British Thoracic Society

NICE National Institute for Health and Care Excellence

Healthcare Improvement Scotland | SIGN

Final

Asthma: diagnosis, monitoring and chronic asthma management (update)

[L] Evidence reviews for symptom diary for monitoring asthma

BTS/NICE/SIGN collaborative guideline NG245

Evidence reviews underpinning recommendation 1.5.2 in the guideline

November 2024

Final

Developed by BTS, NICE and SIGN

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1. Symptom diary

1.1 Review question

In people with asthma, what is the clinical and cost-effectiveness of using symptom scores/diaries or validated questionnaires measuring symptom control (e.g. ACT, ACQ, CACT, RCP 3 questions) and/or health related quality of life (e.g. AQLQ, PAQLQ) to monitor asthma?

1.1.1 Introduction

Asthma is, characteristically, a disease which varies over time – people have some days which are worse than others. A symptom diary can be used to help people with asthma monitor how they are on particular days with regard to their symptoms and medication use and help identify any triggers for these. If people are asked to spend time doing these, and if decisions are made based on what is recorded in a diary, it is important to understand the evidence around whether they are effective.

1.1.2 Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	People with a diagnosis of asthma (physician diagnosis/definitive diagnosis by objective test) All ages, stratified into the following 3 different groups: • Children (<5 years old) • Children and young people (5-16 years) • Adults (>17 years old)

Interventions	Monitoring the following, and using the outcomes of scores/questionnaires to adjust management/therapy according to physician decision or personalised treatment plan:
	• Symptom score or diaries
	• Symptom/control questionnaires
	  ○ Asthma Control Test, ACT (including caregivers or paediatric version, CACT)
	  ○ Asthma Control Questionnaire, ACQ (including mini ACQ or paediatric ACQ)
	  ○ RCP 3 questions
	• Quality of life questionnaires (asthma specific)
	  ○ Health-related QoL
	  ○ Asthma Quality of Life Questionnaire, AQLQ (including paediatric version, PAQLQ)

Comparison	Comparison of adjustment of asthma therapy based on symptom scores or questionnaires to: • Usual care: e.g. clinical symptoms (with/without spirometry/PEF) according to guidelines (including BTS/SIGN, GINA) Comparison of adjustment of asthma therapy based on: • Symptom scores or diaries vs questionnaires • Control questionnaire vs other control questionnaire

	• QOL questionnaire vs asthma control questionnaire
Outcomes	All outcomes are considered equally important for decision making and therefore have all been rated as critical: • Mortality • Unscheduled healthcare utilisation (ED/A&E visit; hospital admissions; GP out of hours or walk-in centre) • Severe asthma exacerbations (defined as asthma exacerbations requiring oral corticosteroid use-dichotomous outcome at ≥6 months, latest time point if more than one) • Asthma control assessed by a validated questionnaires (ACQ, ACT; CACT; PACQ; RCP-3; continuous outcome at ≥3 months) • Quality of life (QoL) (validated scale, including asthma specific questionnaires AQLQ; health related, pAQLQ; St George's respiratory questionnaire; continuous outcome at ≥3 months) • Lung function (FEV1, PEF) • Symptoms (annual symptom free days) • Dose of regular asthma therapy / preventer medication (ICS dose) • Reliever/ Rescue medication use (SABA use – continuous outcome at ≥3 months) • Time off school or work
Study design	• RCTs

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

Seven randomised controlled studies (reported in 8 papers) were included in the review (Mehuys, et al., 2008, Pool, et al., 2017, Rikkers-Mutsaerts, et al., 2012, van den Wijngaart, et al., 2017, van der Meer, et al., 2009, van Gaalen, et al., 2013, Ye, et al., 2021, Zhang, et al., 2020); these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

5 studies were conducted in adults (Mehuys 2008; Pool 2017; van der Meer 2009; van Gaalen 2013; Ye 2021; Zhang 2020) and 2 studies were conducted in children and young people (Rikkers 2012;; van Wijngaart 2017). Of these studies, 4 were newly identified, since the NICE guideline (Asthma: diagnosis, monitoring and chronic asthma management) published in 2017.

A wide range of interventions were used by the 7 studies, and for some studies the intervention involved monitoring by symptoms and/or questionnaire as well as other intervention components; most notably education. Of the 5 studies in adults, studies by Mehuys 2008 and van der Meer 2009 (and van Gaalen 2013) used interventions that included educational components (in intervention arm only) as well as monitoring. Both studies in children and young people (the Rikkers 2012 and van der Wijngaart 2017 studies) used interventions that included educational components (in intervention arm only) as well as monitoring.

The most common symptom control questionnaire used in the interventions was the asthma control test (ACT) and its paediatric version C-ACT (Mehuys 2008; Ye 2021; Zhang 2020; van Wijngaart 2017), followed by the asthma control questionnaire (ACQ) (Rikkers 2012; van der Meer 2009). Pool 2017 used an unvalidated questionnaire focusing on asthma symptoms.

The route by which asthma management or therapy changed in response to questionnaire monitoring varied widely from studies where there was clear involvement of a healthcare professional reviewing the questionnaires and adjusting treatment, to use of algorithms to prompt participants to alter self-management behaviours. Studies were excluded if it was not clear that management or therapy had changed in response to questionnaire monitoring. Due to the wide variability in nature of the interventions, the studies were not pooled in this review.

See also the study selection flow chart in Appendix C, study evidence tables in Appendix D, forest plots in Appendix E and GRADE tables in Appendix F.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix I.

1.1.5 Summary of studies included in the effectiveness evidence

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Mehuys 2008 (Mehuys et al., 2008)	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on	Adults aged 18-50 years with a prescription for asthma medication and treated for	Unscheduled healthcare utilisation (emergency department visits	Strata: adults Intervention indirectness: intervention group received education,

Study	Intervention and comparison	Population	Outcomes	Comments
	ACT score, plus education) Personal education session (1) from pharmacist on topics including correct use of inhaler, symptom triggers, understanding asthma Sessions (2) and (3) at 1 mo and 3 mo for pharmacist advice based on ACT score: i. ACT <15: immediate referral to GP or specialist ii. ACT 15-19: review inhaler technique and check controller adherence iii. ACT >19: no advice, inform patient asthma is well-controlled vs Usual pharmacist care	asthma >12 months, using controller medication N=201 Mean age (range): 35.5 (18-51) years Belgium	or hospitalisations) Asthma exacerbations (requiring treatment with oral glucocorticoids or an emergency department visit or hospital admission due to asthma) Asthma control (ACT) Quality of life [Asthma quality of life questionnaire (AQLQ)] Lung function (Morning PEF) Reliever/rescue mediation use At 6 months	but not the usual care group.
Pool 2017 (Pool et al., 2017)	Symptom scores or diaries (Symptom questions with feedback to support self-management) Intervention participants were asked to use an online tool at least once each month (and within 14 days of their next scheduled health care provider visit), in which they would answer 11 questions about their asthma	Adults aged 21-60 years. with persistent asthma based on their pattern of medication use specific to asthma, emergency room visits or hospitalizations with a principal diagnosis of asthma, and outpatient visits coded by the provider with a diagnosis of asthma.	Unscheduled healthcare utilisation (number of emergency room visits; number of outpatient visits) Asthma control (ACT) Dose of regular asthma therapy/preventer medication (number of asthma medications;	Strata: adults Intervention indirectness: an unvalidated symptom questionnaire. 4 of 11 questions relate to asthma care rather than symptoms.

Study	Intervention and comparison	Population	Outcomes	Comments
	symptoms (e.g., rescue inhaler frequency, night symptom frequency), availability of oral corticosteroids at home for exacerbations, and asthma care received from providers, such as an asthma management plan. Participants were also asked to enter their current asthma medications, the number of days each week that each medication was used and identify if any medicines bothered them; and record their next scheduled visit with their asthma care provider. Based on their answers and pre-written rules, the online tool provided tailored feedback reminding patients to ask providers specific questions about their asthma medications and perform specific asthma self-care, to improve adherence to the 2007 NAEPP treatment guidelines. Feedback included lay-person explanations and links to an external website that supported the recommendation. Vs	N=408 Mean age (SD): 47.4 (9.3) years United States (members of a health insurance company)	number of asthma controller medications) At 12 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Control condition received questions and were given feedback about preventive services (e.g., colon cancer screening) that would be unlikely to change asthma care.			
Rikkers 2012 (Rikkers-Mutsaerts et al., 2012, van der Meer et al., 2009)	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) Internet-based self-management: consisting of all four components of self-management support programs: education, self-monitoring, an electronic action plan, and regular medical review. Education was provided as web-based portal including interactive communication with a specialized nurse, and 2 face-to-face group based education sessions focussing on self-management. Patients monitored their asthma weekly by completing an electronic version of the ACQ and receiving feedback and 4 types of self-treatment advice on how to adjust their treatment according to a predefined treatment plan:	Adolescents aged 12-17 years, with a doctor's diagnosis of mild to severe persistent asthma characterised by a prescription of ICS more than 3 months in the previous years. N=90 Mean age (range): 13.5 (12-17) years The Netherlands	Asthma exacerbations (deterioration in asthma that required oral steroids for 3 days or more, as reported in 3-monthly questionnaires) Asthma control (ACQ) Quality of life (Paediatric Asthma QOL questionnaire) Symptoms (symptom-free days) Dose of regular asthma therapy / preventer medication (daily ICS dose) At 12 months	Strata: children and young people SMASHING trial Intervention indirectness: intervention group received additional web-based and face-to-face education sessions. Population indirectness: unknown proportion of 17 year olds.

Study	Intervention and comparison	Population	Outcomes	Comments
	i.4 consecutive ACQ scores of 0.5 or less= decrease treatment according to treatment plan. ii. 2 consecutive scores > 0.5 but < 1.0= increase treatment according to treatment plan. iii. 1 score ≥1.0 but < 1.5 = immediately increase treatment according to treatment plan. iv. 1 score ≥ 1.5= immediately increase treatment and contact the asthma nurse. Vs Usual care: care by their physician according to the Dutch guidelines on asthma management in children in general practice and in hospitals. Commonly, they visited their general practitioner or paediatrician every 3 months or twice per year once control of asthma had been achieved.			
Van der Meer 2009(van der Meer et al., 2009)	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) Internet-based self-management:	Adults with asthma treated with ICS for 3 months or more during the previous year and who had access to the internet. N=200	Asthma exacerbations [deterioration requiring emergency treatment or hospitalization or the need for oral steroids for 3 days or more (as judged by the	Strata: Adults Multicentre RCT (SMASHING trial) Same intervention as Rikkers-Mutsaerts 2012

Study	Intervention and comparison	Population	Outcomes	Comments
	including weekly asthma control monitoring and treatment advice, online and group education and remote Web communications. Education was provided as web-based portalincluding interactive communication with a specialized nurse, and 2 face-to-face group based education sessions focussing on self-management. Patients monitored their asthma weekly by completing an electronic version of the ACQ and receiving feedback and 4 types of self-treatment advice on how to adjust their treatment according to a predefined treatment plan: i.4 consecutive ACQ scores of 0.5 or less= decrease treatment according to treatment plan. ii. 2 consecutive scores > 0.5 but < 1.0= increase treatment according to treatment plan. iii. 1 score ≥1.0 but < 1.5 = immediately increase treatment	Mean age (range): 36.6 (18-50) years The Netherlands	attending physician)] Asthma control (ACQ) Quality of life (Asthma-related QOL) Lung function (FEV1) Symptoms (symptom free days) Dose of regular asthma therapy / preventer medication (daily ICS use) At 12 months	Intervention indirectness: intervention group received additional web-based and face-to-face education sessions.

Study	Intervention and comparison	Population	Outcomes	Comments
	according to treatment plan. iv. 1 score ≥ 1.5= immediately increase treatment and contact the asthma nurse. Vs Usual care: asthma care according to the Dutch general practice guidelines on asthma management in adults, which recommend a medical review and treatment adjustment every 2 to 4 weeks in unstable asthma and medical review once or twice yearly for patients whose asthma is under control.			
Van Gaalen 2013(van Gaalen et al., 2013)	as Van der Meer 2009	N=107 Otherwise, as Van der Meer 2009	Asthma control (ACQ) Quality of life (AQLQ) At 30 months	Strata: adults Longer-term follow-up of Van der Meer (2009) (intervention ceased at 12 months)
Van den Wijngaart 2017 (van den Wijngaart et al., 2017)	Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) Virtual asthma clinic: a web-based portal with a chat and forum module for peers, an information module to enhance knowledge about asthma, and a secure and private module in which the child/parent can	Children aged 6-16 years, with a doctor's diagnosis of asthma based on symptoms and a bronchodilator response of forced expiratory volume in 1 s (FEV1) % pred >9%, and/or airway hyperresponsiveness, and/or signs of eosinophilic airways inflammation. All had to have at least one allergy for airborne	Unscheduled healthcare utilisation (unscheduled outpatient visits; visits to emergency departments; hospital admissions) Asthma exacerbations (exacerbations treated with systemic corticosteroids)	Strata: children and young people Intervention indirectness: intervention group received interactive web-based education.

