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Effectiveness of home visits in adult patients with asthma: a systematic review of randomized controlled trials.

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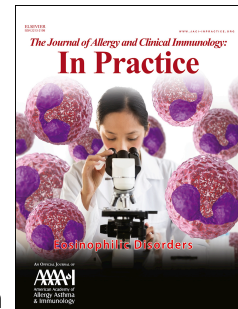
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Effectiveness of home visits in adult patients with asthma: a systematic review of randomized controlled trials.

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Conflict of interest

All authors declared no potential conflicts of interest concerning the research, authorship, and publication of this systematic review.

Abstract

Background

The effectiveness of home visits is well discussed for children with asthma, but limited in adults.

Objective

The present systematic review aims to investigate the potential role of home visits in improving outcomes among adult patients with asthma.

Methods

The systematic review was performed in line with the PRISMA statement. An extensive literature search was conducted using databases such as PubMed, ProQuest, CINAHL, The Cochrane Library, PsycINFO, and Google Scholar from inception to June 2019. The studies included were randomized controlled trials (RCTs), which reported asthma outcomes in adult patients.

Results

The literature search yielded 8331 publications, of which 63 studies were selected for full-text review, and of these studies, 9 studies with a total of 2011 patients were included in the final analysis. The included RCTs reported quality of life (QoL), asthma symptoms, exacerbations, healthcare utilization, and pulmonary function. Improvements in asthma outcomes were observed predominantly in QoL. The effects on asthma symptom control were inconsistent. The evidence on the impact of home visits in asthma exacerbations and healthcare utilization was rather limited. There were no significant differences observed between intervention versus control arms in terms of pulmonary function; however, one study reported significant improvements in PEFr.

Conclusion

Home visits may serve as an adjuvant activity that complements existing healthcare system based initiatives. It may be concluded that home visits have the potential to improve outcomes in adult patients with asthma; however, the RCTs reviewed in the present systematic review reported several limitations that warrant further investigation.

Keywords: home visit, adult asthma, systematic review, domiciliary, outcome, randomized

Highlights Box

1. What is already known about this topic?

The effectiveness of home visit programs in improving asthma control among children has been well established and proven to be cost-effective. However, evidence in adult patients with asthma is limited.

2. What does this article add to our knowledge?

The present systematic review highlights that home visits have the potential to improve outcomes in adult patients with asthma. They may serve as an adjuvant activity that complements existing healthcare system based initiatives.

3. How does this study impact current management guidelines?

Further studies are needed to explore the full potentials of home visits among adult patients with asthma before the management guidelines can make appropriate

controlled trial.

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68 Abbreviations

69	ATS:	American Thoracic Society
70	EPR-3:	Expert Panel Report 3
71	PRISMA:	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
72	RCTs:	Randomised controlled trials
73	QoL:	Quality of life
74	ACT™:	Asthma Control Test
75	NS:	Non-significant
76	CHW:	Community health worker
77	AQLQ:	Asthma Quality of Life Questionnaire
78	RT:	Respiratory therapist
79	OCS:	Oral corticosteroid
80	ACQ:	Asthma Control Questionnaire
81	SGRQ:	St. George's Respiratory Questionnaire
82	CHWs:	Community health workers

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85 Introduction

86 Asthma is a heterogeneous lung disease, usually characterized by chronic airway
87 inflammation (1). It affects more than 300 million people worldwide and leads to an
88 estimated 400 000 deaths annually (1, 2). The long-term goals of asthma management are to
89 achieve: 1. Good control of symptoms and maintain normal activity levels. 2. To minimize
90 future risk of exacerbations, fixed airflow limitation, and medication adverse drug reactions
91 (1). The REALISE (REcognise Asthma and LInk to Symptoms and Experience) survey in
92 Europe revealed that asthma control was poor (3) and the REALISE Asia survey documented
93 a crisis-oriented, reactive approach to asthma management related to a high number of
94 emergency department (ED) visits, hospitalizations, reliever and oral corticosteroids (OCS)
95 use (4). Across the globe, asthma management guidelines suggest a patient-centered
96 approach, with key recommendations, including ongoing self-management and regular
97 review of the patient's treatment (1, 5). These periodic reviews can be conducted by having
98 the patients attend at their regular primary or specialist physician, however often in the case

of asthma patients, this is very challenging in daily practice (6, 7). Meeting patients where they are, rather than always expecting them to present at venues where healthcare professionals are, maybe a way to improve outcomes in chronic diseases (8). Home visits may serve as an effective strategy. Moreover, patients may face exposures at home, i.e., triggers, particularly crucial in asthma, that are not easily identified at the clinic (9).

Indeed, the American Thoracic Society (ATS) identified asthma as one of the respiratory disorders that may benefit from home visits (10). The National Asthma Council, Australia has highlighted the potential role of a Home Medicines Review (HMR), which involves patients, their general practitioners (GPs) and pharmacists (11). In the setting of an HMR, an accredited pharmacist visits the patient at their home, reviews their medication use and appropriateness, and provides a report to the patient's regular community pharmacy (if the accredited pharmacist is not also the patients' regular community pharmacist) and their GPs. The aims of the HMR include identifying and resolving patients' drug-related problems, improving their medication-related knowledge, and medication use (11). The Expert Panel Report 3 from the National Asthma Education and Prevention Program, USA, also incorporates multifaceted patient education at all points of care, including patients' homes (12).

The effectiveness of home visit programs in improving asthma control among children has been well established (13-15) and proven to be cost-effective (16). However, evidence in adult patients with asthma is limited. A systematic review which evaluated the effectiveness of home-based interventions with an environmental focus (children and adult) was unable to determine the effectiveness in the adult population; however, the authors acknowledged that only a small number of studies with adult participants were included (14, 15). Since the publication of the above-mentioned systematic review, several new studies have been reported. The present systematic review thus aims to determine the potential role of home visits in improving outcomes among adult patients with asthma.

Methods

The systematic review was performed in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (17). The systematic review protocol was registered with the National Medical Research Register (NMRR-18-3219-45148), Ministry of Health Malaysia.

Literature search.

An extensive literature search was performed using databases such as PubMed, ProQuest, CINAHL (via EBSCOhost), The Cochrane Library (Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials), PsycINFO (via EBSCOhost) and Google Scholar from inception to June 2019. Additional relevant articles were identified by reviewing the bibliography of retrieved articles. Emails were sent to some experts to obtain further information. The search was conducted by using several keywords and relevant subject headings. The details of the search strategies are described in Table 1.

Inclusion and exclusion criteria

The criteria to include studies in this review were that such reported studies needed to be:

1. Randomized controlled trials (RCTs), which included home visits as an ‘intervention’ in adult patients with asthma, 2. Available in full text and English language, 3. Reporting asthma outcomes in accordance either with the American Thoracic Society/European Respiratory Society Statement (18) or Asthma Outcomes Workshop (19); expected outcomes included asthma symptom control, exacerbations, healthcare utilization, quality of life (QoL), pulmonary functions and others and 4. Those that included data from the adult asthma population (*if both children and adults were included in the study, then the data from adult asthma patients had to be extractable*).

The following studies were not included:

1. Correspondences, editorials, reviews, commentaries, notes, letters, or conference proceedings, 2. Studies without a detailed description of asthma-related home visits and procedures, 3. Studies which only focused on home environmental trigger interventions, 4. Studies which used home interventions as a substitute for hospital-level care at patients’ home, and 5. Studies where participants were residing in nursing home/ aged care facilities.

Study selection and review

Two reviewers undertook the literature selection and review process. The reviewers independently screened the studies based on published study titles and abstracts to identify potentially relevant articles. This was an over-inclusive process, and irrelevant records were removed. The reviewers then reviewed the full text of papers selected at this stage, which were potentially includable in concordance with the pre-determined inclusion and exclusion criteria. Any disagreement between the reviewers was discussed and resolved using a

consensus-based approach, and if necessary, a third reviewer was consulted for the final decision.

