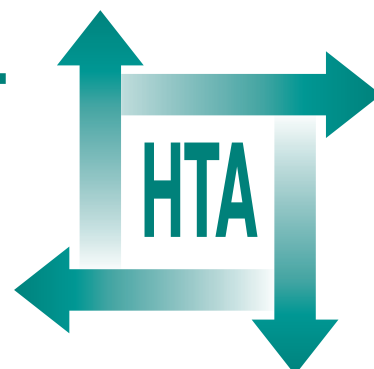


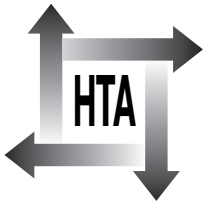
A systematic review to examine the impact of psycho-educational interventions on health outcomes and costs in adults and children with difficult asthma

JR Smith, M Mugford, R Holland, B Candy,
MJ Noble, BDW Harrison, M Koutantji,
 Upton and I Harvey

June 2005

**Health Technology Assessment
NHS R&D HTA Programme**





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A systematic review to examine the impact of psycho-educational interventions on health outcomes and costs in adults and children with difficult asthma

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Abstract

A systematic review to examine the impact of psycho-educational interventions on health outcomes and costs in adults and children with difficult asthma

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Objectives: Prior research has highlighted the importance of psychosocial factors in 'difficult' asthma. This study aimed to review the content, effectiveness and cost-effectiveness of psycho-educational interventions designed to address these factors in patients with severe and difficult asthma.

Data sources: Thirty-two electronic databases and other sources were searched for studies of educational, self-management, psychosocial and multifaceted interventions.

Review methods: Abstracts were screened in duplicate, against prior definitions, to identify eligible interventions targeted to patients with forms of or risk factors for difficult asthma. Studies were classified by patient group (child, adult) and graded along two dimensions related to study design and relevance in terms of the degree to which they were judged to have targeted difficult asthma. Detailed data were extracted from studies meeting a minimum design and relevance threshold. Characteristics of studies were tabulated and results qualitatively synthesised. Where sufficiently similar studies reported adequate data about comparable outcomes, quantitative syntheses of results were undertaken using a random effects approach to calculate pooled relative risks (RR) or standardised mean differences (SMD), with 95% confidence intervals (CI).

Results: Searches identified over 23,000 citations. After initial screening and removal of duplicates, 4240 possibly relevant abstracts were assessed. Papers associated with 188 studies were initially obtained and

classified. Fifty-seven studies including control groups and those that were judged to have at least 'possible' targeting of difficult asthma (35 in children, 21 in adults, 1 in both) were selected for in-depth review. The delivery, setting, timing and content of interventions varied considerably even within broad types. Reporting of interventions and methodological quality was often poor, but studies demonstrated some success in targeting and following up at-risk patients. Studies reporting data suitable for calculation of summary statistics were of higher quality than those that did not. There was evidence from these that, compared to usual or non-psycho-educational care, psycho-educational interventions reduced admissions when data from the latest follow-ups reported were pooled across nine studies in children (RR = 0.64, CI = 0.46–0.89) and six studies with possible targeting of difficult asthma in adults (RR = 0.57, CI = 0.34–0.93). In children, the greatest and only significant effects were confined to individual studies with limited targeting of difficult asthma and no long-term follow-up. Limited data in adults also suggested effects may not extend to those most at risk. There was no evidence of pooled effects of psycho-educational interventions on emergency attendances from eight studies in children (RR = 0.97, CI = 0.78–1.21) and four in adults (RR = 1.03, CI = 0.82–1.29). There were overall significant reductions in symptoms, similar in different sub-groups of difficult asthma, across four paediatric studies that could be combined (SMD = -0.45, CI = -0.68 to -0.22), but mixed results

across individual adult studies. A few individual studies in children showed mainly positive effects on measures of self-care behaviour, but with respect to all other outcomes in adults and children, studies showed mixed results or suggested limited effectiveness of psycho-educational interventions. No studies of psychosocial interventions were included in any quantitative syntheses and it was not possible to draw clear conclusions regarding the relative effectiveness of educational, self-management and multifaceted programmes. Data on costs were very limited. Of the two well-designed economic evaluations identified, both of multifaceted interventions, one in children suggested an additional cost of achieving health gain in terms of symptom-free days. Provisional data from the other study suggested that in adults the significantly increased costs of providing an intervention were not offset by any short-term savings in use of healthcare resources or associated with improvements in health outcomes.

Conclusions: There was some evidence of overall positive effects of psycho-educational interventions on hospital admissions in adults and children, and on

symptoms in children, but limited evidence of effects on other outcomes. The majority of research and greatest effects, especially in adults, were confined to patients with severe disease but who lacked other characteristics indicative of difficult asthma or likely to put them at risk. A lack of good-quality research limited conclusions about cost-effectiveness. Although psycho-educational interventions may be of some benefit to patients with severe disease, there is currently a lack of evidence to warrant significant changes in clinical practice with regard to the care of patients with more difficult asthma. Further research is needed to: (1) standardise reporting of complex interventions; (2) extend and update this review; (3) improve identification of patients at risk from their asthma; (4) develop and test appropriate outcome measures for this group; and (5) design and evaluate, via the conduct of high-quality pragmatic RCTs, more powerful psycho-educational interventions that are conceptualised in terms of the ways in which psychosocial factors and asthma interact.



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List of abbreviations

| | | | |
|------------------|---|-------|--|
| A&E | accident and emergency (used interchangeably with emergency department) | ICS | inhaled corticosteroid |
| ATS | American Thoracic Society | ICU | intensive care unit |
| BTS | British Thoracic Society | ITT | intention-to-treat |
| CCT | controlled clinical trial (i.e. non-randomised) | MA | meta-analysis |
| CI | confidence interval | NAEPP | National Asthma Education and Prevention Program |
| COPD | chronic obstructive pulmonary disease | NFA | near-fatal asthma |
| COS | controlled observational study | NRR | NHS National Research Register |
| CPOS | controlled prospective observational study | OR | odds ratio |
| CRD | NHS Centre for Reviews and Dissemination | PEF | peak expiratory flow |
| CROS | controlled retrospective observational study | QoL | quality of life |
| ED | emergency department (used interchangeably with accident and emergency) | RCT | randomised controlled trial |
| FEV ₁ | forced expiratory volume in 1 second | RR | relative risk (ratio) |
| FVC | forced vital capacity | SA | sensitivity analysis |
| HMO | health maintenance organisation | SD | standard deviation |
| | | SE | standard error of the mean |
| | | SES | socio-economic status |
| | | SH | subject heading (in database searching) |
| | | SMD | standardised mean difference |

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.



Executive summary

Background

Despite effective treatments and management guidelines, there are a significant minority of asthma patients who suffer from severe or poorly controlled disease. When persistent, this is sometimes referred to as 'difficult' asthma. Research highlights the association of psychosocial factors with difficult asthma and its related adverse consequences (e.g. fatal and near-fatal attacks). It is suggested that psycho-educational interventions designed to address these factors might improve outcomes in at-risk patients. Existing reviews of programmes involving interactive education, training in self-management and/or targeting specific psychosocial issues resulting from or impacting on asthma, suggest that **some** psycho-educational interventions are effective and potentially cost-effective in **general** asthma populations. However, findings are unlikely to be generalisable to patients with **difficult** asthma in whom a complex interplay of factors complicate management and who are therefore often excluded from or fail to attend standard programmes.

Objectives

- Do psycho-educational interventions improve outcomes for patients with difficult asthma?
- Do psycho-educational interventions constitute an efficient use of healthcare resources for patients with difficult asthma?

Methods

Data sources

Asthma terms combined with complex permutations for describing interventions were used to search 32 electronic data sources (including research registers, grey literature and non-English language databases) and guide handsearching of reference lists, conference proceedings, current contents and three key journals up to the end of 2002.

Study selection

Abstracts and/or titles were assessed in duplicate, against definitions developed at the start of the

review, to identify potentially eligible interventions targeting patients with forms of or one or more risk factors/outcomes associated with difficult asthma. Final inclusion decisions were made on the basis of viewing full texts. Two reviewers classified the studies initially included by patient group (child, adult) and graded them along dimensions related to study design and relevance in terms of the degree to which they were judged to target difficult asthma (insufficient, possible, probable, definite). A third reviewer resolved disagreements or uncertainties.

Data extraction

Descriptive, methodological, outcome and cost data were extracted from studies meeting a minimum design (having a control group) and relevance (at least 'possible' targeting of difficult asthma) threshold. Authors were contacted for additional information as necessary.

Data synthesis

Characteristics of studies in children and adults selected for in-depth review were tabulated separately and results qualitatively synthesised. Where sufficiently similar studies reported adequate data about comparable outcomes, quantitative syntheses (meta-analyses) of results were undertaken using a random effects approach to calculate pooled relative risks (RRs), or standardised mean differences (SMDs) with 95% confidence intervals (CIs).

Results

Extent of research

From over 23,000 citations identified, 4240 abstracts and/or titles were considered for further review. A total of 278 citations reporting on 188 different studies were initially included and classified. Of these, 57 (35 in children, 21 in adults and one including child and adult subgroups) were considered suitable for in-depth review.

Study characteristics

There has been a rapid and continuing growth of research in this field, with several important UK studies being recently completed or in progress at

the time of this review. The largest proportion of research to date has been conducted in the USA.

The delivery, setting, timing and content of interventions varied considerably even within broad types. Reporting of interventions and methodological quality was often poor but studies demonstrated some success in targeting and following up at-risk patients. The range of outcomes assessed and variations in the ways they were measured and reported precluded quantitative synthesis for most. Studies reporting data suitable for calculation of summary statistics were of higher quality than those that did not.

Effectiveness

There was evidence that, compared with usual or non-psycho-educational care, psycho-educational interventions reduced admissions when data from the latest follow-ups reported were pooled across nine studies in children (RR = 0.64, 95% CI = 0.46 to 0.89) and six studies with **possible** targeting of difficult asthma in adults (RR = 0.57, 95% CI = 0.34 to 0.93). In children, the greatest and only significant effects were confined to individual studies with limited targeting of difficult asthma and no long-term follow-up. Limited data in adults also suggested that effects may not extend to those most at risk. There was no evidence of pooled effects of psycho-educational interventions on emergency attendances from eight studies in children (RR = 0.97, 95% CI = 0.78 to 1.21) and four in adults (RR = 1.03, 95% CI = 0.82 to 1.29).

There were overall significant reductions in symptoms, similar in different sub-groups of difficult asthma, across four paediatric studies that could be combined (SMD = -0.45, 95% CI = -0.68 to -0.22), but mixed results across individual adult studies. A small number of individual studies in children showed mainly positive effects on measures of self-care behaviour but, with respect to all other outcomes in adults and children where sufficient data allowed conclusions to be drawn, studies showed mixed results or suggested limited effectiveness of psycho-educational interventions. No studies of psychosocial interventions were included in any quantitative syntheses and it was not possible to draw clear conclusions regarding the relative effectiveness of educational, self-management and multifaceted programmes.

Cost-effectiveness

Data on costs were very limited in quantity and quality for children and adults. Of the two well-designed economic evaluations identified, both of

multifaceted interventions, one in children suggested that, from the health provider's viewpoint, there would be an additional cost of achieving health gain in terms of symptom-free days. Provisional data from the other study suggested that in adults the significantly increased costs of providing an intervention were not offset by any short-term savings in use of healthcare resources or associated with improvements in health outcomes. Several relevant well-designed UK studies which plan to assess cost-effectiveness are yet to be published.

Conclusions

There was some evidence of overall positive effects of psycho-educational interventions on hospital admissions in adults and children, and on symptoms in children, but limited evidence of effects on other outcomes. The majority of research and greatest effects, especially in adults, were confined to patients with severe disease but who lacked other characteristics indicative of difficult asthma or likely to put them at risk. A lack of quality research limits conclusions regarding cost-effectiveness. Limited findings, trends in the evidence base and theoretical developments suggest that multidisciplinary, multifaceted interventions incorporating formal self-management and medical care may be the most promising broad-based approaches warranting further evaluation, but an alternative conceptualisation of interventions in the light of the ways in which psychosocial factors and asthma interact may be necessary.

Implications for healthcare

With the aim of reducing asthma morbidity and mortality, based on the evidence in this review, we suggest that:

- In adults and children with **severe** asthma, provision of psycho-educational interventions (especially those incorporating formal self-management) may reduce hospital admissions and, in children, improve symptoms, but potentially at increased overall cost. There is currently a lack of evidence to warrant significant changes in clinical practice with regard to care of patients with more **difficult** asthma.
- Better identification and recognition of patients with difficult asthma, taking into account the different pathophysiological, clinical, compliance and psychosocial risk factors, might

improve their care, enhance the value of future audit, and aid in the targeting of any new interventions.

- Until further research is available, the emphasis should be on optimisation of medical care, taking account of potential complicating psychosocial factors, for patients with difficult asthma, to ensure that the number of patients continuing to experience poor control of symptoms and frequent exacerbations is minimised.

Recommendations for research

In priority order, reflecting the reviewers' viewpoint, our findings suggest there is a need for further research in the following areas.

In general:

1. Standardisation of reporting of complex interventions.

In asthma/difficult asthma:

2. An update of this review incorporating the results of the good-quality randomised controlled trials (RCTs) with economic evaluations that were in progress or remained unpublished.
3. Primary and secondary research to clarify key risk factors and develop tools for identifying patients susceptible to adverse asthma outcomes.
4. Secondary research extending this review to examine psycho-educational interventions aimed **solely** at those providing care for patients with difficult asthma, and potentially asthma more generally (e.g. family members, school teachers, health professionals).
5. Further development, validation and standardisation of patient-focused, clinically relevant and age-appropriate measures of

intermediate (self-management behaviour and its correlates) and final health outcomes (especially symptom-based and quality of life scales), plus measures of benefit suitable for inclusion as end-points in economic studies, for use in research on asthma and particularly, severe and difficult asthma.

6. Further work on the conceptualisation of interventions, particularly with a view to the development of individualised, multidisciplinary interventions, incorporating application of psycho-educational theories, which can be delivered to a broad spectrum of patients, potentially in primary care or community settings.
7. Development and conduct of pragmatic RCTs to evaluate and compare different well-defined, theory-based interventions in practice which should:
 - (a) take account of guidance on the development and conduct of complex interventions;
 - (b) be piloted or based on prior modelling of possible effectiveness and cost-effectiveness to inform sample-size calculations and feasibility of full-scale evaluations;
 - (c) focus on broad-based multifaceted approaches adapted to individual needs for a wide spectrum of at-risk patients or evaluate specific interventions matched to the needs of particular groups, especially in areas where evidence is lacking (e.g. psycho-social interventions, adults, complex patients);
 - (d) have sufficient power and length of follow-up (preferably ≥ 12 months) to assess all important health and intermediate outcomes using validated measures;
 - (e) incorporate, where possible, assessment of relevant costs and end-points suitable for inclusion in economic analyses.

Chapter I

Background

Introduction

Asthma is the most common chronic disease that affects all age groups in Britain. Estimates suggest that around one in seven children and at least one in 20 adults have asthma.^{1,2} Its prevalence has also been increasing.² Asthma is a chronic inflammatory disease of the airways. The inflammation periodically causes the airways to narrow in response to certain internal or external stimuli, referred to as trigger factors. This causes the characteristic symptoms of breathlessness, cough, wheeze and chest tightness.^{3,4} Asthma is recognised as a chronic disease usually characterised by episodes of symptoms, which if uncontrolled can result in an asthma attack or exacerbation, interspersed with periods of reduced or no symptoms. It is therefore often unpredictable and can have a variable impact on a person's life.⁴

Effective drug therapies in the form of preventative anti-inflammatory medication, usually inhaled corticosteroids (ICSs), along with bronchodilator inhalers for immediate relief of symptoms, are available for the treatment of asthma.^{4,5} Pharmacological treatment is recommended for most patients with asthma and aims to eliminate or control symptoms to allow normal or best possible functioning and reduce the risk of attacks.³ Diagnosis and medical management of asthma have been refined in recent years with the publication of national and international guidelines which recommend a stepwise approach to treatment.³⁻⁸

Poorly controlled asthma

Disease burden

Despite the availability of effective medical treatment and consensus guidelines for asthma management, a significant minority of patients continues to suffer from severe or poorly controlled disease. Poorly controlled asthma is characterised by peak expiratory flow (PEF) rates, measuring airflow obstruction, which are habitually <80% of predicted or best and vary from morning to evening by >20%.⁷ The most common clinical indicators of poor asthma control are overuse of reliever medication,³ difficulty in

sleeping because of asthma, daytime symptoms and limitations on usual activities due to symptoms.⁹ These are influenced by the extent to which patients receive and follow advice regarding medical treatment but also by underlying disease severity and symptom perception. Thus, in the absence of objective testing, poor control, resulting from inadequate treatment, poor compliance or heightened perception of symptoms, and severity are often indistinguishable in practice.^{4,5} The terms are, therefore, often used interchangeably in the literature.

Accurate data on levels of asthma control amongst populations of asthma patients are currently lacking, since validated measures incorporating indicators of poor control have only recently been developed.¹⁰ However, the UK National Asthma Campaign¹ estimate that about 20% of people with asthma can be described as having severe asthma, which results in daily symptoms, reduced quality of life (QoL), time off work and school and frequent use of health services. In one large UK survey,¹¹ 27% of respondents felt that asthma totally controlled or had a major effect on their lives. In another,¹² 19% of respondents who had experienced wheezing in the last month had their sleep disturbed more than once a week and half said that their symptoms interfered with daily activities.

The burden of poorly controlled asthma is most evident through its adverse consequences, namely fatal and near-fatal asthma (NFA) attacks, hospital admissions and emergency healthcare attendances. Although they appear to have declined in recent years, deaths from asthma represent one of the major causes of preventable mortality and there remain around 1500 deaths annually in the UK with asthma registered as the cause.² Hospital admissions for asthma remained stable in the UK during the 1990s following increases since the early 1960s, with almost 74,000 admissions in 1999.² Children account for nearly half of these.^{1,13} A small proportion of admitted patients require intensive care unit (ICU) treatment. This is a commonly used indicator of a near-fatal attack.¹⁴ NFA, also known as severe life-threatening asthma, is defined as severe asthma requiring intermittent positive pressure ventilation

with raised inflation pressures or a raised arterial partial pressure of carbon dioxide.¹⁵ Attendance at accident and emergency (A&E) or emergency departments (ED) and unscheduled clinician visits for asthma are harder to quantify but contribute further to the significant healthcare burden associated with poorly controlled disease.²

Economic burden

In parallel with evidence on the health and social burden of asthma, and poorly controlled asthma in particular, there is a growing volume of literature regarding its economic burden. For example, a report from the US National Asthma Education and Prevention Program (NAEPP) Working Group on the Cost-effectiveness of Asthma Care¹⁶ identified that patients with severe and/or poorly controlled asthma consume a disproportionate amount of healthcare resources, incur greater personal costs and account for the majority of societal costs due to asthma. One review of cost-of-illness studies¹⁷ estimated that 10% of asthma patients account for >50% of costs and that three-quarters of the costs result from uncontrolled disease. However, the majority of costs result from inpatient stays and emergency attendances,¹⁸ many of which should be preventable with adequate management of asthma.¹⁹

Difficult asthma

Poor medical management has been identified as a contributing factor in studies of asthma deaths,^{20–22} NFA^{15,23} and admissions for asthma.²⁴ Undoubtedly misdiagnosis, failure to monitor asthma and under-treatment with anti-inflammatory medication continue to contribute to the problem of poorly controlled disease.³ However, even when medical management appears to be in line with recommended guidelines,^{4,5} a proportion of patients continue to suffer from the adverse consequences associated with poor asthma control. Such patients are considered by some to have what is referred to as ‘difficult asthma’.^{25–29} Central to a definition of difficult asthma is, therefore, disease which remains poorly controlled despite medical treatment which would usually be effective.^{26,30,31} A more detailed discussion of the concept of difficult asthma is provided in Chapter 2 and part of this review is concerned with further clarification of definitions and indicators for patients at risk from their asthma.

It is estimated that <10% of patients have difficult asthma.^{2,26,31} Inevitably, it has profound effects on

QoL for patients and prevention of emergency attendances,³² hospitalisations,^{24,33} ICU admissions¹⁴ and deaths²² associated with difficult asthma represents a challenge to clinicians. Again, although patients with difficult asthma make up a small proportion of the whole population with asthma, they account for a large and disproportionate share of mortality, morbidity and costs.^{34,35}

Several clinical subgroups of difficult asthma have been identified.^{30,34,36} Some patients with difficult asthma have ‘brittle’ asthma, of which Ayres³⁷ identifies two types. The first is characterised by wide diurnal PEF variation despite maximal therapy and the second is manifested in asthma attacks which are extremely sudden in their onset, often resulting in loss of consciousness.³⁷ Other patients with inherently severe, refractory or therapy-resistant asthma, and a large proportion of those dying from asthma, suffering near-fatal attacks and experiencing frequent admissions or emergency attendances for asthma, represent others whose asthma might be defined as ‘difficult’.^{25,30}

Psycho-social factors in asthma

Underlying disease severity is obviously an important factor in difficult asthma.^{25,38,39} Most patients suffering fatal and near-fatal attacks or experiencing admissions use three or more classes of asthma drugs²⁴ and/or have previous admissions^{21,22} and various pathophysiological mechanisms to account for difficult asthma have been proposed.^{25,27,31,40–42} In recent years, however, the role of patient-related factors in difficult asthma has become increasingly apparent.⁴³ Adverse psychological characteristics and social problems have been identified as the major potentially modifiable factors in preventing asthma deaths.^{21–23,44,45} For example, in two British studies,^{21,22} >70% of patients dying from asthma had significant psychological or social factors which may have contributed to their deaths. In an Australian study the figure was 86%.²³ Studies of NFA in adults^{15,23,46,47} and children⁴⁸ have shown similar findings to those of asthma deaths. Adverse home environments⁴⁹ and other psychosocial problems, including previous abuse,⁵⁰ also appear to be common in patients with brittle asthma.

Poor compliance has frequently been identified amongst patients experiencing a range of adverse outcomes from their asthma.^{15,48} Patterson and

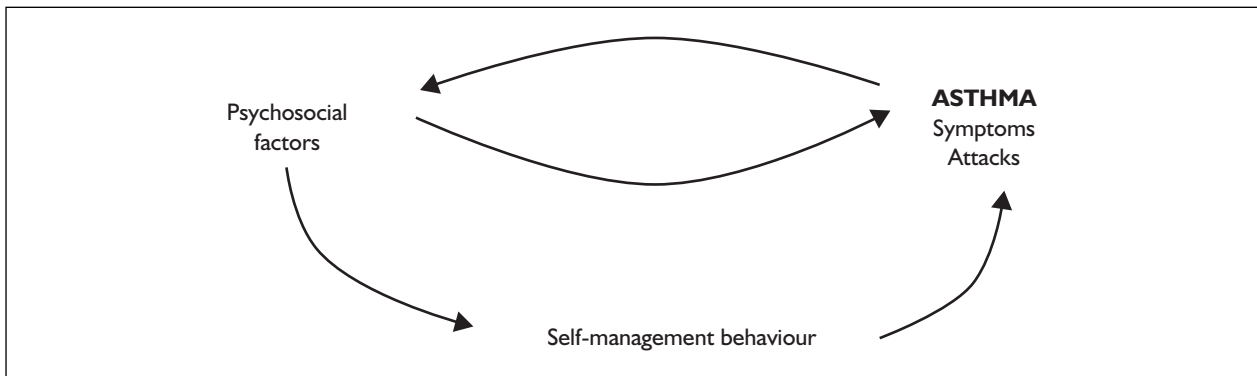


FIGURE 1 Relationships between psychosocial factors and asthma

Greenberger⁵¹ recognise both problem asthma and problem patients with asthma, and indeed patients who do not attend hospital outpatient or GP appointments, do not adhere to medication regimens or fail to comply with recommended management of their asthma in other ways can be considered to have difficult-to-manage asthma.²² Research suggests that there is a complex relationship between psychosocial factors and compliance.^{52,53} For example, in a study of patients admitted to hospital, management errors mainly related to inadequate self-management behaviour, which was predicted by social, economic and psychological characteristics.⁵⁴ Further findings in this area are reviewed elsewhere.⁵⁵ Harrison⁵⁶ concluded that all these patients have so many psychosocial characteristics in common that they can be regarded as a spectrum of patients with difficult asthma. He suggests that even when the medical management of such patients is optimised, patient factors would still present major impediments to effective control of their asthma.

The role of patient-related factors in asthma and the complex relationship between psychosocial characteristics and asthma have long been recognised.^{57,58} Relationships of asthma morbidity and mortality with psychosocial factors are likely to be two way (*Figure 1*). The experience of asthma, and particularly severe outcomes such as impairments in daily functioning, hospital admissions and near-fatal attacks, may increase psychological morbidity, reduce social functioning and have socio-economic consequences.⁵⁹ Asthma may, for example, affect a person's ability to work or study and thus contribute to problems such as poverty, poor housing and depression. Asthma, and in particular acute events, can also interfere with normal family functioning and relationships. Such psychological and social consequences may then in turn also impact on asthma directly. For example, blue-collar occupations or poor housing

may result in increased exposure to irritants and allergens, and stress may trigger asthma symptoms via neuro-immunological pathways.⁶⁰

Psychosocial factors can also affect asthma via their influence on a patient's ability to manage their condition, in particular through adherence to medication.^{55,61-63} Specific interest in psychosocial influences on asthma has indeed re-emerged in recent years,⁶⁴ with increasing emphasis being placed on patient self-management.^{4,5} Broadly, self-management involves patients making therapeutic, behavioural and environmental adjustments in accordance with advice from health professionals.⁶⁵ A central component of asthma self-management focuses on patients adjusting their medication according to action plans based on objective monitoring of PEF and/or identification of key symptoms.⁶⁶ Patients are expected to monitor and detect changes in their condition, assess them accurately and respond to them appropriately. Clark and Nothwehr⁶⁷ refer to the importance of patients practising attack prevention, attack management and social skills. Wilson and colleagues⁶⁸ further break these components down into medication, precipitant avoidance, symptom intervention, communication and health promotion skills. Ultimately, a patient's ability to perform behaviours central to effective self-management such as adjusting medications, avoiding triggers, seeking medical attention when needed, attending regular appointments and communicating problems, is affected by internal psychosocial characteristics and external psychosocial influences.^{61,69,70}

Psycho-educational interventions

Many psychosocial factors are potentially amenable to intervention. Programmes involving education, training in self-management and/or targeting

specific psychological or social issues resulting from or impacting on asthma are increasingly being implemented alongside conventional medical treatment to address them. The emphasis on patient self-care has meant that training in self-management and asthma education in particular have become central to the overall management of asthma in recent years.^{4,5} Asthma education and self-management interventions for children began to be developed during the 1980s,⁷¹ and in the last 10 years programmes for adults⁷² and children⁷³ have proliferated. Recommended components of asthma education programmes have been identified by a number of authors.^{71,74–76}

There is increasing overlap between self-management education and other psychological and social support interventions, with recognition that there is a need for all programmes to take account of psychological theories of behaviour change^{67,70,77–79} and to be tailored to address specific psychosocial and behavioural needs.^{80,81} This is especially true in difficult patient groups.⁸² An increasing number of programmes also attempt to intervene at various points in the cyclical relationship between psychological factors and asthma (*Figure 1*) by incorporating, for example, education and training in self-management, relaxation and other stress management techniques and support for coping with the impact of chronic disease. For this reason, psychotherapeutic, social support, educational and self-management interventions in asthma are considered together here as ‘psycho-educational’ interventions, as has been done in a previous review.⁸³

Evidence on the effectiveness of psycho-educational interventions

The following provides a summary of existing research on a range of psycho-educational interventions for asthma available at the time of this review (2002). It is based on accessible literature obtained primarily to guide planning of the review. It is therefore not intended to be exhaustive but is presented to provide the context and justification for the review of psycho-educational interventions for difficult asthma that follows. Further details on the methods and results of the individual reviews summarised below are provided in Appendix 1.

Psycho-educational interventions in mixed diseases

Several studies have examined psycho-educational interventions for asthma in the context of broader

reviews of interventions across a range of diseases.^{84–93} An early review of psychotherapy for medically ill patients of all ages, which failed to define search methods but involved a formal appraisal of 18 studies, included two controlled studies of group psychotherapy in asthma with conflicting findings.⁸⁴ Three reviews of psycho-educational interventions across a range of diseases conducted in the late 1990s focused specifically on children.^{85–87} One identified 15 psychosocial interventions for children with a range of chronic conditions⁸⁵ using strict selection criteria and fairly explicit review methods. Included amongst these were seven studies in asthma, of which three were found to have a positive impact on one or more psychological or behavioural outcome (health outcomes were not examined in this review). Another⁸⁶ found, across 42 studies, that psychological interventions for children with a range of chronic medical conditions were effective in improving a range of outcomes (mean overall effect size = 1.12, $p < 0.001$), but within this review results for six asthma studies identified were not assessed separately. A further review of psychological treatments for asthma, diabetes and cancer in children⁸⁷ undertook limited searching and quality assessment but graded evidence on interventions to make recommendations for practice and future research. This did not quantitatively synthesise results but concluded that, in asthma, relaxation therapies were ‘probably efficacious’, especially for children with emotional triggers, certain forms of biofeedback constituted a ‘well-established’ therapy, and family therapy represented a ‘promising approach’. The studies reviewed in each case were, however, limited in quantity and quality and highlighted the need for research examining these interventions in conjunction with up-to-date medical treatment.

In the field of reviews, systematic reviews using Cochrane methodology are generally considered more rigorous than other reviews⁹⁴ and this has been shown to be the case in asthma specifically.⁹⁵ A Cochrane review by Haynes and colleagues^{88,89} examined a diverse range of interventions designed to promote adherence with prescribed medications across a number of medical and psychiatric conditions. Five relevant interventions in asthma were included amongst the total of 33 studies reviewed, two of which showed clear effects on adherence and treatment outcomes in favour of the intervention.

Several further relevant reviews have focused specifically on respiratory diseases.^{90–93} A review⁹⁰

of pulmonary rehabilitation programmes for adults with chronic obstructive pulmonary disease (COPD) and asthma identified three studies from a total of 18 in which patients with asthma were included. In another review of a range of psycho-educational interventions for adults with COPD,⁹¹ 28% of the interventions also included asthma patients. Significant pooled effects on a number of outcomes were observed in both reviews, but neither summarised results from studies including asthma patients separately.

Two health technology assessment reports, which aimed to inform health policy in New Zealand⁹² and Quebec, Canada,⁹³ respectively, have summarised evidence on self-management strategies for asthma within broader reviews of interventions for respiratory diseases. The first⁹² assessed whether a variety of outpatient interventions reduced hospital admissions for a range of respiratory conditions. This concluded that there was no evidence from one systematic review and three randomised controlled trials (RCTs) reviewed, and evidence from only one of six observational studies identified, to suggest that self-management strategies reduced admissions for acute asthma. It noted, however, that there was often a lack of power in studies to detect differences, follow-up was relatively short, patients with severe asthma tended to be excluded and there was some evidence of positive effects of self-management on emergency department visits and other health service use. The other report⁹³ summarised levels of evidence in providing recommendations for implementation of a range of self-management and education programmes in asthma and COPD. In relation to asthma, it concluded that there was sufficient evidence from systematic reviews to recommend implementation of self-management education in adults, but further research was required in children and to establish the relative effectiveness of different types of self-management strategies, to identify which patients benefit most and to assess effectiveness in different settings and contexts. Other reviews that have examined these aspects in more depth are summarised in the sections that follow.

Psycho-educational interventions in patients of mixed ages with asthma

Four reviews of psycho-educational interventions for asthma were identified which examined studies in both adults and children.^{75,96-98} A descriptive review of hypnosis and asthma highlighted some positive effects of hypnosis amongst uncontrolled and non-randomised studies, especially in

susceptible individuals and children, but results from RCTs were equivocal.⁹⁶ A further discussion paper⁷⁵ considered some of the evidence on psychological approaches to treatment of asthma and concluded that these interventions, and in particular relaxation and psycho-education, may be a useful adjunct to treatment. One well-conducted systematic review⁹⁷ examined a range of relaxation techniques in asthma but across the nine RCTs identified, only two of mental and muscular relaxation showed significant effects. Finally, a Cochrane review⁹⁸ assessing individual written action plans for adults and children with asthma concluded on the basis of six RCTs that there was no consistent evidence that provision of plans alone produced better patient outcomes than no plan and highlighted conflicting results regarding the best type of plan. All these reviews identified the need for further high-quality research in each of the areas investigated.

Psycho-educational interventions in children with asthma

A two-part narrative review, conducted by one of the pioneering researchers in this field, Thomas Creer, and colleagues^{99,100} described 19 self-management programmes for childhood asthma developed between 1972 and 1988. This concluded that overall the programmes produced positive changes in the lives of children with asthma and their families,⁹⁹ although serious shortcomings in relation to the selection of patients, design of interventions, research methods used and interpretation of results were identified in all but a handful of studies.¹⁰⁰ Two papers^{101,102} that effectively constituted an update to this review discussed a further 18 studies of self-management programmes conducted during the 1990s. These identified that some progress had been made towards addressing identified gaps in the research literature but the authors did not discuss the findings or quality of these studies in depth and no attempt was made in these or the previous review to apply systematic review methods or formally pool results.⁹⁹⁻¹⁰² This was done, however, by Bernard-Bonin and colleagues,⁷³ who provided fairly detailed information on searching, study selection and quality assessment. They combined results from 11 RCTs in meta-analyses and found that self-management interventions were largely ineffective in reducing absenteeism, asthma attacks, hospitalisations, hospital days or emergency visits in children with asthma.

Further evidence on the effectiveness of psycho-educational interventions for children with asthma

comes from four Cochrane reviews.^{103–106} One examined family therapy and, on the basis of the two trials identified, concluded that it may be a useful adjunct to standard pharmacological therapy, but that there is a need for further research.¹⁰³ A second¹⁰⁴ included 32 trials of self-management education programmes for children with asthma. Meta-analyses combining results from these demonstrated effects on lung function, absenteeism, levels of restricted activity, emergency department visits and self-efficacy, but no effects on attacks, severity or other healthcare use. However, another Cochrane review of eight similar interventions targeting children who had attended the emergency department or been hospitalised for asthma in the previous 12 months concluded, on the basis of meta-analyses of eight trials conducted despite significant heterogeneity in results, that they did not reduce subsequent healthcare use.¹⁰⁵ A further Cochrane review remained in protocol form at the time of our review¹⁰⁶ (2002) and planned to consider a range of formal psychotherapeutic therapies (excluding family therapy), relaxation therapies, counselling and patient education incorporating formal psychotherapeutic techniques for children with asthma. Contact with the review authors suggested that high-quality research on these types of interventions in asthma is extremely limited.

Psycho-educational interventions in adults with asthma

Several reviews have examined psycho-educational interventions for adults with asthma.^{67,72,83,107–114} A 1997 narrative review of interventions designed to enhance self-management⁶⁷ concluded, on the basis of a qualitative assessment of 18 trials which involved random assignment and sufficient sample sizes, that there was impressive evidence of the benefits of self-management education in adults in terms of a range of health and psychological outcomes. A review conducted at a similar time,¹⁰⁷ which provided little detail on its methods, focused specifically on self-management programmes incorporating self-treatment guidelines and was much more cautious in its conclusions, highlighting the need for further good-quality research on the important components of such interventions. A broader review by Devine⁸³ examined a range of ‘psycho-educational’ interventions (education, behavioural and cognitive therapies, counselling) in adults with asthma, and provided some details on search and review methods. On the basis of meta-analyses of 31 studies (58% randomised, 77% with control groups), this concluded that such interventions have a positive impact on a range of physiological,

health, behavioural and psychological outcomes. More recently, a New Zealand health technology assessment report, in which review methods were clearly described,¹⁰⁸ considered 18 quality-assessed studies of asthma education and self-management in adults published since 1998. Results of studies were tabulated and all but three studies showed positive effects on at least one outcome at one or more time points; however, no attempt was made to synthesise results qualitatively or quantitatively. A systematic review of patient education programmes for adults with asthma¹⁰⁹ summarised details of the content and methods applied in, but not results from, 94 studies of such programmes and concluded that interventions were generally poorly described and reported.

Six Cochrane reviews examine psycho-educational interventions specifically in adults with asthma.^{72,110–114} Gibson and colleagues^{72,110–111} have conducted three reviews of interventions involving education, self-monitoring, regular review and/or use of a written action plan. The first followed from the need to assess evidence in support of the recommendation to ‘educate and review regularly’ in the Australian asthma management guidelines and considered 36 RCTs of self-management education and regular practitioner review.⁷² Meta-analyses showed that self-management interventions, particularly those including use of a written action plan, self-monitoring and regular review (i.e. optimal self-management), were effective in improving a range of objective and subjective health-related outcomes compared with usual care. The second review¹¹⁰ considered educational interventions not included in the first (i.e. asthma education not involving changes in therapy, self-monitoring or use of a written action plan) and, in contrast, on the basis of results from 11 trials, concluded that limited, information only, education was largely ineffective. A further review¹¹¹ reporting on 15 RCTs that compared two of more types of self-management education suggested, on the basis of qualitative syntheses and limited meta-analyses of results, that self-management options involving adjustment of medications by medical review or patients themselves, and self-monitoring based on PEF or symptoms, were largely equivalent in terms of their impact on health outcomes. Three remaining Cochrane reviews of psycho-educational interventions for adults with asthma remained in protocol form at the time of our review (2002).^{112–114} One is examining psychotherapeutic interventions¹¹² for which, as in the similar review in children,¹⁰⁶ contact with the authors has suggested that high-quality research in asthma is

lacking. The second is examining educational interventions specifically targeting adults attending the emergency room for asthma.¹¹³ The final proposed review of educational interventions for adults with asthma¹¹⁴ does not appear to be distinct from existing Cochrane reviews^{72,110–111} and, given that it has remained in protocol form for some time, it is not clear whether this is still planned.

Multifaceted and related interventions for asthma

A number of reviews have examined broader interventions in asthma of which some have psycho-educational components. The New Zealand health technology assessment report discussed above⁹² examined medical and organisational, in addition to self-management, interventions and concluded that there was a lack of or conflicting research on the utility of observational units, nurse clinics and organisational strategies to improve outpatient management of asthma and prevent admissions. Another review of organisational methods for asthma management¹¹⁵ also concluded that evidence was lacking, but suggested that specialist care may be more effective than generalist care and shared care as good as hospital-led care. A US review of community-based asthma interventions for inner-city disadvantaged children with asthma,¹¹⁶ that gave information on study selection but no other methodological details, considered five studies using strategies such as case management, patient, professional and community education, outreach and surveillance in schools. Although not a formal review, a further paper described 10 US-based managed care programmes for asthma.¹¹⁷ Both papers gave recommendations for key components of these multifaceted interventions and presented data to suggest that they improve outcomes, but the results and quality of studies were not formally used to draw conclusions regarding effectiveness.

Breathing retraining techniques, which sometimes combine physiotherapeutic and psychotherapeutic components or form part of broader interventions, have been the subject of two systematic reviews,^{118,119} including one for the Cochrane collaboration.¹¹⁸ Reviewing five¹¹⁸ and six¹¹⁹ studies respectively, both these reviews concluded that there were insufficient data to draw firm conclusions. One further Cochrane review¹²⁰ of primary care-based clinics for asthma identified only one study of sufficient quality for inclusion, highlighting the need for further research.

Evidence on the cost-effectiveness of psycho-educational interventions

The provision of any additional programmes for management of asthma requires resources that have an 'opportunity cost'. Healthcare funders, providers and other policy makers need evidence not only that programmes are acceptable, feasible and effective (in the short and long-term), but also that the costs of providing these programmes are justified by their outcomes and any prevented costs. That is, they need to be sure that they are as beneficial a use of resources as any alternatives. Many researchers in the asthma field have been aware of these questions for some years.

There have been several published discussion papers on economic aspects of asthma,^{16,121–125} which indicate a growing awareness that socio-economic conditions for patients, and resource constraints in the health service are factors affecting the need for and success of any healthcare programmes, including those directed at improving asthma management. Reviews focusing more formally on economic studies of a range of asthma treatments^{126–130} stress the limited nature of many of these. They highlight that the majority of economic studies in this field are cost-minimisation analyses of management strategies in routine asthma care,¹²⁶ with emphasis on effective delivery and uptake of pharmacological treatments. The importance of considering outcomes and costs comprehensively is emphasised.^{126–128} However, the specific problem of measuring economic benefits of interventions for asthma is noted. Obstacles to economic analysis lie in the difficulty of defining, measuring and valuing asthma outcomes which can be used for informing economic decisions,^{128,131,132} and in the lack of good observational data on people with asthma, and services and costs.^{128,129} However, there are an increasing number of studies where some aspects of resource use or cost have been included. There is also a growing empirical literature on outcomes measurement in asthma.^{132–139}

In 1996, a US NAEPP Task Force report on the Cost Effectiveness, Quality and Financing of Asthma Care¹³¹ identified that, apart from for drug therapies, little evidence was available on the cost-effectiveness of treatments and alternative management strategies for asthma. As the number of primary research studies of psycho-educational interventions has increased, however, reviews focusing specifically on economic studies of such

interventions in asthma have been published,^{121,123,140–142} some of which have taken a systematic and critical approach (for example, Volmer¹⁴²). These tend to highlight a number of individual studies that suggest self-management education programmes are more cost-effective than routine care in **general** asthmatic populations,^{143,144} but in common with many concurrent reviews of economic studies in general, the quantity and quality of economic analyses in this field have been found wanting.¹²⁹ Where there were sufficient studies, reviewers' conclusions echo those of the NAEPP cost-effectiveness task force¹³¹ about the difficulty of generalisation from the current research evidence, particularly to interventions for severe asthma and, given that the majority of existing studies have been conducted in the USA, the UK health service setting.¹²⁹

Psycho-educational interventions in difficult asthma: context for this review

The above summary of existing research suggests that there is good evidence from systematic and other well-conducted reviews of trials that self-management education and related interventions for adults with asthma can improve a range of health outcomes.^{67,72,92–93,108,111} High-quality reviews of similar interventions for children suggest more mixed results.^{73,92,93,104} Evidence on the optimal form and methods for delivery of self-management education,^{72,98,104,107,109,111} other types of psycho-educational programmes (e.g. psychotherapeutic approaches)^{96,97,103,106,112} and multifaceted interventions^{92,115,120} appears to be more sparse and a number of these areas have been identified for further research or consideration in ongoing Cochrane reviews.

With this in mind, this review aims to complement and, in a specific subgroup of patients, further expand on existing reviews of psycho-educational programmes in asthma. Distinctions between current Cochrane reviews of different types of psycho-educational interventions have developed on the basis of individual researchers' interests or local guidelines, differing in adults and children and appearing somewhat arbitrary. There is therefore potential for studies of complex psycho-educational interventions (e.g. multifaceted programmes incorporating self-management and psychotherapeutic techniques) to span two or more existing reviews, or some types of related interventions (e.g. social support strategies) to be omitted from reviews where narrow definitions are

applied. In order to overcome this, our review will consider a broad range of well-defined psycho-educational interventions, but test the utility of Cochrane review classifications as a framework for describing these and assessing subgroups of intervention types. In order to provide an overview of the breadth of available options for the management of difficult asthma in particular, and especially in the UK context, it will also not confine itself in the first instance, as the Cochrane reviews have done, only to those interventions that have been subject to evaluation via RCTs. This review will therefore contribute to an identified need further to classify and describe components of psycho-educational interventions, and continue to clarify the types of interventions that require more formal evaluation.

Although there is good evidence for the effectiveness of certain types of psycho-educational interventions, where there were sufficient studies, a number of existing reviews have identified the potential for differential effects of interventions across different settings and patient groups.^{93,104,105,111,119} For example, one Cochrane review in children suggests that the benefits of self-management education are greater in those with moderate–severe, as opposed to mild–moderate, asthma.¹⁰⁴ In contrast, the only completed systematic review discussed above which focused on a subgroup of patients likely to be at greater risk of adverse outcomes than a general community sample, namely children attending A&E, concluded that self-management education was largely ineffective.¹⁰⁵ There are therefore contradictory assertions in the literature regarding whether psycho-educational interventions are likely to be more effective, given greater capacity to benefit from both clinical¹⁴⁵ and economic¹⁶ perspectives, or less effective, given potential psychosocial barriers to education and behaviour change,^{54–56,63,146} in patients with severe, poorly controlled and difficult asthma.

Studies aimed at broad groups of asthma patients, which have been summarised in most reviews conducted to date, tend to exclude patients with severe asthma or adverse psychosocial characteristics, such as those associated with difficult asthma.^{56,92} Attendance of disadvantaged and at-risk groups in broad-based programmes also appears to be problematic.⁵³ For these reasons, results of systematic reviews and individual studies considering general samples of asthma patients are unlikely to be generalisable to those with severe and difficult asthma. The only previous review of psycho-educational

interventions to focus specifically on high-risk patients examined eight asthma education programmes in adults and children.¹⁴⁵ It was conducted as a 'narrative' review and did not define the types of patients and interventions under consideration, describe search methods or explicitly synthesise and evaluate results. Data on the effectiveness of psycho-educational interventions in difficult asthma have therefore not been formally summarised and there appears to be a need for further research in this context.

With regard to cost-effectiveness, only two of the Cochrane reviews in this field appear to have made explicit reference to data on costs in the studies they have evaluated,^{72,104} but economic data have not been formally extracted and synthesised, the quality of the economic evaluations has not been assessed and, again, results of the bulk of studies reviewed to date are unlikely to be generalisable. It therefore remains uncertain whether greater use of secondary and emergency health services in patients with severe and difficult asthma could be reduced by better management of the illness, such as might be achieved through psycho-educational interventions. For patients with difficult asthma, interventions may need to be individualised to specific needs^{80,81} and be more intensive, and thus be more costly to deliver.⁶³ However, since this subgroup accounts for most of the poor outcomes and costs in asthma care, if interventions are shown to be effective amongst these patients then this could be an efficient use of healthcare resources.¹⁶ Indeed, the NAEP report¹³¹ on the cost-effectiveness of asthma care concluded, on the basis of its review of studies on the economics of educational interventions, that more favourable economic results were seen where the intervention targeted 'high-risk or more costly' patients. However, it identified a lack of primary data on illness costs by disease severity and observed that 'the ability to generalise from these studies is minimal'.¹³¹

Since the only existing review of psycho-educational interventions for high-risk asthma patients was published, our research team have been involved in a randomised trial and economic evaluation of a home-based psycho-educational nurse intervention for adult patients with severe asthma who fail to comply with recommended management. Contact with other researchers in the field and review work undertaken as a result of our study suggests that there is a growing body of published literature and ongoing research on the effectiveness and cost-effectiveness of psycho-

educational interventions for difficult asthma, particularly in the UK. These recent research studies were designed to address perceived gaps in the UK and international research literature. However, the rationale for conducting them was not based on an up-to-date or systematic review of available evidence in this field. Furthermore, these studies only included patients with specific types of difficult asthma. Thus, even if results show that their respective interventions are effective and cost-effective, there is still a host of unanswered questions regarding optimal management of patients with difficult asthma.

In order to address some of these questions and gaps in the evidence base, the review presented in the following chapters uses systematic methods to identify, evaluate and summarise results from relevant studies of a range of psychological and educational interventions for patients with difficult asthma. The rationale for applying systematic methods to reduce bias in assimilating research information has been well documented elsewhere^{147,148} and will not be repeated here. Wide variations in the existing management of difficult asthma have been documented and imply uncertainty in clinical practice regarding the benefits and costs of various interventions.¹⁴⁹ The following review therefore aims to inform NHS clinicians, planners and purchasers in identifying options for current best practice and researchers and funders in identifying areas where further research is required in what, in recent years, appears to be a rapidly expanding research field in an area of increasing clinical need. In summary, this review of psycho-educational interventions for difficult asthma complements and expands on existing evidence in the following ways:

- In contrast to existing Cochrane reviews, it will consider a broad range of psycho-educational interventions together, examine novel approaches that may yet not have been subject to formal evaluation using rigorous research designs and test the utility of distinctions made in existing reviews further to identify and describe the key components of such interventions and clarify areas for future research.
- It will focus on the subgroup of patients with severe and difficult asthma in whom clinical and psychosocial factors interact with asthma, complicate management, potentially influence the need for and effectiveness of any interventions and to whom the evidence formally summarised to date is therefore unlikely to be generalisable.

- Unlike the only previous review to focus on psycho-educational interventions in high-risk asthma patients, it will take a systematic and critical approach to identifying and reviewing the literature and formally synthesise results.
- As an addition to existing reviews, it will formally consider, evaluate and synthesise data

on costs alongside health outcomes to aid decision-making further regarding the optimal management of patients with difficult asthma, particularly in the UK context.

Chapter 2

Review questions, definitions and scope

Research questions

The main objective of this project was systematically to identify and review available research evidence to address the primary question:

- Are psycho-educational interventions effective in patients with difficult asthma and, if so, are they cost-effective?

The question can therefore be divided into one of effectiveness:

- Do psycho-educational interventions improve outcomes in patients with difficult asthma?

and one of cost-effectiveness:

- Do psycho-educational interventions constitute an efficient use of healthcare resources in patients with difficult asthma?

It was anticipated from prior work and searching in this area that the number of good-quality studies in patients with difficult asthma would be relatively small in proportion to the body of research on psycho-educational interventions in asthma as a whole. A comprehensive approach to addressing these questions therefore entailed undertaking a thorough assessment of the volume and nature of potentially relevant literature and providing a detailed description of the subgroup of studies considered most directly relevant to addressing the review questions. These tasks therefore comprised a major component of the review and, although it aimed to explore best practice where data were available, from the start a large part of it was concerned with describing and defining options for current practice in this field, further developing definitions of psycho-educational interventions and difficult asthma and synthesising a knowledge base of what research has been undertaken. The review also aimed to build upon as yet unpublished, recently completed and ongoing research in this area, including that of our own group.

Definitions

In line with recommendations,¹⁵⁰ the review question, subsequent review procedures and, to a

large extent, the structure of key sections of this report are framed in terms of the problem and patients targeted, interventions and comparators assessed and outcomes, study types and study designs considered of relevance. Owing to the complexity of this review in relation to these dimensions, this chapter provides some background on how definitions were developed to frame the scope of the review and guide the review process.

Problem and patients

The review is concerned with studies targeting patients of all ages (i.e. children, adolescents, adults and elderly adults) who have 'difficult' asthma.

Difficult asthma is, however, not a distinct illness subgroup. It has proved problematic to characterise because the reasons for difficult asthma are often unclear¹⁵¹ or appear to be associated with a complex interplay of a wide range of clinical, pathophysiological and psychosocial risk factors and/or outcomes.¹⁵² For this reason, prior to the main review, a search of literature already held on various forms of severe and difficult asthma (e.g. asthma deaths, NFA, brittle asthma, severe asthma, asthma admissions and emergency attendances) and key medical bibliographic databases (MEDLINE, Web of Science) was undertaken and expert advice sought from the review team clinicians. This was done in order to develop a working definition of difficult asthma and formulate a checklist of relevant terms, indicators and outcomes associated with it to be used as a framework to guide the identification, selection and prioritisation of studies targeting a wide range of potentially appropriate patients.

A book,²⁵ two journal special issues^{28,38} and numerous papers that discussed definitions of difficult asthma in general^{26,27,30,31,38,151,153–158} and specifically in children^{29,49,152,159,160} were identified. Two papers report on consensus opinions resulting from task forces convened to address issues related to difficult asthma in Europe²⁷ and the USA (here referred to as 'refractory asthma').³¹ Certain aspects of defining difficult asthma were found to have been explored

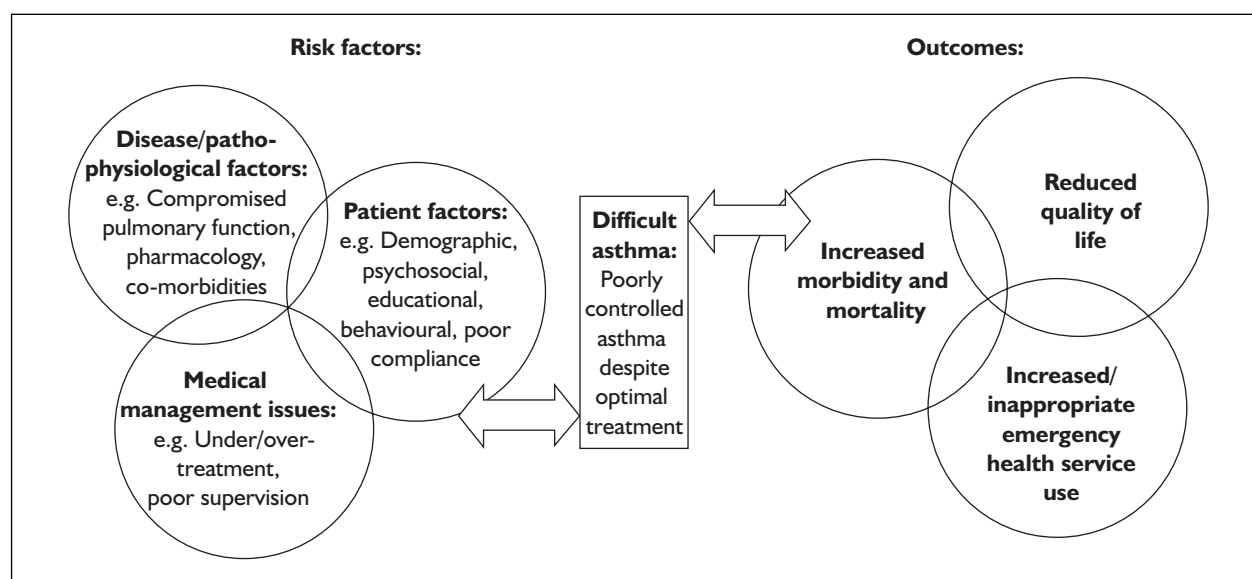


FIGURE 2 Interacting factors in the aetiology and outcomes of difficult asthma

in one or two papers only, whilst in other areas there was some broad level of agreement. The uncontentious areas were that:

- Central to a definition of difficult asthma is that asthma remains poorly controlled despite provision of optimal medical therapy, defined as adherence to national or international asthma management guidelines now recommending a stepwise approach to pharmacological treatment and regular ICS for all but those with the mildest asthma.¹⁶¹ This implies that the definition of difficult asthma may change over time as standard treatment improves.
- Poor control can be defined in terms of poor QoL and/or an increase in risk of death, health service use, unpredictable acute exacerbations, chronic persistence of symptoms, impaired lung function and side-effects from asthma medications.¹⁵⁴
- It is generally accepted that a definition of difficult asthma can be defined as difficult from a combination of the patient's and/or clinician's perspective.
- A patient is likely to see difficulty in terms of reduced QoL or side-effects of medication, whereas a clinician will see it as an increase in risk of severe attacks or death.²⁵
- People with difficult asthma are a heterogeneous group, in terms of clinical presentation and description, natural history and response to current therapies.^{26,28,30,36,154,156}
- Difficult asthma can be seen as either therapy resistant or as resulting from a failure of therapy, which may be due to poor compliance.¹⁵¹
- The risk factors for difficult asthma can be expressed under three broad categories: pathophysiological mechanisms (relating to an absence of scientific knowledge regarding underlying causes), medical management issues (relating to clinical expertise and access to services) and patient-related factors (such as environmental influences, psychosocial characteristics and compliance).^{38,156}
- Different combinations of these factors may produce difficult asthma. Pathophysiologically severe asthma may be difficult, however good the management and compliance of the patient, but inadequate treatment by clinicians or poor adherence by patients may make milder disease difficult. Likewise, not all dangerous or even life-threatening forms of asthma would be recognised as 'difficult'.^{34,154}
- The outcomes resulting from difficult asthma can be broadly expressed as those relating to an increase in morbidity (symptoms, attacks), health service use and mortality and a reduction in QoL. Some of these outcomes appear to act as further risk factors for future emergency service use, hospital admissions, NFA and fatal asthma, producing a downward spiral of disability.
- There is a longitudinal aspect to a definition of difficult asthma such that several papers suggest that patients should be assessed over a year before making a diagnosis of asthma that is difficult **because it is uncontrolled**.^{27,156}

From reviewing the literature, a framework was devised to illustrate the overlap between different risk factors for, and outcomes of, difficult asthma. This emphasises that outcomes can further affect

control of asthma and act as risk factors in themselves and highlights that central to defining difficult asthma is poorly controlled asthma despite optimal treatment. This framework is inclusive. It is not intended to act as a definitive model of difficult asthma. Instead, it was devised for the purpose of guiding decisions regarding whether studies specifically targeted patients with forms of 'difficult' asthma or a group/subgroup with characteristics of such who are likely to be at increased risk of adverse outcomes from asthma and in which a greater proportion than in a general sample of asthma patients are likely to have difficult asthma. The various components of the framework's risk factors and outcomes are shown in *Figure 2*. A detailed breakdown of the terms, characteristics, risk factors, indicators and outcomes commonly associated with difficult asthma is provided in Appendix 2.

In planning the review, it was anticipated that characteristics of patients and their problem (i.e. difficult asthma) would vary considerably across studies. To deal with this potential clinical diversity, in the first instance it was agreed that a broad distinction throughout the review would be maintained, where possible, between studies of children and adults. This is in line with the majority of reviews of asthma interventions conducted for the Cochrane collaboration, took account of the potential for interventions aimed at children to take a different approach to those aimed at adults (particularly with respect to involvement of additional family members) and considered the fact that there were likely to be two distinct specialist clinical audiences for the review, namely those involved in the care of adult and paediatric patients, respectively. In addition, it was planned that potentially relevant studies of patients with one or more characteristics associated with difficult asthma would be graded according to the type of difficult asthma and/or the degree to which difficult asthma was judged to be targeted (for further details, see Chapter 3). This was with a view to accommodating the need to focus on the most relevant literature if a large body was identified, whilst allowing for a more general review if not. It also allowed for descriptions and analyses of results to be broken down as necessary into prespecified subgroups and differences between these used in interpreting results. Further patient and disease characteristics varying across studies, particularly those pertinent to defining difficult asthma, would then be documented during data extraction. Given that the definition of difficult asthma is dependent on an assessment of what is considered to be 'good'

or 'optimal' medical treatment in line with asthma management guidelines, it was anticipated that it would also be important to document, where possible, details relevant to an evaluation of this.

Interventions

Prior to the main review, a search of literature already held and a number of secondary research databases [Cochrane Database of Systematic Reviews, York Centre for Reviews and Dissemination (CRD) Database of Abstracts of Reviews of Effectiveness and Effective Health Care Bulletins, UK HTA website, Bandolier Library] was undertaken to identify existing reviews and discussions of psychological and educational interventions in asthma and other conditions (see list of reviews in Appendix 1). On the whole, previous reviews of a broad range of psycho-educational interventions failed to provide explicit definitions. However, along with expert advice from the review psychologist, liaison psychiatrist and other team members, information gained from these searches was used to formulate a working definition of psycho-educational interventions.

For the purposes of this review, psycho-educational interventions were defined as:

1. Individual or group programmes in any setting and delivered by any provider or therapist that involved direct **interaction** between a person delivering the intervention (i.e. more than just didactic transfer of information) and the patient and of which **a major component**
 - (a) involved taking an educational, cognitive, behavioural and/or social approach to improving outcomes in asthma; and/or
 - (b) addressed educational, cognitive, behavioural or social issues impacting on asthma or its management; and/or
 - (c) addressed cognitive, behavioural or social issues resulting from the consequences of living with asthma.

It was anticipated that interventions providing patients with information, support, self-management strategies and/or psychological (e.g. cognitive-behavioural) techniques to assist in the management of asthma and/or in coping with its consequences would be eligible for the review. A range of different types of interventions, broadly classified as educational, self-management and psychosocial (i.e. psychotherapeutic and social support) therapies, were seen to come under the umbrella of psycho-educational interventions. It was recognised that psycho-educational programmes could be multifaceted and include

adjunctive physical therapies (e.g. exercise, breathing retraining, medical treatment) or environmental control measures (e.g. use of physical or chemical methods for reduction or elimination of triggers).

The definition of psycho-educational interventions also excluded certain related interventions. Interventions working **primarily** at the physical or environmental level or using physical or environmental therapies alone were excluded from this definition. Alternative therapies such as yoga, meditation and spiritual therapies were also not specifically sought for inclusion in the review. These have been reviewed elsewhere and in general were deemed unlikely to be evaluated in those with severe disease or difficult asthma. However, in some instances they were anticipated to be working primarily at a cognitive or behavioural level, and it was agreed that where they were identified via searching in this context they would be considered for inclusion on an individual basis against the defined eligibility criteria. Programmes that involved only passive or didactic transfer of information (e.g. video, written material or lectures alone) or that were aimed **solely** at third parties (e.g. parents of children with asthma, school teachers or health professionals) and therefore did not actively involve the patient in management of their asthma were also not considered as meeting our definition of psycho-educational.

Possible types of interventions identified in advance for inclusion were:

Educational:

- active/interactive teaching incorporating verbal, written (e.g. booklets), visual (e.g. video, computer) or audio transfer of information
- structured or unstructured learning
- problem solving
- role playing
- skills training
- discussion.

Self-management:

- education involving training in self-monitoring (of symptoms or PEF) and use of formal self-management or action plans.

Psychosocial:

- cognitive-behavioural therapies
- cognitive therapies
- behavioural therapies
- psychodynamic therapies
- psychoanalytic therapy

- psychosomatic therapy
- stress management and relaxation therapies
- progressive relaxation
- autogenic therapy
- guided imagery
- biofeedback
- hypnotherapy
- systematic desensitisation
- counselling (counseling)
- group therapies
- family therapies
- other psychotherapies
- alternative therapies (e.g. meditation, yoga, hypnosis, spiritual therapies) primarily working at a psychotherapeutic level and justified on this basis
- social support interventions.

Multifaceted:

- Psycho-educational interventions with elements of two or more of the above
- specialist multidisciplinary centres, clinics or programmes incorporating aspects of one or more of the above as core components.