Study	Intervention and comparison	Population	Outcomes	Comments
	log in to consult an individual treatment plan and communicate with the asthma management team. Outpatient visits every 8 months. Digital (c-)ACT completed monthly: If the (C-)ACT score was ⩾20, automatic default messages were emailed with positive and encouraging content. If the (C-)ACT score was <20 feedback to the participants included advice to check their medication use, an individual action plan and a request to contact their asthma team when symptoms persisted. Feedback also sent to the asthma team to prompt contacting the participant within 2 working days to address clinical status. Vs Usual care: routine outpatient visits every 4 months, during which patients completed a digital version of the (C-)ACT to assess asthma control. Results of/feedback from (C-)ACT not available to	allergens confirmed by positive skin prick tests and/or blood tests N=210 Mean (SD) age: 11.3 (2.8) years The Netherlands	Asthma control (C-ACT and ACT) Lung function (FEV1 % predicted) Symptoms (symptom-free days) At 16 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	physician or patient.			
Ye 2021(Ye et al., 2021)	Symptom/control questionnaires (ACT-guided treatment) ACT guided treatment comprising of: i. ACT score=25, ≥3 months; step down treatment ii. ACT score= ≥20, <25 or ACT score=25, <3 months; no change iii. ACT score ≤19; treatment adjustment: step-up Vs Usual care: treatment based on physicians' subjective judgment asking questions including: 'what is the major symptom you have', 'what kind of medicines did you take'	People aged 18–70 years with an ACT score <20, documented clinical history of asthma for ≥6 months, and using ICS alone or ICS/LABA treatment within 1 year prior to or at Visit 0 N=530 Mean age (SD): 48 (13) years China	Asthma exacerbations (moderate/severe asthma exacerbations, not defined) Asthma control (ACT) Lung function (FEV1) Quality of life (AQLQ) At 24 weeks	Strata: Adults Cluster-RCT; multicentre study. Patients in both groups were required to record PEF, symptoms and medication in a paper diary record card every day. These were checked to evaluate therapeutic compliance. Use of ICS/bronchodilators was modified according to GINA recommendations.
Zhang 2020 (Zhang et al., 2020)	Symptom/control questionnaires (ACT monitoring with results sent to physician) Observational group: in addition to the control group treatment, participants undertook a self-reported ACT questionnaire at the end of each month and were asked to bring the results to physicians/pharmacists at the next visit/submit them via email/webchat; they were guided by	Adults with asthma diagnosed according to the diagnostic criteria for bronchial asthma prevention and treatment guidelines developed by the Asthma workgroup of the Chinese Medical Association Respiratory Diseases Branch. N=627 Mean age (SD): 42.7 (11.8) years	Lung function (FEV1 and PEF) At 6 months	Strata: Adults Intervention indirectness: unclear what adjustments to treatment and/or self-management made in response to ACT monitoring, though results were sent to physician Both arms received training in pulmonary function measurement and inhaler techniques

Study	Intervention and comparison	Population	Outcomes	Comments
	physicians/pharmacists on the significance of the ACT and given knowledge related to disease, symptom control and inhalation therapy. Vs Control group: patients were treated with standardised medication of combination of ICS/LABA for asthma control and health education involving inhaler technique training.	China		

See Appendix D for full evidence tables.

1.1.6 Summary of the effectiveness evidence

Table 3: Clinical evidence summary: Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) vs usual care (by pharmacists) in adults

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care (by pharmacists) in adults	Risk difference with ACT-score & pharmacist advice	Comments
Asthma exacerbations (severe exacerbations, final score, lower is better)	150 (1 RCT) Follow-up: 6 months	⊕◯◯◯ Very low[a,b,c]	**RR 1.09** (0.46 to 2.62)	114 per 1,000	**10 more per 1,000** (62 fewer to 185 more) No clinically important difference	MID (imprecision) = 0.8 – 1.25 MID (clinical importance) = 30 per 1000
Unscheduled healthcare utilisation (emergency department visits or hospitalisation, final scores, lower is better)	150 (1 RCT) Follow-up: 6 months	⊕◯◯◯ Very low[b,c,d]	**RR 0.17** (0.02 to 1.46)	71 per 1,000	**59 fewer per 1,000** (70 fewer to 33 more) Clinically important difference favouring symptom/control questionnaires	MID (imprecision) = 0.8 – 1.25 MID (clinical importance) = 30 per 1000
Asthma control (ACT score, range 0 to 25, final score, higher is better)	150 (1 RCT) Follow-up: 6 months	⊕◯◯◯ Very low[b,e,f]	-	The mean asthma control (ACT score, range 0 to 25, final score, higher is better, FUP 6 mo) was **19.7**	MD **0.5 higher** (0.86 lower to 1.86 higher) No clinically important difference	MID= 3 (established MID)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care (by pharmacists) in adults	Risk difference with ACT-score & pharmacist advice	Comments
Quality of life (asthma-QoL questionnaire, scale 0 to 7, final score, higher is better)	150 (1 RCT) Follow-up: 6 months	⊕◯◯◯ Very low[b,e,f]	-	The mean quality of life (asthma-QoL questionnaire, scale 0 to 7, final score, higher is better, FUP 6 Mo) was **5.8**	MD **0.2 higher** (0.06 lower to 0.46 higher) No clinically important difference	MID= 0.5 (established MID)
Lung function (morning PEF, % predicted, final score, higher is better)	150 (1 RCT) Follow-up: 6 months	⊕◯◯◯ Very low[b,g,h]	-	The mean lung function (morning PEF, % predicted, final score, higher is better, FUP 6 Mo); at 6 months) was **79.1**	MD **4.9 higher** (1.25 lower to 11.05 higher) No clinically important difference	MID=9.05 (calculated as baseline SD/2)
Reliever/rescue medication use (puff/day; mean over previous 14 days, final score, lower is better)	150 (1 RCT) Follow-up: 6 months	⊕◯◯◯ Very low[b,e,f]	-	The mean reliever/rescue medication use (puff/day; mean over previous 14 days, final score, lower is better, FUP 6 Mo) was **0.9**	MD **0.23 lower** (0.66 lower to 0.2 higher) No clinically important difference	MID= 0.81 (established MID)

a. Downgraded by one increment due to some concerns about risk of bias (no info about prespecified analyses)

b. Downgraded by one increment for intervention indirectness (intervention group received education as well and questionnaire monitoring)

c. Downgraded by two increments for imprecision because the confidence interval crosses both MIDs (0.8-1.25)

d. Downgraded by one increment due to some concerns about risk of bias (no info about prespecified analyses and no information about outcome assessment)

e. Downgraded by two increments because study at high risk of bias (self-reported outcome and unblinded: no information in prespecified analyses and unclear why ITT analysis presented for primary outcomes and per-protocol analysis for secondary outcomes)

f. Published MIDs: ACT=3; AQLQ=0.5; reliever/rescue medication=0.81 puffs/day

g. Downgraded by one increment due to some concerns about risk of bias (no information about prespecified analyses and unclear why PP used for secondary outcomes but ITT for primary outcomes)

h. Downgraded by one increment for imprecision because the confidence interval crosses one MID (calculated as baseline SD of control and intervention groups /2=9.05)

Table 4: Clinical evidence summary: Symptom/control questionnaires (ACT-guided treatment) vs usual care (physician's judgment) in adults

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care (physician's judgment) in adults	Risk difference with ACT-guided treatment	Comments
Asthma exacerbations (moderate/severe exacerbations, final score, lower is better)	507 (1 RCT) Follow-up: 24 weeks	⊕◯◯◯ Very low[a,b,c]	**RR 0.88** (0.35 to 2.18)	38 per 1,000	**5 fewer per 1,000** (25 fewer to 45 more) No clinically important difference	MID (imprecision) = 0.8 – 1.25 MID (clinical importance) = 30 per 1000

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with usual care (physician's judgment) in adults	Risk difference with ACT-guided treatment	
Asthma control (LS mean change in ACT score, change score, higher is better)	504 (1 RCT) Follow-up: 24 weeks	⊕⊕◯◯ Low[d,e]	-	The mean asthma control (LS mean change in ACT score, change score, higher is better, FUP 24 weeks) was **5.6**	MD **1.3 higher** (0.5 higher to 2.1 higher) No clinically important difference	MID= 3 (established MID)
Lung function (FEV1 (% change score; higher is better)	504 (1 RCT) Follow-up: 24 weeks	⊕⊕⊕◯ Moderate[f,g]	-	The mean lung function (FEV1 (% change score; higher is better, FUP 24 weeks) was **3.83**	MD **1.85 higher** (1.58 lower to 5.28 higher) No clinically important difference	MID=9.8 (calculated as follow-up SD/2)
Quality of life (AQLQ symptom domain, range 1-7; change score; higher is better)	504 (1 RCT) Follow-up: 24 weeks	⊕◯◯◯ Very low[d,h]	-	The mean quality of life (AQLQ symptom domain, range 1-7; change score; higher is better, FUP 24 weeks) was **1.2**	MD **0.3 higher** (0 to 0.6 higher) No clinically important difference	MID= 0.5 (established MID)

a. Downgraded by two increments due to concerns about risk of bias (exacerbations determined by patients record card and unblinded; no information about pre-specified analyses in protocol.)

b. Downgraded by one increment for outcome indirectness (not defined and so not clear whether meets protocol definition)

c. Downgraded by two increments for imprecision because the confidence interval crossed both MIDs (MIDs for dichotomous outcomes: 0.8 and 1.25)

d. Downgraded by two increments due to concerns about risk of bias (subjective outcome and assessors aware of intervention; no information about prespecified analyses)

e. Published MID for ACT=3

f. Downgraded by one increment due to some concerns about risk of bias (no information about prespecified analyses)

g. MID= Follow-up SD/2=9.8 (baseline SDs not available)

h. Downgraded by one increment for imprecision because confidence interval crosses one MID (published MID for AQLQ=0.5)

Table 5: Clinical evidence summary: Symptom control/questionnaires (ACT monitoring with results sent to physician)) vs usual care (ICS/LABA & education) in adults

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care (ICS/LABA & education) in adults	Risk difference with ACT self-management	Comments
Lung function (FEV1 % predicted, change score, higher is better)	627 (1 RCT) Follow-up: 6 months	⊕◯◯◯ Very low[a,b,c]	-	The mean lung function (FEV1 % predicted, change score, higher is better, 6 mo FUP) was **19.94**	MD **16.78 higher** (15.85 higher to 17.71 higher) Clinically important benefit favouring intervention	MID=6.63 (calculated as baseline SD/2)
Lung function (PEF % predicted, change score, higher is better)	627 (1 RCT) Follow-up: 6 months	⊕◯◯◯ Very low[a,b,c]	-	The mean lung function (PEF % predicted, change score, higher is better, 6 Mo FUP) was **23.65**	MD **17.84 higher** (17.14 higher to 18.54 higher) Clinically important benefit favouring intervention	MID=3.52 (calculated as baseline SD/2)

a. Downgraded by two increments because the study is at high risk of bias (no details about randomisation and pre-specified analyses)

b. Downgraded by one increment for intervention indirectness (unclear what adjustments to treatment and/or self-management made in response to ACT monitoring, though results were sent to physician)

c. MID calculated using baseline SD (of intervention + control groups/2)/2; FEV1: 6.63; PEF: 3.52

Table 6: Clinical evidence summary: Symptom control/questionnaires (ACQ monitoring with feedback to support self-management, plus education) vs usual care (Dutch guidelines) in adults

