Nurse versus physician led-care for the management of paediatric asthma
Küthe, M.C.

Citation for published version (APA):
Küthe, M. C. (2014). Nurse versus physician led-care for the management of paediatric asthma

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Nurse versus physician-led care for the management of asthma (Review)

Kueth MC, Vaessen-Verberne AAPH, Elbers RG, Van Aalderen WMC

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library 2013, Issue 2

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[Intervention Review]

**Nurse versus physician-led care for the management of asthma**

Maarten C Kuethe¹, Anja A P H Vaessen-Verberne¹, Roy G Elbers², Wim MC Van Aalderen³

¹Paediatrics, AMPHIA Hospital, Breda, Netherlands. ²Dutch Cochrane Centre, Academic Medical Center, Amsterdam, Netherlands. ³Department of Paediatric Respiratory Medicine and Allergy, Emma Children’s Hospital, Academic Medical Center, Amsterdam, Netherlands

Contact address: Maarten C Kuethe, Paediatrics, AMPHIA Hospital, PO Box 90157, Breda, 4800 RL, Netherlands. kuethe@planet.nl. mkuethe@amphia.nl.

**Editorial group:** Cochrane Airways Group.

**Publication status and date:** New, published in Issue 2, 2013.

**Review content assessed as up-to-date:** 30 August 2012.

**Citation:** Kuethe MC, Vaessen-Verberne AAPH, Elbers RG, Van Aalderen WMC. Nurse versus physician-led care for the management of asthma. Cochrane Database of Systematic Reviews 2013, Issue 2. Art. No.: CD009296. DOI: 10.1002/14651858.CD009296.pub2.

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**ABSTRACT**

**Background**

Asthma is the most common chronic disease in childhood and prevalence is also high in adulthood, thereby placing a considerable burden on healthcare resources. Therefore, effective asthma management is important to reduce morbidity and to optimise utilisation of healthcare facilities.

**Objectives**

To review the effectiveness of nurse-led asthma care provided by a specialised asthma nurse, a nurse practitioner, a physician assistant or an otherwise specifically trained nursing professional, working relatively independently from a physician, compared to traditional care provided by a physician. Our scope included all outpatient care for asthma, both in primary care and in hospital settings.

**Search methods**

We carried out a comprehensive search of databases including The Cochrane Library, MEDLINE and EMBASE to identify trials up to August 2012. Bibliographies of relevant papers were searched, and handsearching of relevant publications was undertaken to identify additional trials.

**Selection criteria**

Randomised controlled trials comparing nurse-led care versus physician-led care in asthma for the same aspect of asthma care.

**Data collection and analysis**

We used standard methodological procedures expected by The Cochrane Collaboration.

**Main results**

Five studies on 588 adults and children were included concerning nurse-led care versus physician-led care. One study included 154 patients with uncontrolled asthma, while the other four studies including 434 patients with controlled or partly controlled asthma. The studies were of good methodological quality (although it is not possible to blind people giving or receiving the intervention to which group they are in). There was no statistically significant difference in the number of asthma exacerbations and asthma severity...
after treatment (duration of follow-up from six months to two years). Only one study had healthcare costs as an outcome parameter, no statistical differences were found. Although not a primary outcome, quality of life is a patient-important outcome and in the three trials on 380 subjects that reported on this outcome, there was no statistically significant difference (standardised mean difference (SMD) - 0.03; 95% confidence interval (CI) -0.23 to 0.17).

Authors’ conclusions

We found no significant difference between nurse-led care for patients with asthma compared to physician-led care for the outcomes assessed. Based on the relatively small number of studies in this review, nurse-led care may be appropriate in patients with well-controlled asthma. More studies in varied settings and among people with varying levels of asthma control are needed with data on adverse events and health-care costs.

PLAIN LANGUAGE SUMMARY

Nurse- versus physician-led care for the management of asthma

Asthma is a very common chronic condition and symptoms are breathlessness, coughing, wheezing and chest tightness. Symptoms may be persistent or intermittent. In order for asthma to be managed well, and symptoms controlled, regular visits to a healthcare professional are needed. During these visits, a number of aspects should be addressed (prescribing of medication, asthma self-management education including inhaler technique assessment, written asthma treatment plans, self-monitoring of symptoms and regular medical review). Consultations such as these, although important, are time-consuming, placing a burden on healthcare resources and the workload of the doctors treating these patients. Since the 1990s, nurse-led care has been introduced to treat people with asthma. We investigated if nurse-led care is as effective as that delivered by a physician.

We reviewed the medical literature to find randomised controlled trials on care delivered by specialised nurse compared to care by a doctor in the management of asthma. We found five studies on 588 adults and children. The studies were of good methodological quality. The number of asthma exacerbations (flare-ups) and the level of asthma severity did not differ at the end of the study period between the intervention and the control group. Only one study reported information about the costs associated with both kinds of care and there was no significant difference between them. There was also no difference in quality of life. We found no difference between nurse-led care and physician-led care. Based on the relatively small number of studies in this review, nurse-led care may be appropriate in patients with well-controlled asthma. More studies in varied settings and among people with varying levels of asthma control are needed with data on adverse events and health-care costs.
### Summary of Findings for the Main Comparison

Nurse-led versus physician-led care for the management of asthma

**Patient or population:** the management of asthma  
**Settings:** primary care and hospital  
**Intervention:** nurse-led versus physician-led

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<td>The mean quality of life at 12 months in the intervention groups was 0.03 standard deviations lower (0.23 lower to 0.17 higher)</td>
<td>SMD -0.03 (-0.23 to 0.17) 380 (3 studies)</td>
<td>moderate</td>
<td>As studies reported quality of life on different scales, we pooled using SMD. There was no clinically important difference in quality of life between the 2 groups</td>
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<td>Hospital admissions</td>
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<td>Risks were calculated from pooled risk differences</td>
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*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval; RR: risk ratio; SMD: standardised mean difference.

---

**GRADE Working Group grades of evidence**

**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

1 Blinding of participants not possible.

2 Heterogeneity was found in this outcome ($I^2 = 59\%$).
BACKGROUND

Asthma is the most common chronic disease in childhood, and the high childhood prevalence persists into adulthood (Akinbami 2009; Wenzel 2006), placing a considerable burden on healthcare resources. Thus effective asthma management is important to reduce morbidity and to optimise utilisation of healthcare facilities. This led to the development of (inter)national guidelines for diagnosis and management (GINA 2011; SIGN 2011; de Jongste 2007; Levy 2009). The cornerstone of asthma management is treatment with an inhaled corticosteroid (ICS) (CAMP 2000). Good asthma management is of the utmost importance in achieving control and should include: institution of (inhaled) medication; asthma self-management education including inhaler technique assessment; written asthma plans; self-monitoring of symptoms or airflow, and regular medical review (GINA 2011; Guarnaccia 2007; O’Byrne 2006). Until recently, care was mainly provided by physicians and the role of the asthma nurse supportive in the implementation of these aspects. However, educational interventions, including self-management and self-monitoring by specialised asthma nurses (in nurse-led care) is already widely implemented in many (but not all) general practices and hospitals in high-income countries for more than two decades and have proved to be effective (Gibson 2008 Gibson 2009 Jones 2009; Nathan 2006; Wolf 2008).

The increasing need for asthma management in general and hospital practice emphasises the importance of adequate ‘manpower-planning’ in primary and secondary care settings (Akinbami 2009). Many general practitioners as well as paediatricians lack sufficient time for such comprehensive care. Several studies suggested that treatment provided in nurse-led care is non-inferior compared to physician-led care (Kamps 2003; Kuethe 2011; Tsai 2005). Furthermore, from a health economic perspective, substitution of workload from physicians to specialised nurses may lead to financial savings. These professionals may be able to work more efficiently than physicians who are often distracted from chronic care tasks by interfering urgent matters.

Taking these factors into account, we formulated the following research question; is nurse-led care in asthma equivalent and not inferior to care delivered by a physician?

Why it is important to do this review

Health economics are increasingly important and intelligent use of human resources is an important issue with regards to effective healthcare. Nurse-led outpatient management may be provided at a lower cost than medical care by a physician. For this reason, is it useful to review the literature in order to find support for the assumption that nurse-led care is not inferior. Until now a systematic literature review on this issue has not been performed.

OBJECTIVES

To review the effectiveness of nurse-led asthma care provided by a specialised asthma nurse, a nurse practitioner, a physician assistant or an otherwise specifically trained nursing professional, working relatively independently from a physician, compared to traditional care provided by a physician. Our scope included all outpatient care for asthma, both in primary care and in hospital settings.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs).

Types of participants

Adults and children with the clinical diagnosis of asthma, as defined by the authors, reviewed on a regular basis in primary or in hospital care. No restrictions were made for co-morbidities.