Again, it was anticipated in advance that the characteristics of the interventions would vary considerably across studies. For this reason, it was planned that interventions would initially be classified into four broad categories as described above, which generally reflect distinctions made between different Cochrane reviews in this field conducted to date (for further details, see Chapter 3). This allowed for studies to be divided into subgroups for further review if there was considerable heterogeneity between them. It was intended that further key characteristics of interventions would then be documented during data extraction and, where possible, examined in describing and assessing results. In particular, attempts were made in this review to address, where there were sufficient data, the following secondary questions in relation to the interventions:

1. Which type(s) of psycho-educational interventions for difficult asthma are most effective?
2. What are the components of effective psycho-educational interventions?
3. Are interventions based on established psychological or educational theories more effective than those that are not?

Comparison groups

It was expected that interventions or control treatments to which psycho-educational

interventions would be compared in studies reviewed would likely vary to include:

- other psycho-educational interventions
- minimal/passive education or 'placebo' interventions
- other active non-psycho-educational treatments
- routine or usual care.

All comparative interventions/control treatments were considered relevant to the review in the first instance and it was planned that studies would be tagged at an early stage of the review according to the type of comparison made (for further details, see Chapter 3). Again, further efforts were planned to describe the comparison interventions in detail by documenting key characteristics important from the perspective of patients, clinicians, purchasers and future researchers during data extraction.

Outcomes

It was anticipated that a wide range of final and intermediate outcomes measured in various ways and on various scales would be reported by studies in different ways and contribute to a high degree of clinical diversity amongst them. These would include:

Final health outcomes:

- mortality
- morbidity (attacks, symptoms, severity)
- healthcare resource use and associated direct costs (hospital admissions, emergency attendances, routine attendances, medication use, patient resources)
- time lost from work or school, associated productivity losses and other costs to households and society
- health status, QoL (generic, respiratory and asthma specific) and associated preference-based valuations of outcomes (e.g. quality-adjusted life-years, willingness to pay)
- psychological morbidity (anxiety, depression, general).

Intermediary/explanatory outcomes:

- respiratory function [forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), PEF, bronchial challenge, lung volume, airway resistance, blood tests for inflammatory markers, etc.]
- self-care behaviour (compliance, trigger avoidance, attack management, general health-related behaviours, behavioural coping strategies)
- cognitions (self-efficacy/perceived control,

- cognitive coping strategies, attitudes, beliefs, knowledge, perceived social support)
- satisfaction with care.

It was planned that during study classification, the broad types of outcomes reported by each study would be noted to guide how best evidence might be combined for each outcome to examine the effectiveness of the various types of interventions amongst different patient groups (for further details, see Chapter 3). It was proposed that all reported patient outcomes (including intermediary outcomes), but not those related to effects on any third parties involved in the interventions (e.g. parents, health professionals), would be documented during data extraction since different outcomes are important from the perspective of patients, clinicians, purchasers and society. However, it was anticipated that outcome data extraction and subsequent analysis might be limited to primary health (as opposed to intermediary) outcomes specified by studies if there were a sufficient number of good-quality studies which assessed these in the various domains of the review.

Study types and designs

Studies of any design which examined appropriate interventions in patients with difficult asthma were considered for review in the first instance. It was proposed that the type (qualitative or quantitative, examining effectiveness, costs or cost-effectiveness) and design of studies would be classified after initial study selection (for further details, see Chapter 3). Priority for further review and data extraction would then be given to the best available evidence, namely controlled experimental studies, followed by observational studies with control groups, and then uncontrolled studies if little or no evidence was available from the former.

It was agreed prior to commencement of the review that qualitative and descriptive studies identified via searching would be documented and, where possible, matched to quantitative evaluative studies of the same interventions to provide additional details on patients, interventions and outcomes for data extraction. However, it was not proposed that these studies would be considered for further review in their own right unless there was a particular paucity of literature in a given area and time permitted. If a body of highly relevant qualitative research (e.g. related to experiences of patients with difficult asthma receiving psycho-educational interventions or the implementation of such programmes in the

NHS setting) was identified during searching, it was also agreed that advice would be sought from a qualitative reviewer on incorporating aspects of this into the review.

For the purposes of the review, any papers reporting assessment of costs in monetary units were considered economic studies, whether or not the authors had expressed intention to conduct a formal economic evaluation.

It was thought that there would likely be considerable methodological diversity amongst studies in terms of study designs and quality characteristics, from both clinical and economic perspectives, which would be documented and, where possible, examined in describing and assessing results.

Scope of the review

The discussion above highlights the scope of the review and its complexity. The review was focused in terms of the problem (difficult asthma) and type of intervention (psycho-educational) under consideration. However, since the relative importance of different comparators and outcomes varies depending on the perspective taken (e.g. that of health service providers, purchasers, health professionals and patients), and potentially according to the type of intervention under evaluation, the focus of the review was not restricted with respect to these parameters. Classification of studies early in the review process according to the dimensions highlighted was designed to deal with the complexity inherent in the review and ensure that within different

domains of the review, priority was given to extracting data from, and further reviewing, the best available evidence in terms of both study design and patients targeted. Along with further details documented during data extraction, this classification also guided qualitative data synthesis and was used to determine the feasibility and appropriateness of quantitative synthesis of effectiveness results.

Given the complexity, it was anticipated that refinements might need to be made to questions and definitions during the course of the review as alternative ways of conceptualising these become apparent. The implications of identifying a much larger than anticipated evidence base on the need to narrow the proposed broad scope was also considered in advance and handled by grading of studies according to their relevance. Where queries arose in the course of the review regarding whether particular patient samples and, to a lesser extent, certain types of interventions that were assessed matched the definitions developed, the review team was consulted and a consensus reached on the basis of expert opinion and consideration of the core thrust of the review. Further details on how the definitions were finally translated into study inclusion and exclusion criteria in relation to patients and interventions are therefore provided in Chapter 3. It was agreed that the motivation behind any refinements made, the influence of seeing study results and the applicability of the search strategy and data collection methods to the refined definitions would be considered and reported. Decisions leading to any changes made were therefore carefully documented.

Chapter 3

Review methods

This review was undertaken in line with the CRD guidelines on undertaking systematic reviews.¹⁵⁰ A detailed protocol outlining proposed methods for the review was developed during the early stages of the project. This was published as an internal departmental report¹⁶² and is available on request from the authors. The review was conducted in the School of Medicine, Health Policy and Practice at the University of East Anglia between early 2002 and mid-2003 by a review team comprising:

- Jane Smith (JS) and Bridget Candy (BC), who were employed as research associates (part-time and full-time, respectively) on the project and were responsible for day-to-day conduct and management of the review.
- Miranda Mugford (MM), Professor of Health Economics, who served as the project principal investigator and provided overall management in addition to expertise and practical input in relation to the economic aspects of the review.
- Richard Holland (RH), Lecturer in Public Health, and Ian Harvey (IH), Professor of Public Health and Epidemiology, who provided methodological and some clinical expertise and acted as secondary reviewers.
- Maria Koutantji (MK), Lecturer in Health Psychology, who provided advice related to psycho-educational interventions and outcomes and served as a secondary reviewer.
- Brian Harrison (BH), Consultant Respiratory Physician, Mike Noble (MN), General Practitioner and Asthma Liaison Psychiatrist, and Chris Upton (CU), Consultant Paediatrician, who provided invaluable clinical advice and acted as secondary reviewers. Mike Noble provided additional psychological expertise.

Further advice on searching and systematic review methods was obtained from Julie Glanville and Jos Kleijnen, respectively, from the York CRD. Additional help with searching and study assessment in relation to the economic aspects of the review was also received from Charlotte Davis (CD), an MSc Health Economics student at the University of York during a 3-month placement in the department.

Review procedure

A detailed description of each stage of the review is provided in the rest of this chapter. The following provides an overview of the review procedures.

1. Primarily one reviewer (BC) **searched** for all possibly relevant studies using predefined search terms in sources available locally. Additional searching using the same methods was undertaken at the CRD (see search strategy).
2. One reviewer (BC) **screened** titles obtained from searches to eliminate studies which appeared obviously irrelevant. To check validity, a second reviewer (JS) checked a subsample of search results. Studies considered potentially relevant by either reviewer were considered for further review (see study screening).
3. Study titles, abstracts and, where necessary, full papers were assessed by two primary reviewers (BC, JS) for **inclusion/exclusion** (see study selection). Reference to a secondary reviewer with relevant expertise (MM, MK, RH, IH, BH, MN, CU) was sought if there were disagreements or queries regarding selection. A second screening of titles, against criteria developed to prioritise those for which full text documents would be obtained, was undertaken for the large number of studies without abstracts whose eligibility status was initially deemed unclear by one of the primary reviewers (JS, BC). Since this represented a change to the protocol, a small methodological study to assess the validity of this approach was conducted. Attempts were made to obtain full copies of all studies selected for inclusion. Additional information was sought for papers which could not be obtained or for studies where eligibility remained unclear even after full articles had been retrieved.
4. **Study classification and grading** was undertaken by two primary reviewers (BC, JS). This initially categorised studies by the type of and/or degree to which difficult asthma was targeted, study type and design, patient age group and intervention type and also allowed initial documentation of comparison

TABLE 1 Electronic data sources searched

| | |
|---|--|
| <p>General health and social science databases: MEDLINE on Ovid EMBASE on Ovid Pre-MEDLINE on Ovid CINAHL (Cumulative Index of Nursing and Allied Health Literature) on Ovid Web of Science Citation Index Web of Science Social Science Citation Index Web of Science ISI Proceedings database PsycINFO ASSIA (Applied Social Sciences Index and Abstracts) ERIC (Educational Resources Information Centre) Mental Health Abstracts British Nursing Index Royal College of Nursing Library</p> <p>Health economics databases: CRD NHS EED (Economic Evaluation Database) Office of Health Economics HEED (Health Economic Evaluations Database)</p> <p>Grey literature databases: SIGLE (System for Information on Grey Literature in Europe) Dissertation Abstracts International ASLIB Index to UK and Ireland Theses</p> | <p>Databases of current/recent research: MetaRegister of Current Controlled Trials NHS NRR (National Research Register) ReFer (UK Department of Health Research Findings Register) Conference Papers Index NLM Gateway, incorporating: Meeting Abstracts HSRProj Database of Projects in Progress</p> <p>Foreign databases: Latin American and Caribbean Center on Health Sciences Information Virtual Health Library, incorporating: AdSuaDe (Latin American Health Services Administration) LILACS (Latin American and Caribbean Literature on the Health Sciences) ADOLEC (Latin American Adolescent Health) BDENF (Latin American Nursing) MedCarib (Caribbean Health Science Literature) WHOLIS (World Health Organization Library Information System) JICST (Japanese Information Center for Science and Technology) PASCAL (French health database)</p> |
|---|--|

- interventions and outcomes evaluated (see study classification). Reference to a secondary reviewer (MM, MK, RH, IH, BH, MN, CU) was made if there was disagreement or need for clarification and further information was sought from authors where classification details remained unclear. Classification details were used, in the first instance, to grade studies in children and adults along two dimensions related to study design and the extent to which they were judged to target patients with difficult asthma. Any studies reporting assessment of costs in monetary terms were also tagged at this stage for inclusion in the economic part of the review.
- Studies meeting a minimum grading at step four were prioritised for **extraction of descriptive data**. Data describing general study characteristics, patients, interventions, methodological quality, outcomes assessed and a descriptive summary and the significance of reported findings (see data extraction) were extracted by one reviewer (BC, JS, MM, CD) and checked by a second reviewer (BC, JS, MM, MK, RH, IH, BH, MN, CU) with any disagreements or uncertainties resolved via discussion.
 - Extraction of economic data** from all studies identified at step four as reporting assessment

of costs in monetary terms was conducted by one reviewer (CD, MM, JS) and checked by a second (MM, JS) with any disagreements or uncertainties resolved via discussion (see data extraction).

7. Selective **extraction of effectiveness data** was conducted retrospectively after an assessment had been made, blind to study results, of the number of controlled studies in each domain of the review which reported outcomes of similar types, in similar ways and over similar time frames (see data extraction).
8. A qualitative synthesis of all reported results was conducted. Additionally, where data were available in a suitable format, **summary statistics** were calculated for individual studies and combined in meta-analyses using a random effects approach if there was non-significant statistical heterogeneity between them (see data synthesis).

Search strategy

Data sources

Expert advice was sought from CRD advisers and reference made to previous reviews regarding the sources of data to be searched. The choice of data sources was limited by accessibility, time and the

TABLE 2 Journals included in British Library current contents alert

| | |
|---|---|
| <i>Allergy and Asthma Supplement</i> | <i>Journal of Behavioral Medicine</i> |
| <i>Allergy and Asthma Proceedings</i> | <i>Journal of Clinical Epidemiology</i> |
| <i>Allergy and Clinical Immunology International</i> | <i>Journal of Critical Illness</i> |
| <i>American Journal of Health Behavior</i> | <i>Journal of Epidemiology and Community Health</i> |
| <i>American Journal of Health Promotion</i> | <i>Journal of Health Education</i> |
| <i>American Journal of Medicine</i> | <i>Journal of Health Psychology</i> |
| <i>American Journal of Preventive Medicine</i> | <i>Journal of Pediatric Health Care</i> |
| <i>American Journal of Psychology</i> | <i>Journal of Pediatric Nursing</i> |
| <i>American Journal of Respiratory and Critical Care Medicine</i> | <i>Journal of Psychosomatic Research</i> |
| <i>Annals of Allergy Asthma and Immunology</i> | <i>Journal of Respiratory Diseases</i> |
| <i>Annals of Behavioral Medicine</i> | <i>Journal of the American Medical Association</i> |
| <i>Archives of Disease in Childhood</i> | <i>Lancet</i> |
| <i>Asthma in General Practice (became Primary Care Respiratory Journal)</i> | <i>Lung Biology in Health and Disease</i> |
| <i>Asthma Journal</i> | <i>Medical Care</i> |
| <i>Behavioral Medicine</i> | <i>Monaldi Archives for Chest Disease</i> |
| <i>British Journal of Health Psychology</i> | <i>Patient Education and Counseling</i> |
| <i>British Journal of Medical Psychology</i> | <i>Pediatric Allergy and Immunology</i> |
| <i>British Journal of Psychology</i> | <i>Pediatric Annals</i> |
| <i>British Medical Bulletin</i> | <i>Pediatric Asthma Allergy and Immunology</i> |
| <i>British Medical Journal</i> | <i>Pediatric Clinics of North America</i> |
| <i>Canadian Respiratory Journal</i> | <i>Pediatric Emergency Care</i> |
| <i>Chest</i> | <i>Pediatric Pulmonary Supplement</i> |
| <i>Clinical Allergy and Immunology</i> | <i>Pediatric Research</i> |
| <i>Clinical and Experimental Allergy</i> | <i>Pediatrics</i> |
| <i>Consultant, UK and US editions</i> | <i>Pediatrics in Review</i> |
| <i>European Journal of Pediatrics</i> | <i>Pediatrics International</i> |
| <i>European Respiratory Journal</i> | <i>Postgraduate Medical Journal</i> |
| <i>European Respiratory Review</i> | <i>Postgraduate Medicine</i> |
| <i>Health Economics</i> | <i>Practice Nurse</i> |
| <i>Health Education and Behavior</i> | <i>Practice Nursing</i> |
| <i>Health Education Research</i> | <i>Practitioner</i> |
| <i>Health Psychology</i> | <i>Preventive Medicine</i> |
| <i>Health Psychology Update</i> | <i>Psychological Bulletin</i> |
| <i>International Archives of Allergy and Immunology</i> | <i>Psychological Review</i> |
| <i>International Archives of Occupational and Environmental Health</i> | <i>Psychology and Health</i> |
| <i>International Journal of Behavioral Medicine</i> | <i>Psychology Health and Medicine</i> |
| <i>Journal of Adolescent Health</i> | <i>Psychosomatic Medicine</i> |
| <i>Journal of Allergy and Clinical Immunology</i> | <i>Respiratory Medicine</i> |
| <i>Journal of Asthma</i> | <i>Seminars In Respiratory and Critical Care Medicine</i> |
| <i>Journal of Behavioral Health Services and Research</i> | <i>Social Science and Medicine</i> |
| | <i>Thorax</i> |

perceived relevance of each source to the topic under review, but aimed to provide as comprehensive a retrieval as possible of world-wide published and unpublished studies, including those in languages other than English. A full listing of the 32 electronic data sources searched is provided in *Table 1*.

Searching of electronic databases was undertaken between May and July 2002. Searches were updated for key databases (MEDLINE, CINAHL, EMBASE, Web of Science) in October 2002 and search alerts sent when new citations matching search criteria were added to MEDLINE, CINAHL and EMBASE were scanned until the end of

December 2002. The British Library current contents alerting service (ZETOC) was also used to provide information on publications to December 2002 in the 81 key general health, specialist medical and social science journals listed in *Table 2*. Weekly updates on research news in pulmonary medicine were also received from the WebMD Medscape service.

On the basis of their frequency of occurrence in the research group's existing database of associated literature and direct relevance to the topic under review, the following journals were handsearched for the past 5 years (1997–2002):

TABLE 3 Meetings for which conference proceedings searched

| |
|--|
| American Academy of Allergy, Asthma and Immunology Meeting, New York, March 2002 |
| British Psychological Society Conference, Blackpool, March 2002 |
| Thoracic Society of Australia and New Zealand, Australia, March 2002 |
| Royal College of Paediatrics and Child Health meeting, York, April 2002 (abstracts published in a supplement to <i>Archives of Disease in Childhood</i>) |
| American Thoracic Society, Atlanta, May 2002 (abstracts published in supplement to the <i>American Journal of Respiratory and Critical Care Medicine</i>) |
| European Academy of Allergy and Clinical Immunology Congress, Italy, June 2002 |
| International Primary Care Respiratory Group Conference, The Netherlands, June 2002 |
| British Thoracic Society Summer Meeting, Manchester, June 2002 (abstracts published in a supplement to <i>Thorax</i>) |
| British Association for Behavioural and Cognitive Psychotherapies, Warwick, July 2002 |
| European Respiratory Society Congress, Sweden, September 2002 (abstracts published in a supplement to the <i>European Respiratory Journal</i>) |
| British Psychological Society Division of Health Psychology Conference, Sheffield, September 2002 |
| European Conference on Paediatric Asthma, London, October 2002 |
| European Health Psychology Conference, Portugal, October 2002 |
| Chest – Assembly of the American College of Chest Physicians, San Diego, November 2002 (abstracts published in a supplement to <i>Chest</i>) |
| Association of Respiratory Nurse Specialists Conference, Warwick, November 2002 |
| British Thoracic Society Winter Meeting, London, December 2002 (abstracts published in a supplement to <i>Thorax</i>) |

- *Journal of Asthma* (main journal solely dedicated to asthma)
- *Thorax* (main UK respiratory journal)
- *Patient Education and Counselling* (key journal on patient education programmes).

Conference proceedings or programmes from the 2002 specialist respiratory and psychology meetings listed in *Table 3* were also searched by hand.

Flyers requesting additional information relevant to the review were distributed at the European Health Psychology conference (October 2002) and Cochrane Colloquium. Further contact with all known UK researchers with an interest in the field was made via the Psychosocial Research in Asthma Group mailing list (<http://www.uea.ac.uk/mailman/listinfo/asthma>). Links were also established with members of the Cochrane Airways Group.

Reference lists from all relevant review articles already held and identified during searching and primary studies from which data were extracted were scanned for further potentially relevant articles not identified elsewhere. Although time did not permit structured Internet searching, websites for specialist respiratory funding bodies, professional organisations, charities and consumer bodies and the general web search engine 'Google' were used to trace authors and further details of studies for which minimal information existed or full papers could not be obtained. References to

any additional studies found during these searches were also followed up.

Search terms

A preliminary search of previously held literature, including reviews in asthma and of psycho-educational interventions in other conditions, was made to identify terms to be used for searching the main literature databases (for details of terms used in previous asthma-related reviews of psycho-educational interventions, see Appendix 1). Consideration was given to inclusion of possible synonyms, use of words in alternative contexts and changes in terminology over time in selecting search terms. Expert advice was also sought from York CRD advisers regarding the search terms and how they were combined to optimise sensitivity and specificity in searching.

Patients and problem

Based on initial work conducted to define difficult asthma (Chapter 2, Appendix 2), it was felt that it was impossible to generate a definitive list of terms used to describe 'difficult' asthma or its indicators without the potential for missing relevant studies. The decision was therefore made later, at the study selection stage, regarding whether studies targeted patients with difficult asthma. For this reason, the search for studies targeting relevant patients was only limited by using expanded subject headings for 'asthma' (where available) and free text searching of titles and abstracts using the truncated term 'asthma'

(see Appendix 3). This was in line with the forms used by Cochrane and other reviews in this field (see Appendix 1). Other terms to describe symptoms of asthma, such as wheeze, which have been used in some previous reviews of treatments for general asthmatic populations, were not used in the present review. It was found during scoping searches of MEDLINE that they were unlikely to identify additional studies of patients with disease at the more severe end of the spectrum that the term 'asthma' would not. Given the focus on a range of patient age groups in the review, no other limits were set in searching with regard to the types of patients.

Interventions

Previous reviews and background work conducted to define psycho-educational interventions (Chapter 2) were used to generate a list of possible search terms and subject headings for the interventions under consideration. In addition, a further preliminary search of PsycINFO was conducted to identify terms for specific psychotherapeutic interventions. Attempts were made to maximise sensitivity by including terms reflecting all possibly relevant educational, self-management, psychosocial and multifaceted interventions and to maximise specificity by excluding papers which did not describe or assess individual interventions (e.g. discussion papers, epidemiological studies of risk factors and outcomes) and studies of drug and other therapies. Different permutations for combining terms describing psycho-educational interventions using AND, OR and adjacency operators (ADJ, NEAR, SAME) were optimised using scoping searches on MEDLINE.

Comparison interventions, outcomes and study designs

Terms were not used to limit the search to studies examining particular comparison interventions, outcomes or study designs given the scope of the review as defined in Chapter 2. No further limits were set on dates, language or publication types within the sources searched.

Combined search terms

For specialist databases and others deemed likely to contain only small collections of asthma-related literature, where the scope for complex searching was often limited (e.g. NHS EED, OHE HEED, ASSIA, ERIC), asthma-related headings and text word searches were used in isolation to avoid missing potentially relevant studies. For all large databases, asthma search terms were combined with the complex permutations for describing

psycho-educational interventions and subject headings included or amended as appropriate to each. Details of search strategies for the major databases are provided in Appendix 3.

Study screening

Titles obtained from individual searches were screened as searches were conducted to exclude obviously irrelevant papers. Decisions to retain citations were guided by reference to the following questions:

- Is the paper primarily about asthma?
- Might the paper describe or evaluate an intervention of some form (i.e. it is not a discussion paper or epidemiological study)?
- Is there a possibility that the intervention in the paper is something other than a drug or physical/environmental therapy alone?

If the answer to **all** of the above questions was 'yes' or 'unclear', the citation was marked for retrieval, and if the answer to **any** one of the above questions was 'no', the citation was not considered further. Emphasis was placed on the need to be inclusive at this stage to ensure that no potentially relevant articles were missed.

All marked records from searches, and abstracts where available, were downloaded and imported directly into Procite reference management software or printed and entered manually where this was not possible. The number of citations downloaded from each data source was recorded. Databases containing citations from each of the data sources were then combined. Duplicates were removed with retention of the citation which contained most information. Owing to the method used to eliminate duplicates and the large number of records involved, it was not possible to record all original sources against each reference to assess overlap or the relative productivity of each database in identifying relevant articles.

A sample search (restricted to the year 1999) on the main medical databases (MEDLINE, EMBASE, CINAHL) was repeated by a second reviewer who also screened study titles according to the above criteria. Citations retrieved by the second reviewer for this year were compared with those obtained by the first to check the validity of the study screening procedure. References identified by either reviewer were retained for assessment of study eligibility.

Study selection

Eligibility criteria

Study type

Papers were included for further review only if they reported primary research projects that described or evaluated one or more interventions (i.e. intervention studies). General discussion papers, commentaries, policy articles or epidemiological surveys were excluded. Reviews reporting on individual studies of psycho-educational interventions, although excluded in their own right, were tagged as such and obtained for further references. Owing to the large number of citations assessed, papers stating that they were individual or descriptive case studies, even if other inclusion criteria were met, were not consistently retrieved since there was ambiguity regarding whether these could be considered primary research.

Interventions

Studies were included only if one or more of the interventions assessed could be described as psycho-educational according to the definition outlined in Chapter 2. Within this broad definition, the following interventions of borderline relevance were also excluded following agreement by the review team:

- Interventions that involved no obvious interaction between provider and patient, appeared to consist only of passive/didactic education or gave no information to suggest that delivery methods were to the contrary.
- Psycho-educational interventions that relied solely on use of computer-based technology in their delivery which, although potentially interactive, were agreed following consultation with the review team not to be appropriate for inclusion given the relatively limited scope for their implementation at present amongst patients from disadvantaged backgrounds.
- Interventions aimed solely at training health professionals, teachers, parents or other family members involved in the care of asthma patients, even if the patients were judged to have difficult asthma, where no information was given to suggest that the patients themselves participated in the study in any way.
- Routine and specialist clinics or care systems that mainly focused on medical assessment and treatment in which only minimal (and likely didactic) adjunctive education or training was provided.
- Rehabilitation or similar programmes in which limited (and likely didactic) education was provided secondary to exercise training.

- Breathing retraining techniques delivered in isolation (e.g. Buteyko) unless explicitly presented within the context of influencing interactions of psychological factors with the physiological processes concerned.
- Programmes aimed at controlling or reducing exposure to environmental triggers where, despite such interventions often involving some degree of education and behavioural change, the primary focus was on provision of equipment (e.g. anti-allergy bedding) or direct assessment and/or adaptation of home environments.
- Alternative spiritual and relaxation therapies which did not make explicit reference to addressing the influence of psychosocial factors on asthma.

Patients

Studies were included only if:

1. they explicitly targeted patients with an identified form of difficult asthma, or used terms that were suggestive of such
2. they explicitly targeted patients demonstrating characteristics associated with difficult asthma where these patients were argued by authors to be, in some sense, 'at risk', or
3. they identified and presented at least some results for a subgroup of such patients (1 or 2) within a more general sample.

The conceptualisation of difficult asthma and identification of indicators associated with it described in Chapter 2 were used to guide decisions regarding whether studies targeted patients with relevant characteristics. A broad approach to inclusion of studies on the basis of patient characteristics was taken at this stage in the knowledge that further grading of studies would be undertaken later. Within the broad definition of difficult asthma initially used, however, studies of the following potentially ambiguous patient groups were excluded following agreement by the review team:

- Studies aimed solely at adolescents who, despite being at potentially higher risk of experiencing difficulties with asthma than patients of other ages, in the absence of further targeting according to severity or other psychosocial risk factors were felt to be unlikely to be representative of a difficult asthma group.
- Studies of patients considered to have moderate-severe asthma only (whether or not this was defined), who were selected solely on the basis of being on daily or regular ICS

(regardless of dose) or were identified as being symptomatic or experiencing exacerbations of symptoms where no details were given with regards to the severity, frequency or time frame for these occurrences.

- Studies of patients demonstrating some characteristics associated with difficult asthma where this merely resulted from the study being undertaken in a particular geographical location (e.g. inner city) and authors did not make explicit reference to the target sample being at risk.

Given that patients with difficult asthma are often the least likely to agree to participate in studies or attend programmes, it was felt that the broad targeting approaches used in the above types of studies would be unlikely to lead to recruitment of more than a very small minority of patients with difficult asthma.

Studies of samples in which the majority of patients were children under 2 years of age were also not considered for the review because of the difficulty in diagnosing asthma and delivering psycho-educational interventions to this group.

Outcomes and study design

Initial inclusion and exclusion decisions were not made on the basis of comparison groups assessed, outcomes reported or study design/methodological quality characteristics.

Assessment procedures

Two reviewers independently viewed all titles and abstracts (where available) retained after initial screening to complete study eligibility checklists that assessed the suitability of studies for inclusion against the above criteria. The checklist was piloted on a sample of papers already held to confirm that it could be reliably interpreted. A longer structured checklist was used to guide discussion regarding eligibility with translators for non-English language papers. Questions regarding whether the paper (1) reported a primary research study, (2) described or evaluated a psycho-educational intervention, (3) targeted a sample or subgroup of patients with difficult asthma or characteristics thereof and (4) targeted a sample in which over half of the patients were aged over 2 years were answered Yes, Unclear or No. If the answer to **all** the questions on the study eligibility checklist was 'yes', the paper was considered included, if the answer to **any** one of the questions was 'no', the paper was considered excluded and if the answer to any questions was 'unclear', further action was taken (see below). The

initial overall assessment made by each reviewer with regard to the eligibility of studies (i.e. whether included, excluded or unclear) was recorded against citations in the Procite database and inter-rater agreement (kappa score) calculated.

Efforts were made to retrieve full copies of articles for all studies considered included by either reviewer. It was also intended that full papers would be obtained for all studies where inclusion was judged to be unclear by either reviewer. However, owing to the large number of potentially relevant references identified overall and the large proportion of these lacking abstracts, there were many references judged on the basis of the content of their titles alone that fell into this category. Owing to the anticipated time and high costs involved in obtaining many of these papers via inter-lending services, in a change to the original protocol, a further screening of references lacking abstracts was undertaken to prioritise papers for ordering on the basis of their likely relevance. On this basis the following were excluded:

- References which included information in citation fields other than the title to suggest that they were reviews, commentaries on previous studies, discussion papers or case studies.
- References with titles that did not appear to make reference to a single intervention programme and thus appeared to use terms such as education, self-management, compliance or psychotherapeutic techniques in the context of a general discussion.
- References where titles used only general terms such as asthma 'therapy', 'management' or 'treatment' without any other context in referring to an intervention, which were assumed to be primarily concerned with medical treatment.
- References with titles including only terms that were suggestive of primarily physical or environmental interventions (e.g. acupuncture, exercise, physiotherapy, allergen reduction).
- References with titles that did not mention asthma or mentioned another disease (e.g. COPD) as the main or joint focus of the article.

Retrieval of full text was always attempted for citations with titles where the wording appeared to make reference to a single intervention or programme, included terms reflective of the intervention possibly involving education, self-management, psychosocial techniques or multiple

components **and** gave some indication of potential risk factors (e.g. being at risk, ethnic, low income, inner city, adolescent, poorly compliant) or asthma severity (e.g. hospitalised, severe) in the patients targeted. Citations with titles that made reference to patients having only mild, moderate or well-controlled asthma or targeting what appeared to be general community or primary care samples were generally not retrieved. Where no reference was made to the type of patients targeted, all articles that could be obtained locally or online were retrieved and attempts made to obtain others with priority given to more recent publications.

A separate methodological study with departmental colleagues involved in a systematic review of randomised trials of non-pharmacological treatments for heart failure was conducted to examine the validity of making judgements regarding the eligibility of studies on the basis of information contained in titles alone. A summary of this exercise is reported in Appendix 4.

The eligibility status of references ordered based on the original assessment regarding inclusion being unclear was reassessed independently by each reviewer as necessary in the light of details contained in the full text. Where there were disagreements regarding inclusion, reference was made to a third reviewer with appropriate expertise depending on the nature of the disagreement. Where eligibility after examination of the full article remained unclear, further information was sought from accompanying papers, if available, via direct contact with authors or via Internet searching. The eligibility status of a small number of studies remained unclear in the absence of any further information (e.g. where articles could not be obtained, contact with authors failed or no response was received and/or additional Internet searching proved fruitless). A list of these studies was maintained.

Records of all papers reviewed for inclusion/exclusion, with broad reasons for exclusion added where applicable, were maintained on the Procite database and the number of inclusions and exclusions documented.

Multiple publications and unpublished data

Details of each study identified were carefully checked in order to match up, as early in the review process as possible, multiple publications of the same data and/or intervention. Clarification regarding the independence of publications was

also sought from authors for several studies. A number of papers, excluded in their own right, were later identified as providing additional information on patients, interventions or outcomes assessed in included studies and were subsequently retrieved to aid data extraction. The first author and year of a key paper, judged to be the most recent or important publication of the series, were used to identify each unique study. Studies were added to an Access database designed for the review where they were also assigned a unique identification number and details of related papers were linked.

Where no published papers existed, principal investigators were contacted for further information and their surname and the default year of 2002 used to identify studies.

Study classification

Two reviewers independently completed a form (see Appendix 5) during a brief scan of all selected papers to document key characteristics of each study. These key features related to:

- indicators or terms used which were suggestive of difficult asthma
- whether or not difficult asthma patients represented a subgroup of the total study sample
- study design
- study type (effectiveness, cost, effectiveness with some information on costs, cost-effectiveness)
- patient age group
- main components of intervention (education, formal self-management, psychotherapeutic techniques, social support, other)
- type(s) of comparison intervention/control group
- types of outcomes assessed.

Reference was made to an algorithm adapted from that used for a US Centers for Disease Control review of Community Preventive Services^{163,164} in categorising studies by design (see Appendix 6). All studies reporting assessment of costs in monetary units anywhere in the paper were tagged as economic studies. Mention of economic consequences or implications but without actual cost data did not qualify a study as economic, although a note was made of these. Where there were disagreements or uncertainties regarding categorisation, usually in relation to study design, reference was made to a third reviewer with appropriate methodological or other expertise.

Completed classification forms allowed studies to be categorised initially into two subgroups according to the age of patients targeted, namely (1) adults (generally over 18 years old or according to the criteria used in individual studies) and (2) children (generally under 18 years old or according to the criteria used in individual studies). This division is in line with distinctions maintained in Cochrane reviews conducted to date. Where study samples included a broad spectrum of ages the study was classified according to the age group of the **majority** of patients where this could be determined, unless there were subgroup analyses by age, in which case they were included in both categories. If the age of the majority of patients was unclear or no details on age were provided, additional papers on the study were consulted if available or authors contacted for clarification.

Within each of the patient age groups, studies were graded in tables along two dimensions. The first related to broad methodological quality expressed in terms of a study design hierarchy ranging from randomised and controlled experimental studies [RCTs, controlled clinical trials (CCTs)], through to controlled prospective observational studies (CPOSs) and controlled retrospective observational studies (CROSs) and finally uncontrolled observational studies (time series and before-and-after studies) and descriptive or non-comparative studies as detailed in the study design algorithm (Appendix 6). The second dimension related to a judgement, based on the data recorded in the study classification form and informed by emerging evidence from the review, regarding the extent to which the study targeted patients with difficult asthma. There were four levels broadly reflecting:

1. studies targeting patients with identified forms of difficult asthma or multiple risk factors (labelled 'DEFINITE')
2. studies targeting patients with multiple indicators of asthma severity/poor control or a single good indicator of asthma severity/poor control **plus** at least one other well-defined risk factor (labelled 'PROBABLE')
3. studies targeting patients with a single good indicator of asthma severity/poor control **or** a weaker indicator of asthma severity/poor control coupled with another single well-defined risk factor (labelled 'POSSIBLE')
4. studies of patients selected on the basis of a single emergency attendance with or without subsequent hospitalisation alone **or** targeting a

potentially at-risk, low socio-economic and/or ethnic minority population on the basis of geographical location only (labelled 'INSUFFICIENT').

This assessment was designed to grade studies according to the certainty with which they targeted patients with difficult asthma or, expressed another way, the approximate proportions of patients in each study sample likely to have difficult asthma [ranging from (1) virtually all to (2) a majority, (3) a large minority and (4) a small minority]. Further justification for this approach is provided in Chapter 4.

Studies were also tagged on the basis of the type of intervention studied, namely whether it primarily involved:

1. education without reference to use of a formal self-management or action plan (labelled 'EDUCATION')
2. education with reference to use of a formal self-management or action plan (labelled 'SELF-MANAGEMENT')
3. psychotherapeutic or social support techniques (labelled 'PSYCHOSOCIAL') or
4. education and formal self-management plus other add-ons (labelled 'MULTIFACETED').

These distinctions were broadly in line with divisions made in different Cochrane reviews conducted to date and were designed to allow further classification of studies into prespecified subgroups.

Classification details and other information recorded on the forms completed by the two reviewers were entered on to the database of selected studies. Tables summarising the quantity and quality of studies overall and in each patient age group were produced and the final classifications agreed upon. These tables enabled the review team, prior to detailed data extraction and viewing of results, to prioritise studies representing the best available evidence in the field (in terms of study design and targeting of difficult asthma), and in the light of the size of the evidence base as a whole, for data extraction. Decisions regarding classification of studies were further verified and adapted as necessary as detailed data on the patients, interventions, study type and design were documented during data extraction (see below). Additional issues pertinent to the type, design and focus of each study under consideration were also documented during the data extraction phase.

Data extraction

The development of data extraction forms was informed by background work on defining difficult asthma and psycho-educational interventions plus examination of data extracted in previous reviews (Appendix 1). Data to be extracted included information important from the perspective of different users of the review concerned with understanding characteristics of the patients and interventions, the validity of the results, applying the results in practice, informing policy and informing future research. In the light of the total number of studies identified, detailed data extraction was limited to studies judged to represent the best available evidence with respect to the dimensions of study design and relevance in terms of the degree to which difficult asthma was targeted as defined above (for further details on studies selected for in-depth review, see Chapter 4). The data extraction process was divided into three parts for which forms were designed and piloted.

Descriptive data extraction

The first part of the data extraction process recorded data on general study characteristics, aims, patients and details of the interventions and comparison treatments. Data on study methodology, outcomes assessed, measures and methods of assessment used and information pertaining to the quality of the study [for further details see the section 'Quality assessment' (p. 28)] were also extracted at this point. In addition, details of the type of statistics (if any) reported in results and a descriptive summary of findings plus their stated significance (*p*-values) in relation to each outcome were extracted for all studies where these were reported.

Extraction of data from economic studies

The second part of the data extraction process was applied to studies identified during the study classification stage or at a later point as reporting assessment of costs in monetary terms. It involved extraction of data pertinent to describing and assessing the quality of cost and cost-effectiveness studies [for further details, see the section 'Quality of economic studies' (p. 29)]. Items for extraction were developed from the *BMJ* checklist for reviewers of economic studies,¹⁶⁵ a form designed for a review of Community Preventive Services conducted by the US Centers for Disease Control¹⁶⁶ and the York NHS Economic Evaluation Database data abstraction forms.¹⁶⁷ Other recommendations for assessing and

summarising economic studies were also consulted.^{150,168,169}

Effectiveness, cost and cost-effectiveness data extraction

The final part of the data extraction process focused on the extraction of numerical data on effectiveness, costs and cost-effectiveness. Owing to anticipated clinical diversity, heterogeneity in outcomes assessed and poor reporting, extraction of actual numerical results data was conducted retrospectively on selected studies, and for selected outcomes within studies, after an assessment had been made of the outcomes for which there were a sufficient number of controlled trials in each domain of the review which reported data of similar types, in similar ways and over similar time frames to allow comparison, and potentially quantitative synthesis, across studies. Decisions to extract numerical data were, however, made blind to actual results. Cost and cost-effectiveness data were extracted as far as possible from all studies that reported costs in monetary units.

Procedures

Items were recorded as not reported or unclear where necessary on all data extraction forms as it was not possible within the time frame of the review to contact all authors for missing details or data. Data for each study were extracted using all accompanying papers and any further documents provided by authors or identified via Internet searching. Data from studies in progress, recently completed or for which minimal information was available (e.g. abstracts) were extracted as far as possible. For non-English language papers, data were either extracted directly by student translators who had become familiar with the field through assisting with study inclusion decisions or by reviewers on the basis of a full translation of the text.

Once completed, copies of all data extraction forms were sent with accompanying papers for checking to a second reviewer. Any disagreements or uncertainties regarding data extraction were resolved via discussion. Descriptive data, details of outcomes, study quality characteristics, statistics reported and descriptive summaries of results were entered on to the Access database of included studies. Data considered relevant for extraction by either reviewer were entered. Effectiveness data extracted retrospectively for selected outcomes were entered directly into Cochrane RevMan software (version 4.1) and all details of economic studies along with cost and cost-effectiveness data were entered directly into Excel spreadsheets. All data entry was checked.

Data synthesis

Descriptive data synthesis

Previous experience of research in this complex field had suggested that the number of good-quality studies, similar enough in terms of the patients targeted and interventions, comparisons and outcomes assessed to make quantitative synthesis of results appropriate and worthwhile, would be limited. A major focus of the review was therefore to summarise the broad range and types of research studies in this field and in those representing the best available evidence, within the previously specified subgroups as appropriate, to describe in detail study patients, interventions, methodological characteristics and reported observations related to effectiveness, costs and cost-effectiveness. Tabular summaries of characteristics across different patient groups and for different interventions were therefore planned to allow comparisons of similarities and differences and an assessment of the overall quantity and quality of research evidence. In the same way as for quantitative synthesis, weight was given to the best research evidence available and it was intended that the likely effects of clinical and methodological diversity on the general patterns of results and variations amongst them would be explored.

Quantitative data synthesis

The appropriateness of undertaking quantitative data synthesis (meta-analysis) was assessed by the review team on the basis of tabular summaries of study characteristics in the absence of any actual results data. This determined whether it was appropriate, and practical, to pool studies for given outcomes on the basis that they appeared to be sufficiently similar in terms of patients, interventions, comparisons, study designs and outcome assessment and reporting, or large enough in number to divide into the prespecified patient and intervention subgroups identified during study classification. The time frame for the project did not permit follow-up of authors for specific results data and the potential for meta-analyses was therefore additionally limited by the (often inadequate) reporting of results in published papers. Furthermore, although descriptive summaries of results were extracted for studies of all designs considered for in-depth review, it was agreed that only results from the highest quality studies (randomised and non-randomised controlled trials) would be considered for inclusion in meta-analyses owing to the potential for bias in observational studies. The number of controlled trials included in the review

and their similarity therefore also influenced decisions regarding whether meta-analyses were conducted for particular outcomes.

Broad categories of anticipated outcomes had been specified prior to data extraction. Selection of outcomes for quantitatively summarising effectiveness results was then largely determined by the frequency with which they were reported or identified as primary outcomes by individual studies. However, only outcomes directly related to patients, and not those concerned with the impact of asthma on or behaviour and knowledge of third parties (e.g. family members, treating clinicians), were considered. In addition, although descriptive summaries of results for all patient-focused outcomes were extracted, the focus for extraction of effectiveness data was on final (rather than intermediary) outcomes such as measures of asthma morbidity, QoL and healthcare resource use since the links between factors such as patient behaviour and cognitions and health status are yet to be clearly determined.

Where sufficient trials reported appropriate statistics for similar outcomes over similar time frames, standard meta-analytic approaches to calculating summary effect size statistics for individual studies and combining results were adopted¹⁷⁰ using RevMan software (version 4.1). Care was taken to include only one outcome per patient per meta-analysis if multiple time points and outcomes were reported in studies. Special attention was also given to crossover and cluster trials where unit of analysis errors are common. Summary relative risk ratio (RR) statistics for binary outcomes and standardised mean differences (SMDs) for continuous data were calculated for individual studies. If observations of Forest plots of these summary statistics with 95% confidence intervals (CIs) and statistical tests suggested that there was not significant statistical heterogeneity between individual study estimates ($p > 0.05$), pooled effect sizes were calculated using a random effects model.¹⁷⁰ Where significant statistical heterogeneity was observed, summary statistics for individual studies were tabulated so that comparisons between them could be made, but an overall effect statistic was not calculated since the studies were usually too few in number to allow meaningful division into subgroups.

It was intended that prespecified subgroup analyses to address the secondary questions posed in the review in relation to the relative effectiveness of interventions of different types,

with different components and using psycho-educational theories, in addition to differential effects across different patient groups, would be conducted where possible. Where studies were smaller in number, more limited sensitivity analyses were conducted to explore effects of patient groups, intervention types and methodology on results. Where opportunities for conducting formal sensitivity and subgroup analyses were limited, explorations of variations in effects were mainly limited to casual observations in the patterns of descriptive results.

Publication bias

For the outcome most commonly reported in studies of children and adults, funnel plots were constructed from individual summary statistics using RevMan.

Economic data synthesis

Economic data were qualitatively summarised to describe cost and resource implications of interventions, where possible considering resource consequences from different viewpoints. For comparison of costs between countries and over time, data were converted to UK pounds sterling at 2002–03 values based on WHO purchasing power parity conversion ratios¹⁷¹ and annual pay and price inflation rates.¹⁷² The simple pooling of cost-effectiveness ratios from different studies has been widely criticised, mainly on the grounds of the very wide range of heterogeneity in these complex variables.^{173–175} A further aim of the descriptive review of economic studies was to derive suggested structures for simple decision models to assess cost-effectiveness of psycho-educational interventions for difficult asthma.

Quality assessment

Methodological quality

Although a broad quality assessment, in terms of a hierarchy of research designs, was made at the study classification stage, as recommended,¹⁵⁰ detailed methodological quality characteristics were also extracted from all studies reviewed in depth. Owing to problems identified with using existing quality scales and scores¹⁷⁶ and anticipated diversity in terms of study designs, relevant components from existing checklists for experimental (randomised and non-randomised trials) and observational studies were selected to assess quality characteristics considered important in general and in light of the specific nature of this review. Most items came from checklists included in the CRD report on undertaking

systematic reviews,¹⁵⁰ but additional sources discussing broader quality issues were also consulted.^{176–179} Features related to recruitment and retention of participants (given the focus on difficult asthma) and outcome assessment (given lack of agreement on ways to assess asthma outcomes) were quality issues that were felt to be particularly important to assess in this review. The final components selected for extraction in relation to assessment of the internal validity, external validity and quality of reporting of studies are shown in *Table 4*.

Difficulties with disentangling methodological quality from the quality of reporting^{176,177} were handled in this review by assuming that if no reference was made to a particular quality component in the sources from which data were extracted, the component was assumed to be lacking. This represents a conservative approach in that there is potential for well-conducted studies that are badly reported to appear of poor quality; however, there is evidence that methodological and reporting quality are related.¹⁷⁷ Where necessary, to aid interpretation, additional explanatory information in relation to individual studies was included in tables summarising quality characteristics.

Outcome validity

Quality characteristics related to measurement issues (e.g. reliability, validity, recall) were extracted along with details of outcome measures and are reported alongside descriptions of these in the sections summarising results in relation to each outcome.

Intervention quality characteristics

Standard ways of assessing intervention quality are not available, but there is increasing emphasis on the importance of quality in designing and evaluating complex interventions¹⁸⁰ and growing interest in the systematic review field regarding reporting and summarising relevant features of such interventions.¹⁸¹ In this review, data deemed relevant to assessment of intervention quality and the quality of reporting in this context were extracted and are summarised in results sections describing features of the interventions.

'Quality' of targeting difficult asthma

In addition to the quality issues outlined above in relation to methodology, outcomes and interventions which are common to many systematic reviews, an added dimension of complexity in this review which required some consideration is the extent to which the patients

TABLE 4 Methodological and reporting quality components assessed

| |
|--|
| <p>Internal validity</p> <ul style="list-style-type: none"> • Randomisation methods/selection of comparison group (as appropriate) • Concealment of allocation sequence and methods for doing so (where applicable) • Blinding of outcome assessors^a <p>External validity</p> <ul style="list-style-type: none"> • Specification of clear inclusion/exclusion criteria • Patient participation rate • Total sample size • Minimum follow-up • Comparability of non-participants • Comparability of withdrawals • Specification and conduct of ITT analysis (where applicable) <p>Quality of reporting</p> <ul style="list-style-type: none"> • Details of analyses provided • Appropriate data reported for results (numerator and denominator for binary outcomes, point estimates and measures of variability for continuous outcomes) <p>Other issues</p> <ul style="list-style-type: none"> • Specification of primary outcome • Specification of primary endpoint • Power calculation • Baseline comparability of groups <p>^a Blinding of providers and patients is difficult, usually impossible, for psycho-educational interventions, so these components were not assessed.</p> |
|--|

targeted by studies were judged to have difficult asthma. An assessment of this was crudely achieved by grading studies, as described earlier, according to the degree to which they were judged to have targeted difficult asthma. In the light of the definition of difficult asthma used for this review, which makes reference to poor asthma control despite good medical care, an assessment of the quality of standard medical care was also

made where possible by documenting whether studies made reference to use of asthma guidelines.

Quality of economic studies

Quality assessment of economic studies was judged according to the total number of items from the *BMJ* checklist for economic evaluations¹⁶⁵ that had been fully reported.

Chapter 4

Results: extent and general quality of research

Overview

This chapter provides an assessment of the review searching and selection processes and a summary of the quantity and characteristics of research identified. It also documents the rationale behind the decision to exclude certain portions of the research from further in-depth review.

Throughout the chapter and the rest of the report, a distinction is made between 'citations' referencing published and unpublished research papers, abstracts or other documents and the 'studies' which were reported in these as individual, independent research projects. Each study could therefore be associated with more than one retrieved document so the number of studies considered is always less than the number of citations. Where there was no clear evidence of studies being independent (e.g. multiple analyses in the same sample of patients) they were considered to be one study. For ease of identification and consistency, individual studies are referred to by the surname of the first author and, where there are multiple authors of the same name, date of the main or most recent paper or other document reporting on them. Where available, all references associated with studies are provided when they are first mentioned in the text but these are not repeated at every mention. Referral to individual studies is only consistently made in the text where the study-level data reported are not available in appendices.

Review process

Search results

Over 23,000 citations were identified across all data sources searched. The largest number of hits was obtained from MEDLINE, followed by EMBASE and the combined Web of Science Science and Social Science Citation Indices, all of which produced over 4000 citations each.

Study screening

On average, initial screening on the main health databases eliminated around two-thirds of citations, although this varied from elimination of <50% in CINAHL to nearly 85% in PsycINFO where the search strategy was less specific. Overall, 4240 citations were retained after study screening and removal of duplicates from across the different data sources, representing about 18% of the total number identified.

The results of the citation screening validity check conducted by the second reviewer for a single sample year (1999) across three of the main health databases are shown in *Table 5*. The data suggest that the reviewer (BC) who conducted the primary searches and screening tended to be more inclusive than the second reviewer (JS). She included, on average across these three databases, approximately 40% (5% on MEDLINE to 68% on CINAHL) more citations than the second reviewer (JS). This may be explained by the fact that the second reviewer was more familiar with the field

TABLE 5 Numbers of citations saved from searches and included and excluded studies identified uniquely by each reviewer across three health databases for the year 1999

| | Reviewer BC (primary search) | | | Reviewer JS (subsample search) | | |
|----------------------------|------------------------------|--|----------|--------------------------------|--|----------|
| | Citations saved | Citations identified uniquely that were ultimately | | Citations saved | Citations identified uniquely that were ultimately | |
| | | Excluded | Included | | Excluded | Included |
| MEDLINE 1999 | 101 | 30 (30%) | 0 | 96 | 25 (26%) | 0 |
| CINAHL 1999 | 96 | 49 (51%) | 0 | 57 | 5 (9%) | 0 |
| EMBASE 1999 | 114 | 53 (46%) | 0 | 72 | 11 (15%) | 0 |
| Total (duplicates removed) | 311 | 111 (36%) | 0 | 225 | 28 (12%) | 0 |

TABLE 6 Details of reviewers' initial assessments regarding study eligibility

| | | Reviewer JS | | | Totals |
|-------------|---------|-------------|---------|---------|--------|
| | | Include | Unclear | Exclude | |
| Reviewer BC | Include | 80 | 19 | 35 | 134 |
| | Unclear | 32 | 261 | 305 | 598 |
| | Exclude | 17 | 145 | 3346 | 3508 |
| | Totals | 129 | 425 | 3686 | 4240 |

and literature in this area. Ultimately, only 17 of the additional 28 studies uniquely identified by the second reviewer across the three databases for the year 1999 were not identified by the first reviewer when other data sources searched by the primary reviewer were also taken into consideration. If this pattern was assumed to remain consistent across all searches, as a worst case scenario around 330 potentially relevant citations may have been missed. However, none of the additional citations identified by the second reviewer were ultimately included in the review, suggesting that the screening strategy used by the reviewer who conducted the main searches was unlikely to have missed any relevant studies. The fact that none of the 111 citations uniquely identified by the reviewer who conducted the primary searches were ultimately included in the review also suggests that the second reviewer's more stringent screening would have been unlikely to miss any relevant studies. In any event, this exercise suggests that we can be confident that the number of potentially relevant studies excluded at the study screening stage is likely to be very small.

Study selection

Details of the initial assessments regarding study eligibility made by each of the two primary reviewers (JS, BC) on the basis of viewing titles and abstracts only are provided in *Table 6*. Overall, there was 87% absolute agreement between reviewers. The kappa score for inter-rater agreement was 0.51 (95% CI 0.47 to 0.55) representing a moderate level of agreement. As described in the methods chapter, final inclusion and exclusion decisions by each reviewer for papers whose eligibility status was initially rated by one or both reviewers as unclear were made on the basis of rescreening titles for studies without abstracts and/or viewing full text papers. The agreement between reviewers regarding final inclusion decisions was therefore higher but this was not formally documented.

Of the 762 citations for which eligibility status was initially rated as unclear by one or both of the

reviewers, 472 (62%) did not have abstracts and were rescreened according to the criteria described in the methods section to prioritise for full text retrieval only those most likely to be references to relevant studies. Results of the separate exercise designed to assess the validity and likely impact on reviews of making eligibility decisions on the basis of titles alone are briefly described in Appendix 4.

Seven citations initially judged to be eligible for inclusion by both reviewers on the basis of titles and/or abstracts were excluded when examined in more detail during full text assessment (three papers), study classification (two papers) or data extraction (two papers). Two of these were commentaries on included studies and therefore did not represent primary research and three were ultimately judged not to have targeted patients with difficult asthma despite indications to the contrary in the abstracts. A further two described interventions that, as detailed in Chapter 3, it was decided did not ultimately meet inclusion criteria, namely computer-based education and a programme that appeared to be aimed **solely** at parents of children with difficult asthma.

A total of 276 citations associated with 188 independent studies were ultimately selected for inclusion in the review and classified.¹⁸²⁻⁴⁵⁷ The eligibility status of the largest proportion of the included citations (38%) was initially assessed as unclear by both reviewers, 30% were initially judged to be unclear by one reviewer and 26% were initially identified as suitable for inclusion on the basis of titles and abstracts alone by both reviewers. There was disagreement at the initial inclusion stage regarding 5% of the citations ultimately included and 1% were in the first instance excluded by both reviewers but later included on the basis of information contained in other papers associated with the same studies. A further 19 citations excluded in their own right^{53,458-475} were retrieved to provide additional information on the patients or interventions assessed in included studies. A listing of all

documents identified in relation to each study is provided in Appendix 7.

There were an additional 29 papers^{476–504} associated with 28 studies, whose eligibility status remained unclear in the absence of additional information. Brief details of these are provided in Appendix 8. Five potentially relevant papers identified too late for assessment and inclusion in the review, are listed in Appendix 9. Details of all excluded references are not provided in this report owing to their large number but are available on request from the authors. Around one-third of citations were excluded on the basis that they were not or did not appear to be references to primary research studies. Of those that were primary research, the main reason for exclusion was lack of evidence to suggest that patients with difficult asthma were targeted.

Author contacts

Contacts with authors were attempted or made in relation to around 100 studies at various stages in the review process. Queries mainly related to:

- needing further details to determine eligibility in relation to the patients and/or interventions studied
- needing further details (e.g. on age of patients targeted) to allow study classification
- clarification regarding overlap of multiple publications by the same authors
- follow-up for further publication of studies in progress, reported only as abstracts or providing only descriptive information

Responses were received from approximately 40 authors. Details of author contacts in relation to included studies are provided in Appendix 7 and those attempted in relation to studies where eligibility status remained unclear in Appendix 8.

General characteristics of included studies

Language

Twenty citations associated with 20 different studies (11% of total) were to documents in languages other than English (seven Japanese,^{328,329,354–357,435} four French,^{196,220,274,293} two each of German,^{320,421} Italian^{326,451} and Spanish^{254,300} and one each of Swedish,⁴²⁰ Russian³⁴¹ and Portuguese⁴¹⁰). Of these, 10 (three French,^{196,220,274} two each of Spanish^{254,300} and German^{321,421} and one each of Italian⁴⁵¹ and Portuguese⁴¹⁰) did not have English abstracts.

Details of only three of the studies represented by these papers had also been published in English language articles (one each of the Spanish,^{252–254} German^{319–322} and Swedish^{419,420} papers).

Types of publication

Of all the 276 citations providing information relevant to included studies, 197 were references to published journal articles, short research reports, news items or magazine-style articles. Fifty-four were references to conference abstracts, 14 to abstracts from current research registers, nine to theses and two to book chapters.

There were 31 studies for which published articles or short reports in journals or magazines were not identified. Details of 26 studies were found in abstracts from conferences or research registers only and five in theses. The majority of these were from the last 3 years and therefore tended to represent recently completed or ongoing research. This still left six studies from the late 1990s, two from the early 1990s and two from the 1980s that appeared to remain unpublished in journals by the end of 2002. Further details of the types of data sources consulted in relation to each study are provided in Appendix 7.

Publication dates

The number of studies included in this review by their latest year of publication in 5-yearly intervals is shown in *Figure 3*. There appears to have been a rapid increase in research in this area over the last 10 years, with the largest number of studies in total (26 or 14% of the total) identified as either published or ongoing in 2002. However, this may also be reflective of the increasing number of research publications in general.

Study classification

All 188 included studies underwent classification. Of these, 108 (57%) were studies of children (107) or primarily children (1), 68 (36%) were studies of adults (65) or primarily adults (3), in nine (5%) the age group targeted was unclear and three (2%) targeted all ages but included adult and child subgroups. As shown in *Table 7*, in the first instance, classification details were used to grade studies along two dimensions related to study design and the degree to which difficult asthma was judged to have been targeted.

It is immediately apparent that the number of studies representing the best available evidence in this field, according to the two dimensions related to methodological quality and relevance, is relatively small as a proportion of the whole.

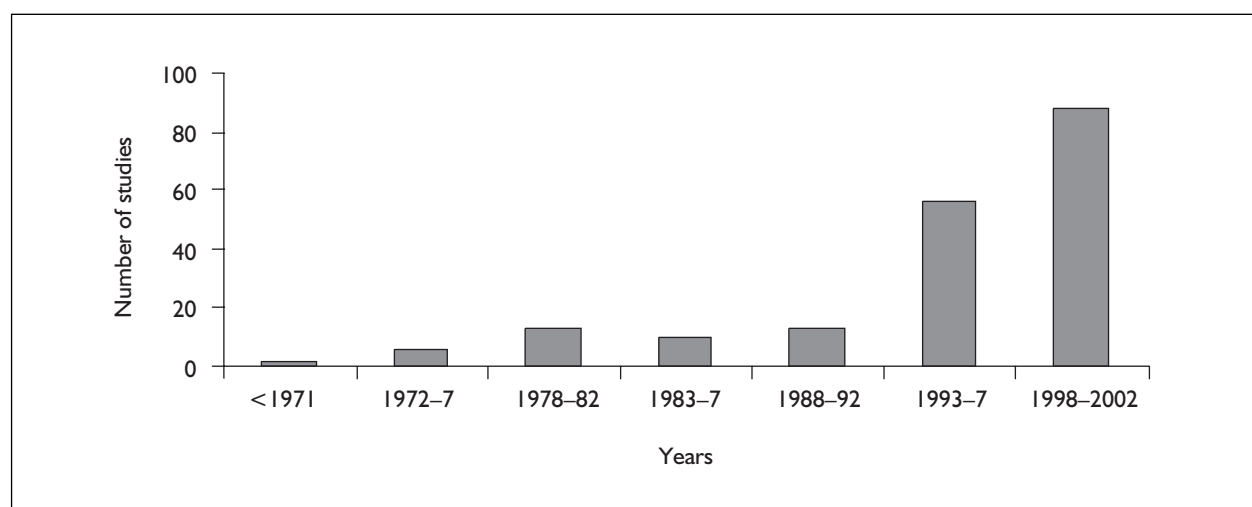


FIGURE 3 Included studies by date of most recent publication

TABLE 7 Grading of included studies along dimensions related to study design and the degree to which they were judged to have targeted difficult asthma

| Targeting of difficult asthma | Randomised trials | Controlled trials | Controlled prospective observational | Controlled retrospective observational | Before-and-after studies | Descriptive studies | Total |
|-------------------------------|-------------------|-------------------|--------------------------------------|--|--------------------------|---------------------|----------|
| Definite | 1 | 1 | 2 | 1 | 11 | 5 | 21 (11%) |
| Probable | 16 | 2 | 1 | 3 | 25 | 4 | 51 (27%) |
| Possible | 21 | 3 | 4 | 2 | 26 | 12 | 68 (36%) |
| Insufficient | 23 | 0 | 2 | 2 | 9 | 12 | 48 (26%) |
| Total | 61 (32%) | 6 (3%) | 9 (5%) | 8 (4%) | 71 (38%) | 33 (18%) | 188 |

There are only 20 studies, representing 11% of the total, in the first two categories along each dimension. Data extraction was only undertaken on studies meeting a minimum threshold in terms of their study design and targeting of difficult asthma but, owing to the small numbers of studies of high quality and relevance, the cut-off was at a level where it was felt that studies could provide potentially useful information to answering the review questions posed without introducing a high degree of bias or excessively diluting the pool of difficult asthma patients in which effects were examined. A brief commentary on other details documented during study classification for the studies which were not reviewed further is provided below with reference to summary tables in Appendices 10–12. Further details of the studies from which data were extracted are provided in the following two chapters, divided according to whether they targeted children or adults.

Descriptive studies

Attempts were made to match descriptive studies or publications that did not report formal evaluations of interventions to reports of quantitative evaluations and authors were contacted, where possible, to establish whether one had been conducted. However, in the absence of any further information being obtained or identified, 33 studies (23 in children,^{182–212} five in adults^{213–217} and five in which the age group targeted was unclear^{218–222}) were not reviewed beyond the study classification stage on the basis that they were not formal evaluations and simply described characteristics of an individual psycho-educational programme, presented data on characteristics of participants at baseline only or reported narrative case studies of patients recruited to such programmes. Brief descriptions of patients targeted and details on the components of the interventions in these studies

TABLE 8 Breakdown of descriptive studies by age group, degree to which they targeted difficult asthma and intervention type

| Intervention type | Targeting of difficult asthma | | | | | | | | | All |
|-------------------|-------------------------------|-------|----------|-------|-------------|----------|-------|--------------|-------------|-----|
| | Definite | | Probable | | | Possible | | Insufficient | | |
| | Child | Adult | Child | Adult | Age unclear | Child | Adult | Child | Age unclear | |
| Education | 0 | 1 | 0 | 0 | 0 | 6 | 1 | 6 | 3 | 17 |
| Self-management | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 2 |
| Psychosocial | 2 | 0 | 1 | 2 | 0 | 1 | 1 | 0 | 0 | 7 |
| Multifaceted | 2 | 0 | 0 | 0 | 1 | 2 | 0 | 1 | 1 | 7 |
| All interventions | 4 | 1 | 1 | 2 | 1 | 10 | 2 | 8 | 4 | 33 |
| | 5 | | 4 | | | 12 | | 12 | | |

are provided in Appendix 10. A summary breakdown of studies by age group, the degree to which they targeted difficult asthma and intervention type is provided in *Table 8*. No formal qualitative studies of relevant interventions in appropriate patients were identified.