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care (Dutch guidelines) in adults	Risk difference with ACQ-feedback + self-management	Comments
Asthma exacerbations, final score, lower is better)	200 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[a,b,c]	**HR 1.18** (0.51 to 2.73)	101 per 1,000	**17 more per 1,000** (48 fewer to 151 more) No clinically important difference	MID (imprecision) = 0.8 – 1.25 MID (clinical importance) = 30 per 1000
Asthma control (ACQ, range 0 to 7, lower is better)	200 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[b,d,e]	-	The mean asthma control (ACQ, range 0 to 7, lower is better, FUP 12 Mo) was **-0.06**	MD **0.47 lower** (0.64 lower to 0.3 lower) No clinically important difference	MID= 0.5 (established MID)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care (Dutch guidelines) in adults	Risk difference with ACQ-feedback + self-management	Comments
Asthma control (ACQ, range 0 to 7, final score, lower is better)	107 (1 RCT) Follow-up: 30 months	⊕◯◯◯ Very low[b,e,f]	-	Not reported	MD **0.33 lower** (0.61 lower to 0.05 lower) No clinically important difference	MID= 0.5 (established MID)
Quality of life (AQLQ , range 1 to 7, change score, higher is better)	200 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[b,d,e]	-	The mean quality of life (AQLQ , range 1 to 7, change score, higher is better, FUP 12 Mo) was **0.18**	MD **0.38 higher** (0.2 higher to 0.56 higher) No clinically important difference	MID= 0.5 (established MID)
Quality of life (AQLQ, range 1 to 7, final score, higher is better)	107 (1 RCT) Follow-up: 30 months	⊕◯◯◯ Very low[b,e,f]	-	Not reported	MD **0.29 higher** (0.01 higher to 0.57 higher) No clinically important difference	MID= 0.5 (established MID)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care (Dutch guidelines) in adults	Risk difference with ACQ-feedback + self-management	Comments
Lung function (FEV1, L, change score, higher is better)	200 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[a,b,e]	-	The mean lung function (FEV1, L, change score, higher is better, FUP 12 Mo) was **-0.01**	MD **0.25 higher** (0.03 higher to 0.47 higher) Clinically important benefit favouring intervention	MID= 0.23 (established MID)
Symptoms (symptom-free days, %, change score, higher is better)	200 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[b,d,g]	-	The mean symptoms (symptom-free days, %, change score, higher is better, FUP 12 Mo) was **7.3**	MD **10.9 higher** (0.05 higher to 21.75 higher) No clinically important difference	MID=19.55 (SD calculated from 95%CI/2)
Dose of regular asthma therapy / preventer medication (daily ICS use, mcg, change score)	200 (1 RCT) Follow-up: 12 months	⊕⊕◯◯ Low[b,h,i]	-	The mean dose of regular asthma therapy / preventer medication (daily ICS use, mcg, change score, FUP 12 Mo) was **-48**	MD **57 higher** (38 lower to 152 higher) No clinically important difference	MID=171.35 (SD calculated from 95%CI/2)

a. Downgraded by one increment due to some concerns about risk of bias (no information about prespecified analyses)

b. Downgraded by one increment for intervention indirectness (intervention group received additional web-based and face-to-face education sessions)

c. Downgraded by two increments for imprecision because the confidence interval crosses both MIDs (0.8 to 1.25)

d. Downgraded by two increments because study at high risk of bias (self-reported outcome and unblinded study (ACQ measurement part of intervention); no information about pre-specified analyses)

e. Downgraded by one increment for imprecision because the confidence interval crosses one MID (published MIDs: ACQ=0.5; AQLQ=0.5; FEV1=0.23L))

f. Downgraded by two increments because study at high risk of bias (self-reported subjective outcome and unblinded; post-hoc analysis; investigators likely to know 12 month results before reporting 30 month results; unclear information on missing data as longer follow-up participants were re-recruited)

g. Downgraded by one increment for imprecision because the confidence interval crosses one MID (SD calculated from 95%CI/2=19.55)

h. Downgraded by one increment due to some concerns about risk of bias [self-reported outcome and unblinded (but not completely subjective an outcome); no information on prespecified outcomes]

i. MID: SD from 95%CI/2=171.35

Table 7: Clinical evidence summary: Symptom scores or diaries (symptom questions with feedback to support self-management) vs control questions and feedback in adults

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with Control-Qs +feedback	Risk difference with Symptom-Qs + feedback +self-management	Comments
Unscheduled healthcare utilisation (number of emergency room visits, change score, lower is better)	326 (1 RCT) Follow-up: 12 months	⊕⊕⊕◯ Moderate[a,b]	-	The mean unscheduled healthcare utlisation (number of emergency room visits, change score, lower is better, FUP 12 Mo) was **-0.08**	MD **0.18 lower** (0.43 lower to 0.07 higher) No clinically important difference	MID=0.98 (calculated as baseline SD/2)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with Control-Qs +feedback	Risk difference with Symptom-Qs + feedback +self-management	Comments
Unscheduled healthcare utilisation (number of outpatient visits, change score, lower is better)	326 (1 RCT) Follow-up: 12 months	⊕⊕⊕◯ Moderate[a,b]	-	The mean unscheduled healthcare utilisation (number of outpatient visits, change score, lower is better, FUP 12 Mo) was **0**	MD **0.13 lower** (0.7 lower to 0.45 higher) No clinically important difference	MID=1.99 (calculated as baseline SD/2)
Asthma control (ACT, range 5 to 25, change score, higher is better)	325 (1 RCT) Follow-up: 12 months	⊕⊕⊕◯ Moderate[a,c]	-	The mean asthma control (ACT, range 5 to 25, change score, higher is better, FUP 12 Mo) was **1.2**	MD **1.05 higher** (0.17 higher to 1.93 higher) No clinically important difference	MID= 3 (established MID)
Dose of regular asthma therapy / preventer medication (number of asthma medications, change score, lower is better)	326 (1 RCT) Follow-up: 12 months	⊕⊕◯◯ Low[b,d]	-	The mean dose of regular asthma therapy / preventer medication (number of asthma medications, change score, lower is better, FUP 12 Mo) was **0.25**	MD **0.17 higher** (0.05 lower to 0.39 higher) No clinically important difference	MID=1.0 (calculated as baseline SD/2)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with Control-Qs +feedback	Risk difference with Symptom-Qs + feedback +self-management	Comments
Dose of regular asthma therapy / preventer medication (number of asthma controller medications, change score, lower is better)	326 (1 RCT) Follow-up: 12 months	⊕⊕◯◯ Low[b,d]	-	The mean dose of regular asthma therapy / preventer medication (number of asthma controller medications, change score, lower is better, FUP 12 Mo) was **0.12**	MD **0.06 higher** (0.09 lower to 0.21 higher) No clinically important difference	MID=0.78 (calculated as baseline SD/2)

a. Downgraded by 1 increment due to indirectness of intervention (use of non-validated asthma symptom questionnaire. Only 7/11 Q are directly about asthma symptoms)

b. MIDs= SD/2 of the intervention and control group; SDs were calculated using the baseline mean (95% CI) of the intervention and control group to get the standard error and then convert it to SD; MIDs: ED visits: 0.98; outpatient visits: 1.99; asthma medications: 1.0; asthma controller medications: 0.78

c. Published MID for ACT=3

d. Downgraded by 2 increments due to indirectness of intervention (use of non-validated asthma symptom questionnaire. Only 7/11 Q are directly about asthma symptoms) and outcome [not identical to dose of regular asthma therapy / preventer medication (ICS dose)]

Table 8: Clinical evidence summary Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) compared to usual care (Dutch guidelines) in children and young people

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care (Dutch guidelines) in CYP	Risk difference with ACQ-feedback + self-management	Comments
Asthma exacerbations (lower is better)	90 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[a,b,c]	**RR 0.96** (0.33 to 2.74)	136 per 1,000	**5 fewer per 1,000** (91 fewer to 237 more) No clinically important difference	MID (imprecision) = 0.8 – 1.25 MID (clinical importance) = 30 per 1000
Asthma control (ACQ, change score, lower is better)	90 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[a,b,d]	-	The mean asthma control (ACQ, change score, lower is better, FUP 12 Mo) was **0.79**	MD **0.05 lower** (0.35 lower to 0.25 higher) No clinically important difference	MID= 0.5 (established MID)
Quality of life (paediatric asthma-QOL-q, change score, higher is better)	90 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[a,b,d]	-	The mean quality of life (paediatric asthma-QOL-q, change score, higher is better, FUP 12 Mo) was **6.05**	MD **0.05 lower** (0.5 lower to 0.4 higher) No clinically important difference	MID= 0.5 (established MID)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care (Dutch guidelines) in CYP	Risk difference with ACQ-feedback + self-management	Comments
Dose of regular asthma therapy / preventer medication (daily ICS dose, change score, lower is better)	90 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[a,b,e]	-	The mean dose of regular asthma therapy / preventer medication (daily ICS dose, change score, lower is better, FUP 12 Mo) was **265** mcg	MD **14 mcg higher** (75 lower to 103 higher) No clinically important difference	MID=107.7 (calculated using 95%CI of mean difference to calculate SD/2)
Symptoms (symptom free days, change score, higher is better)	90 (1 RCT) Follow-up: 12 months	⊕◯◯◯ Very low[a,b,f]	-	The mean symptoms (symptom free days, change score, higher is better, FUP 12 Mo) was **80**	MD **4 higher** (9.7 lower to 17.7 higher) No clinically important difference	MID=16.7 (calculated using 95%CI of mean difference to calculate SD/2)

a. Downgraded by two increments because study at high risk of bias (>10% differential rate of missing data between groups at 12 months; subjective self-reported outcome & lack of blinding; No information on pre-specified analyses)

b. Downgraded by two increments for indirectness for population (mixed age group including people >16 years) and intervention (intervention group received additional web-based and face-to-face education sessions).

c. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs (MID for dichotomous outcomes: 0.8 and 1.25)

d. Based on MID for ACQ& pediatric QoL in children and young people: 0.5 for both measures

e. Downgraded by one increment for imprecision because the confidence interval crossed one MID (MID calculated using 95%CI of mean difference to calculate SD =215.34; MID=SD/2=107.7)

f. Downgraded by 1 increment as the confidence interval crossed one MID (MID calculated using 95% CI of the mean difference by calculating the standard error and converting to SD; MID:SD/2= 16.7)

Table 9: Clinical evidence summary Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) vs usual care in children and young people

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care	Risk difference with C-ACT-feedback + self-management	Comments
Unscheduled healthcare utilisation (visits to emergency department, final score, lower is better)	210 (1 RCT) Follow-up: 16 months	⊕◯◯◯ Very low[a,b,c]	**RR 1.50** (0.26 to 8.79)	19 per 1,000	**10 more per 1,000** (14 fewer to 148 more) No clinically important difference	MID (imprecision) = 0.8 – 1.25 MID (clinical importance) = 30 per 1000
Hospital admissions (final score, lower is better)	210 (1 RCT) Follow-up: 16 months	⊕◯◯◯ Very low[a,b,c]	**RR 0.50** (0.05 to 5.43)	19 per 1,000	**10 fewer per 1,000** (18 fewer to 84 more) No clinically important difference	MID (imprecision) = 0.8 – 1.25 MID (clinical importance) = 30 per 1000