Data extraction

One reviewer abstracted data into a standardized and data extraction form. The following study information and characteristics were extracted from the full text of the eligible studies into the predefined data fields: 1. Identification of study source (authors, citation, contact details, country), 2. Study details (study design, setting, duration, and sampling), 3. Characteristics of the study patients (age, gender, total number, inclusion/exclusion criteria), 4. Intervention details, 5. Outcome measures, 6. Results (summary of results for each asthma outcome assessed, including exploring missing data/drop-out handling, sub-group analysis), 7. Conclusion, 8. Miscellaneous comments: strengths, limitations, and recommendations. A second reviewer verified the entry of data from studies into the data extraction table.

Risk of bias assessment

The included studies were assessed for potential bias in accordance with the Cochrane Collaboration's Risk of Bias Tool for RCTs (20). The following domains were used: random sequence generation, allocation concealment; blinding of participants and personnel selection; blinding of outcome assessment; incomplete outcome data; selective reporting; and other potential biases. Registered or published study protocols for the selected studies were also assessed for completeness of the information. Corresponding authors were contacted through email to obtain further details of the selected studies if required. Two reviewers independently appraised the selected studies. Discrepancies were resolved by consensus.

Results

The literature search yielded 8331 publications, of which 5350 articles were excluded based on their titles and abstracts relevance. Sixty-three studies were selected for full-text review, and of these studies, nine studies were selected to be included in the final evaluation. The final selection of articles sampled for the review from the initial screening to final inclusion is highlighted in the PRISMA diagram (Figure 1). The general overviews, descriptions of the home visit interventions, and outcomes of the RCTs are presented in Tables 2, 3, and 4, respectively.

A total of 2011 adult patients with asthma were included in this review. The follow-up period varied across the studies, ranging between 6 (21-24) to 12 months (25-29). Two studies (23, 28) recruited both adults and children; however, only data specific to the adult population are presented in the systematic review. The health personnel who conducted the home visits were nurses (21, 23, 24, 29), community health workers (CHWs) (22, 26, 27), respiratory therapists (RTs) (21, 28), and asthma care coaches (25). The risk of bias assessments for each included study and summative assessments by domains are described in Figures 2 and 3.

Pulmonary function

Two studies analyzed the impact of home visits on pulmonary function as a secondary outcome at 6 (21) and 12 months using spirometric indices (27). The studies measured forced expiratory volume in one second (FEV₁), FEV₁ % predicted, forced vital capacity (FVC), FEV₁/FVC, and peak expiratory flow rate (PEFR). Both studies demonstrated no significant differences in FEV₁, FEV₁ % predicted, FVC and FEV₁/FEV between intervention and control arms (21), although there were improvements within the intervention arm (change from baseline) after multiple imputations (27). However, in the study reported by Shelledy and colleagues, there were demonstrated improvements in the PEFR in the intervention arm (AMP-RT) compared with the control arm (mean 6.0 ±2.2 L/s vs. 4.9 ±1.7 L/s; p = 0.03) (21). The interventional arm had higher SpO₂ (%) values compared with the control arm (mean AMP-RN=97.4±1.5, AMP-RT=97.2±1.1 vs 96.4± 1.7; p < 0.05) (21).

Asthma exacerbations and healthcare utilization.

Federman et al. reported a fewer number of patients with ED visits in both home (OR 0.7, 95% CI 0.5 to 1.0; p=0.03) and clinic-based intervention arms (25). In a study which used home visits delivered by RTs or nurses (AMP-RT or AMP-RN), analyses identified that both interventional arms had significantly fewer hospitalisations (mean, AMP-RT=0.04 ±0.2, AMP-RN=0±0 vs C= 0.20 ±0.5; p = 0.014 and p = 0.005) and inpatient hospital days (mean, AMP-RT=0.09 ±0.04, AMP-RN=0±0 vs C=0.46±0.20; p = 0.02 and p=0.015) during the 6 month study period (21). The study by Apter et al., which combined home visits with Web-based portal training, demonstrated a significant reduction in annualized hospitalization rate among the home visit arm (mean difference -0.53, 95% CI -1.08 to -0.024) (26). The Home-Based Asthma Support and Education (HomeBASE) study demonstrated that asthma exacerbations were significantly lower in the intervention arm (adjusted mean difference

–0.55, 95% CI –0.87 to –0.24; $p=0.001$) (27).

No significant differences were demonstrated between the intervention and control arms in the ED visits and hospitalizations rate by Vojta and colleagues in their trial (24). Krieger et al. reported that there were no significant differences in annual asthma-related urgent health care use between their intervention and control arms (27). Similarly, the annualized ED visit rates were not statistically different between groups in the study by Apter and colleagues (26). Brown et al. reported no significant difference in the time to first asthma relapse between intervention and usual care group during the 6 month follow-up period (23). In another large scale study, there were no significant differences in time to first asthma event and asthma-related health care utilization rates (28). There were no significant differences in the mean number of ED or clinic visits between the groups in the study by Shelledy et al. (21). The use of OCS bursts was not statistically significant between groups either in trials that measured this outcome (26-28).

Asthma symptoms

The Supporting Asthma Self-Management Behaviors in Older Adults (SAMBA) study demonstrated improvements in Asthma Control Test (ACT™) score at 3 (mean, 16.6 ± 4.4 , Cohen's $d=0.47$) and 6 months (mean, 16.8 ± 4.3 , Cohen's $d=0.39$), but changes in this outcome were not significantly different between arms at 12 months (25). Krieger et al.'s trial also demonstrated an improvement in asthma symptom-free days in the intervention arm (mean adjusted difference 2.02, 95% CI 0.94 to 3.09; $p < 0.001$, effect size=0.33) (27). This study also reported that the ACQ score (mean adjusted difference –0.55, 95% CI –0.74 to –0.37; $p < 0.001$) and proportions of patients with very poorly controlled asthma was significantly lower (OR 0.43, 95%CI 0.27 to 0.68; $p < 0.001$) in the home visit arm compared with the control arm (27). Additionally, the study reported a significant decline in the number of nights that patients experienced asthma symptoms (adjusted mean difference –1.65, 95% CI –2.59 to –0.72; $p=0.001$) and the number of days that trial participants required rescue medication use (adjusted mean difference –1.38, 95% CI –2.44 to –0.32; $p=0.01$) in the home visit group (27). Galbreath et al. also reported that the patients receiving home visit interventions demonstrated more significant improvements in symptoms score ($p=0.001$), which was measured using the Lara Asthma Symptom Scores (LASS) (28).

Asthma symptom control, as measured by the Asthma Control Questionnaire (ACQ), did not differ significantly in the study by Apter et al. (26). Smith and colleagues reported no significant improvement in symptom scores in the intervention arm. The additional intention-

to-treat (ITT) analyses also demonstrated no significant differences between arms at 2, 6, or 12 months of follow-ups (29). The asthma symptoms were measured using the asthma morbidity questionnaire (29). In the study by Shelledy and colleagues, the home visit arm revealed no significant difference in asthma symptoms (Borg and Asthma Symptoms Scores) compared with the usual care arm (21). Symptomatic days and nights were not statistically different between the intervention and control arms in the trial by Martin et al. either (22).