Studies with insufficient targeting of difficult asthma

Of the studies reporting a formal evaluation of a psycho-educational intervention, 36 were not reviewed further because they were judged to have insufficient targeting of patients with difficult asthma (18 in children,²²³⁻²⁵¹ 13 in adults,²⁵²⁻²⁶⁹ three in which the age group was unclear²⁷⁰⁻²⁷² and two that included adult and child subgroups^{273,274}). Further descriptions of patients, details on the components of the interventions and types of outcomes assessed in these studies are provided in Appendix 11.

This category of studies covered those in which the sample could include patients recruited solely on the basis of a single emergency attendance and studies that targeted a population with identified socio-demographic/economic risk factors for difficult asthma (e.g. ethnic minority, poor) purely on the basis of geographical location. These types of studies were not reviewed further for a number of reasons, as outlined below.

In relation to the studies targeting accident and emergency attenders, first, there is an existing Cochrane review in children¹⁰⁵ and a protocol for a Cochrane review in adults¹¹³ which examine educational interventions for patients attending the emergency room for asthma. Given the potential substantial overlap with this review, we did not want to duplicate work already being

done. Second, it was evident in some studies, where no mention was made of the sample targeted being potentially at risk, that A&E attenders appeared to be recruited solely on the basis of convenience. Third, although providing some evidence of poor asthma control, in comparison with other risk factors, a single emergency attendance was deemed not to be a strong indicator of potentially difficult asthma. Emergency attendance can be influenced by many factors other than asthma severity, asthma control or psychosocial factors indicative of patients being at risk, in particular the absence of alternative medical care. Indeed in the USA in particular, use of emergency departments has until relatively recently been the normal point of access to care for some population subgroups.

For the studies that targeted potentially at-risk populations on the basis of geographical locations alone, it was not always clear whether the characteristics of the population provided an *a priori* reason for conducting the study or were simply observed during the course of the study when its location had been purely coincidental. In targeting an entire population with asthma, it was also felt by the review team that without any further explicit selection criteria, those most at risk within these populations would be least likely to participate or remain in studies.

Of the 36 studies judged to have insufficient targeting of difficult asthma, half targeted patients on the basis of geographical location and half recruited at least some patients on the basis of a single emergency attendance alone. In both types of studies, the proportion of patients with difficult asthma in the samples recruited, although probably higher than in a general population of asthmatic patients, was expected to be small.

TABLE 9 Breakdown of studies with insufficient targeting of difficult asthma by age group, method of targeting and intervention type

| Intervention type | Child | | Adult | | Age unclear | | Child and adult subgroups | | All |
|-------------------|-------|------------|-------|------------|-------------|------------|---------------------------|------------|-----|
| | A&E | Geographic | A&E | Geographic | A&E | Geographic | A&E | Geographic | |
| Education | 4 | 9 | 2 | 1 | 0 | 2 | 1 | 0 | 19 |
| Self-management | 2 | 2 | 7 | 1 | 0 | 0 | 1 | 0 | 13 |
| Psychosocial | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Multifaceted | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 4 |
| All interventions | 18 | | 13 | | 3 | | 2 | | 36 |

TABLE 10 Breakdown of studies with insufficient targeting of difficult asthma by age group and study design

| Design | Child | Adult | Age unclear | Child and adult subgroups | All |
|------------------|-------|-------|-------------|---------------------------|-----|
| RCT | 11 | 11 | 0 | 1 | 23 |
| CCT | 0 | 0 | 0 | 0 | 0 |
| CPOS | 2 | 0 | 0 | 0 | 2 |
| CROS | 0 | 0 | 1 | 1 | 2 |
| Before-and-after | 5 | 2 | 2 | 0 | 9 |
| All designs | 18 | 13 | 3 | 2 | 36 |

TABLE 11 Outcomes reported as assessed by studies with insufficient targeting of difficult asthma

| Outcome type | Child | Adult | Age unclear | Child and adult subgroups | All |
|----------------|-------|-------|-------------|---------------------------|-----|
| A&E attendance | 15 | 12 | 2 | 1 | 30 |
| Admissions | 13 | 8 | 2 | 0 | 23 |
| Symptoms | 8 | 6 | 2 | 0 | 16 |
| Medication use | 5 | 7 | 2 | 1 | 15 |
| Self-care | 6 | 6 | 1 | 1 | 14 |
| QoL | 6 | 6 | 2 | 0 | 14 |

A breakdown of studies with insufficient targeting of difficult asthma by age group, method of targeting and intervention type is provided in *Table 9*. As can be seen, there were no studies within this category that examined psychosocial interventions.

A breakdown of studies with insufficient targeting of difficult asthma by age group and study design is provided in *Table 10*. As can be seen, the majority were RCTs. Six studies provided some information on both costs and effectiveness (see Appendix 11).

As shown in *Table 11*, the most commonly reported types of outcomes for these studies were emergency attendances, admissions, symptoms, medication use, self-care behaviour and QoL.

Before-and-after studies

Although they represented the largest proportion of studies identified (nearly 40% of the total), the 62 before-and-after studies (32 in children,^{275–313} 29 in adults^{314–361} and one in which the age group was unclear³⁶²) that were judged to have sufficiently targeted patients with difficult asthma were not reviewed beyond the study classification stage. There were deemed to be a sufficient number of controlled studies to contribute useful data for the review and, owing to the problem of regression to the mean, particularly when targeting high-risk groups, it was expected that before-and-after studies would introduce unnecessary bias in assessing results. Although potentially able to inform the review in terms of clarifying descriptions of patients and highlighting

TABLE 12 Breakdown of before-and-after studies by age group, degree to which they targeted difficult asthma and intervention type

| Intervention type | Targeting of difficult asthma | | | | | | | All |
|-------------------|-------------------------------|-------|----------|-------|----------|-------|-------------|-----|
| | Definite | | Probable | | Possible | | | |
| | Child | Adult | Child | Adult | Child | Adult | Age unclear | |
| Education | 2 | 3 | 5 | 1 | 6 | 4 | 0 | 21 |
| Self-management | 0 | 0 | 1 | 1 | 2 | 3 | 1 | 8 |
| Psychosocial | 3 | 0 | 4 | 5 | 4 | 3 | 0 | 19 |
| Multifaceted | 1 | 2 | 3 | 5 | 1 | 2 | 0 | 14 |
| All interventions | 6 | 5 | 13 | 12 | 13 | 12 | 1 | 62 |
| | 11 | | 25 | | 26 | | | |

TABLE 13 Outcomes reported as assessed by before-and-after studies

| Outcome type | Child | Adult | Age unclear | All |
|----------------------|-------|-------|-------------|-----|
| A&E attendance | 22 | 18 | 1 | 41 |
| Admissions | 18 | 14 | 1 | 33 |
| Medication use | 8 | 11 | 1 | 20 |
| Self-care | 11 | 9 | 0 | 20 |
| Symptoms | 10 | 9 | 0 | 20 |
| Knowledge | 11 | 7 | 0 | 18 |
| Respiratory function | 8 | 9 | 0 | 17 |

further options for intervention, time did not permit the extraction of descriptive data related to these factors from all studies identified. Readers are referred to Appendix 12 for further descriptions of patients, details on the components of the interventions and types of outcomes assessed in individual before-and-after studies.

A breakdown of the before-and-after studies by age group, degree to which they targeted difficult asthma and intervention type is provided in *Table 12*. There were a very wide range of interventions evaluated and different patient groups targeted in these studies. In nine studies (eight in adults, one in children), the patients demonstrating characteristics associated with difficult asthma comprised only a subgroup of the total sample (see Appendix 12).

Fourteen before-and-after studies (seven in children, seven in adults) provided some information on both costs and effectiveness (see Appendix 12). As can be seen in *Table 13*, the most commonly reported types of outcomes for these studies were emergency attendances, admissions, medication use, self-care behaviour, symptoms, knowledge and respiratory function.

Studies selected for in-depth review

After removal of descriptive studies, studies with insufficient targeting of difficult asthma and before-and-after studies, 57 studies with independent control groups remained for data extraction and in-depth review.³⁶³⁻⁴⁵⁷ Of these, 18 were initially tagged as reporting assessment of costs in monetary terms for consideration in the economics part of the review.

Descriptions of controlled studies and assessment of their results in the light of the review questions are provided in the following two chapters, which divide studies according to whether they targeted children or adults. One study (Garrett⁴⁰⁴) targeted adults and children but provided some information on subgroups by age and is therefore included in both chapters. Where data were not reported for child and adult subgroups separately in this study, results are presented in the adult chapter since the majority of the sample were adult patients aged over 15 years (55% in the intervention group, 53% in the control group). A recently completed study (Griffiths³⁹⁰⁻³⁹³) targeted both adults and children, although the sample was comprised of marginally more children (53%) than adults, so this is reviewed in the chapter on children.

Chapter 5

Results: studies in children

Overview

The initial part of this chapter provides a descriptive overview of characteristics associated with general features, patients, interventions and methodological quality for the studies of psycho-educational interventions in children that were selected for in-depth review. Reference is made to Appendices 13–20 for detailed information in relation to these facets for individual studies. Unless indicated otherwise by the use of quotation marks, all data presented rely on paraphrasing from original data sources.

The latter part of this chapter begins with an overview of the comparisons, outcomes and follow-up assessed in studies considered for inclusion in a qualitative and quantitative synthesis of effectiveness results and then provides a summary of results in relation to each outcome.

The final section presents information on study quality, costs and cost-effectiveness for the smaller number of studies in children identified for inclusion in the economics part of the review. Reference is made to Appendices 22 and 23 for detailed data in relation to individual studies.

Quantity and quality of information available for data extraction

Detailed data were extracted from 66 published papers and other documents^{363–428} associated with 35 studies in children and one study which included adult and child subgroups (Garrett⁴⁰⁴). For the majority of studies, data were available from one or more published English language journal articles, sometimes accompanied by foreign language papers, conference abstracts, theses and unpublished manuscripts. For two studies data were extracted from unpublished PhD theses (Catrambone,³⁸⁶ Gold⁴¹⁸), for one study data came from a short research report, thesis and two abstracts (McNabb^{412–415}) and one further study was published as a short research report only (Shields³⁷⁷), but additional abstracts excluded in their own right were consulted to provide additional details on the intervention.^{464–467} All of these were in English.

For six studies, available data were more limited. For three, information was extracted from one or more conference abstracts alone (Kirk,^{426–428} Weder,³⁸⁴ Wilkening⁴²¹), the last of which was translated from German. One Portuguese paper could not be obtained so data extraction was based solely on a translation of the study abstract (Westphal⁴¹⁰). An unpublished manuscript (subsequently published some time after completion of our review⁵⁰⁵) was provided by the author in relation to one recently completed study and supplemented various abstracts identified from searches (Griffiths^{390–393}). In the case of one further ongoing study, the only available data came from an abstract of research in progress supplemented by information from the Internet and contact with the study principal investigator (Madge, 2002³⁷⁵).

Summary data presented in this chapter therefore reflect details of studies as they were reported at the time our review was conducted and not necessarily in terms of what was actually done as this could not always be determined.

General study characteristics

Overall study quality and relevance

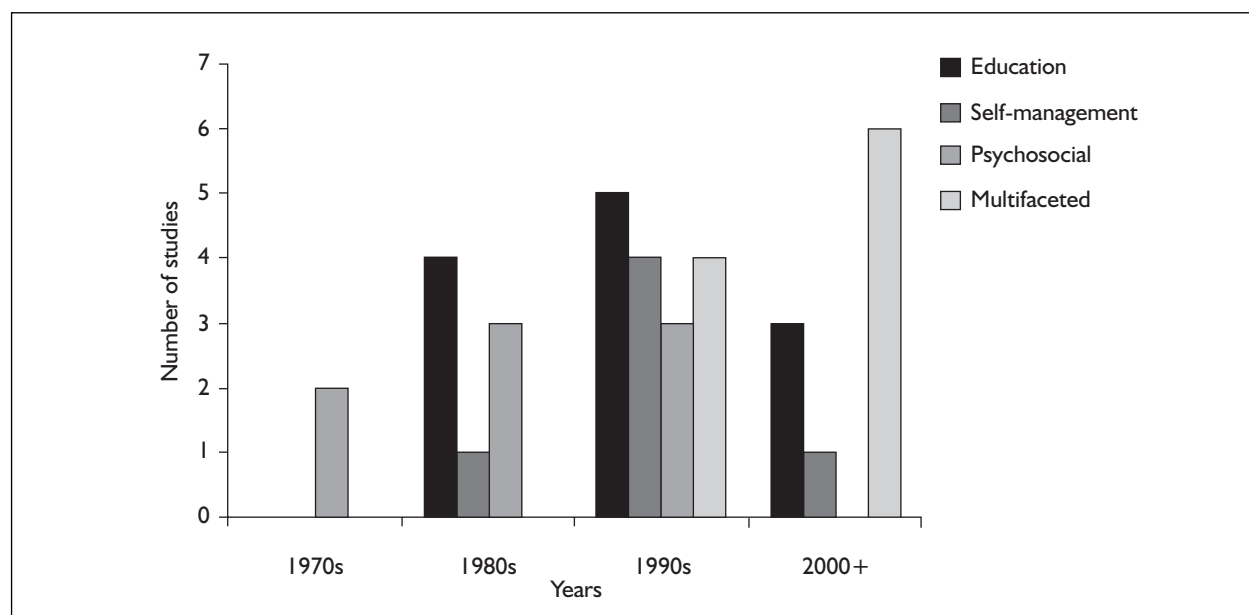
The distribution of studies in children from which data were extracted along the two dimensions related to study design and degree to which difficult asthma was targeted is shown in *Table 14*. A full listing of these studies with basic information collated at the study classification stage on the patients, types and main components of the interventions and types of outcomes assessed is provided in Appendix 13.

Publication dates

Two studies were published in the 1970s (Alexander, 1972,³⁶³ Davis^{382,383}), eight in the 1980s (Alexander, 1988,⁴⁰² Backman,³⁸⁵ Evans,⁴⁰³ Gold,⁴¹⁸ Gustafsson,^{419,420} McNabb,^{412–415} Mitchell,³⁷⁶ Westphal⁴¹⁰), 16 in the 1990s (Colland,³⁷⁸ Collins,⁴⁰⁷ Dahl,³⁸¹ Fisher,^{408,409} Garrett,⁴⁰⁴ Greineder,^{387–389} Hanson,^{394–396} Lewis,^{424,425,472,473} Madge, 1997,⁴¹¹ Ronchetti,⁴¹⁶ Shields,^{377,464–467} Vazquez,⁴⁰⁶ Weder,³⁸⁴ Weinstein,^{364–373} Wesseldine,⁴¹⁷ Wilkening⁴²¹) and

TABLE 14 Grading of studies in children along dimensions related to study design and degree to which they were judged to have targeted difficult asthma

| Targeting of difficult asthma | RCTs | CCTs | CPOS | CROS | Total |
|-------------------------------|----------|---------|---------|--------|----------|
| Definite | 0 | 1 | 0 | 1 | 2 (5%) |
| Probable | 11 | 2 | 1 | 1 | 15 (42%) |
| Possible | 14 | 1 | 3 | 1 | 19 (53%) |
| Total | 25 (69%) | 4 (11%) | 4 (11%) | 3 (8%) | 36 |

**FIGURE 4** Studies of different types of interventions in children by date of most recent publication

10 have been published since 2000 or have been recently completed and remained unpublished as journal articles at the time of this review (Bonner,⁴²² Catrambone,³⁸⁶ Cowie,³⁷⁴ Griffiths,³⁹⁰⁻³⁹³ Harish,⁴²³ Kelly,^{379,380} Kirk,⁴²⁶⁻⁴²⁸ Krieger,^{405,471} Madge, 2002,³⁷⁵ Sullivan^{397-401,468-470}). The breakdown of studies by decade of publication according to the main type of intervention evaluated is shown in *Figure 4*. In line with similar research in the paediatric asthma field as a whole, psycho-educational interventions for difficult asthma in children really began to be developed during the 1980s with a rapid growth in this area during the 1990s, which seems to be continuing to the present day. There appear to have been an increasing number of studies of multifaceted interventions in recent years.

Readers are referred to the 'Overview' section in Chapter 4 (p. 31) for conventions used in referring to and referencing individual studies throughout this chapter. Please note that references associated with each study (referred to

by key author surname and year where necessary) are provided when they are first mentioned in this chapter but are not repeated throughout subsequent sections or tables. For ease of reference, details of all associated citations are provided with the alphabetical listing of studies in Appendix 7.

Country and setting

Over half of the studies in children were conducted in the USA (Alexander, 1972, 1988, Bonner, Catrambone, Davis, Evans, Fisher, Gold, Greineder, Hanson, Harish, Kelly, Kirk, Krieger, Lewis, McNabb, Shields, Sullivan, Weinstein), five were conducted in the UK (Collins, Griffiths, Madge, 1997, 2002, Wesseldine), eight in other European countries [two each in Switzerland (Weder, Wilkening) and Sweden (Dahl, Gustafsson), one each in The Netherlands (Colland), Finland (Backman), Spain (Vazquez) and Italy (Ronchetti)], two in New Zealand (Garrett, Mitchell) and one each in Canada (Cowie) and Brazil (Westphal). This is shown in

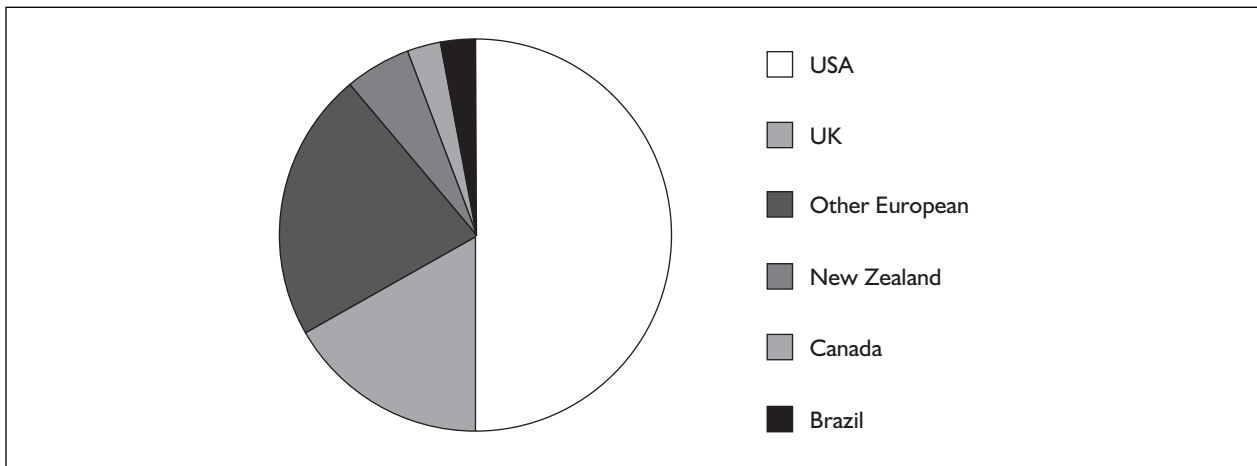


FIGURE 5 Countries in which studies in children were undertaken

Figure 5. There were no clear patterns regarding the type of interventions studied in different countries; however, the only two studies judged definite in terms of their targeting of difficult asthma were conducted in the USA.

Three studies were set in tertiary care centres (Alexander, 1972, Davis, Weinstein), 21 in secondary care (Alexander, 1988, Backman, Colland, Collins, Cowie, Dahl, Gold, Gustafsson, Harish, Kelly, Kirk, Lewis, Madge, 1997, 2002, McNabb, Ronchetti, Vazquez, Weder, Wesseldine, Westphal, Wilkening), three in primary care (Catrambone, Greineder, Griffiths), six in the community (Fisher, Garrett, Hanson, Kreiger, Mitchell, Shields), one in a school (Evans) and two across combinations of secondary care, primary care and the community (Bonner, Sullivan). All the studies set in the community or school environment evaluated educational interventions. Perhaps not surprisingly, the only studies that were judged to be definite in terms of their targeting of difficult asthma were set in tertiary centres.

Collaborations and funding

Most studies (21) were conducted via collaborations between clinical and academic institutions, of which five also involved collaborations with government and/or community organisations. Five involved academic departments alone, five clinical organisations alone, three academic institutions with other (government or commercial) organisations and one a government health department alone. In one study for which only an abstract was available, the organisation(s) involved was unclear (Westphal). Twenty-three of the 36 studies provided details of research funding sources. Of these, half (12 studies) received

funding from more than one source with 10 in receipt of funding from what appeared to be charitable organisations, 11 from government departments, four from research councils or bodies, five from commercial organisations and three from other sources.

Patients

Summary characteristics of the patients targeted by each individual study, graded from definite to possible in terms of the degree to which they were judged to target patients with difficult asthma, are provided in Appendix 14. This supplements the brief description of patients collated at the study classification stage and given in Appendix 13.

Targeting of difficult asthma

Only two studies were rated as definite in terms of their targeting of difficult asthma. One described asthma as intractable to treatment (Alexander, 1972) and the other identified eligible patients on the basis of them having a combination of multiple risk factors related to the use of services, psychosocial factors or absence from school (Weinstein).

Fifteen studies were rated as probable in terms of their targeting of difficult asthma (Backman, Catrambone, Colland, Cowie, Dahl, Davis, Greineder, Griffiths, Hanson, Kelly, Madge, 2002, Mitchell, Shields, Sullivan, Weder). The patient samples for studies included in this category appeared relatively heterogeneous, but in most cases studies relied upon identification of patients on the basis of good indicators of severe or poorly controlled asthma (e.g. diagnosis of severe asthma,

hospitalisation, high medication use, multiple emergency attendances) in combination with other socio-demographic (e.g. ethnic minority), socio-economic (e.g. low income) or behavioural (e.g. inadequate self-care) risk factors.

Nineteen studies were rated as possible in terms of their targeting of difficult asthma (Alexander, 1988, Bonner, Collins, Evans, Fisher, Garrett, Gold, Gustafsson, Harish, Kirk, Krieger, Lewis, Madge, 1997, McNabb, Ronchetti, Vazquez, Wesseldine, Westphal, Wilkening). Of these, eight targeted patients on the basis of relatively weak indicators of asthma severity or control (e.g. prior emergency attendance with or without hospitalisation, relatively severe asthma, three or more episodes of symptoms in a year) in combination with socio-demographic (e.g. ethnic minority) and/or socio-economic characteristics (e.g. low income, no other source of care) which were often identified on the basis of geographical location alone (Alexander, 1988, Evans, Fisher, Garrett, Gold, Harish, Kirk, Lewis). Six studies targeted patients on the basis of good indicators of severity or poor asthma control alone, namely a diagnosis of severe asthma (Gustafsson, Ronchetti, Westphal) or hospitalisation (Collins, Madge, 1997, Wesseldine). In two studies, patients were included on the basis of demonstrating poor compliance in combination with an emergency attendance or low socio-economic status (Bonner, McNabb). In one study the sample consisted of low income, mostly ethnic minority patients (Krieger), and in another (Vazquez) a subsample of patients with low self-care abilities was identified (although it was stated that they did **not** have severe asthma). In the remaining study (Wilkening), patients were recruited solely on the basis that they were identified as in need of psychological treatment and no further details on the criteria for this were given in the abstract from which data were extracted.

Three studies met difficult asthma criteria for inclusion and/or in-depth review only on the basis of reporting subgroup analyses of patients judged to be at greater risk as part of a larger sample. In one a severe subgroup was identified (Ronchetti), in another a group of patients with low self-care abilities (Vazquez) and in a third study some results were presented separately for an ethnic minority subgroup amongst a larger sample of patients who were admitted to hospital or attending for emergency treatment (Griffiths). A further three studies targeted patients who demonstrated characteristics of difficult asthma in their own right but provided additional subgroup

analyses in those most at risk (Davis, Mitchell, Sullivan). These last studies were graded according to the characteristics of patients included in the subgroup; however, only two (Davis, Mitchell) presented complete results for these patients.

The categories used to grade studies according to their degree of targeting were often not distinct and indeed could be seen to represent an underlying continuum related to degrees of difficult asthma. There was some movement of studies between categories after the study classification stage when detailed data were extracted, and classification was inevitably subjective and influenced by the quality of reporting and specific terms used in papers. In the absence of research evidence on the relative importance of different risk factors in contributing to adverse asthma outcomes, it was also difficult to rate different types of indicators (e.g. ethnicity versus multiple accident and emergency attendances) or combinations of these against each other. Agreement between two reviewers regarding classification was reached, however, in an attempt to minimise subjectivity. The assessment of all studies graded as at least possible in terms of difficult asthma for in-depth data extraction also ensured that relevant studies are unlikely to have been excluded from the discussion contained in this chapter.

A further dimension considered in relation to describing patients for the purposes of the review stems from the fact that our definition of difficult asthma makes reference to 'poor control of asthma despite good medical treatment'. We considered that good medical treatment can be defined as treatment in line with recommended guidelines; however, this implies that what constitutes difficult asthma has changed over time as treatment has improved. In the 10 studies in children published prior to 1990 (see above) and hence the advent of the first asthma guidelines, it is extremely unlikely that the medical care received by patients was in line with current recommendations, although details of this are rarely provided. This may, therefore, call into question the targeting of difficult asthma in these studies. However, even in later studies details of standard medical care against which the definition of difficult asthma can be considered are sparse. Of the 26 studies completed since 1990, 17 made at least some reference to guidelines, but, only in two of these (Hanson, Garrett) was this in relation to the provision of standard care. In most others (Bonner, Cowie, Fisher, Greineder, Griffiths, Harish, Kelly, Kirk, Lewis, Madge, 1997, Sullivan,

Wesseldine) guidelines were referenced in the context of the intervention being based on or involving promotion of guidelines, often owing to identified inadequacies in standard medical care in general or for the particular patients targeted.

Although our grading of studies provides a useful guide regarding the extent to which they targeted difficult asthma, and were therefore relevant to addressing the review questions, the above discussion highlights the complexity of defining difficult asthma and the need for consideration of other factors in making a true assessment of whether individual study samples adequately represent a difficult asthma group. Readers are therefore encouraged to consider the information on patients within individual studies (Appendix 14) in interpreting results which follow later in this chapter.

Recruitment and justification of sample selection

Only 17 of the 36 studies reviewed in depth were judged to provide clear details regarding patient recruitment procedures (i.e. methods, timing and use of incentives for recruitment) and these varied amongst studies (Alexander, 1988, Bonner, Colland, Fisher, Garrett, Gold, Greineder, Griffiths, Harish, Kelly, Kreiger, Madge, 1997, 2002, Mitchell, Ronchetti, Weinstein, Wesseldine). All but two studies, for which only data from abstracts were available (Westphal, Wilkening), were judged to have provided a clear description of the target population, which was usually justified on the basis of disproportionate mortality, morbidity or service use and costs within the types of patients studied. Reference was also made in several studies to complications of asthma as a result of the impact of adverse psychosocial characteristics (e.g. Backman, Colland, Dahl, Kelly, Madge, 2002, Weder). A small number of studies, although they appeared to target patients with potentially difficult asthma, did not make explicit reference to patients being 'at risk' (e.g. Alexander, 1972, Collins, Evans, Gustafsson). Eight studies also included specific criteria related to the severity of asthma or presence of physical, psychosocial or behavioural co-morbidities that would have excluded some of the most at-risk patients from their sample (Alexander, 1972, Gold, Gustafsson, Hanson, Krieger, McNabb, Mitchell, Vazquez). Of note is that one of the studies graded as definite in terms of its targeting of difficult asthma (Alexander, 1972) both failed to provide any explicit reference to patients being at risk and had limiting exclusion criteria.

Further details on patient recruitment rates, retention rates and indications of samples being representative of the target population are provided in the section on 'Study quality' (p. 54).

Age of patients

All but eight studies made reference to the specific age range of children targeted. For those lacking this information, several simply made reference to recruitment of children (Bonner, Collins, Dahl, Ronchetti, Weder, Westphal) and in the others the approximate age of patients was able to be ascertained from additional information reported (Backman, Wilkening). Amongst the 26 studies that solely recruited children and provided detailed information on age, 13 targeted school-aged children within the age range 4–19 years (Alexander, 1972, Colland, Davis, Evans, 1987, Fisher, Gold, Gustafsson, Kirk, Krieger, Lewis, McNabb, Sullivan, Vazquez), two specifically targeted teenagers (Cowie, Madge, 2002) and one younger children (Hanson). The others all targeted broad age ranges (Alexander, 1988, Catrambone, Greineder, Harish, Kelly, Madge, 1997, Mitchell, Shields, Weinstein, Wesseldine).

Interventions

Overview

All studies considered in this chapter, by nature of their selection for in-depth review, included two or more groups of patients receiving alternative forms of care. Within all studies, one or more of the groups received an active psycho-educational intervention and if there were multiple interventions meeting the definition of psycho-educational, one was usually identified as primary on the basis of the author's description or it being the most active or intense. Most, but not all, studies also included one or more groups that were referred to as, or could be considered to have received, a non-psycho-educational control treatment, although the nature of this varied and further details are provided in the section that follows. For the purposes of describing the interventions and comparators, all groups within studies were classified as either intervention (i.e. psycho-educational) or control treatments (i.e. non-psycho-educational) on the basis of the terms used by the author or a judgement made regarding the nature and intensity of the care provided.

As described in previous chapters, all studies were classified as educational, self-management, psychosocial or multifaceted on the basis of the

TABLE 15 Intervention providers involved in delivery of psycho-educational interventions of different types to children

| Provider | Education | Self-management | Psychosocial | Multifaceted | All |
|--|-----------|-----------------|--------------|--------------|-----|
| Nurse | 6 | 5 | 1 | 6 | 18 |
| All doctors | 2 | 3 | 2 | 8 | 15 |
| Respiratory specialist | 1 | 1 | 1 | 2 | 5 |
| GP/primary care physician | 0 | 0 | 0 | 2 | 2 |
| Other/unspecified doctor | 1 | 2 | 1 | 4 | 8 |
| Psychologist | 1 | 1 | 4 | 2 | 8 |
| Social worker | 0 | 2 | 2 | 2 | 6 |
| Physio/respiratory therapist | 1 | 0 | 1 | 1 | 3 |
| Pharmacist | 0 | 0 | 0 | 1 | 1 |
| Health educator | 2 | 0 | 0 | 1 | 3 |
| Community worker | 2 | 0 | 0 | 0 | 2 |
| Peer or lay educator | 2 | 0 | 0 | 1 | 3 |
| Researcher | 0 | 0 | 1 | 0 | 1 |
| Other (teacher, 'trainer', 'family coordinator') | 0 | 0 | 0 | 3 | 3 |

main components of the primary intervention they evaluated, brief details of which are documented in Appendix 13. For consistency, in the section that follows and in associated Appendices 15–19, summary characteristics and details of studies are presented within the four categories of intervention types and studies are described in relation to the primary intervention evaluated. A discussion of the validity of the intervention classification and its relevance in combining and assessing results of studies in light of an examination of detailed intervention characteristics is made in the 'Summary' at the end of this section (p. 54).

Types of interventions and comparison groups

The 36 studies in children included 43 groups of patients who were judged to have received a psycho-educational intervention. In 12 of these the primary intervention was classified as mainly educational (Alexander, 1988, Collins, Cowie, Evans, Fisher, Garrett, Krieger, Madge, 2002, Mitchell, Shields, Vazquez, Westphal), in six studies a self-management intervention was evaluated (Colland, Kelly, Madge, 1997, McNabb, Ronchetti, Wesseldine), in eight a psychosocial intervention (Alexander, Backman, Dahl, Davis, Gold, Gustafsson, Weder, Wilkening) and in 10 a multifaceted programme involving education, self-management and other add-ons (Bonner, Catrambone, Greineder, Griffiths, Hanson, Harish, Kirk, Lewis, Sullivan, Weinstein).

All but two studies, which compared two educational interventions incorporating environmental assessments of different intensities (Krieger) and multifaceted inpatient versus outpatient rehabilitation (Weinstein), included a

comparison with at least one non-psycho-educational control group. Three included two different forms of control group, two of these a usual care/waiting list control and 'placebo' control comprising minimal education (Colland, Gold), and one (Westphal) medical care delivered via outpatient clinics and usual medical care delivered via emergency services. In all, 26 studies included a comparison with a group of patients who received usual care, of which 16 gave at least some description. Where comparisons of psycho-educational interventions were made with non-standard care, this generally comprised a brief, didactic or unstructured education session or a 'placebo' condition (e.g. sitting quietly for comparison with relaxation training interventions). In one study, for which only an abstract was available, the nature of the comparison treatment was unclear as it just made reference to a comparison with patients from a previous study (Weder). Further details of control groups for the 34 individual studies that included them are provided in Appendix 15.

A number of studies compared more than one psycho-educational intervention with a control group. One evaluated standard and shortened versions of two different self-management programmes, making four interventions in total, against usual care (Ronchetti), one compared education with and without relaxation training to a control condition (Vazquez) and one study assessed two different forms of relaxation training against a control (Davis).

Providers

All but five studies indicated the type of intervention provider. Full details are provided in

Appendix 16. *Table 15* shows that the majority of studies (18) involved nurses in delivery of the intervention and, nearly half (15) involved a medical doctor. Nurses were least commonly involved in psychosocial interventions and, perhaps not surprisingly, psychologists were most commonly involved in delivering interventions of these types. Doctors were most commonly involved in multifaceted interventions, which often included additional medical treatment. A range of other health professionals also contributed to programme delivery across the range of intervention types. In four studies of educational interventions, four of self-management interventions, one of a psychosocial intervention and seven of multifaceted interventions, a team comprising providers of more than one profession were involved in delivery of the intervention.

Just under half of the studies (17) reported on the number of interventionists involved in the delivery of the intervention (Alexander, 1972, Bonner, Catrambone, Colland, Davis, Fisher, Garrett, Gold, Greineder, Gustafsson, Harish, Kelly, Krieger, Madge, 1997, McNabb, Ronchetti, Wesseldine). Details of the number of interventionists were most commonly provided for the self-management interventions, where only one of six studies failed to provide this information, and were least commonly reported for educational interventions where only three of 12 studies provided this information. The number of interventionists ranged from one, in seven studies of self-management, psychosocial and multifaceted interventions, to more than 20, in two studies of educational interventions, with a median number of two.

Although previous specialist training was implicit in the positions held by some of the intervention providers (e.g. Respiratory Nurse Specialists), 15 studies (five educational, three self-management, three psychosocial and four multifaceted interventions) made reference to specific training undertaken or supervision given in relation to provision of the intervention (Alexander, Bonner, Catrambone, Fisher, Garrett, Gold, Greineder, Hanson, Kreiger, Madge, 1997, 2002, Mitchell, Ronchetti, Sullivan, Wesseldine). Seven of these provided some details on the content of the training or supervision, which included education in asthma and its management, instruction in techniques or theory relevant to delivery of the intervention and information on ethical and practical aspects of specific projects. Six studies provided further information on the amount and intensity of the training provided, which ranged

from two meetings with project staff (Gold) to 40 hours of initial training plus 10–20 hours of continuing education (Krieger).

It was apparent in three studies that the intervention provider was also involved in study management, analysis or reporting (Gold, Madge, 1997, Wesseldine). In four studies the intervention provider appeared to be independent from the research aspects of the study (Fisher, Hanson, Krieger, Sullivan). However, in all other cases, it was unclear whether the intervention provider was involved in the study in other ways.

Only eight studies (two educational, one self-management, one psychosocial and four multifaceted interventions) provided additional information on the intervention providers (Bonner, Colland, Garrett, Gold, Greineder, Hanson, Krieger, Sullivan). This included detail about the provider's relevant experience (seven studies), gender (three studies) and shared ethnic, linguistic or cultural background with study participants (four studies).

Structure and timing

Details on the overall structure and timing of the interventions for children are presented in Appendix 16.

Thirty-two of the 36 studies provided information on the size of groups to which the intervention was delivered. In half of these (16 studies) the intervention was delivered to a single child with one or more family members present. Five studies delivered the intervention in medium-sized groups of 5–15 children and one in small groups. In both group formats, family members were also sometimes involved. Six studies delivered the intervention on a one-to-one basis, although it is likely in these that for the youngest participants, adult family members were also in attendance. Four studies used a combination of delivery approaches at different stages of the intervention (Bonner, Fisher, Hanson, Sullivan).

Three-quarters of the studies (27) provided information on the number of intervention sessions delivered, although in some studies the numbers varied according to need (e.g. Alexander, 1988, Garrett, Krieger). The number of sessions ranged from one, in a study of a self-management intervention (Wesseldine), up to a maximum of 21, in a study of family therapy (Gustafsson), although the majority of studies appeared to provide between four and six sessions.

TABLE 16 Intervention settings for psycho-educational interventions of different types in children

| Intervention site | Education | Self-management | Psychosocial | Multifaceted | All |
|------------------------------------|-----------|-----------------|--------------|--------------|-----|
| Inpatient | 1 | 1 | 3 | 0 | 5 |
| Outpatient | 2 | 2 | 2 | 2 | 8 |
| Primary care | 0 | 0 | 0 | 1 | 1 |
| Home | 2 | 0 | 0 | 2 | 4 |
| School | 1 | 0 | 0 | 0 | 1 |
| Other (specific research site) | 1 | 0 | 0 | 0 | 1 |
| Combination (two or more of above) | 3 | 2 | 1 | 5 | 11 |

Twenty-three studies provided details on the frequency of intervention sessions. This ranged from twice daily for one study of relaxation training (Alexander, 1972) up to regular bimonthly contact in two studies of multifaceted interventions (Krieger, Sullivan). In a number of studies the frequency of contacts varied according to patients' needs or at different stages of the intervention (e.g. Alexander, 1988, Greineder, Hanson, Kelly). The majority of studies reporting this information appeared to provide either weekly or monthly sessions. In all cases, however, the frequency of sessions appeared to be related to the duration of the sessions and entire intervention.

Twenty-two studies provided details of the duration of individual intervention sessions. Where stated, this ranged from 20 minutes for a self-management intervention (Wesseldine) and relaxation training (Alexander, 1972) to up to 2 hours for a multifaceted intervention (Greineder). Again, there were sometimes variations according to the needs of individual patients (e.g. Hanson, Sullivan). For the majority of studies intervention sessions appeared to last between 30 and 60 minutes.

The duration of the entire intervention package was able to be ascertained for 29 studies. This ranged from the time required to deliver a single self-management intervention session (Wesseldine) to up to 2 years in a study of a multifaceted intervention (Hanson). In a number of studies the duration varied according to the needs of individual patients (e.g. Garrett, Weinstein). It was not possible to estimate a total measure of the intensity of interventions (i.e. number of sessions multiplied by the duration of sessions) for more than a small number of studies owing to poor reporting and the different ways in which data were provided; however, where this could be ascertained, it ranged from 20 minutes (Wesseldine) to approximately 8 hours (Ronchetti).

In one-quarter of studies the intervention followed an asthma episode, either a hospital admission for asthma, emergency attendance or recent attack (Collins, Cowie, Garrett, Griffiths, Harish, Mitchell, Madge, 1997, Wesseldine, Wilkening). The timing of the start of the intervention from the acute event was not always clear.

Only 14 studies provided all of the above details related to the structure and timing of the intervention. There did not appear to be any clear patterns with respect to these characteristics across interventions of different types and there were large variations with respect to format, intensity and timing.

Setting

All but five studies indicated the setting for delivery of the primary intervention evaluated. Full details for individual studies are provided in Appendix 16 and summarised for different types of interventions in *Table 16*. This shows that for 11 of the 31 studies in which details of the intervention setting were provided, the intervention was delivered in two or more of an inpatient, outpatient, primary care, home, school or other setting. The most commonly reported single site for psycho-educational interventions in children was an outpatient facility, followed by delivery during an inpatient stay and at home. Only one multifaceted intervention was delivered solely in primary care (Griffiths) and one educational intervention in a school (Evans). There did not appear to be any clear patterns with respect to the setting for interventions of different types.

Intervention quality issues

Piloting and standardisation

Eight studies, three of educational interventions (Evans, Kreiger, Garrett), two of self-management (McNabb, Ronchetti), one of a psychosocial intervention (Gustafsson) and two of multifaceted programmes (Greineder, Lewis), made reference to

a pilot study being conducted. One study of an educational intervention was itself stated to be a pilot study (Collins). Nineteen studies made reference to attempts at standardisation of the intervention (Alexander, Bonner, Colland, Collins, Dahl, Davis, Evans, Gold, Hanson, Krieger, Lewis, Madge, 1997, McNabb, Ronchetti, Shields, Sullivan, Vazquez, Wesseldine, Wilkening). This included the use of predeveloped and tested standardised programmes (three studies), use of an intervention protocol, guidelines or booklet (seven studies), recording delivery of the intervention (two studies), training of providers (three studies) and maintaining consistency in terms of the intervention provider (two studies) and/or setting and timing of the intervention (two studies). One intervention was referred to as standardised but no details were provided in the abstract available for data extraction on how this was ensured (Wilkening).

Rationale and use of theory

Twenty-two studies, eight of educational interventions, two of self-management, five of psychosocial interventions and seven of multifaceted interventions, provided a specific rationale to justify the use of the intervention evaluated (Alexander, 1988, Backman, Bonner, Catrambone, Colland, Collins, Dahl, Davis, Evans, Fisher, Garrett, Gold, Gustafsson, Hanson, Krieger, Lewis, Madge, 2002, McNabb, Sullivan, Vazquez, Weinstein, Wesseldine). Most commonly, this was phrased in terms of the intervention being appropriately targeted or adapted to engage the patients under study, provided justification for the intervention content or presented a rationale for use of specific techniques or delivery methods. Nineteen studies, six of educational interventions, two of self-management, five of psychosocial and six of multifaceted interventions, made reference to application of a specific psycho-educational theory, model or approach in the planning or delivery of the intervention. Most commonly cited were Bandura's social learning and social cognitive theories⁵⁰⁶ and concepts (e.g. self-efficacy) associated with these (McNabb, Sullivan, Hanson, Kreiger, Evans, Colland) and generic behavioural or cognitive-behavioural principles and approaches (Colland, Dahl, Gold, Vazquez, Weinstein, Garrett), which were each referred to by six studies. Two studies each made reference to Prochaska and DiClemente's stages of change model⁵⁰⁷ (Bonner, Kreiger), Leventhal's self-regulation theory⁵⁰⁸ (Madge, 1997, Bonner), specific family therapy approaches (Gustafsson, Weinstein), theories of relaxation training

(Alexander, 1972, Davis) and the Orem self-care nursing model⁵⁰⁹ (Alexander, 1988, Catrambone). One study applied the Preceed-Proceed model⁵¹⁰ in the design and evaluation of the intervention (Fisher) and two made reference to theories from developmental psychology (Evans, Colland). A few studies cited more than one theory or model.

Tailoring

Two aspects of intervention tailoring were assessed: (1) whether there was evidence of tailoring to the needs of the patient group and (2) whether there was tailoring to the needs of individuals.

Thirteen studies (seven educational, one self-management, five multifaceted interventions) were judged to have made reference to tailoring to the needs of the patient group as a whole, in terms of the intervention being tailored to the general age (five studies), educational or care needs (four studies) and language or socio-cultural background (four studies) of the patients under study (Colland, Collins, Cowie, Evans, Fisher, Greineder, Krieger, Lewis, Madge, 2002, McNabb, Sullivan, Weinstein, Garrett). Two studies also made reference to the timing and delivery of the intervention being arranged to accommodate the anticipated needs of the teenagers under study (Madge, 2002, Cowie).

The second area of tailoring about which a judgement was made related to whether the study referred to the content or delivery of the intervention being individualised in any way. Twenty-two studies explicitly reported that this had been done (Alexander, 1988, Backman, Bonner, Catrambone, Colland, Collins, Cowie, Dahl, Gold, Greineder, Gustafsson, Kelly, Kreiger, Lewis, Madge, 1997, McNabb, Sullivan, Vazquez, Weinstein, Wesseldine, Garrett, Griffiths). However, the degree of individualisation ranged from provision of an individualised management or action plan only (five studies) to complex tailoring of intervention content and delivery on the basis of some form of assessment (eight studies). It should be noted that although some studies did not appear to make specific reference to group or individual tailoring, this could be argued to be explicit in the nature and format of particular interventions (e.g. individual psychotherapy).

Methods and tools for intervention delivery

Details of the broad methods and tools that were reported as being used for delivery of

TABLE 17 Methods of delivery used in psycho-educational interventions of different types for children

| Primary intervention type | Lecture/didactic | Discussion | Skills training | Problem solving | Goal setting | Role play | Games/fun | Formal therapeutic |
|---------------------------|------------------|------------|-----------------|-----------------|--------------|-----------|-----------|--------------------|
| Education | 6 | 8 | 11 | 3 | 1 | 4 | 3 | 3 |
| Self-management | 4 | 4 | 5 | 2 | 1 | 1 | 1 | 2 |
| Psychosocial | 1 | 3 | 3 | 1 | 1 | 2 | 0 | 8 |
| Multifaceted | 3 | 9 | 8 | 4 | 1 | 4 | 2 | 3 |
| All studies | 14 | 24 | 27 | 10 | 4 | 11 | 6 | 16 |

TABLE 18 Details of formal psychotherapeutic techniques used in psychosocial interventions for children

| Study | Group | Details of psychotherapeutic techniques |
|-----------------|---|---|
| Alexander, 1972 | Systematic relaxation training | Modified Jacobsonian relaxation training procedure involving successively tensing and relaxing muscles in order of hands and forearms, biceps, upper face, calves and feet; no tension, relaxation and warmth emphasised |
| Backman | Psychotherapy and family therapy | Psychotherapy and family therapy (no details provided) |
| Dahl | Behaviour therapy | Behavioural techniques: symptom discrimination training, self-control (relaxation, abdominal breathing, distraction), contingency management (time out) for over-users of services, compliance training, systematic desensitisation to phobic stimuli |
| Davis | Jacobsonian relaxation training assisted by biofeedback | Biofeedback using EMG electrodes attached to forehead amplified to produce feedback signal into headphones. Subject 'hears' muscle tension and told to 'lower the tone' via relaxation techniques (no details of this given but refers to manual/studies) |
| | Jacobsonian relaxation training alone | Relaxation techniques (no details of this given but refers to manual/studies) |
| Gold | Problem-solving conflict management | Problem-solving steps: define problem, generate solutions, evaluate, plan |
| Gustafsson | Family therapy | Family therapy: psychological and pedagogical methods aimed at changing interpersonal relations |
| Weder | Individual psychotherapy | Psychotherapy (no details on content as abstract only) |
| Wilkening | Standardised behavioural therapeutic group programme | Behaviour therapy |

interventions in individual studies are provided in Appendix 17. Summaries are provided in *Tables 17–19*. These data reflect information reported in papers describing studies or details obtained from authors and are particularly subject to variations in the quality of reporting. Four studies, two of educational interventions (Mitchell, Westphal) and two of multifaceted interventions (Catrambone, Kirk), provided little detail on the methods and tools used for delivery of their interventions in the sources available for data extraction.

Delivery methods

A summary of the delivery methods used in interventions of different types is shown in *Table 17*.

As can be seen, the primary intervention in 14 studies involved a lecture or didactic education, although by nature of their inclusion in the review, this was always supplemented by additional delivery methods. Twenty-four studies included formal or informal discussion and/or questioning in groups, families or individually with intervention providers. This commonly covered issues such as experiences with and problems related to asthma management. The most frequently used method for delivery of interventions, applied in 27 studies, was skills training, including training in correct use of inhalers, related equipment and peak flow meters, training in self-management procedures, training in relaxation, breathing or other psychotherapeutic techniques, training in trigger management or training in social skills. Problem

TABLE 19 Supplementary tools used for delivery of psycho-educational interventions of different types to children

| Primary intervention type | Telephone | Written information | Video | Audio | Computer |
|---------------------------|-----------|---------------------|-------|-------|----------|
| Education | 4 | 9 | 1 | 1 | 0 |
| Self-management | 2 | 5 | 0 | 1 | 0 |
| Psychosocial | 0 | 1 | 0 | 0 | 0 |
| Multifaceted | 5 | 4 | 0 | 0 | 1 |
| All studies | 11 | 19 | 1 | 2 | 1 |

solving, in the form of encouraging identification of problems, solutions and strategies for decision-making, was used in 10 studies and in one psychosocial intervention (Gold) enhancement of problem solving skills was the primary focus (see *Table 18*). Four studies used goal-setting or a similar form of behavioural self-monitoring involving action plans, contracts, assignment and/or homework tasks with follow-up or reporting back. Role play or rehearsal of scenarios in relation to management of asthma generally and during attacks, use of communication skills, social situations and family conflicts were used in 11 studies. Despite targeting children, only six studies used educational games, puzzles or fun activities to promote learning.

Sixteen studies made use of formal psychotherapeutic techniques in delivering one or more aspects of the intervention. One educational intervention made use of behavioural techniques (Evans) and another behavioural techniques and formal progressive relaxation training (Vazquez). Two self-management interventions used a range of behavioural or cognitive-behavioural techniques plus relaxation (McNabb, Colland). Amongst multifaceted interventions, two made reference to use of behavioural techniques (Bonner, Weinstein) and one relaxation techniques (Lewis), and in the study by Weinstein a formal psychological assessment was provided along with family therapy where indicated. Since use of formal psychotherapeutic techniques was central to the eight studies classified as examining psychosocial interventions, a detailed summary of the techniques applied in these is provided in *Table 18*.

There were no clear patterns or differences across intervention types in terms of the delivery methods used, except that, not surprisingly, psychosocial interventions more commonly made use of formal psychotherapeutic techniques. The median number of intervention delivery methods used across interventions of all types was four, and this was similar across educational, self-

management and multifaceted interventions. Psychosocial interventions tended to use fewer intervention delivery methods although, as highlighted above, all focused on use of formal psychotherapeutic techniques which are likely to be more powerful than other methods.

Supplementary tools

In addition to use of a range of delivery methods, some interventions supplemented direct patient and provider interaction with other tools. Details of these in relation to individual studies are again provided in Appendix 17 and a summary of tools used by interventions of different types is presented in *Table 19*.

Nineteen studies made use of additional written information, in the form of booklets, information sheets, visual aids, manuals, workbooks, action plans, handouts or diaries, in the provision of their primary intervention. Telephone contact for advice or follow-up comprised part of the intervention in 11 studies and very small numbers of studies made use of information presented via videos (Alexander, 1988), audio material (Vazquez, Colland) and computers (Harish).

One study made reference to the use of a particularly innovative technique in the delivery of the intervention that was not covered by the categories described. There was extensive use of analogy in the study by Lewis, whereby a theme of 'you're in the driver's seat' was used to structure education on management of asthma around references to driving and maintaining a car and obeying warning signs in a similar way to red, yellow and green traffic light signals.

Rationale for delivery methods

Three studies of educational interventions (Evans, Kreiger, Vazquez), two of self-management (McNabb, Colland), three of psychosocial interventions (Alexander, 1972, Backman, Dahl) and one of a multifaceted programme (Bonner) provided a clear rationale for the delivery techniques or tools used. This was phrased in

TABLE 20 Asthma-specific topics covered in psycho-educational interventions of different types for children

| Primary intervention type | Asthma general | Asthma management | | | | | |
|---------------------------|----------------|---------------------|----------------------------|-------------------|--------------------|--------------------|-------------|
| | | Symptom recognition | Self-management principles | Attack management | Symptom monitoring | PEF use/monitoring | Action plan |
| Education | 11 | 6 | 2 | 6 | 3 | 3 | 2 |
| Self-management | 6 | 6 | 6 | 6 | 5 | 4 | 6 |
| Psychosocial | 1 | 2 | 2 | 3 | 1 | 1 | 1 |
| Multifaceted | 9 | 6 | 10 | 9 | 4 | 9 | 10 |
| All studies | 27 | 20 | 20 | 24 | 13 | 17 | 19 |

| Primary intervention type | Asthma medication | | | | Triggers | | |
|---------------------------|-------------------|-------------|------------|--------------|----------|-----------|-------------------|
| | General | Inhaler use | Compliance | Side-effects | General | Avoidance | Attendance issues |
| Education | 9 | 6 | 7 | 2 | 9 | 9 | 4 |
| Self-management | 5 | 4 | 4 | 2 | 5 | 5 | 3 |
| Psychosocial | 2 | 1 | 1 | 1 | 2 | 2 | 0 |
| Multifaceted | 9 | 10 | 7 | 3 | 9 | 9 | 4 |
| All studies | 25 | 21 | 19 | 8 | 25 | 25 | 11 |

terms of proven effectiveness or use of theory in justifying the techniques (with reference to previous research) or use of techniques appropriate to the aims of the intervention.

Content

Asthma-specific topics

An assessment was made of the asthma-specific topics covered by the primary psycho-educational interventions evaluated in studies of children. It should be noted, however, that the accuracy of this information is likely to be extremely susceptible to variations in the quantity and quality of information available for data extraction and the quality of reporting. Details of asthma-specific topics covered by individual studies are provided in Appendix 18 and a summary by intervention type is presented in *Table 20*. Two studies of educational interventions (Madge, 2002, Westphal), two of psychosocial interventions (Weder, Wilkening) and one of a multifaceted intervention (Kirk) provided relatively limited information on the content of their programmes in the sources available for data extraction.

The most commonly covered asthma-specific topics related to development of a general understanding of asthma (e.g. its nature, pathophysiology, causes) and medications for its treatment, followed by general information on triggers and trigger avoidance, attack management, inhaler use, symptom recognition, general principles of self-management, use of an

action plan and issues related to compliance with medications. All these were considered by over half of studies. The median number of topics covered across all interventions was nine, although multifaceted and self-management interventions tended to cover a greater range of asthma-specific topics than educational interventions, and educational interventions more than psychosocial interventions. It is interesting that on the basis of an examination of the detailed content of programmes, the distinction between educational and self-management interventions in particular may be called into question. Two studies initially classified as educational interventions included use of formal self-management plans for at least some of the patients under study (Cowie, Garrett) and one of the self-management interventions did not clearly make reference to use of self-monitoring of symptoms or peak flow in relation to the action plan provided (Ronchetti).

Issues indirectly related to asthma and its management

In addition to topics directly related to understanding asthma and its management, many studies, in line with a more general approach to addressing factors impacting on asthma, evaluated interventions which considered broader issues. Again, it should be noted that the information presented with regard to these factors for individual studies in Appendix 19 and the summary presented in *Table 21* is susceptible to variations in the quantity and quality of

TABLE 21 Issues indirectly related to asthma and its management covered in psycho-educational interventions of different types for children

| Primary intervention type | Smoking | Other health behaviours | Attitude/beliefs | Other psychological issues | Social/family issues | Economic issues | Other issues |
|---------------------------|---------|-------------------------|------------------|----------------------------|----------------------|-----------------|--------------|
| Education | 3 | 2 | 2 | 4 | 5 | 2 | 7 |
| Self-management | 0 | 1 | 1 | 3 | 3 | 0 | 2 |
| Psychosocial | 0 | 1 | 2 | 8 | 4 | 0 | 1 |
| Multifaceted | 4 | 1 | 2 | 5 | 6 | 1 | 1 |
| All studies | 7 | 5 | 7 | 20 | 18 | 3 | 12 |

information available for data extraction and quality of reporting. As above, limited information on content was available from data sources in relation to five studies (Madge, 2002, Westphal, Weder, Wilkening, Kirk).

The most commonly covered topics indirectly related to management of asthma were psychological issues other than those to do with attitudes and beliefs (e.g. management of psychological triggers such as anxiety, concerns, fears or feelings related to asthma, self-esteem, adjustment, symptom perception). Half of studies addressed social, family or communication issues impacting on asthma or its management (e.g. communication with parents, peers and health providers, social support issues, family dynamics, conflicts, social consequences of asthma). Smaller numbers of studies covered issues related to smoking, other health-related behaviours (e.g. exercise, diet), attitudes and beliefs in relation to asthma and its management and the impact of financial problems on management of asthma. A range of other issues, for example, information on services, appropriate use of health services, the impact of asthma on school and career and correct breathing techniques, were also addressed in a number of studies. The median number of issues indirectly related to asthma and its management that were covered across all interventions was two. There was little difference in the number of these issues addressed across interventions of different types but, not surprisingly, a larger number of psychosocial than other interventions considered additional psychological issues impacting on asthma management.

Add-ons to interventions

Although by nature of their inclusion in the review a primary component of the main programme assessed in each study was a psycho-educational intervention, many programmes included non-psycho-educational add-ons that were not received by control groups, where present. As a result of the

definition used, studies classified as evaluating self-management interventions comprised only education plus formal self-management without any additional facets. Two of the five studies classified as assessing self-management interventions, however, did contain minimal medical interventions which were not felt to warrant their classification as multifaceted. One (Madge, 1997) simply provided a supply of oral steroids along with the self-management plan and another (Kelly) provided a flu vaccination and allergy test without any formal instruction related to the latter.

Studies in which the primary programme evaluated was judged to be multifaceted, in addition to education and formal self-management, always included add-ons. Interventions classified as primarily educational or psychosocial could, but were not required to, include other facets and neither included formal self-management. In fact, no psychosocial interventions in children actually included other add-ons. A summary of the numbers of studies of educational and multifaceted interventions including different types of add-ons is therefore provided in *Table 22*.

Details of the add-ons incorporated into educational and multifaceted interventions that included them are provided for individual studies in *Tables 23* and *24*.

Medical treatment

Three educational programmes included medical treatment. The nurse-managed programme of Alexander (1988) included an initial medical evaluation and change in medication under supervision. The young adult asthma programme of Cowie included a medical assessment and adjustment of therapy, details of which were given to the family physician. The intercritical treatment and education programme of Westphal incorporated multi-professional outpatient

TABLE 22 Numbers of studies in children including add-ons of different types

| Primary intervention type | Medical treatment | Exercise | Environmental control | Referral to services | Professional education | Community education |
|---------------------------|-------------------|----------|-----------------------|----------------------|------------------------|---------------------|
| Education | 3 | 2 | 2 | 2 | 1 | 1 |
| Multifaceted | 9 | 1 | 4 | 1 | 5 | 1 |
| All studies | 12 | 3 | 6 | 3 | 6 | 2 |

TABLE 23 Additional components of educational interventions in children

| Study | Intervention | Medical care | Exercise | Environmental control | Referral | Professional education | Community education |
|-----------------|---|--------------|----------|-----------------------|----------|------------------------|---------------------|
| Alexander, 1988 | Nurse-managed programme | Yes | | | | | |
| Cowie | Young adult asthma programme | Yes | | | | | |
| Westphal | Intercritical treatment and education | Yes | | | | | |
| Fisher | Neighbourhood asthma coalition | | Yes | | | Yes | Yes |
| Garrett | Community health care intervention | | | | Yes | | |
| Evans | Self-management programme (Open Airways) | | Yes | | | | |
| Krieger | High intensity education and environmental assessment | | | Yes | Yes | | |
| | Limited education and environmental assessment | | | Yes | | | |

treatment that was only provided to one of the comparison control groups.

Nine of the ten multifaceted programmes were reported to incorporate medical treatment. The inpatient and outpatient rehabilitation programmes evaluated in the study by Weinstein included assessment, medication and treatment of other conditions and the intervention in the Sullivan study incorporated assignment to a primary care physician for those without one. In the study by Bonner, the individualised asthma education intervention included allergy testing and direct contact with doctors as necessary. The paediatric asthma centre evaluated in the study by Harish provided medical assessment and treatment along with allergy testing, and the comprehensive medical care plus education programme provided by Hanson included free comprehensive medical care during clinic visits.

In the study of asthma case management by Catrambone, the intervention incorporated team assessment and primary care physician support. In the study by Greineder, the asthma outreach programme included revision of medication and an allergy consultation for those at risk. The Asma Control y Tratamiento Para Niños (ACTPN) programme in the study by Lewis included initial medical assessment and was adapted to provide additional medical care and community nursing input owing to inadequacies with existing care being identified. In the liaison nurse intervention in the study by Griffiths, an assessment and review of medication was provided.

Exercise

Two educational programmes included exercise as an adjunct to psycho-educational intervention. Sports and other physical activities were incorporated into the Neighbourhood Asthma

TABLE 24 Additional components of multifaceted interventions in children

| Study | Intervention | Medical care | Exercise | Environmental control | Referral | Professional education | Community education |
|------------|---|--------------|----------|-----------------------|----------|------------------------|---------------------|
| Weinstein | Inpatient rehabilitation programme | Yes | Yes | Yes | | | |
| | Outpatient rehabilitation programme | Yes | Yes | Yes | | | |
| Sullivan | Intervention | Yes | | Yes | Yes | Yes | |
| Bonner | Individualised asthma education intervention | Yes | | Yes | | Yes | |
| Harish | Paediatric asthma centre | Yes | | Yes | | | |
| Hanson | Comprehensive medical care plus education intervention (Open Airways programme) | Yes | | | | Yes | |
| Catrambone | Asthma case management | Yes | | | | | |
| Greineder | Asthma outreach programme (education plus follow-up) | Yes | | | | | |
| Lewis | Asma Control y Tratamiento Para Ninos (ACTPN) | Yes | | | | | |
| Griffiths | Liaison nurse intervention | Yes | | | | Yes | |
| Kirk | Education and case management | | | | | Yes | Yes |

Coalition initiative evaluated by Fisher, and the Open Airways self-management programme of Evans included physical activities. Only one multifaceted study appeared to include exercise. The inpatient rehabilitation programme evaluated in the study by Weinstein included 1 hour of training twice daily (running, bicycle, swimming) to assess the effectiveness of pharmacological therapy and increase cardiovascular and pulmonary endurance. The frequency of exercise training in the outpatient programme was unclear.

Environmental control

One study of two educational programmes included environmental control measures (Kreiger). The high-intensity education and environmental assessment intervention evaluated in this study included provision of allergy tests, environmental assessments, equipment, roach and rodent eradication plus advocacy for improved housing. The limited education and

environmental assessment with which it was compared included only the environmental assessment component and provision of bedding covers.