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care	Risk difference with C-ACT-feedback + self-management	Comments
Unscheduled healthcare utilisation (unscheduled visits to outpatients, final score, lower is better)	210 (1 RCT) Follow-up: 16 months	⊕◯◯◯ Very low[a,b,d]	**RR 1.35** (0.88 to 2.07)	248 per 1,000	**87 more per 1,000** (30 fewer to 265 more) Clinically important difference favouring usual care	MID (imprecision) = 0.8 – 1.25 MID (clinical importance) = 100 per 1000
Asthma exacerbations (final score, lower is better)	210 (1 RCT) Follow-up: 16 months	⊕◯◯◯ Very low[a,b,c]	**RR 0.89** (0.48 to 1.65)	171 per 1,000	**19 fewer per 1,000** (89 fewer to 111 more) No clinically important difference	MID (imprecision) = 0.8 – 1.25 MID (clinical importance) = 30 per 1000
Asthma control (ACT, range 5 to 25, final score; higher is better)	210 (1 RCT) Follow-up: 16 months	⊕◯◯◯ Very low[b,e,f]	-	The mean asthma control (ACT) was **16**	MD **0.8 higher** (0.04 lower to 1.64 higher) No clinically important difference	MID= 3 (established MID)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		
				Risk with usual care	Risk difference with C-ACT-feedback + self-management	Comments
Asthma control (C-ACT, range 0 to 27, final score; higher is better)	210 (1 RCT) Follow-up: 16 months	⊕◯◯◯ Very low[b,e,g]	-	The mean asthma control (C-ACT) was **22.3**	MD **1.4 higher** (0.48 higher to 2.32 higher) No clinically important difference	MID= 2 (established MID)
Lung function (FEV1, % predicted, final score, higher is better)	210 (1 RCT) Follow-up: 16 months	⊕◯◯◯ Very low[b,h,i]	-	The mean lung function (FEV1, % predicted, final score; FUP 16 Mo) was **92.3**	MD **0.2 lower** (4.02 lower to 3.62 higher) No clinically important difference	MID=7.05 (calculated as baseline SD/2)
Symptoms (symptom free days, final score; higher is better)	210 (1 RCT) Follow-up: 16 months	⊕◯◯◯ Very low[e,i,j]	-	The mean symptoms (symptom free days, final score; higher is better, FUP 16 Mo) was **27.3**	MD **1.2 higher** (0.44 higher to 1.96 higher) No clinically important difference	MID=2.25 (calculated as baseline SD/2)

a. Downgraded by 2 increments as the evidence was at very high risk of bias (due to lack of information about outcome assessment, adherence, and pre-specified analyses. Intervention-related deviations from protocol also possible due to availability of FEV1 and FENO to treating physicians in both arms)

b. Downgraded by one increment for intervention indirectness because intervention included web-based education as well as C-ACT monitoring

c. Downgraded by 2 increments for imprecision because the confidence interval crossed both MIDs (MIDs for dichotomous outcomes: 0.8 and 1.25)

d. Downgraded by one increment because the confidence interval crossed one MID (MIDs for dichotomous outcomes: 0.8 and 1.25)

e. Intervention-related deviations from protocol possible due to availability of FEV1 and FENO to treating physicians; no information about protocol, missing data or adherence; outcome based on self-reports (unblinded)

f. Published MID for ACT=3

g. Downgraded by one increment for imprecision because confidence interval crosses one MID (published MID for C-ACT=2)

h. Unblinded outcome assessors, no information about missing data, protocol or adherence; intervention-related deviations from protocol possible due to availability of FEV1 and FENO to treating physicians

i. MID for FEV1 % predicted calculated using baseline SD/2= 7.05; for symptom free days: 2.25

j. Downgraded by two increments for intervention indirectness (intervention included web-based education as well as C-ACT monitoring) and outcome indirectness (based on C-ACT)

See Appendix F for full GRADE tables.

1.1.7 Economic evidence

1.1.7.1 Included studies

No health economic studies were included.

1.1.7.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G.

1.1.8 Summary of included economic evidence

None.

1.1.9 Economic model

This area was not prioritised for new cost-effectiveness analysis.

1.1.10 Evidence statements

1.1.10.1 Economic

- No relevant economic evaluations were identified.

1.2 The committee's discussion and interpretation of the evidence

1.2.1 The outcomes that matter most

The Committee considered the outcomes of mortality, unscheduled healthcare utilisation, asthma exacerbations, asthma control, quality of life, lung function, symptoms, dose of regular asthma therapy/preventer medication, reliever/rescue medication use and time off school or work. For the purposes of decision making, all outcomes were considered equally important and were rated as critical.

For this review there was no outcome data for mortality, time off school or work or asthma control based on the Royal College of Physicians (RCP) 3 questions questionnaire.

Asthma exacerbations were defined in the protocol as exacerbations requiring oral corticosteroid use. Definitions for exacerbations varied across studies: Mehuys (2008) and van der Meer (2009) defined exacerbations as severe exacerbations requiring treatment with oral glucocorticoids or an emergency department visit or hospital admission due to asthma. Rikkers (2012) defined exacerbations as deterioration in asthma that required oral steroids for 3 days or more as reported in 3-monthly questionnaires. Van den Wijngaart et al (2017) defined asthma exacerbations as exacerbations treated with systemic corticosteroids. Ye et al (2021) did not report a definition for moderate/severe exacerbations.

Asthma control or quality of life measured by questionnaire [for example Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), Asthma Quality of Life Questionnaire (AQLQ) and Paediatric Asthma Quality of Life Questionnaire (PAQLQ)] are preferably reported as continuous outcomes, in line with the review protocol.

Some outcomes were identified in the review that were related to, but not identical to, those pre-specified in the protocol, and have therefore been downgraded due to indirectness of the outcome: number of asthma medications; number of asthma controller medications.

1.2.2 The quality of the evidence

No evidence was found in children aged 1-5 years old.

Using GRADE criteria, the quality of the evidence for most outcomes in adults was low or very low. Evidence was downgraded due to risk of bias (including risk of selection bias, lack of details on randomisation and imbalance in characteristics at baseline, unclear information on missing data and issues with analyses) and indirectness of the intervention (the intervention included education as well as monitoring by symptom diary/questionnaire). This evidence was further downgraded due to imprecision when the confidence intervals around the effect estimate crossed MIDs (minimal clinically important differences).

Evidence for three outcomes (number of emergency room visits; number of outpatient visits and ACT) from Pool et al (2017) was moderate in certainty; this study was at low risk of bias but was downgraded due to indirectness of intervention. An unvalidated asthma symptom questionnaire was used that included questions on asthma care as well as symptoms. Two outcomes (number of asthma medications and number of asthma controller medications) were further downgraded due to indirectness of outcomes (these were related, but not identical to, outcomes specified in the review protocol) and were therefore graded as being of low certainty.

Using GRADE criteria, the quality of the evidence for all outcomes in children and young people was very low. This is because all included studies in children were at very high risk of bias. Issues included: lack of blinding and outcomes self-reported; unbalanced missing data

across trial arms; use of a dichotomous outcome instead of a continuous outcome and lack of information reported on pre-specified analyses. Evidence was further downgraded due to indirectness of the intervention (which also included education as well as symptom diary/questionnaire monitoring) and outcome (when symptom-free days were calculated from the Childhood Asthma Control Test, (C)ACT). Several outcomes were further downgraded due to imprecision when the confidence intervals around the effect estimate crossed MIDs.

The potential bias and widespread uncertainty in the evidence, for both children and young people, and adults, influenced the Committee's view of the evidence. They considered there to be insufficient evidence to support a strong statement on the use of symptom diaries/questionnaires for monitoring of asthma. The wide variability in route by which asthma therapy/management was adjusted in response to symptom diaries/questionnaires in the trial interventions (ranging from healthcare professionals directly adjustment treatment to use of algorithms to direct self-management) was an additional concern. The committee also noted that, although the studies generally used validated questionnaires which will reliably reflect asthma control, the action points for adjusting treatment in response to questionnaire results were not validated.

1.2.3 Benefits and harms

When assessing the clinically significant impact of the evidence, the GC agreed an approach for use of MIDs. For continuous outcomes, published MIDs were applied for ACT (3); (C)ACT (2); ACQ (0.5); AQLQ (0.5); and FEV1 (L) (0.23). In the absence of published MIDs, default calculations for MID were applied based on baseline SD (where available), for the rest of the continuous outcomes. For dichotomous outcomes, a threshold of 100/1000 people for changes in absolute effects was applied when assessing unscheduled visits to outpatients. A threshold of 30/1000 people for changes in absolute effects was applied when assessing the following outcomes: asthma exacerbations; emergency department visits; and hospital admissions. This is because the committee considered small differences between the intervention and comparison groups likely to be important for these outcomes.

As the study interventions varied widely, and a number were downgraded due to indirectness, no pooling of studies was conducted; assessment of each outcome was therefore based on a single RCT.

Evidence in adults

Evidence from one RCT showed there was no clinically important difference of ACT-monitoring (plus education) compared to usual care in adults in terms of asthma control (ACT), quality of life (AQLQ), rescue medication use; lung function (morning PEF % predicted) or asthma exacerbations (severe exacerbations). However, this RCT, which involved asthma-management advice delivered by a pharmacist based on ACT score, showed a clinically important benefit in unscheduled healthcare utilisation (emergency room visits or hospitalisation) for those who received the intervention.

Evidence from one RCT showed there was no clinically important difference of ACT guided treatment compared to usual care in terms of asthma exacerbations, asthma control (ACT), lung function (FEV1% predicted) or quality of life (AQLQ) in adults.

Evidence from one RCT showed a clinically important benefit of ACT monitoring compared to usual care for lung function (FEV1 % predicted and PEF % predicted) in adults.

Similarly, another RCT showed a clinically important benefit of ACQ monitoring (plus education) compared to usual care for lung function (FEV1 L). However, this RCT also showed no clinically important difference for a range of outcomes: asthma exacerbations; asthma control (ACQ); quality of life (AQLQ); symptoms (symptom-free days); and dose of regular asthma therapy/preventer medication (ICS) use.

Where there was evidence of clinically important benefit in adults, it was predominantly for objective outcomes on lung function in two RCTs, but the certainty of the evidence was very

low. However, one further RCT provided moderate certainty evidence for a comparison of online symptom monitoring versus usual care and reported no clinically importance differences in a wide range outcomes [unscheduled healthcare utilisation (number of visits to emergency room, number of outpatient visits)] asthma control (ACT), dose of regular asthma therapy/preventer medication (number of asthma medications and number of asthma controller medications)].

Overall, the Committee considered the relatively small number of clinically important benefits identified in adults, together with concerns over the quality of the evidence, did not support regular monitoring with symptom questionnaires at the frequencies used in the studies.

Evidence in children and young people

Evidence from children and young people showed no clinically important benefit of asthma symptom/questionnaire monitoring for the outcomes included.

One RCT showed no clinically important difference of ACQ monitoring (plus education) compared to usual care for asthma exacerbations, asthma control (ACQ), quality of life (paediatric AQLQ), dose of regular asthma therapy/preventer medication (ICS dose) and symptoms (symptom-free days).

Evidence from one RCT reported on (C)ACT monitoring (plus education) compared to usual care and showed no clinically important difference for unscheduled healthcare utilisation (emergency department visits and hospital admissions) and) asthma exacerbations, lung function (FEV1 % predicted), asthma control [ACT or (C)ACT], or symptoms (symptom-free days). There was a clinically important difference favouring usual care for unscheduled healthcare utilisation (visits to outpatients).

Overall, the Committee considered the evidence-base in children and young people to be to be very limited. They noted the lack of clinically important difference in outcomes, the small number of studies available and the concerns about the certainty in the evidence.

1.2.4 Cost effectiveness and resource use

No relevant published health economic analyses were identified for this review. The committee made a recommendation to use a validated questionnaire to assess asthma control in annual reviews. Asthma control questionnaires are already recommended as part of annual reviews for asthma, so no change in practice or additional resource use is anticipated.

1.2.5 Other factors the committee took into account

The Committee discussed the different contexts in which monitoring of asthma control by symptoms/questionnaire could take place, namely in a clinical setting (where the results are directly used by physicians or other clinical professionals to adjust treatment or therapy) or in self-management, where the results are used directly by patients to support their self-management of asthma. By consensus, the Committee agreed that an appropriate alternative focus for self-management symptom monitoring is a personalised asthma action plan.

Although the evidence reviewed did not support a role for symptom diaries/questionnaires in routine monitoring, the Committee did not want to infer that such diaries or questionnaires had no use at all. The questionnaires have been formally validated, and the committee agreed that asking the focussed questions within them is a much better way of assessing asthma control than a general “how have you been?” approach. Furthermore, the committee were aware of evidence that asthma control questionnaires are predictive of future risk of severe asthma attacks. They noted that the study protocols employed the questionnaires

over short periods of time (they were filled in at weekly intervals in one study) and while they concluded that the evidence showed this was not a worthwhile exercise, they agreed by consensus that filling in a questionnaire at a person's regular review (which will be an annual review in most people with asthma) should provide useful information. It was also suggested that it would be useful to fill in a questionnaire when any treatment change was being contemplated, to provide an objective baseline against which any improvement could be measured. However, the committee recognised that this was a separate issue from that of regular monitoring and did not make a recommendation on this point.

In keeping with the above, the Lay Committee members noted that validated questionnaires such as ACT and ACQ are chronic management tools that require the patient to recall symptoms over several weeks, rather than an acute management tool (to assess symptoms on a day-to-day basis). The recall element of the questionnaires can be difficult to complete. This view further supports the Committee's agreement that daily or weekly monitoring of asthma should not rely on symptom questionnaires.

