children under 1 year of age, so-called bronchiolitis (Grade 2). Adding inhalant anticholinergics to beta-2 stimulants has a favorable effect in children (Grade 2) and reduces the need for hospitalization in treating adults (Grade 1).

Maintenance therapy for asthma

Continued maintenance therapy via short-acting beta-2 stimulants as the only medication, or as a supplement to other therapy, does not provide better asthma control in adults (Grade 2). However, the evidence is insufficient to determine the value of maintenance therapy in children (Grade 4). Long-acting beta-2 stimulants have effects in both children (Grade 3) and adults (Grade 1) as a supplement to inhaled steroids or other treatment. Evidence is lacking or deficient for determining the effects of maintenance therapy with inhaled anticholinergics in children and adults with asthma (Grade 4).

Acute exacerbation in COPD

The evidence is deficient for judging the value of both beta-2 stimulants and anticholinergics for this indication, despite a treatment tradition that has lasted many years (Grade 4).

Maintenance therapy for COPD

Long-acting beta-2-stimulants provide small improvements in symptoms and quality of life in maintenance therapy (Grade 1). Maintenance therapy with anticholinergics has effects on symptoms and quality of life (Grade 2), but does not reduce the need for hospitalization and does not influence mortality (Grade 3).

Theophylline

Xanthine derivatives such as caffeine have some bronchodilating effects on asthma. One such derivative, theophylline, was introduced in the 1930s and was used widely in Sweden until the 1980s, both in acute and maintenance treatment of asthma and to some extent for COPD. Since then, its use has progressively declined, due in part to its adverse side effects.

The review shows that oral maintenance treatment with theophylline for asthma in adults has no favorable effects (Grade 1), while the evidence for determining the effects in children and in COPD is deficient (Grade 4). Given intravenously for acute asthma, theophylline has the same effects as inhalation of beta-2 stimulants, but unfavorable side effects (Grade 2). The drug has a supplementary effect in acute asthma when the effect of inhaled beta-2 stimulants is insufficient (Grade 2).

Glucocorticoids

Glucocorticoids in the form of cortisone, etc (usually called steroids) were first used for asthma in the early 1950s and were quickly found to have dramatic effects on asthma when used in high oral doses. Severe side effects such as growth inhibition in children and osteoporosis in adults gave the treatment a bad reputation. Inhalation steroids were introduced in the early 1970s, and were established as first line treatment for asthma in both children and adults during the 1990s, due in part to the increasing knowledge about the effects of steroids on underlying inflammation in the bronchi during asthma.

Although COPD is an inflammatory bronchial disease, the inflammation is of a different character than in asthma. Hence, it is not surprising that the clinical effects of steroids on COPD are not as apparent. However, the scientific documentation is also more limited. Compared to oral administration, inhalation steroids have a clear advantage as regards the relation between effects and side effects. Therefore, the working group's review has focused on this type of medication. Based on comparative studies that have been published, the group did not find it meaningful to assess the possible differences among available inhalation steroids and their different delivery mechanisms since the studies seldom meet the requirements that should be placed on such comparative studies.

The side effects of inhalation steroids are rare and often depend on dosage: hoarseness, increased risk for superficial bruising, and often a minor and temporary influence on height growth in children.

Asthma in children over 2 years of age and in adults

Maintenance therapy using inhaled steroids has important effects both in children and adults with asthma (Grade 1). In adults with severe asthma, inhaled steroids reduce the need for oral steroids (Grade 1) and reduce the risk for death from asthma (Grade 3). In maintenance therapy of children with mild asthma, inhalation steroids reduce the symptoms better than long-acting beta-2 stimulants (Grade 3), and inhaled steroids reduce symptoms better than theophylline in adults with mild asthma (Grade 3). The addition of long-acting beta-2 stimulants to inhalation steroids provides better asthma control in both children (Grade 3) and adults (Grade 1). Unfortunately, there is no

evidence for permanent treatment effects following discontinued treatment. Symptoms return after exposure, even after a longer period of treatment with inhalation steroids for mild asthma in both children and adults (Grade 2).