Types of interventions

Intervention

Any aspect of asthma management, on a regular basis in primary or hospital care, led by an allied health professional (i.e. specialised asthma nurse, nurse practitioner, physician assistant or an otherwise specifically trained nursing professional), supervised by a physician (nurse-led care).

Control

The same aspect of asthma management provided by a physician.

Types of outcome measures

We assessed effects of interventions on three categories of outcomes where available: patient-related, health economic, and objective measures of lung function, airway reactivity and inflammation.

Primary outcomes

- Frequency of exacerbations.
- Asthma severity and symptoms: measured by validated asthma control questionnaires (e.g. Asthma Control Questionnaire (ACQ) (Juniper 1999; Juniper 2006) or Asthma Control Test (ACT) (Schatz 2006).
- Healthcare costs; direct and indirect.
Secondary outcomes

A. Patient-related variables
- Quality of life: measured by disease specific or generic questionnaires (e.g. Asthma Quality of Life Questionnaire (AQoL) (Juniper 1993).
- Symptom-free days (as measured in symptom diaries).
- Patient satisfaction with care.
- Quality of care, including:
  - patient knowledge of asthma and understanding of disease;
  - use of an action plan;
  - prescription of ICS;
  - verifying of appropriate inhalation technique.
- Compliance with medication.
- Use of rescue medication.

B. Health-economics
- Absence from school or work due to asthma.
- Hospital admissions.
- Referrals from primary to hospital care.
- Duration of consultation and consultations with the specialised asthma nurse, nurse practitioner, physician assistant or an otherwise specifically trained nursing professional and the physician.
- Evidence of stepping down therapy.

C. Objective tests: lung function, airway reactivity, airway inflammation
- Forced expiratory volume in 1 second (FEV₁).
- Peak expiratory flow rate (PEF).
- Airway hyper-reactivity (including PD/PC₂₀ methacholine/histamine (where PD is the provocative dose and PC₂₀ is the concentration inhaled aerosol of methacholine or histamine leading to a fall in FEV₁ of 20%)).

Search methods for identification of studies

Electronic searches
We identified trials from the Cochrane Airways Group Specialised Register of trials (CAGR), which were derived from systematic searches of bibliographic databases including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, AMED and PsycINFO, and handsearching of respiratory journals and meeting abstracts (see Appendix 1 for further details). All records in the CAGR coded as ‘asthma’ were searched using the following terms: nurse* or nursing* or allied*.

Additional searches of MEDLINE, EMBASE, CINAHL, CENTRAL, AMED and prospective trial registers (the World Health Organization (WHO) trial register and other registers listed in the Cochrane Handbook for Systematic Reviews of Interventions (Section 6.2.3.1; Higgins 2011)) using the keywords: nurse or nursing or allied combined with MeSH terms and free-text words for asthma, combined with the sensitive Cochrane RCT filter were conducted. A search of ClinicalTrials.gov was conducted.

We searched all databases from their inception to August 2012 without restriction to language or status of publication.

Searching other resources
We checked reference lists of all primary studies included in this systematic review and review articles identified by the search strategy for additional references.

Data collection and analysis

Selection of studies
Two review authors (WvA, MCK) independently screened all studies identified by the search strategy on title and abstract for eligibility. Once agreement was obtained on studies to be considered for inclusion, we retrieved full-text articles. Two review authors (WvA, MCK) independently assessed each study for inclusion, based on the pre-defined criteria for study selection. Any disagreement was resolved by discussion.

Data extraction and management
A data extraction form was developed and tested before two review authors (WvA, MCK) independently extracted data from the included studies. MCK entered the data in RevMan 2008. In case of missing data, we attempted to contact authors to confirm data for accuracy and completeness. We extracted the following characteristics:

Study design
- Randomisation method.
- Follow-up procedures and withdrawals.
- Sample size.
- Inclusion criteria.
- Exclusion criteria.

Demographic
- Age.
- Gender.
Clinical

- Asthma diagnosis.
- Asthma severity.
- Other medical diagnosis.

Intervention

- Nurse-led care.

Control

- Physician led care.

Outcomes

- Data on all outcomes as listed in the section Types of outcome measures.

Assessment of risk of bias in included studies

Two review authors (WvA, MCK) independently assessed the risk of bias for each study using the criteria outlined below and judged the risk of bias as high, low or unclear for the criteria listed according to recommendations in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). Since it was not possible to blind nurses, physicians and participating patients in these studies these criteria were all scored as high risk of bias and the potential impact of non-blinding was reflected in the discussion of the results.

The criteria assessed were:

- adequate sequence generation;
- adequate allocation concealment;
- adequate blinding of assessors;
- incomplete outcome data adequately assessed;
- free of suggestion of selective outcome reporting;
- free of other bias.

Measures of treatment effect

We calculated a mean difference (MD) with 95% confidence intervals (CI) for continuous variables measured on identical metrics.

A standardised mean difference (SMD) with 95% CI was used for the same continuous variable measured with different metrics and for dichotomous outcomes, we calculated the risk ratio (RR) and risk difference (RD) with 95% CI.

When incorporating results from cluster randomised studies for continuous and dichotomous variables we extracted direct estimates of effect measures from an analysis that properly accounted for the cluster design and combined results from studies using the generic inverse variance (GIV) method in RevMan 2008.

Dealing with missing data

Investigators or study sponsors were contacted in order to verify key study characteristics and obtain missing numerical outcome data where possible.

Assessment of heterogeneity

We assessed heterogeneity by comparing clinical characteristics of the included studies such as type of patients, intervention, comparison and outcome measures. We discussed clinical homogeneity in the review team. Based on this discussion we decided whether pooling of results was sensible. We initially investigated statistical heterogeneity by visual inspection of the forest plots. We applied the Chi² test for homogeneity and calculated the I² statistic. To increase the power of the test for homogeneity we used a P value less than 0.1 for rejecting the null-hypothesis of homogeneity. Interpretation of statistical heterogeneity was according to the recommendation of Higgins et al. (Higgins 2011), as follows:

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

When interpreting the results of the test for heterogeneity and the I² statistic, we took into account the size of the studies that were included in the meta-analysis. If statistical heterogeneity was observed (Chi²; P value < 0.1 and I² > 30%), we explored factors, other than the pre-defined subgroups, that can explain heterogeneity such as clinical or methodological characteristics of studies.

Assessment of reporting biases

Where we suspected reporting bias, we attempted to contact study authors asking them to provide missing outcome data. Where this was not possible, and the missing data were thought to introduce serious bias, we explored the impact of including such studies in the overall assessment of results using a sensitivity analysis. We planned to explore publication bias using visual inspection of a funnel plot, if 10 or more studies had been incorporated into a meta-analysis.

Data synthesis

If studies were sufficiently comparable in relation to subjects, interventions and outcome variables, we combined data in a meta-analysis. For continuous outcome variables we calculated a weighted MD or a weighted SMD with 95% CI using the GIV method. For dichotomous outcomes, we estimated a pooled RR or RD using the Mantel-Haenszel method. We hypothesised that the individual studies that evaluated the effect of asthma management provided by an allied health professional may contain different, but related, real values per study for the effect; therefore we combined the results using a random-effects model.
Subgroup analysis and investigation of heterogeneity

We planned to carry out the following subgroup analyses:

- adults versus children;
- disease severity (using hospital admissions as a surrogate marker for disease severity);
- doctor-led clinics versus nurse-led clinics versus nurse/doctor shared clinics;
- duration of intervention.

Sensitivity analysis

We planned sensitivity analyses to test the robustness of the results based on the risk of bias assessment. We excluded studies according to the following categories: high risk of bias for allocation concealment, high risk of bias for assessor blinding or high risk of bias for incomplete follow-up. If a limited number of studies (≤ four) were included in a meta-analysis, the random-effects model was tested for its robustness using a fixed-effect model. Dichotomous outcomes (RD) were tested for robustness using the Peto odds ratio (OR).

'Summary of findings' table

The quality of the body of evidence was evaluated according to the GRADE system (Higgins 2011), using GRADE pro software (Grade Working Group 2004) to generate a 'Summary of findings' table. We used the most relevant outcomes (number of exacerbations, asthma severity and symptoms, healthcare costs, quality of life, hospital admissions).

Results of RCTs were considered initially as 'high level' evidence. The level of evidence was decreased (downgraded) based on potential risk of bias of the included studies, indirectness of evidence, unexplained heterogeneity or inconsistency in results, imprecision of results or high probability of publication bias (Higgins 2011). The necessity to apply downgrading was evaluated according to previously published criteria (Grade Working Group 2004; Higgins 2011).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The search yielded 360 records; 358 records were found by the search strategy and two studies were identified by handsearching (see Figure 1). Of these records, 154 studies did not address the issue of nurse-led care at all and 181 studies did address the issue of interventions by means of nurse-led care in general but were not related to follow-up. Twenty-five studies were assessed in full text of which five (seven articles) were included.
Included studies
The characteristics of included studies are summarised in the Characteristics of included studies table. Five studies (Kamps 2003; Kuethe 2011; Nathan 2006; Pilotto 2004; van Son 2004) were included. The results of two of these studies were each presented in two separate publications (Kamps 2003 and Kuethe 2011).