Four studies of multifaceted interventions included environmental control measures. The inpatient and outpatient rehabilitation programmes of Weinstein included a home assessment visit. In the study by Sullivan, patients were provided with pillow and mattress covers, insecticides for cockroach-allergic children and a five-module individualised intervention to deal with specific allergens. The individualised asthma education intervention evaluated in the study by Bonner incorporated a home assessment and provision of equipment or referral to extermination services where necessary. The paediatric asthma centre evaluated in the study by Harish provided anti-allergy equipment and environmental assessment.

Referral to other services

Two studies of educational interventions incorporated referral to other services. The community healthcare intervention in the study by Garrett included referral to or links with a patient's GP as necessary plus contact with other health, mental health or social service agencies or support structures as appropriate. In the high-intensity education and environmental assessment evaluated by Krieger, referrals were made for assistance with toxins and other indoor health concerns and smoking cessation.

Only one study of a multifaceted programme, that of Sullivan, included referral to other agencies, in this case referral for assistance with smoking cessation and psychological or social issues.

Professional education

One educational intervention incorporated professional education. In the study by Fisher, A&E and other staff were involved in the Neighbourhood Asthma Coalition evaluated.

Five multifaceted interventions involved professional education. In the Sullivan study, primary care physicians of intervention patients were sent a care plan, peak flow, spacer and guidelines and followed up if the care was deemed inadequate. The intervention in the Bonner study encouraged use of action plans and diaries by direct contact with professionals where necessary. In the comprehensive medical care plus education intervention programme provided by Hanson, educational contact was made with primary care providers and emergency rooms to emphasise the use of guidelines. As part of the intervention evaluated in the study by Griffiths, nurses liaised with practice staff via two visits regarding guidelines for management of high-risk patients. The intervention evaluated by Kirk involved education of school personnel and primary care physicians.

Community education

One educational programme (Fisher) and one multifaceted intervention (Kirk) incorporated wider community education. The Neighbourhood Asthma Coalition evaluated by Fisher incorporated promotional campaigns via the media and distribution of leaflets. The intervention provided in the Kirk study formed part of a larger community-wide paediatric asthma network initiative.

Summary

In children, no educational or self-management interventions were evaluated in studies with

definite targeting of difficult asthma and multifaceted interventions were the least frequently evaluated types of interventions in studies with possible targeting. There therefore appeared to be a tendency, as might be expected, for interventions aimed at more difficult patient groups to be those considered generally most intensive.

As described in the definitions and methods chapters of this review (Chapters 2 and 3), the initial classification of studies by intervention type was based on the distinctions broadly made to date in Cochrane reviews of psycho-educational interventions for asthma. In the light of the above-detailed assessment of intervention characteristics, however, it appears that this classification is not particularly useful. There appear to be few clear distinctions between educational, self-management, multifaceted and a subset of psychosocial interventions and it is likely in many cases that classification was influenced by the quantity of information available for extraction of data on interventions and the quality of reporting. Further attention to this issue and suggestions for alternative ways of conceptualising interventions are provided in the discussion.

Given the lack of distinction between the different types of intervention, by agreement of the review team, it was decided that all types of psycho-educational interventions would be considered together in the qualitative and quantitative syntheses of results that follow later in this chapter. Although prespecified subgroup analyses are undertaken in relation to intervention types, these should be treated with caution and reference made to specific intervention characteristics provided for individual studies in interpreting and evaluating results.

Study quality

Tables of detailed quality characteristics for individual studies in children, divided by study design, are provided in Appendix 20.

Randomised controlled trials

Twenty-five of the 36 studies in children were classified as RCTs on the basis that they described allocation to groups as random. In 21 studies, the unit of randomisation was the patient. In the remaining four studies, cluster randomisation was undertaken using schools (Evans), general practices (Griffiths), counties (Hanson) and study centres (Ronchetti) as the unit of randomisation.

In the last study there was allocation of patients within study centres to control and intervention groups, but each centre was randomised to receive one of two different intervention programmes. Only the study by Griffiths made clear reference to assessment of clustering effects on the results via conduct of adjusted analyses.

In several studies, randomisation was not straightforward. In five, patients or other units were matched on key characteristics prior to randomisation of one of each pair to groups (Evans, Hanson, Colland, Greineder, McNabb) and four studies undertook stratification of randomisation on one or more variables anticipated to be related to outcomes (Griffiths, Ronchetti, Mitchell, Sullivan).

Randomisation

Only 10 of the 25 RCTs actually described their methods for generating randomisation sequences. Seven used random number tables (Greineder, Lewis, Shields), computer-generated sequences (Griffiths, Wesseldine) or a coin toss (Hanson, McNabb), which are considered adequate approaches to randomisation. One used patient birth dates (Harish) and one date of admission (Wilkening) to determine allocation to groups, both of which are considered inadequate methods.¹⁵⁰ One further study stated that randomisation was based on drawing cards (Madge, 1997) although from the information provided it was unclear whether this constituted an adequate or inadequate approach to the generation of allocation sequences.

Just two studies made reference to concealment of the allocation sequence at randomisation. One of these used central generation of codes to ensure the sequence could not be altered (Cowie), which is deemed to be an adequate method of concealment. The other used serially numbered envelopes (Wesseldine), which are considered still to be open to manipulation.

Outcome assessment

Ten RCTs (Bonner, Evans, Garrett, Griffiths, Gustafsson, Harish, Krieger, Ronchetti, Sullivan, Wesseldine) made reference to at least some degree of blinding for those involved in assessing or scoring outcomes. It should be noted, however, that in several other studies outcome data were largely reliant on self-report, which is less susceptible to detection bias (e.g. Cowie) but potentially more prone to other forms of bias. Blinding of patients and intervention providers is extremely difficult, often impossible, in studies of

psycho-educational interventions, so this aspect of study quality was not formally assessed.

Most RCTs reported the assessment of multiple outcomes over multiple time points (between one and six follow-ups with a median of two), so there was potential for selective reporting and Type I errors given multiple significance testing. Seven studies specified a single primary outcome *a priori* (Catrambone, Cowie, Griffiths, Madge, 1997, McNabb, Sullivan, Wesseldine) and in three further studies a primary outcome was apparent from the reporting of results (Alexander, Harish, Ronchetti). In two ongoing studies (Madge, 2002, Krieger), multiple outcomes were specified as primary, still leaving them open to selective reporting. In 10 studies outcomes were assessed at a single end-point (Alexander, 1988, Bonner, Dahl, Evans, Garrett, Greineder, Krieger, Madge, 1997, Ronchetti, Wilkening), in a further two studies a single primary end-point was specified *a priori* (Cowie, Wesseldine) and in another five a primary end-point was apparent in the results (Catrambone, Griffiths, Lewis, McNabb, Sullivan). Overall, in only nine studies was there clearly both a single primary outcome and end-point (Alexander, 1988, Catrambone, Cowie, Griffiths, Madge, 1997, McNabb, Ronchetti, Sullivan, Wesseldine).

Study samples and attrition

Sample sizes in the RCTs were highly variable, ranging from just 16 patients (McNabb) to 1033 patients in one large multi-centre study (Sullivan). The mean sample size overall was 171 patients, but excluding the large studies by Sullivan and Garrett; where in the latter, analyses in subgroups of children and adults were considered separately for the purposes of this review, the mean sample size was 118.

Only seven studies reported that power calculations, to estimate the required sample size, had been conducted (Catrambone, Cowie, Garrett, Griffiths, Harish, Sullivan, Wesseldine), but it was apparent in at least one of these (Harish) that the final numbers analysed did not meet prespecified targets. There were six studies which were judged to have failed to provide clear patient selection criteria (Catrambone, Harish, Krieger, Madge, 2002, Ronchetti, Wilkening).

The proportion of patients approached who agreed to participate could not be ascertained for 10 studies (Alexander, 1988, Colland, Dahl, Hanson, Madge, 2002, McNabb, Mitchell, Ronchetti, Wesseldine, Wilkening). For only two of these was data extraction limited to abstracts or

information obtained from authors (Madge, 2002, Wilkening), highlighting inadequate reporting of patient flow in a large number of published studies. In the 15 studies that did report patient participation rates, successful recruitment from the population targeted ranged from 28% (Bonner) to 100% (Shields), with a mean participation rate of 68%. In three of the five studies (Griffiths, Garrett, Sullivan, Madge, 1997, Cowie) that assessed the comparability of non-participants, there was some evidence of differences, suggesting only moderate success in recruiting patients representative of the target population as a whole.

Five RCTs (Gustafsson, Krieger, Madge, 2002, Mitchell, Wilkening) failed to present data or report on assessment of the comparability of control and intervention groups at baseline in terms of key prognostic and outcome variables. In two of these, however, data extraction was limited to abstracts or information obtained from authors (Madge, 2002, Wilkening). In one study (Cowie), minor differences between groups were apparent but these were judged unlikely to have any major impact on results. In six studies (Alexander, 1988, Dahl, Evans, Gold, Hanson, Madge, 1997), more major differences were apparent; however, three of these (Evans, Hanson, Madge, 1997) examined the impact of these differences on results by conducting adjusted analyses. In all other studies, groups were reported to be, or appeared to be, similar.

Numbers of patients lost to follow-up could not be ascertained for five studies (Colland, Dahl, Gold, McNabb, Wilkening). Within individual studies, follow-up rates often varied for different outcomes and at different time points. A crude assessment of the minimum follow-up reported by studies suggested this ranged from 52% (Hanson) to 100% (Alexander, 1988, Greineder) with a mean of 80%. Seven studies (Alexander, 1988, Garrett, Greineder, Griffiths, Lewis, McNabb, Sullivan) reported <15% loss to follow-up across all major outcomes, which on some quality scales is considered a maximum acceptable level to prevent attrition bias. In three of the nine studies (Bonner, Cowie, Garrett, Hanson, Harish, Madge, 1997, Mitchell, Ronchetti, Shields) that reported assessment of the comparability of withdrawals with patients remaining in the study, differences were found (Hanson, Harish, Mitchell). In two of these (Hanson, Mitchell) ethnic minority patients were more likely to drop out of the study.

Analysis and reporting of results

Details of the analyses conducted were reported by or could be ascertained from 20 of the 25 RCTs.

Amongst the remaining five, results were not presented in the information obtained in relation to two studies (Madge, 2002, Kreiger), for another data was extracted from an abstract only (Wilkening), but in both the others, details of analyses were not reported in published papers (Mitchell, Shields). Five studies (Catrambone, Cowie, Garrett, Gustafsson, Sullivan) specified that analyses were undertaken on an intention-to-treat (ITT) basis. However, one of these (Cowie) did not actually conduct a full ITT analysis and one presented ITT analyses for some outcomes only (Garrett). A further seven studies, although they did not report doing so, did in fact conduct ITT analyses for one or more outcomes (Alexander, 1988, Greineder, Griffiths, Madge, 1997, Mitchell, Shields, Wesseldine). Fifteen of the 25 RCTs were judged to have adequate reporting of outcome data whereby numerators and denominators were provided for binary outcomes and point estimates (means, medians) plus measures of variability (standard deviations, ranges) for continuous measures. Two of the studies lacking these data were incomplete (Kreiger, Madge, 2002) and for another, information for data extraction was limited to an abstract (Wilkening), again highlighting poor reporting in a significant minority of all the RCTs.

Controlled trials

Four studies in children (Alexander, 1972, Davis, Kelly, Vazquez) were classified as CCTs on the basis that patients were systematically allocated to groups, but this was not done on a random basis. One study in fact described patients as being randomly divided but also stated that groups were matched on key characteristics as far as possible, suggesting that the method of allocation was not truly random (Alexander, 1972). For this reason, the study was classified as a CCT rather than an RCT. Two of the other CCTs (Davis, Vazquez) also made reference to groups being matched on key variables (e.g. age, severity).

Outcome assessment

Only one CCT (Kelly) made reference to those involved in assessing or scoring outcomes being blind to group allocation. Two studies (Davis, Kelly) assessed outcomes at a single time point alone, and the others made assessments at three (Vazquez) and six (Alexander, 1972) time points. In only one of these (Alexander, 1972) was a primary time point apparent in the reporting of results. The results presented for this study also suggested identification of a primary outcome, but no other studies distinguished amongst the multiple outcomes assessed in each case.

Study samples and attrition

Sample sizes for the subgroups of interest in two of the CCTs were extremely small, comprising 12 patients only in each case (Davis, Vazquez). In the other two CCTs, the overall sample sizes were 44 (Alexander, 1972) and 80 patients (Kelly). Patient selection criteria were judged to be clear in all studies but none made reference to power calculations being conducted to estimate required sample size. Only two of the studies reported on patient participation rates, which in both cases were relatively high: 78% in the study by Kelly and 87% in the study by Vazquez. However, neither of these reported on the comparability of non-participants. All CCTs presented data or reported on assessment of the comparability of control and intervention groups at baseline in terms of key prognostic and outcome variables. In two studies, differences between groups were apparent (Kelly, Vazquez) and adjustments to analyses were made in one study to examine the impact of these on results (Vazquez). All but one study (Vazquez) provided details on patient attrition, with the minimum proportion followed up being relatively high in all cases, ranging from 82% (Alexander, 1972) to 100% (Davis). None of the CCTs reported on the comparability of patients who were lost to follow-up.

Analysis and reporting of results

Details of the analyses conducted were reported by or could be ascertained for all four CCTs but none appeared to conduct the equivalent of an ITT analysis by including all patients in the groups to which they were assigned. None of the CCTs were judged to have provided adequate data (numerator and denominator for binary outcomes, point estimates plus measures of variability for continuous data) in reporting results.

Controlled observational studies

Four studies (Collins, Weder, Fisher, Westphal) were initially classified as CPOs in that they appeared to follow-up prospectively an intervention group selected to receive a novel treatment but identified a naturally occurring control group who did not receive this treatment. A further three studies (Backman, Kirk, Weinstein) were initially classified as CROSs since they appeared to identify retrospectively intervention and control groups exposed to different treatments. However, on detailed data extraction, often due to poor reporting or limited information being available for several studies (Weinstein, Kirk, Weder, Westphal), there was considerable uncertainty in some cases regarding whether one or more of the intervention and

control groups was followed prospectively and also considerable overlap between the two categories of observational studies. Although two of the CPOs clearly identified and followed up intervention and control groups prospectively (Collins, Fisher), for one study (Weder) the control group was historical in that it comprised patients from a previous study, and in another, for which only a translated abstract was available, the methods of identification and follow-up were extremely unclear (Westphal). Likewise, in one of the studies classified as a CROS (Kirk), although the control group was clearly identified retrospectively it was unclear how the intervention group had been identified and followed up. In the remaining two studies (Backman, Weinstein), methods of identification and follow-up were also extremely unclear, such that there appeared to be scope for either or indeed both of the groups in each case to be identified and followed up prospectively. For this reason, all these studies are considered together here as controlled observational studies (COSs) although throughout the rest of the report the initial distinction made between them is maintained.

Outcome assessment

None of the COSs made any reference to those involved in assessing or scoring outcomes being blind to group membership. Only one study (Collins) clearly assessed outcomes via a self-reported postal questionnaire, hence in other studies there was potential for considerable bias in assessment of outcomes. Six of the seven observational studies appeared to assess outcomes at a single time point; only the study by Weder, which had four assessment points, did not. A single primary outcome was apparent in the reporting of results for two studies (Weinstein, Backman), but in neither case had this been specified *a priori*.

Study samples and attrition

Sample sizes in the COSs were variable, ranging from just 20 patients (Collins) to 249 (Fisher), with a mean of 77. Data on numbers were not reported in the abstract available for one study (Westphal). Four of the seven studies were judged to have provided clear patient selection criteria (Fisher, Weder, Kirk, Weinstein). None made reference to power calculations being conducted to estimate required sample size. Only three studies provided data on the patient participation or inclusion rates, with two reporting inclusion of 100% of patients identified (Backman, Weinstein) and one a 72% participation rate (Fisher). Two studies (Westphal, Collins) did not report assessment of or

present data on the comparability of groups at baseline. In the remaining five, three (Backman, Kirk, Weinstein) found differences between the groups but none examined the impact of these on results by conducting adjusted analyses, hence outcome data must be interpreted with extreme caution. Four studies reported on rates of follow-up for major outcomes, which were 72, 79, 88 and 100% in the studies by Collins, Backman, Fisher and Weinstein, respectively. None of the studies checked the comparability of patients lost to follow-up.

Analysis and reporting of results

Details of the analyses conducted were reported or could be ascertained for only one study (Fisher) and just a single study (Kirk) was judged to have provided adequate data in reporting results. The principle of ITT analyses was not considered appropriate for observational studies.

Implications of quality characteristics in summarising effectiveness results

The overall quality of studies across the multiple dimensions assessed was relatively poor. For example, none of the RCTs or CCTs provided or adequately met all quality criteria assessed in relation to randomisation (where applicable), outcome assessment, sample characteristics and attrition and analysis and reporting. Only a small number (e.g. Wesseldine, Sullivan, Madge, 1997, Cowie, Garrett) reported on and adequately met all criteria within one or more of these dimensions. Poor methodological quality was, however, particularly striking in the COSs. It had been expected that well-designed observational studies could make a useful contribution, in a field in which research is relatively difficult and limited, to an overall assessment of the effectiveness of psycho-educational interventions for difficult asthma. However, owing to the limited information available from abstracts describing some of these (Weinstein, Westphal, Weder, Kirk), the overall lack of clarity regarding methods used and baseline differences between control and intervention groups or lack of detail on this in five of the seven observational studies, the potential for bias in the results of these studies was judged to be extremely high. For this reason, and since a higher than expected number of controlled trials had been identified, a decision was taken to exclude the COSs from the summary of effectiveness results in children. It was anticipated in any case that given inadequate reporting or limited data sources, the ability to extract any meaningful results data from these would likely be extremely limited.

For the remaining RCTs and CCTs, in some instances methodological quality may have been masked by the limited sources available for data extraction. This is a particular issue for the recently completed or ongoing studies reviewed (Madge, 2002, Griffiths, Krieger). Poor reporting, apparent in the number of studies which failed, for example, to provide details of patient flow, baseline group comparability and statistical analyses, may also have masked study quality. The generally poor quality of studies and potential for quality characteristics to be masked by limited information and poor reporting must be taken into consideration in interpreting the results described in the section which follows. However, it will be clear in reading this section that the better quality studies are generally those which consistently report outcome data and report these data in a form which allowed for summary statistics to be calculated and, in some cases, statistically pooled. Where such summaries are provided, therefore, results and the conclusions which follow are based on the best evidence available in this field.

Effectiveness

This section initially provides a summary of characteristics related to comparisons conducted, duration of follow-up and outcomes assessed for the 25 RCTs and CCTs included in the summary of effectiveness results which follows. These introductory descriptions, in addition to highlighting issues important to consider in the interpretation of the results, explain the rationale for the method of presentation of the effectiveness results.

Descriptive information on outcomes assessed for the controlled observational studies which are not reviewed in this section are provided in Appendix 21. For the reasons highlighted above, no further summary of results for these studies is provided and interested readers are referred to the original sources for details of these.

Comparisons

Detailed information on the comparison groups for each individual study is provided in Appendix 15 and was summarised earlier in this chapter [see the section 'Interventions' (p. 43)] and will not be repeated here. Only two studies did not include a comparison with some form of control treatment and one of these was an observational study for which results are not discussed (Weinstein). The other (Krieger) conducted a comparison between

two educational interventions varying in intensity to examine their relative impacts on a range of outcomes and is discussed alongside other studies in the summary of results that follows. However, results data for this study were not published or available from the author at the time of this review so it does not contribute to any formal qualitative or quantitative analysis of results. For the purposes of summarising results on the effectiveness of psycho-educational interventions, all other control comparisons, including usual care, alternative forms of delivery of medical care, minimal or passive education and placebo conditions, were considered similar enough to combine for both qualitative and quantitative syntheses. The following summary of results therefore represents a comparison of psycho-educational interventions with a range of non-psycho-educational control treatments.

Duration of follow-up

In summarising and synthesising results across studies, it is important to consider variations in the time at which follow-up assessments of outcomes were made. The point from which follow-up was measured (e.g. recruitment, baseline assessment, start of intervention, completion of intervention) varied across studies and for the purposes of comparison between them was standardised as far as possible to represent follow-up from the start of the intervention or baseline assessment (which were assumed to be close together). Where length of follow-up varied across individual patients within studies, the average duration or mid-point of a range for follow-up is reported. With the definition of follow-up described above in mind, the maximum duration of follow-up across all the studies in children ranged from 8 days in one study, representing the end of the final session of a relaxation intervention (Alexander, 1972), to up to 29 months from the start of an educational intervention of unspecified duration (Shields). For one study in progress, details of the duration of follow-up were not reported in available data sources (Madge, 2002). Amongst the remaining studies, the median length of follow-up was 12 months.

Around half of studies included more than one follow-up point for assessment of outcomes. Amongst the majority of these and across all the studies as a whole, there appeared to be some consistency in the time points at which outcomes were assessed. Many included a short-term assessment of outcomes, often during an early intensive phase of longer interventions or

immediately at the end of shorter interventions, a medium-term assessment of outcomes and longer term assessment of outcomes beyond the end of any intervention. For the purposes of summarising effectiveness results in the following sections and to reduce heterogeneity between studies in terms of the duration of follow-up, where there are a sufficient number of studies reporting on a particular outcome, reporting of results is divided into short-, medium- and long-term follow-up. In this case, short-term follow-up equates to assessment of outcomes at a time point prior to 6 months from the start of the intervention, medium-term follow-up equates to assessment at a time point of 6 months or more but less than 12 months from the start of the intervention with long-term follow-up being at 12 months or more from the start of the intervention. Reference is made within each of these categories to the studies reporting **assessment** of a given outcome within the time frame **and** the studies actually reporting **outcome results** for the appropriate time point. In addition, for a number of key outcomes, results across all time points, using data from the last assessment point reported by each study, are also summarised as this provided sufficient numbers of studies for some limited subgroup analyses. Where the number of studies reporting on an outcome was limited, the discussion of results was not broken down into different time points and the duration of follow-up is simply commented on.

Outcomes assessed

The types of outcomes reported as being assessed by studies, in order of frequency, are shown in *Table 25*.

As can be seen, no single outcome was reported as being assessed by all trials. The most commonly assessed outcomes were hospital admissions and A&E attendances for asthma (reported as assessed by over two-thirds of studies), followed by symptoms, self-care behaviour, health status/QoL (reported as assessed by over half of studies) and then medication use, other unscheduled healthcare attendances, respiratory function, scheduled healthcare attendances and school and work time lost (reported as assessed by over one-third of studies). Of these, admissions, A&E attendances, symptoms, other unscheduled healthcare attendances and respiratory function were identified as primary outcomes by one or more studies.

Although a descriptive summary of results from each study (including *p*-values where these were reported) in relation to all patient-focused

TABLE 25 Numbers of trials in children reporting assessment of outcomes of different types

| Type of outcome | Number of studies reporting | | |
|--|-----------------------------|------|-------|
| | RCTs | CCTs | Total |
| Admission/readmission ^a | 20 | 1 | 21 |
| A&E/ED attendance ^a | 17 | 1 | 18 |
| Symptoms/asthma control ^a | 14 | 1 | 15 |
| Self-care behaviour | 13 | 1 | 14 |
| Health status/QoL | 11 | 2 | 13 |
| Medication use | 10 | 2 | 12 |
| Other unscheduled healthcare attendance ^a | 9 | 1 | 10 |
| Respiratory function ^a | 7 | 3 | 10 |
| Scheduled healthcare attendance | 8 | 1 | 9 |
| School or patient work time lost | 8 | 1 | 9 |
| Knowledge | 6 | 0 | 6 |
| Severity | 6 | 0 | 6 |
| Psychological morbidity | 4 | 1 | 5 |
| Self-efficacy/perceived control | 4 | 1 | 5 |
| Exacerbations | 3 | 1 | 4 |
| Beliefs/attitudes | 2 | 0 | 2 |
| Satisfaction | 2 | 0 | 2 |
| Death | 0 | 0 | 0 |
| Other | 10 | 3 | 13 |

^a Identified prior to or after reporting of results as a primary outcome by one or more studies.

outcomes was extracted and summaries of these are provided for all outcomes in the sections that follow, extraction of actual outcome data (e.g. numbers, means), where this was appropriate and worthwhile (see below), was limited to the above outcomes highlighted as being primary or reported by at least one-third of studies. The summaries of effectiveness results are presented under headings by outcome in the order in which they appear in *Table 25* to ensure a focus on the outcomes for which there are most data and which are considered primary.

Table 25 above summarises the numbers of studies reporting **assessment** of the different types of outcomes. The number of studies reporting **actual results** data for intervention and control groups in relation to each outcome was often smaller, in some cases much smaller (e.g. for QoL), than the numbers reporting to have assessed the outcome in *Table 25*. As will be apparent in the sections that follow, some of the outcomes (e.g. self-care behaviour, medication use, respiratory function) were also assessed and reported in very different ways across studies, precluding direct comparisons between them and preventing the calculation of any meaningful summary statistics. In these cases, extraction of outcome data was not undertaken and only a summary of the descriptive results is provided. In addition, of the studies that did report results, the quantity and quality of data

reported were often variable, ranging from casual comments regarding the significance of results and/or probability (*p*) values alone to provision of detailed summary data [e.g. numbers, means and standard deviations (SDs) as appropriate]. However, even in some cases where detailed data were provided, the statistics reported were occasionally not deemed appropriate summaries for the type of outcome assessed. For example, in a number of studies means and SDs were given for total numbers of admissions, the distribution of which is likely to be highly skewed across study samples. This meant that adequate, appropriate data for the calculation of individual study summary statistics to facilitate comparisons and potentially allow pooling across studies were limited. Nevertheless, where more than one study reported such data for a given outcome, statistical data were extracted and summary statistics, in the form of RRs for binary outcomes and SMDs for continuous outcomes, along with CIs were calculated and are presented in tables. As stated in Chapter 3, summary statistics from three or more individual studies were then pooled in a meta-analysis where observation of a Forest plot and statistical tests suggested that there was non-significant statistical heterogeneity between them. Forest plots of the results from meta-analyses are presented where these were undertaken. In some instances, sensitivity analyses involving removal of studies or use of alternative data reported by

studies (e.g. at different time points or for a subgroup of patients) were also conducted to examine the effects of these factors on overall results.

Admissions

Twenty-one studies, 20 RCTs (Catrambone, Cowie, Greineder, Hanson, Madge, 1997, 2002, Mitchell, Shields, Sullivan, Alexander 1988, Gustafsson, Harish, Kreiger, Lewis, McNabb, Ronchetti, Wesseldine, Garrett, Griffiths, Colland) and one CCT (Kelly), reported assessment of hospital admissions for asthma. This was the most commonly reported outcome amongst the studies in children. Of the 17 studies which reported their method of assessment, the majority (11 studies) relied on extraction of data from medical or financial records with the rest using self-report data from interviews or questionnaires completed by patients or caregivers for recall periods ranging from 1 to 3 months. Two studies specified admissions as their primary outcome (Madge, 1997, Wesseldine).

Two studies (McNabb, Colland) did not ultimately report any results in relation to admissions in published papers and no results were yet available for one further study described in two recent papers (Krieger) and another study in progress (Madge, 2002). Admissions data were not reported separately for the subgroup of patients classified as probable in terms of difficult asthma in the study by Griffiths.

Short-term follow-up of admissions

Of the 16 remaining studies, three RCTs (Cowie, Catrambone, Wesseldine) reported on assessment of admissions in the short-term (<6 months) at follow-up points ranging from 6 weeks (Wesseldine) to 3 months (Cowie, Catrambone). One study (Cowie) did not present admissions data separately for this time point. Another (Catrambone) presented means and SDs for numbers of hospital days at 3 months, during the intensive phase of the multifaceted intervention provided to 28 patients classified as probable in terms of difficult asthma. However, no significant differences between groups were observed ($p = 0.94$). The remaining RCT (Wesseldine) presented data on the numbers of patients from a sample of 160 (classified as possible in terms of difficult asthma) admitted in each group at 6 weeks after baseline assessment and following the single self-management intervention session provided. There were reported to be no significant differences between groups at this time point (p -value not reported).

Medium-term follow-up of admissions

Eight RCTs (Cowie, Hanson, Mitchell, Lewis, Madge, 1997, Wesseldine, Catrambone, Garrett) assessed admissions at a follow-up point between 6 (Cowie, Catrambone, Hanson, Mitchell, Lewis, Wesseldine) and 9 months (Catrambone, Garrett) from baseline (medium-term). One study (Hanson) commented on admissions but did not present any actual supporting data and another (Lewis) did not report results separately for this time point. The study by Garrett, although reporting no significant differences in admissions between groups for children in the study at 9 months ($p = 0.14$), only presented data on the proportion of patients who were admitted following their educational intervention for the whole sample, the majority of whom were adults aged over 15 years. One further study (Catrambone) presented means and SDs for numbers of admissions at 6 and 9 months amongst 28 patients, but reported no significant difference between groups at either time point ($p = 0.88$ and 0.42 , respectively).

The remaining four studies (Cowie, Mitchell, Madge, 1997, Wesseldine), which were all RCTs, presented data on the proportions or numbers of patients admitted in each group, from which RR statistics could be calculated. For three studies the follow-up was at 6 months (Cowie, Mitchell, Wesseldine). In the Madge (1997) study, the follow-up varied from 2 to 14 months so, although not reported, the midpoint of 8 months was assumed to be the average duration of follow-up. There was significant statistical heterogeneity between these studies ($p = 0.039$) so they were not combined in a meta-analysis, but individual RRs are presented in *Table 26*.

In three of the four studies, the proportion admitted in the intervention group was lower than that in the control group. However, only the two self-management studies (Madge, 1997, Wesseldine), both of which targeted patients classified as possible in terms of difficult asthma, provided clear evidence of effectiveness, with RRs in each case suggesting >60% fewer patients admitted in intervention compared with control groups.

Long-term follow-up of admissions

Long-term follow-up of admissions (≥ 12 months) was reported to be undertaken in 11 RCTs (Greineder, Hanson, Mitchell, Shields, Sullivan, Alexander, Gustafsson, Lewis, Ronchetti, Catrambone, Harish) and one CCT (Kelly). Follow-up ranged from 12 months, reported by the

TABLE 26 Comparisons of proportion of children admitted in psycho-educational intervention versus control groups at medium-term follow-up (6–11 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) admitted | | RR (95% CI) |
|-------------|-------------------------------|-------------------|-----------------------------|-----------------------------|------------------------|
| | | | Intervention | Control | |
| Mitchell | Probable | Education | 27/84 ^a (32%) | 23/84 ^a (27%) | 1.17 (0.74 to 1.87) |
| Cowie | Probable | Education | 0/29 (0%) | 4/33 (12%) | 0.13 (0.01 to 2.24) |
| Madge, 1997 | Possible | Self-management | 8/96 (8%) | 26/105 (25%) | 0.34 (0.16 to 0.71) |
| Wesseldine | Possible | Self-management | 12/80 (15%) | 30/80 (38%) | 0.40 (0.22 to 0.72) |

^a Estimated from percentages provided.

majority of studies, to up to 29 months, reported in one study (Shields). Several studies reported multiple follow-ups beyond 12 months (Hanson, Shields, Sullivan, Harish).

Three studies commented on admissions, two suggesting no differences between groups (Hanson, Alexander, 1988), without presenting any data to support their statements. One study ultimately reported only baseline admissions data (Ronchetti) and one presented admission results for the intervention group alone (Gustafsson).

One study reported means and SDs for hospital days due to asthma and other conditions for 253 patients classified as probable in terms of difficult asthma (Shields). At 12 months and up to 29 months from baseline following an educational intervention, there were reported to be no significant differences between groups (p -values were not reported). The Kelly study of 78 patients classified as probable in terms of difficult asthma reported significantly lower mean admission rates and hospital days per child per year in the group who received a self-management intervention compared with the control group (both $p < 0.001$). An adjusted RR statistic for the control group versus the intervention was presented in the paper. This indicated that the control group admission rate was on average nearly 2.5 times that in the intervention group (RR = 2.4, 95% CI = 1.04 to 5.40, $p = 0.04$). The data presented were such that the complementary RR statistic for reductions in admissions in the intervention group compared with the control could not be recalculated for inclusion in the meta-analysis presented below.

Six remaining studies (Greineder, Mitchell, Sullivan, Lewis, Catrambone, Harish), all RCTs,

presented data on the proportions or numbers of patients admitted in each group. Follow-up was at 12 months in the study by Lewis, 18 months in the studies by Catrambone and Mitchell and between 1 and 2 years in the Greineder study. Sullivan and Harish reported data at 1- and 2-year follow-ups but results at each point were similar so the 12-month data were used in the first instance. Results for each study are summarised in *Table 27*. There was no significant statistical heterogeneity between these studies ($p = 0.53$) so they were combined in a meta-analysis. The Forest plot of the results of this is presented in *Figure 6*.

As shown in *Table 27*, all but one of the studies included in the meta-analysis assessed a multifaceted intervention, the other a primarily educational intervention (Mitchell). Four of the six were classified as probable in terms of their targeting of difficult asthma with the two remaining studies classified as possible. Four of the six studies demonstrated effects on admissions in favour of the intervention group but none showed significant differences between groups and pooled results (RR = 0.84, 95% CI = 0.68 to 1.02) suggested a small reduction in the proportion of patients admitted at long-term follow-up following a psycho-educational intervention but just failed to reach traditional levels of statistical significance ($p = 0.08$). A repeat of the analysis using the 2-year follow-up data from the Sullivan and Harish studies did not alter the results (RR = 0.82, 95% CI = 0.65 to 1.03, $p = 0.09$). Removal of the Mitchell study of an educational intervention also did not influence the conclusions (RR = 0.80, 95% CI = 0.64 to 1.01, $p = 0.06$).

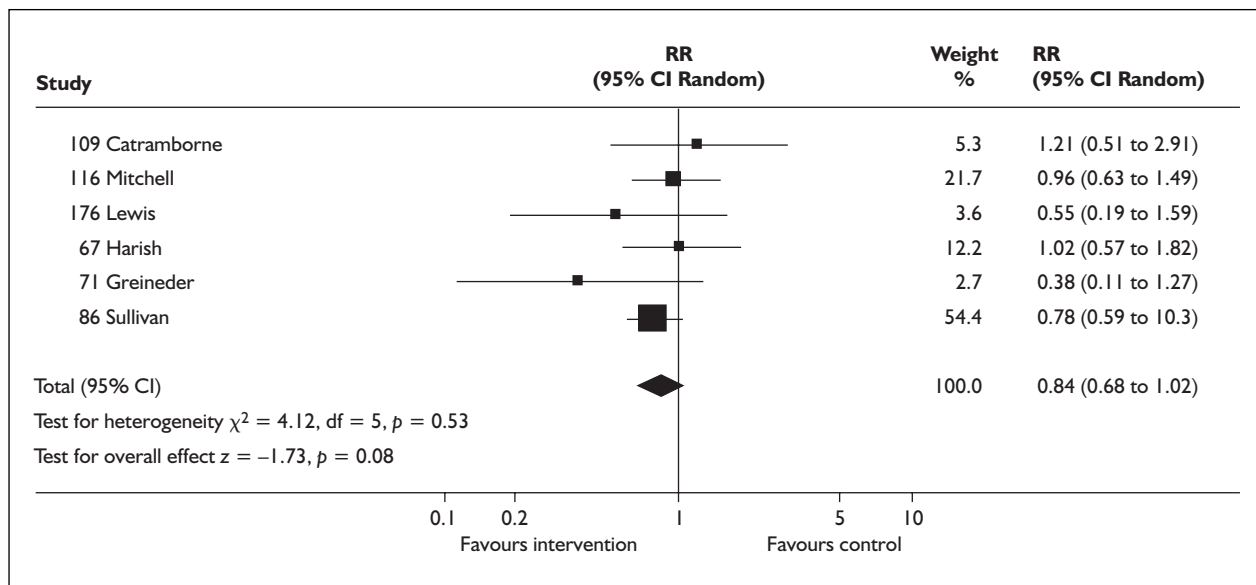
Admissions across all follow-up time points

Owing to the small numbers of studies reporting

TABLE 27 Comparisons of proportion of children admitted in psycho-educational intervention versus control groups at long-term follow-up (> 12 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) admitted | |
|------------|-------------------------------|-------------------|------------------------------|------------------------------|
| | | | Intervention | Control |
| Mitchell | Probable | Education | 27/84 ^a (32%) | 28/84 ^a (33%) |
| Catrambone | Probable | Multifaceted | 7/15 ^a (47%) | 5/13 ^a (38%) |
| Greineder | Probable | Multifaceted | 3/29 (10%) | 8/28 (29%) |
| Sullivan | Probable | Multifaceted | 76/515 ^a (15%) | 98/518 ^a (19%) |
| Harish | Possible | Multifaceted | 16/60 (27%) | 18/69 (26%) |
| Lewis | Possible | Multifaceted | 5/66 (8%) | 8/58 (14%) |

^a Estimated from percentages provided.

**FIGURE 6** Forest plot showing meta-analysis for proportions of children admitted at long-term follow-up (> 12 months)

data on admissions within short, medium- and long-term follow-up periods, a reanalysis across all studies reporting appropriate statistics (nine RCTs) using data from the latest follow-up reported in each study was conducted. This allowed studies to be divided into subgroups according to the degree to which they targeted difficult asthma and type of intervention evaluated. Since overall there was non-significant statistical heterogeneity between them ($p = 0.073$), they were combined in meta-analyses by subgroup. The results of these are presented in *Figures 7* and *8*.

The summary statistic calculated from all nine studies suggests that psycho-educational interventions can reduce admissions in children by up to 36% (RR = 0.64, 95% CI = 0.46 to 0.89), an effect which is significant ($p = 0.009$). However, the meta-analysis presented in *Figure 7* suggests that the effects are more marked in the subgroup of studies classified as possible in terms of their targeting of difficult asthma where a significant reduction ($p = 0.0007$) of >50% is observed (RR = 0.47, 95% CI = 0.30 to 0.73), compared with those classified as probable, where there is a

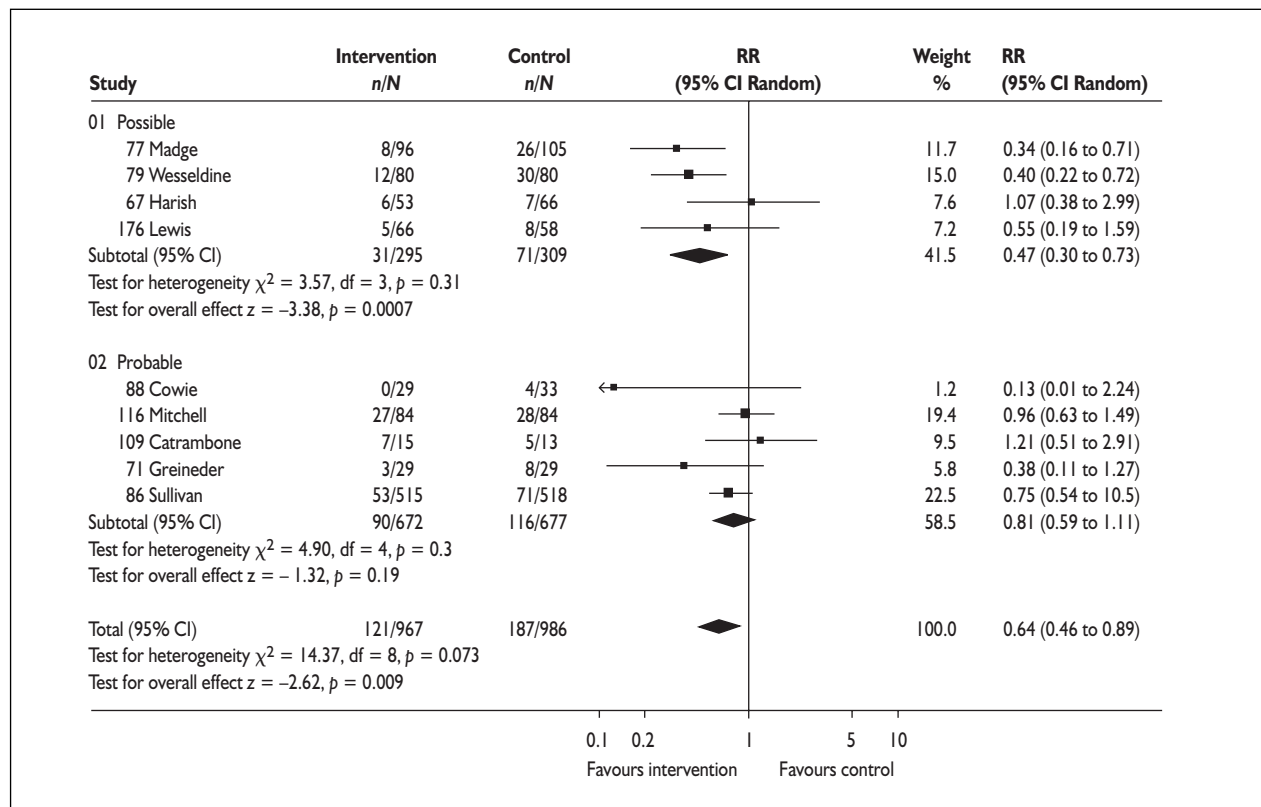


FIGURE 7 Forest plot showing meta-analysis divided by difficult asthma subgroups (possible and probable targeting) for proportions of children admitted at latest follow-up reported

non-significant reduction ($p = 0.3$) of less than 20% (RR = 0.81, 95% CI = 0.59 to 1.11), despite the larger overall sample size for the latter subgroup.

The meta-analysis of admissions data by type of intervention suggests that the greatest and only significant effects ($p = 0.00003$) are seen for self-management interventions for which a reduction of more than 60% is observed (RR = 0.37, 95% CI = 0.24 to 0.59). Despite including all the components of self-management in addition to other add-ons, the 24% reduction in admissions following multifaceted interventions (RR = 0.76, 95% CI = 0.58 to 1.01) just failed to reach traditionally accepted levels of statistical significance ($p = 0.06$). However, since more of the studies of multifaceted interventions were classified as probable in terms of their targeting of difficult asthma, this will undoubtedly have reduced the effects observed given the results of the meta-analysis presented in *Figure 7*.

Accident and emergency department attendances

Eighteen studies, 17 RCTs (Catrambone, Cowie, Greineder, Hanson, Madge, 1997, 2002, Shields, Sullivan, Alexander 1988, Gustafsson, Harish, Kreiger, Lewis, Ronchetti, Wesseldine, Garrett,

Griffiths) and one CCT (Kelly), reported assessment of A&E or ED attendances or their equivalent for asthma. Of the 15 studies which reported their methods of assessment, the majority (nine studies) relied on extraction of data from medical or financial records with the rest using self-report data from interviews or questionnaires completed by patients or caregivers over recall periods ranging from 1 to 3 months. A&E attendances appeared to be the primary outcome in four studies (Alexander, 1988, Cowie, Harish, Ronchetti), but in only one of these was this specified in advance (Cowie).

No results were yet available for one study described in two recent papers (Krieger) and another study in progress (Madge, 2002), and for one other study, data on A&E attendances were only collected for use in calculating a composite measure of unscheduled attendance (Griffiths), results for which are presented in a later section.

Short-term follow-up of A&E attendances

Three studies, all RCTs, reported assessment of A&E attendances in the short term (<6 months) ranging from 6 weeks from baseline in one study (Wesseldine) to 3 months in two studies (Cowie, Catrambone). However, the study by Cowie did

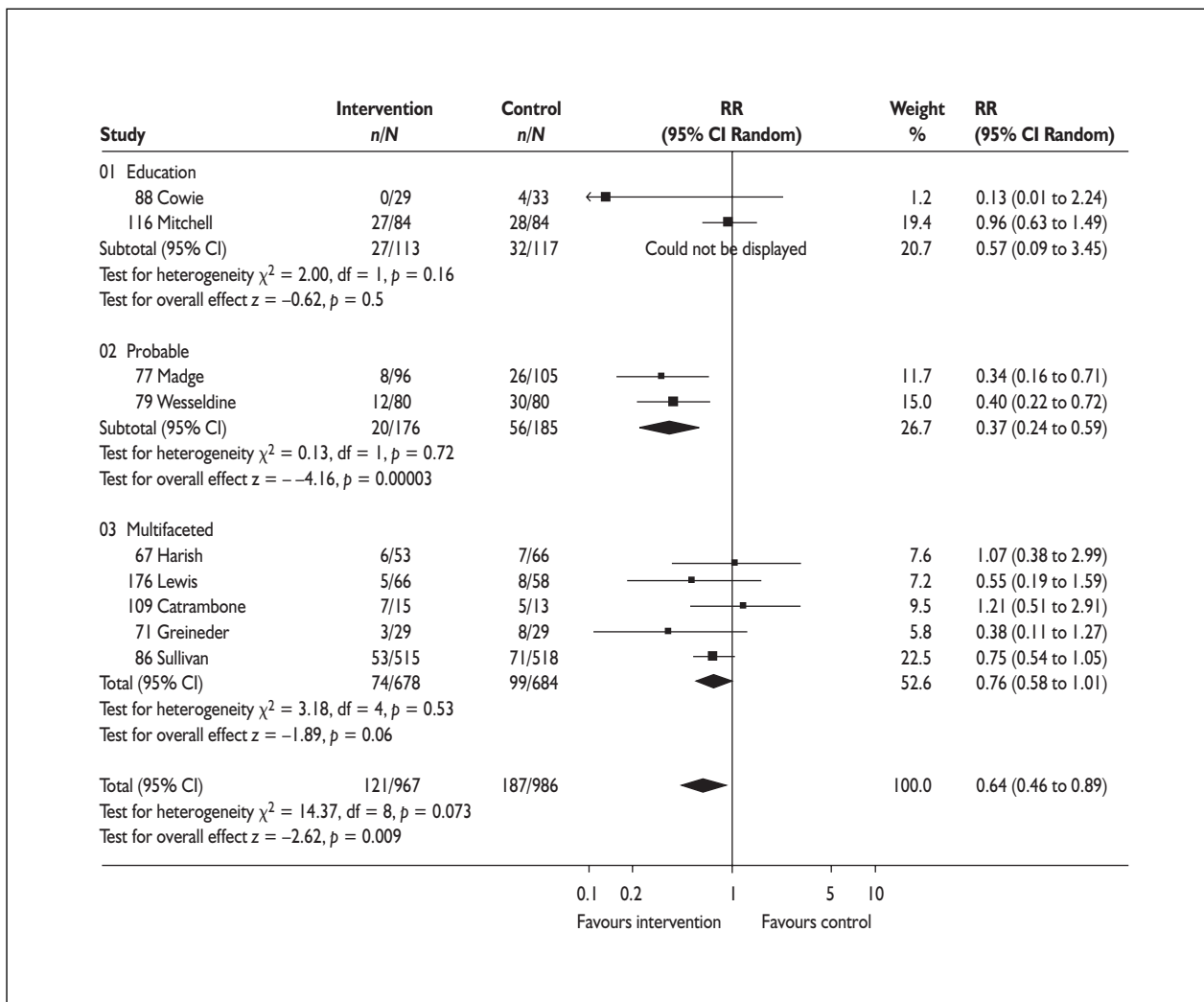


FIGURE 8 Forest plot showing meta-analysis divided by intervention types (education, self-management, multifaceted) for proportions of children admitted at latest follow-up reported

not present emergency attendance data separately for this time point. Catrambone presented means and SDs for numbers of emergency department attendances amongst 28 patients classified as probable in terms of their difficult asthma during a multifaceted intervention, but found no significant difference between groups ($p = 0.77$). The remaining RCT (Wesseldine) presented data on the numbers of patients from a sample of 160 (classified as possible in terms of difficult asthma) attending in each group following the single self-management intervention session provided. There were reported to be significantly fewer attendances in the intervention compared with the control group at 6 weeks ($p < 0.05$).

Medium-term follow-up of A&E attendances

Seven studies, all RCTs (Garrett, Catrambone, Cowie, Hanson, Lewis, Wesseldine, Madge 1997), reported assessment of A&E attendance at a

follow-up point between 6 and 11 months (medium-term). The follow-up in all but two studies was 6 months from baseline. Of the remaining two, one assessed A&E attendance at 9 months (Garrett) and in the other the follow-up varied from 2 to 14 months, so the midpoint of 8 months was assumed to be the average (Madge, 1997).

One study (Hanson) commented on there being no significant differences between groups in terms of A&E attendances but did not present any actual data to support this statement and another (Lewis, 1994) did not report results separately for this time point. The study by Garrett reported no significant differences in emergency room visits between groups for children in the study at 9 months ($p = 0.6$), but presented only data on the proportion of patients who attended following their educational intervention for the whole

TABLE 28 Comparisons of proportion of children attending A&E in psycho-educational intervention versus control groups at medium-term follow-up (6–11 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) admitted | | RR (95% CI) |
|-------------|-------------------------------|-------------------|---------------------|----------------|------------------------|
| | | | Intervention | Control | |
| Cowie | Probable | Education | 9/29 (31%) | 13/33 (39%) | 0.79 (0.40 to 1.57) |
| Madge, 1997 | Possible | Self-management | 7/96 (7%) | 7/105 (7%) | 1.09 (0.40 to 3.00) |
| Wesseldine | Possible | Self-management | 6/80 (8%) | 31/80 (39%) | 0.19 (0.09 to 0.44) |

sample, the majority of whom were adults.

One study (Catrambone) presented means and SDs for numbers of ED attendances at 6 and 9 months amongst 28 patients during the intensive phase of the multifaceted intervention provided, but reported no significant difference between groups at either time point ($p = 0.18$ and 0.39 , respectively).

The remaining three studies (Cowie, Madge, 1997, Wesseldine), which were all RCTs, presented data on the numbers of patients attending A&E in each group, from which summary RR statistics could be calculated. For three studies the follow-up was at 6 months and for the Madge (1997) study an average of 8 months. There was significant statistical heterogeneity between these studies ($p = 0.0087$) so they were not combined in a meta-analysis, but individual study results and RRs calculated from them are presented in *Table 28*.

In two of the three studies, the proportions attending A&E in the intervention group are lower than those in the control group. However, only one of the self-management studies (Wesseldine), targeting patients classified as possible in terms of difficult asthma, provides clear evidence of effectiveness, with 95% CIs demonstrating between an estimated 56% and 91% fewer patients attending A&E in the intervention compared with the control group.

Long-term follow-up of A&E attendances

Eleven studies, 10 RCTs (Catrambone, Greineder, Hanson, Shields, Sullivan, Alexander, 1988, Gustafsson, Harish, Lewis, Ronchetti) and one CCT (Kelly), reported assessment of A&E attendances at a follow-up point 12 months or more from baseline (long-term). All but two studies assessed attendances at 12 months and in five of these (Catrambone, Hanson, Shields,

Sullivan, Harish) an additional assessment was made beyond 12 months at time points ranging from 15 to up to 29 months. The two remaining studies assessed A&E attendance at a time point ranging from 1 to 2 years (Greineder) and at 16 and 26 months (Gustafsson).

One study ultimately did not report results for A&E attendances (Gustafsson), and another (Hanson) commented on there being no significant differences between groups in terms of A&E attendances, but did not present any actual data to support this statement.

One RCT (Alexander, 1988) presented totals, means and SDs for the number of ED attendances at the end of their 1-year educational intervention targeting 21 patients classified as possible in terms of difficult asthma. There were reported to be significantly fewer attendances in the intervention compared with the control group ($p < 0.05$). The RCT by Ronchetti presented means and standard errors for ED attendance rates per patient per 2 months amongst the severe subgroup of patients of interest. Overall there were significantly lower rates of attendance amongst the severe subgroup who received one of the four self-management interventions evaluated compared with equivalent control patients ($p < 0.05$). Sullivan reported no significant differences between groups in the 2-year rate of ED visits per patient at final follow-up ($p > 0.05$) amongst 1033 patients graded as probable in terms of difficult asthma and following a 4-month multifaceted intervention.

The Kelly study of 78 patients classified as probable in terms of difficult asthma reported significantly lower mean ED attendance rates per child per year in the group who received a self-management intervention ($p < 0.05$) compared with the control group. An adjusted RR for the

TABLE 29 Comparisons of proportion of children attending A&E in psycho-educational intervention versus control groups at long-term follow-up (> 12 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) admitted | | RR (95% CI) |
|------------|-------------------------------|-------------------|-----------------------------|----------------------------|-------------------------|
| | | | Intervention | Control | |
| Shields | Probable | Education | 24/101 (24%) | 18/104 (17%) | 1.37 (0.80 to 2.37) |
| Catrambone | Probable | Multifaceted | 12/15 ^a (80%) | 9/13 ^a (69%) | 1.16 (0.74 to 1.80) |
| Greineder | Probable | Multifaceted | 11/29 (38%) | 14/28 (50%) | 14/28 (0.78 to 1.21) |
| Harish | Possible | Multifaceted | 32/60 (53%) | 46/69 (67%) | 0.80 (0.60 to 1.07) |
| Lewis | Possible | Multifaceted | 25/66 (38%) | 20/58 (34%) | 1.10 (0.69 to 1.76) |

^a Estimated from percentages provided.

control versus the intervention group was presented. This indicated that the control group emergency attendance rate was on average nearly 1.5 times that in the intervention group (RR = 1.4, 95% CI = 1.02 to 1.9, $p = 0.04$). The data presented were such that the RR for reductions in the intervention compared with the control group could not be recalculated.

Five remaining studies, all RCTs (Catrambone, Greineder, Shields, Harish, Lewis), presented data on the proportions or numbers of patients attending A&E in each group. Follow-ups in each case were at 12 months (Lewis, Shields), between 1 and 2 years (Greineder) and 18 months (Catrambone). The study by Harish reported outcomes at 1 and 2 years but results at each point were similar so the 12-month data were used in the first instance. Results for each study are summarised in *Table 29*. There was no significant statistical heterogeneity between these studies ($p = 0.3$) so they were combined in a meta-analysis. The Forest plot of the results of this is presented in *Figure 9*.

All but one of the studies included in the meta-analysis assessed a multifaceted intervention, the other a primarily educational intervention (Shields). Three of the five studies were classified as probable (Shields, Greineder, Catrambone) in terms of their targeting of difficult asthma with the others classified as possible (Lewis, Harish). Only two of the five studies demonstrated effects on A&E attendance in favour of the intervention group, none showed significant differences

between groups and the combined RR (RR = 0.97, 95% CI = 0.78 to 1.21) suggested no overall long-term effect of psycho-educational interventions on A&E attendances ($p = 0.8$). A repeat of the analysis using the 2-year follow-up data from the Harish study did not alter the results (RR = 1.03, 95% CI = 0.82 to 1.29, $p = 0.8$). Removal of the Shields educational study also did not influence the conclusions (RR = 0.91, 95% CI = 0.74 to 1.12, $p = 0.4$).

A&E attendances across all follow-up time points

Owing to the small numbers of studies reporting data on A&E attendance within short-, medium- and long-term follow-up periods, a re-examination across all studies reporting appropriate statistics (eight RCTs) using data from the latest follow-up point reported in each study was conducted. This allowed studies to be divided into subgroups according to the degree of targeting of difficult asthma and type of intervention evaluated. There was significant statistical heterogeneity between studies ($p = 0.0059$) so they were not combined in meta-analyses by subgroup. However, examination of individual summary statistics calculated for studies (presented in the tables above) suggests mainly non-significant effects of psycho-educational interventions on A&E attendances and little difference in effects between studies classified as possible, rather than probable, in terms of their targeting of difficult asthma. There were no clear patterns across different types of interventions when the small numbers within subgroups were taken into consideration.

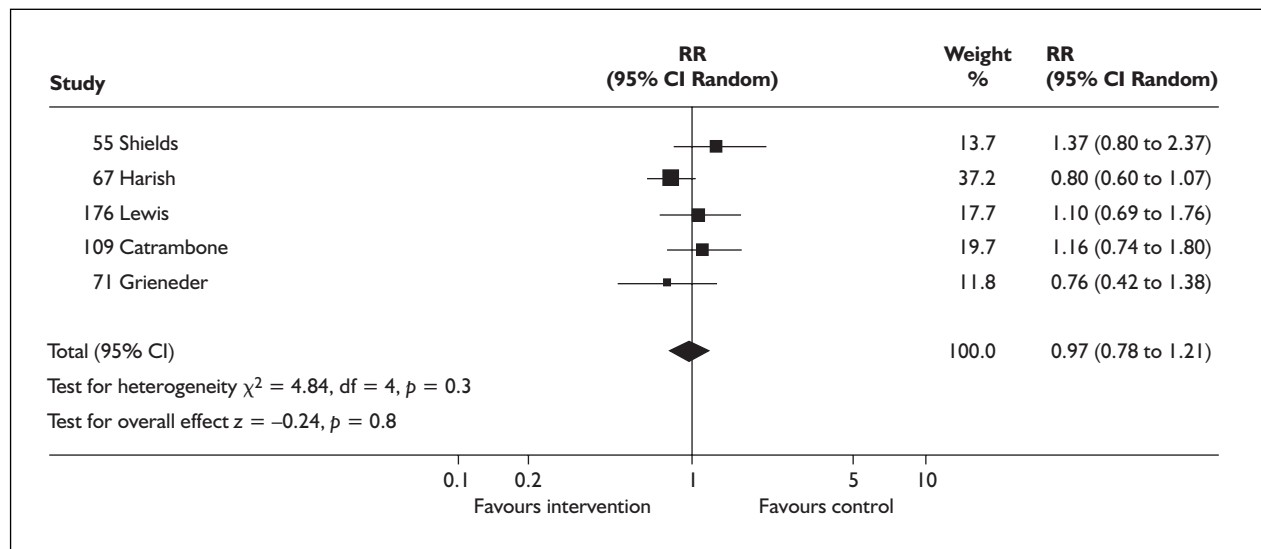


FIGURE 9 Forest plot showing meta-analysis for proportions of children attending A&E at long-term follow-up (> 12 months)

Symptoms

Fifteen studies, 14 RCTs (Catrambone, Cowie, Dahl, Sullivan, Bonner, Gold, Gustafsson, Krieger, Madge, 1997, Wesseldine, Garrett, Griffiths, Colland, Evans) and one CCT (Vazquez), reported assessment of symptoms or asthma control. All but one study (Gustafsson), which assessed symptoms via a clinical evaluation, used diaries or questions administered via interviews or questionnaires to assess patient or caregiver reported frequency and, in some cases, severity of symptoms. As is increasingly being recommended,⁹ five studies (Madge, 1997, Bonner, Sullivan, Garrett, Griffiths) reported assessment of some combination of day-time symptoms, night-time symptoms and restrictions to daily living or impacts due to symptoms. Three studies (Wesseldine, Krieger, Catrambone) assessed day- and night-time symptoms only and two just night-time symptoms (Cowie, Colland). The remaining five studies (Gustafsson, Gold, Vazquez, Evans, Dahl) reported on global assessment of time with symptoms, which in two cases was combined with a rating of symptom severity (Gustafsson, Gold). Most studies, however, did not report that the assessment methods used were standard or validated measures. Of those that did, one (Vazquez) made reference to use of a standard tested diary⁵¹¹ for assessment of symptoms, one (Madge, 1997) to a questionnaire based on a previously used morbidity index⁵¹² and one (Cowie) to a questionnaire used in a previous study by the author and shown to be correlated with measures of severity and control. One further study used novel items to assess symptoms as part of a caregiver interview but reported an alpha

coefficient for the items (Bonner). Two studies reported symptom measures as their primary outcome (Catrambone, Sullivan).

One study did not ultimately report any outcome data for symptoms (Wesseldine), one did not report symptom measures separately for the subgroup of interest (Griffiths) and two reported data for the intervention group only (Gustafsson, Dahl). For one recently completed RCT, symptom results were not yet available (Kreiger).

Short-term follow-up of symptoms

Seven studies, six RCTs (Gold, Bonner, Cowie, Catrambone, Madge, 1997, Colland) and one CCT (Vazquez), reported assessment of symptoms in the short-term, at follow-ups ranging from 3 to 4 weeks (Madge, 1997) to 4 months (Colland). Two studies did not ultimately report data separately for this time point (Colland, Cowie). Vazquez and Gold reported means for the total time with symptoms and asthma problems, respectively, and both found no significant differences between groups (no p -values were reported). The study by Madge (1997) reported medians and ranges for scores on three subscales of a morbidity index and found significant differences in day-time symptom scores ($p = 0.0005$) and night-time symptom scores ($p = 0.0002$), but not disability scores ($p = 0.078$). Catrambone presented means and SDs and reported no significant differences for the number of days with symptoms ($p = 0.10$) and frequency of night-time waking ($p = 0.41$) and night-time coughing ($p = 0.98$). Bonner reported scores on a scale of symptom persistence and found

TABLE 30 Symptom scores for psycho-educational intervention and control groups plus standardised mean differences at short-term follow-up (<6 months) in children

| Study | Targeting of difficult asthma | Intervention type | Mean (SD) | | SMD (95% CI) |
|------------|-------------------------------|-------------------|------------------------------------|------------------------------------|---------------------------|
| | | | Intervention | Control | |
| Bonner | Possible | Multifaceted | N = 50 5.46 (1.80) ^a | N = 50 6.78 (1.91) ^a | -0.71 (-1.11 to -0.30) |
| Catrambone | Probable | Multifaceted | N = 15 3.53 (7.62) ^b | N = 13 9.00 (9.61) ^b | -0.62 (-1.38 to 0.15) |

^a 3–9 scale of symptom frequency.
^b Days with symptoms over past 4 weeks.

TABLE 31 Frequency of night-time waking in psycho-educational intervention and control groups plus standardised mean differences at medium-term follow-up (6–11 months) in children

| Study | Targeting of difficult asthma | Intervention type | Mean (SD) | | SMD (95% CI) |
|------------|-------------------------------|-------------------|------------------------------------|------------------------------------|--------------------------|
| | | | Intervention | Control | |
| Cowie | Probable | Education | N = 29 1.00 (2.20) ^a | N = 33 2.00 (2.90) ^a | -0.38 (-0.88 to 0.12) |
| Catrambone | Probable | Multifaceted | N = 15 1.13 (2.39) ^b | N = 13 2.38 (4.50) ^b | -0.34 (-1.09 to 0.40) |

^a 3–9 scale of symptom frequency.
^b Days with symptoms over past 4 weeks.

significantly reduced symptoms in the intervention compared with the control group at 3 months ($p < 0.01$). Summary results for the last two RCTs reporting means and SDs for generic symptom measures are provided in *Table 30*.