Short-term, oral steroid regimens after treatment for acute asthma reduce the number of new asthma attacks that require treatment and the number of hospital admissions (Grade 1).

Treatment effects following COPD

Long-term treatment with inhalation steroids does not prevent progressive deterioration of pulmonary function in COPD (Grade 1). In advanced COPD, inhaled steroids reduce the number of acute exacerbations (Grade 3). In episodes that require treatment, oral and intravenous steroids have minor, but clinically relevant, effects (Grade 2).

Chromoglicate

Chromoglicate is an antiinflammatory drug that has been used in Sweden since the early 1970s to treat asthma and allergic eye and nose problems. The drug has local effects only and no serious side effects. The review shows that chromoglicate has favorable effects mainly in mild to moderate asthma in children over 4 years of age and in adults (Grade 1). The effects of treatment in children are less pronounced than the effects of inhaled steroids (Grade 3), but data for comparisons in adults is lacking (Grade 4).

Antileukotrienes

Antileukotrienes, a new group of drugs for treating asthma were introduced in the late 1990s and have not yet secured a position in the treatment arsenal. To date, only one drug in the antileukotriene group has been registered in Sweden. This drug is delivered orally. Maintenance treatment with antileukotrienes reduces the frequency of attacks and the need for additional medication. It also improves quality of life in mild and moderate asthma cases in both children and adults (Grade 1), but treatment in adults has a lesser effect than inhaled steroids in moderate doses (Grade 2).

Antihistamines

Since the 1950s, antihistamines have been used for effective treatment of nose, eye, and skin allergies. Our review concludes that the evidence is too weak for determining their effects on asthma symptoms related to pollen allergies and on year-round asthma (perennial asthma) (Grade 4).

Cough medicine

Coughing and expectoration are common, important, and often disturbing symptoms in both asthma and COPD, but also appear in many other diseases involving the bronchi and lungs. Regardless of the cause for coughing, treatment should be aimed at the basic cause and not at the symptoms. Traditionally, a large number of different decoctions and mixtures have been used to inhibit coughing (cough suppressants) or to promote expectoration. Modern documentation is lacking for all of these agents. Sales of cough medicine remain high in Sweden, particularly in self-care.

Evidence is lacking to assess the effects on coughing and expectoration in long-term treatment with cough medicines for asthma and COPD (Grade 4). Long-term treatment

with acetylcysteine provides a small reduction in the number of acute episodes in patients with chronic bronchitis at various grades of COPD (Grade 1).

Immunosuppression

In some cases, patients with severe asthma may not achieve satisfactory asthma control through high doses of inhaled steroids in combination with other drugs. This often leads to repeated oral steroid treatment, in some cases even to continual steroid treatment. Adding drugs that inhibit immunological processes has been tested. The review shows that methotrexate can lead to a reduction in oral steroid doses for severe asthma, but the treatment also carries troublesome side effects (Grade 2). The evidence for cyclosporine is weaker (Grade 3).

Specific immunotherapy with allergen extracts

Specific immunotherapy - or hyposensitization as it was formerly called - has been used since the early 1900s in people with allergic hay fever and asthma. In the late 1970s, allergen extracts with standardized contents of allergens were introduced and gradually replaced earlier, unspecified extracts. The effects of allergic asthma have been questioned from time to time. Immunotherapy is given over a long period, usually 3 years, as injections in the skin. Serious, acute side effects may appear. The review shows that immunotherapy has favorable effects on allergy-triggered asthma symptoms (Grade 1). The effects are best documented for pollen and cat allergies (Grade 1), less well documented for mite allergies (Grade 3), and the evidence is lacking as regards dog allergies (Grade 4).