No significant harms were reported, and the committee therefore did not recommend against using the questionnaires over short periods of time if the person with asthma and the relevant healthcare professional agreed that this served a useful purpose.

1.2.6 Recommendations supported by this evidence review

This evidence review supports recommendation 1.5.2.

1.3 References

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Appendices

Appendix A Review protocols

Review protocol for symptom diary for monitoring

ID	Field	Content
0.	PROSPERO registration number	CRD42023443030
1.	Review title	Symptom scores / diaries or validated questionnaires measuring symptom control to monitor asthma.
2.	Review question	In people with asthma, what is the clinical and cost-effectiveness of using symptom scores / diaries or validated questionnaires measuring symptom control (eg ACT, ACQ, CACT, RCP 3 questions) and/or health related quality of life (eg AQLQ, PAQLQ) to monitor asthma?
3.	Objective	To evaluate the clinical and cost-effectiveness of using symptom scores / diaries or validated questionnaires that measure symptoms or HRQoL to monitor asthma? Questionnaires that measure current disease impact and future risk of exacerbation; does measuring symptom control and QoL in asthma patients, improve patient outcomes?
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos Searches will be restricted by:

		• English language studies • Human studies • Date- year 2014 onwards Other searches: • Inclusion lists of systematic reviews The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
5.	Condition or domain being studied	Asthma
6.	Population	Inclusion: People with a diagnosis of asthma (physician diagnosis/definitive diagnosis by objective test) All ages, stratified into the following 3 different groups: • Children (<5 years old) • Children/young people (5-16 years old) • Adults (>17 years old) Exclusion:

		Severe asthma

7.	Intervention	Monitoring the following, and using the outcomes of scores/questionnaires to adjust management/therapy according to physician decision or personalised treatment plan
		
		• Symptom scores or diaries
		• Symptom/control questionnaires
		  ○ Asthma Control Test, ACT (including caregivers or paediatric version, CACT)
		  ○ Asthma Control Questionnaire, ACQ (including mini ACQ or paediatric ACQ)
		  ○ RCP 3 questions
		• Quality of life questionnaires (asthma specific)
		  ○ Health-related QoL
		Asthma Quality of Life Questionnaire, AQLQ (including paeds version, PAQLQ)

8.	Comparator	Comparison of adjustment of asthma therapy based on symptom scores or questionnaires to: • Usual care: e.g. clinical symptoms (with/without spirometry/PEF) according to guidelines (including BTS/SIGN, GINA) Comparison of adjustment of asthma therapy based on: • Symptom scores or diaries vs questionnaires • Control questionnaire vs other control questionnaire • QOL questionnaire vs asthma control questionnaire
9.	Types of study to be included	• RCTs • SRs of RCTs
10.	Other exclusion criteria	• Observational cohort studies and NRS unless limited evidence from RCTs • Studies not in English • Occupational asthma /allergens
11.	Context	Primary, secondary and community care settings

12.	Primary outcomes (critical outcomes)	• All outcomes are considered equally important for decision making and therefore have all been rated as critical: • Mortality • Unscheduled healthcare utilisation (ED/A&E visit; hospital admissions; GP out of hours or walk-in centre) • Severe asthma exacerbations (defined as asthma exacerbations requiring oral corticosteroid use-dichotomous outcome at ≥6 months, latest time point if more than one) • Asthma control assessed by a validated questionnaire (ACQ, ACT; CACT; PACQ; RCP-3, continuous outcome at ≥3 months) • Quality of life (QoL) (validated scale, including asthma specific questionnaires AQLQ; health related, pAQLQ; St George's respiratory questionnaire; continuous outcome at ≥3 months) • Lung function (FEV1, PEF) • Symptoms (annual symptom free days) • Dose of regular asthma therapy / preventer medication (ICS dose) • Reliever/ Rescue medication use (SABA use – continuous outcome at ≥3 months) • Time off school or work
13.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately

		• a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary. Study investigators may be contacted for missing data where time and resources allow.
14.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For Intervention reviews the following checklist will be used according to study design being assessed: • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
15.	Strategy for data synthesis	Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects. • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias will be considered with the guideline committee, and if suspected will be tested for when there are more than 5 studies for that outcome.

		The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.		
16.	Analysis of sub-groups	Subgroups that will be investigated if heterogeneity is present: • Ethnic groups (e.g. south Asians, African Americans, Hispanics) • Education levels • Language (non-English speaking)		
17.	Type and method of review	☒	Intervention	
		☐	Diagnostic	
		☐	Prognostic	
		☐	Qualitative	
		☐	Epidemiologic	
		☐	Service Delivery	
		☒	Other – monitoring	
18.	Language	English		
19.	Country	England		
20.	Anticipated or actual start date			
21.	Anticipated completion date	31 July 2024		
22.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	☑	☑

		Piloting of the study selection process	☐	☐
		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
23.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail asthmachronicmanagement@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Centre.		
24.	Review team members	From the National Guideline Centre: Bernard Higgins Sharon Swain Melina Vasileiou Qudsia Malik		

		Toby Sands Alfredo Mariani Lina Gulhane Amy Crisp
25.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
26.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10186
28.	Other registration details	N/A
29.	Reference/URL for published protocol	
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.

31.	Keywords	Asthma	
32.	Details of existing review of same topic by same authors	N/A	
33.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
34.	Additional information	N/A	
35.	Details of final publication	www.nice.org.uk	

Health economic review protocol

Table 10: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.

Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2006, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).(National Institute for Health and Care Excellence) **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland).

	• Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2006 or later but that depend on unit costs and resource data entirely or predominantly from before 2006 will be rated as 'Not applicable'. • Studies published before 2006 be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B Literature search strategies

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 10: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	2014 – 28 Dec 2023	Randomised controlled trials Systematic review studies Validation Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	2014 – 29 Dec 2023	Randomised controlled trials Systematic review studies Validation Exclusions (conference abstracts, animal studies, letters, comments, editorials, case studies/reports) English language
The Cochrane Library (Wiley)	Cochrane Reviews 2014 to 2023 Issue 12 of 12 CENTRAL to 2023 Issue 12 of 12	Exclusions (clinical trials, conference abstracts)
Epistemonikos (The Epistemonikos Foundation)	2014 to 28 Dec 2023	Exclusions (Cochrane reviews) English language

Medline (Ovid) search terms

1.	exp Asthma/
2.	asthma*.ti,ab.
3.	1 or 2
4.	letter/
5.	editorial/
6.	news/

7.	exp historical article/
8.	Anecdotes as Topic/
9.	comment/
10.	case reports/
11.	(letter or comment*).ti.
12.	or/4-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animals/ not humans/
16.	exp Animals, Laboratory/
17.	exp Animal Experimentation/
18.	exp Models, Animal/
19.	exp Rodentia/
20.	(rat or rats or mouse or mice or rodent*).ti.
21.	or/14-20
22.	3 not 21
23.	limit 22 to English language
24.	(diary or diaries).ti,ab,kf.
25.	(symptom* adj2 scor*).ti,ab,kf.
26.	(CACT or "C ACT" or ATAQ or ACQ 6 or ACQ 7 or ACQ? or PACQ or RCP-3 or RCP3 or PAQLQ or AQLQ or PACQLQ or QOL).ti,ab,kf.
27.	(("quality of life" or control* or test* or assessment) adj5 (questionnaire* or survey*)).ti,ab,kf.
28.	(control* adj3 test*).ti,ab,kf.
29.	("rcp3 question*" or "rcp 3 question*" or "rcp three question*" or "royal college of physician* 3 question*" or "royal college of physician* three question*" or "St George* respiratory question*").ti,ab,kf.
30.	or/24-29
31.	23 and 30
32.	randomized controlled trial.pt.
33.	controlled clinical trial.pt.
34.	randomi#ed.ab.
35.	placebo.ab.
36.	randomly.ab.
37.	clinical trials as topic.sh.
38.	trial.ti.
39.	or/32-38
40.	Meta-Analysis/
41.	Meta-Analysis as Topic/
42.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
43.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
44.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
45.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.

46.	(search* adj4 literature).ab.
47.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
48.	cochrane.jw.
49.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
50.	or/40-49
51.	Validation Studies as Topic/
52.	reproducibility of results/
53.	validation study.pt.
54.	(valid* or reliab*).ti,ab.
55.	observer variation/
56.	((inter* or intra* or observer* or rater*) adj3 (bias* or variation* or agree* or concordan*)).ti,ab.
57.	or/51-56
58.	31 and (39 or 50 or 57)

Embase (Ovid) search terms

1.	exp Asthma/
2.	asthma*.ti,ab.
3.	1 or 2
4.	letter.pt. or letter/
5.	note.pt.
6.	editorial.pt.
7.	case report/ or case study/
8.	(letter or comment*).ti.
9.	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
10.	or/4-9
11.	randomized controlled trial/ or random*.ti,ab.
12.	10 not 11
13.	animal/ not human/
14.	nonhuman/
15.	exp Animal Experiment/
16.	exp Experimental Animal/
17.	animal model/
18.	exp Rodent/
19.	(rat or rats or mouse or mice or rodent*).ti.
20.	or/12-19
21.	3 not 20
22.	limit 21 to English language
23.	(diary or diaries).ti,ab,kf.
24.	(symptom* adj2 scor*).ti,ab,kf.
25.	(CACT or "C ACT" or ATAQ or ACQ 6 or ACQ 7 or ACQ? or PACQ or RCP-3 or RCP3 or PAQLQ or AQLQ or PACQLQ or QOL).ti,ab,kf.

26.	(("quality of life" or control* or test* or assessment) adj5 (questionnaire* or survey*)).ti,ab,kf.
27.	(control* adj3 test*).ti,ab,kf.
28.	("rcp3 question*" or "rcp 3 question*" or "rcp three question*" or "royal college of physician* 3 question*" or "royal college of physician* three question*" or "St George* respiratory question*").ti,ab,kf.
29.	or/23-28
30.	22 and 29
31.	random*.ti,ab.
32.	factorial*.ti,ab.
33.	(crossover* or cross over*).ti,ab.
34.	((doubl* or singl*) adj blind*).ti,ab.
35.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
36.	crossover procedure/
37.	single blind procedure/
38.	randomized controlled trial/
39.	double blind procedure/
40.	or/31-39
41.	Systematic Review/
42.	Meta-Analysis/
43.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
44.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
45.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
46.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
47.	(search* adj4 literature).ab.
48.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
49.	cochrane.jw.
50.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
51.	or/41-50
52.	validation study/
53.	reproducibility of results/
54.	(valid* or reliab*).ti,ab.
55.	observer variation/
56.	((inter* or intra* or observer* or rater*) adj3 (bias* or variation* or agree* or concordan*)).ti,ab.
57.	or/52-56
58.	30 and (40 or 51 or 57)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Asthma] explode all trees
#2.	asthma*:ti,ab
#3.	#1 or #2

#4.	((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or eudract* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp)):an
#5.	#3 not #4
#6.	conference:pt
#7.	#5 not #6
#8.	(diary or diaries):ti,ab
#9.	(symptom* near/2 scor*):ti,ab
#10.	(CACT or "C ACT" or ATAQ or ACQ 6 or ACQ 7 or ACQ? or PACQ or RCP-3 or RCP3 or PAQLQ or AQLQ or PACQLQ):ti,ab
#11.	(("quality of life" or control* or test* or assessment) near/5 (questionnaire* or survey*)):ti,ab
#12.	(control* near/3 test*):ti,ab
#13.	("rcp3" or "rcp 3" or "rcp three" or "royal college of physicians" or "St Georges" or "St George's") near/2 questionnaire*:ti,ab
#14.	(or #8-#13)
#15.	#7 and #14 with Cochrane Library publication date Between Jan 2014 and Dec 2023

Epistemonikos search terms

1.	(title:(asthma*) OR abstract:(asthma*)) AND (title:(diary OR diaries OR (symptom* adj2 scor*) OR CACT OR "C ACT" OR ATAQ OR ACQ 6 OR ACQ 7 OR ACQ? OR PACQ OR "RCP-3" OR RCP3 OR PAQLQ OR AQLQ OR PACQLQ OR QOL OR (("quality of life" OR control* OR test* OR assessment) adj5 (questionnaire* OR survey*)) OR (control* adj3 test*) OR "rcp3 questionnaire" OR "rcp 3 questionnaire" OR "rcp three questionnaire" OR "royal college of physicians 3 questionnaire" OR "royal college of physicians three questionnaire" OR "St Georges respiratory questionnaire") OR abstract:(diary OR diaries OR (symptom* adj2 scor*) OR CACT OR "C ACT" OR ATAQ OR ACQ 6 OR ACQ 7 OR ACQ? OR PACQ OR "RCP-3" OR RCP3 OR PAQLQ OR AQLQ OR PACQLQ OR QOL OR (("quality of life" OR control* OR test* OR assessment) adj5 (questionnaire* OR survey*)) OR (control* adj3 test*) OR "rcp3 questionnaire" OR "rcp 3 questionnaire" OR "rcp three questionnaire" OR "royal college of physicians 3 questionnaire" OR "royal college of physicians three questionnaire" OR "St Georges respiratory questionnaire"))

B.2 Health economic literature search strategy

Health economic evidence was identified by conducting searches using terms for a broad Asthma population. The following databases were searched: NHS Economic Evaluation Database (NHS EED - this ceased to be updated after 31st March 2015), Health Technology Assessment database (HTA - this ceased to be updated from 31st March 2018) and The International Network of Agencies for Health Technology Assessment (INAHTA). Searches for recent evidence were run on Medline and Embase from 2014 onwards for health economics, and all years for quality-of-life studies and modelling.