Setting
Two studies were executed in primary care (Pilotto 2004; van Son 2004). One of these studies was performed in two academic primary care centres (van Son 2004). Two studies were executed in general hospitals (Kamps 2003; Nathan 2006) and one study combined primary- and hospital care (Kuethe 2011).

Type of patients
Three studies included adult patients (Nathan 2006; Pilotto 2004; van Son 2004). One of these studies (van Son 2004) also included nurse-led care for patients with another chronic condition (diabetes rather than asthma); however, these patients were analysed separately in a subgroup and therefore we were able to exclude the diabetic patients from our analysis. Two studies included children (Kamps 2003; Kuethe 2011).

Years of publication and countries of origin
All included studies were published after 2000. Three studies originated from the Netherlands (Kamps 2003; Kuethe 2011; van Son 2004). One study (van Son 2004) was published in Dutch. One study was performed in the UK (Nathan 2006) and one study in Australia (Pilotto 2004).

Aspects of intervention
In two studies, the asthma nurse worked strictly according to an algorithm derived from guidelines, whereas the physician in the control group had to work according to same guideline (Kamps 2003; Kuethe 2011). In two studies the intervention group as
well as the control group received a similar co-intervention at the beginning of the study (Kamps 2003; Nathan 2006). In the two studies there were co-interventions at the beginning of a follow-up period, without an apparently similar co-intervention in the control group (Pilotto 2004; van Son 2004).

**Asthma severity**
In four studies (Kamps 2003; Kuethe 2011; Pilotto 2004; van Son 2004) the patients had stable asthma and were treated in an outpatient clinic setting in either primary or secondary care. One study included patients who were recently admitted for an asthma exacerbation. These patients were apparently not well controlled (Nathan 2006).

**Excluded studies**
Eighteen studies were excluded after reading the full text and reasons of exclusion are summarised in the Characteristics of excluded studies table. Of these 18 studies, nine did not cover the subject of the review but concerned "added care" to usual care by means of nurse-led care (Alexander 1988; Castro 2003; Catrambone 2000; Charlton 1994; Grieneder 1999; Griffiths 2004; Hughes 1991; Kernick 2002; Levy 2000). Nine studies did compare nurse led care versus physician led care but were either "pre/post" studies (Cave 2001; Charlton 1991; Dickinson 1997; Jones 1995; Lindberg 2002; Weng 2007), were abstracts presented too concise to extract data (Webb 1997) or had co-interventions distracting from our objective or had no clear diagnosis of asthma (Lenz 2004; Mundinger 2000).

**Risk of bias in included studies**
Most of the included studies were well designed and scored on most items low risk of bias. The results of the risk of bias assessment are summarised in Figure 2 and full details can be found in the Characteristics of included studies tables.
Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.
Allocation
One study did not describe the randomisation procedure in detail (van Son 2004) and in one study randomisation per participating centre took place, this procedure was computer generated and statistical analyses were adjusted for clustering (Pilotto 2004). Two studies did not clearly describe allocation concealment (Kamps 2003; van Son 2004). It was unclear whether this resulted in selection bias.

Blinding
Blinding of participants was not possible as a consequence of the subject involved. None of the studies clearly reported whether the outcome assessor was blinded for allocation. Regarding the objective character of the outcome measures we did not expect a high risk of bias.

Incomplete outcome data
In two studies drop-out was very low and unlikely to lead to attrition bias (Kamps 2003; Kuethe 2011). The reasons for drop-out were described in the text and were not related to the intervention. In two studies there was moderate drop-out or partly incomplete outcomes (Pilotto 2004; van Son 2004). The drop-outs in the intervention group and in the control group were about the same and the reason for drop-out was not described, therefore the risk of attrition bias was scored unclear.

Selective reporting
No selective reporting bias was detected, in all studies the predefined outcomes were presented.

Other potential sources of bias
No major forms of other bias were found.

Effects of interventions
See: Summary of findings for the main comparison Nurse-led versus physician-led care for the management of asthma

Primary outcomes: frequency of exacerbations
One study on 154 patients who had recently suffered from an exacerbation were randomised to receive either nurse-led or physician-led care (Nathan 2006). This study reported the number of exacerbations as a primary endpoint. Altogether 98 exacerbations occurred in the nurse-led group and 76 in the physician-led group (rate ratio 1.23; 95% CI 0.91 to 1.66; P = 0.368). Thirty-one patients (45.6%) in the nurse-led group and 32 patients (49.2%) in the physician-led group had one or more exacerbations over the six-month follow-up period. The difference between groups was not statistically significant (OR 0.86; 95% CI 0.44 to 1.71; P = 0.674) (Nathan 2006). The definition for an exacerbation was well described in this study, as a drop in PEF of at least 30% accompanied by increased ICS, emergency nebuliser treatment or a course of oral corticosteroids. In one study in a stable paediatric asthma population (Kuethe 2011), there were no differences between groups regarding the number of exacerbations as expressed by the number of prednisolone courses. In the groups as a whole, few exacerbations occurred (two in general practice group, two in paediatric group and three in nurse-led group). The same applies for the other study in a group of children with stable asthma (Kamps 2003) (median of zero in both groups; P = 0.37); however, no definition of an exacerbation was given. A study in a primary care population (van Son 2004) used exacerbations as the outcome parameter, though they were not well defined in the text. The difference between the intervention and the control groups was also not statistically significant (P = 0.68). It was not possible to pool the data for exacerbations for two reasons. First, in two studies (Kamps 2003; van Son 2004) exacerbations were not defined, and the definitions of exacerbation used in the other two studies (Kuethe 2011; Nathan 2006) were not the same. Second, the raw data (standard deviations (SD)) of these studies could not be retrieved after contacting the authors.

Primary outcomes: asthma severity and symptoms
One study investigated asthma control (Kuethe 2011) making use of the ACQ (Juniper 1999; Juniper 2006). This paediatric study had three arms; general practitioner-led care, paediatrician-led care and asthma nurse-led care. The median ACQ scores after two years in both the general practitioner-led group and the paediatrician-led group did not significantly differ from the nurse-led group (P = 0.18 and 0.28, respectively), demonstrating non-inferiority for the asthma control in the nurse-led group (Kuethe 2011).

Primary outcomes: healthcare costs, direct and indirect
One trial addressed the issue of healthcare costs in nurse- versus physician-led care (Kamps 2003). The costs of outpatient visits was statistically significant lower in the nurse-led group (outpatient visits costs per patient per year; EURO156 in the nurse-led group versus EURO189 in the physician-led group; P < 0.001). This difference led to a lower total costs in the healthcare sector, though not statistically significantly (total health costs EURO343 in nurse led group versus EURO357 in physician-led group; P = 0.62).
Secondary outcomes: patient-related variables

Quality of life

Three studies had various forms of quality of life scores as outcome parameter. One study (Kamps 2003) used the Dutch version of the Paediatric Asthma Quality of Life Questionnaire (PAQoL) (Juniper 1993; Juniper 1996a; Juniper 1996b). Two studies (Nathan 2006; Pilotto 2004) used the St George’s Respiratory Questionnaire (SGRQ; Barley 1998; Jones 1991). In these studies, quality of life improved from baseline over time, but in none of these studies there was a statistically significant difference between the nurse-led groups and the physician-led groups. After meta-analysis no effect was found (SMD -0.03; 95% CI -0.23 to 0.17; Figure 3). Sensitivity analysis using a fixed-effect model yielded the same results (SMD -0.03; 95% CI -0.23 to 0.17). Kamps 2003 also used two other instruments relating to quality of life; the ‘Functional health status FS II score’ and the ‘RAND general health rating index’ (Post 1998a; Post 1998b; Stein 1990). The MD in FSII score between the two treatment groups at the end of the study was 10.1 (95% CI -0.3 to 19.8). The MD in RAND score between both groups at the end of the study was 0.1 (95% CI 22.8 to 2.7).

Symptom-free days

One study had symptom-free days as the primary outcome parameter (defined as symptom score and use of rescue medication in a diary for the two weeks preceding a follow-up visit) (Kamps 2003). The mean percentage of symptom-free days throughout the study was comparable between the two treatment groups (70.5% in the paediatrician-led group and 68% in the nurse-led group; P = 0.54).

Patient satisfaction with care

One study (van Son 2004) presented data relating to “patient satisfaction with care”. However, this study made use of a Dutch scoring system (van Weel 1990) that is derived from an instrument constructed by the “Dartmouth Primary Care Cooperative Project” and is mainly meant to score “ability to perform daily life activities” instead of “patient satisfaction with care” (Nelson 1990).