Both studies were similar in terms of the type of intervention evaluated (multifaceted) but the study by Catrambone was classified as probable in terms of its targeting of difficult asthma and the study by Bonner as possible. Both showed short-term reductions in symptoms in favour of the intervention group as a result of psycho-educational intervention; however, only in the Bonner study was the difference between groups significant.

Medium-term follow-up of symptoms

Five studies, four RCTs (Cowie, Catrambone, Garrett, Colland) and one CCT (Vazquez), reported assessment of symptoms in the medium-term, at follow-ups ranging from 6 (Vazquez, Cowie, Catrambone) to 9 months (Colland, Garrett, Catrambone). One study did not ultimately report data separately for this time point (Colland). Vazquez reported means for the total time with

symptoms and found no significant differences between groups (no p -value was reported). The study by Garrett reported a higher proportion of children coughing and getting breathless from activities in the control compared with the intervention group (both $p = 0.05$), but only reported data on waking at night for the whole study sample, the majority of whom were adults.

Catrambone presented means and SDs but reported no significant differences at 6 or 9 months for the number of days with symptoms ($p = 0.08, 0.47$) and frequency of night-time waking ($p = 0.51, 0.77$) and night-time coughing ($p = 0.85, 0.07$). Cowie reported means and SDs for the frequency of night-time waking per week and found no significant differences between groups ($p = 0.2$). Summary results for the last two RCTs reporting means and SDs for night-time waking (using the later, 9-month follow-up data from the Catrambone study) are provided in *Table 31*.

Both studies were similar in terms of their targeting of difficult asthma (probable), but the study by Cowie evaluated an educational

TABLE 32 Annual symptom days for psycho-educational intervention and control groups plus standardised mean differences at long-term follow-up (> 12 months) in children

| Study | Targeting of difficult asthma | Intervention type | Mean (SD) | | SMD (95% CI) |
|--------------------|-------------------------------|-------------------|-------------------------|-------------------------|--------------------------|
| | | | Intervention | Control | |
| Evans ^a | Possible | Education | N = 93 18.10 (33.50) | N = 68 30.30 (58.30) | -0.27 (-0.58 to 0.05) |
| Catrambone | Probable | Multifaceted | N = 15 25.17 (36.55) | N = 13 71.361(88.01) | -0.69 (-1.46 to 0.08) |

^a Cluster RCT, data not adjusted for clustering.

intervention and that by Catrambone a multifaceted intervention. Both showed similar medium-term reductions in night-time waking in favour of the intervention group; however, in neither study were the effects significant.

Long-term follow-up of symptoms

Five studies, four RCTs (Catrambone, Sullivan, Colland, Evans) and one CCT (Vazquez), reported assessment of symptoms in the longer term. All but one study, which reported follow-up at 15 months (Colland), reported symptom measures at 12 months. Two studies reported additional follow-ups at 15, 18 (Catrambone) and 24 months (Sullivan). Colland reported significantly less waking at night in the intervention group compared with the control ($p < 0.02$) but did not present data to support this statement. Vazquez reported means for the total time with symptoms and found no significant differences between groups (no p -value was reported).

In the study by Sullivan, the mean maximum number of symptom days for each group were presented. The intervention group experienced significantly reduced symptoms at 1 ($p < 0.004$) and 2 years ($p < 0.007$), with the greatest effects at 1 year being seen in the subgroups of patients with severe symptoms, who had been previously hospitalised or had two or more unscheduled care visits in the past 2 months (mean differences with 95% CIs but no p -values were reported for these subgroup analyses). Evans presented means and SDs for the number of days with symptoms and reported significantly greater reductions in the intervention compared with the control group ($p = 0.004$). However, this was a cluster RCT and it was not clear that the results had been adjusted for clustering. Catrambone presented means and SDs but reported no significant differences at 12, 15 or 18 months for the number of days with symptoms ($p = 0.57, 0.40, 0.54$), frequency of night-time waking ($p = 0.38, 0.13, 0.83$) and

night-time coughing ($p = 0.81, 0.47, 0.73$). There were also no significant differences in cumulative 18-month estimates of night-time waking ($p = 0.80$) or coughing ($p = 0.89$). However, the intervention group experienced significantly fewer annual symptom days ($p = 0.02$). Summary results for the latter two RCTs reporting annual days with symptoms are provided in *Table 32*.

The two studies evaluated different types of interventions in different patient groups. Although both showed long-term effects on symptoms in favour of the intervention groups, SMDs suggest that in neither study were the effects significant.

Symptoms across all follow-up time points

Owing to the small numbers of studies reporting data on symptoms within short-, medium- and long-term follow-up periods, a reanalysis across all studies reporting appropriate statistics (four RCTs) using data from the latest follow-up reported in each study was conducted. For the studies by Catrambone, Evans and Bonner, data related to generic measures of time with or persistence of symptoms, and for the Cowie study, data related to frequency of night-time symptoms alone. The reanalysis across all time points allowed studies to be divided into subgroups according to the degree to which they targeted difficult asthma (two studies in each subgroup) and type of intervention (two multifaceted, two educational). There was non-significant statistical heterogeneity between the studies ($p = 0.35$), so they were combined in meta-analyses by difficult asthma and intervention type subgroups. The results of these are presented in *Figures 10* and *11*.

The summary statistic calculated from data for all four studies suggests that psycho-educational interventions can reduce occurrence of symptoms in children (SMD = -0.45, 95% CI = -0.68 to -0.22), an effect which is significant ($p = 0.0001$). Unlike for admissions, there appears to be no

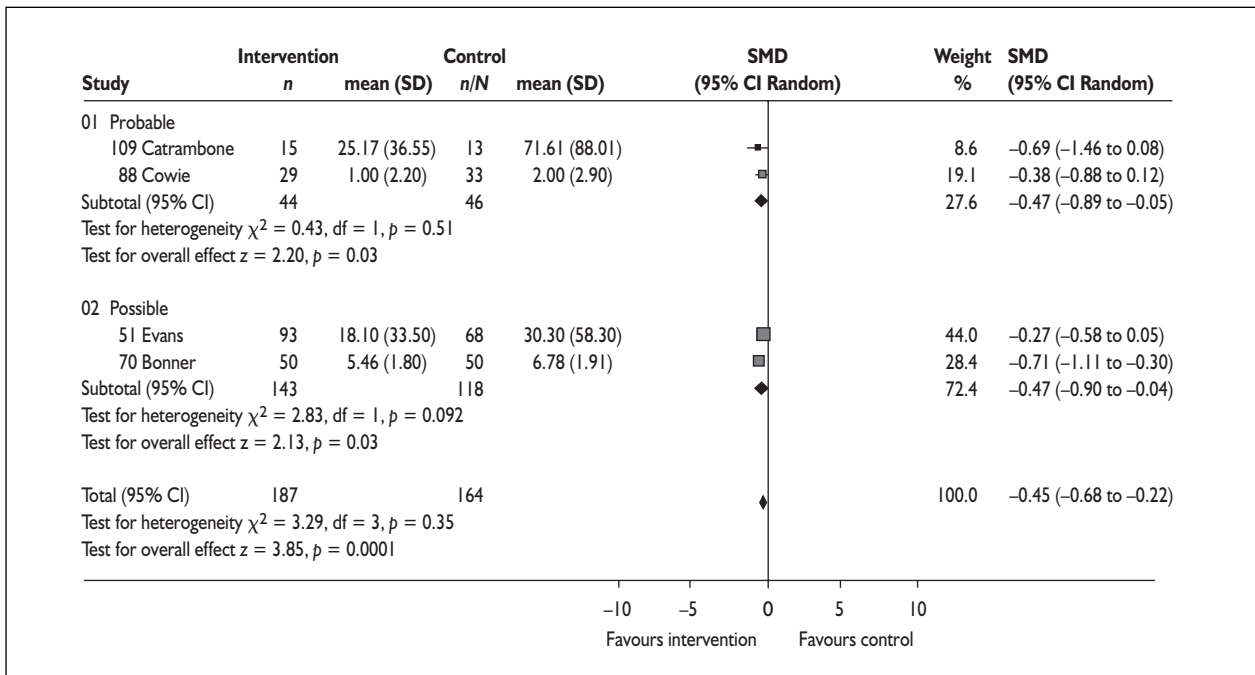


FIGURE 10 Forest plot showing meta-analysis divided by difficult asthma subgroups (possible and probable targeting) for symptom measures in children at latest follow-up reported

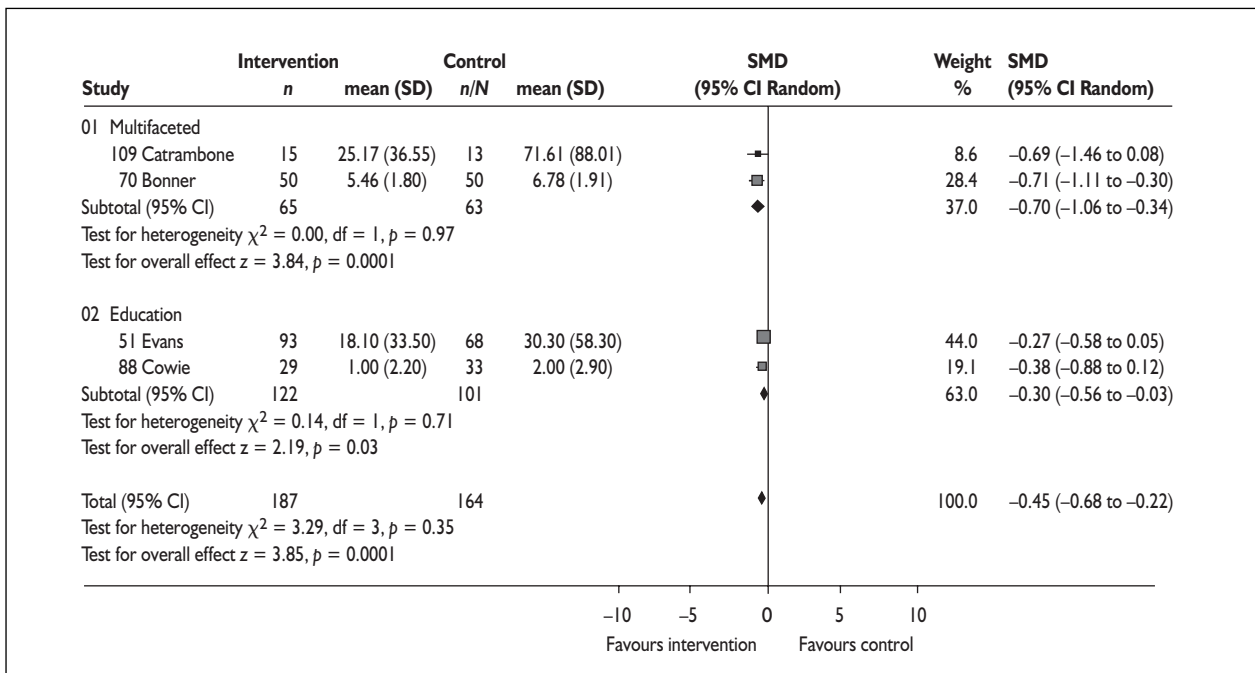


FIGURE 11 Forest plot showing meta-analysis divided by intervention types (multifaceted, educational) for symptom measures in children at latest follow-up reported

differential effect by difficult asthma subgroup, with the effects of psycho-educational interventions on symptoms being virtually identical and significant ($p = 0.03$) in studies graded as both probable and possible in terms of

their targeting of difficult asthma. The meta-analysis of symptom data by type of intervention suggests greater effects of multifaceted (SMD = -0.70, 95% CI = -1.06 to -0.34) than educational interventions (SMD = -0.30, 95%

CI = -56 to -0.03), but significant effects in both cases ($p = 0.0001$ and 0.03 , respectively). It should be noted that the study by Evans is a cluster RCT, results for which were not adjusted for clustering before inclusion in the meta-analyses. There is, therefore, potential for this study, and the meta-analysis including it, to overestimate effect sizes. A repeat of the analysis with the Evans study removed did not, however, influence overall conclusions (SMD = -0.59, 95% CI = -0.89 to -0.30).

Self-care behaviour

Thirteen RCTs (Cowie, Hanson, Bonner, Gold, Gustafsson, Kreiger, Lewis, McNabb, Wilkening, Griffiths, Garrett, Colland, Evans) and one CCT (Vazquez) reported assessment of one or more aspects of self-care behaviour. On closer examination, two studies (Krieger, Hanson) appeared to assess only parent's self-management practices so these data were not considered further. Only three studies reported the use of previously published measures: the compliance subscale from the author's own Asthma Knowledge and Compliance Test for children and Asthma Coping Test was used in the study by Colland, a List of Asthma Self-management Practices derived from the Asthma Problem Behaviour Checklist⁵¹³ was used by Vazquez and the attack scenarios from Avery and colleagues⁵¹⁴ and Sibbald⁵¹⁵ were used by Garrett. All studies assessed one or more aspects of self-care behaviour, such as medication compliance, trigger avoidance, symptom and attack management, communication about symptoms or need for treatment and self-monitoring, in a variety of different ways and at different time points. This made results very difficult to compare across studies. However, of the six studies that reported follow-up comparative data in the patients of interest, five reported some significant effects of the intervention. Significant differences between control and intervention groups were seen in relation to a composite index of self-management behaviours (Evans) ($p = 0.05$), coping with asthma in various daily situations (Colland) (no p -values reported), coping with attacks (Wilkening) (no p -values reported), medication adherence (Bonner) ($p < 0.001$) and use of peak flow meters ($p < 0.05$) and action plans ($p < 0.0001$) (Garrett). The remaining study reported no significant differences between groups (p -value not reported) with regard to trigger avoidance (Cowie) and one study reporting significant differences on some measures as highlighted above (Garrett) reported no significant differences in further measures of attack management ($p = 0.5$) and inhaler technique ($p > 0.05$).

Health status/quality of life

Thirteen studies, 11 RCTs (Garrett, Griffiths, Catrambone, Cowie, Dahl, Bonner, Gustafsson, Krieger, Wesseldine, Wilkening, Colland) and two CCTs (Kelly, Vazquez) reported assessment of health status or QoL.

One study (Griffiths) assessed generic health status using the EuroQol 5D.⁵¹⁶ Five studies assessed asthma-specific QoL using four different validated scales: the Juniper adult Asthma Quality of Life Questionnaire⁵¹⁷ (Krieger, Cowie), the Juniper Pediatric Asthma Quality of Life Questionnaire⁵¹⁸ (Kelly), the 'Inventory of Negative Consequences of Asthma' from Creer's Asthma Problem Behaviour Checklist⁵¹³ (Vazquez) and Barley's AQ20⁵¹⁹ (Griffiths). One further study specified use of an 'FAP quality of life questionnaire' (Wilkening) for which no reference or further details were given. Another (Garrett) referenced a review article⁵²⁰ on measurement of disease-specific QoL but did not provide further details on the actual questionnaire used. One study simply assessed, via interview, parent's perceptions of their child's health over the past 3 months, rated from excellent to poor (Catrambone). The remaining five studies (Dahl, Bonner, Gustafsson, Wesseldine, Colland) used data collected from diaries, questionnaires or interviews to make an assessment of restrictions to daily activities in terms of days or a calculated score. One of these (Bonner) provided an alpha coefficient for the items used but no other studies made reference to the psychometric properties or validity of the measures.

Follow-up data were not available for one recently reported study (Krieger), two further studies ultimately did not report results in relation to QoL or health status (Dahl, Wesseldine) and one reported results only for a subsample of intervention group patients (Kelly). For the recently completed study by Griffiths, data from the EuroQol questionnaire were not yet reported and data for the AQ20 were not reported separately for the subgroup of patients of interest.

Of the remaining eight studies, the study by Garrett reported no group differences across the total, primarily adult, sample, but did not present any data to support this statement or for the subgroup of children separately. Wilkening commented on improvements in some QoL subscales for intervention patients compared with worsening in control patients at 6 months but did not provide any data to support this claim. Colland reported that intervention group patients

were significantly less limited in their daily activities at 12 months than control patients ($p < 0.009$), but again presented no supportive data. Gustafsson reported that a significantly higher proportion of intervention than control group patients improved in terms of their functional impairment ($p < 0.05$) at 26 months; however, only three patients from the total of nine in the intervention group appeared to have been included in the analysis. Bonner reported significantly fewer activity restrictions in intervention compared with control patients at 3 months ($p < 0.01$). In the study by Cowie, intervention group patients showed significantly better scores at 6 months than control patients on symptom ($p = 0.048$) and emotional subscales ($p = 0.028$), but not activity ($p = 0.4$) or environmental subscales ($p = 0.13$), of an asthma-specific questionnaire. The overall improvement in QoL in intervention group patients compared with controls in this study was of borderline significance ($p = 0.06$). Catrambone reported no significant differences between groups in parent's perceptions of their child's health at any of the 3-monthly follow-up points at which this was assessed (all $p > 0.41$) or in cumulative estimates over 18 months ($p = 0.84$). The final study reporting QoL outcomes (Vazquez) suggested that the self-management intervention evaluated significantly reduced the negative consequences of asthma for children at 12 months ($p < 0.005$) but not for the family or overall (p -values were not reported for the latter measures).

Medication use

Twelve studies, 10 RCTs (Cowie, Dahl, Mitchell, Bonner, Gustafsson, Krieger, McNabb, Ronchetti, Garrett, Griffiths) and two CCTs (Kelly, Vazquez), reported assessment of medication use. Of the 11 studies reporting on methods of assessment, six obtained data on medications from medical records or health professional reports and five from patient or caregiver reports via interviews, questionnaires or diaries over a maximum recall period of 2 months. Most studies specified that they assessed beta-agonist use (Cowie, Dahl, Mitchell, Bonner, Gustafsson, Krieger, Vazquez), four ICS use (Bonner, Mitchell, Cowie, Kelly), two oral steroid courses (Mitchell, Garrett) and two studies one or more of theophylline, cromoglycate, long-acting beta-agonists and non-steroidal anti-inflammatory medication (Mitchell, Bonner). In other studies it was stated that medication use in general was assessed. Results were difficult to interpret since data that appeared to be collected were not consistently reported, several studies calculated composite medication counts or scores

(Mitchell, Gustafsson, McNabb, Ronchetti) and time points for assessment varied.

One study did not report data for the eligible subgroup (Griffiths), no results were yet available for another (Krieger) and two did not present any formal comparison between groups (Ronchetti, Kelly). Of the remaining studies reporting results, three showed significant effects in at least one domain of medication use: one (Dahl) a significant reduction in beta-agonist use at 8 weeks in the intervention compared with the control group ($p < 0.05$) and two increased use of preventive medication in intervention patients at three (Bonner, $p < 0.03$) and 9 months (Garrett, $p < 0.05$). The other five studies reported no significant differences between groups in any of the domains of medication use assessed (Gustafsson, Cowie, Mitchell, McNabb, Vazquez) at follow-up points ranging from 6 to 18 months.

Other unscheduled healthcare attendances

Ten studies, nine RCTs (Griffiths, Wesseldine, McNabb, Garrett, Madge, 1997, Sullivan, Krieger, Colland, Evans) and one CCT (Vazquez), reported assessment of other unscheduled healthcare attendances. Data comprised emergency attendances apart from those at A&E departments (e.g. to physicians, clinics or GPs) and composite measures of emergency attendance. All studies reported their methods of assessment with four relying on extraction of data from medical records (Griffiths, McNabb, Wesseldine, Vazquez), five using self-report data from interviews or questionnaires completed by patients or caregivers over recall periods ranging from 2 to 12 months (Sullivan, Krieger, Madge, 1997, Colland, Evans) and one obtaining data from GPs (Garrett). Two studies specified unscheduled attendances as their primary outcome (Griffiths, McNabb). No results were yet reported for one study described in two recent papers (Krieger).

Short-term follow-up of other unscheduled healthcare attendances

Five studies, four RCTs (Griffiths, Wesseldine, McNabb, Colland) and one CCT (Vazquez), reported assessment of other unscheduled attendances in the short term, with follow-up ranging from 1 month (Vazquez, Colland) to 3 months (McNabb). One study did not ultimately report data separately for this time point (Griffiths) and another (Colland) reported significantly fewer unscheduled attendances in the intervention compared with the control group at 1 month ($p < 0.02$) but did not present any data

TABLE 33 Comparisons of proportion of children attending for other unscheduled care in psycho-educational intervention versus control groups at medium-term follow-up (6–11 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) attending | | RR (95% CI) |
|-------------|-------------------------------|-------------------|----------------------|----------------|------------------------|
| | | | Intervention | Control | |
| Madge, 1997 | Possible | Self-management | 11/96 (11%) | 7/105 (7%) | 1.72 (0.69 to 4.25) |
| Wesseldine | Possible | Self-management | 31/78 (40%) | 72/77 (94%) | 0.43 (0.32 to 0.56) |

to support this statement. Vazquez reported no significant differences in mean attendances between groups (no p -value was reported). McNabb presented means and SDs for numbers of emergency treatments per patient at 3 months and reported significantly fewer in the intervention compared with the control group ($p = 0.019$). Only Wesseldine provided data on the number of patients in each group within the total sample of 150 attending for unscheduled care. These data suggested that almost 50% fewer patients in the intervention group had consulted their GP for problematic asthma 6 weeks after the intervention, a difference that was statistically significant ($p = 0.001$).

Medium-term follow-up of other unscheduled healthcare attendances

Six studies, five RCTs (Griffiths, Wesseldine, Garrett, Madge, 1997, Colland) and one CCT (Vazquez), reported assessment of other unscheduled attendances in the medium term, with follow-up ranging from 6 months, reported in the majority of studies (Vazquez, Colland, Wesseldine, Griffiths), to 9 months (Garrett). Again, one study did not ultimately report data separately for this time point (Griffiths) and another (Colland) reported significantly fewer unscheduled attendances in the intervention compared with the control group ($p < 0.02$) but did not present any data to support this statement. Vazquez reported no significant differences in mean attendances between groups (no p -value was reported). The study by Garrett reported no significant differences in emergency visits between groups for children in the study at 9 months ($p = 0.53$), but presented data on the proportion of patients who attended only for the whole sample, the majority of whom were adults.

Two studies (Wesseldine, Madge, 1997) provided data on the number of patients in each group attending for unscheduled care, from which summary statistics could be calculated. In the

Wesseldine study the follow-up was at 6 months. In the Madge (1997) study, the midpoint of 8 months was assumed to be the average duration of follow-up. Individual study results and RRs calculated from them are presented in *Table 33*.

Both studies were similar in terms of the degree to which they were judged to have targeted difficult asthma (possible) and type of intervention (self-management). However, one showed a non-significant effect in favour of the control group (Madge, 1997) and the other a significant effect in favour of the intervention, suggesting >50% fewer intervention patients attending for other unscheduled care, compared with controls.

Long-term follow-up of other unscheduled healthcare attendances

Six studies, five RCTs (Sullivan, McNabb, Colland, Griffiths, Evans) and one CCT (Vazquez), reported long-term follow-up of other unscheduled healthcare attendances. All studies reported follow-up at 12 months and Sullivan reported additional data at 2 years.

Colland did not ultimately report any data for the 12-month follow-up. No significant differences in mean numbers of emergency attendances between groups were reported by Sullivan ($p = 0.32$ at 12 months, $p = 0.75$ at 2 years), Evans (no p -value reported) and Vazquez (no p -value reported). McNabb reported mean total numbers of attendances per group at 12-months which suggested maintenance of the differences observed at 3 months; however, no formal comparison was conducted. Griffiths provided data on the proportions of patients in each group attending for unscheduled care and time to reattendance, within the subgroup of 164 ethnic minority patients of interest. Preliminary results obtained from the author suggest no significant effect of the intervention on the proportions attending (adjusted odds ratio = 0.54, 95% CI = 0.25 to 1.16) or time to reattendance (hazard ratio = 0.72,

95% CI = 0.48 to 1.09) in the south Asian subgroup, despite increases in the time to re-attendance in the white participants also included in the total sample (hazard ratio = 0.57, 95% CI = 0.38 to 0.85).

Other unscheduled healthcare attendances across all follow-up time points

Since there were only three studies in total reporting appropriate data for calculation of summary statistics, an analysis of studies combined across different time points was not conducted since this would not allow any meaningful assessment of results across different subgroups.

Respiratory function

Ten studies, seven RCTs (Dahl, Hanson, Gustafsson, Kreiger, Ronchetti, Wilkening, Garrett), and three CCTs (Alexander, 1972, Davis, Vazquez), reported assessment of respiratory function at time points ranging from 8 days to 32 months. Respiratory function appeared to be the primary outcome in one study (Alexander, 1972), although this was not specified in advance.

Of these studies, seven (Vazquez, Dahl, Gustafsson, Wilkening, Alexander, 1972, Davis, Garrett) presented PEF data in various forms (e.g. percentage predicted, mean change, categories of improvement, variability), five reporting no significant differences between groups (Vazquez, Davis, Garrett, Dahl, Gustafsson) and two (Alexander, 1972, Wilkening) significant improvements in intervention patients relative to controls. One of the latter studies (Alexander, 1972) reported significantly greater improvements ($p < 0.005$) in intervention patients than control patients during the final three sessions of their 8-day relaxation training intervention provided to half of the sample of 36 patients classified as definite in terms of difficult asthma. The other (Wilkening) reported improvements in PEF amongst 30 intervention group patients who received a behavioural programme as compared with worsening PEF amongst 26 control patients at 6 months (p -values were not reported), but presented no actual data to support this claim.

Two studies reported assessment of FEV₁ using spirometry equipment (Krieger, Ronchetti) and one study other measures of respiratory function (Hanson). For one of these no results data were yet available (Krieger) and the others reported no significant effects of interventions on the respiratory function measures assessed. However, neither reported any actual data to support these claims.

Scheduled healthcare attendances

Nine studies, eight RCTs (Griffiths, Wesseldine, McNabb, Catrambone, Lewis, Garrett, Shields, Alexander, 1988) and one CCT (Kelly), reported assessment of scheduled healthcare attendances. All nine studies reported their methods of assessment, and of these six relied on extraction of data from medical records (Griffiths, McNabb, Weinstein, Kelly, Lewis, Shields), two used self-report data from interviews or questionnaires completed by patients or caregivers over recall periods ranging from 2 to 4 weeks (Catrambone, Wesseldine) and one obtained data from GPs (Garrett). Ultimately, one study did not report outcome data for the subgroup of interest (Griffiths). It is not entirely clear in the majority of studies whether a reduction or an increase in scheduled healthcare attendances constitutes a good outcome.

Short-term follow-up of scheduled healthcare attendances

Only three studies, all RCTs (Catrambone, McNabb, Wesseldine), reported assessment of scheduled attendances in the short term, with follow-up ranging from 6 weeks (Wesseldine) to 3 months (Catrambone, McNabb). Two studies reported means and SDs for the number of visits, with one (McNabb) reporting reductions in the intervention compared with the control group ($p = 0.04$) and one (Catrambone) the opposite ($p = 0.05$). Wesseldine presented data on the numbers attending in each group that suggested little difference between groups (p -value not reported).

Medium-term follow-up of scheduled healthcare attendances

Four studies, all RCTs (Catrambone, Lewis, Wesseldine, Garrett), reported assessment of scheduled attendances in the medium term, with follow-up ranging from 6 (Wesseldine, Lewis, Catrambone) to 9 months (Catrambone, Garrett). Two studies did not ultimately report data for this time point (Lewis, Wesseldine) and Garrett commented on there being no differences between groups without presenting any data to support this statement. The remaining study by Catrambone presented means and SDs for the number of visits at 6 and 9 months but showed no differences between groups at either time point ($p = 0.92$, 0.33 respectively).

Long-term follow-up of scheduled healthcare attendances

Six studies, five RCTs (Catrambone, Lewis, Shields, Alexander, 1988, McNabb) and one CCT

TABLE 34 Comparisons of proportion of children attending for scheduled care in psycho-educational intervention versus control groups at long-term follow-up (> 12 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) attending | | RR (95% CI) |
|------------|-------------------------------|-------------------|-----------------------------|-----------------------------|------------------------|
| | | | Intervention | Control | |
| Lewis | Possible | Multifaceted | 8/15 (53%) | 8/13 (62%) | 0.87 (0.46 to 1.64) |
| Catrambone | Probable | Multifaceted | 30/66 ^a (45%) | 24/58 ^a (41%) | 1.10 (0.73 to 1.65) |

^a Estimated from percentages reported.

(Kelly), reported long-term follow-up of scheduled healthcare attendances. All studies except Catrambone, where the final follow-up was at 18 months, reported follow-up at 12 months. Shields also reported follow-up data for an additional time point at up to 29 months.

In the study by Kelly, scheduled allergy clinic visits were costed, but details on numbers of attendances were provided disaggregated for the intervention group only. McNabb commented that there were no differences between groups in scheduled attendances but did not provide any data to support this statement and Alexander (1988) presented means and SDs for total numbers of attendances throughout the study and commented that the groups were similar but did not present a formal comparison. In the study by Shields, means and SDs for numbers of office visits for asthma and other conditions were presented but there were reported to be no significant differences between groups (no *p*-value was provided).

Two RCTs presented data on the number of patients attending for scheduled care (Catrambone, Lewis) and summary results for these are presented in *Table 34*.

Both studies were similar in terms of the type of intervention evaluated (multifaceted) but the study by Catrambone was classified as probable in terms of its targeting of difficult asthma and Lewis as possible. Catrambone showed non-significantly higher attendance in the control group and Lewis non-significantly higher attendance in the intervention group.

Scheduled healthcare attendances across all follow-up time points

Since there were only three studies in total reporting appropriate data for calculation of summary statistics, an analysis of studies combined across different time points was not conducted

since this would not allow any meaningful assessment of results across different subgroups.

School or work time lost

Nine studies, eight RCTs (Cowie, Dahl, Wesseldine, Mitchell, Krieger, Garrett, Colland, Evans) and one CCT (Vazquez), assessed days of children's absence from school or work due to asthma. Follow-up data were not yet available for one study (Kreiger).

Short-term follow-up of school or work time lost

Five studies, four RCTS (Wesseldine, Dahl, Cowie, Colland) and one CCT (Vazquez), reported assessment of absence from school or work in the short term at follow-ups ranging from 1 (Vazquez) to 4 months (Colland). Three studies ultimately did not report data separately for this time point (Colland, Wesseldine, Cowie). Vazquez presented mean numbers of days of children's absence from school and reported no significant differences between groups at an unspecified time point (no *p*-values were reported). Dahl reported the percentage change in absence from baseline and reported significantly greater reductions in the intervention compared with the control group (*p* < 0.05).

Medium-term follow-up of school or work time lost

Six studies, five RCTs (Wesseldine, Cowie, Mitchell, Garrett, Colland) and one CCT (Vazquez), reported assessment of time lost from work or school in the medium term at follow-up points ranging from 6 months in four studies (Wesseldine, Cowie, Mitchell, Vazquez) to 9 months in two studies (Garrett, Colland). Colland ultimately did not report outcome data separately for this time point and Garrett did not present results separately for children. The four remaining studies (Wesseldine, Cowie, Mitchell, Vazquez) reported absence from school or work in various ways but none showed significant differences between groups.

Long-term follow-up of school or work time lost

Three studies, two RCTs (Colland, Evans) and one CCT (Vazquez), reported long-term assessment of school or work time lost, two at 12 months from baseline (Vazquez, Evans) and one at 15 months (Colland). Colland reported significantly lower absence from school in intervention compared with control patients ($p < 0.05$) but presented no data to support this claim and the two remaining studies reported no significant differences between groups (p -values were not reported).

School or work time lost across all follow-up time points

Calculation of summary statistics to allow analysis of studies combined across different time points was not possible.

Knowledge

Six RCTs (Mitchell, Colland, Krieger, McNabb, Bonner, Lewis) reported assessment of knowledge related to asthma and its management. On detailed data extraction it was apparent that two of these assessed knowledge of caregivers only (Kreiger, Bonner), so outcome data for these were not considered further. Two studies appeared to assess knowledge in the children and caregivers (Lewis, Mitchell), although in the results it was not entirely clear which data were reported. One study (Colland) administered to the children studied a knowledge subscale from a previously published questionnaire, the Asthma Knowledge and Compliance Test for Children, designed by the author. In another study, open-ended knowledge questions relating to asthma prevention, intervention, medication taking and adjustment were administered during diagnostic interviews (McNabb).

Of the four studies that appeared to assess patient knowledge, one ultimately did not report results in relation to knowledge (Lewis) and one reported outcome data only for the intervention group (McNabb). The study by Mitchell reported that there were no significant differences in the proportions of patients with appropriate knowledge between groups at follow-up for the subgroup of patients of interest. Colland reported significantly improved knowledge scores in the intervention compared with the control group at 1 and 6 months but provided no details of results at the 12-month follow-up point.

Severity

Six studies, all RCTs (Garrett, Gustafsson, Harish, Lewis, Ronchetti, Colland), reported assessment of some global measure of asthma severity. These

assessments were made on the basis of clinical evaluations, broad classifications or composite scores calculated from two or more indices of symptoms, attacks, medication use, daily functioning, respiratory function and/or health service use. Two studies (Ronchetti, Lewis) did not ultimately report severity as an outcome. The study by Garrett did not report severity results separately for the subgroup of children examined in the sample. Harish reported a higher proportion of severe patients in the intervention group compared with the control group at 1 year follow-up (no p -value was reported); however, it was unclear whether this was simply due to greater loss to follow-up of milder patients from the intervention group. Of the remaining studies, one reported significantly higher proportions of patients who were judged to have improved from baseline in terms of their severity compared with the control group ($p < 0.05$) at 18 months following a psychosocial intervention targeting patients judged possible in terms of difficult asthma (Gustafsson). The final study reported differences of borderline significance ($p < 0.06$) in severity between groups at 12 months following a self-management intervention in patients classified as probable in terms of difficult asthma (Colland).

Psychological morbidity

Five studies, four RCTs (Colland, Garrett, Sullivan, Wilkening) and one CCT (Davis), reported assessment of psychological morbidity. One (Garrett) assessed, via an interview, levels of anxiety at the time of an attack only in the caregivers of the children in the study, hence these data were not considered further. The other studies used published measures to assess psychological morbidity in children: one (Wilkening) the Hospital Anxiety and Depression Scale,⁵²¹ one (Sullivan) the Child Behaviour Checklist,⁵²² one (Davis) the Mood Adjective Checklist⁵²³ and one (Colland) the State-Trait Anxiety Questionnaire for Children.⁵²⁴

One study (Sullivan) reported baseline data only and two studies (Davis, Wilkening) reported no significant differences between groups but did not present any data to support their statements. Colland reported significantly reduced anxiety scores in the intervention compared with the control at 1 month ($p < 0.042$), but no difference at 6 months (p -values not reported) except in extremely anxious children ($p < 0.05$). Twelve-month data were not reported.

Self-efficacy/perceived control

Five studies, four RCTs (Hanson, Bonner, Evans,

Colland) and one CCT (Vazquez), reported assessment of a construct similar to self-efficacy or perceived control. However, on detailed data extraction it became apparent that two studies (Hanson, Bonner) assessed parental or caregiver and not patient self-efficacy/confidence, so results in relation to these were not considered further. Of the remaining three studies, one (Vazquez) used a validated generic Children's Health Locus of Control Scale⁵²⁵ and one (Colland) a self-efficacy subscale from a validated Asthma Coping Test designed by the author, where reference was made to a submitted paper. The final study (Evans) derived an index of self-efficacy in relation to 13 asthma management behaviours from the baseline interviews conducted.

One study did not ultimately report results for the self-efficacy subscale of the questionnaire used (Colland) and another did not report results for the subgroup of interest (Vazquez). The remaining study reported significantly greater improvements in child self-efficacy ($p = 0.04$) in the intervention compared with the control group amongst patients classified as possible in terms of difficult asthma at 1 year following an educational intervention (Evans).

Exacerbations

Four studies, three RCTs (Ronchetti, Mitchell, Evans) and one CCT (Vazquez), reported assessment of exacerbations at follow-up time points ranging from 1 (Vazquez) to 18 months (Mitchell). One study did not report outcome data in relation to exacerbations (Ronchetti). Of the three remaining studies, one (Mitchell) reported no differences between groups in terms of the proportions of patients who had experienced an attack at 6 months follow-up (p -value not provided) and one reported significantly greater reductions in the number ($p = 0.024$) and duration ($p = 0.007$) of attacks in the educational intervention group compared with the control group of patients classified as possible in terms of difficult asthma (Evans). The final study (Vazquez) reported that the self-management intervention alone significantly reduced duration of attacks and level of therapeutic response ($p < 0.05$) compared with the control group but had no significant effect on the frequency or intensity of attacks at 12 months (no p -values reported).

Beliefs/attitudes

Only two RCTs (Bonner, Gold) reported assessment of beliefs and/or attitudes related to asthma and its management. It became apparent on detailed data extraction that Bonner examined

parental or caregiver beliefs and attitudes alone, so these data were not considered further. The other study (Gold) referenced use of a standard Asthma Attitude Scale⁵²⁶ of which a subscale was used to assess children's attitudes; however, no significant differences between groups were found (p -values for the group comparison were not reported).

Satisfaction

Two studies, both RCTs, reported assessment of patient satisfaction with interventions provided; however, formal results were not yet available for one study (Kreiger) and the other did not ultimately present any data in relation to satisfaction (Hanson).

Deaths

No studies in children were recorded as reporting on deaths.

Other outcomes

Other patient outcomes reported in studies of children, for which detailed data were not extracted, were as follows:

- academic performance (Evans)
- child's influence on parent's decision-making (Evans)
- receipt of flu vaccination (Kelly)
- levels of relaxation (Davis, Alexander, 1972)
- infections (Wesseldine)
- barriers to improved management (Lewis)
- allergen exposure (Krieger)
- family conflict behaviour (Gold)
- self-regulation (Bonner)
- family adaptation (Hanson)
- improvement (possibly equivalent to severity?) (Mitchell)
- social support (Garrett).

Summary of effectiveness results

Psycho-educational interventions compared with routine or other non-psycho-educational care

Table 35 presents a summary of the findings and main conclusions in relation to the key outcomes assessed in trials comparing psycho-educational interventions with routine or non-psycho-educational care in children. Where results within individual studies varied across different measures of the same outcome or at different follow-up points, or multiple studies suggested conflicting findings, results are described as mixed. Qualifications to conclusions on the basis of available data and in light of any subgroup analyses conducted are also provided.

TABLE 35 Summary of effectiveness results for psycho-educational interventions (PEI) compared with usual or non-psycho-educational care (UC) in children

| Type of outcome | Length of follow-up | Number of and reported findings from studies providing any results data | Number of studies reporting data for calculation of summary statistic and findings based on these | Meta-analysis conducted? | Conclusions |
|-----------------|---------------------------------|---|--|--------------------------------|---|
| Admissions | Short | 2 studies 2 no sig. differences | 1 study 1 non-sig. effects favouring PEI | N/A | Limited data on which to base valid conclusions |
| | Medium | 6 studies 2 sig. effects favouring PEI 4 no sig. differences | 4 studies 2 sig. effects favouring PEI 1 non-sig. effects favouring PEI 1 non-sig. effects favouring UC | No – significant heterogeneity | Clear evidence of medium-term effectiveness confined to only 2 individual studies of self-management with possible targeting of difficult asthma |
| | Long | 8 studies 1 sig. effects favouring PEI 7 no sig. differences | 6 studies 3 non-sig. effects favouring PEI 2 no clear differences 1 non-sig. effects favouring UC | Yes | Small, and non-significant, pooled effect favouring intervention (RR = 0.84, 95% CI = 0.68 to 1.02). Individual study data provide little evidence of long-term effectiveness |
| | Latest reported (min. 6 months) | 12 studies 3 sig. effects favouring PEI 9 no sig. differences | 9 studies 2 sig. effects favouring PEI 4 non-sig. effects favouring PEI 2 no clear differences 1 non-sig. effects favouring UC | Yes – with subgroup analyses | Significant pooled effect in favour of intervention (RR = 0.64, 95% CI = 0.46 to 0.89), but individual study data show greatest and only significant effects confined to 2 trials of self-management with possible targeting of difficult asthma and lacking long-term follow-up. Subgroup analyses suggest lesser and non-significant effect in studies with probable (RR = 0.81, 95% CI = 0.59 to 1.11) compared to possible (RR = 0.47, 95% CI = 0.30 to 0.73) targeting of difficult asthma. Also, greatest and only significant effects seen in studies of self-management (RR = 0.37, 95% CI = 0.24 to 0.59), with effects of multifaceted interventions of borderline significance (RR = 0.76, 95% CI = 0.58 to 1.01), but these findings are confounded by the fact that more studies of multifaceted interventions had probable, compared with possible targeting of difficult asthma |

continued

TABLE 35 Summary of effectiveness results for psycho-educational interventions (PEI) compared with usual or non-psycho-educational care (UC) in children (cont'd)

| Type of outcome | Length of follow-up | Number of and reported findings from studies providing any results data | Number of studies reporting data for calculation of summary statistic and findings based on these | Meta-analysis conducted? | Conclusions |
|------------------|---------------------------------|---|--|--------------------------------|--|
| A&E attendance | Short | 2 studies 1 sig. effects favouring PEI 1 no sig. differences | 1 study 1 non-sig. effects favouring PEI | N/A | Limited data on which to base valid conclusions |
| | Medium | 5 studies 1 sig. effects favouring PEI 4 no sig. differences | 3 studies 1 sig. effects favouring PEI 1 non-sig. effects favouring PEI 1 no clear differences | No – significant heterogeneity | Individual study data provide little evidence of effectiveness, with only significant effects seen in a single study of self-management with possible targeting of difficult asthma |
| | Long | 9 studies 4 sig. effects favouring PEI 5 no sig. differences | 5 studies 2 non-sig. effects favouring PEI 3 non-sig. effects favouring UC | Yes | No overall pooled effect (RR = 0.97, 95% CI = 0.78 to 1.21), with individual study data showing mixed results |
| | Latest reported (min. 6 months) | 12 studies 4 sig. effects favouring PEI 8 no sig. differences | 8 studies 1 sig. effects favouring PEI 3 non-sig. effects favouring PEI 1 no clear differences 3 non-sig. effects favouring UC | No – significant heterogeneity | Individual study data show mixed results, with only clearly significant effect confined to a single study of self-management with possible targeting of difficult asthma and lacking long-term follow-up |
| Symptoms/control | Short | 5 studies 1 sig. effects favouring PEI 1 mixed results 3 no sig. differences | 2 studies 1 sig. effects favouring PEI 1 non-sig. effects favouring PEI | N/A | Limited individual study data show mixed results, with only significant effects confined to a single study of a multifaceted intervention with possible targeting of difficult asthma |
| | Medium | 4 studies 1 sig. effects favouring PEI 3 no sig. differences | 2 studies 2 non-sig. effects favouring PEI | N/A | Individual study data provide little evidence of effectiveness |
| | Long | 4 studies 2 sig. effects favouring PEI 1 mixed results 1 no sig. differences | 2 studies 2 non-sig. effects favouring PEI | N/A | Individual study data provide little evidence of effectiveness |

continued

TABLE 35 Summary of effectiveness results for psycho-educational interventions (PEI) compared with usual or non-psycho-educational care (UC) in children (cont'd)

| Type of outcome | Length of follow-up | Number of and reported findings from studies providing any results data | Number of studies reporting data for calculation of summary statistic and findings based on these | Meta-analysis conducted? | Conclusions |
|--|----------------------------------|--|---|------------------------------|--|
| | Latest reported (min. 3–4 weeks) | 9 studies 4 sig. effects favouring PEI 2 mixed results 3 no sig. differences | 4 studies 1 sig. effects favouring PEI 3 non-sig. effects favouring PEI | Yes – with subgroup analyses | Significant pooled effect in favour of intervention (SMD = -0.45, 95% CI = -0.68 to -0.22), but individual study data show mixed results with only clearly significant effects confined to a single study of a multifaceted intervention with possible targeting of difficult asthma and lacking long-term follow-up. Subgroup analyses showed effects similar in studies with probable versus possible targeting of difficult asthma and greater for multifaceted compared with educational interventions (although effects significant for both) |
| Self-care behaviour | All | 6 studies 4 some sig. effects favouring PEI 1 mixed results 1 no sig. differences | N/A | N/A | Comparison and synthesis across studies difficult as all assessed different aspects; however, individual study data suggest effects mainly favour intervention |
| Health status/QoL | All | 5 studies 2 sig. effects favouring PEI 2 mixed results 1 no sig. differences | N/A | N/A | Comparison and synthesis across studies difficult as all used different types of measures. Individual study data show mixed results |
| Medication use | All | 8 studies 3 some sig. effects favouring PEI 5 no sig. differences | N/A | N/A | Comparison and synthesis across studies difficult as all assessed different outcomes. Individual study data show mixed results |
| Other unscheduled healthcare attendances | Short Medium | 3 studies 2 sig. effects favouring PEI 1 no sig. differences 4 studies 1 sig. effects favouring PEI 3 no sig. differences | 1 study 1 sig. effects favouring PEI 2 studies 1 sig. effects favouring PEI 1 non-sig. effects favouring UC | N/A N/A | Limited individual study data show effects mainly favour intervention Individual study data show mixed results |

continued

TABLE 35 Summary of effectiveness results for psycho-educational interventions (PEI) compared with usual or non-psycho-educational care (UC) in children (cont'd)

| Type of outcome | Length of follow-up | Number of and reported findings from studies providing any results data | Number of studies reporting data for calculation of summary statistic and findings based on these | Meta-analysis conducted? | Conclusions |
|---------------------------------|---------------------------------|---|--|--------------------------|--|
| | Long | 5 studies 1 unclear 4 no sig. differences | 1 study 1 non-sig. effects favouring PEI | N/A | Individual study data provide little evidence of effectiveness |
| | Latest reported (min. 3 months) | 8 studies 2 sig. effects favouring PEI 6 no sig. differences | 3 studies 1 sig. effects favouring PEI 1 non-sig. effects favouring PEI 1 non-sig. effects favouring UC | N/A | Individual study data provide little evidence of effectiveness |
| Respiratory function | All | 6 studies 1 sig. effects favouring PEI 5 no sig. differences | N/A | N/A | Comparison and synthesis across studies difficult as all used assessed and reported outcomes in different ways. Individual study data provide little evidence of effectiveness |
| Scheduled healthcare attendance | Short | 3 studies 1 sig. effects favouring PEI 1 no sig. differences 1 sig. effects favouring UC | 1 study No clear differences | N/A | Limited individual study data show mixed results |
| | Medium | 1 study 1 no sig. differences | N/A | N/A | Limited data on which to base valid conclusions |
| | Long | 3 studies 3 no sig. differences | 2 studies 1 non-sig. effects favouring PEI 1 non-sig. effects favouring UC | N/A | Individual study data provide little evidence of effectiveness |
| | Latest reported (min. 3 months) | 5 studies 1 sig. effects favouring PEI 4 no sig. differences | 3 studies 1 non-sig. effects favouring PEI 1 no clear differences 1 non-sig. effects favouring UC | N/A | Individual study data show mixed results. |

continued

TABLE 35 Summary of effectiveness results for psycho-educational interventions (PEI) compared with usual or non-psycho-educational care (UC) in children (cont'd)

| Type of outcome | Length of follow-up | Number of and reported findings from studies providing any results data | Number of studies reporting data for calculation of summary statistic and findings based on these | Meta-analysis conducted? | Conclusions |
|--------------------------|--------------------------------|---|---|--------------------------|--|
| School or work time lost | Short | 2 studies 1 sig. effects favouring PEI 1 no sig. differences | N/A | N/A | Limited data on which to base valid conclusions |
| | Medium | 4 studies 4 no sig. differences | N/A | N/A | Individual study data provide no evidence of effectiveness |
| | Long | 2 studies 2 no sig. differences | N/A | N/A | Limited data on which to base valid conclusions |
| | Latest reported (min. 8 weeks) | 6 studies 1 sig. effects favouring PEI 5 no sig. differences | N/A | N/A | Comparison and synthesis across studies difficult as all assessed and reported in different ways. Individual study data provide little evidence of effectiveness |

Although all of the outcomes summarised in *Table 35* were reported as assessed by more than one-third of studies, and in a number of cases identified as primary outcomes (see *Table 25*), as can be seen, the number of studies actually reporting any results data for intervention and control groups (rather than just commenting on findings) in relation to these outcomes and, amongst these, reporting data in a format suitable for calculation of summary statistics, is more limited. Generally, the studies reporting valid statistics for calculation of summary effect sizes were of higher quality than those that did not, hence additional weight may be given to these in interpreting results.

In no studies for any outcome were there significant effects in favour of the control group, suggesting that psycho-educational interventions are unlikely to do harm or to be less effective than routine or other non-psycho-educational care alone. The data overall suggest that psycho-educational interventions, as compared with routine care or minimal intervention, may reduce hospital admissions for asthma in children, although the greatest and only significant effects appear to be confined to studies with possible, as opposed to probable, targeting of difficult asthma and lacking long-term follow-up. There was little evidence of effects on A&E attendances. Psycho-educational interventions may reduce symptoms in children and in this case effects appear similar across different subgroups of difficult asthma; however, data are more limited. Studies also showed mainly positive effects on various measures of self-care behaviour but, with respect to all other outcomes where sufficient data allowed conclusions to be drawn, studies showed mixed results or provided no clear evidence of the effectiveness of psycho-educational interventions for difficult asthma in children.

Where this could be examined, self-management interventions appeared to have the greatest effects, followed by multifaceted and educational interventions. However, studies of self-management interventions tended to have possible targeting of difficult asthma and those of multifaceted interventions probable targeting, making it difficult to draw any valid conclusions regarding the relative effectiveness of interventions of different types. No studies of psychosocial interventions were ultimately included in any quantitative synthesis of results, so the effectiveness of these remains unclear. None of the studies with definite targeting of difficult asthma reported data in a format which allowed

them to be included in quantitative syntheses, so it is also uncertain whether any effects of psycho-educational interventions extend to the most at-risk patients.

Comparisons of different psycho-educational interventions

As highlighted earlier, the two studies in children that compared two different forms of psycho-educational intervention without reference to a control group were not included in the formal summary of results, one because it was an observational study (Weinstein) and the other because no results had yet been reported (Kreiger). Amongst the three other studies which compared more than one psycho-educational intervention with a control group, Ronchetti reported that the more interactive Open Airways self-management programme evaluated showed significantly greater effects on emergency treatments than the Living with Asthma programme and only for the standard, as opposed to reduced length, programmes were outcomes significantly different to the control group. There were no significant differences between an educational intervention incorporating relaxation training and a standard educational programme in the study by Vazquez and in the study by Davis it was unclear whether the two different forms of relaxation training differed. There is therefore a paucity of evidence on the relative effectiveness of psycho-educational interventions of different types in children with difficult asthma.

Assessment of publication bias

A funnel plot constructed for the most commonly reported outcome in studies of children (admissions) is shown in *Figure 12*.

No small trials reporting negative results, to mirror the one reporting the greatest positive effects in favour of the intervention, were apparent amongst the studies in children. Owing to the small number of such trials overall, however, it is unclear whether this resulted from publication bias *per se*.

Costs and cost-effectiveness

Quantity and characteristics of economic studies

This section reports on studies that were tagged as relevant to the economic section of the review in that they reported assessment of cost data in monetary units. Studies that were identified as including costs but were not reviewed further on

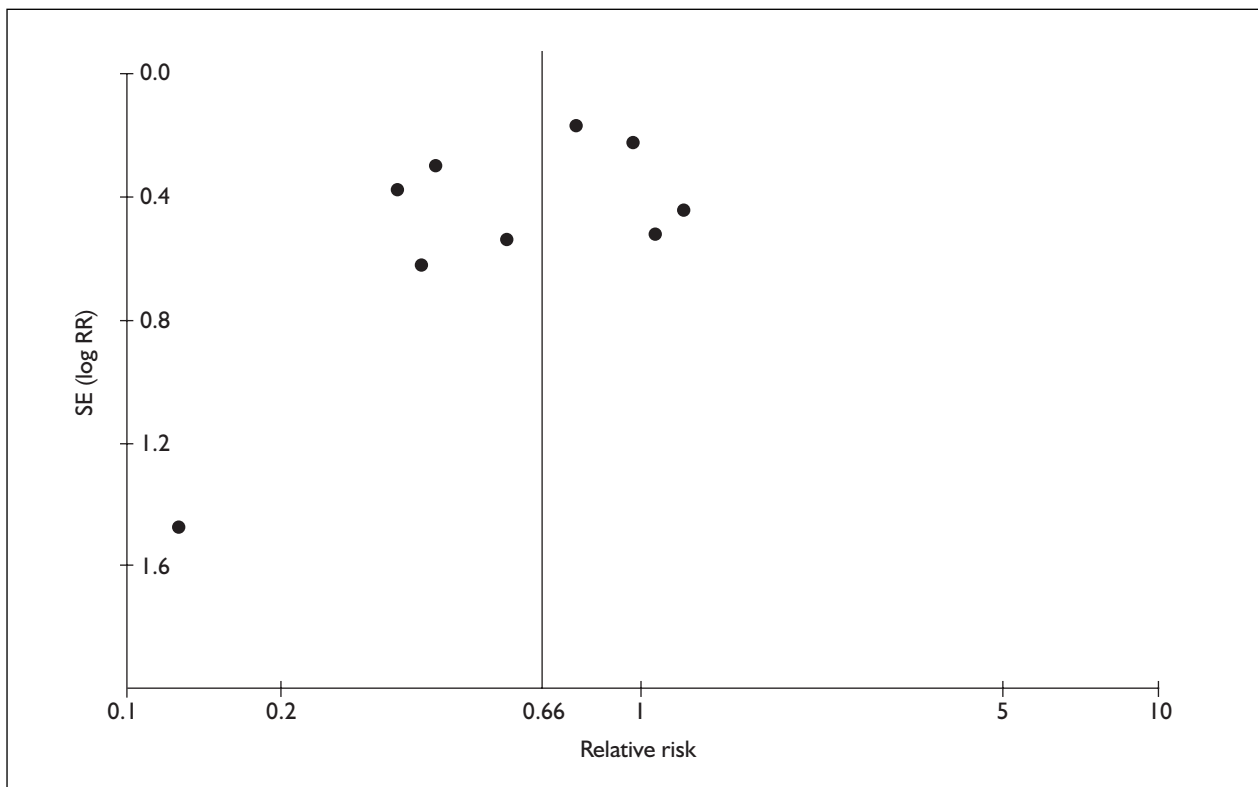


FIGURE 12 Funnel plot constructed from admissions data in children at latest follow-up reported by studies

the basis of insufficient evidence for targeting of difficult asthma or poor study design are listed in Appendices 11 and 12. A total of 12 studies with independent control groups graded as at least possible in terms of their targeting of difficult asthma were initially tagged as economic studies and considered for economic data extraction. One further study (Ronchetti) was noted as including conclusions regarding cost-effectiveness without presentation of any cost data, so this study was not considered further.

Economic data were ultimately extracted from eight of the 12 studies in children identified for economic review. Two recently completed RCTs (Griffiths, Hanson) had been described as cost-effectiveness studies in data sources reviewed but could not be assessed further as economic studies because costing methods and cost data had not yet been reported and could not be obtained from authors. The study by Lewis had conducted a limited assessment of costs but did not report data separately for the at-risk subgroups of interest. One further study (Kirk) reported only very limited hospital charge data for intervention group patients before and after the multifaceted programme they evaluated in the abstract available for data extraction. These studies are therefore not reviewed further in this section.

All of the remaining eight studies were conducted in the USA and reported costs in US dollars. A classification of these, comprising six RCTs (Alexander, 1988, Greineder, McNabb, Shields, Sullivan, Harish), one CCT (Kelly) and one COS (Weinstein), is provided in *Table 36*.

As can be seen, only one study (Sullivan) was considered to be a cost-effectiveness analysis based on an effectiveness study of a sound design. The others were effectiveness studies which provided some, often very limited, planned or unplanned assessment of costs. It should also be noted that although controlled studies for the purposes of assessing effectiveness, four studies (Greineder, Harish, Kelly, Weinstein) only provided before-and-after cost data for intervention group patients, sometimes in separate papers from the effectiveness results.

Quality of economic studies

The *BMJ* checklist for peer reviewers of economic studies¹⁶⁵ was used to identify features of the studies pertinent to an assessment of their quality. Detailed data for individual studies are provided in Appendix 22 and a summary given in *Table 37*.

The *BMJ* checklist¹⁶⁵ includes some categories which may be mutually exclusive (such as items 9

TABLE 36 Classification of economic studies in children by design of effectiveness study

| Source of effectiveness data | Cost-effectiveness analysis | Effectiveness study with some costs | Study reporting costs only | All |
|------------------------------|-----------------------------|-------------------------------------|----------------------------|-----|
| RCT | 1 | 5 | 0 | 6 |
| CCT | 0 | 1 | 0 | 1 |
| COS | 0 | 1 | 0 | 1 |
| All | 1 | 7 | 0 | 8 |

TABLE 37 Quality of economic studies in children

| Number of BMJ checklist items included | Number of studies |
|--|-------------------|
| 0–10 | 4 |
| 11–20 | 3 |
| 21–35 | 1 |
| Total | 8 |

and 10 on sources of effectiveness data), so a score of 35 is extremely unlikely. We scored studies only where it was clear that the answer was true. Where it was partially true or not applicable, no score was given. Only the study considered to be a cost-effectiveness analysis in *Table 36* (Sullivan) met most of the criteria for consideration as a good economic evaluation and included any formal incremental and sensitivity analyses. Along with one other study (Greineder), this was also the only one to state specifically the economic question that the research was addressing, although two others (Alexander, Kelly) emphasised the importance of the economic problem, the high cost of care for severe asthma and the scarcity of funds and resources for this patient group.

Even though most of the studies did not aim to be formal economic evaluations, and would not be formally classified as such, we have summarised the findings of all the included studies which estimated costs in some form in the following section. The evidence should clearly be considered with reference to the quality of the studies.

Costs

Details of cost data reported in the eight individual economic studies are provided in Appendix 23.

Healthcare costs

All eight studies reported some aspect of healthcare costs and, at least implicitly, took the viewpoint of healthcare providers. All included costs of emergency department use. Two studies

included nothing else (Alexander, McNabb) and the other six included other hospital inpatient and/or outpatient costs. Medication costs were not always mentioned, but were explicitly included by Weinstein, and explicitly excluded by Sullivan. The authors of the latter study discussed this omission. Three studies appear to have considered 'out of hospital' health costs such as primary care nurse clinics or home visits (Kelly, Sullivan, Harish).

Intervention costs

Four studies (McNabb, Shields, Weinstein, Harish) reported separately the financial cost of the intervention (see *Table 38*). Estimates of intervention costs, converted to 2002–03 UK prices, varied from £100 per patient for a class based education programme (Shields) to over £4000 per patient for US hospital charges related to an outpatient rehabilitation programme.

The methods for costing the intervention were not always clear, but appeared to vary with regard to what was included. 'Estimated programme administration costs' were included by McNabb, Shields estimated the education programme expenditure per year per child, Weinstein compared hospital charges for the intervention and control groups and Harish estimated an approximate annual figure for operating the paediatric asthma centre evaluated.

Combined healthcare and intervention costs

Several studies reported differences in costs of healthcare for control and intervention children in the study. In seven of the eight studies, the intervention was compared with usual care. In the remaining study (Weinstein), patients receiving outpatient rehabilitation were compared with a group receiving inpatient rehabilitation, the costs and effectiveness of which had been evaluated previously, in a before-and-after study, comparing inpatient care with prior usual management.³⁶⁸ *Table 39* summarises the findings for studies which reported the difference in costs including the intervention cost.

TABLE 38 Intervention costs from economic studies in children

| Study | Intervention | No. of patients receiving intervention | Currency and price year | Approx. cost per patient | | Comments |
|-----------|---|--|-------------------------|-------------------------------|---|----------------------------------|
| | | | | Local currency and price year | £ sterling 2003 prices (to nearest £10) | |
| McNabb | Tailored education programme in US health maintenance organisation | 7 | US\$ pre-1985 | \$180 | £220 | 'Estimated administration costs' |
| Shields | Education by classes and telephone for patients and parents | 101 | US\$ 1984 | \$96 | £100 | Programme expenditure per year |
| Weinstein | Outpatient rehabilitation programme | 11 | US\$ pre-1998 | \$5781 | £4440 | Hospital charges |
| Harish | Referral from ED to multidisciplinary asthma clinic with tailored care review plus education with home visits | 59 | US\$ pre-2000 | \$625 | £440 | Estimated from data in paper |

TABLE 39 Mean differences in healthcare costs per patient from economic studies in children

| Study | Intervention | Period for costs (months) | Reported mean difference in cost per patient (US\$) | Mean difference in cost per patient in £ sterling 2003 prices | Comments |
|----------|---|---------------------------|---|---|--|
| McNabb | Tailored education programme in US health maintenance organisation | 12 | -\$507 | -£630 | Insufficient information to judge quality of economic results |
| Kelly | Education and nurse outreach in tertiary level US asthma clinic | 12 | -\$515 | -£371 | Insufficient information to judge quality of economic results |
| Harish | Referral from ED to multidisciplinary asthma clinic with tailored care review plus education with home visits | 12 | -\$1316 | -£919 | Insufficient information to judge quality of economic results Cost estimate based on before-and-after comparison of intervention group patients |
| Sullivan | Social worker-led community-based tailored education programme including home visits | 24 | \$245 | £166 | Based on resource use by patients included in the study |

Three studies (McNabb, Kelly, Harish) reported net cost savings over 1 year compared with locally provided usual care and one (Sullivan) reported an increase in net costs over 2 years.

Productivity costs

No studies reported productivity costs arising out of changes in either school attendance or parents' working time. This was discussed as an important omission by Sullivan and Shields.

Patient costs

Although poverty and the cost to families of meeting health and self-care costs was discussed in several papers (Alexander, Sullivan, Harish, Shields) as a possible obstacle to good care, costs were not measured or reported from this viewpoint in any of the reviewed studies.