Table 11: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 29 Dec 2023	Health economics studies Quality of life studies Modelling Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
	Quality of Life 1946 – 29 Dec 2023	
	Modelling 1946 – 29 Dec 2023	
Embase (OVID)	Health Economics 1 January 2014 – 29 Dec 2023	Health economics studies Quality of life studies Modelling Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
	Quality of Life 1974 – 29 Dec 2023	
	Modelling 1974 – 29 Dec 2023	
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception - 29 Dec 2023	English language

Medline (Ovid) search terms

1.	exp Asthma/
2.	asthma*.ti,ab.
3.	1 or 2
4.	letter/
5.	editorial/
6.	news/

7.	exp historical article/
8.	Anecdotes as Topic/
9.	comment/
10.	case reports/
11.	(letter or comment*).ti.
12.	or/4-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animals/ not humans/
16.	exp Animals, Laboratory/
17.	exp Animal Experimentation/
18.	exp Models, Animal/
19.	exp Rodentia/
20.	(rat or rats or mouse or mice or rodent*).ti.
21.	or/14-20
22.	3 not 21
23.	limit 22 to English language
24.	quality-adjusted life years/
25.	sickness impact profile/
26.	(quality adj2 (wellbeing or well being)).ti,ab.
27.	sickness impact profile.ti,ab.
28.	disability adjusted life.ti,ab.
29.	(qal* or qtime* or qwb* or daly*).ti,ab.
30.	(euroqol* or eq5d* or eq 5*).ti,ab.
31.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
32.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
33.	(hui or hui1 or hui2 or hui3).ti,ab.
34.	(health* year* equivalent* or hye or hyes).ti,ab.
35.	discrete choice*.ti,ab.
36.	rosser.ti,ab.
37.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
38.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
39.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
40.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
41.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
42.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
43.	or/24-42
44.	exp models, economic/
45.	*Models, Theoretical/

46.	*Models, Organizational/
47.	markov chains/
48.	monte carlo method/
49.	exp Decision Theory/
50.	(markov* or monte carlo).ti,ab.
51.	econom* model*.ti,ab.
52.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
53.	or/44-52
54.	Economics/
55.	Value of life/
56.	exp "Costs and Cost Analysis"/
57.	exp Economics, Hospital/
58.	exp Economics, Medical/
59.	Economics, Nursing/
60.	Economics, Pharmaceutical/
61.	exp "Fees and Charges"/
62.	exp Budgets/
63.	budget*.ti,ab.
64.	cost*.ti.
65.	(economic* or pharmaco?economic*).ti.
66.	(price* or pricing*).ti,ab.
67.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
68.	(financ* or fee or fees).ti,ab.
69.	(value adj2 (money or monetary)).ti,ab.
70.	or/54-69
71.	23 and 43
72.	23 and 53
73.	23 and 70

Embase (Ovid) search terms

1.	exp Asthma/
2.	asthma*.ti,ab.
3.	1 or 2
4.	letter.pt. or letter/
5.	note.pt.
6.	editorial.pt.
7.	case report/ or case study/
8.	(letter or comment*).ti.
9.	(conference abstract or conference paper).pt.

10.	or/4-9
11.	randomized controlled trial/ or random*.ti,ab.
12.	10 not 11
13.	animal/ not human/
14.	nonhuman/
15.	exp Animal Experiment/
16.	exp Experimental Animal/
17.	animal model/
18.	exp Rodent/
19.	(rat or rats or mouse or mice or rodent*).ti.
20.	or/12-19
21.	3 not 20
22.	limit 21 to English language
23.	quality adjusted life year/
24.	"quality of life index"/
25.	short form 12/ or short form 20/ or short form 36/ or short form 8/
26.	sickness impact profile/
27.	(quality adj2 (wellbeing or well being)).ti,ab.
28.	sickness impact profile.ti,ab.
29.	disability adjusted life.ti,ab.
30.	(qal* or qtime* or qwb* or daly*).ti,ab.
31.	(euroqol* or eq5d* or eq 5*).ti,ab.
32.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
33.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
34.	(hui or hui1 or hui2 or hui3).ti,ab.
35.	(health* year* equivalent* or hye or hyes).ti,ab.
36.	discrete choice*.ti,ab.
37.	rosser.ti,ab.
38.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
39.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
40.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
41.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
42.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
43.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
44.	or/23-43
45.	statistical model/
46.	exp economic aspect/
47.	45 and 46
48.	*theoretical model/

49.	*nonbiological model/
50.	stochastic model/
51.	decision theory/
52.	decision tree/
53.	monte carlo method/
54.	(markov* or monte carlo).ti,ab.
55.	econom* model*.ti,ab.
56.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
57.	or/47-56
58.	health economics/
59.	exp economic evaluation/
60.	exp health care cost/
61.	exp fee/
62.	budget/
63.	funding/
64.	budget*.ti,ab.
65.	cost*.ti.
66.	(economic* or pharmaco?economic*).ti.
67.	(price* or pricing*).ti,ab.
68.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
69.	(financ* or fee or fees).ti,ab.
70.	(value adj2 (money or monetary)).ti,ab.
71.	or/58-70
72.	22 and 44
73.	22 and 57
74.	22 and 71

NHS EED and HTA (CRD) search terms

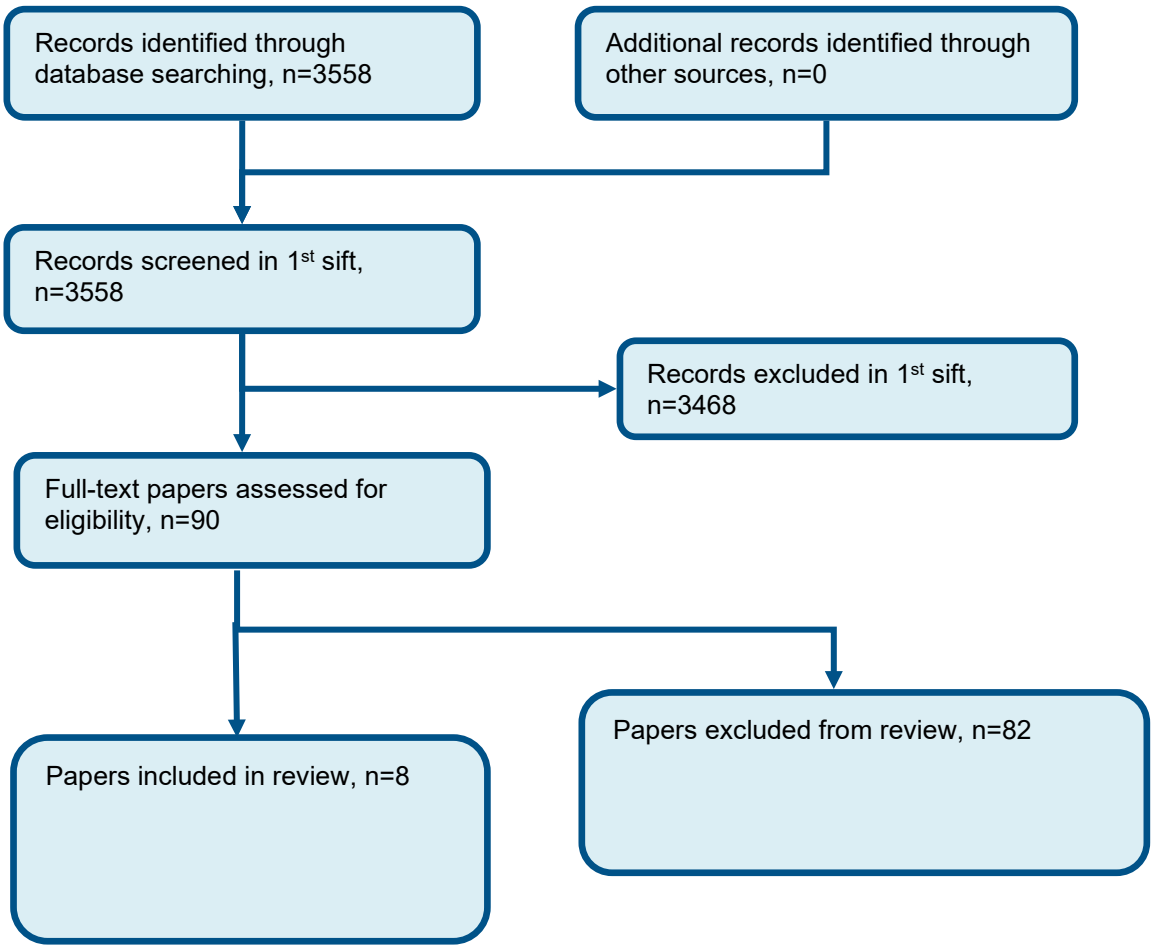
#1.	MeSH DESCRIPTOR Asthma EXPLODE ALL TREES
#2.	(asthma*)
#3.	#1 OR #2

INAHTA search terms

1.	(Asthma)[mh] OR (asthma*)[Title] OR (asthma*)[abs]

Appendix C Effectiveness evidence study selection

Figure 1: Flow chart of clinical study selection for the review of Symptom diary



Appendix D Effectiveness evidence

Mehuys, 2008

Bibliographic Reference	Mehuys, E.; Van Bortel, L.; De Bolle, L.; Van Tongelen, I.; Annemans, L.; Remon, J. P.; Brusselle, G.; Effectiveness of pharmacist intervention for asthma control improvement; Eur Respir J; 2008; vol. 31 (no. 4); 790-9

Study details

Study type	Randomised controlled trial (RCT)
Study location	Flanders, Belgium
Study setting	66 randomly selected pharmacies.
Study dates	January 2006 and October 2006 (patient recruitment period: January–April 2006)
Sources of funding	not specified.
Inclusion criteria	To be eligible, patients were required to carry a prescription for asthma medication (R03, Anatomical Therapeutic Chemical classification); aged between 18–50 yrs; being treated for asthma for >12 months; ‘‘using’’ controller medication; and 4) regular visitor to the pharmacy. All patients entering the run-in phase had to keep an asthma diary for 2 weeks. At the end of the run-in phase, patients were eligible for randomisation if they returned to the pharmacy with a diary that was completed for ≥90%.
Exclusion criteria	Exclusion criteria included a smoking history of .10 pack-yrs, suffering from another severe disease (e.g. cancer) and having an ACT score at screening of ,15 (indicating seriously uncontrolled asthma; for ethical reasons, these patients were

	immediately referred to their general practitioner (GP) or respiratory specialist) or equalling 25 (indicating complete asthma control; no room for improvement).
Recruitment / selection of participants	Consecutive; In consecutive order, patients visiting the pharmacy were invited to participate in the study when they fulfilled the inclusion criteria.
Intervention(s)	Before the start of the present study, the participating pharmacists had a training session about asthma (pathophysiology), its non-pharmacological and pharmacological treatment (GINA guidelines) and about the use of the study protocol. Patients in the intervention group received a protocol-defined intervention at the start of the study and at the 1- and 3-month follow-up visit: Session 1: at start of intervention period Personal education from the pharmacist about the following topics: Correct use of the inhaler device, Understanding asthma (using the Dutch version of the Global Initiative for Asthma Patient Guide ‘‘What You and Your Family Can Do About Asthma’’) , Symptoms, Triggers, Early warnings Understanding asthma medication, Difference between controller and reliever medication, Facilitate adherence to controller medication, Smoking cessation (if relevant). Sessions 2 and 3: at 1-month and 3-month follow-up, respectively Pharmacist advice based on the ACT score of the patient: If ACT score <15 (‘‘uncontrolled’’ asthma): immediate referral to general practitioner or respiratory specialist If ACT score 15–19 (‘‘insufficiently controlled’’ asthma): review inhalation technique and check controller medication adherence If ACT score ≥20 (‘‘well-controlled’’ asthma): no specific advice needed, inform patient asthma is well controlled
Population subgroups	
Ethnicity	Not reported/unclear

Education Level	Mixed
Language of Participants	Not reported/unclear
Comparator	Patients in the control group received usual pharmacist care; No education at start of study as in intervention group.
Number of participants	201 randomised (150 analysed)
Duration of follow-up	6 months; The study had a 2-week run-in period, followed by 6 months of randomised treatment. There were five scheduled visits to the pharmacy as follows: at the start of the run-in period, at randomisation and at 1, 3 and 6 months after randomisation.
Indirectness	Intervention included education as well as ACT monitoring (intervention indirectness)
Additional comments	The primary outcome, i.e. the ACT score, was analysed using an intention-to-treat approach. A linear mixed model was used, with the maximum-likelihood method used to handle missing data. The secondary outcomes were analysed on a per-protocol approach. The continuous parameters measured at baseline, and at 3 and 6 months were analysed using a repeated measures multivariate ANOVA with baseline values as covariates. Secondary outcomes included the patient's peak expiratory flow, rescue medication use, severe exacerbations and quality of life.