Quality of life

The SAMBA study reported significant improvements in the Mini Asthma Quality of Life Questionnaire (AQLQ) at 3 (mean, 4.8 ± 1.8 , effect size=0.34) and 6 (mean, 4.9 ± 1.2 , effect size=0.34) months but was not significant at 12 months. Galbreath et al. demonstrated that the intervention, which included home visits, significantly improved QoL scores from the baseline ($p < 0.0001$) and compared with the control arm (28). Krieger et al. reported a significant improvement in QoL (Mini AQLQ) scores among the patients with home visit intervention (mean difference 0.50, 95% CI 0.28 to 0.71; $p < 0.001$, effect size=0.53) (27). The same study utilized the SF 12 Physical and Mental Health Scale (27) and reported that the intervention arm demonstrated significant improvements in the SF Physical Health Scale (adjusted mean difference 4.54, 95%CI 2.56 to 6.52; $p = 0.001$), while the SF Mental Health Scale was not significantly different compared with the control arm (27). In the trial reported by Martin et al., there was a significant improvement in the QoL score (Mini AQLQ) evident among the recipients of home visits at 6 months (mean difference 1.8, 95% CI 0.8-2.9; $P = 0.002$) (22). Shelledy and colleagues measured QoL with St. George's Respiratory Questionnaire (SGRQ) and the Short Form – 36 (SF-36) and demonstrated significant improvements in the total SGRQ scores in the intervention arm (AMP-RT) compared with the control arm (mean change -11.0 ± 15 vs. -2.5 ± 15 ; $p = 0.04$) (21). The symptom domain score (mean change -8.4 ± 21 vs. 2.7 ± 17 ; $p = 0.03$) also improved significantly in the home intervention arm (AMP-RT) compared with the usual care. The activity and impact domain were not statistically different (21). Similarly, significant improvements were seen in SF-36 Physical Component Summary (PCS) score in both interventional arms, AMP-RN (mean change 9.4 ± 18 vs. -3.1 ± 15 ; $p = 0.005$) and AMP-RT (mean change 16.9 ± 23 vs. -3.1 ± 15 ; $p = 0.0002$). However, the SF-36 Mental Component Summary (MCS) score change was not significantly different between arms (21). The SF-36 was also measured by Smith et al. and there was an improvement in the mental health component (additional ITT analysis, adjusted mean difference -7.65, 95% CI -15.33 to 0.19; $p = 0.05$) at 2 months but the physical function

score was not significantly different from the control arm throughout the study. The study also used the Living with Asthma Questionnaire which delineated significant improvement in the interventional arm after an additional ITT analysis at 2 months (adjusted mean difference 0.14, 95% CI 0.04 to 0.23; $p=0.01$), 6 months (adjusted mean difference 0.13, 95% CI 0.03 to 0.23; $p=0.01$) and 12 months (adjusted mean difference 0.13, 95% CI 0.02 to 0.25; $p=0.03$) (29). The changes in QoL measured by using Mini AQLQ were not significantly different between arms in the study by Apter and colleagues (26).

Discussion

The present systematic review is, to the best of our knowledge, the first review to collate data on the effectiveness of home-based visits on asthma outcomes of adult patients. The review included and analyzed nine RCTs. There were variations in the study outcomes measured, the nature of home interventions tested, professionals involved in-home visit delivery, and study duration/follow up. Four studies reported symptom control as the primary outcome (Federman et al., Apter et al., Krieger et al. and Smith et al.) (25-27, 29) and home visits had a positive impact on symptoms in two (Federman et al. and Krieger et al.) of these four studies (25, 27). Four studies reported symptom assessment as a secondary outcome (21, 22, 27, 28), and improvements were documented in two of these four studies as well (27, 28). The effect size reported in two studies for home visit interventions for this outcome (symptom control) ranged between 0.33 and 0.47 (25, 27); these are moderate effect sizes. The benefits of home visits in asthma symptom control have been previously observed in a systematic review focusing on pediatric asthma populations (14); however, the present systematic review highlights an inconsistent trend in adults. Recently, two published RCTs also demonstrated inconsistencies in asthma symptom outcomes despite patients in both trials being treated with similar interventions (30-32). There may be several factors that underpin these inconsistencies in asthma symptom improvement wrought by home visit interventions in our systematic review. Firstly, there were variations in the symptom assessment methods utilized in the RCTs included in the present review. Further, broader inclusion criteria across studies may also have compromised comparable outcomes. For example, in the study by Smith et al. (29), a large proportion of patients were using long term OCS (54%) at baseline, which indicates patients with more 'severe asthma.' Such patients likely have more challenging needs and require longer timeframes for effective change to take place compared to patients not on long term OCSs (29, 33). The variability in the premise for study sample calculations could have led to underpowered studies. In the study by Smith et al., the authors

had used a minimal clinically important difference (MCID) for asthma morbidity questions in their sample size and power calculations (29). However, the validity of the method is questionable as MCID for the asthma morbidity questionnaire used in the study is not established. Finally, participants' environmental circumstances may have also affected the outcomes, for example, Apter et al. highlighted that poor neighborhood living conditions and limited internet access were barriers for patients to complete the protocol and for CWHs to make home visits (26). Interestingly, the study protocol in the Apter et al. study did not include asthma education but only care coordination (26).

The RCTs in the present systematic review also analyzed asthma exacerbations and healthcare utilization. Six studies reported these outcomes as the primary outcome (21, 23-25, 27, 28), and out of these studies, only Federman et al. (25) and Shelledy et al. (21) reported positive outcomes regarding asthma hospitalizations, in-patient days and ED visits. The findings were published as secondary outcomes in three studies (26-28), where positive improvements in asthma annual hospital admission and exacerbation rate were documented in Krieger et al. (27) and Apter et al. (26). Poor patient compliance with the home visit interventions was reported in three of these studies (23, 24, 28), and this could potentially have impacted the results of the reviewed RCTs. For example, in the study authored by Vojta et al., only 18% of the recruited patients completed the planned home visiting program, which further leads to concerns of compliance and its influence on the results (24). Moreover, Brown et al. and Galbreath et al. acknowledged that poor compliance might have limited the results of their studies (only 67% and 57% completers respectively) (23, 28).

Study power and intervention 'dose' (study duration) may be other limitations of the pooled results around improvements in hospitalization and exacerbation rates in the systematic review. The study by Vojta et al. did not specify the exact number of samples required in their methodology, making it difficult to deduce whether the study was adequately powered (24). The sample size was calculated and targeted for both adult and pediatric patients (combined) in the study by Brown et al., so stratification of the results based on age should be interpreted with caution (23). Even though the present systematic review was not able to definitively conclude that studies conducted with longer duration consistently produced positive results, the suggested duration for interventions aimed at improving asthma exacerbations and health care-utilization rates is 12 months (34). Three RCTs (21, 23, 24) in the present systematic review used a follow-up period of 6 months, which may not have allowed the intervention to affect maximal improvements. Brown et al. highlighted that a

longer follow-up is needed to see the real benefit of interventions on acute asthma relapses (23). A similar limitation was stated by Vojta et al. (24).

Home visits were linked with consistent improvements in QoL in all studies that reported it as a primary outcome (25, 27, 28). Four (21, 22, 27, 29) out of five studies (21, 22, 26, 27, 29), which reported QoL as a secondary outcome, also showed improvements. The RCTs in the present systematic review included home environment control strategies as one of the components in the intervention protocols. Interventions that evaluated the effectiveness of home-based interventions with environmental focus unveiled a positive impact in improving the overall QoL (14). We speculate that the inclusion of this component, along with patient education, self-management, medication/ inhaler review, and other interventions, may serve as an effective strategy.

Pulmonary function was assessed in 2 studies (21, 27). Spirometry provides an objective and highly reproducible measure of airflow limitation caused by smooth muscle contraction or structural changes (18). The two studies in the present systematic review failed to demonstrate a significant impact on FEV₁, FEV₁ % predicted, FVC, and FEV₁/FVC. However, it is essential to note that both studies were not powered to detect differences in the pulmonary function, as these were reported as the secondary outcomes in the respective studies. Despite no significant effect, Krieger et al. reported significant improvements in asthma symptoms (27). The finding is not surprising as pulmonary function measures may be weakly correlated with asthma symptoms (35). Several systematic reviews that have analyzed interventions to improve asthma outcomes also reported inconsistencies in pulmonary function outcomes (36-38), and this warrants further investigations. Shelledy et al. presented significant improvements in PEFr and SpO₂ in the home visit intervention arm (21). PEFr is generally considered to be inferior to FEV₁ as a clinic-measured parameter of airways obstruction, although it may have a place in ambulatory monitoring (18). However, a recent post hoc analysis by Halpin et al. reported a strong association between pre-dose PEFr and FEV₁, thus supporting PEFr, as a reasonably valid endpoint for trials in adult patients with asthma (39).