Antibiotic treatment for acute exacerbation in chronic bronchitis

Patients with chronic bronchitis, with or without COPD, are often afflicted with respiratory tract infections and acute exacerbations. Some, but not all, of these episodes are caused by bacteria. Placebo-controlled studies suggest that treatment with tetracyclines, amoxicillin, and trimethoprim-sulfamethoxazole of patients with chronic bronchitis, with or without COPD, shortens the exacerbation and reduces symptoms (Grade 2).

Oxygen therapy at home

Oxygen deficiency may appear in case of severe COPD. In the beginning, it may occur only during acute exacerbations, but later it may become chronic. Chronic oxygen deficiency substantially reduces survival. Chronic oxygen deficiency can be treated with well-controlled, continual administration of oxygen. Treatment is technically rather complicated, relatively expensive, and requires that the patient can follow the instructions and not smoke. Since 1987, Sweden has kept a national registry of patients on home oxygen therapy, which makes it possible to monitor the treatment strategies, survival, etc. The review led to the conclusions that continuous oxygen therapy extends survival in COPD patients with severe chronic oxygen deficiency (Grade 1), but it has no proven effect on mild or moderate daytime oxygen deficiency (Grade 2).

To facilitate oxygen therapy and improve the condition of patients with severe COPD, different home healthcare nursing models have been tested. Specific clinical guidelines, eg, involving home visits by special nurses, have not shown any effects on quality of life or hospital admissions for patients with severe COPD (Grade 2).

Cardiovascular drugs in COPD

In severe cases of COPD with chronic oxygen deficiency, some patients develop elevated pressure in the pulmonary circulatory system, resulting in edema. Traditionally, these patients have been treated with diuretics and, in some cases, digitalis. Vasodilators have been proposed as a treatment strategy for elevated pressure in pulmonary circulation. The review concludes that vasodilating agents have no effect on survival in COPD (Grade 3). Remarkably, the data are insufficient for assessing the almost routine use of diuretics in severe COPD (Grade 4).

Lung surgery for emphysema

Volume reducing lung surgery as treatment in selected patients with severe COPD and emphysema was tested as early as the 1950s, but has been used on a wider scale since the early 1990s. Only a small percentage of these patients are candidates for surgery. The method has received major attention in the mass media because of patients in whom the initial effects were very good. However, the scientific evidence supporting the method is scant. Mortality in conjunction with surgery has been 0% to 6% in uncontrolled studies. Preliminary results from an ongoing Swedish controlled study suggest that health-related quality of life improves for at least 1.0 to 1.5 years following surgery (Grade 3).

Reflux treatment

In addition to acid reflux and heartburn, regurgitation of acid stomach contents into the esophagus can also cause problems in the respiratory tract and exacerbate asthma, particularly at night. Asthma and reflux problems co-vary, and certain asthma drugs, eg, theophylline, increase the tendency for reflux. Various studies have assessed the treatment of reflux using both drugs and surgery, but without confirmed effects on asthma symptoms (Grade 2).

Antioxidants

Epidemiological and immunological studies suggest that low levels of antioxidants in the blood, eg, vitamins C, E, etc, may be associated with asthma. However, there is insufficient evidence to determine whether the administration of antioxidants has any effect in treating asthma (Grade 4).

Conclusions

- Asthma and COPD are both chronic public health diseases that are on the rise in Sweden. For asthma, the increase is most obvious among children and young adults, while COPD is increasing among older smokers, particularly women.
- The cause behind the increase in asthma is unknown. However, the dominant, confirmed cause behind COPD is tobacco smoking. To prevent the advancement of COPD, it is important to detect the disease early. The most important preventive measure is to intervene effectively against smoking.
- COPD is associated with substantial limitations in everyday life and a lower quality of life despite medication. Although asthma also leads to a lower quality of life, individuals with asthma have a greater chance of becoming symptom-

free through modern medication. To assess the treatment of asthma and COPD, it is essential to use outcome measures that reflect the impact of the disease on an individual's life (health-related quality of life, symptom scales, need for acute care, mortality).