Cost-effectiveness

All eight studies drew conclusions about the effect of the intervention on healthcare costs. Several

had only measured outcome in terms of utilisation of services (Alexander, Greineder, Shields, Weinstein). Of those that reported health outcomes, only two studies (Kelly, Sullivan) related estimated costs to health outcomes. Kelly found a net reduction in costs (estimated at £371 per child per year) and improvement in health-related QoL in the limited number of intervention families who responded (15 out of 38), but did not include the cost of the intervention in this analysis (estimated at an annual equivalent cost of £11,000 at UK 2003 prices for a part-time nurse salary). Sullivan performed a cost-effectiveness and probabilistic sensitivity analysis which showed a cost of US\$9.20 (£6 at 2003 UK prices) for an additional symptom-free day, with 95% CIs of -£8 to 37 (at 2003 UK prices).

Chapter 6

Results: studies in adults

Overview

The initial part of this chapter provides a descriptive overview of characteristics associated with general features, patients, interventions and methodological quality for the studies of psycho-educational interventions in adults that were selected for in-depth review. Reference is made to Appendices 24–31 for detailed information in relation to these facets for individual studies. Unless indicated otherwise by the use of quotation marks, all data presented rely on paraphrasing from original data sources.

The latter part of this chapter begins with an overview of the comparisons, outcomes and follow-up assessed in studies considered for inclusion in a qualitative and quantitative synthesis of effectiveness results and then provides a summary of results in relation to each outcome.

The final section of the chapter presents information on study quality, costs and cost-effectiveness for the smaller number of studies in adults identified for inclusion in the economics part of the review. Reference is made to Appendices 32 and 33 for detailed data in relation to individual studies.

Quantity and quality of information available for data extraction

Detailed data were extracted from 30 papers and other documents associated with 21 studies in adults^{429–457} and one study which included adult and child subgroups (Garrett).⁴⁰⁴ For all but six studies, data were extracted from one or more published English language journal articles, sometimes accompanied by abstracts or other documents. For two studies (Ford,⁴³² Yoon⁴⁴⁶), additional information on patients or interventions was obtained from two papers^{53,474} and an abstract⁴⁷⁵ excluded in their own right.

With regard to the studies not reported in English language journal articles, data from one Italian article were extracted directly by a translator (Ciurluini⁴⁵¹). For three studies, data extraction

was limited to one or more conference abstracts alone (Gibson,⁴⁵⁷ White,^{453–456} Zimmermann⁴⁴⁰) supplemented with limited information provided by authors or obtained via Internet searching. One of these was published as a journal article⁵²⁷ subsequent to completion of our review (Zimmermann), so readers are referred to this for additional data to supplement those presented here. For one study, descriptive results from a pilot study had been published (Mildenhall^{438,439}) and the first author for these publications is used to refer to this study. However, preliminary unpublished data on a recently completed full trial which followed the pilot study were provided by the current investigators (Smith and colleagues) and are reported throughout this chapter. Another recently completed study (Parry^{449,450}) also relied heavily on information provided by project investigators as a supplement to abstracts of research in progress identified via searching. Readers are referred to further data published in abstract form subsequent to completion of our review (Mildenhall,^{528–529} Parry⁵³⁰) and advised to contact authors for additional information on these studies.

Summary data presented in this chapter therefore reflect details of studies as they were reported at the time our review was conducted and not necessarily in terms of what was actually done, as this could not always be determined.

General study characteristics

Overall study quality and relevance

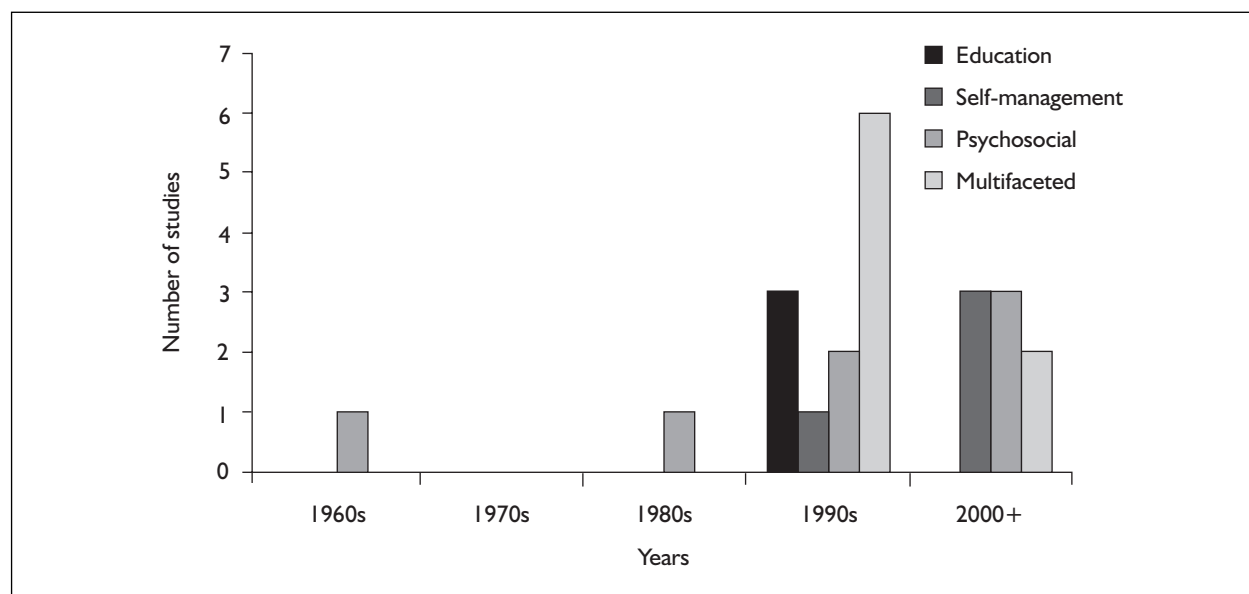
The distribution of studies in adults from which data were extracted along the two dimensions related to study design and the degree to which difficult asthma was targeted is shown in *Table 40*. A full listing of these studies with basic information collated at the study classification stage on patients, types and main components of the interventions and types of outcomes studied is provided in Appendix 24.

Publication dates

One study of a psychosocial intervention was published in 1960 (Groen⁴³⁶), another study of a psychosocial intervention in 1980 (Ago⁴³⁵), four

TABLE 40 Grading of studies in adults along dimensions related to study design and the degree to which they were judged to have targeted difficult asthma

| Targeting of difficult asthma | RCTs | CCTs | CPOS | CROS | Total |
|-------------------------------|----------|--------|---------|---------|----------|
| Definite | 1 | 0 | 2 | 0 | 3 (14%) |
| Probable | 5 | 0 | 0 | 2 | 7 (32%) |
| Possible | 8 | 2 | 1 | 1 | 12 (55%) |
| Total | 14 (64%) | 2 (9%) | 3 (14%) | 3 (14%) | 22 |

**FIGURE 13** Studies of different types of interventions in adults by year of publication

studies were published in the early 1990s (Garrett,⁴⁰⁴ Mayo,⁴²⁹ Yoon,^{53,446} Ciurluini⁴⁵¹), eight in the late 1990s (Kelso, 1996,⁴³⁰ Kelso, 1995,⁴³¹ Ford,^{432,474,475} George,⁴³⁷ Brewin,⁴⁴¹ Bowler,⁴⁴⁷ Mildenhall,^{438,439} Gibson⁴⁵⁷) and a further eight have been published since 2000 or have been recently completed and thus remained unpublished as journal articles at the time of this review (Blixen,^{433,434} Zimmermann,⁴⁴⁰ Morice,^{442,443} Osman,^{444,445} Manocha,⁴⁴⁸ Parry,^{449,450} Ross,⁴⁵² White^{453–456}). The breakdown of studies by decade of publication according to the type of intervention evaluated is shown in *Figure 13*. It is clear that, unlike in children, research on psycho-educational interventions for difficult asthma in adults only really began to develop in the last 10 years with an apparent rapid and continuing increase in research in this field since the late 1990s.

Readers are referred to the ‘Overview’ section in Chapter 4 (p. 31) for conventions used in referring to and referencing individual studies throughout this chapter. Please note that references associated with each study (referred to by key author surname and year where necessary)

are provided when they are first mentioned in this chapter but are not repeated throughout subsequent sections or tables. For ease of reference, details of all associated citations are provided with the alphabetical listing of studies in Appendix 7.

Country and setting

Seven of the 22 studies in adults were conducted in the USA (Blixen, George, Ford, Zimmermann, Mayo, Kelso, 1995, 1996), six in the UK (Mildenhall, Osman, White, Morice, Brewin, Parry), four in Australia (Yoon, Manocha, Bowler, Gibson), two in other European countries [Italy (Ciurluini) and The Netherlands (Groen)] and one each in Canada (Ross), New Zealand (Garrett) and Japan (Ago). This is shown in *Figure 14*. There were no clear patterns regarding the type of interventions studied in different countries; however, the three studies judged to have definite targeting of difficult asthma were all conducted in the USA.

One adult study was set in a tertiary care centre (Blixen), 13 were set in secondary care (George, Ford, Gibson, Morice, Brewin, Zimmermann,

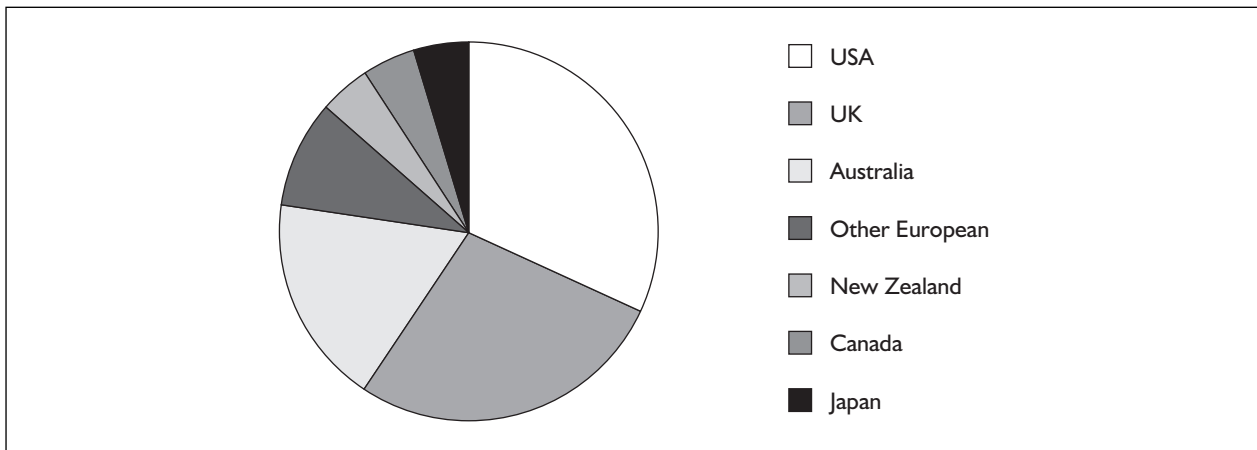


FIGURE 14 Countries in which studies in adults were undertaken

Yoon, Osman, Mildenhall, Mayo, Kelso, 1995, 1996, Parry), one across primary and secondary care (White) and two in the community (Garrett, Bowler). Three studies of psychosocial interventions were set in other locations (Groen, Ago, Ciurluini) and in two studies the setting was unclear (Ross, Manocha). There were no clear patterns regarding the types of interventions studied in relation to the study settings; however, all of the studies that were judged to have definite targeting of difficult asthma were set in secondary care.

Collaborations and funding

Most studies (15) were conducted via collaborations between clinical and academic institutions, four involved clinical organisations alone and three academic departments alone. Sixteen of the 22 studies provided details of research funding sources. Of these, half received funding from more than one source with six studies in receipt of funding from what appeared to be charitable organisations, six from government departments, five from commercial organisations and four from other sources.

Patients

Characteristics of the patients targeted by each individual study, graded from definite to possible in terms of the degree to which they were judged to target patients with difficult asthma, are summarised in Appendix 25. This supplements the brief description of patients collated at the study classification stage and given in Appendix 24.

Targeting of difficult asthma

Three studies were rated as definite in terms of their targeting of difficult asthma. Two of these

were separate studies by the same investigators (Kelso 1995, 1996) which targeted ethnic minority patients with moderate to severe asthma who had multiple hospitalisations, emergency department attendances or an ICU admission. The other study identified patients on the basis of them having 'difficult' asthma (Mayo). They were primarily low-income, ethnic minority patients, again with multiple hospitalisations or emergency department attendances.

Seven studies were rated as probable in terms of their targeting of difficult asthma (Ago, Blixen, Ford, George, Groen, Mildenhall, Zimmermann). Most of these identified patients on the basis of good indicators of severe or poorly controlled asthma (e.g. diagnosis of severe asthma, hospitalisation, high medication use, multiple emergency attendances) in combination with other socio-demographic (e.g. ethnic minority) or behavioural (e.g. poor compliance) risk factors.

Twelve studies were rated as possible in terms of their targeting of difficult asthma (Bowler, Brewin, Ciurluini, Gibson, Manocha, Morice, Osman, Parry, Ross, White, Yoon, Garrett). Half of these targeted patients on the basis of them having experienced a hospital admission for asthma (Brewin, Gibson, Morice, Osman, White, Yoon). A further three studies selected patients on the basis of other good indicators of poor control, namely substantial medication use (Bowler), being symptomatic on moderate- to high-dose ICS (Manocha) and recurrent exacerbations not related to allergies (Ciurluini). Two studies selected patients with high anxiety/panic alone (Parry, Ross) and one (Garrett) targeted patients on the basis of a relatively weak indicator of severity/poor control (emergency attendance with or without

hospitalisation) in combination with social deprivation identified on the basis of geographic location alone.

Two studies met criteria for inclusion and/or in-depth review only on the basis of reporting subgroup analyses of patients judged to be at greater risk within a larger sample. One of these reported a reanalysis of data from subgroups of ethnic minority and poorly compliant patients recruited to a previously conducted RCT excluded from this review in its own right (Ford). The other study reported results for a subgroup of patients who had been hospitalised within a larger sample (White). One further study that was judged possible in terms of its targeting of difficult asthma since it identified patients during a hospital admission (Osman), provided a separate analysis for the subgroup of patients within the whole sample who had had previous admissions and were thus graded as probable in terms of difficult asthma.

As was identified for studies in children (see Chapter 5), the categories used to grade studies according to their degree of targeting were often not entirely distinct and indeed could be seen to represent an underlying continuum related to degrees of difficult asthma. Perhaps owing to the smaller number of studies in adults, however, the difficult asthma subgroups appeared clearer and the patients within them less heterogeneous than for the studies in children. Despite this, there were still uncertainties regarding the relative importance of different risk factors or combinations thereof in contributing to adverse asthma outcomes.

As was done in children, an assessment was made of whether adult studies referenced asthma management guidelines as an indicator of good medical treatment against which the definition of difficult asthma could be considered. In the two studies in adults published prior to 1990 (see above) and hence the advent of the first asthma guidelines, it is evident that the medical care received by patients was not in line with current recommendations. This may, therefore, particularly call into question the targeting of difficult asthma in these studies. However, even amongst the studies published since 1990, eight (Manocha, Mayo, Parry, Ciurluini, Ford, Gibson, Ross, White) did not make any references to guidelines, although the description of medical treatment given in two of these (Manocha, Mayo) suggests that it is broadly in line with early guidelines. Four studies referenced guideline

documents (Zimmermann, Blixen, Bowler, George) but did not provide any information on the context for these. The rationale for intervention in five studies (Kelso, 1995, 1996, Morice, Yoon, Osman) was based on identification of inadequacies in medical care in light of guidelines, either generally or for the particular patients targeted. Lack of provision of education as part of routine care was identified as a particular issue in two studies and under-use of preventive medication for ethnic minority patients a key issue in another. Three studies did make reference to guidelines in the provision of standard care (Mildenhall, Garrett, Brewin), although two of these also identified inadequacies with this.

Although our grading of studies provides a useful guide regarding the extent to which they targeted difficult asthma, and were therefore relevant to addressing the review questions, the above discussion highlights the complexity of defining difficult asthma and the need for consideration of other factors in making a true assessment of whether individual study samples adequately represent a difficult asthma group. Readers are therefore encouraged to consider the information on patients within individual studies (Appendix 25) in interpreting results which follow later in this chapter.

Recruitment and justification of sample selection

Twelve of the 22 adult studies reviewed in depth were judged to provide clear details regarding patient recruitment procedures (i.e. methods, timing and use of incentives for recruitment) and these varied amongst studies (Kelso, 1995, 1996, Mayo, Blixen, Mildenhall, Zimmermann, Brewin, Manocha, Osman, Parry, Yoon, Garrett). All studies were judged to have provided a clear description of the target population, which was usually justified on the basis of the patients identified being at increased risk of mortality, morbidity or high service use. Reference was also made in two studies to complications of asthma related to adverse psychosocial factors (Ciurluini, Ross). A small number of studies, although judged to target patients with potentially difficult asthma, did not make explicit reference to patients being in any sense 'at risk' (e.g. Ago, Bowler). Ten studies, including the three graded as definite in terms of their targeting of difficult asthma, also included specific criteria related to the severity of asthma or presence of physical, psychosocial or behavioural co-morbidities that would have excluded some of the most at-risk patients from

their sample (Kelso, 1995, 1996, Mayo, Ford, George, Bowler, Manocha, Morice, Parry, Yoon).

Further details on patient recruitment rates, retention rates and indications of samples being representative of the target population are provided in the section on 'Study quality' (p. 102).

Age of patients

Sixteen studies made reference to the specific age range of patients targeted. Those lacking this information made reference to recruitment of adults in general. In addition to the Garrett study, which included subgroups of adults and children, three included small numbers of children aged <16 years, with one specifying a lower age limit of 12 years (Bowler), one 14 years (Osman) and one 15 years (White). Amongst the other studies that provided a specific age range, eight set a lower age limit of 18 and four of 16 years. Eleven studies set an upper age limit for inclusion which ranged from 40 to 72 years.

Interventions

Overview

All studies considered in this chapter, by nature of their selection for in-depth review, included two or more groups of patients receiving alternative forms of care. Within all studies, one or more of the groups received an active psycho-educational intervention and if there were multiple interventions meeting the definition of psycho-educational one was usually identified as primary on the basis of the author's description or it being the most active or intense. Most, but not all, studies also included one or more groups that were referred to as, or could be considered to have received, a non-psycho-educational control treatment, although the nature of this varied and further details are provided in the section that follows. For the purposes of describing the interventions and comparators, all groups within studies were classified as either intervention (i.e. psycho-educational) or control treatments (i.e. non-psycho-educational) on the basis of the terms used by the author or a judgement made regarding the nature and intensity of the care provided.

As described in previous chapters, all studies were classified as educational, self-management, psychosocial or multifaceted on the basis of the main components of the primary intervention they evaluated, brief details of which are documented in Appendix 24. For consistency, in the section that

follows and in associated Appendices 26–30 summary characteristics and details of studies are presented within the four categories of intervention types and studies are described in relation to the primary intervention evaluated. A discussion of the validity of the intervention classification and its relevance in combining and assessing results of studies in light of an examination of detailed intervention characteristics is made in the 'Summary' at the end of this section (p. 102).

Types and comparisons

The 22 studies in adults evaluated a total of 26 groups of patients who were judged to have received a psycho-educational intervention. In four of these the primary intervention was classified as mainly educational (Brewin, Ciurluini, Ford, Garrett), in four studies a self-management intervention was evaluated (Blixen, Morice, Osman, Yoon), in six a psychosocial intervention (Ago, Bowler, Groen, Manocha, Parry, Ross) and in eight a multifaceted programme involving education, self-management and other add-ons (George, Gibson, Kelso, 1995, 1996, Mayo, Mildenhall, White, Zimmermann).

All but three studies (Manocha, Bowler, Ciurluini) included a comparison with at least one non-psycho-educational control group. Only one older study (Groen) included two different forms of control group, namely treatment with preventive and symptomatic therapy and symptomatic therapy alone. In all, 18 studies included a comparison with a group of patients who received usual care, of which 12 gave at least some description. In the one study that did not include a comparison with usual care, control patients received general medical assessment and treatment as a supplement to their usual care; however, this did not appear to be significantly different from the usual care provided in many other studies. Further details of control groups for the 19 individual studies that included them are provided in Appendix 26.

In two of the three studies lacking comparisons to non-psycho-educational care, two provided what were referred to as 'control interventions'. In one study of a yoga intervention, this comprised training in standard relaxation methods, group discussion and cognitive behavioural therapy-type exercises (Manocha). In the other study, reporting a comparison of Buteyko training with a 'control intervention', comparison patients received general asthma education and training in abdominal breathing exercises that did not involve hypoventilation. In both of these studies, the

TABLE 41 Intervention providers involved in delivery of psycho-educational interventions of different types to adults

| Provider | Education | Self-management | Psychosocial | Multifaceted | All |
|--|-----------|-----------------|--------------|--------------|-----|
| Nurse | 3 | 3 | 1 | 5 | 12 |
| All doctors | 0 | 0 | 2 | 5 | 7 |
| Respiratory specialist | 0 | 0 | 0 | 2 | 2 |
| GP/primary care physician | 0 | 0 | 0 | 1 | 1 |
| Other/unspecified doctor | 0 | 0 | 2 | 2 | 4 |
| Psychologist | 0 | 0 | 3 | 1 | 4 |
| Pharmacist | 0 | 0 | 0 | 1 | 1 |
| Health educator | 0 | 0 | 0 | 1 | 1 |
| Community worker | 1 | 0 | 0 | 0 | 1 |
| Researcher | 0 | 0 | 1 | 0 | 1 |
| Other (medical caseworker, Buteyko trainer, yoga instructor) | 0 | 0 | 3 | 0 | 3 |

control treatments were considered to be psycho-educational interventions in their own right and the studies were therefore considered to be comparisons of two interventions. In the remaining study which did not include a comparison with non-psycho-educational care, three different psychotherapeutic techniques (autogenic training, cognitive-behavioural techniques, psychotherapy with biofeedback) were evaluated (Ciurluini). There were no studies that compared more than one psycho-educational intervention with a non-psycho-educational control group.

Providers

Only one study (Yoon) failed to provide information on the type of intervention provider. Full details are provided in Appendix 27. *Table 41* shows that the majority of studies (12) involved nurses in delivering the intervention and just under one-third (seven studies) involved a medical doctor. Nurses were least commonly involved in psychosocial interventions and, perhaps not surprisingly, psychologists were most commonly involved in delivering interventions of these types. Doctors were most commonly involved in multifaceted interventions, which often included additional medical treatment. A range of other health professionals also contributed to programme delivery in other single studies. In one study of an educational intervention, one of a psychosocial intervention and five of multifaceted interventions, a team comprising providers of more than one profession was involved in delivery of the intervention.

Half of the studies reported on the number of intervention providers involved in the delivery of the intervention (Ford, Blixen, Morice, Osman,

Bowler, Groen, Manocha, Mayo, Mildenhall, White, Garrett). There was one provider involved in six studies, two in four studies and four in the study by Garrett, with no clear differences in reporting of this information or numbers of providers by intervention type.

Although previous specialist training was implicit in the positions held by some of the intervention providers (e.g. Respiratory Nurse Specialists), six studies (three educational interventions and one each of self-management, psychosocial and multifaceted interventions) made reference to specific training undertaken by or supervision given in relation to provision of the intervention (Brewin, Ford, Osman, Groen, Mildenhall, Garrett). Two of these (Mildenhall, Groen) provided some details on the content of the training or supervision, which included education in asthma and its management and instruction in techniques or theory relevant to delivery of the intervention. Only one study (Mildenhall) provided further information on the amount and intensity of supervision provided.

It was apparent in eight studies that the intervention provider was also involved in study management, analysis or reporting (Mildenhall, Brewin, Osman, Groen, Parry, Kelso, 1995, 1996, White). In one study, the intervention provider appeared to be independent from the research aspects of the study (Bowler). However, in all other cases, it was unclear whether the intervention provider was involved in the study in other ways.

Only five studies (one educational, two psychosocial and two multifaceted interventions) provided additional information about the intervention providers (Groen, Manocha,

Mildenhall, White, Garrett). This included detail about the provider's relevant experience (three studies), gender (two studies) and shared ethnic, linguistic or cultural background with study participants (one study).

Structure and timing

Details on the overall structure and timing of the interventions for adults are presented in Appendix 27.

Seventeen studies provided information on the size of groups to which the primary intervention was delivered. The majority of these (13 studies) delivered the intervention on an individual basis, three to medium-sized groups (5–15 people) and one to a large group (>15 people). Unlike in the interventions for children, none were explicitly delivered to family groups or used a combination of approaches at different stages of the intervention.

More than three-quarters of the studies (17) provided information on the number of intervention sessions delivered. In four this varied according to need (Brewin, Garrett, Ago, Mayo). The number of sessions ranged from one in one study of self-management (Yoon) and another of a multifaceted intervention (Kelso, 1995) to 16 in a yoga intervention (Manocha).

Half of studies provided information on the frequency of intervention sessions. This ranged from daily in one self-management programme (Morice) and a multifaceted intervention (Zimmermann) conducted on an inpatient basis, to regular contact at 2–3-monthly intervals in another multifaceted intervention (Kelso, 1996). In a number of studies the frequency of contacts varied according to patients' needs or at different stages of the intervention (e.g. Kelso, 1995, 1996, Mayo). There were no clear patterns in the frequency of sessions reported across other studies owing to the relatively small numbers providing information on this aspect of the intervention. In many cases, however, the frequency of sessions appeared to be related to the duration of the sessions and entire intervention.

Fifteen of the 22 studies provided details of the duration of individual intervention sessions. Where stated, this ranged from a minimum of 20 minutes for a psychosocial intervention (Ago) to 3 hours for a single session self-management intervention (Yoon). In most studies, intervention sessions appeared to last between 30 and 60 minutes. Again, there were sometimes

variations according to the needs of individual patients (e.g. Garrett).

The duration of the entire intervention package was able to be ascertained for 12 studies. This ranged from the time required to deliver a single intervention session in one of the self-management interventions (Yoon) up to an average of 22 months or several years in two studies of psychosocial interventions (Ago, Groen). In a number of studies the duration appeared to vary depending on patients' needs (Morice, George, Garrett). It was not possible to estimate a total measure of the intensity of interventions (i.e. number of sessions multiplied by the duration of sessions) for more than a small number of studies owing to poor reporting and the different ways in which data were provided.

In 13 studies, including all those of education or self-management, the intervention followed an asthma episode, either a hospital admission for asthma, emergency attendance or recent attack (Kelso, 1995, Mayo, White, Zimmermann, Brewin, Ford, Garrett, Blixen, George, Gibson, Morice, Osman, Yoon). The exact timing of the start of the intervention from the acute event was not, however, always clear. It is notable that none of the psychosocial interventions were timed to follow an asthma episode.

Only five studies provided all of the above details related to the structure and timing of the intervention. There did not appear to be any clear patterns with respect to these characteristics across interventions of different types and there were large variations with respect to format, intensity and timing.

Setting

All but four studies (all of psychosocial interventions) indicated the setting for delivery of the primary intervention evaluated. Full details for individual studies are provided in Appendix 27 and summarised for different types of interventions in *Table 42*. This shows that amongst the 18 studies in which details of the intervention setting were provided, the most commonly used sites were outpatient and inpatient environments. Four studies delivered the intervention across a combination of intervention settings. Most self-management interventions were delivered on an inpatient basis and most multifaceted interventions involved at least some delivery on an outpatient basis, in one case in combination with inpatient care. Only one multifaceted intervention for adults was set partly in primary care (White)

TABLE 42 Intervention settings for psycho-educational interventions of different types in adults

| Intervention site | Education | Self-management | Psychosocial | Multifaceted | All |
|------------------------------------|-----------|-----------------|--------------|--------------|-----|
| Inpatient | 1 | 3 | 0 | 1 | 5 |
| A&E | 1 | 0 | 0 | 1 | 2 |
| Outpatient | 0 | 1 | 2 | 3 | 6 |
| Primary care | 0 | 0 | 0 | 0 | 0 |
| Home | 0 | 0 | 0 | 1 | 1 |
| Combination (two or more of above) | 1 | 0 | 1 | 2 | 4 |

and only two included any home visits (Garrett, Mildenhall).

Intervention quality issues

Piloting and standardisation

Two studies, one of an educational intervention and one of a multifaceted intervention, made reference to a pilot study being conducted (Mildenhall, Garrett). One study of a self-management intervention was itself stated to be pilot study (Blixen). Eight studies made reference to attempts at standardisation of the intervention (Blixen, Ciurluini, Groen, Kelso, 1995, Mildenhall, Morice, Osman, Yoon). This included structuring the programme around specific educational tools (three studies), use of an intervention protocol, guidelines or booklet (five studies) and recording delivery of the intervention (two studies).

Rationale and use of theory

Ten studies, two of educational interventions, two of self-management, three of psychosocial interventions and three of multifaceted programmes, provided a specific rationale to justify use of the intervention evaluated (Ago, Blixen, Bowler, Ciurluini, Ford, George, Kelso, 1995, Mildenhall, Osman, Garrett). Most commonly, this was phrased in terms of the intervention being appropriately targeted or adapted to engage the patients under study, providing justification for the intervention content or presenting a rationale for use of specific techniques or delivery methods. An identified failure in current provision of care was also cited by two studies.

Only four studies, three examining psychosocial interventions (Manocha, Parry, Ross) and one a multifaceted intervention (Mildenhall), made reference to the application of specific psycho-educational theories, models or approaches in the planning or delivery of the intervention. Three made reference to general cognitive-behavioural principles (Parry, Ross, Mildenhall) and one was based on yogic principles and philosophy (Manocha).

Tailoring

Two aspects of intervention tailoring were assessed: (1) whether there was evidence of tailoring to the needs of the patient group and (2) whether there was tailoring to the needs of individuals.

Five studies (one of an educational intervention, one of self-management, one of a psychosocial intervention and three of a multifaceted programme) were judged to have made reference to tailoring to the needs of the patient group as a whole (Ago, Blixen, Kelso, 1995, Mildenhall, Garrett). This was done in terms of the intervention being tailored to the general educational or care needs (one study), language or socio-cultural background (three studies) of the group. Three studies also made reference to the timing and/or delivery of the intervention being arranged to accommodate patient needs.

Twelve studies reported that the content or delivery of the intervention was further individualised in some way (Ago, Bowler, Kelso, 1995, 1996, Manocha, Mayo, Mildenhall, Morice, Osman, Parry, Zimmermann, Garrett). The degree of individualisation ranged from provision of an individualised management or action plan only (four studies) to provision of extra intervention sessions as needed (two studies). Three studies made reference to the intervention or aspects of it being individualised to patient's needs but no specific details on the methods used for tailoring were described. It should be noted that although some studies did not appear to make specific reference to group or individual tailoring, this could be argued to be explicit in the nature and delivery of the intervention (e.g. individual psychotherapy).

Methods and tools for intervention delivery

Details of the broad methods and tools that were reported as being used for delivery of interventions in individual studies are provided in

TABLE 43 Methods of delivery used in psycho-educational interventions of different types for adults

| Primary intervention type | Lecture/didactic | Discussion | Skills training | Problem solving | Goal setting | Role play | Games/fun | Formal therapeutic |
|---------------------------|------------------|------------|-----------------|-----------------|--------------|-----------|-----------|--------------------|
| Education | 0 | 3 | 3 | 1 | 0 | 0 | 0 | 1 |
| Self-management | 3 | 4 | 4 | 0 | 0 | 0 | 0 | 0 |
| Psychosocial | 0 | 4 | 4 | 2 | 1 | 1 | 0 | 7 |
| Multifaceted | 3 | 7 | 8 | 1 | 1 | 1 | 0 | 1 |
| All studies | 6 | 18 | 19 | 4 | 2 | 2 | 0 | 9 |

TABLE 44 Details of formal psychotherapeutic techniques used in psychosocial interventions for adults

| Study | Group | Details of psychotherapeutic techniques |
|-----------|--|--|
| Ago | Psychosomatic treatment | Psychosomatic treatment in 5 stages including: stress reduction, relaxation, release of negative emotions, recognition of emotional and behavioural triggers for asthma, modifying distorted perceptions and inadequate behaviours, promoting acquisition of coping mechanisms, reinforcement throughout |
| Bowler | Buteyko breathing techniques | Standard Buteyko techniques to reduce depth and frequency of respiration and breath-holding exercises |
| | 'Control intervention' | Relaxation techniques with abdominal breathing exercises that did not involve hypoventilation |
| Ciurluini | Cognitive-behavioural techniques | Cognitive-behavioural techniques |
| | Autogenic training | Seven relaxation exercises |
| | Psychotherapy with biofeedback | Psychotherapy with biofeedback |
| Groen | Group psychotherapy | Group psychotherapy including questioning, psychodrama, discussion (little detail) |
| Manocha | Sahaja yoga | Relaxation, meditation, achievement of state of 'thoughtless awareness', 'mental silence' |
| | 'Control intervention' | Relaxation methods involving visualisation and stress management techniques plus cognitive-behavioural therapy-like exercises |
| Parry | Cognitive-behavioural therapy | Cognitive-behavioural therapy |
| Ross | Cognitive-behavioural treatment and asthma education | Cognitive-behavioural techniques (little detail provided as abstract only) |

Appendix 28. A summary is provided in Tables 43–45. These data reflect information reported in papers describing studies or details obtained from authors and are particularly subject to variations in the quality of reporting. Two studies, one of a psychosocial intervention (Ross) and one of a multifaceted intervention (Gibson), provided little detail on the methods and tools used.

Delivery methods

A summary of the delivery methods used in interventions of different types is shown in Table 43.

As can be seen, the primary intervention in six studies included a lecture or didactic education, although by nature of their inclusion in the review, this was always supplemented by additional delivery methods. Eighteen studies involved formal or informal discussion and/or questioning either in groups, or individually with intervention providers. This commonly covered issues such as experiences with and problems related to asthma management. The most frequently used method for delivery of the intervention, applied in 19 studies, was skills training, including training in correct use of inhalers, related equipment and peak flow meters, training in self-management

procedures, training in relaxation, breathing or other psychotherapeutic techniques, training in trigger management or training in social skills. Four studies made reference to use of problem-solving strategies, but little detail was provided on what this entailed. Two studies made reference to use of goal setting or behavioural self-monitoring techniques, but again lacked detail on what this involved. Role play in the form of rehearsal of attack management scenarios was used in two studies. No studies in adults made use of games or fun activities to support learning.

Only nine studies made reference to the use of formal psychotherapeutic techniques in delivering one or more aspects of the intervention. One educational intervention made use of relaxation techniques (Ford) and one multifaceted intervention applied cognitive-behavioural techniques (Mildenhall) in delivery of the intervention. The remaining studies to make use of psychotherapeutic techniques were all psychosocial interventions, and since this was a primary component of these interventions, a detailed summary of the techniques applied in these studies is provided in *Table 44*.

There were no clear patterns or differences across interventions types in terms of the delivery methods used, except that, not surprisingly, psychosocial interventions more commonly made use of formal psychotherapeutic techniques. The median number of intervention delivery methods used across interventions of all types was four, and this ranged from a median of three in educational and psychosocial interventions to 4.5 in self-management interventions.

Supplementary tools

In addition to the use of a range of delivery methods, some interventions supplemented direct patient and provider interaction with other tools. Details of these in relation to individual studies are provided in Appendix 28 and a summary of tools used by interventions of different types is presented in *Table 45*.

Thirteen studies made use of written information, in the form of booklets, information sheets, visual aids, manuals, workbooks, action or self-management plans, handouts, diaries and medication or equipment product literature, in the provision of their primary intervention. Telephone contact to follow-up on progress or non-attendance was used in seven studies, three made use of videos and one supplemented training via use of an audio cassette. No studies of adults made use of computers to supplement education; however, two made reference to use of other tools, namely homework or practice sessions to reinforce principles learnt.

Rationale for delivery methods

One study of a psychosocial intervention (Parry) and one of a multifaceted intervention (Mayo) provided a clear rationale for the techniques or tools used in delivery of the intervention. One made reference to previous research documenting proven effectiveness and a theory base for the techniques used (Parry) and in the other study the approach taken was applied because many patients were unable to read and write (Mayo).

Content

Asthma-specific topics

An assessment was made of the asthma-specific topics covered by the primary psycho-educational interventions evaluated in studies of adults. It should be noted, however, that the accuracy of this information is likely to be extremely susceptible to variations in the quantity and quality of information available for data extraction and quality of reporting. Details of asthma-specific topics covered by individual studies are provided in Appendix 29 and a summary of this information by intervention type is presented in *Table 46*. Two studies of psychosocial interventions (Groen, Ross) and two of multifaceted interventions (Gibson, White) provided limited information on the content of their programmes in the sources available for data extraction.

TABLE 45 Supplementary tools used for delivery of psycho-educational interventions of different types to adults

| Primary intervention type | Telephone | Written information | Video | Audio | Computer |
|---------------------------|-----------|---------------------|-------|-------|----------|
| Education | 0 | 3 | 0 | 1 | 0 |
| Self-management | 0 | 4 | 2 | 0 | 0 |
| Psychosocial | 1 | 1 | 1 | 0 | 0 |
| Multifaceted | 6 | 5 | 0 | 0 | 0 |
| All studies | 7 | 13 | 3 | 1 | 0 |

TABLE 46 Asthma-specific topics covered in psycho-educational interventions of different types for adults

| Primary intervention type | Asthma general | Asthma management | | | | | |
|---------------------------|----------------|---------------------|----------------------------|-------------------|--------------------|--------------------|-------------|
| | | Symptom recognition | Self-management principles | Attack management | Symptom monitoring | PEF use/monitoring | Action plan |
| Education | 3 | 0 | 3 | 2 | 1 | 2 | 2 |
| Self-management | 4 | 3 | 4 | 4 | 3 | 4 | 4 |
| Psychosocial | 1 | 2 | 2 | 2 | 1 | 1 | 1 |
| Multifaceted | 7 | 5 | 8 | 6 | 3 | 6 | 7 |
| All studies | 15 | 10 | 17 | 14 | 8 | 13 | 14 |

| Primary intervention type | Asthma medication | | | | Triggers | | |
|---------------------------|-------------------|-------------|------------|--------------|----------|-----------|-------------------|
| | General | Inhaler use | Compliance | Side-effects | General | Avoidance | Attendance issues |
| Education | 3 | 2 | 1 | 1 | 3 | 2 | 1 |
| Self-management | 4 | 3 | 3 | 1 | 3 | 3 | 0 |
| Psychosocial | 2 | 0 | 2 | 1 | 2 | 2 | 0 |
| Multifaceted | 7 | 7 | 5 | 5 | 4 | 4 | 5 |
| All studies | 16 | 12 | 11 | 8 | 12 | 11 | 6 |

TABLE 47 Issues indirectly related to asthma and its management covered in psycho-educational interventions of different types for adults

| Primary intervention type | Smoking | Other health behaviours | Attitudes/beliefs | Other psychological issues | Social/family issues | Economic issues | Other issues |
|---------------------------|---------|-------------------------|-------------------|----------------------------|----------------------|-----------------|--------------|
| Education | 2 | 1 | 2 | 1 | 2 | 1 | 1 |
| Self-management | 1 | 0 | 0 | 2 | 2 | 0 | 3 |
| Psychosocial | 0 | 0 | 2 | 6 | 2 | 0 | 2 |
| Multifaceted | 1 | 2 | 2 | 2 | 3 | 2 | 1 |
| All studies | 4 | 3 | 6 | 11 | 9 | 3 | 7 |

The most commonly covered asthma-specific topics related to the development of a general understanding of asthma (e.g. its nature, pathophysiology, causes), medications for its treatment and broad principles of self-management. This was followed by advice on attack management, peak flow use, use of an action plan, correct use of inhalers, general information on triggers, trigger avoidance and compliance with medications. All these were considered by over half of studies.

The median number of topics covered across all interventions was 9.5, although multifaceted and self-management interventions tended to cover a greater range of asthma-specific topics than educational interventions, and educational interventions more than psychosocial interventions. It is interesting that on the basis of an examination of the detailed content of programmes, the distinction between educational and self-management interventions in particular

may be called into question. Two studies classified as educational interventions included the use of formal self-management plans for at least some of the patients under study (Brewin, Garrett).

Issues indirectly related to asthma and its management

In addition to topics directly related to understanding asthma and its management, many studies, in line with a more general approach to addressing factors impacting on asthma, evaluated interventions which considered broader issues. Again, it should be noted that the information presented with regard to these factors for individual studies in Appendix 30 and the summary presented in *Table 47* are susceptible to variations in the quantity and quality of information available for data extraction and quality of reporting. As above, limited information on content was available from data sources in relation to four studies (Groen, Ross, Gibson, White).

TABLE 48 Numbers of adult studies including add-ons of different types

| Primary intervention type | Medical treatment | Exercise | Environmental control | Referral to services | Professional education | Community education |
|---------------------------|-------------------|----------|-----------------------|----------------------|------------------------|---------------------|
| Education | 0 | 0 | 0 | 2 | 0 | 0 |
| Psychosocial | 3 | 0 | 0 | 0 | 0 | 0 |
| Multifaceted | 8 | 1 | 0 | 2 | 1 | 0 |
| All studies | 11 | 1 | 0 | 4 | 1 | 0 |

The most commonly covered topics indirectly related to management of asthma were psychological issues other than those related to attitudes and beliefs (e.g. management of psychological triggers such as anxiety, concerns, fears or feelings related to asthma). Nine studies addressed social, family or communication issues impacting on asthma or its management (e.g. communication with health providers, social support, social consequences of asthma). Smaller numbers of studies covered issues related to attitudes and beliefs in relation to asthma and its management, smoking, other health-related behaviours (e.g. exercise, diet) and the impact of financial problems on management of asthma. A range of other issues, for example, information on services, the impact of other medications on asthma and factors related to occupation were also addressed by a number of studies. The median number of issues indirectly related to asthma and its management that were covered across all interventions was 1.5. There was little difference in the number of these issues addressed across interventions of different types but, not surprisingly, a larger number of psychosocial than other interventions considered additional psychological issues impacting on asthma management.

Add-ons to interventions

Although by nature of their inclusion in the review a primary component of the main programme assessed in each study was a psycho-educational intervention, many programmes included non-psycho-educational add-ons that were not received by control groups where present. As a result of the definition used, studies classified as evaluating self-management interventions comprised only education plus formal self-management without any additional facets. However, although not an explicit part of the intervention, one self-management intervention did appear to influence subsequent medical treatment (Osman), but this was not deemed sufficient to warrant its classification as a multifaceted intervention.

Studies in which the primary programme evaluated was judged to be multifaceted, in

addition to education and formal self-management, always included other add-ons. Interventions classified as primarily educational or psychosocial could, but were not required to, include other facets and neither included formal self-management. One educational intervention (Brewin) and four psychosocial interventions did not include any add-ons (Parry, Manocha, Bowler, Ross). A summary of the numbers of other studies of each type including different types of add-ons is provided in *Table 48*.

No adult studies included environmental control or community education. Details of the additional facets incorporated into educational, psychosocial and multifaceted interventions that included them are provided for individual studies in *Tables 49–51*.

Medical treatment

Three studies of psychosocial interventions and all eight multifaceted interventions included medical treatment. In the study by Ago, the first stage of the psychosomatic treatment evaluated consisted of general medical assessment and treatment, which was sustained throughout the intervention. In the study by Groen, psychotherapy was supplemented by provision of preventative therapy that was given only to one of the control groups with which this intervention was compared. All three of the psychotherapeutic approaches evaluated by Ciurluini involved provision of additional drug treatment.

Amongst the multifaceted interventions, the programme evaluated by Kelso (1995) included prescriptions for ICS, beta-agonists, emergency prednisolone and other medications as necessary. In the Kelso (1996) study, the intervention evaluated also involved optimisation of therapy and focused on linking this to use of a self-management plan. Mayo evaluated a specialist clinic programme that involved a reduction in or minimal use of medications required to control symptoms. The comprehensive inpatient education programme in the study by George involved use of bedside spirometry, discharge planning and outpatient follow-up which were not

TABLE 49 Additional components of educational interventions in adults

| Study | Intervention | Medical care | Exercise | Referral | Professional education |
|---------|-----------------------------------|--------------|----------|----------|------------------------|
| Ford | Educational intervention | | | Yes | |
| Garrett | Community healthcare intervention | | | Yes | |

TABLE 50 Additional components of psychosocial interventions in adults

| Study | Intervention | Medical care | Exercise | Referral | Professional education |
|-----------|----------------------------------|--------------|----------|----------|------------------------|
| Ago | Psychosomatic treatment | Yes | | | |
| Groen | Group psychotherapy | Yes | | | |
| Ciurluini | Psychotherapy with biofeedback | Yes | | | |
| | Autogenic training | Yes | | | |
| | Cognitive-behavioural techniques | Yes | | | |

TABLE 51 Additional components of multifaceted interventions in adults

| Study | Intervention | Medical care | Exercise | Referral | Professional education |
|-------------|--|--------------|----------|----------|------------------------|
| Kelso, 1995 | Education and long-term therapeutic intervention | Yes | | | |
| Kelso, 1996 | Educational intervention with long-term management programme | Yes | | | |
| Mayo | Specialist clinic programme | Yes | | | |
| George | Comprehensive inpatient educational programme | Yes | | Yes | |
| Mildenhall | Coping with asthma programme | Yes | Yes | Yes | |
| Zimmermann | Asthma intervention programme | Yes | | | |
| Gibson | Asthma management service | Yes | | | |
| White | Specialist consultation-liaison | Yes | | | Yes |

provided as part of usual care. The home-based programme evaluated by Mildenhall incorporated liaison with medical services, additional testing and recommendations for adjustment of medication where necessary. In the studies by Zimmermann and Gibson, the interventions involved optimisation of medical care and a key feature of the specialist consultation-liaison evaluated by White was coordination of inpatient and primary care management.

Exercise

One multifaceted intervention (Mildenhall) included provision of exercise programmes as required on an individual basis.

Referral to services

Two of three studies of educational interventions (Garrett, Ford) included referral to other services. One made referrals to or links with GPs and contact with other health, mental health or social

service agencies or support structures as appropriate (Garrett). The other made referrals to smoking cessation programmes (Ford). Two studies of multifaceted interventions (Mildenhall, George) included referral to other services, one (George) included liaison with social workers as needed and the other (Mildenhall) made referrals to medical, psychological and social services as necessary.

Professional education

One multifaceted intervention included professional education (White) which comprised education sessions with ward staff and consultation liaison with GPs and practice nurses to improve care and provide advice on management of difficult asthma.

Summary

In adults, no educational or self-management interventions were evaluated in studies with definite targeting of difficult asthma and

multifaceted interventions were the least frequently evaluated types of interventions in studies with possible targeting of difficult asthma. There therefore appeared to be a tendency, as would be expected, for interventions aimed at more difficult patient groups to be those considered generally most intensive.

As described in the definitions and methods chapters of this review (Chapter 2 and 3), the initial classification of studies by intervention type was based on the distinctions broadly made to date in Cochrane reviews of psycho-educational interventions for asthma. In the light of the above-detailed assessment of intervention characteristics, however, it appears that this classification is not entirely useful. There appear to be few clear distinctions between educational, self-management, multifaceted and a subset of psychosocial interventions and it is likely in many cases that classification was influenced by the quantity of information available for extraction of data on interventions and the quality of reporting. Further attention to this issue and suggestions for alternative ways of conceptualising interventions are provided in the discussion.

Given the lack of distinction between the different types of intervention, by agreement of the review team, it was decided that all types of psycho-educational interventions would be considered together in the qualitative and quantitative syntheses of results that follow later in this chapter. Although prespecified subgroup analyses are undertaken in relation to intervention types, these should be treated with caution and reference made to specific intervention characteristics provided for individual studies in interpreting and evaluating results.

Study quality

Tables of detailed quality characteristics for individual studies in adults, divided by study design, are provided in Appendix 31.

Randomised controlled trials

Fourteen of the 22 studies in adults were classified as RCTs on the basis that they described allocation to groups as random. In all of these, the unit of randomisation was the patient. One additional study (Brewin) was initially classified as an RCT since it made reference in the introduction to patients being randomly assigned to groups; however, on detailed data extraction this was clearly not the case. Intervention group patients

comprised those admitted to the study hospital and control group patients those admitted to other hospitals in the district. This study was thus re-classified as a CPOS.

Randomisation

Only four of the RCTs actually described their randomisation methods. Three used random number tables (George, Osman) or computer-generated sequences (Mildenhall), which are considered adequate approaches to randomisation, and one used patient record numbers (Mayo), which is considered inadequate.¹⁵⁰ Four studies made reference to concealment of the allocation sequence at randomisation (Bowler, Zimmermann, Manocha, Osman); however, only three of these described their methods for doing so, namely use of serially numbered envelopes (Osman, Manocha, Bowler), which are still considered open to manipulation. The study by Zimmermann simply described randomisation as 'blinded' in the abstract reviewed.

Outcome assessment

Seven studies (Blixen, Bowler, Ford, Garrett, Manocha, Osman, Yoon) made reference to at least some degree of blinding for those involved in assessing or scoring outcomes. It should be noted, however, that in several other studies outcome data were largely reliant on self-reported data which are less susceptible to detection bias (e.g. Mildenhall, Morice), although potentially more prone to other forms of bias. Blinding of patients and intervention providers is extremely difficult in studies of psycho-educational interventions, so this aspect of study quality was not formally assessed. It was noted, though, that in the studies by Bowler and Manocha of Buteyko breathing and yoga, respectively, attempts were made to blind participants and others involved in treatment to which group received training in the active, as opposed to sham, techniques.

Most RCTs reported assessment of multiple outcomes over multiple time points (between one and three follow-ups, with a median of two), so there was potential for selective reporting and Type I errors given multiple significance testing. One study reported only one outcome at one time point (White). Of the remaining 13 RCTs, three specified a single primary outcome *a priori* (Ford, Mildenhall, Osman) and in one further study a primary outcome was apparent from the reporting of results (Mayo). In several studies (Manocha, Kelso, 1996, Zimmermann) multiple outcomes were specified as primary, still leaving them open

to selective reporting. In addition to the study by White, another five studies (Bowler, Garrett, George, Mayo, Zimmermann) assessed outcomes at a single time point, in a further three a single primary end-point was specified *a priori* (Blixen, Mildenhall, Osman) and in a further two a primary end-point was apparent in the results (Ford, Yoon). Overall, in only five of the 14 RCTs was there clearly both a single primary outcome and endpoint (Ford, Mayo, Mildenhall, Osman, White).

Study samples and attrition

Sample sizes in the RCTs ranged from 28 patients (Blixen) to 500 patients (Garrett); however, the latter study performed some analyses in subgroups of children and adults which were considered separately for the purposes of this review. The mean sample size excluding the large Garrett study was 102 patients. Only six studies reported that power calculations to estimate the required sample size had been conducted (Blixen, Ford, Manocha, Osman, Parry, Garrett), but it was apparent in several of these that the final numbers analysed did not always meet prespecified targets. All but one recently completed study, for which data were limited to information obtained from investigators (Parry), were judged to have reported clear patient selection criteria.

The proportion of patients approached who agreed to participate could not be ascertained for four studies (Morice, Parry, White, Zimmermann), but for three of these data were extracted from abstracts or information obtained from authors only (Parry, White, Zimmermann). In the remaining 10 studies, successful recruitment from the population targeted ranged from 41% (Yoon) to 100% (Mayo), with a mean participation rate of 65%. In two of the three studies (Ford, Garrett, Yoon) that assessed the comparability of non-participants, there was some evidence of differences, suggesting limited success in recruiting patients representative of the target population as a whole.

All but two recently completed RCTs, for which limited data were available (Parry, White), presented data on, or reported assessment of, the comparability of control and intervention groups at baseline in terms of key prognostic and outcome variables. In four studies (Blixen, Manocha, Morice, Zimmermann) minor differences between groups were apparent but these were judged unlikely to have any major impact on results. In two studies (Mildenhall,

Osman) more major differences were apparent; however, both these studies examined the effects of these differences on results by conducting adjusted analyses. In all other studies, groups were reported to be, or appeared to be, similar.

Numbers lost to follow-up could not be ascertained for four studies (Bowler, Parry, White, Zimmermann), but for three of these data were extracted from abstracts or information obtained from authors only (Parry, White, Zimmermann). Within individual studies, follow-up rates often varied for different outcomes and at different time points. A crude assessment of the minimum follow-up reported by studies suggested this ranged from 43% (Blixen) to 100% (Ford, Mayo), with a mean of 81%. Only four studies (Ford, Garrett, Mayo, Osman) reported a <15% loss to follow-up, which on some quality scales is considered a maximum acceptable level to prevent attrition bias. However, in the two studies that reported assessment of the comparability of withdrawals with patients remaining in the study, no differences were found (Garrett, Manocha).

Analysis and reporting of results

Details of the analyses conducted were reported or could be ascertained from 12 of the 14 RCTs. For the remaining two (Parry, Zimmermann) details were not provided in the abstracts or information obtained from authors from which data were extracted. Four studies (Ford, Garrett, George, Manocha) specified that analyses were undertaken on an ITT basis. However, one of these (Manocha) did not actually conduct a full ITT analysis and two presented ITT analyses for some outcomes only (Garrett, George). A further three studies, although they did not report doing so, did in fact conduct ITT analyses for one or more outcomes (Mayo, White, Morice). Eight of the 14 RCTs (Blixen, Bowler, Ford, Manocha, Mildenhall, Osman, White, Yoon) were judged to have adequate reporting of outcome data whereby numerators and denominators were provided for binary outcomes and point estimates (means, medians) plus measures of variability (standard deviations, ranges) were provided for continuous measures. For two of the studies lacking these data (Parry, Zimmermann), sources of information for data extraction were limited.

Controlled trials

Two studies in adults (Ciurluini, Ross) were classified as CCTs on the basis that patients were systematically allocated to groups, but this was not described as being done on a random basis.

Outcome assessment

Neither of the CCTs made reference to those involved in assessing or scoring outcomes being blind to group allocation. It was largely unclear how outcomes were assessed in each case, and hence the degree to which results may have been subject to detection bias. One assessed outcomes at a single time point alone and specified a primary outcome *a priori* (Ciurluini). The other (Ross) made no reference to a primary outcome or end-point despite multiple assessments in each case; however, the data for this study were obtained only from a conference abstract.

Study samples and attrition

Sample sizes in both the CCTs were small, namely 36 (Ciurluini) and 25 patients (Ross). Patient selection criteria were judged to be clear in both cases. Neither made reference to power calculations being conducted to estimate required sample size or reported on patient participation or follow-up rates. It is therefore unclear whether the patients for which outcomes were assessed are likely to be representative of the populations targeted in each case. Only one study (Ciurluini) provided data on the comparability of groups at baseline, which suggested that they were largely similar.

Analysis and reporting of results

Details of the analyses conducted were reported or could be ascertained for both CCTs and one study (Ciurluini) conducted what appeared to be equivalent to an ITT analysis by including all patients in the groups to which they were assigned. However, that this was done was not specified in advance. Neither study was judged to have provided adequate data (numerator and denominator for binary outcomes, point estimates plus measures of variability for continuous data) in reporting results.

Controlled prospective observational studies

Three studies (Brewin, Kelso, 1995, 1996) were classified as CPOs in that they prospectively followed up an intervention group selected to receive a novel treatment but identified a naturally occurring control group who did not receive this treatment. In one study (Brewin) the control group, comprising patients admitted to other hospitals in the same district as the study site, also appeared to be identified prospectively. However, in the two studies by Kelso (1995, 1996), the control groups, comprising patients meeting the study eligibility criteria but treated elsewhere in the district, were identified retrospectively.

Outcome assessment

Only one of the three CPOs (Brewin) made any reference to those involved in assessing or scoring outcomes being blind to group membership. It was largely unclear how outcomes were assessed and thus the degree to which results were subject to detection bias in the two studies by Kelso (1995, 1996). Two of the three studies (Brewin, Kelso, 1995) assessed outcomes at a single time point only, but neither of these specified a primary outcome from amongst the multiple outcomes assessed. In contrast, the 1996 study by Kelso did not specify which of the two end-points at which outcomes were assessed was primary but did specify two outcomes from amongst the eight assessed as primary.

Study samples and attrition

Sample sizes in all three CPOs were small, namely 39 (Kelso, 1996), 45 (Brewin) and 52 (Kelso, 1995). All were judged to have provided clear patient selection criteria. None made reference to power calculations being conducted to estimate required sample sizes and only one (Brewin) reported on patient participation (100%) or follow-up rates (70%). This study did not attempt to ascertain whether there were any differences between those who dropped out of the study and those who provided results. In all cases, therefore, it was unclear whether the patients for whom outcomes were assessed were likely to be representative of the populations targeted. Only the two studies by Kelso (1995, 1996) provided data on the comparability of groups at baseline. In one (Kelso, 1996) the groups were similar, but in the other (Kelso, 1995) there were differences in age and the proportions in each group with adult-onset asthma so adjustments were made to examine whether these affected the results.

Analysis and reporting of results

Details of the analyses conducted were reported or could be ascertained for only one study (Kelso, 1996). The Kelso (1995) study conducted what appeared to be equivalent to an ITT analysis by including all patients. Only the two Kelso studies (1995, 1996) were judged to have provided adequate data (numerator and denominator for binary outcomes, point estimates plus measures of variability for continuous data) in reporting results.

Controlled retrospective observational studies

Three studies (Ago, Gibson, Groen) were classified as CROs in that they retrospectively identified

intervention and control groups. In two studies (Ago, Groen), the patients for both groups appeared to be identified from the same site over similar time frames. However, it was extremely unclear how those in the Gibson study were identified, and hence whether they were likely to be comparable.

Outcome assessment

None of the CROs made any reference to those involved in assessing or scoring outcomes being blind to group membership. Since in two of the studies (Ago, Groen) outcomes were assessed on the basis of clinical evaluation and in the other study (Gibson) methods of outcome assessment were unclear, there is great potential for bias to influence results for these studies. All three CROs assessed only a single primary outcome at a single end-point but since these had been chosen retrospectively, again results should be viewed with caution.

Study samples and attrition

Sample sizes in all three CROs were relatively large in comparison with those in studies of other designs. The study by Groen included 162 patients, that by Ago 166 patients and Gibson identified 135 patients for the intervention group but did not provide details of the number in the control group. Only the studies by Ago and Groen were judged to have provided clear patient selection criteria. None made reference to power calculations being conducted to estimate required sample sizes. Although all patients identified were included in the studies by Ago and Groen, the Gibson study only obtained data for just over half of the intervention patients selected (53%) and factors of comparability for those not included could not be checked. Only the studies by Ago and Groen provided data on the comparability of control and intervention groups at baseline and in the latter study differences were found, the effects of which were examined in analysing results. The fact that no data were provided on the comparability of groups at baseline in the study by Gibson serves to reinforce the fact that, given the methods used for identifying patients, any results from this must be viewed with extreme caution.

Analysis and reporting of results

Details of the analyses conducted were reported or could be ascertained for only one of the three CROs (Groen). The principle of ITT analyses cannot be applied to retrospective studies. Only two of the three studies (Ago, Groen) were judged to have provided adequate data, in both cases details of the numerator and denominator for binary outcomes, in reporting results.

Implications of quality characteristics in summarising effectiveness results

The overall quality of studies across the multiple dimensions assessed was poor. For example, none of the RCTs or CCTs provided or adequately met all quality criteria assessed in relation to randomisation (where applicable), outcome assessment, sample characteristics and attrition and analysis and reporting. In fact, none reported on or adequately met all criteria within any one of these dimensions. Unlike in children, the majority of the controlled observational studies in adults were relatively well conducted and reported. It was therefore agreed that these studies could make a useful contribution, in a field in which research is relatively difficult and limited, to an overall assessment of the effectiveness of psycho-educational interventions for difficult asthma in adults. However, based on recommendations,¹⁵⁰ it was not considered appropriate to consider these studies for inclusion in any quantitative synthesis of results.

In some instances, methodological quality may have been masked by the limited sources available for data extraction. This is a particular issue for the recently completed or ongoing studies reviewed for which data extraction relied on abstracts or unpublished information from authors (Parry, Ross, Zimmermann, White, Mildenhall). Poor reporting, apparent in the number of studies which failed, for example, to provide details of patient flow, baseline group comparability and statistical analyses, may also have masked study quality. The generally poor quality of studies and potential for quality characteristics to be masked by limited information and poor reporting must be taken into consideration in interpreting the results described in the section which follows. However, it will be clear in reading this section that the better quality studies are generally those consistently reporting outcome data and reporting these data in a form which allowed for summary statistics to be calculated and, in some cases, statistically pooled. Where such summaries are provided, therefore, results and the conclusions which follow are based on the best evidence available in this field.

Effectiveness

This section initially provides a description of characteristics related to comparison groups, duration of follow-up and outcomes assessed for the 14 RCTs, two CCTs, three CPOs and three CROs included in the summary of effectiveness

results that follows. These introductory descriptions, in addition to highlighting issues important to consider in the interpretation of the results, also explain the rationale for the method of presentation of the effectiveness results.

Comparisons

Detailed information on the comparison groups for each individual study is provided in Appendix 26 and was summarised earlier in this chapter [see the section 'Interventions' (p. 93)] and will not be repeated here. Three studies did not include a comparison with some form of non-psycho-educational control treatment (Ciurluini, Manocha, Bowler). Although the focus of the following section is on summarising results from the majority of studies that compared psycho-educational interventions with usual care or other non-psycho-educational treatment (considered similar enough to combine for both qualitative and quantitative syntheses), the assessment of outcomes in and descriptive results for the three studies that did not include such a comparison are discussed alongside those for other studies. The comparisons undertaken in these studies is, however, always made clear and for obvious reasons these studies are not included in any of the quantitative syntheses of results.

Duration of follow-up

In summarising and synthesising results across studies, it is important to consider variations in the time at which follow-up assessments of outcomes were made. The point from which follow-up was measured (e.g. recruitment, baseline assessment, start of intervention, completion of intervention) varied across studies and for the purposes of comparison between them was standardised as far as possible to represent follow-up from the start of the intervention or baseline assessment (which were assumed to be close together). Where length of follow-up varied across individual patients within studies, the average duration or mid-point of a range for follow-up is reported. With the definition of follow-up described above in mind, the maximum duration of follow-up across all the studies in adults ranged from 1 month after a two-session inpatient self-management intervention in one study (Osman) to over 5 years from the start of a psychosocial intervention lasting, on average, nearly 2 years in another study (Ago). Amongst the controlled trials, the maximum duration of follow-up was 18 months (Morice) after a brief inpatient education programme. Across all studies, and controlled trials considered separately, the median length of follow-up was 9 months.