The present systematic review has highlighted the potential value of home visits in improving specific outcomes among adult patients with asthma, such as QoL. The impact of such interventions on asthma symptoms was inconsistent; the effects of home visits on asthma exacerbations, healthcare utilization, and pulmonary function were less pronounced, perhaps in part attributable to the limitation in the population studied, study sample size, and durations (i.e., intervention dose). Home visits provide an opportunity to educate patients and

to help them effectively manage their disease. A home visit offers an ideal setting to educate, review medication plans, and help families to identify environmental factors that affect asthma in their homes (40, 41). These are essential factors in asthma disease management (41). Patients are more receptive of the asthma follow-up care and assessment in their homes (21). Patients with uncontrolled asthma in a qualitative study conducted by LaCava et al. reported a positive perception of home visits and increased understanding of their disease severity (42). The study also documented improved motivation for treatment adherence, access to knowledge, preparation for medical visits along with better recognition of treatment methods, and asthma trigger factors (42). Home visits may also benefit patients who have defaulted their regular appointments. The study by Smith and colleagues demonstrated improvement in patients' QoL (additional ITT analysis) among clinic appointment defaulters (29). Another retrospective cohort study demonstrated that a single home visit improved patient adherence and reduced exacerbations among patients with established non-compliance to office visits (43). Another important aspect that determines the success of asthma treatment is the involvement of family members and friends. A patient's family and friends may be involved in treatment plans, through the home visiting programs. Their understanding of the disease condition can help them provide supporting roles (44). Home visits also demonstrated benefits amongst elderly asthma patients. Federman and colleagues tested an individualized self-management support program in patients more than 60 years old and reported improvements in ACT™, QoL, and reduced ED visits (25). Improvements in inhaler technique and medication adherence were also noted in the intervention group (25). While the study highlighted the importance of personalized care in asthma management, it also highlighted the challenges of engaging vulnerable populations in self-management support, including modest retention rates and reduced impact over time despite repeated encounters designed to sustain its effects (25). It is important to note that Federman et al. also highlighted that the SAMBA program conducted at the office was as effective as the program where interventions were delivered in the patients' homes, although the study was not powered to detect the differences between the two interventions (25). However, home and clinic environments each may offer different opportunities for patient care, which warrants further research on the effects of combined or individual intervention venues as variables under test (25).

In general, the RCTs reviewed in the present systematic review have several limitations. The sample sizes and power calculations of the included studies warrant further discussion. We found that only three studies (Apter et al. , Galbreath et al., and Krieger et al.) had adequate

sample size and power (26-28). In the case of other studies included in the review, there were some issues in reported sample/power calculations. The study by Martin et al. had a small sample size, and it was powered to detect the differences in patients' self-efficacy (not the clinical outcomes such as QoL and asthma symptoms) (22); meanwhile, the SAMBA study did not achieve the planned sample size (25). An explanation as to which variable the study based power calculations around was not clarified by Shelledy et al. (21). The sample size and power calculation issues in the remaining studies were explained earlier in the discussion segment. Another limitation is the benefits observed from the home visits may not be exclusive to the interventions, as the home visit programs in this review were not stand-alone but complex multifactorial interventions that were complementing the existing healthcare system. The asthma patients included in the RCTs can be categorized as high-risk patients; thus, the generalisability of the findings to milder patients is not known. The majority of the studies were classified as "high risk of bias" for the blinding of participants, personnel, and outcome assessment domains. This was due to the nature of the studies where blinding was a cumbersome/unrealistic process. Three studies (23, 24, 28) had poor patients' compliance with the home visiting program in the intervention group, and this could have affected the results of the studies. Finally, the present systematic review did not report any information related to the cost-effectiveness of the home visits. Well powered studies need to be conducted in the future using standardized outcome measures that have been endorsed by the international asthma guidelines. Such forthcoming research work should also focus on the strategies to reduce biases and improvement of the home visiting program compliance rate. We are also eagerly waiting for publications of several ongoing studies, including the Houston Home-based Integrated Intervention Targeting Better Asthma Control (HIITBAC) trial (professional abstract was recently published at <https://www.pcori.org/>) (45).

Conclusion

Home visits may serve as an adjuvant activity that complements existing healthcare system based initiatives. For the studies reviewed, improvements in asthma outcomes were observed predominantly in QoL. The results for intervention effects on asthma symptom control were inconsistent. The evidence on the impact of home visits in asthma exacerbations and healthcare utilization was rather limited. There were no significant differences observed between interventions versus control arms in terms of pulmonary function, however one of two studies measuring these reported significant improvements in PEFr. It may be concluded that home visits have the potential to improve outcomes in adult patients with asthma;

however, the RCTs reviewed in the present systematic review reported several limitations that warrant further investigation.

Authors' contributions

All authors have equally participated in the drafting and revision of the manuscript. JM, MAH, BS, BI, AAN, and IAHA drafted the protocol. JM, AKV, AAN, and RH were involved in study registration. JM, AuR, RH, and AKV conducted the literature search and assessed eligibility of studies for inclusion. JM and AKV were involved in the acquisition and entry of the data. JM, MAH, BS, RH, and IAHA analyzed the data. JM and BI conducted study risk assessments. JM wrote the first draft of the article, while MAAH, BI, BS, RH, AuR, and AAN provided input on the draft. All authors revised the final version of the manuscript and provided inputs and authorizations. JM, AKV, AuR, AAN, and RH were involved in manuscript submission to the journal.

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Figure 1: Flow chart for study screening and selection using the PRISMA flow diagram.

Figure 2: Assessment of risk of bias using the Cochrane Collaboration Tool

Figure 3: Summative assessment of the risk of bias

Table 1: Search strategies used in the literature retrievals.

Database	Search strategies
PubMed	((("asthma"[MeSH Terms] OR "asthma"[All Fields]) OR "Asthma"[Mesh]) AND (((((((home visit[All Fields] OR home visitation[All Fields] OR home visitations[All Fields] OR home visited[All Fields] OR home visiting[All Fields] OR home visitor[All Fields] OR home visitors[All Fields] OR home visits[All Fields] OR home visits studies[All Fields]) OR ("nursing"[Subheading] OR "nursing"[All Fields] OR ("home"[All Fields] AND "care"[All Fields]) OR "home care"[All Fields] OR "home care services"[MeSH Terms] OR ("home"[All Fields] AND "care"[All Fields] AND "services"[All Fields]) OR "home care services"[All Fields] OR ("home"[All Fields] AND "care"[All Fields]))) OR (domiciliary visit[All Fields] OR domiciliary visiting[All Fields] OR domiciliary visits[All Fields])) OR ("home care services"[MeSH Terms] OR ("home"[All Fields] AND "care"[All Fields] AND "services"[All Fields]) OR "home care services"[All Fields] OR ("domiciliary"[All Fields] AND "care"[All Fields]) OR "domiciliary care"[All Fields])) OR (house visit[All Fields] OR house visiting[All Fields] OR house visits[All Fields])) OR ("Home Care Services"[Mesh] OR "Home Care Services, Hospital-Based"[Mesh] OR "Home Care Agencies"[Mesh] OR "Home Nursing"[Mesh])) OR "House Calls"[Mesh]) AND ("humans"[MeSH Terms] AND English[lang] AND "adult"[MeSH Terms]))
ProQuest	((mainsubject.Exact("asthma") OR asthma) AND (mainsubject.Exact("gp visits to patients' homes") OR mainsubject.Exact("domiciliary visits" OR "gp visits to patients' homes") OR (home visit*) OR mainsubject.Exact("domiciliary visits" OR "home care group" OR "home care" OR "gp visits to patients' homes" OR "home care services" OR "home care services, hospital-based") OR (domiciliary care) OR (house visit*))) AND (stype.exact("Scholarly Journals") AND subt.exact("asthma" NOT ("child" OR "children & youth" OR "pediatrics" OR "child, preschool" OR "children" OR "infant" OR "animals"))) AND la.exact("ENG"))
CINAHL (via EBSCOhost)	(asthma OR (MH "Asthma+")) AND (((MH "Home Visits") OR (MH "Home Rehabilitation+") OR (MH "Home Health Care+") OR "home visit*") OR ("domiciliary visit*") OR ((MH "Home Respiratory Care+") OR (MH "American Academy of Home Care Physicians") OR "home care") OR ("domiciliary care") OR ("house visit*"))
PsycINFO (via EBSCOhost)	(DE "Asthma" OR asthma) AND (home visit* OR home care OR domiciliary visit* OR domiciliary care OR house visit* OR DE "Home Care Personnel" OR DE "Home Care" OR DE "Home Visiting Programs")
Cochrane Library	#1 (asthma) #2 MeSH descriptor: [Asthma] explode all trees #3 (Home visit*) #4 MeSH descriptor: [House Calls] explode all trees #5 (home care) #6 MeSH descriptor: [Home Care Services] explode all trees #7 (domiciliary visit*) #8 (domiciliary care)