Quality of care

One study briefly addressed the issue of knowledge of asthma and understanding of disease, but the way of scoring was only vaguely described and seemed to favour nurse-led care (van Son 2004). Two studies in children described explicitly the use of ICS and the prescribed dose (Kamps 2003; Kuethe 2011). In none of these studies did the prescribed dose differ significantly between the nurse-led group and the physician-led group at the end of the study period. The use of an “action plan” and “checking of appropriate inhalation technique” was not presented as an outcome measure in any of the studies.

Kuethe 2011 assessed quality of care and patient satisfaction in a paediatric population with asthma using a revised version of the QUality Of care Through the patient’s Eyes-Chronic Non Specific Lung Disease (QUOTE-CNSLD) questionnaire (van Campen 1997), containing a process-, structure- and asthma-specific domain plus a simple five-item child-specific scale; in three arms; general practitioner-led care, paediatrician-led care and nurse-led care. After one year for process and structure quality no statistical differences were found between groups. For asthma-specific and child-specific quality the ratings for the paediatrician-led care and nurse-led were higher than for the general practitioner-led care (P < 0.05).

Compliance with medication
None of the included studies presented data about compliance as an outcome measure.

**Use of rescue medication**

One study in paediatric patients with stable asthma presented the percentage of “rescue medication free days” (Kamps 2003) without a statistically significant difference at the end of the study period (75.8% in nurse-led group versus 76.8% in physician-led group; \( P = 0.40 \)).

One study in patients with asthma that was not stable, all older than 16 years, totaled the number of “emergency room nebulizations” and the number of “hospital admissions” in both groups without a statistically significant difference between groups (Nathan 2006). Mean number of exacerbations requiring emergency treatment was 0.59 in nurse-led group versus 0.43 in the physician-led group.

**Secondary outcomes: health economics**

**Absence from school/work due to asthma**

Three studies presented data about absence from school or work due to asthma. One study (Kamps 2003) reported a median of zero days school absence in both groups at the end of the study period (median 0 (range 0 to 23) in the nurse-led group, median 0 (range 0 to 21) in the paediatrician-led group (\( P = 0.80 \)). Another study (Kuethe 2011) also reported no significant difference in school absence between groups. In an adult population, Pilotto and colleagues (Pilotto 2004) reported that 20.6% of patients in the physician-led group had more than one day of absence from work opposed to no patients in the nurse-led group (\( P = 0.04 \)).

**Hospital admissions**

Four studies presented data about hospital (re)admissions (Kamps 2003; Kuethe 2011; Nathan 2006; Pilotto 2004). The pooled data showed substantial heterogeneity (RD -0.02; 95% CI -0.06 to 0.02; \( I^2 = 59\% \)) as shown in Figure 4. Therefore data are also presented in a subgroup analysis. We performed a subgroup analysis by excluding the study with patients who were discharged from hospital after experiencing an exacerbation (Nathan 2006) from the meta-analysis, including only patients with stable asthma: the summary was again not statistically significant, but the heterogeneity disappeared (RD -0.01; 95% CI -0.04 to 0.02; see Figure 5). Sensitivity analyses using a fixed-effect model and the Peto OR yielded comparable results for the patients with stable asthma (RD -0.01; 95% CI -0.04 to 0.02; Peto OR 0.15; 95% CI 0.01 to 2.42).

**Figure 4. Forest plot of comparison: 1 Nurse-led versus physician-led, outcome: 1.2 Hospital admission.**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Nurse-led Events</th>
<th>Physician-led Events</th>
<th>Risk Difference M-H, Random, 95% CI</th>
<th>Risk Difference M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kamps 2003</td>
<td>0</td>
<td>37</td>
<td>0.00 [0.05, 0.05]</td>
<td></td>
</tr>
<tr>
<td>Kuethe 2011</td>
<td>0</td>
<td>86</td>
<td>0.00 [0.05, 0.05]</td>
<td></td>
</tr>
<tr>
<td>Nathan 2006</td>
<td>5</td>
<td>80</td>
<td>-0.01 [-0.02, 0.00]</td>
<td></td>
</tr>
<tr>
<td>Pilotto 2004</td>
<td>0</td>
<td>80</td>
<td>-0.02 [-0.08, 0.02]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>221</td>
<td>226</td>
<td>-0.02 [-0.06, 0.02]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>5</td>
<td>14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Test \( \chi^2 = 25.65; \text{df} = 3 (P = 0.00), \text{I}^2 = 59\%\).

Test for overall effect: \( Z = 0.90 (P = 0.37)\).
Figure 5. Forest plot of comparison: 1 Nurse-led versus physician-led, outcome: 1.4 Hospital admission subgroup analysis.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Nurse led Events</th>
<th>Total</th>
<th>Physician led Events</th>
<th>Total</th>
<th>Risk Difference</th>
<th>Risk Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M-H, Random, 95% CI</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td>1.4.1 Patients with stable asthma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kamps 2003</td>
<td>0</td>
<td>0</td>
<td>37</td>
<td>37</td>
<td>26.0%</td>
<td>0.00 [-0.05, 0.05]</td>
</tr>
<tr>
<td>Kuethe 2011</td>
<td>0</td>
<td>0</td>
<td>36</td>
<td>34</td>
<td>26.8%</td>
<td>0.00 [-0.05, 0.05]</td>
</tr>
<tr>
<td>Pilotto 2004</td>
<td>0</td>
<td>0</td>
<td>80</td>
<td>90</td>
<td>33.3%</td>
<td>-0.02 [-0.08, 0.02]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>153</td>
<td>161</td>
<td>88.7%</td>
<td>-0.01 [-0.04, 0.02]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>0</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity</td>
<td>Test 2 = 0.00; CH² = 0.06, df = 2 (P = 0.81); P = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.01 (P = 0.22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4.2 Patients after exacerbation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nathan 2006</td>
<td>6</td>
<td>12</td>
<td>65</td>
<td>65</td>
<td>11.3%</td>
<td>-0.11 [-0.22, 0.00]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>68</td>
<td>65</td>
<td>11.3%</td>
<td>-0.11 [-0.22, 0.00]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>5</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity</td>
<td>Not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.53 (P = 0.05)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>221</td>
<td>226</td>
<td>100.0%</td>
<td>-0.02 [-0.06, 0.02]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>5</td>
<td>14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity</td>
<td>Test 2 = 0.00; CH² = 7.25, df = 3 (P = 0.08); P = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.90 (P = 0.36)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: CH² = 2.86, df = 1 (P = 0.08), P = 65.1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Referrals from primary to hospital care

No data presented in any of the included studies.

Duration of consultation and consultations with the asthma nurse and the physician

Kamps and colleagues (Kamps 2003) reported the duration of consultation in the nurse-led group. The mean (SD) duration of the first nurse-led follow-up visit was 29.0 (5.2) minutes. The second and third follow-up visits lasted 19.4 (7.2) and 18.3 (6.3) minutes, respectively. Subsequent nurse-led follow-up visits lasted approximately 15 minutes. No data about duration of consultation were presented for the paediatrician-led group.

One study (Kuethe 2011) reported the extra workload for the physician caused by consultation with the paediatrician by the asthma nurse. In 58% of children the professional providing nurse-led care was confident to provide asthma management without support from the paediatrician. In 34% of the children one or two short oral communications with a paediatrician took place to assist the nurse with management. Eight per cent of the children had problems that required more frequent input from the paediatrician.

Evidence of stepping down therapy

One study (Kamps 2003) presented data about stepping down of ICS. At the end of the study period there were no statistically significant differences. (See also prescription of inhaled corticosteroids under subheading “quality of care”).

Objective tests: lung function, airway reactivity, airway inflammation

Forced expiratory volume in 1 second (FEV₁)

FEV₁ was an outcome parameter in three studies (Kamps 2003; Kuethe 2011; Pilotto 2004). None of the studies found a statistically significant difference between the nurse-led group and the physician-led group. The pooled data are presented in Figure 6. No clear difference was found (MD -0.54% predicted; 95% CI -4.20 to 3.12). Sensitivity analysis using a fixed-effect model showed the same results (MD -0.54% predicted; 95% CI -4.20 to 3.12).
**Figure 6. Forest plot of comparison: Nurse-led versus physician-led, outcome: 1.3 FEV<sub>1</sub> % predicted.**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Nurse led</th>
<th>Physician led</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
<td>Mean</td>
</tr>
<tr>
<td>Kamps 2003</td>
<td>101.4</td>
<td>15</td>
<td>37</td>
<td>103.3</td>
</tr>
<tr>
<td>Kuethe 2011</td>
<td>101.2</td>
<td>14.4</td>
<td>36</td>
<td>103.1</td>
</tr>
<tr>
<td>Pilote 2004</td>
<td>91.2</td>
<td>16.6</td>
<td>71</td>
<td>75.8</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>153</td>
<td></td>
</tr>
</tbody>
</table>

N = 105, I² = 0%, Test for overall effect: Z = 0.29 (P = 0.77)

**Peak expiratory flow rate (PEF)**

Two studies presented change in peak flow over the course of the study. Nathan and colleagues (Nathan 2006) compared the maximum PEF measurement at first hospital visit with the six-month follow-up measurement. In this study there was a decrease of PEF over time. Mean drop was 2.53% (SD 11.5) in the physician-led group and 3.92% (SD 12.4) in the nurse-led group. No significant difference in change in PEF between the two groups (P = 0.122) was observed. One study (van Son 2004) presented the change in PEF over the study period of one year. In this study there was an increase over time (5.3% in the nurse-led group and 3.94% in the physician-led group), but no statistical significant between group differences were found (P = 0.66).