Just under half of studies included more than one follow-up point for assessment of outcomes. Amongst the majority of these and across all the studies as a whole, there appeared to be some consistency in the time points at which outcomes were assessed. Many included a short-term assessment of outcomes, often during an early intensive phase of longer interventions or soon after the end of shorter interventions, a medium-term assessment of outcomes and longer term assessment of outcomes beyond the end of any intervention. For the purposes of summarising effectiveness results in the following sections and to reduce heterogeneity between studies in terms of the duration of follow-up, where there are a sufficient number of studies reporting on a particular outcome, reporting of results is divided into short-, medium- and long-term follow-up. In this case short-term follow-up equates to assessment of outcomes at a time point prior to 6 months from the start of the intervention, medium-term follow-up equates to assessment at a time point of >6 months but <12 months from the start of the intervention, with long-term follow-up being at >12 months from the start of the intervention. Reference is made within each of these categories to the studies reporting **assessment** of a given outcome within the timeframe and the studies actually reporting **outcomes** for the appropriate time point. In addition, for a number of key outcomes, results across all time points, using data from the last assessment point reported by each study, are also summarised as this provided sufficient numbers of studies for some limited subgroup analyses. Where the number of studies reporting on an outcome was limited, the discussion of results was not broken down into different time points and the duration of follow-up is simply commented on.

Outcomes assessed

The types of outcomes reported as being assessed by studies in adults, in order of frequency, are shown in *Table 52*.

As can be seen, no single outcome was reported as being assessed by all studies. The most commonly assessed outcomes amongst the controlled studies in adults were hospital admissions for asthma and symptoms (reported as assessed by over half of studies), followed by A&E attendance, health status/QoL, psychological morbidity and medication use (reported as assessed by over one-third of studies). Admissions, A&E attendance, symptoms, exacerbations and other outcomes in the form of global assessments of improvement

TABLE 52 Numbers of studies in adults reporting assessment of outcomes of different types

| Type of outcome | Number of studies reporting | | | | |
|---|-----------------------------|------|------|------|-------|
| | RCTs | CCTs | CPOs | CROs | Total |
| Admission/readmission ^a | 12 | 0 | 2 | 1 | 15 |
| Symptoms/asthma control ^a | 9 | 1 | 2 | 1 | 13 |
| A&E/ED attendance ^a | 8 | 0 | 2 | 0 | 10 |
| Health status/QoL | 8 | 1 | 1 | 0 | 10 |
| Psychological morbidity | 6 | 2 | 0 | 1 | 9 |
| Medication use | 6 | 0 | 2 | 0 | 8 |
| Respiratory function | 5 | 1 | 0 | 1 | 7 |
| Self-care behaviour | 5 | 0 | 1 | 1 | 7 |
| Knowledge | 3 | 0 | 3 | 0 | 6 |
| Scheduled healthcare attendance | 5 | 0 | 0 | 0 | 5 |
| Time lost from work | 4 | 0 | 1 | 0 | 5 |
| Other unscheduled healthcare attendance | 4 | 0 | 0 | 0 | 4 |
| Death | 1 | 0 | 1 | 1 | 3 |
| Exacerbations ^a | 1 | 1 | 1 | 0 | 3 |
| Self-efficacy/perceived control | 3 | 0 | 0 | 0 | 3 |
| Beliefs/attitudes | 3 | 0 | 0 | 0 | 3 |
| Severity | 2 | 0 | 0 | 0 | 2 |
| Satisfaction | 1 | 0 | 0 | 0 | 1 |
| Other ^a | 1 | 0 | 1 | 2 | 4 |

^a Identified prior to or after reporting of results as a primary outcome by one or more studies.

were identified as primary outcomes by one or more studies.

Although a descriptive summary of results from each study (including *p*-values where these were reported) in relation to all patient-focused outcomes was extracted and summaries of these are provided for all outcomes in the sections that follow, extraction of actual outcome data (e.g. numbers, means), where this was appropriate and worthwhile (see below), was limited to the above outcomes highlighted as being primary or reported by at least one-third of studies. The summaries of effectiveness results are presented under headings by outcome in the order in which they appear in the above table to ensure a focus on the outcomes for which there are most data.

Table 52 above summarises the numbers of studies reporting **assessment** of the different types of outcomes. The number of studies reporting **actual results** data for intervention and control groups in relation to each outcome was often smaller, in some cases much smaller (e.g. for QoL), than the numbers reporting to have assessed the outcome in Table 52. As will be apparent in the sections that follow, some of the outcomes (e.g. self-care behaviour, medication use, respiratory function) were also assessed and reported in very different ways across studies precluding direct comparisons between them and preventing calculation of any

meaningful summary statistics. In these cases, extraction of outcome data was not undertaken and only a summary of the descriptive results is provided. In addition, of the studies that did report results, the quantity and quality of data reported was often variable, ranging from casual comments regarding the significance of results and/or probability (*p*) values alone to provision of detailed summary data (e.g. numbers, means and SDs as appropriate). However, even in some cases where detailed data were provided, the statistics reported were occasionally not deemed appropriate summaries for the type of outcome assessed. For example, in a number of studies means and SDs were given for total numbers of admissions, the distribution of which is likely to be highly skewed across study samples. This meant that adequate, appropriate data for the calculation of individual study summary statistics to facilitate comparisons, and potentially allow pooling across studies, were limited. Nevertheless, where one or more study reported such data for a given outcome, statistical data were extracted and summary statistics, in the form of RRs for binary outcomes and SMDs for continuous outcomes, along with appropriate confidence intervals (CIs), were calculated and are presented in tables. As stated in the methods chapter, summary statistics from three or more individual studies were then pooled in a meta-analysis where observation of a Forest Plot and statistical tests suggested that there

was non-significant statistical heterogeneity between them. Forest plots of the results from meta-analyses are presented where these were undertaken. In some instances, sensitivity analyses involving removal of studies or use of alternative data reported by studies (e.g. at different time points or for a sub-group of patients) were also conducted to examine the effects of these factors on overall results.

Admissions

Fifteen studies, 12 RCTs (Mayo, Blixen, Ford, George, Mildenhall, Zimmermann, Bowler, Morice, Osman, White, Yoon, Garrett), two CPOs (Kelso 1995, 1996) and one CROS (Gibson) reported assessment of hospital admissions for asthma. This was the most commonly reported outcome amongst the studies in adults. One of the studies (Ford), however, did not ultimately report admissions data separately for the subgroup of patients of interest. Of the 12 studies that reported methods of assessment, eight relied on extraction of data from medical or financial records with the rest using self-report data from interviews or questionnaires completed by patients for recall periods ranging from 3 to 6 months. Admissions appeared to be the primary outcome in four studies (Mayo, Osman, White, Gibson), but in only one of these was this specified in advance (Osman).

Short-term follow-up of admissions

Five RCTs (Blixen, Bowler, Morice, Yoon, Osman) reported assessment of admissions in the short-term (<6 months), ranging from 1 to 5 months. Two studies ultimately did not present data separately for this time point (Morice, Yoon). One (Blixen) commented on there being no significant differences in admissions at 3 months but did not present relevant data to support this statement. In the studies by Osman and Bowler, very small numbers of patients were admitted prior to 1- and 3-month follow-ups, respectively. The results from these are presented in *Table 53*.

The study by Osman showed effects in favour of the self-management intervention over usual care. In the Bowler study, the comparison was between Buteyko breathing training and an alternative psycho-educational intervention. Owing to the small event rates in both studies, neither demonstrated any significant differences between groups.

Medium-term follow-up of admissions

Eight RCTs (Mayo, Blixen, George, Mildenhall, Zimmermann, Morice, Yoon, Garrett) assessed admissions at a follow-up point between 6 and 11 months (medium term). Most of these reported assessment at 6 months (Blixen, George, Mildenhall, Zimmermann, Morice) and one each at 8 (Mayo), nine (Garrett) and 10 months (Yoon). Ultimately, however, the study by Morice did not report admissions data separately for this time point. One study (Blixen) commented on there being no significant differences in admissions at 6 months but did not present any actual data to support this statement. The study by George reported significant reductions in the total number of admissions amongst those receiving the multifaceted intervention compared with the control group ($p = 0.04$). Mayo reported significantly fewer admissions per patient ($p < 0.004$) and days per patient ($p < 0.02$) following their multifaceted intervention targeting 104 patients classified as definite in terms of difficult asthma. Another study judged to have probable targeting of difficult asthma presented total numbers of admissions per group, and reported significantly fewer due to asthma ($p = 0.03$) and overall ($p = 0.06$) in the intervention compared with the control group (Zimmermann).

The remaining three studies (Garrett, Mildenhall, Yoon) presented data on the proportions or numbers of patients admitted in each group. For two of these the follow-up was at 6 months (Mildenhall, Yoon). In the Garrett study, follow-up

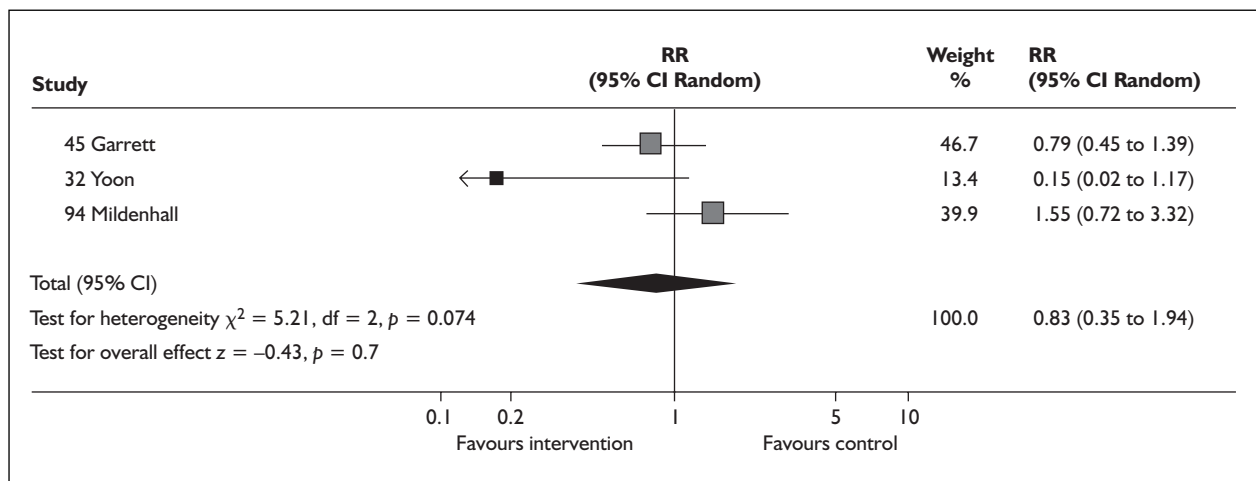
TABLE 53 Comparisons of proportion of adult patients admitted in psycho-educational intervention versus comparison groups at short-term follow-up (<6 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) admitted | | RR (95% CI) |
|--------|-------------------------------|--------------------------------------|---------------------|---------------|------------------------|
| | | | Intervention | Control | |
| Osman | Possible | Self-management (vs routine care) | 1/108 (1%) | 4/118 (3%) | 0.27 (0.24 to 4.59) |
| Bowler | Possible | Psychosocial (vs psychosocial) | 3/19 (16%) | 3/20 (15%) | 1.05 (0.03 to 2.41) |

TABLE 54 Comparisons of proportion of adult patients admitted in psycho-educational intervention versus control groups at medium-term follow-up (6–11 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) admitted | | RR (95% CI) |
|------------|-------------------------------|-------------------|-----------------------------|------------------------------|------------------------|
| | | | Intervention | Control | |
| Garrett | Possible | Education | 20/251 ^a (8%) | 25/249 ^a (10%) | 0.79 (0.45 to 1.39) |
| Yoon | Possible | Self-management | 1/37 (3%) | 7/39 (18%) | 0.15 (0.02 to 1.17) |
| Mildenhall | Probable | Multifaceted | 13/41 (32%) | 8/39 (21%) | 1.55 (0.72 to 3.32) |

^a Estimated from percentages provided.

**FIGURE 15** Forest plot showing meta-analysis for proportions of adults admitted at medium-term follow-up (6–11 months)

was at 9 months. Results for each study are summarised in *Table 54*. The heterogeneity between these studies was not statistically significant ($p = 0.074$) so they were combined in a meta-analysis. The Forest plot for this is presented in *Figure 15*.

The three studies included in the meta-analysis all evaluated different types of intervention, two in patients classified as possible in terms of difficult asthma (Yoon, Garrett) and one as probable (Mildenhall). Two of the three showed reductions in admissions in favour of the intervention group but none suggested significant differences between groups and the combined relative risk (RR = 0.83, 95% CI = 0.35 to 1.94) suggested a minimal and non-significant ($p = 0.7$) effect of psycho-educational interventions on admissions in the medium term.

Long-term follow-up of admissions

Long-term follow-up of admissions (≥ 12 months) was reported to be undertaken in four RCTs

(Mildenhall, Osman, White, Morice), two CPOs (Kelso 1995, 1996) and one CROS (Gibson). Follow-up data were collected at 12 months for all but one of the studies (Morice), which reported outcomes at 18 months, and Kelso (1996) presented additional 2-year follow-up data.

Kelso (1995) reported no significant differences in average hospital admissions by group ($p = 0.37$), but Kelso (1996) reported significantly greater reductions in mean numbers of admissions in the multifaceted intervention compared with the control group at 1 and 2 years (both $p < 0.05$). The CROS by Gibson reported that a significantly lower proportion of patients referred to their multifaceted intervention compared to control patients not referred were readmitted ($p = 0.001$). However, there were no details on the number or comparability of patients selected as controls so these results must be treated with caution. The four remaining studies were RCTs that presented data on the numbers of patients admitted in each group (Osman, Mildenhall, White, Morice). There

TABLE 55 Comparisons of proportion of adult patients admitted in psycho-educational intervention versus control groups at long-term follow-up (> 12 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) admitted | | RR (95% CI) |
|------------|-------------------------------|-------------------|---------------------|-----------------|------------------------|
| | | | Intervention | Control | |
| Morice | Possible | Self-management | 10/40 (25%) | 11/40 (28%) | 0.91 (0.44 to 1.90) |
| Osman | Possible | Self-management | 22/131 (17%) | 38/140 (27%) | 0.62 (0.39 to 0.99) |
| | Probable subgroup | Self-management | 19/62 (31%) | 25/72 (35%) | 0.88 (0.54 to 1.44) |
| White | Possible | Multifaceted | 4/54 (7%) | 32/92 (35%) | 0.21 (0.08 to 0.57) |
| Mildenhall | Probable | Multifaceted | 14/38 (37%) | 12/41 (29%) | 1.26 (0.67 to 2.37) |

was significant heterogeneity between these studies ($p = 0.017$) so they were not combined in a meta-analysis but individual study results are summarised in *Table 55*. Results from the subgroup analysis in patients with multiple admissions amongst the sample of admitted patients targeted by Osman are also presented.

Two of the studies assessed a multifaceted intervention, one in patients classified as possible in terms of difficult asthma (White) and the other as probable (Mildenhall). The other two studies (Osman, Morice) evaluated self-management alone in patients classified as possible in terms of difficult asthma, but the study by Osman also presented a subgroup analysis for patients meeting criteria for classification as probable difficult asthma. Results from White, Morice and the entire sample in the Osman study are in favour of the intervention, suggesting between 10 and 80% fewer patients admitted in the intervention compared with the control groups. However, only the study by White demonstrated a clearly significant effect and the borderline significance in the Osman study was negated when a summary statistic was calculated from data for the subgroup of higher risk patients in the study. The Mildenhall study, which targeted patients classified as probable in terms of difficult asthma, showed no favourable effects of the intervention on admissions.

Admissions across all follow-up time points

Owing to the small numbers of studies reporting data on admissions within short-, medium- and long-term follow-up periods, using data from the latest follow-up point, a re-examination across all studies comparing psycho-educational

interventions with routine care or a non-psycho-educational intervention and reporting appropriate statistics (six RCTs) was conducted. There was significant statistical heterogeneity between studies ($p = 0.027$) so they were not initially combined in a meta-analysis. However, all but one (Mildenhall) of the studies (excluding the additional subgroup analysis conducted in the Osman study) were graded as possible in terms of their targeting of difficult asthma. Consideration of the studies graded as possible alone allowed a meta-analysis to be conducted since removal of the Mildenhall study reduced the heterogeneity ($p = 0.11$). This is presented in *Figure 16*.

The summary statistic calculated across all five studies with possible targeting of difficult asthma suggests that psycho-educational interventions can reduce admissions in this group by approximately 40% (RR = 0.57, 95% CI = 0.34 to 0.93), an effect which is statistically significant ($p = 0.02$). However, results from the Mildenhall study and the subgroup analysis in the Osman study, neither of which was included in the meta-analysis, suggest that this effect may not be maintained when there is clearer targeting of difficult asthma. Since the five studies included in the above meta-analysis assessed three different types of intervention (three self-management, one multifaceted, one educational), it was not possible to make any meaningful comparisons across subgroups of intervention types.

Symptoms

Thirteen studies, nine RCTs (Garrett, Blixen, Mildenhall, Bowler, Manocha, Morice, Osman, Parry, Yoon), one CCT (Ross), two CPOs (Kelso, 1996, Brewin) and one CROS (Gibson), reported

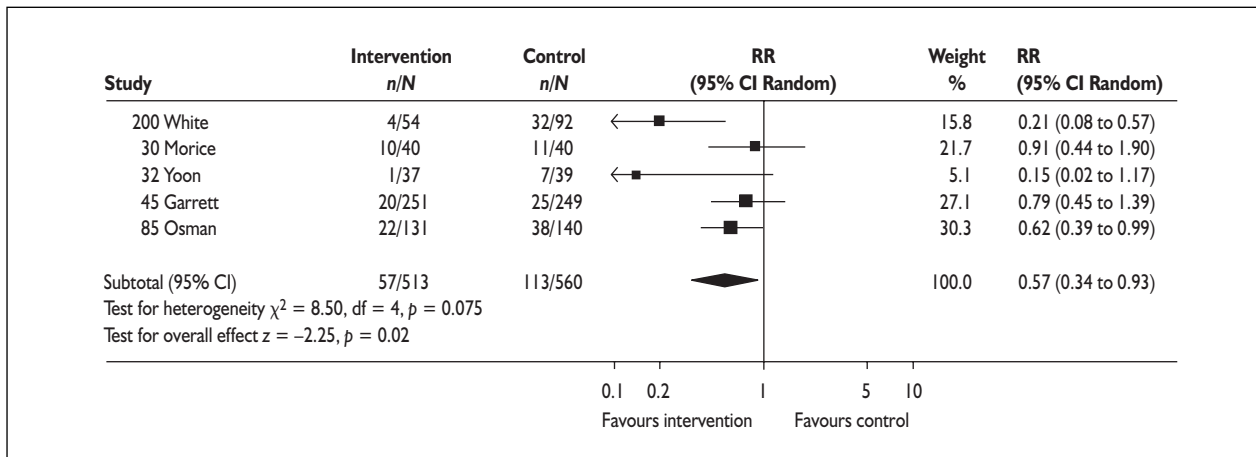


FIGURE 16 Forest plot showing meta-analysis of studies with possible targeting of difficult asthma for proportions of adults admitted at latest follow-up reported

assessment of symptoms or asthma control. All but one study (Morice), which used GP-reported symptoms, used diaries or questions administered via interviews or questionnaires to assess patient-reported frequency and, in some cases, severity of symptoms. As is increasingly being recommended,⁹ two studies (Osman, Mildenhall) reported assessment of some combination of day-time symptoms, night-time symptoms and restrictions to daily living or impacts due to symptoms. One study (Brewin) assessed day- and night-time symptoms only, two just night-time symptoms (Kelso, 1996, Gibson) and one just day-time symptoms (Blixen). The remaining seven studies (Ross, Yoon, Parry, Morice, Manocha, Bowler, Garrett) reported on some global assessment of symptoms, which in two cases was combined with a rating of symptom severity (Yoon, Parry). Only two studies made reference to the use of tested measures for assessment of symptoms. One of these (Manocha) referenced a tested scoring system⁵³¹ and one (Kelso, 1996) used a measure referred to as the Asthma Sleep Scale for which a conference abstract was cited. One study specified symptoms as its primary outcome (Mildenhall).

Follow-up symptom data were not available for one recently completed RCT (Parry), four studies ultimately did not report any symptom data (Kelso, 1996, Blixen, Morice, Bowler) and one presented results only for the intervention group (Gibson).

Short-term follow-up of symptoms

Of the remaining seven studies, four RCTs (Yoon, Osman, Manocha, Mildenhall), one CCT (Ross) and one CPOS (Brewin) reported assessment of symptoms in the short term with follow-up

ranging from 1 (Osman) to 5 months (Yoon). The study by Yoon, however, did not ultimately report symptom outcomes separately for this time point. The CCT by Ross reported significantly lower symptom scores in the intervention compared with the control group at the end of cognitive behavioural treatment ($p < 0.05$), but no further data were provided to support this statement in the abstract from which data were extracted and the exact time of follow-up was not specified. Osman reported a significantly lower proportion of patients experiencing day- and night-time symptoms in the intervention compared with the control group at 1 month (both $p = 0.01$) but no differences in the proportions experiencing restrictions to activity due to symptoms ($p = 0.12$). The study by Brewin presented symptom data at follow-up between 3 and 5 months in a number of different ways but reported no significant differences between educational intervention and control groups (a p -value was not reported). Only one study reported means and SDs for scores on a composite symptom measure (Mildenhall), but no significant differences between groups were found following provision of a multifaceted intervention ($p = 0.3$).

In the study by Manocha comparing yoga with a psycho-educational control treatment involving relaxation and cognitive behaviour therapy exercises, there was no significant difference between control and intervention groups in mean symptom improvement scores ($p = 0.3$).

Medium-term follow-up of symptoms

Five studies, four RCTs (Yoon, Garrett, Manocha, Mildenhall) and one CCT (Ross), reported assessment of symptoms in the medium term with

TABLE 56 Symptom scores for psycho-educational and control groups plus standardised mean differences at medium-term follow-up (6–11 months) in adult patients

| Study | Targeting of difficult asthma | Intervention type | Mean (SD) | | SMD (95% CI) |
|------------|-------------------------------|-------------------|------------------------------------|------------------------------------|--------------------------|
| | | | Intervention | Control | |
| Yoon | Possible | Self-management | N = 28 5.43 (2.50) ^a | N = 28 5.67 (2.24) ^a | -0.10 (-0.62 to 0.42) |
| Mildenhall | Probable | Multifaceted | N = 41 4.27 (3.53) ^b | N = 39 4.05 (2.99) ^b | 0.07 (-0.37 to 0.50) |

^a 3–12 scale.
^b 0–9 scale (both where higher score = greater symptoms/worse control).

follow-up ranging from 6 months in the majority of studies (Mildenhall, Manocha, Ross) to 10 months (Yoon). The CCT by Ross reported significantly lower symptom scores in the intervention compared with the control group at follow-up ($p < 0.05$), but no data were provided to support this statement in the abstract from which data were extracted and the exact time point was not specified. Garrett reported a significantly lower proportion of patients waking at night in the intervention group compared with the control group ($p = 0.02$) but other symptom outcomes were not reported for the adults or overall sample in the study. Only two studies reported means and SDs for scores on two similar composite symptom measures (Yoon, Mildenhall) from which summary SMD statistics could be calculated. These are shown in *Table 56*.

Both studies showed very small differences between groups, one in favour of the self-management intervention provided (Yoon) and one in favour of the control group (Mildenhall), but neither of which approached statistical significance.

In the study by Manocha comparing yoga with a psycho-educational control treatment involving relaxation and cognitive behaviour therapy exercises, there was no significant difference between control and intervention groups in mean symptom improvement scores at 6 months ($p = 0.6$).

Long-term follow-up of symptoms

Only one study reported long-term follow-up assessment of symptoms (Mildenhall). However, results for the 12-month follow-up were not yet available for this recently completed study.

Symptom outcomes across all follow-up time points

Since there were only two studies in total reporting appropriate symptom data for calculation of summary statistics, an analysis of studies combined across different time points was not conducted.

Accident and emergency department attendances

Ten studies, eight RCTs (Blixen, Ford, Yoon, George, Morice, Mildenhall, Zimmermann, Garrett) and two CPOs (Kelso, 1995, 1996), reported assessment of A&E attendances or an equivalent for asthma. Of the nine that reported methods of assessment, four relied on extraction of data from medical or financial records, four used self-report data from interviews or questionnaires completed by patients over recall periods ranging from 3 to 6 months and one study (Morice) obtained data from GPs. One study reported A&E attendances as a primary outcome (Ford).

Short-term follow-up of A&E attendances

Three studies, all RCTs, reported assessment of A&E attendances in the short term (<6 months), one each at 3 (Blixen), 4 (Ford) and 5 months (Yoon). Two of these (Ford, Yoon), however, did not ultimately report data separately for this time point and Blixen simply commented on there being no significant differences in ED attendances but did not present any data to support this statement.

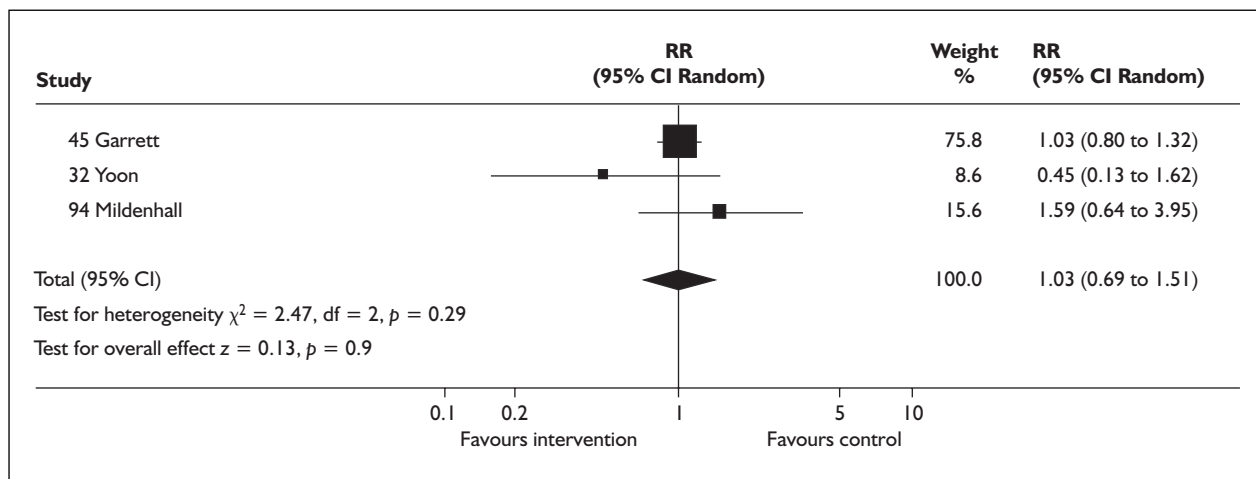
Medium-term follow-up of A&E attendances

Eight studies, all RCTs (Garrett, Yoon, Zimmermann, Mildenhall, Morice, George, Ford, Blixen), reported assessment of A&E attendances

TABLE 57 Comparisons of proportion of adult patients attending A&E in psycho-educational intervention versus control groups at medium-term follow-up (6–11 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) attending | | RR (95% CI) |
|------------|-------------------------------|-------------------|------------------------------|------------------------------|------------------------|
| | | | Intervention | Control | |
| Garrett | Possible | Education | 85/251 ^a (34%) | 82/249 ^a (33%) | 1.03 (0.80 to 1.32) |
| Yoon | Possible | Self-management | 3/37 (8%) | 7/39 (18%) | 0.45 (0.13 to 1.62) |
| Mildenhall | Probable | Multifaceted | 10/41 (24%) | 6/39 (15%) | 1.59 (0.64 to 3.95) |

^a Estimated from percentages provided.

**FIGURE 17** Forest plot showing meta-analysis for proportions of adults attending A&E at medium-term follow-up (6–11 months)

at a follow-up point between 6 and 11 months (medium term). The follow-up in five of these (Blixen, George, Morice, Mildenhall, Zimmermann) was 6 months from baseline, and one study each assessed A&E attendances at 8 (Ford), 9 (Garrett) and 10 months (Yoon).

Two studies (Ford, Morice), however, did not ultimately report data separately for this time point and the Blixen study simply commented on there being no significant differences in ED attendances without presenting any actual data to support this statement. Two studies of multifaceted interventions with probable targeting of difficult asthma reported on the total numbers of A&E attendances in each group, one of which (Zimmermann) demonstrated no significant differences between groups ($p = 0.28$) and the other (George) significant reductions in the intervention compared with the control group ($p = 0.04$).

The three remaining studies (Mildenhall, Yoon, Garrett) presented data on the proportions or numbers of patients attending A&E in each group, from which summary RR statistics could be calculated. These are presented in *Table 57*. There was no significant statistical heterogeneity between these studies ($p = 0.29$) so they were combined in a meta-analysis, the results for which are presented in *Figure 17*.

The three studies included in the meta-analysis all evaluated different types of intervention, two in patients classified as possible in terms of difficult asthma (Garrett, Yoon) and one as probable (Mildenhall). Only one study showed results in favour of the intervention group but none suggested significant differences between groups and the pooled results (RR = 1.03, 95% CI = 0.69 to 1.51), suggested no overall effect of psycho-educational interventions on A&E attendance in the medium term ($p = 0.9$).

TABLE 58 Comparisons of proportion of adult patients attending A&E in psycho-educational intervention versus control groups at long-term follow-up (> 12 months)

| Study | Targeting of difficult asthma | Intervention type | Number (%) attending | | RR (95% CI) |
|------------|-------------------------------|-------------------|----------------------|----------------|--------------------------|
| | | | Intervention | Control | |
| Morice | Possible | Self-management | 2/40 (5%) | 0/40 (0%) | 5.00 (0.25 to 100.97) |
| Mildenhall | Probable | Multifaceted | 15/38 (39%) | 14/41 (34%) | 1.16 (0.65 to 2.15) |

Long-term follow-up of A&E attendance

Five studies, three RCTs (Ford, Mildenhall, Morice) and two CPOs (Kelso, 1995, 1996), reported assessment of A&E attendances at a follow-up point ≥ 12 months from baseline (long term). Follow-up data were collected at 12 months for all but one of the studies (Morice), which reported outcomes at 18 months, and Kelso (1996) presented additional 2-year follow-up data.

Both Kelso studies (1995, 1996) with definite targeting of difficult asthma reported significantly greater reductions in ED attendances in the patients receiving the multifaceted interventions compared with the control groups at 12 months ($p < 0.01$ and $p < 0.05$, respectively). In the Kelso (1996) study, differences were also significant at 2 years ($p < 0.05$). Ford reported significant reductions in the monthly average ED use over 12 months ($p = 0.0005$) with no differential effect in the ethnic minority ($p = 0.6$) and non-compliant ($p = 0.76$) subgroups of patients classified as possible in terms of difficult asthma. However, the overall effects of the intervention mainly appeared to be due to differences during the initial 4 months of follow-up ($p = 0.003$) rather than the last 4 months, which when examined alone did not show significant differences ($p = 0.42$).

The two remaining studies presented data on the numbers of patients attending A&E at follow-up points of 12 (Mildenhall) and 18 months (Morice), from which valid summary statistics could be calculated. These are presented in *Table 58*.

Both studies showed effects on A&E attendance in favour of the control group but in neither of the studies were the differences significant.

A&E attendances across all follow-up time points

Owing to the small numbers of studies reporting data on A&E attendances within short-, medium- and long-term follow-up periods, using data from the latest follow-up point reported, a

re-examination across all studies reporting appropriate statistics (four RCTs) was conducted. There was no significant statistical heterogeneity between studies ($p = 0.42$) so they were combined in a meta-analysis. Only one of the studies was graded as probable in terms of its targeting of difficult asthma (Mildenhall) and the four studies evaluated three different types of interventions (two self-management, one education, one multifaceted). It was therefore not possible to divide the studies into any meaningful subgroups but the overall results from the meta-analysis are presented in *Figure 18*.

As can be seen in *Figure 18*, only one of the four studies, of a self-management intervention and with possible targeting of difficult asthma, showed effects on A&E attendances in favour of the intervention and there was no overall effect of psycho-educational interventions on A&E attendances in adults (RR = 1.03, 95% CI = 0.82 to 1.29, $p = 0.8$).

Health status/quality of life

Ten studies, eight RCTs (Garrett, Blixen, Ford, Mildenhall, Zimmermann, Bowler, Manocha, Parry), one CCT (Ross) and one CPO (Kelso, 1996), reported assessment of health status or QoL. Three studies (Mildenhall, Kelso, 1996, Blixen) assessed generic health status using the Short-Form 36⁵³² and one (Parry) using the EuroQol EQ5D.⁵¹⁶ Six studies assessed asthma-specific QoL using four different validated scales: the Hyland Living with Asthma Questionnaire⁵³³ (Mildenhall), the Juniper Asthma Quality of Life Questionnaire⁵¹⁷ (Blixen, Zimmermann), the Marks Asthma Quality of Life Questionnaire⁵³⁴ (Manocha, Bowler) and the Asthma Bother Profile⁵³⁵ (Parry, Kelso, 1996), five of these in addition to assessing generic health status (Mildenhall, Parry, Blixen, Parry, Kelso, 1996). One study (Garrett) referenced a review article on measurement of disease-specific QoL⁵²⁰ but did not provide further details on the specific questionnaire used, one used an asthma-specific

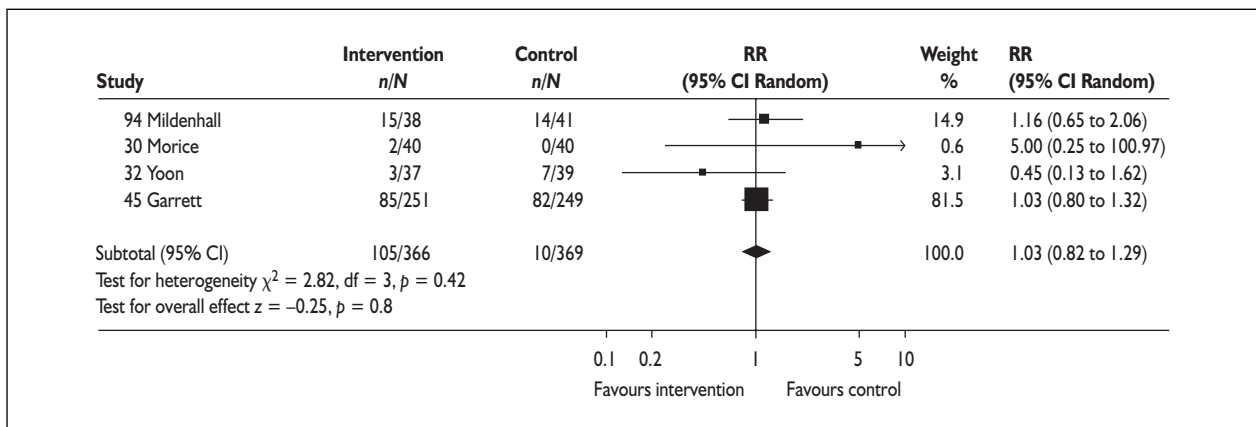


FIGURE 18 Forest plot showing meta-analysis for proportions of adults attending A&E at latest follow-up reported

scale but did not provide details in the abstract consulted (Ross) and one simply assessed the number of limited activity days (Ford).

One study presented QoL data for intervention group patients only (Kelso, 1996) so no further data from this study are reported here.

Short-term follow-up of quality of life

Seven studies, six RCTs (Blixen, Ford, Mildenhall, Bowler, Manocha, Parry) and one CCT (Ross), reported assessment of health status or QoL in the short term, at follow-ups ranging from 2 (Mildenhall) to 4 months (Manocha). One study ultimately did not present data separately for this time point in the subgroup of patients of interest (Ford). One (Ross) reported a significant improvement in asthma-specific QoL post-treatment in the intervention compared with the control group ($p < 0.05$) but did not present any data in the abstract assessed to support this statement. Another recently completed study (Parry) reported a significant improvement in a daily living dimension from an asthma-specific scale for intervention compared with control patients post-treatment ($p < 0.05$), but data to support this statement were again unavailable and no details of scores for other subscales or generic health status measures were reported for this time point. Blixen did not ultimately report results for generic health status but presented means and SDs for overall scores on an asthma-specific scale which showed no significant differences between self-management intervention and control groups ($p = 0.29$). Mildenhall found no significant differences between control and multifaceted intervention groups in relation to asthma-specific QoL scores ($p = 0.905$) and physical functioning ($p = 0.966$) and mental health ($p = 0.776$) subscales scores on a generic health status measure.

In the study by Manocha comparing yoga with a psycho-educational control treatment involving relaxation and cognitive behaviour therapy exercises, there were no significant differences between groups in overall asthma-specific QoL ($p = 0.07$) or subscale scores apart from a significantly greater improvement in mood dimension scores in the yoga group (no p -value was reported). Bowler also found no differences in mean asthma-specific QoL scores ($p = 0.09$) between groups provided with Buteyko training and a discussion-based psycho-educational intervention.

Medium-term follow-up of quality of life

Nine studies, seven RCTs (Blixen, Ford, Mildenhall, Manocha, Parry, Garrett, Zimmermann) and one CCT (Ross), reported assessment of health status or QoL in the medium term at time points ranging from 6 months, for the majority of studies (Blixen, Mildenhall, Zimmermann, Manocha, Parry, Ross), to 9 months (Garrett). One study ultimately did not present data separately for this time point in the subgroup of interest (Ford). Two studies (Ross, Garrett) reported no significant differences between groups in asthma-specific and generic QoL, respectively, but did not present any data to support their statements. Limited information available for the recently completed study by Parry suggested a significant improvement in overall QoL scores on the EuroQoL generic health status measure for the intervention compared with the control group at 6 months but there were no differences on the visual analogue scale incorporated into this questionnaire. No data were available to support these statements, and outcomes at this time point for the asthma-specific scale used were not available. The remaining three studies comparing psycho-educational interventions with routine care

reported no significant differences in average scores or improvement scores between groups overall on any of the asthma-specific (Zimmermann, Mildenhall, Blixen) or generic scales (Mildenhall) used.

In the study by Manocha comparing yoga with a psycho-educational control treatment involving relaxation and cognitive behaviour therapy exercises, there were no significant differences between groups in overall asthma-specific QoL ($p = 0.3$) or subscale scores.

Long-term follow-up of quality of life

Only two RCTs reported assessment of QoL in the longer term, both at 12 months (Mildenhall, Ford). However, for one recently completed study, data were not yet available (Mildenhall). The other study (Ford) reported significant decreases in the monthly average number of limited activity days for educational intervention compared with control patients in the entire sample ($p = 0.04$) and suggested that there was no differential effect for the ethnic minority subgroup of interest ($p = 0.43$ for the interaction). It was observed, however, that differences were mainly due to effects in the initial 4 months ($p = 0.03$) and not the final 4 months ($p = 0.65$) of follow-up.

Quality of life across all follow-up time points

Owing to the various ways in which health status and QoL were assessed and reported, it was not possible to calculate any meaningful summary statistics for studies or examine effects across all time points.

Psychological morbidity

Nine studies, six RCTs (Mildenhall, Parry, Blixen, Manocha, Yoon, Garrett), two CCTs (Ross, Ciurluini) and one CROS (Ago), reported assessment of psychological morbidity. Of these, six used validated measures: two (Mildenhall, Parry) the Hospital Anxiety and Depression Scale,⁵²¹ one (Blixen) the Center for Epidemiological Studies Depression Scale,⁵³⁶ one (Mildenhall) the General Health Questionnaire,⁵³⁷ one (Manocha) the Profile of Mood States,⁵³⁸ one (Parry) the panic-fear sub-scale of the Asthma Symptom Checklist⁵³⁹ and one (Ciurluini) the Minnesota Multiphasic Personality Inventory.⁵⁴⁰ In addition to using questionnaires, the study by Ciurluini also made a psychiatric diagnosis according to criteria from the Diagnostic and Statistical Manual III for mental disorders.⁵⁴¹ The study by Ross reported an anxiety score and numbers of panic attacks but details of assessment

methods were not given. One study made general observations on psychological status (Ago) and another used four questions on psychosocial disturbance due to asthma based on a previous study and for which some psychometric data were reported (Yoon). The study by Garrett made reference to a review publication⁵²⁰ in relation to assessment of levels of anxiety/panic at the time of an asthma attack.

One study (Ciurluini) did not ultimately report outcome data related to psychological morbidity, and the study by Ago reported informal observations only. Ross reported significantly less anxiety and fewer panic attacks after cognitive behavioural treatment and at 6 months in the intervention compared with the control group ($p < 0.05$) but no further data were presented in the abstract assessed to support this statement. Parry reported no significant differences in anxiety but a significant reduction in depression and panic-fear scores in the intervention group compared with the control at the end of a psychosocial programme but not at 6 months (p -values were not reported). Four studies (Yoon, Mildenhall, Blixen, Garrett) reported no significant differences in various aspects of psychological morbidity between groups at follow-up time points ranging from 2 to 10 months.

The study by Manocha comparing yoga with a psycho-educational control treatment involving relaxation and cognitive behaviour therapy exercises reported significantly greater improvements in overall mood scores and tension and fatigue subscale scores in the yoga group compared with the control treatment at 4 but not 6 months (p -values were not given). Differences on four other subscales were not significant.

Medication use

Eight studies, six RCTs (Mayo, Mildenhall, Bowler, Manocha, Morice, Garrett) and two CPOs (Kelso, 1995, 1996), reported assessment of medication use. Of the six that reported their methods of assessment, the majority (Mildenhall, Bowler, Manocha, Morice) relied on patient self-reported use or diaries, with one obtaining information from medical notes (Mayo) and one data from GPs (Garrett). Most stated that medication use in general was assessed, but one study did not report medication use at follow-up (Manocha), three studies reported results in relation to medication for the intervention group only (Kelso, 1995, 1996, Mayo) and there appeared to be selective reporting of outcomes for most of the other studies.

Two studies reported significant reductions in beta-agonist use in intervention compared with control groups at follow-up points at two (Mildenhall, $p = 0.044$) and 6 months (Morice, $p < 0.01$); however, in the former study effects were not maintained at 6 months ($p = 0.225$). One study (Garrett) reported greater use of preventive medication in the intervention group at 9 months ($p < 0.0005$).

In a comparison of Buteyko breathing and a discussion-based psycho-educational programme, Bowler found reduced beta-agonist use in the Buteyko group at 3 months ($p = 0.005$).

Respiratory function

Seven studies, five RCTs (Garrett, Yoon, Manocha, Mildenhall, Bowler), one CCT (Ross) and one CROS (Gibson), reported assessment of respiratory function at time points ranging from 2 to 12 months.

All studies reported measurement of PEF; however, one of these stated that insufficient data were obtained from patients to report this as an outcome (Mildenhall) and one presented results for the intervention group only (Gibson). All other studies reported some peak flow data but this was done in a variety of ways (e.g. mean PEF, mean change, categories of improvement, variability). All but one study reported no significant differences between groups, this (Ross) reporting significantly improved post-intervention (the exact time point for this follow-up was not stated) PEF scores for the cognitive behavioural treatment group compared with control patients ($p < 0.05$); however, these effects were not maintained at the 6-month follow-up and no other data were presented to support this claim.

In addition to PEF data, one study comparing a self-management intervention with a control group presented FEV₁ and FVC values assessed using spirometry equipment (Yoon). This reported significant declines in FEV₁ and FVC in the control group relative to the self-management intervention group at 5 months ($p = 0.01$, $p < 0.05$, respectively), but no differences at 10 months (p -values not reported).

The two studies comparing different psycho-educational interventions reported other respiratory function measures. Manocha reported significant differences in mean improvement scores in relation to a methacholine challenge test at the end of the 4-month yoga intervention compared with patients receiving a control

intervention comprising relaxation and cognitive behaviour therapy exercises ($p = 0.047$), but this difference was not apparent at the 6-month follow-up ($p = 0.3$). No differences were apparent in this study for FEV₁ values assessed using spirometry equipment at 4 (both $p > 0.9$) or 6 months (both $p > 0.3$). Bowler presented means and SDs in relation to FEV₁, end tidal CO₂ and minute volume and reported significant differences between Buteyko training and relaxation groups at 3 months in minute volume only ($p = 0.004$).

Self-care behaviour

Seven studies, five RCTs (Mildenhall, Garrett, Blixen, Morice, Yoon), one CPOS (Kelso, 1995) and one CROS (Gibson), reported assessment of one or more aspects of self-care behaviour. Only two reported use of previously published measures, one (Mildenhall) using the Asthma Coping Questionnaire⁵⁴² and subscales from the Revised Asthma Problem Behaviour Checklist⁵⁴³ and one (Garrett) previously published attack management scenarios.^{514,515} All studies assessed one or more aspects of self-management behaviour related to medication compliance, inhaler technique, trigger avoidance, symptom and attack management and self-monitoring in a variety of different ways and at different time points. This made it very difficult to compare results across studies. However, of the only four studies for which comparative follow-up data were available in the patients of interest, three reported at least some significant effects of the intervention. Significant differences between control and intervention groups related to use of an action plan (Yoon, $p = 0.001$; Garrett, $p < 0.01$; Morice, $p < 0.001$), knowledge ($p < 0.01$) and use of ($p < 0.005$) peak flow meters (Morice), differentiation of mild from severe attacks (Yoon, $p = 0.005$), PEF technique ($p < 0.005$) and management of slow ($p < 0.005$) and fast onset attacks ($p < 0.01$) (Garrett). However, the study by Blixen found no significant differences between groups in relation to a variety of self-care behaviours and, despite positive effects of the intervention in other domains, the study by Garrett reported no differences between groups in inhaler technique ($p > 0.1$) and commented that there were no differences in smoking status.

Knowledge

Six studies, three RCTs (Ford, Morice, Yoon) and three CPOSs (Kelso 1995, 1996, Brewin), reported assessment of knowledge related to asthma and its management, most commonly medications and use of inhalers. Four developed questionnaires to assess knowledge, of which two reported some

data on psychometric properties (Yoon, Ford). It was not clear how knowledge was assessed in the other two studies, although it appeared to involve some kind of observation or informal assessment (Kelso, 1995, 1996). Follow-up knowledge data were not reported for one study (Morice) and two reported results for the intervention group only (Kelso, 1995, 1996). Of the remaining three studies, one (Brewin) reported that perceived knowledge was significantly higher in the control group ($p = 0.000001$), but actual knowledge significantly higher in the intervention group ($p = 0.000029$) at follow-up between 3 and 5 months. Yoon reported increases in scores for knowledge of asthma ($p < 0.07$) and medications ($p < 0.05$) in the intervention group compared with the control group at 10 months. In the final study (Ford), the effects of the intervention on knowledge in the overall sample were not formally assessed (they appeared minimal), but it was reported that there were no differential effects of the intervention on knowledge by race ($p = 0.51$ for interaction) or compliance level ($p = 0.88$ for interaction).

Scheduled healthcare attendances

Five studies, all RCTs (Blixen, Ford, George, Mildenhall, Garrett), reported assessment of scheduled healthcare attendances at follow-up points ranging from 1 (George) to 12 months (Mildenhall). Three of these relied on self-report data obtained from patients (Blixen, Mildenhall, Ford) using recall periods of between 3 and 6 months, one obtained data from GPs (Garrett) and one from medical records (George).

No data were available for one recently completed study (Mildenhall) and for another results were not presented separately for the subgroup of interest (Ford). Two studies commented that there were no significant differences between groups (Blixen, Garrett) but presented no data in support of this statement. The remaining study (George) presented data on the numbers and proportions of

patients attending scheduled appointments within 1 month of their multifaceted intervention, which suggested that more than double the proportion of intervention compared with control patients attended for outpatient follow-up, a difference that was statistically significant ($p = 0.01$).

Time lost from work

Five studies, four RCTs (Garrett, Mildenhall, Zimmermann, Yoon) and one CPOS (Brewin), reported assessment of patient-reported days lost from work or school due to asthma at follow-up time points ranging from between 3 and 5 (Brewin) to 12 months (Mildenhall). Follow-up data on time lost from work were not yet available for one recently completed study (Mildenhall). Of the others, three (Brewin, Yoon, Garrett) reported no significant differences between groups and one (Zimmermann) reported a significant reduction in days lost for patients who had received the multifaceted intervention compared with the control group at 6 months ($p = 0.01$).

Other unscheduled healthcare attendances

Four studies, all RCTs (Mildenhall, Ford, Morice, Garrett), reported assessment of other unscheduled healthcare attendances, with follow-ups ranging from 4 (Morice) to 12 months (Mildenhall, Ford). Two of these relied on self-report data obtained from patients (Ford, Mildenhall) using recall periods of 4 and 6 months, respectively, and two obtained data from GPs (Garrett, Morice).

For one recently completed study follow-up data were not yet available (Mildenhall) and another did not report data separately for the subgroup of interest (Ford). The remaining studies reported on the numbers or proportions of patients attending for other unscheduled care, one at 4 months (Morice) and one at 9 months from baseline (Garrett). Summary results for these studies are presented in *Table 59*.

TABLE 59 Comparisons of proportion of adult patients attending for other unscheduled care in psycho-educational intervention versus control groups

| Study | Targeting of difficult asthma | Intervention type | Number (%) attending | | RR (95% CI) |
|---------|-------------------------------|-------------------|----------------------|-----------------|------------------------|
| | | | Intervention | Control | |
| Garrett | Possible | Education | 39/228 (17%) | 49/223 (22%) | 0.78 (0.53 to 1.14) |
| Morice | Possible | Self-management | 13/40 (33%) | 14/40 (35%) | 0.93 (0.50 to 1.72) |

These two studies evaluated educational and self-management interventions in patients classified as possible in terms of difficult asthma. Both showed effects of psycho-educational interventions on the proportions of patients attending for unscheduled care in favour of the intervention; however, the results suggest that these were minimal and non-significant.

Deaths

Three studies, one RCT (Mayo), one CPOS (Kelso, 1996) and one CROS (Groen), made reference to all-cause and asthma-related mortality. There was one death amongst patients classified as definite in terms of difficult asthma in each of two studies (Mayo, Kelso, 1996), with the deceased being in the control group in one study and the intervention group in the other. In the Groen retrospective study conducted prior to 1960 there were reported to be significantly fewer deaths from all causes at follow-up in the psychotherapy compared with the control group, but this effect was not significant when adjusted for age differences ($p = 0.14$).

Exacerbations

Three studies, one RCT (Ford), one CCT (Ciurluini) and one CPOS (Brewin), reported assessment of exacerbations at follow-up time points of between 3 and 5 months (Brewin), 3 and 6 months (Ciurluini) and 12 months (Ford). However, one study did not ultimately present results in relation to exacerbations (Brewin) and in the Ford study they were not presented for the subgroup of interest. In the remaining study, in which exacerbations were specified to be the primary outcome (Ciurluini), a decrease in the number of attacks was observed across the three different intervention groups with a slightly greater improvement in the biofeedback group compared with the others (no p -values were reported).

Self-efficacy/perceived control

Three studies, all RCTs (Mildenhall, Parry, Zimmermann), reported assessment of a construct similar to self-efficacy or perceived control. One study (Parry) used the validated Asthma Multidimensional Health Locus of Control Scale,⁵⁴⁴ one (Mildenhall) a validated Perceived Control of Asthma Questionnaire⁵⁴⁵ and one (Zimmermann) reported assessment of self-efficacy within a range of beliefs related to the Health Belief Model.⁵⁴⁶ For one study (Zimmermann), baseline observations only were reported, one reported no significant differences in mean perceived control scores between intervention and control groups at 2 and 6 months following a multifaceted intervention (Mildenhall) and the

other (Parry) reported increases in internal locus of control in the cognitive-behavioural intervention group at 6 months. However, no data have yet been reported for the latter study to support this statement and it was unclear how this compared with the control group.

Beliefs/attitudes

Three studies, all RCTs (Zimmermann, Ford, Yoon), reported assessment of beliefs and/or attitudes related to asthma and its management. All three constructed their own measures for which two reported some data on psychometric properties (Ford, Yoon). For one study, observations of beliefs from the Health Belief Model⁵⁴⁶ were reported at baseline only (Zimmermann), both others presented mean scores and SDs at 10 and 12 months of follow-up. One found a significant increase in the health beliefs score in the intervention compared with the control group (Yoon) and for the other (Ford) the effects of the intervention on beliefs overall were not formally assessed (they appeared minimal), but it was reported that there were no differential effects of the intervention on beliefs by race ($p = 0.51$ for interaction) or compliance level ($p = 0.88$ for interaction).

Severity

Only two adult studies, both RCTs (Garrett, Yoon), reported assessment of some global measure of severity. One used a visual analogue scale to assess patients' overall perceptions of the severity of their asthma over the previous 6 months and presented means and SDs of scores (Yoon). In this study, no differences between groups were observed at 10 months following a self-management intervention for 76 patients classified as possible in terms of difficult asthma. The other study (Garrett) reported on the proportions of patients, also classified as possible in terms of difficult asthma, who were judged to have improved, remained the same or deteriorated in terms of the overall severity of their asthma at 9 months following the commencement of their educational intervention. Although analyses for the subgroup of adults examined in the study were not presented separately, for the overall sample composed primarily of adults, intervention patients were significantly more likely to report improvement than control patients ($p = 0.0005$).

Satisfaction

Two studies, both RCTs, reported assessment of patient satisfaction with interventions or usual care provided. Results were not yet available for one recently completed study (Mildenhall). The other

(Osman) reported that overall, and in the subgroup of patients with multiple admissions, a higher proportion of the intervention compared to the control group was satisfied with the advice they had been given as part of the self-management programme ($p < 0.001$).

Other outcomes

Only four studies reported outcomes other than those discussed above. Two older studies of psychotherapeutic interventions (Groen, Ago) presented results from composite clinical assessments of remission or improvement in asthma, the assessment of which appeared to be based on the premise that asthma could in some sense be 'cured'. Both studies reported that a higher proportion of intervention patients were judged to have improved at follow-up compared with the respective control groups ($p < 0.001$ for Ago and $p = 0.0004$ for Groen). The study by Brewin evaluated the intensity and level of education received by control and intervention groups but did not report outcome data from the questionnaire administered. Garrett assessed social support, and found that adults in the intervention group were more likely than those in the control group to have someone to help with asthma attacks at the 9-month follow-up ($p < 0.05$).

Summary of effectiveness results

Psycho-educational interventions compared with routine or other non-psycho-educational care

Table 60 presents a summary of the findings and main conclusions in relation to the key outcomes assessed in trials comparing psycho-educational interventions with routine or non-psycho-educational care in adults. Where results within individual studies varied across different measures of the same outcome or at different follow-up points, or multiple studies suggested conflicting findings, results are described as mixed. Qualifications to conclusions on the basis of available data and in light of any subgroup analyses conducted are provided.

Although all of the outcomes summarised in Table 60 were reported as assessed by more than one-third of studies, and in a number of cases identified as primary outcomes (see Table 52), as can be seen, the number of studies actually reporting any results data for intervention and control groups (rather than just commenting on findings) in relation to these outcomes, and amongst these, reporting data in a format suitable for calculation of summary statistics, is more limited. Generally, the studies reporting valid statistics for calculation of summary effect sizes

were of higher quality than those that did not, hence additional weight may be given to these in interpreting results.

In no studies for any outcome were there significant effects in favour of the control group, suggesting that psycho-educational interventions are unlikely to do harm or to be less effective than routine or other non-psycho-educational care alone. When compared with routine or non-psycho-educational care, the only clearly significant effects of psycho-educational interventions in adults were seen in admissions data pooled from the latest follow-up reported in individual studies. However, only studies with possible targeting of difficult asthma were included in the meta-analysis for this outcome and in the one study reporting admissions data in a form to allow calculation of a summary statistic amongst patients graded as probable in terms of difficult asthma (Mildenhall), positive effects on admissions were not observed. Furthermore, in another study (Osman), although reductions in admissions of borderline significance were seen amongst the overall sample, when the analysis was confined to the subgroup of patients judged probable in terms of their difficult asthma, the effect was reduced and significance lost. There is therefore limited evidence to suggest that the effects of psycho-educational interventions on admissions in adults may not extend to the most difficult patient groups.

The data suggest that psycho-educational interventions have no effect on A&E attendances in adults, but the number of studies reporting A&E outcome data in a format suitable for pooling was small. Where effects in favour of the intervention group were seen in relation to other outcomes (e.g. medication use), the number of studies reporting outcome data was very limited, preventing any valid conclusions being drawn. With respect to all other outcomes in adults, where sufficient data allowed conclusions to be drawn, studies showed mixed results or provided no clear evidence of the effectiveness of psycho-educational interventions for difficult asthma.

In adults, conclusions regarding the relative effectiveness of interventions of different types could not be drawn since no subgroup analyses by intervention type were possible. It should be noted, however, that only educational, self-management and multifaceted interventions were ultimately included in any quantitative synthesis of results, hence the effectiveness of psychosocial interventions remains unclear. None of the studies

TABLE 60 Summary of effectiveness results for psycho-educational interventions (PEI) compared with usual or non-psycho-educational care (UC) in adults

| Type of outcome | Length of follow-up | Number of and reported findings from studies providing any results data | Number of studies reporting data for calculation of summary statistic and findings based on these | Meta-analysis conducted? | Conclusions | |
|------------------|---------------------|---|--|--|--|---|
| Admissions | Short | 1 study 1 no sig. difference | 1 study 1 non-sig. effects favouring PEI | N/A | Limited data on which to base valid conclusions | |
| | Medium | 6 studies 3 sig. effects favouring PEI 3 no sig. differences | 3 studies 2 non-sig. effects favouring PEI 1 non-sig. effects favouring UC | Yes | Small, and non-significant, pooled effect favouring intervention (RR = 0.83, 95% CI = 0.35 to 1.94). Individual study data show mixed results | |
| | Long | 7 studies 4 sig. effects favouring PEI 3 no sig. differences | 4 studies 2 sig. effects favouring PEI 1 no clear differences 1 non-sig. effects favouring UC | No – Significant heterogeneity | Individual study data show mixed results with only clearly significant effects favouring intervention confined to a single study of a multifaceted intervention with possible targeting of difficult asthma. Effects of borderline significance in a study of self-management with possible targeting of difficult asthma were reduced and non-significant when the analysis was confined to a subgroup in this study with probable difficult asthma | |
| Symptoms/control | Short | Latest reported (min. 6 months) | 12 studies 7 sig. effects favouring PEI 5 no sig. differences | 6 studies 2 sig. effects favouring PEI 2 non-sig. effects favouring PEI 1 no clear differences 1 non-sig. effects favouring UC | Yes – with single study with probable targeting of difficult asthma removed to reduce heterogeneity | Significant pooled effect in favour of intervention (RR = 0.57, 95% CI = 0.34 to 0.93) amongst studies with possible targeting of difficult asthma. A single study with probable targeting of difficult asthma from which a summary statistic could be calculated, and a subgroup analysis of the most at-risk patients in one of the studies included in the meta-analysis suggest that positive effects on admissions may not extend to patients with probable difficult asthma. A subgroup analysis by intervention type was not possible as 5 studies included in the meta-analysis evaluated 3 different types of intervention |
| | | 4 studies 1 sig. effects favouring PEI 1 mixed results 2 no sig. differences | 1 study 1 non-sig. effects favouring UC | N/A | Individual study data show mixed results | |
| | Medium | 4 studies 2 sig. effects favouring PEI 2 no sig. differences | 2 studies 2 no clear differences | N/A | Individual study data show mixed results | |

continued

TABLE 60 Summary of effectiveness results for psycho-educational interventions (PEI) compared with usual or non-psycho-educational care (UC) in adults (cont'd)

| Type of outcome | Length of follow-up | Number of and reported findings from studies providing any results data | Number of studies reporting data for calculation of summary statistic and findings based on these | Meta-analysis conducted? | Conclusions |
|-------------------|---------------------------------|---|--|--------------------------|--|
| | Long | – | – | N/A | No data on long-term effects on symptoms |
| | Latest reported (min. 1 month) | 6 studies 2 sig. effects favouring PEI 1 mixed results 3 no sig. differences | 2 studies No clear differences | N/A | Mixed results from individual study data |
| A&E attendance | Short | – | – | N/A | No data on short-term effects on A&E attendance |
| | Medium | 5 studies 1 sig. effects favouring PEI 4 no sig. differences | 3 studies 1 non-sig. effects favouring PEI 1 no clear differences 1 non-sig. effects favouring UC | Yes | No overall pooled effect (RR = 1.03, 95% CI = 0.69 to 1.51) amongst limited number of studies for which results could be combined. Individual study data provide limited evidence of effectiveness |
| | Long | 5 studies 3 sig. effects favouring PEI 2 no sig. differences | 2 studies 2 non-sig. effects favouring UC | N/A | Individual study data show mixed results, but there is limited evidence of effectiveness in two studies reporting appropriate statistics for comparison |
| | Latest reported (min. 6 months) | 9 studies 4 sig. effects favouring PEI 5 no sig. differences | 4 studies 1 non-sig. effects favouring PEI 1 no clear differences 2 non-sig. effects favouring UC | Yes | No overall pooled effect (RR = 1.03, 95% CI = 0.82 to 1.29) amongst limited number of studies for which results could be combined. Individual study data show mixed results. Subgroup analyses were not possible |
| Health status/QoL | Short | 4 studies 2 sig. effects favouring PEI 2 no sig. differences | N/A | N/A | Comparison and synthesis across studies difficult as all used different types of measures. Individual study data show mixed results |
| | Medium | 4 studies 1 mixed results 3 no sig. differences | N/A | N/A | Comparison and synthesis across studies difficult as all used different types of measures. Individual study data provide little evidence of effectiveness |
| | Long | 1 study 1 sig. effects favouring PEI | N/A | N/A | Limited data on which to base valid conclusions |
| | Latest reported (min. unclear) | 6 studies 3 sig. effects favouring PEI 3 no sig. differences | N/A | N/A | Comparison and synthesis across studies difficult as all used different types of measures. Individual study data show mixed results |

continued

TABLE 60 Summary of effectiveness results for psycho-educational interventions (PEI) compared with usual or non-psycho-educational care (UC) in adults (cont'd)

| Type of outcome | Length of follow-up | Number of and reported findings from studies providing any results data | Number of studies reporting data for calculation of summary statistic and findings based on these | Meta-analysis conducted? | Conclusions |
|-------------------------|---------------------|---|---|--------------------------|--|
| Psychological morbidity | All | 5 studies 1 sig. effects favouring PEI 1 mixed results 3 no sig. differences | N/A | N/A | Comparison and synthesis across studies difficult as all used different types of measures. Individual study data provide little evidence of effectiveness |
| Medication use | All | 3 studies 2 sig. effects favouring PEI 1 mixed results | N/A | N/A | Comparison and synthesis across studies difficult as all assessed different outcomes. Limited individual study data suggest effects mainly favour intervention |

with definite targeting of difficult asthma reported data in a format which allowed them to be included in quantitative syntheses, so it is also uncertain whether any effects of psycho-educational interventions extend to the most at-risk patients.