	#9	(house visit*)
	#10	#1 OR #2
	#11	#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
	#12	#10 AND #11

Table 2: General overviews of the RCTs

Author, Country	Study Aim	Number of patients, gender and age	Patients' baseline characteristics and requirement methods	Study Duration	Power analysis	Patient compliance to program
1. Federman AD et al. 2019, USA (25).	To test the effect of a comprehensive, patient-tailored asthma self-management support intervention (Supporting Asthma Self-Management Behaviors in Older Adults -SAMBA) for older adults in clinical and self-management outcomes. The SAMBA intervention was carried out either at the patients' home or primary care clinic.	N: 391 patients I: SAMBA-Home: 128 and SAMBA-Clinic: 129 C: 134 ♂: 58, ♀: 333 Mean age (years): 67.8 ±7.4	Eligible patients: Adult patients more than 60 years with uncontrolled, moderate, or severe persistent asthma. Patients were recruited from 3 primary care practices. They were identified by electronic health record query and screened by telephone for eligibility.	12 months	Power analysis was conducted to detect the difference in symptom control and QoL. Hundred fifty patients per arm were needed.	Number (%) of patients completed the program: SAMBA-Home: 90 (70) SAMBA-Clinic: 76 (59) C: 95 (71) There were no significant differences in baseline characteristics between I and C among the completers. Analyses that addressed missing data did not show a difference.
2. Apter AJ et al. 2019, USA (26).	To estimate the effect on asthma outcomes of an intervention using home visits plus Web-based patient portal (PT) compared with PT and usual care only.	N: 301 patients I: 151 C: 150 ♂: 31, ♀: 270 Mean age (years): 49 ±13	Eligible patients: Adult patients with uncontrolled asthma; required prednisone, an ED visit, or hospitalization for asthma in the past year. Patients were recruited from primary care and asthma specialty practices serving low-income urban neighborhoods.	12 months	Power analysis was conducted to detect the difference in symptom control. Hundred fifty patients per arm were needed.	Number (%) of patients completed the program: I: 135 (89) C: 138 (92) Sensitivity analysis was conducted to determine if there was a selection bias from loss to follow-up. Differences between groups in changes over time remained not significant at conventional levels.

3. Martin MA et al. 2009, USA (22).	To pilot test an intervention to improve asthma self-efficacy for appropriate self-management behaviors.	N: 42 patients I: 20 C: 22 ♂: 13, ♀: 29 Mean age (years): I: 33±9 C: 37±8	Eligible patients: Adult patients with persistent asthma (defined as >2 days bothered by asthma symptoms on recall of past 14 days and ≥1 urgent care or emergency department visit or requirement for oral corticosteroid in the past 12 months. Patients were recruited from 2 primary care clinics using pharmacy records and chronic disease registries.	6 months	Power analysis was conducted to detect the difference in asthma self-efficacy. The study was not powered for any clinical outcomes.	Number (%) of patients completed the program: I : 17 (85) C: 17 (77)
4. Brown MD et al. 2006, USA (23).	To evaluate the effect of an asthma education program among discharged patients from ED. A home visit was conducted approximately 6 weeks after the ED visit.	N: 110 patients (adults) I: 51 C: 59	Eligible patients: Adult and children patients with acute asthma and history consistent with moderate to severe persistent asthma or had used the ED for asthma care at least once in the last year. Patients were recruited during their ED visits.	6 months	Power analysis was conducted to detect the difference in the risk of relapse. Two hundred forty-two patients were needed (adult and children combined). However, the study was not powered to evaluate differences based on age stratification.	Number (%) of patients completed the program*: I: 34 (67) C: 46 (78) *Adult population
5. Galbreath AD et al. 2008, USA (28).	To compare the effectiveness of 2 disease management (DM and DM+Home Visit) programs with usual care. DM focused on patients' current self-management strategies, health status and educational needs. It	N: 429 patients (adults) I: DM:143, DM + Home Visit:143 C: 143 ♂: 333, ♀: 96	Eligible patients: Adult and children patients with persistent asthma. The authors proposed five criteria. Potential study patients were identified through physician referral, self-referral, referrals from asthma education seminars, mass mailings to school nurses, review of patient lists from	12 months.	Power analysis was conducted to detect the difference in first asthma inpatient or ED event, QoL, rates of asthma-related ED visits, and hospitalizations. Four hundred and seventy patients were needed.	Number (%) of patients completed the program*: DM + Home Visit: 82 (57) DM: 92 (64) C: 93 (65) *Adult population

	also aimed to provide individualized advice and training of the asthma action plan.	Mean age (years): I: DM: 42.4 ±12.4, DM+ Home Visit: 42.1±12.8 C: 43.7±11.7	collaborating clinics and sites, and solicitation through media.			
6. Krieger J et al. 2015, USA (27).	To test the hypothesis that CHW home visits for adults with uncontrolled asthma improve outcomes relative to usual care.	N: 366 patients I: 177 C: 189 ♂: 98, ♀: 268 Mean age (years): I: 41.2 C: 41.3	Eligible patients: Adult patients with not well or very poorly controlled asthma. The authors proposed six criteria. Patients were recruited primarily from the community, public health, and hospital-based clinics, community agencies, Medicaid health plan, and self-referrals.	12 months	Power analysis was conducted to detect the difference in asthma-free days, QoL, and urgent health care events. Hundred sixty-seven and 184 patients were needed in the intervention and control group respectively (the authors expected a higher attrition rate in the control arm).	Number (%) of patients completed the program: I : 161 (91) C: 172 (91)
7. Shelledy DC et al. 2009, USA (21).	To compare the effects of in-home asthma management programs (AMP) provided by RTs (AMP-RT) with an AMP provided by nurses (AMP-RN) and to usual care provided in physician offices or clinics.	N: 159 patients (166 patients entered the study) I: AMP-RT: 46, AMP-RN: 54 C: 59 ♂: 26, ♀: 133 Mean age	Eligible patients: Adult patients with moderate-to-severe asthma following an ED or hospital admission for an acute exacerbation of asthma.	6 months	Power calculation was based on obtaining an effect size of 0.25; however, the targeted outcome variable was not clear. A total of 159 patients were needed.	Number (%) of patients completed the program: 159 (96)