Study arms

Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention) (N = 107)

Usual pharmacist care (N = 94)

Characteristics

Arm-level characteristics

Characteristic	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention) (N = 107)	Usual pharmacist care (N = 94)
% Female Sample size	n = 59 ; % = 55	n = 48 ; % = 51
Mean age (SD) Mean (range) Custom value	35.2 (19-51)	36.3 (17-51)
Smoking status: current smoker % Custom value	23.4%	21.3%
Ex-smoker Custom value	20.7%	29.7%
Passive smoker Custom value	29.4%	30.7%
Asthma duration (years) Mean (range) Custom value	20 (1-47)	22 (1-48)

Characteristic	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention) (N = 107)	Usual pharmacist care (N = 94)
Morning PEF (l/minute) Mean (range) Custom value	409.7 (165.7-717.1)	390.7 (127.9-755.0)
ACT score mean (range) Custom value	19.7 (11-25)	19.3 (10-25)
Rescue medication (puffs per day) mean (range) Custom value	1.24 (0-10.7)	1.33 (0-16.6)
Controller medication: ICS (%) Custom value	25%	23.1%
LABA Custom value	14.5	9.2
ICS/LABA combination Custom value	64.5	70.8
Theophylline Custom value	15.8	12.3

Characteristic	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention) (N = 107)	Usual pharmacist care (N = 94)
leukotriene modifiers Custom value	0.0	1.5
Mean daily dose ICS (range) (µg) expressed as beclomethasone equivalent Custom value	1184 (200-4000)	1211 (200-4000)
Education: no hish-school degree (%) Custom value	1.9	5.3
high-school degree Custom value	50.5	48.9
Higher education Custom value	47.7	44.7

Outcomes

Study timepoints

- Baseline
- 6 month

Continuous outcomes

Outcome	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention), Baseline, N = 107	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention), 6 month, N = 80	Usual pharmacist care, Baseline, N = 94	Usual pharmacist care, 6 month, N = 70
Asthma control (ACT score) scale 0-25, final score Mean (SD)	19.7 (3.1)	20.2 (3.5)	19.3 (3.5)	19.7 (4.8)
Reliever/rescue medication use puffs/day; average over previous 14 days, final score Mean (SD)	1.24 (2.04)	0.67 (1.33)	1.33 (2.36)	0.9 (1.36)
Lung function (morning PEF) % predicted, final score Mean (SD)	80.9 (18)	84 (19.4)	78 (18.2)	79.1 (19)

Outcome	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention), Baseline, N = 107	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention), 6 month, N = 80	Usual pharmacist care, Baseline, N = 94	Usual pharmacist care, 6 month, N = 70
Quality of life (AQLQ) Scale 0-7, final score Mean (SD)	5.9 (0.7)	6 (0.7)	5.7 (1)	5.8 (0.9)

Asthma control (ACT score) - Polarity - Higher values are better
Reliever/rescue medication use - Polarity - Lower values are better
Lung function (morning PEF) - Polarity - Higher values are better
Quality of life (AQLQ) - Polarity - Higher values are better

Dichotomous outcomes

Outcome	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention), Baseline, N = NA	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention), 6 month, N = 80	Usual pharmacist care, Baseline, N = NA	Usual pharmacist care, 6 month, N = 70
Asthma exacerbations (severe exacerbations) Number of people No of events	n = NA ; % = NA	n = 10 ; % = 12.8	n = NA ; % = NA	n = 8 ; % = 11.4
Unscheduled healthcare utilisation (emergency	n = NA ; % = NA	n = 1 ; % = 1.6	n = NA ; % = NA	n = 5 ; % = 10.4

Outcome	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention), Baseline, N = NA	Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) ACT monitoring at month 1 and 3 (pharmacist intervention), 6 month, N = 80	Usual pharmacist care, Baseline, N = NA	Usual pharmacist care, 6 month, N = 70
department visits or hospitalisations) Number of people No of events				

Asthma exacerbations (severe exacerbations) - Polarity - Lower values are better
Unscheduled healthcare utilisation (emergency department visits or hospitalisations) - Polarity - Lower values are better
severe exacerbations were defined as requiring an oral steroid course, an emergency room visit or hospitalisation

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Continuousoutcomes-Asthmacontrol(ACTscore)-MeanSD-Pharmacist intervention-Usual pharmacist care-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Self-reported outcome and unblinded: no information on prespecified analyses and unclear why ITT analysis presented for primary outcomes and per-protocol analysis for secondary outcomes;)*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention indirectness (also received education as well and questionnaire monitoring))*

Continuousoutcomes-Rescuemedication-MeanSD-Pharmacist intervention-Usual pharmacist care-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Self-reported outcome and unblinded: no information in prespecified analyses and unclear why ITT analysis presented for primary outcomes and per-protocol analysis for secondary outcomes)*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention indirectness (also received education as well as monitoring))*

Continuousoutcomes-MorningPEF-MeanSD-Pharmacist intervention-Usual pharmacist care-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns *(No information about prespecified analyses and unclear why PP used for secondaryoutcomes but ITT for primary outcomes)*
Overall bias and Directness	Overall Directness	Partially applicable *(control group did not receive education)*

Continuousoutcomes-Asthmaqualityoflifequestionnaire(AQLQ)-MeanSD-Pharmacist intervention-Usual pharmacist care-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Self-reported outcome and unblinded; no information about prespecified analyses and unclear why ITT analysis presented for primary outcomes and per-protocol analysis for secondary outcomes; only participants in the intervention group received education at the start of the intervention and this could have been confounding with the results)*
Overall bias and Directness	Overall Directness	Partially applicable *(control group did not receive education)*

Dichotomousoutcomes-Severeexacerbations-NoOfEvents-Pharmacist intervention-Usual pharmacist care-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns *(No info about prespecified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(control group did not receive education)*

Dichotomousoutcomes-Emergencydepartmentvisitsorhospitalisations-NoOfEvents-Pharmacist intervention-Usual pharmacist care-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns *(No info about prespecified analyses and no information about outcome assessment)*
Overall bias and Directness	Overall Directness	Partially applicable *(control group did not receive education)*

Pool, 2017

Bibliographic Reference	Pool, Andrew C; Kraschnewski, Jennifer L; Poger, Jennifer M; Smyth, Joshua; Stuckey, Heather L; Craig, Timothy J; Lehman, Erik B; Yang, Chengwu; Sciamanna, Christopher N; Impact of online patient reminders to improve asthma care: A randomized controlled trial.; PloS one; 2017; vol. 12 (no. 2); e0170447

Study details

Secondary publication of another included study- see primary study for details	
Trial name / registration number	Registered at clinicaltrials.gov, NCT00921401
Study type	Randomised controlled trial (RCT)
Study location	United States
Study setting	Participants were members of a large insurer, Highmark Blue Shield, with over 4 million members
Study dates	Recruitment began in 2009 and all follow-up measures were completed by 2012.
Sources of funding	Funding: by grant R01HL088590 from the National Heart, Lung, And Blood Institute and from the National Institutes of Health and by National Center for Advancing Translational Sciences, NIH through Grant UL1RR033184 and KL2RR033180.
Inclusion criteria	1) enrolled in Highmark Blue Shield for at least one year, 2) between the ages of 21–60 years and 3) met Healthcare Effectiveness Data and Information Set (HEDIS) criteria for persistent asthma. The HEDIS criteria identify individuals with persistent asthma based on their pattern of medication use specific to asthma (e.g., albuterol), emergency room visits or hospitalizations with a principal diagnosis of asthma, and outpatient visits coded by the provider with a diagnosis of asthma.
Exclusion criteria	Potential participants were excluded if, during a phone screener, they reported never receiving a diagnosis of asthma from a health care provider, were not able to read and speak English fluently, did not have Internet access at home or work or were pregnant. In addition, those with a history of more than 20 pack-years of cigarette smoking were excluded, as many of these individuals have chronic obstructive pulmonary disease rather than asthma
Recruitment / selection of participants	Participants were members of a large insurer, Highmark Blue Shield, with over 4 million members. Recruitment letters were sent to members who were: 1) enrolled in Highmark Blue Shield for at least one year, 2) between the ages of 21–60 years and 3) met Healthcare Effectiveness Data and Information Set (HEDIS) criteria for persistent asthma
Intervention(s)	Intervention participants were asked to use an online tool at least once each month (and within 14 days of their next scheduled health care provider visit), in which they would answer 11 questions about their asthma symptoms (e.g., rescue

	inhaler frequency, night symptom frequency), availability of oral corticosteroids at home for exacerbations, and asthma care received from providers, such as an asthma management plan. Participants were also asked to enter their current asthma medications, the number of days each week that each medication was used and identify if any medicines bothered them; and record their next scheduled visit with their asthma care provider. Based on their answers and pre-written rules, the online tool provided tailored feedback reminding patients to ask providers specific questions about their asthma medications and perform specific asthma self-care, to improve adherence to the 2007 NAEPP treatment guidelines. Feedback included lay-person explanations and links to an external website that supported the recommendation.
Ethnicity	White 84.2% white
Education Level	Mixed College 4+ years, 58.5%
Language of Participants	Not reported/unclear
Comparator	Control condition received questions and were given feedback about preventive services (e.g., colon cancer screening) that would be unlikely to change asthma care.
Number of participants	408 adults
Duration of follow-up	12 months
Indirectness	4 of the 11 questions (available in paper) relate to asthma care from providers rather than symptoms specifically. These questions may have informed automated feedback (intervention indirectness).
Additional comments	Intention-to-treat.

	To determine the impact of losses to follow-up on the results, a sensitivity analysis using a more conservative approach was conducted that replaced missing data with data from the last visit carried forward (LOCF). These sensitivity analyses revealed similar results to the analyses without replacement, so the results are presented in their original, non-replaced, form.

Study arms

Symptom scores or diaries (Symptom questions with feedback to support self-management) (N = 204)
Intervention participants were asked to use an online tool at least once each month (and within 14 days of their next scheduled health care provider visit), in which they would answer 11 questions about their asthma symptoms (e.g., rescue inhaler frequency, night symptom frequency), availability of oral corticosteroids at home for exacerbations, and asthma care received from providers, such as an asthma management plan. Participants were also asked to enter their current asthma medications, the number of days each week that each medication was used and identify if any medicines bothered them; and record their next scheduled visit with their asthma care provider. Based on their answers and pre-written rules, the online tool provided tailored feedback reminding patients to ask providers specific questions about their asthma medications and perform specific asthma self-care, to improve adherence to the 2007 NAEPP treatment guidelines. Feedback included lay-person explanations and links to an external website that supported the recommendation.