- The new drugs for treating asthma have major advantages. They also have contributed toward a dramatic decline in the cost of hospitalization for asthma patients.
- The review of the scientific literature has shown:
 - that smoking cessation is the single most important intervention against COPD. Smoking cessation increases survival substantially and reduces symptoms. For many individuals with severe COPD, drugs provide only limited relief for their medical, psychological, and social situation.
 - that current maintenance treatment for asthma using long-acting beta-2 stimulants and inhaled steroids is based on solid scientific evidence that shows a positive effect.
 - that treatment as needed with short-acting beta stimulants for asthma symptoms and exacerbations is well founded.
 - that other treatment principles for asthma such as chromoglicate, antileukotrienes, and immunotherapy have documented effects.
 - that the benefits of cough medications in obstructive lung diseases is inadequately studied.
 - that treatment with theophylline tablets is not beneficial for patients.
 - that continual treatment with short-acting beta stimulants is not effective.
 - that preventive measures against asthma symptoms, such as allergen elimination, need to be assessed.
 - that scientific evidence on alternative medicine as a complementary treatment method for asthma and COPD is either weak or completely lacking. There is a major need for controlled, well-executed studies.
- The methods for improving patient compliance with treatment regimens need to be developed and can be strengthened when patients themselves participate in decisions on treatment methods.
- There is a major need to assess special asthma clinics and treatment methods at home for severe COPD. Different forms of COPD rehabilitation play an important role, but need to be developed and assessed.

Appendix

Overview of the effects of various treatments for asthma and COPD

An overview of current knowledge is presented in the following tables, which summarize the most important conclusions from the systematic review. Such tables are necessarily schematic and cannot fully represent the detailed reasoning underlying each of the 24 chapters. Hence, they must be complemented with the more detailed information presented in the summary and the text of the report.

The following symbols are used in the tables to indicate the effects of the methods:

(+) = favorable effects, (o) = no proven favorable effects, (?) = documentation lacking or deficient.

The evidence underlying each evaluation was graded to indicate the strength of the scientific evidence: 1 = strong support by scientific studies, 2 = moderate support, 3 = weak support, 4 = little or no support or consensus among experts (for areas not reviewed by modern scientific methods, eg, treatment with theophylline or beta stimulants in acute asthma).

Asthma treatment in adults

Table 1 Effects of treating acute asthma in adults.

Treatment	Effect	Evidence Grade	Comments	Chapter
Beta-2 stimulants	+	4	Regardless of medication type	2.10
Beta-2 stimulants, inhaled	+	1	Better than intravenous	2.10
Beta-2 stimulants + anticholinergics, inhaled	+	1	Fewer admissions	2.10
Theophylline	+	4	More side effects than beta-2	2.11
Theophylline as complement to beta-2 stimulants	+	2		2.11
Steroids	+	1	No advantage with parenteral administration	2.12

Table 2 Effects of methods and drugs in maintenance treatment of asthma in adults

Treatment	Effect	Evidence Grade	Comments	Chapter
Anti-mite measures	+	3		2.1
Air filters	0	1		2.1
Smoking cessation	?	4		2.2
Education (information only)	0	1		2.3
Physical exercise	?	4		2.3
Self-care program	+	1	Swedish studies lacking	2.3
Asthma clinics in primary care	+	4	Insufficient evidence	2.4
Psychological treatment	?	4		2.6
Alternative medicine methods	?	4	Deficient for acupuncture, homeopathy, and chiropractic. Lacking for others.	2.7
Unsaturated (omega 3) fatty acids	0	1		2.8
Climate management	?	4		2.9
Short-acting beta-2 stimulants in continual treatment	0	2		2.10
Long-acting beta-2 stimulants	+	1		2.10
Anticholinergics	?	4		2.10
Theophylline	0	1	Unfavorable side effects	2.11
Inhaled steroids				
- symptoms, exacerbations, and quality of life	+	1		2.12
- survival	+	3		2.12
Chromogliccate	+	1	Mild-moderate asthma	2.13
Antileukotrienes	+	1	Mild-moderate asthma	2.14
Antihistamines	?	4		2.15
Cough medicine	?	4		2.16
Immunosuppression				
- methotrexate			Less need for oral steroids	2.17
- cyclosporine			Less need for oral steroids	2.17