		(years): I: AMP-RT: 41±12, AMP-RN: 43±14 C: 44±13				
8. Smith JR et al. 2005, UK (29).	To assess the effectiveness of a home-based psychoeducational intervention delivered by a respiratory nurse specialist for adults at risk of adverse asthma outcomes.	N: 92 patients I: 47 C: 45 ♂: 25, ♀: 67 Mean age (years): 36.5 ±10.7	Eligible patients: Adult patients with severe asthma indicated by one or more previous hospital admissions for asthma and/or current (1995) prescription of British Thoracic Society (BTS) step 4 or 5 treatment. Patients who had failed to attend clinic appointments or were considered to have poor adherence to other aspects of their agreed management. Patients were recruited from adult asthma clinics at five hospitals and 10 general practices.	12 months	Power analysis was conducted to detect the difference in asthma symptoms score and QoL. However, the validity of the MCID value use the calculations is questionable. Forty-five patients per arm were needed.	Number (%) of patients completed the program: I: 42(89) C: 42 (93)
9. Vojta CL et al. 1999, USA (24).	To assess the effectiveness of a home-based asthma education program in a Medicaid managed care population.	N: 121 patients I: 62 C: 59 ♂: 16, ♀: 105 Mean age (years): I: 32.2 ±8.1 C: 32.4± 8.2	Eligible patients: Adult patients who experienced 3 or more ED visits and/or 2 hospitalizations related to asthma over 12 months. The Health Partners claims database was used to identify all patients with a claim containing an ICD-9 code for asthma.	6 months	Power analysis was conducted to detect the difference in healthcare utilization. However, no information provided on the required sample size.	Number (%) of patients completed the program: I : 11 (18) (completed 4 th home visit)

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QoL= Quality of Life, PT=Portal Training, CHW=Community health worker, ED= Emergency department, I=Intervention, C=Control, RT= Respiratory therapist, PEFR=Peak expiratory flow rate.

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Table 3: Descriptions of the home visit interventions in the RCTs

Author	Number of home visits	Number of arms	Intervention	Control	Personnel conducted home visits.
1. Federman AD et al. 2019 (25).	Mean 3.3 visits	Three arms (two interventions, delivered at home or clinic and a control)	Received SAMBA intervention either via home visits or in the primary care clinics. The SAMBA intervention comprised of 3 core elements (a) screening to identify barriers to asthma self-management and control, (b) targeted actions to address the barriers, and (c) reinforcement overtime.	Received usual care only	Asthma care coach
2. Apter AJ et al. 2019 (26).	Four home visits were planned	Two-arm study (intervention and control)	Home visits and received PT. Each home visit comprised of 2 parts: (1) Care coordination and promotion of portal use which included goal settings and asthma care plan (2) Improving familiarity with health information technology.	Received PT and usual care	CHW
3. Martin MA et al. 2009 (22).	Six home visits were planned; however, 4 visits were considered sufficient if the participant demonstrated acceptable content mastery in all subject areas.	Two-arm study (intervention and control)	Received 4 clinic group education sessions and 4-6 home visits. Home visits included a general assessment of the participant's asthma status, individualized asthma review, education, and self-management support system. It also addressed medication use, trigger avoidance, and others.	Received mailed asthma education material The material consisted of the same asthma education information presented at group sessions for the intervention participants.	CHW
4. Brown MD et al. 2006 (23).	One home visit was planned	Two-arm study (intervention and control)	Received comprehensive asthma education after an ED visit, and followed up with a home visit. The home visit included medication/	Received usual care only	Nurse

			inhaler technique reviews, identification, and prevention of potential asthma exacerbation triggers. In-house environmental trigger evaluations also were conducted.		
5. Galbreath AD et al. 2008 (28).	Four home visits were planned	Three-arm study (2 interventions and a control)	DM group received a telephonic intervention. DM +Home Visit group received telephonic intervention plus home visits. Home visits included hands-on instruction in the use of equipment, asthma action plan related interventions, and home environmental evaluation.	Received usual care only	RT
6. Krieger J et al. 2015 (27).	Five home visits were planned	Two-arm study (intervention and control)	Received HomeBASE interventions at home. HomeBASE intervention included asthma education, medication use, asthma control assessment, self-management practice, and support. Home environmental/trigger protocols were also part of HomeBASE interventions.	Received usual care plus information about community resources for asthma self-management (such as classes and support groups) and educational pamphlets	CHW
7. Shelledy DC et al. 2009 (21).	Five weekly home visits were planned	Three-arm study (2 interventions and a control)	Received home AMP interventions either by RTs (AMP-RT) or nurses (AMP-RN). AMP intervention included disease severity measurement, therapy monitoring, environmental control, comprehensive pharmacological management, and patient education.	Received usual care only	RT or nurse
8. Smith JR et al. 2005, UK (29).	Four home visits	Two-arm study (intervention and control)	Received psychoeducational program via home visits. Supportive telephone calls were given as reinforcements.	Received usual care only	Nurse

			The home intervention included asthma education, training in self-management skills, advice on coping with asthma and associated difficulties, and support in identifying, prioritizing and addressing other factors compromising an effective management.		
9. Vojta CL et al. 1999 (24).	Four home visits were planned	Two-arm study (intervention and control)	Received home-based asthma educational intervention. The home intervention included an assessment of the patients' knowledge of asthma and medication compliance, recommendations on possible medication changes, medication counseling, PEFr monitoring, identification and avoidance of asthma triggers.	Received usual care only	Nurse

DM=Disease management, AMP= Asthma management programs PT=Portal Training, CHW=Community health worker, ED= Emergency department, RT= Respiratory therapist, PEFr=Peak expiratory flow rate.

Table 4: The outcomes of the RCTs

Author	Outcomes measured (primary outcomes are highlighted in bold and italicized in this column)	Baseline		Change At 3 months from baseline		Difference between groups at 3 months	Change At 6 months from baseline		Difference between groups at 6 months	Change At 12 months from baseline		Difference between groups at 12 months
		I	C	I	C		I	C		I	C	
1. Federman AD et al. 2019 (25). The intervention group comprised of both home- and clinic-based arms. The differences between the home- and clinic-based arms were not statistically significant, except a greater improvement in QoL for home visit recipients at 6 months (DiD, 0.4; 95% CI, 0.1 to 0.8; p=0.02).	Asthma symptom: ACT™ , (mean, SD)	14.8 (3.9)	14.3 (4.0)	16.2 (4.4)	14.6 (4.8)	I>C Adjusted DiD, 1.2 (95% CI, 0.2 to 2.2; p=0.02)	16.2 (4.4)	14.6 (4.9)	I>C Adjusted DiD, 1.0 (95% CI, 0.0 to 2.1; p=0.049)	17.1 (4.7)	16.1 (4.3)	NS
	ED visits (%)	10.5	9.7	-	-	-	-	-	-	6.2	12.7	I>C OR, 0.8 (95% CI, 0.6 to 0.99; p=0.03)
	QoL: Mini AQLQ (mean, SD)	4.3 (1.2)	4.3 (1.1)	4.7 (1.2)	4.3 (1.3)	I>C Adjusted DiD, 0.4 (95% CI, 0.1 to 0.6; p=0.007)	4.7 (1.3)	4.3 (1.3)	I>C Adjusted DiD, 0.4 (95% CI, 0.1 to 0.7; p=0.02)	4.8 (1.3)	4.6 (1.3)	NS

2. Apter AJ et al. 2019 (26).	Asthma symptom: ACQ (95% CI)	2.42 (2.25 to 2.63)	2.39 (2.19 to 2.58)	-	-	-	-	-	-	1.96 (1.69 to 2.22)	2.11 (1.86 to 2.38)	NS
	Annual ED visits (rate per year) (95% CI)	3.64 (2.46 to 5.09)	3.16 (2.43 to 4.17)	-	-	-	-	-	-	0.35 (0.15 to 0.68)	0.48 (0.24 to 0.82)	NS
	Annual hospital admission rate (rate per year) (95% CI)	1.36 (1.00 to 1.72)	1.17 (0.91 to 1.48)	-	-	-	-	-	-	0.17 (0.04 to 0.37)	0.50 (0.26 to 0.82)	I>C Mean difference, -0.53 (95% CI, -1.08 to -0.024)
	Annual rate of OCS bursts (rate per year) (95% CI)	0.42 (0.34 to 0.50)	0.35 (0.27 to 0.43)	-	-	-	-	-	-	0.21 (0.12 to 0.30)	0.23 (0.15 to 0.38)	NS
	QoL: Mini AQLQ (95%	3.68	3.64	-	-	-	-	-	-	4.40	4.05	NS