**Airway hyper-reactivity (including PD/PC<sub>20</sub> methacholine/histamine)**

One study (Kuethe 2011) presented airway hyper-reactivity as a primary outcome, no statistically significant differences were found between the nurse-led group and the physician-led groups (general practitioner or paediatrician). Another study (Kamps 2003) presented airway hyper-reactivity as log<sub>10</sub>PD<sub>20</sub>, which was at the end of the one-year study period (2.4 in nurse-led group and 2.5 in paediatrician-led group; P = 0.63).

**D I S C U S S I O N**

**Summary of main results**

The objective was to review the effectiveness of asthma care provided by a specialised asthma nurse, nurse practitioner, physician assistant or an otherwise specifically trained nursing professional, working relatively independently from a physician, compared to traditional care provided by a physician. We found no statistically significant difference between nurse-led care for patients with asthma compared to physician-led care based on the included studies for the outcomes assessed. A small number of parameters favoured nurse-led care over physician-led care, including savings on healthcare costs. Based on the relatively small number of studies in this review, nurse-led care may be appropriate in patients with well-controlled asthma. We included only one study with uncontrolled patients (Nathan 2006). Therefore we cannot be sure whether nurse-led care might be appropriate in patients with uncontrolled asthma.

**Overall completeness and applicability of evidence**

We did not limit the study search for any language, nevertheless a remarkable proportion of the studies originated from the Netherlands. A probable explanation are the different healthcare settings in different countries. This may limit the extent to which these results may be generalised to countries with different organisation of health care.

This systematic review has some limitations. First, although we had strict selection criteria for inclusion or exclusion (same co-interventions in both groups, active follow-up the same in both groups) it was difficult to apply these criteria on some of the studies. Second, we were not able to perform a funnel plot because of the limited studies included in the review. This makes it difficult to judge whether our findings are biased by publication status. Third, initially we did not include the frequency of consultations with the asthma nurse and the physician in the nurse-led group as an outcome. However, this is an important factor in determining workload for both nurses and physicians. Therefore we decided, post hoc, to add it as an outcome parameter. Fourth, we did not pre-define factors about safety. None of the included studies reported data on adverse events. One study (Kuethe 2011) addressed this issue and proposed a number of prerequisites to be fulfilled: nurse-led care requires working strictly according to guidelines, there should be a low threshold for consulting with a physician when a patient deteriorates or shows unexpected symptoms, and supervision or revision by a physician should always take place when there is uncertainty about the child’s management. Finally, a report by Kuethe 2011 presented clear data about quality of care in the three different settings.
Quality of the evidence

The quality of the body of evidence was evaluated according to the GRADE system. For the pooled outcomes moderate level of evidence was found for health-related quality of life and hospital admission. See Summary of findings for the main comparison.

Agreements and disagreements with other studies or reviews

One Cochrane systematic review (Laurant 2005) investigated the efficacy of nurse-led care in primary practice in people with all types of health problems presenting to primary care (excluding accident and emergency departments). They concluded that appropriately trained nurses can produce as high-quality care as primary care doctors. However, their conclusion should be viewed with caution because of different methodological limitations and small sample size of underlying RCTs. One systematic review about the effectiveness of innovations in nurse-led chronic disease management for patients with chronic obstructive pulmonary disease (COPD; Taylor 2005) found little evidence to support the widespread implementation of nurse-led management interventions for COPD, but the data were too sparse to exclude any clinically relevant benefit or harm arising from such interventions. Another review about specialist nurses in diabetes mellitus care (Loveman 2003) concluded in a similar way that the presence of a diabetes specialist nurse/nurse case manager may improve patients’ diabetic control over short time periods, but from currently available trials the effects over longer periods of time are not evident. These reviews focused on clinical outcome parameters and did not specifically address the issue of workload reduction for physicians neither the issue of non-inferiority or equivalence of care. In the study concerning healthcare costs (Kamps 2003), the reduction of costs of care in the nurse-led group was surprisingly limited compared to physician-led care. An RCT about healthcare costs of nurse-led care in a bronchiectasis clinic reported that nurse-led care for stable patients within a chronic chest clinic may use more resources (Sharples 2002). In that study, unit cost of the nurse practitioner was under half of that of the consultant. However, patients receiving nurse practitioner led care had more clinic visits per year and, on average, nurse-led clinic visits lasted longer. Combining these factors, almost negated the lower unit cost of the nurse practitioner use indicators.

Implications for practice

No significant difference was found between nurse-led care for patients with asthma compared to physician-led care for outcomes assessed. Based on the relatively small number of studies in this review, nurse-led care may be appropriate in patients with well-controlled asthma. Since only one study with uncontrolled patients was included we cannot be sure whether nurse-led care is appropriate in uncontrolled asthma.

Implications for research

The conclusion of this review is based on a small number of studies. Adverse events should be more precisely addressed in future research. Furthermore research on quality of care in different healthcare settings and in different stadia of asthma control is required. Researchers in the future should incorporate outcome parameters fulfilling the following criteria; 1) well-defined and using validated methods where possible; 2) reported in a manner appropriate for meta-analysis; 3) easy to obtain and 4) relevant for carers of, or people with, asthma and people making decisions around healthcare provision. The primary outcome parameters we choose for this review (frequency of exacerbations, asthma severity and symptoms: measured by validated asthma control questionnaires and healthcare costs; direct and indirect) meet these criteria. Exacerbations, and certainly hospital admissions due to exacerbations, are well definable. For asthma severity, there are a number of very well-validated instruments (Juniper 1999; Juniper 2006; Schatz 2006) which can be easily completed by patients. Financing health care is becoming more and more an issue and therefore the importance costs cannot be overstated. From the societal point of view, the indirect costs in term of loss of labour or loss of school education are as relevant as the direct costs. Although speculative rather than based on the evidence presented in this review, extending nurse-led care seems likely to lead to cost reduction. The issue of costs is even more important in countries where the doctors are scarce and where it may be practically or financially prohibitive to access a physician. Therefore research in this field should be specifically encouraged in developing countries.

Authors’ conclusions

No significant difference was found between nurse-led care for patients with asthma compared to physician-led care for outcomes assessed. Based on the relatively small number of studies in this review, nurse-led care may be appropriate in patients with well-controlled asthma. Since only one study with uncontrolled patients was included we cannot be sure whether nurse-led care is appropriate in uncontrolled asthma.

Acknowledgements

Elizabeth Stovold; Trial Search Coordinator, Cochrane Airways Group.

Dr Emma Welsh; Managing Editor, Cochrane Airways Group.
References to studies included in this review

Kamps 2003  {published data only}

Kuethe 2011  {published data only}

Nathan 2006  {published data only}

Pilotto 2004  {published data only}

van Son 2004  {published data only}

References to studies excluded from this review

Alexander 1988  {published data only}

Castro 2003  {published data only}

Catrambone 2000  {published data only}

Cave 2001  {published data only}

Charlton 1991  {published data only}

Charlton 1994  {published data only}

Dickinson 1997  {published data only}

Grieneder 1999  {published data only}

Griffiths 2004  {published data only}

Hughes 1991  {published data only}

Jones 1995  {published data only}

Kernick 2002  {published data only}
Nurse versus physician-led care for the management of asthma (Review)

Additional references

Akinbami 2009

Barley 1998

CAMP 2000

de Jongste 2007

Gibson 2008

Gibson 2009

GINA 2011

Grade Working Group 2004

Guarnaccia 2007

Higgins 2011

Jones 1991

Jones 2009

Juniper 1993

Juniper 1996a

Juniper 1996b

Juniper 1999
Nurse versus physician-led care for the management of asthma (Review)

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Juniper 2006
Juniper EF, Bousquet J, Abetz L, Bateman ED, the GOAL Committee. Identifying “well-controlled” asthma using the Asthma Control Questionnaire. Respiratory Medicine 2006; 100:616–21.