Comparisons of different psycho-educational interventions

There were insufficient studies comparing psycho-educational interventions of different types to draw any strong conclusions regarding their relative effectiveness. Amongst the three psychosocial studies that did make such comparisons (Ciurluini, Manocha, Bowler), one showed reductions in attacks across all three different psychotherapy groups (psychotherapy with biofeedback, autogenic training and cognitive-behavioural techniques) in patients graded as possible in terms of difficult asthma (Ciurluini). There was reported to be a greater reduction in the biofeedback group, but it was unclear whether this effect was significant. The study by Manocha, with possible targeting of difficult asthma, reported significantly greater improvements in airway responsiveness and scores of the mood subscale of an asthma-specific QoL questionnaire immediately after the end of a 4-month yoga intervention compared with a discussion-based group provided with standard relaxation training and cognitive behavioural exercises. These differences were not, however,

maintained at 6 months of follow-up and no differences were observed with respect to other measures of respiratory function, overall QoL, scores on other subscales of the asthma-specific QoL questionnaire or a combined symptom score. In the study by Bowler, Buteyko breathing techniques were compared with general asthma education and training in abdominal breathing exercises that did not involve hypoventilation. There was significantly reduced beta-agonist use and minute volume measures of lung function in the Buteyko group compared with the comparison intervention at 3-month follow-up and trends towards greater improvements in QoL and reduced ICS use. However, the latter effects were not significant and no differences were seen in admissions, prednisolone use or other measures of respiratory function. There is therefore limited evidence on the relative effectiveness of psycho-educational interventions of different types in adults with difficult asthma.

Assessment of publication bias

A funnel plot constructed for the most commonly reported outcome in studies of adults (admissions) is shown in *Figure 19*.

No small studies reporting negative results, to mirror the one reporting the greatest positive effects in favour of the intervention, were apparent amongst the studies in adults. Owing to the small

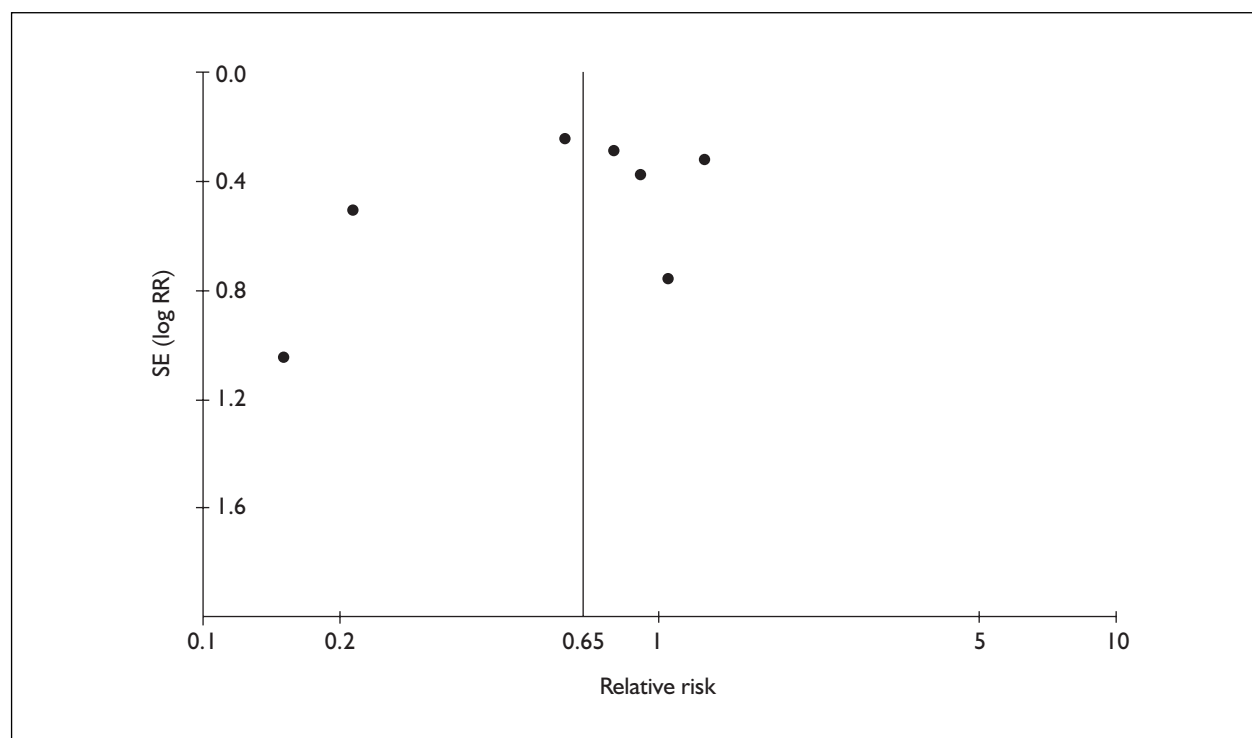


FIGURE 19 Funnel plot constructed from admissions data in adults at latest follow-up reported by studies

TABLE 61 Classification of economic studies in adults by design of effectiveness study

| Source of effectiveness data | Cost-effectiveness analysis | Effectiveness study with some costs | Study reporting costs only | All |
|------------------------------|-----------------------------|-------------------------------------|----------------------------|-----|
| RCT | 1 | 2 | 0 | 3 |
| CCT | 0 | 0 | 0 | 0 |
| COS | 0 | 1 | 0 | 1 |
| All | 1 | 3 | 0 | 4 |

number of such trials overall, however, it is unclear whether this resulted from publication bias *per se*.

Costs and cost-effectiveness

Quantity and characteristics of economic studies

This section reports on adult studies that were tagged as relevant to the economic section of the review in that they reported assessment of cost data in monetary units. Studies that were identified as including costs but were not reviewed further on the basis of insufficient evidence for targeting of difficult asthma or poor study design are listed in Appendices 10 and 11. Seven studies with independent control groups graded as at least possible in terms of their targeting of difficult asthma were initially tagged as economic studies and considered for economic data extraction. Two further studies (George, Kelso, 1996) were noted as including conclusions regarding cost-effectiveness without presentation of any cost data, but were not considered further for the economic section of the review. Economic data were ultimately extracted from four of the seven studies in adults identified for economic review. Two recently completed RCTs (Parry, White) had been described as cost-effectiveness studies in available data sources but could not be reviewed further as economic studies because costing methods and cost data had not been reported at the time of this review. For one further RCT (Ford) separate cost data were not available for the subgroup of patients of interest. A classification of the four remaining studies, three RCTs (Mayo, Mildenhall, Zimmermann) and one prospective observational study (Kelso, 1995), is provided in *Table 61*. All but one of these studies, which was conducted in the UK (Mildenhall), were undertaken in the USA and reported costs in USA dollars.

As can be seen, only one study (Mildenhall) was considered a full cost-effectiveness analysis based on an effectiveness study of a sound design. Zimmermann compared costs and outcomes in a

TABLE 62 Quality of economic studies in adults

| Number of BMJ checklist items included | Number of studies |
|--|-------------------|
| 0–10 | 1 |
| 11–20 | 2 |
| 21–35 | 1 |
| Total | 4 |

study reported as a blinded RCT, but was reported only in abstracts at the time of our review, hence it is difficult to assess methods used for the economic evaluation. The other studies were effectiveness studies which provided some, often very limited, planned or unplanned assessment of costs.

Quality of economic studies

The *BMJ* checklist for peer reviewers¹⁶⁵ was used to identify features of the studies pertinent to an assessment of their quality. Detailed data for individual studies are provided in Appendix 32 and a summary is given in *Table 62*.

Studies were scored only where it was clear that the answer was true. Where it was partially true or not applicable, no score was given. As highlighted in *Table 61*, most studies were not presented as economic evaluation studies. Of those that were, only one study (Mildenhall) met most of the criteria for consideration as a good economic evaluation, but as yet economic analyses are incomplete. Only this study specifically stated the economic question that the research was addressing, although the others emphasised the importance of the economic problem for the patient group. Even though three of the studies did not aim to be formal economic evaluations, and would not be classified as economic evaluations, we have summarised the findings of all the included studies which estimated costs in some form in the following section. The evidence should clearly be considered with reference to the quality of the studies.

TABLE 63 Mean differences in healthcare costs per patient from economic studies in adults

| Study | Intervention | Period for costs (months) | Reported mean difference in cost per patient | Mean difference in cost per patient in £ sterling 2003 prices (to nearest £10) | Comments |
|------------|--|---------------------------|---|--|---|
| Mayo | Vigorous medical regimen and educational programme | 8 | US\$1900 net saving | £1910 net saving | Estimated from data provided |
| Zimmermann | Nurse specialist education for inpatients | 6 | US\$3480 net saving per intervention patient | £2510 net saving | Insufficient information to judge quality of economic results |
| Mildenhall | Specialist nurse-led home-based psycho-educational programme | 6 (12 planned) | £2966 (95% CI £1229 to £4702) increase in mean cost per patient | £2966 increase in costs (95% CI £1229 to £4702) | Based on adjusted comparison, further analyses planned |

Costs

Details of cost data reported in the four individual economic studies in adults are provided in Appendix 33.

Healthcare costs

All four studies reported some aspect of healthcare costs. Two studies reported limited inpatient costs only (Mayo, Kelso, 1995). One study of a nurse outreach programme reported 'direct healthcare costs' (Zimmermann), but it was not clear from the abstracts available what this included. Mildenhall included and costed health and social care contacts and prescriptions reported by trial participants, wherever the healthcare took place, thus including all reported hospital, primary healthcare and social work or social services resources.

Intervention costs

Only one study (Mildenhall) reported separately the financial cost of the intervention (see *Table 63*). Estimates of intervention costs in this study were £1270 per patient (SD £45, 95% CI £1257 to £1283) at 2002–03 UK prices for a specialist nurse-led home-based psycho-educational programme. This estimate included costs for personnel (nurse plus clinical and psychological supervision), travel, telephone calls, liaison with other healthcare professionals and provision of equipment and information and was based on provision of the intervention to the 41 patients available for follow-up at 6 months.

Combined healthcare and intervention costs

Several studies reported differences in costs of healthcare for patients in the study. *Table 63* summarises the findings for those that reported the difference in costs including the intervention cost, in all cases comprising a multifaceted programme.

Two studies (Mayo, Zimmermann) showed a net saving, although this was not formally quantified in the report for the Mayo study, and one study (Mildenhall) a net increase in costs. The Kelso (1995) study did not report sufficient data to estimate the cost difference between groups. The main saving between groups in the US studies resulted from lower healthcare use, with high unit costs of utilisation.

Productivity costs

Lost working and other time due to asthma was estimated in the Mildenhall study but costings based on this had not yet been reported at the time of our review. No other studies reported productivity costs arising either from changes in working time or other activities.

Patient costs

Healthcare costs incurred to patients from prescription charges, purchase of non-prescribed medication and equipment, use of private healthcare, travel to services and telephone calls were assessed in the Mildenhall study, but again, results from these had not been reported at the

time this review was completed. Patient costs were not measured or reported from this viewpoint in any of the other studies reviewed.

Cost-effectiveness

Three of the four economic studies in adults (Mayo, Zimmermann, Mildenhall) drew conclusions about the effect of the intervention on cost-effectiveness; however, two did not report formal economic analyses (Mayo, Zimmermann). Of the studies that reported patient health outcomes, both (Zimmermann, Mildenhall) related estimated costs relative to health outcomes. The

Zimmermann study showed a net reduction in healthcare costs coupled with improvement in asthma-related QoL, and also net reduction in days lost from work. The latter amounted to mean difference of 8.41 days in working days lost over the 6-month follow-up period between groups, but a financial value of this gain was not estimated. Mildenhall found a statistically significant net increase in healthcare costs and no significant difference in primary health outcomes. The authors of this study reported that they planned further sensitivity analyses of the economic data.

Chapter 7

Discussion

Overview

In addition to answering core review questions regarding the effectiveness and cost-effectiveness of psycho-educational interventions for difficult asthma, a major part of this review was concerned with describing the volume and nature of research in the field. Hence this section includes:

- an assessment of the completeness and overall contribution of our review
- an overview of research identified on psycho-educational interventions for difficult asthma
- a summary description of the patients targeted, interventions evaluated, methodological quality and outcomes assessed in studies representing the 'best evidence' research in this field and a discussion of issues arising, points for clarification and areas for future related research
- a summary of results on the effectiveness of psycho-educational interventions for difficult asthma in children and adults, including reference to findings from the limited subgroup and sensitivity analyses that were able to be conducted
- a discussion of the findings regarding the cost-effectiveness of psycho-educational interventions for difficult asthma
- some caveats regarding the review findings.

Specific implications of this review for clinical practice and recommendations for future research which follow from the discussion presented here are summarised in Chapter 8.

Many issues are common to the studies in children and adults and so these are discussed together to avoid repetition, with key differences, particularly with regard to effectiveness results, highlighted as necessary.

Completeness of the review

The searches for this review were wide and thorough, and the results are likely to represent the work that had been published, presented at conferences or included in databases of ongoing research at the time of its completion (early 2003).

Methods were, if anything, over-inclusive and cautious given the amount of research ultimately identified, the results of recent studies investigating the importance of comprehensive searching⁵⁴⁷ and findings from our own methodological investigation of study screening procedures (Appendix 4). We searched for and translated non-English language sources, but in the end these contributed very little to the formal syntheses of results and, therefore, review conclusions. We were aware of the possibility of publication bias, and attempted to include data from unpublished studies described in conference abstracts, theses and other reports by contacting authors. We had some success in doing so, but this was limited by lack of reporting of appropriate statistics in sources available for data extraction and failure to obtain additional information from some authors. The small numbers of studies reporting similar outcomes in the review make the interpretation of funnel plots difficult. Although no small trials reporting negative results were apparent, it is unclear whether this resulted from publication bias *per se*. We suggest that the effect of publication bias on our conclusions is, however, likely to be negligible.

The review was not able to include full outcome and/or cost data from several important studies in progress or recently completed. Data from these would add significantly to the results and strengthen conclusions in this review, especially with regard to findings in adults, in relation to cost-effectiveness and in the UK context. This highlights the fact that, as in many fields, the evidence base on psycho-educational interventions for difficult asthma is changing and emphasises the need for regular updating of systematic reviews.

Contribution of the review

As highlighted in Chapter 1, this review aimed to complement and expand upon existing reviews of psycho-educational interventions for asthma. Our use of systematic review methods, whereby study inclusion and classification decisions were made on the basis of independent assessment by two reviewers, helped to ensure that there was

consistency and transparency regarding studies selected for inclusion and in-depth assessment. Comprehensive searching, methodological rigour and our subsequent attempt formally to pool results from best-evidence sources are key features of this review that were not evident in the only previous, narrative, review of psycho-educational interventions for asthma in at-risk groups.¹⁴⁵

Although several Cochrane systematic reviews of psycho-educational interventions for asthma have been updated or published in full subsequent to completion of our review (readers are referred to the Cochrane library for the latest updates of these), the contributions of this review in the light of these remain unchanged. There is increasing emphasis on patient education and self-management in all asthma management guidelines,^{4,5,8} and interventions to promote these are progressively being implemented as part of routine care in the light of the previous reviews on their effectiveness in general asthmatic populations.^{72,104} Perhaps most importantly, this review has gone some way towards addressing questions raised by reviews of previous research regarding whether these results extend to severe and difficult asthma. It has also contributed to summarising effects of other types of interventions where research evidence, even in general asthmatic populations, appears to be more sparse (e.g. psychosocial and multifaceted interventions). As an addition to existing systematic reviews, this review formally considered, evaluated and synthesised data on costs alongside health outcomes. However, as in many other fields, this exercise highlighted the lack of good-quality data available to aid decision-makers.

Unlike Cochrane reviews, which focus solely on interventions that have been subject to formal evaluation in controlled trials, this review has been able to collate summary descriptive data on the full range of psycho-educational interventions available for care of patients with difficult asthma and present detailed data on interventions from studies reviewed in depth. As a result, it has tested the utility of distinctions made between interventions in existing reviews, begun to explore the relative effectiveness of different types of interventions and, in the section on psycho-educational interventions that follows in this chapter, discusses this further to provide an alternative way of conceptualising these to guide future research.

Preliminary work on definitions and assessment of studies on a wide range of patients undertaken for

this review has highlighted problems in defining difficult asthma, the heterogeneity of patients experiencing poorly controlled disease and the difficulties that they face. The discussion that follows on the patient group of interest to this review covers some of these issues in more depth. It therefore contributes to the debate on defining, characterising and treating severe and difficult asthma, to complement ongoing work in this area, such as that focused on the pathophysiological dimensions of disease being conducted by the European Network for Understanding the Mechanism of Severe Asthma (ENFUMOSA).⁵⁴⁸

Issues that emerged in conducting this review with regard to the adequacy and practicality of systematic review methods, outcome measures for asthma, research quality and reporting of studies are also discussed further in this chapter. In addition to being a timely exercise to inform the direction of future research on psycho-educational interventions and difficult asthma, the points raised here can contribute to broader methodological debates with regard to systematic reviews, asthma research and health services research more generally.

Quantity, quality and nature of research

A broad approach was initially taken with regard to definitions both of 'difficult asthma' and 'psycho-educational interventions' and this review was also inclusive of a range of research designs. The reason for this approach was that research on psycho-educational interventions in difficult asthma was expected to be small compared with the field as a whole, so there was a need to identify all evidence that had the potential to contribute to answering our review questions and a description of options available for the care of patients at risk of poor symptom control and adverse outcomes from their asthma.

Much of the research identified appears to have been opportunistic. Many studies described interventions or reported observational analyses of new services using clinical or administrative data, and were not necessarily set up as formal prospective research evaluations. This was especially true of many 'economic analyses', which seemed to have been driven by the desire to show that a form of management reduced costs in publicly funded services. In the UK, research on difficult asthma seems to have been overshadowed by concern with the burden of asthma as a whole.

The relative ease with which outcomes for the majority of patients can be improved through adequate pharmacological treatment has led to this being an area which is well funded and researched, at the expense of alternative interventions, particularly in at-risk groups. The Department of Health and National Asthma Campaign programmes of research on asthma funded during the late 1990s generated some work of relevance to our review, although results from all of this were yet to be published.

Although not formally assessed here, we had the general impression that, as expected, before-and-after studies tended to report more positive results (in terms of outcomes and costs) than controlled studies. This is likely to be due to regression to the mean when those with initially high use of services or at an extreme in terms of morbidity are targeted.⁵⁴⁹ The studies that we identified potentially provide data for a further methodological study to investigate this. Although not ultimately subject to in-depth review, reports of descriptive and uncontrolled observational studies, and the data that we summarised from them, were, however, useful in defining patients and interventions and would benefit from further scrutiny. Some targeted particularly difficult groups with complex problems (e.g. patients with severe refractory asthma plus multiple clinical, pharmacological, co-morbidity and psychosocial risk factors for adverse outcomes) and may provide insight into ways of identifying these patients and their needs. Some also described particularly novel (e.g. joint psychiatric–medical consultation) or intensive types of interventions (e.g. multifaceted inpatient rehabilitation) and did so in much greater detail than was usual in standard reports of clinical trials.

Recommendations for future research should therefore consider this wider literature in determining the types of interventions and patient groups in which more formal evaluations might be of value.

Owing to potential for bias and the fact that we identified more controlled studies than had been anticipated, the contribution of studies of poorer design to answering the review questions was limited, as data were only extracted from studies with independent control groups. However, the number of high-quality studies most directly relevant in terms of their targeting of difficult asthma was still small, with only 20 RCTs and CCTs (representing 11% of all studies identified) judged to have probable or definite targeting of patients with difficult asthma. There was therefore

limited formal evaluation of the full range of different interventions considered in the most at risk patient groups. This was, however, compensated for to some extent by the fact that the final scope of the review encompassed studies in patients with severe (but not necessarily difficult) asthma and others with more limited characteristics making them potentially at risk from adverse asthma outcomes. Where possible, heterogeneity resulting from inclusion of studies of a broad spectrum of patients was explored by examination of differential effects across the difficult asthma subgroups into which studies had been classified.

Our selection and classification procedures ultimately led to in-depth review of 35 controlled studies in children, 21 in adults and one study including subgroups of both adults and children judged to have at least possible targeting of difficult asthma. A subset of these studies reported formal results data which were qualitatively synthesised, and a smaller portion data from which summary statistics could be calculated for inclusion in one or more meta-analyses. A summary of the literature identified and subsequently reviewed is provided in *Figure 20*.

Most of the research was relatively recent, especially in adults, and the number of recently completed, unpublished and ongoing studies again highlights that the evidence base in this field is changing, albeit relatively slowly given that the total number of studies in this field is small. The largest proportion of the research, including all the studies judged to have definite targeting of difficult asthma, was conducted in the USA. Because care for asthma has been changing rapidly, and is not fully standardised, it was difficult to make comparisons between studies in different places and over time. Older studies did not tend to make a major contribution to summaries of effectiveness owing to poorer designs, limited assessment of outcomes and lack of reporting of appropriate data. Conclusions of this review are usually therefore based on more recent evidence where care is likely to be more in line with current recommendations. The effectiveness and cost-effectiveness results, especially those in children, are, however, dominated by US studies. Although our review clinicians deemed the US⁴ and UK⁵ guidelines for the management of asthma to be sufficiently similar to allow comparisons, with greater variations in care likely at local levels within each country, differences between the guidelines and, more importantly, between US and UK healthcare

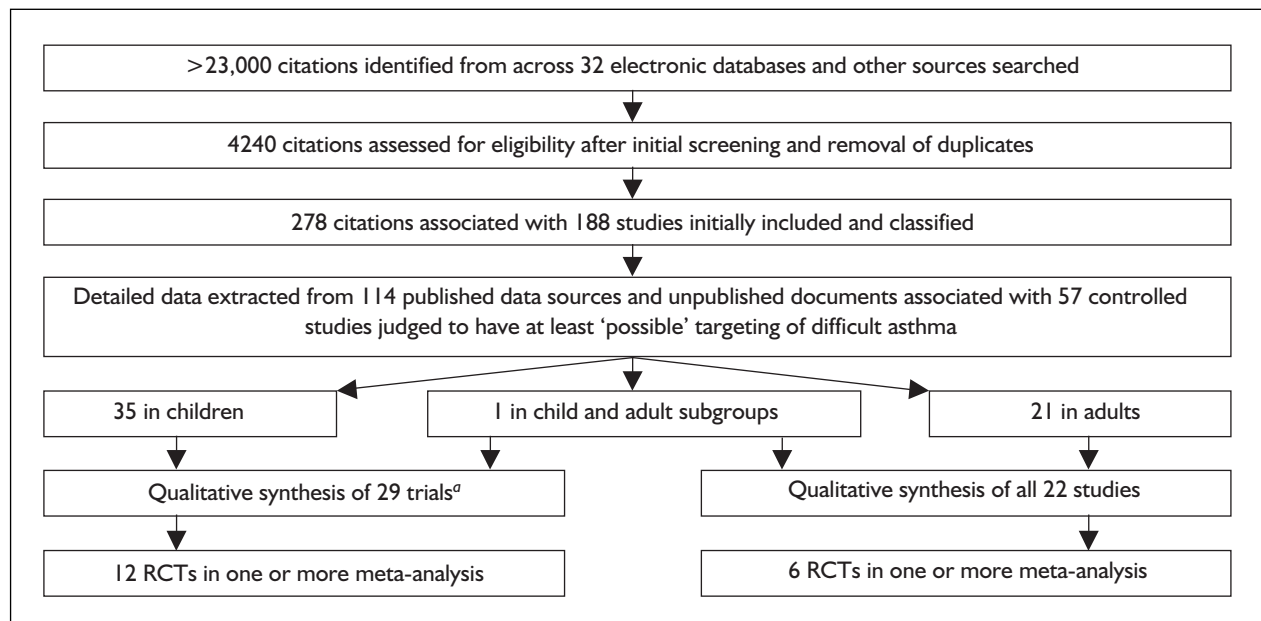


FIGURE 20 Literature identified, reviewed and contributing to conclusions. ^a Results from seven poor quality controlled observational studies were not considered further.

systems are important to consider in extrapolating findings to the UK NHS context.

The research included for in-depth review was still relatively diverse in terms of patients and interventions, but there were some common themes which this review helped to identify. It was also able to clarify further the key features of difficult asthma, of interventions to help patients and of important outcomes. The range of factors affecting outcomes in this review is potentially very large. Therefore, in spite of the fact that the review identified a larger research literature than expected, in most cases the number of studies was too small to examine interactions between all dimensions of difficulty in asthma and the nature of the intervention. The following section, however, discusses how this review has contributed to ideas for classifying and clarifying uncertainty in definitions along a number of dimensions related to patients, interventions and outcomes.

Features and implications of research representing best evidence in the field

Difficult asthma

Studies initially included but later judged to have insufficient targeting of difficult asthma (recruiting A&E attenders and patients from geographical locations demonstrating characteristics associated with increased risk) were excluded from in-depth

review. The effectiveness of educational interventions amongst patients attending the emergency room for asthma is the subject of Cochrane reviews in children¹⁰⁵ and adults,¹¹³ which may be read in conjunction with this review. Despite its exclusions, the results of this review are, however, still based on a broad range of studies deemed possible, probable and definite in terms of their targeting of difficult asthma, reflecting the proportions of patients in study samples likely to have difficult asthma. A judgement regarding the selection and classification of studies on this dimension of relevance to our review was assessed on the basis of a range of criteria and undertaken by two reviewers with agreement reached. The review would have been much more limited in terms of interventions, outcomes and ability to draw any conclusions if very strict criteria had been applied.

Few studies explicitly made reference to 'difficult' asthma, alternative terms used to describe it or to our core definition of 'poorly controlled asthma despite good medical treatment', highlighting problems with using these definitions in practice. In our review, we therefore had to make judgements on the basis of descriptions of a wide range of patient populations and eligibility criteria. Patients were most often identified as at risk of difficult asthma or adverse outcomes because they were from socially deprived backgrounds, had psychological difficulties, poor self-care, severe asthma and/or were high users of

emergency or inpatient services. Criteria used to identify potentially at-risk patients in adults and children were largely similar, although there appeared to be clearer distinctions between different subgroups and less heterogeneity in patients within these in adults, perhaps owing to the smaller number of adult studies. The definition of difficult asthma in adults and children may also differ in some respects, crucially because of the added complexity in children of parental influences on, and involvement in, the management of asthma ('difficult' parents, contributing to a child's problems with management or control of asthma). Such 'family factors' may also be important in adults, but this was rarely considered in the studies reviewed.

In most cases, difficult asthma was assumed to be implied or indicated on the basis of the presence of one or more of a number of identified risk factors and/or poor outcomes. However, these poor outcomes were, particularly in some of the older and US studies (where patients were uninsured and poor), inseparable from the fact that the populations targeted did not have access to good clinical care, which, in the absence of any other descriptors, we defined as care according to current guidelines. Definitions of severe and difficult asthma are therefore influenced by changes over time and variations across settings and countries in pharmacological treatment of asthma, medical management and implementation of guidelines. The fact that patients were not receiving optimal medical treatment was indeed often used as justification for the implementation of many of the interventions evaluated, and in some cases this shortfall in treatment was discovered as a result of implementing an intervention.

There therefore appears still to be room for facilitating access to care and improvements in medical management of patients with difficult asthma, which will further limit patients experiencing problems with disease control to those in which psychosocial factors are the main known contributors to poor outcomes. These are potentially the group for whom psycho-educational interventions are of most value. For this reason, increasing recognition and clarification of the important psychosocial factors affecting asthma and its management by patients are important. Despite this, the focus of many discussion papers on difficult asthma to date is still very biomedical, concentrating on clinical features and pathophysiology. Psychosocial factors have only recently been mentioned in clinical

guidelines and, in the most recent British guideline,⁵ discussion is limited to the context of acute asthma. However, many of the same issues, and additional factors, are important in persistently severe or unstable chronic asthma.

An added complication in assessing the research on difficult asthma is that a key indicator of patients being at risk is poor compliance with medication or other self-care recommendations (and this was a criterion used in some of the studies reviewed). As those who do not attend treatment may also be unwilling to participate in research, it is particularly difficult to be sure that this group was represented in studies. Despite this, the studies reviewed appeared to be relatively successful in targeting and following up patients with characteristics suggestive of them being at risk, with average participation rates similar to those in standard research populations. However, problems of recruitment, retention and compliance of patients were explicitly mentioned as issues by a large number of studies. Several of these indeed had had to be terminated or significantly adapted as a result of these problems. Some limited their assessment of outcomes to avoid the need for following up patients for self-report data.

Some studies targeted patients during critical moments, for example, when admitted to hospital. This is important, since recent research suggests that a patient's psychosocial status and beliefs may have different implications in terms of outcomes, depending on whether a patient has experienced a recent attack or not,⁵⁵⁰ potentially altering the nature and effectiveness of interventions depending on when they were delivered. This might be explored in future research. Longitudinal studies that examine whether patients move in and out of difficult asthma and at-risk categories over time are also important. More generally, further research is needed to assess the relative importance of different pathophysiological, clinical and psychosocial risk factors or combinations thereof in contributing to difficult asthma and the range of poor outcomes associated with it (e.g. reduced QoL, admissions, near-fatal attacks, deaths). This could take the form of secondary research summarising existing epidemiological evidence and primary research studies large enough in scope to assess different types of difficult asthma, from both clinical and psychosocial perspectives, and the existence of interaction and/or multiplication effects, including any changes over time. Further studies assessing practical methods for identifying at-risk patients

in practice, and assessing what screening would be required to inform the types of interventions that might be appropriate, are also important.

Use of the term 'difficult' was convenient in this review, but there could be problems with using this term in clinical practice. 'Difficult to control asthma' might be a better expression from a patient's perspective, and from the clinician's perspective there is a need to distinguish, yet be aware of, interactions between dimensions of 'difficulty' due to complex problems experienced by the patient on the one hand and unexpected pathophysiological or pharmacological responses on the other.

This review has highlighted the variable and multiple factors, and interactions between different factors, giving rise to difficulty in control, management and care of asthma. It has helped to clarify the range of issues, and interactions between them, in different types of severe and difficult asthma and in what might help patients experiencing poor control of their asthma.

Psycho-educational interventions

The review has also helped to clarify complexity in interventions, and what is meant by a 'psycho-educational' programme. As highlighted in Chapter 1, our review confirmed that there appears to be increasing overlap between different types of interventions, including psychological and educational components. When they are well defined for rigorous testing, there is also overlap between interventions commonly considered to be 'alternative' or 'complementary' therapies (e.g. yoga) and more traditional psychotherapies (e.g. relaxation techniques). A number of such interventions were screened for inclusion in the review and two in adults (of Yoga and Buteyko breathing) were actually reviewed in depth. We are therefore confident that although not specifically sought for inclusion in the review, any such alternative therapies which met our definition of a psycho-educational programme were likely to have been picked up by the terms we used for searching.

A contribution of this review has therefore been to test the inclusivity and validity of distinctions made between interventions in previous reviews of psycho-educational, and potentially 'alternative', interventions for asthma. On the basis of previous Cochrane reviews, we classified interventions into different types labelled educational, self-management, psychotherapeutic and multifaceted. Self-management interventions were seen to build

on educational interventions by including formal self-management based on self-monitoring and use of an action plan, with multifaceted interventions being an extension of these in that, in addition to education and formal self-management, they included other components, most often concurrent optimisation of medical treatment. The commonest intervention types were educational in children, multifaceted in adults, with psychosocial programmes the least commonly evaluated in both patient groups. However, this classification was ultimately deemed not to be particularly useful, since there was almost as much variation within interventions of the same type as between those of different types. The delivery, duration, intensity and content of interventions and the presence of non-psycho-educational add-ons (e.g. medical care) were highly varied across programmes, regardless of their type. This has implications for other reviews where interventions may 'fall between the gaps' when strict definitions of interventions are used or where interventions fall into more than one category across different reviews.

We feel that this review has also brought to the fore an alternative way of conceptualising psycho-educational interventions. In Chapter 1, *Figure 1* presented the pathways by which psychosocial factors interact with asthma. Programmes might be classified in terms of the pathways, or number of pathways, that they target. This is shown in *Figure 21*.

If an intervention targets particular groups on the basis of specific psychosocial characteristics, it may focus on just one pathway. For example, patients with poor self-management might be offered skills training and help in addressing the psychosocial determinants of behaviour such as knowledge, attitudes and self-efficacy. There is increasing emphasis on the latter, in particular in the patient education and self-management literature,⁵⁵¹ and this approach is at the core of initiatives such as the expert patient programme for chronic disease management.⁵⁵² Interventions for patients experiencing high anxiety, leading to exacerbations of symptoms, may focus on relaxation or other stress management techniques. However, reasons for anxiety may be also reduced through teaching self-management skills such as objective monitoring of asthma to provide reassurance on levels of airflow obstruction. Interventions for patients with complex psychosocial co-morbidities resulting from the impact of severe asthma may focus on developing skills for coping with these in the first instance, as

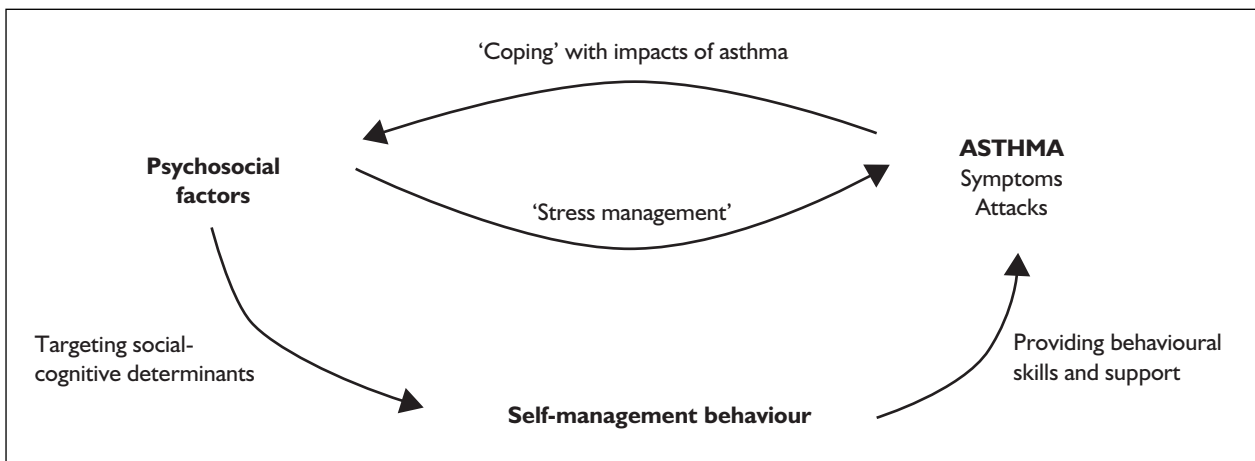


FIGURE 21 Intervention points for psycho-educational programmes

factors such as depression might inhibit motivation for patients actively to manage their disease. Often in complex cases, there may be a need for intervention at different points over time, to allow for feedback and interaction effects. Again, though, self-management would be central to active coping with asthma in the long term. The utility and established effectiveness of self-management interventions suggest that self-management might be offered for all patients. In patients with the most difficulties, comprehensive broad-based psycho-educational interventions might be developed to target generic samples of at-risk patients and potentially adapted to suit individual needs. There is, however, a need for further empirical data to support the implementation of this framework and to establish the effectiveness of specific interventions tailored to patients sharing particular psychosocial characteristics, in addition to broad-based psycho-educational approaches targeting a wider range of patients having problems with symptom control.

Our review has indicated trends over time in the types of interventions evaluated by studies. Early work comprised uni-disciplinary studies of limited short-term psychological interventions (e.g. relaxation training), and studies undertaken from a clinical perspective based on educational models which showed little recognition of psychological principles. Gradually clinical and psychological research seems to have been coming together, with increasing use of psychological theory in educational and self-management interventions and increasing use of health services research methods in evaluating psychosocial programmes. In existing studies, over half of interventions in adults and children involved nurses, one-third doctors, and involvement of a broad range of

other providers across studies appeared to be influenced by the intervention type (e.g. psychologists were primarily involved in psychosocial interventions). In an increasing number of recent studies, however, interventions were delivered by multidisciplinary, multiprofessional teams. The conceptualisation of interventions illustrated in *Figure 21* emphasises the need for a multidisciplinary approach. An asthma nurse may be best placed to provide training in self-management skills, whereas a psychologist may be best placed to address the influence of psychosocial factors on performance of self-management behaviour or provide training for nurses with respect to these aspects of care. Likewise, a respiratory clinician may understand the ways in which psychosocial factors directly impact on pathophysiological mechanisms in asthma, but may in turn need advice or input from a clinical psychologist or interested psychiatrist to find ways of addressing these and treating psychosocial difficulties resulting from living with a chronic disease. There is also a role for social care agencies and referral in dealing with more severe social consequences and determinants of poor asthma control.

In the light of discussions above on the inadequacies in the medical care of patients with difficult asthma, concurrent consideration of diagnostic and pharmacological issues might also be important in this group of patients to ensure that optimal care, according to guidelines, is both delivered by practitioners and agreed with patients as part of a comprehensive management plan. From a practical and theoretical perspective, therefore, multifaceted interventions incorporating formal self-management and delivery of care by a multidisciplinary team

including specialist clinical professionals, may be the most promising approaches warranting further evaluation.

Interventions assessed in this review were most commonly provided in inpatient or outpatient settings. Few were home or community based, despite the fact that the majority of asthma care in the UK is delivered in a primary care setting. Primary care practitioners are likely to have the most frequent contact with these patients, and practice staff may be in the best position to understand the complexity of co-morbidity, psychological, social and environmental issues faced by patients with difficult asthma. There may also be pragmatic and economic arguments for further promotion of appropriate initiatives in primary care. These could capitalise on opportunistic intervention and outreach to overcome many of the barriers to patients with difficult asthma attending organised programmes or accessing secondary care facilities. Our own experience^{528,529} and the rationale for delivery of several recent UK studies of interventions for at-risk patients^{390–393,453–456} also suggests that training for and promotion of guidelines amongst those involved in the care of asthma patients in primary care may be necessary to accompany any such initiatives.

Delivery methods used in interventions were mostly relatively informal – skills training and discussion were the most commonly implemented. Just over half of studies in children but only four studies in adults made reference to the use of one or more formal psycho-educational theory or approach in delivery of their intervention. Clinical, psychological and educational theory (existing organised knowledge) is important but should not inhibit interdisciplinary development. Interventions need to be pragmatic, and a balance in research is needed between practical effectiveness evaluations and concept and theory development. Discussion of issues of complex psychological theory in relation to learning, motivation and behaviour change are beyond the scope of this review. However, use of theory is certainly likely to be important in understanding heterogeneity of effects not explained by chance alone between apparently similar interventions. This is another area for potential future research.

One-quarter of interventions in children and half in adults were timed to follow an asthma episode (e.g. hospital admission). In practice, decisions regarding the timing of interventions often appeared to be influenced by ease of recruitment of patients admitted to hospital or attending for

unscheduled care. The influence of timing on the effectiveness of interventions, and specifically whether effects vary depending on whether they are delivered during or after an exacerbation or during a controlled spell, was unable to be investigated in this review owing to lack of data. Further work is therefore needed to compare similar interventions administered at different times and to determine whether timing is a factor likely to influence uptake by patients.

Around half of interventions examined in this review were delivered to individual families in children or individual patients in adults. Our review of childhood interventions only considered studies of interventions that actively involved paediatric patients in their delivery, with or without parents or other family members, since it was felt that this was important to ensure development of responsibility for self-management and self-care skills from an early age. In the youngest patients, some of the interventions reviewed were inevitably focused primarily on parents. The influence and involvement of care-givers in the management of asthma is an added source of heterogeneity which might usefully be explored in future research, although the data to do so here were limited, often owing to lack of clarity regarding the role of family members or others in the care of the patients under study. There is therefore scope for further review of interventions specifically focused on improving the management of asthma, particularly childhood asthma and difficult asthma, by care-givers (e.g. parents, school teachers, health professionals), which were not considered within the scope of this review.

A frequent problem encountered in the review was that it was not always easy to tell how to classify an intervention on the basis of who did what to whom, with what frequency and in what setting, owing to poor reporting. In line with increasing guidance on the development and evaluation of complex interventions,^{553,554} further research of immediate value would be to develop checklists for research reporting, similar to the CONSORT guidelines for RCTs,⁵⁵⁵ for ensuring consistent reporting of key features of complex interventions such as those in this review (e.g. type and number of providers, format and methods of delivery, techniques or theories used, setting, content, duration, timing and frequency of intervention sessions).

Study quality

As highlighted, there is potential for non-evaluative and poorer quality evaluative studies to

contribute to work on the development of definitions and provide a greater understanding of context. Such studies were, however, not useful for answering the primary clinical and research questions of the review regarding effectiveness and cost-effectiveness. The methodological quality of studies that were used to provide qualitative and quantitative syntheses of results was generally poor, as assessed against standard criteria. For example, of the 39 randomised trials reviewed, less than half in children and less than one-third in adults described randomisation methods, only two in children and four in adults described allocation to groups as being concealed and less than half made reference to blinded outcome assessment. Sample sizes were also often small. As it turned out, however, the studies that included sufficient data for meta-analyses were generally those of better quality. Most studies reporting costs had not been designed and reported as economic evaluations and should be considered poor sources of evidence about costs of the intervention and its consequences. There are, however, a growing number of well-designed RCTs with concurrent economic evaluations of psycho-educational interventions in the UK context, but many of these are yet to report full outcome data or any economic results.

Outcomes

A diverse range of outcomes was reported in studies assessed for in-depth review. Although there is an increased risk of death in patients with difficult asthma, and this was frequently mentioned, very few studies reported this as an outcome, and all were individually too small to address impacts on mortality. Studies were also under-powered to detect effects in other rare events, such as intensive care episodes. The most commonly reported outcomes related to health service use (inpatient care, emergency and other healthcare attendances). Use of admissions and data on utilisation of other services are not always good measures of severity or poor asthma control as they are also influenced by other factors such as clinical practice, patient choices and service availability. Reporting of healthcare use is also not helpful for economic analyses where the measures are not used as indicators for cost measurement, but as primary outcomes. In these cases, economic gain is inferred by comparing some cost savings (reduction in hospital use) with the cost of the intervention, without reference to health gain or QoL.

There is some circularity of definitions around outcomes in asthma in relation to need for

treatment. There is a need to assess patient-reported health and more objective measures of treatment (e.g. drug treatment step^{4,5}) to untangle, for example, differences between asthma control and severity and effects of over-treated mild asthma and under-treated severe asthma. There seems to be increasing consensus on key questions relating to assessment of symptoms and studies evaluating symptoms used variations on this theme. Recommendations⁹ recently incorporated in the British guidelines⁵ will help to ensure that this approach is taken in clinical practice, but this needs to extend to research.

The use of 'symptom-free' or 'episode-free' days,¹³² particularly as a standard outcome in economic studies as was done in the only good-quality economic evaluation we reviewed in children,³⁹⁷ in addition to being subject to general criticisms,^{556,557} may not be sensitive measures of change in those with ongoing severe or poorly controlled disease. An increasing number of generic and asthma-specific standard QoL instruments were reported as used in the reviewed papers. There are valid reasons for both types of measure, but the range made it difficult to summarise outcomes. It may be important, as recommended elsewhere,⁵⁵⁸ and particularly in this patient group, to use both age-appropriate specific and generic measures given the frequent presence of physical and psychological comorbidities. Further standardisation of recommendations on outcomes and testing of these measures in severe and difficult groups would be welcome. There is also scope for future work on the development and testing of wider measures of benefit (e.g. utility measures, willingness to pay) for use in economic studies in difficult asthma to build on the growing empirical literature on this in asthma research more generally.¹³⁵

The goal of psycho-educational interventions is to improve health outcomes by facilitating changes in patients' behaviour, cognitions and emotions related to asthma and its management. It is important to determine that interventions are effective at this level in order to explain effects, or lack thereof, on health outcomes. Therefore, assessment of outcomes matched to the psychological variables being targeted by interventions is necessary to assess intermediary or explanatory effects. There are numerous well-validated measures of emotional status for use in medical patients (e.g. the Hospital Anxiety and Depression Scale⁵²¹) and an increasing number of scales to assess patient cognitions, primarily

perceptions and beliefs, in relation to disease and medication use.⁵⁵⁹ There is, however, a lack of brief, well-validated measures of self-management behaviour and other factors (e.g. self-efficacy) influencing medication use and additional aspects of self-care (e.g. monitoring, trigger avoidance, attendance at routine appointments) in patients with difficult asthma and more generally.⁷⁷ This was reflected in the range of informal questions and techniques used to assess patient behaviour and psychological correlates of this in the studies reviewed. Qualitative investigations of issues of importance to management of asthma in those with difficult asthma and further work on the development and wider validation of measures would aid future evaluations.

The studies reviewed varied with regard to when different health outcomes were measured. Asthma is variable over time, and this suggests a need for multiple time points, measuring immediate effects on behaviour, cognitions and emotion, and also whether this is translated in the longer term into improved symptoms, QoL and later health service use. Long-term impacts may be important especially in children. Early intervention may prevent irreversible effects of poorly controlled disease and side-effects due to overuse of medication. Early improvements may affect educational attendance (measured in a minority of studies reviewed) and long-term educational outcomes (reported in none of the studies reviewed). Sufficiently lengthy follow-up (ideally at least 12 months) in future studies in this field is of crucial importance.

All of the outcomes that we synthesised were reported as having been assessed by more than one-third of studies, and in a number of cases were identified as primary outcomes. The number of studies actually reporting data separately for intervention and control groups (rather than just commenting on findings), and also reporting data in a suitable format for calculation of summary statistics, was, however, much more limited. Generally, the studies reporting valid statistics for calculation of summary effect sizes were of higher quality than those that did not, so additional weight was given to these studies in interpreting results.

Effectiveness of psycho-educational interventions for difficult asthma

This review has primarily attempted to address whether psycho-educational interventions improve

outcomes for patients with difficult asthma. The large range of outcomes measured and their assessment and reporting in different ways across studies precluded meta-analyses of most effectiveness data. However, amongst the most commonly reported outcomes, there was evidence that, compared with usual or non-psycho-educational care, psycho-educational interventions reduced admissions when data from the latest follow-ups reported were pooled across nine studies in children (RR = 0.64, 95% CI = 0.46 to 0.89) and six studies with possible targeting of difficult asthma in adults (RR = 0.57, 95% CI = 0.34 to 0.93). In children, the greatest and only significant effects were confined to two individual studies with limited targeting of difficult asthma and lacking long-term follow-up.^{411,417} Limited data in adults also suggested that effects may not extend to those most at risk. For example, in the one study reporting admissions data in a form to allow calculation of a summary statistic amongst adult patients graded as probable in terms of difficult asthma (unpublished data from recently completed study^{528,529}), positive effects on admissions were not observed (RR = 1.26, 95% CI = 0.67 to 2.37). Furthermore, in another study,⁴⁴⁴ although reductions in admissions of borderline significance in the intervention group were observed amongst the overall sample (RR = 0.62, 95% CI = 0.39 to 0.99), when the analysis was confined to the subgroup of patients judged probable in terms of difficult asthma the effect was reduced and significance lost (RR = 0.88, 95% CI = 0.54 to 1.44).

With regard to other commonly reported outcomes, there was no evidence of effects of psycho-educational interventions on emergency attendances in children (RR = 0.97, 95% CI = 0.78 to 1.21) or adults (RR = 1.03, 95% CI = 0.82 to 1.29), when data from the latest follow-ups reported by eight and six studies, respectively, were pooled across all time points. There were overall significant reductions in symptoms, similar in different subgroups of difficult asthma, across four paediatric studies that could be combined (SMD = -0.45, 95% CI = -0.68 to -0.22), but mixed results across individual adult studies that could not be pooled. Seven individual studies in children also showed mainly positive effects on measures of self-care behaviour. However, with respect to all other outcomes in adults and children where pooling could not be undertaken but sufficient data allowed conclusions to be drawn, studies showed mixed results or suggested limited effectiveness of psycho-educational interventions.

Although to address one of our secondary review questions, limited subgroup and sensitivity analyses were able to be undertaken to examine the relative effectiveness of interventions of different types, these could only be undertaken in children and it was not possible to draw valid conclusions from them. Significant effects on the most commonly reported outcomes were mainly confined to self-management and multifaceted interventions, hence formal self-management may be a key component of effective interventions. However, confounding of results due to the tendency for more intensive interventions to target more at-risk patients means that these findings should be treated with caution. It should be noted that only educational, self-management and multifaceted interventions were ultimately included in any quantitative synthesis of results in adults or children. Echoing findings in general asthma populations,^{106,112} evidence is therefore lacking on the effectiveness of psychotherapeutic and social support interventions. Although stated as questions for consideration in our review, there were insufficient studies using psycho-educational theories and too much variation in terms of components of interventions to examine whether these factors explained heterogeneity in results.

Cost-effectiveness of psycho-educational interventions for difficult asthma

In addition to assessing effectiveness, this review aimed to determine whether psycho-educational interventions constitute an efficient use of healthcare resources for patients with difficult asthma. However, studies examining costs were even more limited in quantity and quality than those reporting key effectiveness outcomes, precluding firm conclusions regarding cost-effectiveness.

Studies on the economics of interventions for treatment and support of patients with asthma have been reviewed by several groups, as referenced in Chapter 1. These reviews covered all forms of intervention for asthma, including medication and medical care, and all levels of severity or difficulty of asthma. They concluded that there had been inadequate economics research in the field in general, and in the area of psycho-educational interventions for asthma in particular. Many reviews pointed to the increased costs of care for the most severe forms of asthma and to the greater potential for interventions for the most severe patients to be cost-effective. For

this to be the case, interventions would need either to improve outcomes at an acceptable increased cost, or to maintain outcomes at reduced overall cost (including the cost of the intervention).

In common with previous reviews, we found very few well-conducted economic studies of psycho-educational interventions and there is currently a lack of evidence to support assertions regarding the potential increased cost-effectiveness of psycho-educational interventions when they target high-risk groups. Only one study in children³⁹⁷ and one in adults^{528,529} have so far met a reasonable number of quality criteria to be considered as good economic evaluations. In the paediatric study, the increased healthcare costs of providing a multifaceted intervention were associated with an increase in symptom-free days, and cost-effectiveness appeared to be within the range for accepted health technology investments in the USA. In the adult study there were higher healthcare costs in the group following provision of a multifaceted intervention, but no differences in health outcomes between groups.

Seven further studies in children and three in adults reported on some more limited assessment of costs, with most drawing conclusions about cost-effectiveness. One recently completed US study reporting on cost-effectiveness in adults had only been reported in abstracts at the time of our review, but subsequent publication of this suggests that it may provide further good economic evidence.⁵²⁷ Several UK RCTs in adults planned to conduct economic analyses of their interventions at the outset but, although one has subsequently published clinical findings,⁵⁰⁵ cost data have not yet been reported from these. This highlights the problem of publication lag for economic studies reported alongside trials.

Where this could be ascertained, the wide variety of costs of interventions reflects the diversity of interventions, methods for estimating costs and settings in which the research took place. Cost data were sometimes based on different cohorts of patients or subgroups from those in the effectiveness studies. The balance between costs of intervention and of long-term healthcare may depend on the period over which costs are followed up. Valuation of lost working time for patients or children's parents or time lost from school in children was not attempted in the studies published to date, but was planned in one recently completed study^{528,529} and recognised by others as important for future research.

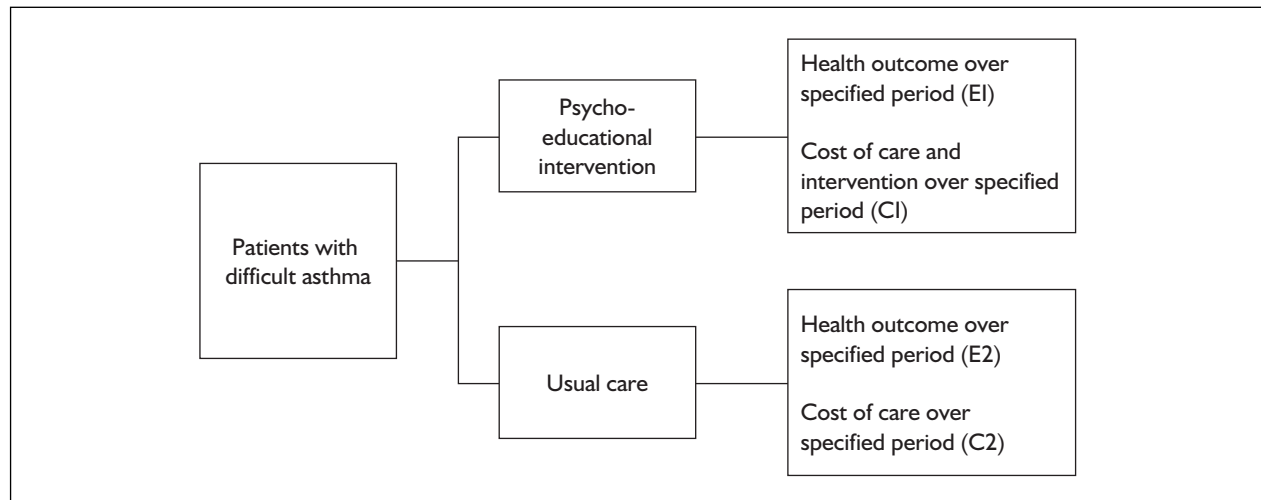


FIGURE 22 Simple decision model for economic evaluation of psycho-educational interventions in difficult asthma

All the ‘economic’ studies identified were primary research studies, basing cost-effectiveness conclusions on data from a single research study population. None took the form of secondary research evaluations based on combining data from secondary sources to model cost-effectiveness. In the protocol for this review, we stated our intention to develop a model for economic evaluation, based on the findings of the reviewed research. Weiss and Sullivan¹⁸ and others have suggested a generic decision-tree approach to building such a model which might take the form shown in *Figure 22*. Cost-effectiveness is estimated as the ratio of cost difference between intervention and usual care groups (C1 minus C2) to the difference in outcome between the two groups (E1 minus E2). In essence, this is the model used in the good-quality economic evaluations identified in our review.^{397,528,529}

This review found few outcomes for which there were sufficient data for meta-analytic synthesis. A cost model could be set up with hypothetical probabilistic variables to fill gaps in missing cost and outcome data, but in our view the gaps are currently too many to make this a worthwhile exercise. As simple decision tree models make no assumptions about time-dependent effects, more work is also needed to find the form of decision model which reflects the changing effects of interventions over time, if these effects indeed exist. In the absence of further modelling, the two good-quality economic studies identified in our review represent the best evidence available on the cost-effectiveness of psycho-educational interventions for difficult asthma. Both studies found net increases in overall costs, one with and

one without accompanying benefits in terms of health gain.

There are some important next steps toward developing evidence about the cost-effectiveness of psycho-educational interventions. The first of these is for new research to adopt agreed comparable outcome measures, including generic QoL, to describe usual care provided in the absence of the intervention, to record the costs of the intervention and to record patients’ use of non-hospital services, patterns of work and/or other usual activity and personal costs over the period of the follow-up. Such studies might consider undertaking some crude modelling of costs and effects to determine sample sizes and feasibility, prior to implementing full-scale evaluations, and should also ensure that reporting of clinical and economic results is in line with recommendations from international guidelines.^{165,555}

Caveats

Our conclusions regarding effectiveness and cost-effectiveness are inevitably cautious given the volume and nature of research on psycho-educational interventions for difficult asthma. We would, however, like to add some further caveats.

There may be some danger of giving undue weight in the report to poorer quality studies reporting multiple outcome measures or time points. However, studies that were included in meta-analyses happened to be the RCTs, as the other studies did not report appropriate data for

calculation of summary statistics. Conclusions are therefore likely to be based primarily on studies classified as RCTs, but the quality and methods used for allocation to groups in these trials were not always clear and this could bias findings. Follow-up of pre-specified outcomes was reported in most included studies, length and completeness of follow-up of patients was variable and there is likely to have been some selective reporting of outcomes and attrition bias. In this high-risk and often socially disadvantaged group of patients, good follow-up rates are particularly difficult and there is always a tendency for data from the less complex patients, particularly those benefiting most from interventions, to be over-represented in results.

In some cases, studies were only included and/or reviewed in depth if they reported data from subgroup analyses of patients with difficult asthma in studies of asthma in general. Given that subgroup analyses are more likely to be reported in published papers and mentioned in abstracts if they demonstrate positive results, the inclusion of these studies may have introduced bias. There were, however, examples of studies where subgroup analyses demonstrated the opposite – namely reduced effectiveness in at-risk groups.

Given the heterogeneity in terms of the types of interventions and patients studied in the research reviewed, we were careful to be cautious in combining results from diverse studies. The fact that we did conduct several meta-analyses might be criticised; however, we felt that these were important to assess whether there were any overall consistent effects in addition to allowing some of the effects of this heterogeneity to be formally

explored. Ultimately, the studies reporting data in a format which allowed results to be pooled were less heterogeneous in terms of interventions and patients than the sample of studies reviewed in-depth as a whole. Only three of the four types of interventions, and those potentially most similar to each other, were considered in meta-analyses and the studies included in these were also only those deemed to have possible or probable targeting of difficult asthma.

Many studies lacked data necessary for quantitative synthesis. The lack of appropriate reporting of data for calculation of summary statistics is a problem common to many systematic reviews and unfortunately, in this one, we were not able in the time frame available to contact authors for specific missing data. As previously highlighted, the studies eventually included in meta-analyses were generally those of highest quality; however, as can be seen in the tables summarising effectiveness results in children and adults (*Table 35* in Chapter 5 and *Table 60* in Chapter 6), the results of these studies were not always representative of the larger number of studies reporting any results data in relation to specific outcomes. Methodological work to allow different types of data (e.g. binary, event rate, continuous data) to be combined into generic effectiveness estimates would greatly aid systematic reviews such as this where there is a lack of standardisation of outcomes and reporting. Ensuring that basic statistical data (e.g. numerators and denominators, point estimates and measures of variability) are reported will also facilitate future meta-analyses and should be encouraged with initiatives such as the CONSORT statement.⁵⁵⁵

Chapter 8

Conclusions

There is some evidence of overall positive effects of psycho-educational interventions on hospital admissions in adults and children, and on symptoms in children, but limited evidence of effects on other outcomes. The majority of research and greatest effects, especially in adults, were confined to patients with severe disease but who lacked other characteristics indicative of difficult asthma or likely to put them at risk. A lack of quality research limits conclusions regarding cost-effectiveness. It was not possible to draw clear conclusions regarding the relative effectiveness of different intervention types, but limited findings, trends in the evidence base and theoretical developments suggest that multidisciplinary, multifaceted interventions incorporating formal self-management and medical care may be the most promising approaches warranting further evaluation. However, we suggest that an alternative conceptualisation of the key components of interventions in the light of the ways in which psychosocial factors and asthma interact may be necessary to guide further research and application of appropriate theories to the development of interventions in this field.

Implications for healthcare

With the aim of reducing asthma morbidity and mortality, based on the evidence in this review, we suggest that:

- In adults and children with **severe** asthma, provision of psycho-educational interventions (especially those incorporating formal self-management) may reduce hospital admissions and, in children, improve symptoms, but potentially at increased overall cost. There is currently a lack of evidence to warrant significant changes in clinical practice with regards to care of patients with more **difficult** asthma.
- Better identification and recognition of patients with difficult asthma, taking into account the different pathophysiological, clinical, compliance and psychosocial risk factors, might improve their care, enhance the value of future audit and aid in the targeting of any new interventions.

- Until further research is available, the emphasis should be on optimisation of medical care, taking account of potential complicating psychosocial factors, for patients with difficult asthma, to ensure that the number of patients continuing to experience poor control of symptoms and frequent exacerbations is minimised.

Recommendations for research

In priority order, reflecting the reviewers' viewpoint, our findings suggest there is a need for further research into the following areas.

In general:

1. Standardisation of reporting of complex interventions.

In asthma/difficult asthma:

2. An update of this review incorporating results of the good-quality RCTs with economic evaluations that were in progress or remained unpublished.
3. Primary and secondary research to clarify key risk factors and develop tools for identifying patients susceptible to adverse asthma outcomes.
4. Secondary research extending this review to examine psycho-educational interventions aimed **solely** at those providing care for patients with difficult asthma, and potentially asthma more generally (e.g. family members, school teachers, health professionals).
5. Further development, validation and standardisation of patient-focused, clinically relevant and age-appropriate measures of intermediary (self-management behaviour and its correlates) and final health outcomes (especially symptom-based and QoL scales), plus measures of benefit suitable for inclusion as end-points in economic studies, for use in research on asthma and, particularly, severe and difficult asthma.
6. Further work on the conceptualisation of interventions, particularly with a view to the development of individualised, multi-disciplinary interventions, incorporating application of psycho-educational theories, that can be delivered to a broad spectrum of

patients, potentially in primary care or community settings.

7. Development and conduct of pragmatic RCTs to evaluate and compare different well-defined, theory-based interventions in practice which should:

- (a) take account of guidance on the development and conduct of complex interventions
- (b) be piloted or based on prior modelling of possible effectiveness and cost-effectiveness to inform sample size calculations and feasibility of full-scale evaluations
- (c) focus on broad-based multifaceted approaches adapted to individual needs for

a wide spectrum of at-risk patients or evaluate specific interventions matched to the needs of particular groups, especially in areas where evidence is lacking (e.g. psychosocial interventions, adults, complex patients)

- (d) have sufficient power and length of follow-up (preferably ≥ 12 months) to assess all important health and intermediary outcomes using validated measures
- (e) incorporate, where possible, assessment of relevant costs and endpoints suitable for inclusion in economic analyses.



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