Specific immunotherapy for allergy-triggered asthma symptoms	+	1	Best for pollen and cat allergies (1), less certain for mite allergies (3), deficient evidence for dog allergies (4)	2.18
Treating reflux	0	2		2.23
Antioxidants	?	4		2.24

Treating asthma in children

Table 3 Effects of treating acute asthma in children.

Treatment	Effect	Evidence Grade	Comments	Chapter
Beta-2 stimulants	+	3		2.10
Beta-2 stimulants + anticholinergics	+	2		2.10
Theophylline	+	4	No advantages compared to beta-2 in inhalation, but a supplementary effect (2)	2.11
Steroids	+	1		2.12

Table 4 Effects of methods and drugs for treatment of asthma in children

Treatment	Effect	Evidence Grade	Comments	Chapter
Anti-mite measures	+	3		2.1
Air filters	0	1		2.1
Reduced smoking by parents	?	4		2.1
Smoking cessation in adolescents	?	4		2.1
Education (information only)	0	1		2.3
Physical exercise	?	4		2.3
Psychological therapy	?	4		2.6
Short-acting beta-2 stimulants, continual treatment	?	4		2.10
Long-acting beta-2 stimulants	+	3		2.10
Anticholinergics	?	4		2.10
Theophylline	?	4		2.11

Inhaled steroids	+	1	Symptoms and exacerbations	2.12
Chromoglicate	+	1	Mild-moderate asthma over 4 years	2.13
Antileukotrienes	+	1	Only shown in adolescents	2.14
Specific immunotherapy for allergy -triggered asthma symptoms	+	1	Best for pollen and cat allergies (1), less certain for mite-allergies (3), deficient for dog allergies (4)	2.18

Treatment of COPD

Table 5 Effects of treatment on acute exacerbation in COPD.

Treatment	Effect	Evidence Grade	Comments	Chapter
Beta-2 stimulants	?	4	-	2.10
Beta-2 stimulants + anticholinergics	?	4		2.10
Theophylline	?	4	-	2.11
Steroids	+	2		2.12
Antibiotics	+	2	Amoxicillin, tetracycline, trimsulfa	2.19

Table 6. Effects of methods and drugs for maintenance treatment of COPD.

Treatment	Effect	Evidence Grade	Comments	Chapter
Smoking cessation				
- survival	+	1	7-year longer survival	2.2
- symptoms	+	1	Best effects on coughing and mucous formation.	2.2
Rehabilitation by physical exercise				
- respiratory distress	+	1		2.3
- quality of life	+	2		2.3
Energy supplements	+	3		2.8
Climate management	?	4		2.9
Long-acting beta-2 stimulants	+	1	Small effects	2.10

Anticholinergics	+	2	Symptoms and quality of life	2.10
Theophylline	?	4		2.11
Inhaled steroids	+	3	Only shown for the number of acute exacerbations	2.12
Antileukotrienes	?	4		2.14
Cough medicine	?	4		2.16
Acetylcystein	+	2	Somewhat fewer acute exacerbations and sick days	2.16
Oxygen - survival	+	1	In severe oxygen deficiency (PaO ₂ <7.3)	2.20
Digitalis and diuretics	?	4		2.21
Vasodilator drugs - survival	0	3		2.21
Volume reducing surgery for emphysema	+	3		2.22
- quality of life	?	4		2.22
- survival in the longer perspective				
Antioxidants	?	4		2.24