[illegible]

	<i>Urgent office visits for asthma</i>	NR	NR	-	-	-	-	-	-	0.37	0.34	NS
	<i>Emergency department visits</i>	NR	NR	-	-	-	-	-	-	0.15	0.37	NS
	<i>Inpatient admissions</i>	NR	NR	-	-	-	-	-	-	0.11	0.15	NS
	Number of OCS bursts	NR	NR	-	-	-	-	-	-	NR	NR	NS
	Asthma symptom: LASS score (estimation from graphs)	23	22	-	-	-	-	-	-	17	18.5	I> C (p=0.001)
	QoL: <i>AQLQ</i> (estimation from graphs)	4.2	4.1	-	-	-	-	-	-	5.0	4.5	I>C (p=0.04)
6. Krieger J et al. 2015 (27).	Asthma symptom: <i>-Asthma symptom-free days (self-reported number of 24-hour periods during the prior 2 weeks without wheeze, tightness in the chest, cough, shortness of breath, slowing down activities, or night-time</i>	3.11	2.81	-	-	-	-	-	-	6.78	4.50	I > C Adjusted mean difference, 2.02 (95% CI 0.94 to 3.09; p <0.001)

	<i>awakening</i>)(mean)											
	-ACQ (mean)	2.77	2.55	-	-	-	-	-	-	1.63	2.10	I>C Adjusted mean difference, -0.55 (95%CI -0.74 to -0.37; p<0.001)
	-Night with symptoms (mean)	6.19	5.56	-	-	-	-	-	-	2.14	3.77	I>C Adjusted mean difference, -1.65 (95%CI -2.59 to -0.72; p=0.001)
	-Days use of rescue medication (mean)	7.30	7.40	-	-	-	-	-	-	4.50	6.08	I>C Adjusted mean difference, -1.38 (95%CI -2.44 to -0.32; p=0.01)
	-Asthma control, proportions of the patients with very poor asthma control (%)	70.8	71.5	-	-	-	-	-	-	39.1	59.9	I>C OR, 0.43 (95%CI 0.27 to 0.68; p<0.001)

	Numbers of urgent health care use episodes in last 12 months (ED, hospital, or unscheduled clinic visit)(mean)	3.46	3.30	-	-	-	-	-	-	1.99	1.96	NS
	Asthma exacerbations (mean)	2.42	2.34	-	-	-	-	-	-	1.07	1.63	I>C Adjusted mean difference, -0.55 (95%CI -0.87 to -0.24; p=0.001)
	OCS bursts (mean)	3.94	5.68	-	-	-	-	-	-	1.16	2.45	NS
	Pulmonary function (mean): -FEV1 -FVC -FEV1 % -FEV1/FVC	2.50 3.37 84.5 72.9	2.60 3.43 87.3 75.4	-	-	-	-	-	-	2.56 3.44 87.3 74.3	2.61 3.46 88.3 75.0	NS NS NS NS
	QoL: - Mini AQLQ (mean)	3.72	3.83	-	-	-	-	-	-	4.66	4.19	I>C Adjusted mean difference, 0.50 (95% CI 0.28 to 0.71; p <0.001)

	-SF-12 Mental Health Scale (mean)	41.7	40.7	-	-	-	-	-	-	44.3	43.5	NS		
	-SF-12 Physical Health Scale (mean)	35.9	37.3	-	-	-	-	-	-	41.5	37.5	I>C Adjusted mean difference, 4.54 (95%CI 2.56 to 6.52; p=0.001)		
	Missed work, school, or normal daily activity days (mean)	1.09	1.01	-	-	-	-	-	-	0.28	0.46	NS		
7. Shelledy DC et al. 2009 (21).	<i>Number of hospitalizations</i> (mean, SD)	AMP -RT	AMP -RN	-	-	-	-	AMP -RT	AMP -RN	0.20 (0.5)	I(AMP-RT & AMP-RN) >C; p = 0.014, p = 0.005	-	-	-
		NR	NR					0.04 (0.2)	0 (0)					
	<i>In-patient days</i> (mean, SD)	NR	NR	-	-	-	-	0.09 (0.04)	0 (0)	0.46 (0.20)	I(AMP-RT & AMP-RN) >C; p = 0.02, p = 0.015	-	-	-
	<i>ED visits</i>	NR	NR	-	-	-	-	0.09 (0.3)	0.26 (0.8)	0.37 (0.9)	NS	-	-	-

	Clinic visits	NR	NR	-	-	-	-	3.3 (5.1)	3.2 (5.2)	4.1 (5.8)	NS	-	-	-
	Pulmonary function (mean, SD):													
	-FVC	2.7 (0.92)	2.8 (0.92)	2.7 (0.94)	-	-	-	2.87 (0.82)	2.74 (0.80)	2.57 (0.73)	NS	-	-	-
	-FEV ₁	2.1 (0.79)	2.1 (0.72)	1.9 (0.70)	-	-	-	2.14 (0.71)	2.02 (0.70)	1.81 (0.65)	NS	-	-	-
	-FEV ₁ /FVC	75 (12)	74 (12)	70 (11)	-	-	-	74 (10)	73 (13)	69 (12)	NS	-	-	-
	-PEFR	5.2 (2.2)	5.2 (2.1)	5.3 (1.9)	-	-	-	6.0 (2.2)	5.3 (2.0)	4.9 (1.7)	I(AMP- RT) > C; p = 0.03	-	-	-
	SpO ₂	97.3 (1.3)	97.0 (2.0)	96.1 (2.6)	-	-	-	97.2 (1.1)	97.4 (1.5)	96.4 (1.7)	I(AMP- RT) & I(AMP- RN) > C; $p < 0.05$	-	-	-
	Asthma symptom (mean, SD):													
	-Borg Score	2.2 (2.2)	1.9 (1.7)	2.3 (2.3)	-	-	-	1.4 (1.3)	1.6 (2.1)	1.7 (1.5)	NS	-	-	-
	-Asthma Symptoms Score.	1.6 (1.3)	1.2 (1.1)	1.5 (1.2)	-	-	-	1.1 (1.3)	1.3 (1.2)	1.8 (1.2)	NS	-	-	-
	QoL:													
	-SGRQ Change Score (mean, SD):													
	Total	56 (19)	56 (17)	56 (19)	-	-	-	-11.0 (15)	-6.0 (14)	-2.5 (15)	I(AMP- RT) > C; p = 0.04	-	-	-
	Symptoms	68 (17)	69 (18)	69 (16)	-	-	-	-8.4 (21)	-5.4 (18)	2.7 (17)	I(AMP- RT) > C; p = 0.03	-	-	-
	Activity	66	64	64 (25)	-	-	-	-9.9	-3.5	1.1 (19)	NS	-	-	-