Laurant 2009

Levy 2009

Loveman 2003

Nelson 1990

O’Byrne 2006

Post 1998a

Post 1998b
Post MWM, Kuyvenhoven MM, Verheij ThJM, de Melker RA, Hoes AW. The Dutch ‘Rand General Health Rating Index for Children’: a questionnaire measuring the general health status of children. [De Nederlandse "RAND general health rating index for children"]; een meetinstrument voor de algemene gezondheid van kinderen.

RevMan 2008

Schatz 2006

Sharples 2002

SIGN 2011

Stein 1990

Taylor 2005

Tsai 2005

van Campen 1997

van Weel 1999

Wenzel 2006

Wolf 2008

References to other published versions of this review

Kuethe 2011

* Indicates the major publication for the study
### Characteristics of included studies

**Kamps 2003**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial</th>
</tr>
</thead>
</table>
| Participants | Chronic persistent asthma. Use of inhaled corticosteroid (ICS)  
Intervention: N = 37, age (mean (standard deviation (SD))) 5.9 (3.6) years  
Control: N = 37, age (mean (SD)) 6.8 (3.5) years |
| Interventions | Before randomisation: both groups received (children and their carers) asthma education by an asthma nurse (triggers of disease, use of controller Rx, management of symptoms, environmental avoidance, inhalation technique) (at 1, 3, 6, and 12 months)  
Intervention: follow-up in nurse-led care  
Control: follow-up in paediatrician-led care |
| Outcomes | Primary outcome symptom-free days; Secondary outcome measures were lung function, airway hyper responsiveness, dose of ICS, use of rescue medication, absence from school, extra visits to the general practitioner, disease-specific quality of life, and functional health status. Measured at baseline, 6 and 12 months  
Healthcare utilisation and healthcare costs after 12 months |
| Notes | The asthma nurses in the intervention group were board certified  
The asthma nurse could consult the paediatrician at all times for medical queries about patients under their follow-up  
Extra (emergency) visits in both intervention and control group as required |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Randomisation by random number tables</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not explicitly specified</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Low risk</td>
<td>&quot;The mother of one patient declined to participate because she was pregnant. Seventy three (99%) of the patients completed the study. One patient followed up by an asthma nurse was diagnosed with tracheomalacia during the study period and excluded from the study&quot;</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All outcomes pre-defined in the method section are presented</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Not feasible in this setting</td>
</tr>
</tbody>
</table>
### Kamps 2003  (Continued)

<table>
<thead>
<tr>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Unclear risk</th>
<th>Unclear if reporting of in of symptom-free days and use of rescue medication in a &quot;diary&quot; is influenced by knowledge about the group to which the subject is randomised&lt;br&gt;Unclear completion of functional health status questionnaires can be biased by knowledge about the group to which the subject is randomised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient reported</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Low risk</th>
<th>Unlikely since outcomes are lung function parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other bias</th>
<th>Low risk</th>
<th>Low risk for other bias</th>
</tr>
</thead>
</table>

### Kuethe 2011

**Methods**

RCT with three study arms. Non-inferiority design (nurse-led care versus general practitioner-led care as opposed to nurse-led care versus paediatric care)

**Participants**

Children with moderate asthma using ICS<br>General practice group N = 37, mean age (SD) 11.2 (2.5)<br>Paediatric group N = 34 subjects mean age (SD) 10.1 (2.6)<br>Asthma nurse group N = 36 subject mean age(SD) 11.2 (2.9)

**Interventions**

Intervention: Follow up in nurse-led care during two years according to the guidelines of the Dutch Paediatric Association. (No fixed scheduled review visits)<br>Control: Follow up in general practitioner-led care during two years<br>Follow up in paediatrician-led care during two years.

**Outcomes**

Primary; Airway hyper responsiveness.<br>Secondary; FEV₁, FE_NO, ACQ, planned visits, unplanned visits, Medication; dose ICS, % use LABA/ICS. At baseline, 12 & 24 months. Quality of care assessed by a revised version of the QUOTE-CNSLD Questionnaire, completed by the parents of the participating children<br>Quality of care assessed by a simple five-item "child-specific" questionnaire, completed by the participating children

**Notes**

The asthma nurses in the intervention group were board certificated<br>The asthma nurse could consult the paediatrician at all times for medical queries about patients under their follow-up<br>Extra (emergency) visits in the nurse-led group, the general practice-led group and the paediatrician-led group as required

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
### Kuethé 2011

<table>
<thead>
<tr>
<th>Bias Type</th>
<th>Risk</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low</td>
<td>Randomised computer-generated list</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low</td>
<td>Sealed numbered envelopes with designated follow-up arms</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low</td>
<td>Very low drop-out</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low</td>
<td>All outcomes pre-defined in the method section are presented</td>
</tr>
<tr>
<td>Blinding of participants and personnel</td>
<td>High</td>
<td>Not feasible in this setting</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear</td>
<td>Unlikely if completion of questionnaires can be biased by about the group</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low</td>
<td>Unlikely since outcomes are lung function parameters</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear</td>
<td>For recruitment and follow-up of children in the general practice group the authors depended on general practitioners who were enthusiastic about participating in research concerning respiratory care in children. An unselected sample of subjects recruited from an unselected sample of general practices was apparently not feasible. This might have caused bias in that the results in this general practice group may differ from results in an unselected sample of general practitioners.</td>
</tr>
</tbody>
</table>

### Nathan 2006

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Open randomised controlled trial</td>
</tr>
<tr>
<td>Participants</td>
<td>Patients &gt; 16 years admitted for an exacerbation of acute asthma</td>
</tr>
<tr>
<td></td>
<td>Intervention: 78 subjects randomised, 70 subject were analysed. Median (range) age 33 years (17 to 83)</td>
</tr>
<tr>
<td></td>
<td>Control: 76 subjects randomised. 66 subject were analysed. Median (range) age 37 years (17 to 91)</td>
</tr>
</tbody>
</table>
Interventions

| Intervention: all patients enrolled into the trial received an initial 30-minute hospital follow-up appointment at 2 weeks after discharge with the specialist nurse. 15-minute follow-up appointments were then arranged as believed necessary by the specialist nurse (no fixed scheduled review visits) |
| Control: all patients enrolled into the trial received an initial 30-minute hospital follow-up appointment at 2 weeks after discharge with the respiratory doctor. 15-minute follow-up appointments were then arranged as believed necessary by the respiratory specialist (no fixed scheduled review visits) |

Outcomes

| The primary outcome was the number of exacerbations within 6 months of hospital admission. Used definition of exacerbation well described. Secondary outcome variables were change in peak flow, quality of life (using the St. George Respiratory Questionnaire (SGRQ) and the Asthma Questionnaire 20 (AQ20)) and clinic attendance after 6 months |

Notes

| Extra (emergency) visits in both intervention and control group as required |

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>randomised envelope system</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>recruitment by an independent research nurse of all admitted patients</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Low risk</td>
<td>Lost to follow up was limited.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All outcomes predefined in the method section are presented.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Not feasible in this setting</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) Patient reported</td>
<td>Unclear risk</td>
<td>Unclear if completion of questionnaires can be biased by about the group to which the subject is randomised</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) Objective</td>
<td>Low risk</td>
<td>Outcome variables were lung function parameters</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>low risk of other bias.</td>
</tr>
</tbody>
</table>
Pilotto 2004

Methods | Open randomised controlled trial
---|---

Participants | Patients aged 18 years and older, who had attended these practices for asthma within the previous 9 months  
| Intervention: N = 80, mean age (SD) 46.8 (15.7) years  
| Control: N = 90, mean age (SD) 49.7 (15.7) years

Interventions | Intervention: treatment in asthma clinic run by 2 respiratory nurses according standardised approach, including spirometry, inhalation technique training, asthma education, if appropriate options for smoking cessation  
| Control: control patients received the usual care provided by their general practitioners, but not in the setting of an asthma clinic

Outcomes | The primary outcome variable was quality of life (St. George Respiratory Questionnaire (SGRQ)), measured after 6 to 9 months  
| Secondary outcome measures were lung function (forced expiratory volume in 1 second (FEV₁)) and asthma-related health service utilisation: attendance at an emergency department; admission to hospital; attendance at a hospital outpatient department; number of general practitioner visits in addition to clinic visits; number of days off work because of asthma (treated as a count and a binary variable); design and use of a written asthma action plan; and smoking cessation measured/recorded after 6 to 9 months

Notes | The nurse-led group received in a standardised approach, an extra intervention next to regular follow-up

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Randomisation per participating centre. Computer generated</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Randomisation per participating centre. Computer generated</td>
</tr>
</tbody>
</table>
| Incomplete outcome data (attrition bias)  
All outcomes | Unclear risk | In intervention group 34 subjects received the standardised intervention, whereas 46 subjects received an incomplete intervention. Loss to follow-up about equal in both arms |
| Selective reporting (reporting bias) | Low risk | All outcomes pre-defined in the method section are presented |
| Blinding of participants and personnel (performance bias)  
All outcomes | High risk | Not feasible |
### Pilotto 2004 (Continued)

<table>
<thead>
<tr>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Author's judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient reported</td>
<td>Unclear risk</td>
<td>Unclear if completion of questionnaires can be biased by about the group to which the subject is randomised</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Author's judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td>Low risk</td>
<td>Lung function parameters, healthcare utilisation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other bias</th>
<th>Author's judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low risk</td>
<td>Low risk of other bias</td>
</tr>
</tbody>
</table>

### van Son 2004

- **Methods**: Open randomised controlled trial

- **Participants**: Patients with asthma in 2 academic primary care healthcare centres. This study also included patients with chronic obstruction pulmonary disease (COPD) and diabetes and result were reported separately

  - Intervention: N = 43, mean age (SD) 45.77 (25.16) years
  - Control: N = 40, mean age (SD) 45.29 (25.39) years

- **Interventions**: Intervention: follow-up in nurse-led care by a primary care nurse practitioner according to a standardised protocol with 2 to 4 review visits/years including; spirometry, inhalation technique training, psychosocial support, promoting of adherence and, if appropriate, options for smoking cessation. 43 subjects with the diagnosis of asthma
  - Control: usual care by general practitioner. 40 subject with the diagnosis of asthma

- **Outcomes**: Forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), peak expiratory flow (PEF), patient satisfaction score, perception of health score, general practitioner workload, outcomes measured after 12 months

- **Notes**: The used patient satisfaction questionnaire and the used health score instrument were not described. Article in Dutch

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Author's judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomisation by research assistant based on rank of receiving informed consent by mail. No details provided</td>
</tr>
</tbody>
</table>

| Allocation concealment (selection bias)          | Unclear risk       | Randomisation by research assistant based on rank of receiving informed consent by mail. No details provided |

| Incomplete outcome data (attrition bias)         | Unclear risk       | Complete data in 29/43 available in intervention group and 26/40 available in control group |

| All outcomes                                    |                    |                                                     |
Selective reporting (reporting bias) | Low risk | All outcomes pre-defined in the method section are presented
---|---|---
Blinding of participants and personnel (performance bias) All outcomes | High risk | Not feasible
Blinding of outcome assessment (detection bias) Patient reported | Unclear risk | Unclear if completion of questionnaires can be biased by about the group to which the subject is randomised. Unclear if used satisfaction questionnaire was validated
Blinding of outcome assessment (detection bias) Objective | Low risk | Lung function parameters
Other bias | Unclear risk | Patients had to give a "report mark" about the received care. The used patient satisfaction score was not defined

**Characteristics of excluded studies** [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexander 1988</td>
<td>In the intervention group medical/pharmaceutical management was done by a physician, while the other aspect of care were performed by a clinical nurse specialist. Thus the study does not cover &quot;nurse-led versus physician-led care&quot;</td>
</tr>
<tr>
<td>Castro 2003</td>
<td>Group of patients admitted for asthma. Intervention was a multifaceted approach by a nurse practitioner as opposed to usual care provided by private primary care physician. The multifaceted approach was not followed by review visits over a certain span of time</td>
</tr>
<tr>
<td>Catrambone 2000</td>
<td>Intervention was a multidisciplinary approach broader than nurse-led care</td>
</tr>
<tr>
<td>Cave 2001</td>
<td>Pre/post design</td>
</tr>
<tr>
<td>Charlton 1991</td>
<td>Pre/post study. Not a randomised controlled trial</td>
</tr>
<tr>
<td>Charlton 1994</td>
<td>The design did not cover &quot;nurse-led versus physician-led care&quot;</td>
</tr>
<tr>
<td>Dickinson 1997</td>
<td>Pre/post study. Not a randomised controlled trial</td>
</tr>
<tr>
<td>Grieneder 1999</td>
<td>Both groups received an educational intervention; however, only the nurse-led group received long-term follow-up, thus the design did not cover &quot;nurse-led versus physician-led care&quot;</td>
</tr>
</tbody>
</table>
Griffiths 2004 | Intervention was added to usual care. The design did not cover "nurse-led versus physician-led care"
---|---
Hughes 1991 | Study about a structured follow-up by a paediatrician in a tertiary care setting versus usual care by a general practitioner. The design did not cover "nurse-led versus physician-led care"
---|---
Jones 1995 | Pre/post study. Not a randomised controlled trial. Authors state that no conclusion can be drawn from this study
---|---
Kernick 2002 | Assessment, education and management from a practice nurse over a period of 4 months, versus usual care by general practitioner. Thus the design did not cover "nurse-led versus physician-led care"
---|---
Lenz 2004 | Complex description. Design and randomisation not clear. High drop-out rate
---|---
Levy 2000 | Intervention consists of 3 extended consultations in the nurse-practitioner group versus none in the control group. This study does not cover the subject "nurse-led versus physician-led care" in a group of stable asthma patients
---|---
Lindberg 2002 | Partly pre/post study. Partly retrospective. No randomisation over groups but random selection of patient files
---|---
Mundinger 2000 | Patients who reported a previous diagnosis of asthma, diabetes, hypertension, or a combination regardless of the reason for the urgent visit, were over-sampled to create a cohort of patients. Therefore there was not a separate group of patients with asthma from which results can be extracted
---|---
Webb 1997 | Abstract of a poster. Methodology section too concise. The control group not described and data of the control group not presented. No other publications of this project or the authors could be traced
---|---
Weng 2007 | Pre/post study. Not a randomised controlled trial
Comparison 1. Nurse-led versus physician-led care for the management of asthma

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Quality of life at 12 months</td>
<td>3</td>
<td>380</td>
<td>Std. Mean Difference (IV, Random, 95% CI)</td>
<td>-0.03 [-0.23, 0.17]</td>
</tr>
<tr>
<td>2 Hospital admission</td>
<td>4</td>
<td>447</td>
<td>Risk Difference (M-H, Random, 95% CI)</td>
<td>-0.02 [-0.06, 0.02]</td>
</tr>
<tr>
<td>3 FEV₁ % predicted</td>
<td>3</td>
<td>297</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-0.54 [-4.20, 3.12]</td>
</tr>
<tr>
<td>4 Hospital admission subgroup</td>
<td>4</td>
<td>447</td>
<td>Risk Difference (M-H, Random, 95% CI)</td>
<td>-0.02 [-0.06, 0.02]</td>
</tr>
<tr>
<td>analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.1 Patients with stable</td>
<td>3</td>
<td>314</td>
<td>Risk Difference (M-H, Random, 95% CI)</td>
<td>-0.01 [-0.04, 0.02]</td>
</tr>
<tr>
<td>asthma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2 Patients after exacerbation</td>
<td>1</td>
<td>133</td>
<td>Risk Difference (M-H, Random, 95% CI)</td>
<td>-0.11 [-0.22, 0.00]</td>
</tr>
</tbody>
</table>

Analysis 1.1. Comparison 1 Nurse-led versus physician-led care for the management of asthma, Outcome 1 Quality of life at 12 months.

Review: Nurse versus physician-led care for the management of asthma

Comparison: Nurse-led versus physician-led care for the management of asthma

Outcome: Quality of life at 12 months

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Nurse led</th>
<th>Physician led</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV/Random,95% CI</td>
<td></td>
<td>IV/Random,95% CI</td>
</tr>
<tr>
<td>Kamps 2003</td>
<td>37 6.5 (2.4331)</td>
<td>37 6.5 (2.4331)</td>
<td>19.5 %</td>
<td>0.0 [-0.46, 0.46]</td>
<td></td>
</tr>
<tr>
<td>Nathan 2006</td>
<td>70 3.94 (14.34)</td>
<td>66 5.02 (16.43)</td>
<td>35.8 %</td>
<td>-0.07 [-0.41, 0.27]</td>
<td></td>
</tr>
<tr>
<td>Pilotto 2004</td>
<td>80 27 (15.9)</td>
<td>90 27.3 (17.1)</td>
<td>44.7 %</td>
<td>-0.02 [-0.32, 0.28]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>187</td>
<td>193</td>
<td>100.0 %</td>
<td>-0.03 [-0.23, 0.17]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.0; Chi² = 0.08, df = 2 (P = 0.96); I² =0.0%

Test for overall effect: Z = 0.32 (P = 0.75)

Test for subgroup differences: Not applicable
Analysis 1.2. Comparison 1 Nurse-led versus physician-led care for the management of asthma, Outcome 2 Hospital admission.