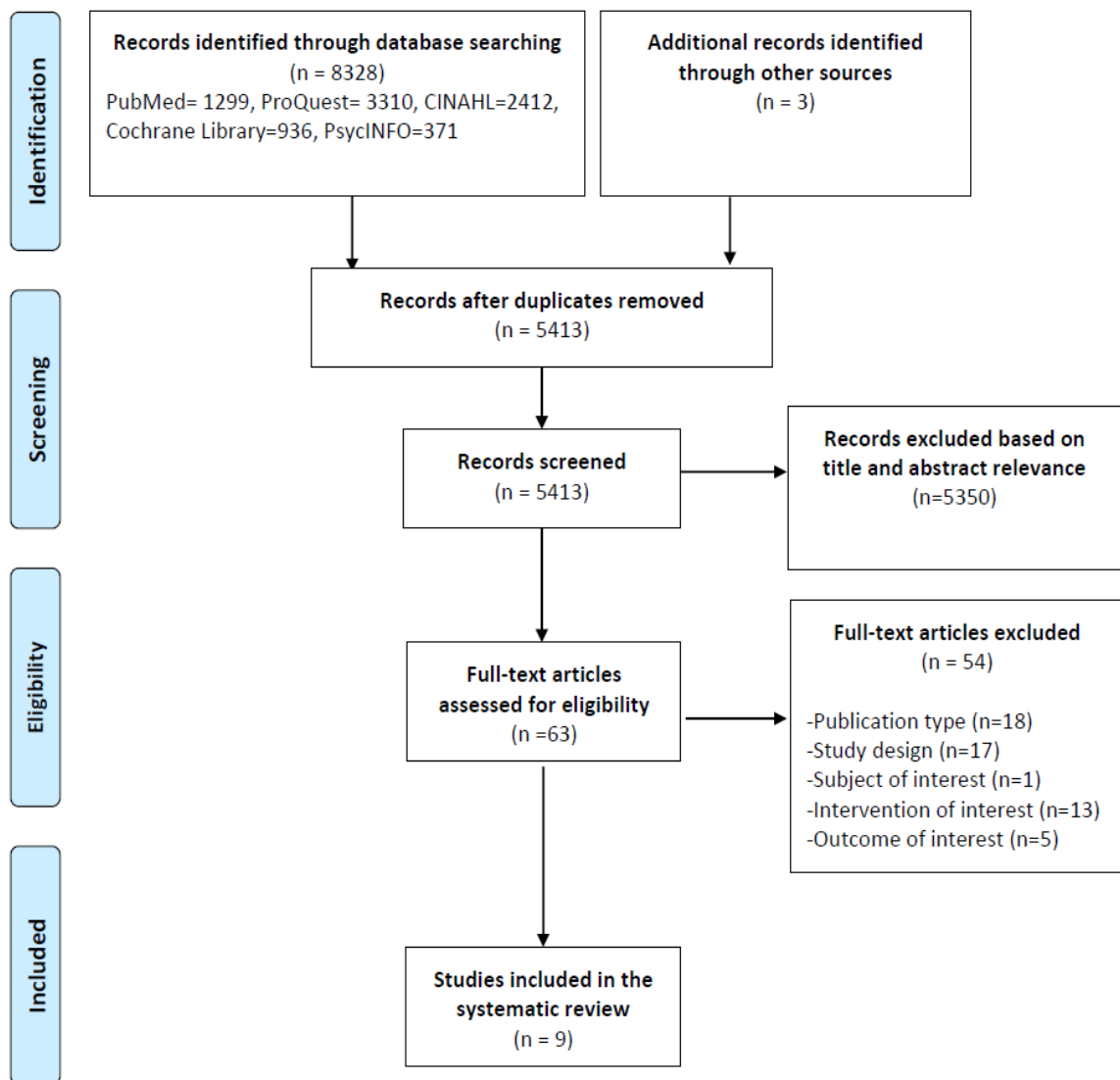
	Impact	(24) 47 (22)	(21) 46 (19)	47 (21)	-	-	-	(23) -12.4 (18)	(21) -7.7 (16)	-6.2 (19)	NS	-	-	-
	-SF-36 Change Scores (mean, SD): PCS	36 (21)	40 (20)	37 (20)	-	-	-	16.9 (23)	9.4 (18)	-3.1 (15)	I(AMP-RT & AMP-RN) >C; $p = 0.0002$, $p = 0.005$	-	-	-
	MCS	45 (23)	44 (22)	45 (26)	-	-	-	15.0 (23)	8.5 (22)	1.9 (25)	NS	-	-	-
8. Smith JR et al. 2005 (29). *Results at 2 months	Asthma symptom: Asthma morbidity questions (mean, SD)	6.06 (3.11)		5.11 (3.00)	*4.29 (3.26)	*5.00 (3.08)	NS	4.21 (3.50)		4.00 (2.91)	NS	4.36 (3.50)	4.48 (3.00)	NS
	QoL (mean, SD) : - Living with Asthma Questionnaire.	1.20 (0.41)		1.14 (0.40)	*1.04 (0.43)	*1.08 (0.41)	NS	1.02 (0.45)		1.04 (0.40)	NS	1.01 (0.45)	1.02 (0.44)	NS
	-SF-36 physical function score	50.85 (31.46)		55.33 (26.83)	*55.71 (33.21)	*51.67 (28.08)	NS	52.98 (31.59)		55.36 (29.56)	NS	55.83 (33.98)	58.45 (30.01)	NS
	SF-36 mental	58.81		62.49	*64.86	*62.57	NS	66.19		66.19	NS		63.81	NS

	health score	(23.01)	(22.14)	(22.60)	(21.16)		(22.30)	(20.82)		66.38 (24.36)	(23.90)	
	<u>Additional ITT analysis</u> Asthma symptom: Asthma morbidity questions (mean, SD)			4.29 (3.26)	5.00 (3.08)	NS	4.21 (3.50)	4.00 (2.91)	NS	4.36 (3.50)	4.48 (3.00)	NS
	QoL (mean, SD) : -Living with Asthma Questionnaire -SF-36 physical function score -SF-36 mental health score			1.04 (0.43)	1.08 (0.41)	I>C mean adjusted difference, 0.14 (95% CI 0.04 to 0.23; p=0.01)	1.02 (0.45)	1.04 (0.40)	I>C mean adjusted difference, 0.13 (95% CI 0.03 to 0.23; p=0.01) NS	1.01 (0.45)	1.02 (0.44)	I>C mean adjusted difference, 0.13 (95% CI 0.02 to 0.25; p=0.03)
				55.71 (33.21)	51.67 (28.08)	NS	52.98 (31.59)	55.36 (29.56)	NS	55.83 (33.98)	58.45 (30.01)	NS
				64.86 (22.60)	62.57 (21.16)	I>C mean adjusted difference, -7.65 (95% CI -15.33 to 0.19; p=0.05)	66.19 (22.30)	66.19 (20.82)		66.38 (24.36)	63.81 (23.90)	NS
9. Vojta CL et al. 1999 (24).	ED visits (mean, SD)	1.27 (1.63)	1.18 (1.50)	-	-	-	0.74 (1.40)	0.45 (0.77)	NS	-	-	-
	Hospitalizations (mean, SD)	0.56 (1.09)	0.59 (0.72)	-	-	-	0.27 (1.40)	0.15 (0.41)	NS	-	-	-

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ACTTM=Asthma Control Test, DiD= Difference in Differences, QoL= Quality of Life, PT=Portal Training, NS= Non-significant, NR= Not reported, CHW=Community health worker, AQLQ= Asthma Quality of Life Questionnaire, ED= Emergency department, I=Intervention, C=Control, > =Better, RT= Respiratory therapist, LASS=Lara Asthma Symptom Scores, OCS=Oral corticosteroids, ACQ=Asthma Control Questionnaire, SGRQ=St. George's Respiratory Questionnaire, PCS=Physical Component Summary Score, MCS=Mental Component Summary Score, ITT=Intention-to-treat, SD=Standard deviation, PEF=Peak expiratory flow rate.

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	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel selection (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other biases	
	?	?	-	-	-	?		Vojta et al. 1999
Smith et al. 2005	+	+	-	-	+	+	-	
Brown et al. 2006	+	+	-	-	-	+	?	
Galbreath et al. 2008	+	+	?	+	-	+	?	
Martin et al. 2009	?	?	-	-	?	?	-	
Shelledy et al. 2009	?	?	+	+	?	?	?	
Krieger et al. 2015	+	+	-	+	+	+	+	
Apter et al. 2019	?	+	+	-	+	+	+	
Federman et al. 2019	+	?	+	-	+	?	+	

+	Low risk of	?	Unclear risk of bias	-	High risk of bias
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