Review: Nurse versus physician-led care for the management of asthma

Comparison: 1 Nurse-led versus physician-led care for the management of asthma

Outcome: 2 Hospital admission

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Nurse led</th>
<th>Physician led</th>
<th>Risk Difference</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>Risk Difference</td>
<td></td>
</tr>
<tr>
<td>Kamps 2003</td>
<td>0/37</td>
<td>0/37</td>
<td>28.0 %</td>
<td>0.00 [-0.05, 0.05]</td>
</tr>
<tr>
<td>Kuethe 2011</td>
<td>0/36</td>
<td>0/34</td>
<td>26.8 %</td>
<td>0.00 [-0.05, 0.05]</td>
</tr>
<tr>
<td>Nathan 2006</td>
<td>5/68</td>
<td>12/65</td>
<td>11.3 %</td>
<td>-0.11 [-0.22, 0.00]</td>
</tr>
<tr>
<td>Pilotto 2004</td>
<td>0/80</td>
<td>2/90</td>
<td>33.9 %</td>
<td>-0.02 [-0.06, 0.02]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>221</strong></td>
<td><strong>226</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>-0.02 [-0.06, 0.02]</strong></td>
</tr>
</tbody>
</table>

Total events: 5 (Nurse led), 14 (Physician led)
Heterogeneity: Tau² = 0.00; Chi² = 7.25, df = 3 (P = 0.06); I² =59%
Test for overall effect: Z = 0.90 (P = 0.37)
Test for subgroup differences: Not applicable
**Analysis 1.3. Comparison 1 Nurse-led versus physician-led care for the management of asthma, Outcome 3 FEV₁ % predicted.**

**Review:** Nurse versus physician-led care for the management of asthma

**Comparison:** 1 Nurse-led versus physician-led care for the management of asthma

**Outcome:** 3 FEV₁ % predicted

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Nurse led</th>
<th>Physician led</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kamps 2003</td>
<td>37</td>
<td>37</td>
<td>101.4 (15)</td>
<td>36.1 %</td>
<td>-1.60 [-7.69, 4.49]</td>
</tr>
<tr>
<td>Kuethe 2011</td>
<td>36</td>
<td>34</td>
<td>101.2 (14.4)</td>
<td>28.2 %</td>
<td>-1.90 [-8.80, 5.00]</td>
</tr>
<tr>
<td>Pilotto 2004</td>
<td>71</td>
<td>82</td>
<td>81.2 (18.6)</td>
<td>35.7 %</td>
<td>1.60 [-4.52, 7.72]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>144</strong></td>
<td><strong>153</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>-0.54 [-4.20, 3.12]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.0; \chi^2 = 7.44, df = 2 (P = 0.06); I^2 = 0.0$

Test for overall effect: $Z = 0.29 (P = 0.77)$

Test for subgroup differences: Not applicable
### Analysis 1.4. Comparison 1 Nurse-led versus physician-led care for the management of asthma, Outcome 4 Hospital admission subgroup analysis.

Review: Nurse versus physician-led care for the management of asthma

Comparison: 1 Nurse-led versus physician-led care for the management of asthma

Outcome: 4 Hospital admission subgroup analysis

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Nurse led</th>
<th>Physician led</th>
<th>Risk Difference M-H, Random, 95% CI</th>
<th>Weight</th>
<th>Risk Difference M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with stable asthma</td>
<td>0/37</td>
<td>0/37</td>
<td></td>
<td>28.0%</td>
<td>0.0 [ -0.05, 0.05 ]</td>
</tr>
<tr>
<td>Kamps 2003</td>
<td>0/37</td>
<td>0/37</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kuethe 2011</td>
<td>0/36</td>
<td>0/34</td>
<td></td>
<td>26.8%</td>
<td>0.0 [ -0.05, 0.05 ]</td>
</tr>
<tr>
<td>Pilotto 2004</td>
<td>0/80</td>
<td>2/90</td>
<td></td>
<td>33.9%</td>
<td>-0.02 [ -0.06, 0.02 ]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>153</td>
<td>161</td>
<td></td>
<td>88.7%</td>
<td>-0.01 [ -0.04, 0.02 ]</td>
</tr>
<tr>
<td>2 Patients after exacerbation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nathan 2006</td>
<td>5/68</td>
<td>12/65</td>
<td></td>
<td>11.3%</td>
<td>-0.11 [ -0.22, 0.00 ]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>68</td>
<td>65</td>
<td></td>
<td>11.3%</td>
<td>-0.11 [ -0.22, 0.00 ]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>221</td>
<td>226</td>
<td></td>
<td>100.0%</td>
<td>-0.02 [ -0.06, 0.02 ]</td>
</tr>
</tbody>
</table>

Heterogeneity: \( \tau^2 = 0.0 \), \( \chi^2 = 0.68, \text{df} = 2 \ (P = 0.71); I^2 = 0.0\% \\
Test for overall effect: \( Z = 0.81 \ (P = 0.42) \)

Heterogeneity: not applicable

Test for overall effect: \( Z = 1.93 \ (P = 0.054) \)

Heterogeneity: \( \tau^2 = 0.00; \chi^2 = 7.25, \text{df} = 3 \ (P = 0.06); I^2 = 59\% \\
Test for overall effect: \( Z = 0.90 \ (P = 0.37) \)

Test for subgroup differences: \( \chi^2 = 2.86, \text{df} = 1 \ (P = 0.09); I^2 = 65\% \)
# APPENDICES

## Appendix 1. Sources and search methods for the Cochrane Airways Group Specialised Register (CAGR)

### Electronic searches: core databases

<table>
<thead>
<tr>
<th>Database</th>
<th>Frequency of search</th>
</tr>
</thead>
<tbody>
<tr>
<td>CENTRAL (The Cochrane Library)</td>
<td>Monthly</td>
</tr>
<tr>
<td>MEDLINE (Ovid)</td>
<td>Weekly</td>
</tr>
<tr>
<td>EMBASE (Ovid)</td>
<td>Weekly</td>
</tr>
<tr>
<td>PsycINFO (Ovid)</td>
<td>Monthly</td>
</tr>
<tr>
<td>CINAHL (EBSCO)</td>
<td>Monthly</td>
</tr>
<tr>
<td>AMED (EBSCO)</td>
<td>Monthly</td>
</tr>
</tbody>
</table>

### Handsearches: core respiratory conference abstracts

<table>
<thead>
<tr>
<th>Conference</th>
<th>Years searched</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Academy of Allergy, Asthma and Immunology (AAAAI)</td>
<td>2001 onwards</td>
</tr>
<tr>
<td>American Thoracic Society (ATS)</td>
<td>2001 onwards</td>
</tr>
<tr>
<td>Asia Pacific Society of Respirology (APSR)</td>
<td>2004 onwards</td>
</tr>
<tr>
<td>British Thoracic Society Winter Meeting (BTS)</td>
<td>2000 onwards</td>
</tr>
<tr>
<td>Chest Meeting</td>
<td>2003 onwards</td>
</tr>
<tr>
<td>International Primary Care Respiratory Group Congress (IPCRG)</td>
<td>2002 onwards</td>
</tr>
<tr>
<td>Thoracic Society of Australia and New Zealand (TSANZ)</td>
<td>1999 onwards</td>
</tr>
</tbody>
</table>
MEDLINE search strategy used to identify trials for the CAGR

**Asthma search**
1. exp Asthma/
2. asthma$.mp.
3. (antiasthma$ or anti-asthma$).mp.
4. Respiratory Sounds/
5. wheez$.mp.
6. Bronchial Spasm/
7. bronchospas$.mp.
8. (bronch$ adj3 spasm$).mp.
9. bronchoconstrict$.mp.
10. exp Bronchoconstriction/
11. (bronch$ adj3 constrict$).mp.
12. Bronchial Hyperreactivity/
13. Respiratory Hypersensitivity/
14. ((bronchial$ or respiratory or airway$ or lung$) adj3 (hypersensitiv$ or hyperreactiv$ or allerg$ or insufficiency$)).mp.
15. ((dust or mite$) adj3 (allerg$ or hypersensitiv$)).mp.
16. or/1-15

**Filter to identify RCTs**
1. exp "clinical trial [publication type]"/
2. (randomised or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. Animals/
10. Humans/
11. 9 not (9 and 10)
12. 8 not 11

The MEDLINE strategy and RCT filter are adapted to identify trials in other electronic databases

**Contributions of Authors**
- Designing of draft (RE, MCK).
- Conceptualisation (MCK, WvA, AVV, RE).
- Writing Draft (MCK).
- Reviewing draft (RE, AVV, WvA).
- Reviewing (WvA, MCK).
- Third assessor (AVV).
DECLARATIONS OF INTEREST

- None known.

SOURCES OF SUPPORT

Internal sources
- New Source of support, Not specified.

External sources
- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The search has been amended.

INDEX TERMS

Medical Subject Headings (MeSH)
- Disease Management; Nurse’s Practice Patterns; Physician’s Practice Patterns; Asthma [*therapy]; Quality of Life; Randomized Controlled Trials as Topic

MeSH check words
- Adult; Child; Humans