Control (non-asthma related preventive Qs and feedback) (N = 204)
Control condition received questions and were given feedback about preventive services (e.g., colon cancer screening) that would be unlikely to change asthma care.

Characteristics

Arm-level characteristics

Characteristic	Symptom scores or diaries (Symptom questions with feedback to support self-management) (N = 204)	Control (non-asthma related preventive Qs and feedback) (N = 204)
% Female Sample size	n = 130 ; % = 63.6	n = 123 ; % = 60.3
Mean age (SD) Mean (SD)	47.6 (9.1)	47.2 (9.6)
White Sample size	n = NR ; % = 81.7	n = NR ; % = 86.8
Hispanic Sample size	n = NR ; % = 3.9	n = NR ; % = 2.9
Education College 4+ years Sample size	n = NR ; % = 58.1	n = NR ; % = 58.8
Current smoker Sample size	n = NR ; % = 3.5	n = NR ; % = 2.9
Smoked More Than 100 Cigarettes Lifetime Sample size	n = NR ; % = 25.1	n = NR ; % = 29.1

Outcomes

Study timepoints

- 12 month

Asthma control

Outcome	Symptom scores or diaries (Symptom questions with feedback to support self-management), 12 month, N = 157	Control (non-asthma related preventive Qs and feedback), 12 month, N = 168
Asthma control (ACT overall score) Change score, range 5-25 Mean (95% CI)	2.3 (1.6 to 2.9)	1.2 (0.6 to 1.8)

Asthma control (ACT overall score) - Polarity - Higher values are better
ACT overall score (continuous and dichotomous variables)

Healthcare utilisation

Outcome	Symptom scores or diaries (Symptom questions with feedback to support self-management), 12 month, N = 158	Control (non-asthma related preventive Qs and feedback), 12 month, N = 168
Unscheduled healthcare utilisation (number of Emergency Room visits) Change score Mean (95% CI)	-0.26 (-0.44 to -0.08)	-0.08 (-0.26 to 0.1)

Outcome	Symptom scores or diaries (Symptom questions with feedback to support self-management), 12 month, N = 158	Control (non-asthma related preventive Qs and feedback), 12 month, N = 168
Unscheduled healthcare utilisation (number of outpatient visits) Change score Mean (95% CI)	-0.13 (-0.54 to 0.28)	0 (-0.41 to 0.4)
Dose of regular asthma therapy / preventer medication (number of asthma medications) Change score Mean (95% CI)	0.42 (0.26 to 0.58)	0.25 (0.09 to 0.4)
Dose of regular asthma therapy / preventer medication (number of asthma controller medications) Change score Mean (95% CI)	0.18 (0.07 to 0.3)	0.12 (0.01 to 0.24)

Unscheduled healthcare utilisation (number of Emergency Room visits) - Polarity - Lower values are better
Unscheduled healthcare utilisation (number of outpatient visits) - Polarity - Lower values are better
Dose of regular asthma therapy / preventer medication (number of asthma medications) - Polarity - Lower values are better
Dose of regular asthma therapy / preventer medication (number of asthma controller medications) - Polarity - Lower values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Asthma control-ACT overall-change score

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Partially applicable *(Indirectness identified due to intervention - use of non-validated asthma symptom questionnaire. 4 of 11 Q are about asthma care. Participants also input information on medications)*

Healthcare utilisation-Number of Emergency Room Visits-change score

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Partially applicable *(Indirectness due to use of non-validated asthma symptom questionnaire. Only 7/11 Q are directly about asthma symptoms))*

Healthcare utilisation-Number of Outpatient Visits-Change score

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low

Section	Question	Answer
Overall bias and Directness	Overall Directness	Partially applicable *(Indirectness identified due to intervention - use of non-validated asthma symptom questionnaire. 4 of 11 Q are about asthma care. Participants also input information on medication)*

Healthcareutilisation-Numberofasthmamedications-MeanNineFivePercentCI-Online tool with 11 questions on asthma symptoms, followed by tailored feedback to ask specific Qs to healthcare providers and prompt self-care-Control (non-asthma related preventive Qs and feedback)-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Partially applicable *(Indirectness identified due to intervention - use of non-validated asthma symptom questionnaire. 4 of 11 Q are about asthma care. Participants also input information on medications. Indirectness also identified for outcome (not identical to protocol))*

Healthcareutilisation-Numberofasthmacontrollermedications-MeanNineFivePercentCI-Online tool with 11 questions on asthma symptoms, followed by tailored feedback to ask specific Qs to healthcare providers and prompt self-care-Control (non-asthma related preventive Qs and feedback)-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Partially applicable *(Indirectness identified due to intervention - use of non-validated asthma symptom questionnaire. 4 of 11 Q*

Section	Question	Answer
		are about asthma care. Participants also input information on medications. Outcome also indirectness in relation to protocol)

Rikkers-Mutsaerts, 2012

Bibliographic Reference	Rikkers-Mutsaerts, ER; Winters, AE; Bakker, MJ; van Stel, HF; van der Meer, V; de Jongste, JC; Sont, JK; Internet-based self-management compared with usual care in adolescents with asthma: a randomized controlled trial; Pediatric pulmonology; 2012; vol. 47 (no. 12); 1170-1179

Study details

Trial name / registration number	ISRCTN 11633371
Study type	Randomised controlled trial (RCT)
Study location	35 practices from the Leiden University Medical Center (LUMC) general practice network and from hospital information systems of eight hospital outpatient clinics (seven general and one academic).
Study setting	Primary/secondary care
Study dates	not specified
Sources of funding	The Netherlands Asthma Foundation
Inclusion criteria	Doctor’s diagnosis of mild to severe persistent asthma characterized by a prescription of ICS more than 3 months in the previous year, age 12–18 years, access to Internet, and understanding of the Dutch language
Exclusion criteria	Patients requiring oral steroids as maintenance or patients with relevant co-morbidity were excluded.

Recruitment / selection of participants	Adolescents were invited by mail and were provided with a web account to complete two different asthma control questionnaires(Asthma Control Questionnaire, ACQ, and the Asthma Therapy Assessment Questionnaire, ATAQ) via a secured website. Only patients with not well-controlled asthma as assessed by ACQ>0.75 and/or ATAQ >1.0 were enrolled in the trial after giving informed consent. After 2 weeks patients were 1:1 randomly assigned to either the IBSM group or the usual care group, stratified according to care provider (primary care vs. secondary care)
Intervention(s)	The intervention consisted of all four components of self-management support programs: education, self-monitoring, an electronic action plan, and regular medical review. Education: Education was provided in two ways: web-based, which included asthma information, news, frequently asked questions and interactive communication with a specialized nurse, and face-to-face group based education. Two asthma self-management education sessions were organized within 6 weeks after entering the trial. Information about asthma self-management was presented in response to participants' questions rather than in lectures. Education was focused on patients' needs and responding to their identified concerns. The first education session also included information on the pathophysiology of asthma, the web-based action plan, and on the inhalation technique. Self-monitoring: Patients in the IBSM group were asked to record asthma control by ACQ and FEV1 every week for 1 year, and to report the results via the study website. They received instant feedback on their level of asthma control and advice how to adjust their medication according to a predefined algorithm and personal treatment plan. A reminder was sent via a phone text message if the weekly results were not reported.

	Electronic Action Plan: depending on the scores participants could receive 4 types of treatment advice, based on a personal treatment plan. To allow for evaluation of a treatment change, it was advised than no medication changes take place during the 4 weeks after treatment was stepped up. Apart from the weekly assessments, patients could always report daily symptoms and lung function by a diary card or contact the asthma nurse, through the web or by phone. As a result, any acute worsening of asthma symptoms, requiring a visit to the attending physician could potentially be detected. Regular Medical Review Patients attended their own physician, as they would normally do, every 3–6 months and extra when needed if their asthma was deteriorating. Treatment plan (based on the Dutch guidelines on asthma management in children in general practice) 1 Rapid acting b2-agonist as needed 2 Low-dose inhaled glucocorticosteroids 3a Medium-dose inhaled glucocorticosteroids 3b Medium-dose inhaled glucocorticosteroids and long-actingb2-agonist 3c Medium-dose inhaled glucocorticosteroids and leukotriene modifier 4 Medium-dose inhaled glucocorticosteroids and long-actingb2-agonist and leukotriene modifier 5 Contact asthma nurse (or other healthcare provider); consider high-dose inhaled glucocorticosteroids and long-actingb2-agonist and leukotriene modifier 6 Contact asthma nurse (or other healthcare provider); consider adding oral glucocorticosteroids

Education Level	Not reported/unclear
Language of Participants	Not reported/unclear
Comparator	Usual care: Adolescents in the usual care group received care by their physician according to the Dutch guidelines on asthma management in children in general practice and in hospitals. Commonly, they visited their general practitioner or paediatrician every 3 months or twice per year once control of asthma had been achieved.
Number of participants	90
Duration of follow-up	12 months
Indirectness	Intervention indirectness (intervention group received additional web-based and face-to-face education sessions)
Additional comments	Intention to treat; Changes in the PAQLQ, the ACQ, and the lung function were analysed using a linear mixed effects model. The primary analysis was aimed at treatment effects after 3 and 12 months. To correct for possibly selective non-response, missing measurements were replaced by 20 imputed values based on regression switching with variables randomization group, baseline values, and available outcomes at all time points. Clinical relevant changes in PAQLQ and ACQ were defined as changes from baseline 0.5, respectively.

Study arms

Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) (N = 46)
consisted of weekly asthma control monitoring with treatment advice by a web-based algorithm.

Usual care (N = 44)

Characteristics

Arm-level characteristics

Characteristic	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) (N = 46)	Usual care (N = 44)
% Female Sample size	n = 26 ; % = 57	n = 19 ; % = 43
Mean age (range) years Custom value	13.4 (12-17)	13.8 (12-17)
FEV1 (L) mean (range) Custom value	2.85 (1.65- 4.62)	3.00 (1.60-5.98)
FEV1 % predicted mean (range) Custom value	88 (49-151)	92 (49-164)
Daily ICS dose (µg) mean (range) Custom value	378 (0-1000)	381 (0-1000)
Inhaled long acting β2 agonist use % Custom value	65.5%	65%

Characteristic	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) (N = 46)	Usual care (N = 44)
Pediatric asthma QOL score mean (range) Custom value	5.60 (3.12-6.97)	5.68 (2.78-7)
Asthma control questionnaire score mean (range) Custom value	1.29 (0.22-3.00)	1.19 (0-3.43)
Symptom-free days (%) mean (range) Custom value	68.3 (0-100)	70.9 (0-100)

Outcomes

Study timepoints

- 12 month

Between-group difference

Outcome	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) vs Usual care, 12 month, N2 = 44, N1 = 46
Asthma control questionnaire (ACQ)	-0.05 (-0.35 to 0.25)

Outcome	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) vs Usual care, 12 month, N2 = 44, N1 = 46
mean difference (95% CI); MID: 0.5 Mean (95% CI)	
Pediatric Asthma QOL questionnaire mean difference (95% CI); MID: 0.5 Mean (95% CI)	-0.05 (-0.5 to 0.41)
Daily ICS dose (µg) mean difference (95% CI) Mean (95% CI)	14 (-75 to 102)
Symptom free days (%) mean difference (95% CI) Mean (95% CI)	4 (-9.7 to 17.9)

Asthma control questionnaire (ACQ) - Polarity - Lower values are better
Pediatric Asthma QOL questionnaire - Polarity - Higher values are better
Daily ICS dose - Polarity - Lower values are better
Symptom free days - Polarity - Higher values are better

Exacerbations

Outcome	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education), 12 month, N = 46	Usual care, 12 month, N = 44
Asthma exacerbations Number of people No of events	n = 6 ; % = 13	n = 6 ; % = 13.6

Asthma exacerbations - Polarity - Lower values are better
Defined as a deterioration in asthma that required oral steroids for 3 days or more, as reported in 3-monthly questionnaires

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Between-groupdifference-Asthmacontrolquestionnaire(ACQ)-MeanNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(lack of blinding and outcomes were subjective and self-reported; >10% difference in missing outcome data between groups at 12 months; no information on pre-specified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(mixed age group including people >16 years; intervention group received additional web-based and face-to-face education sessions.)*

Between-groupdifference-PediatricAsthmaQOLquestionnaire-MeanNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(lack of blinding and outcomes were subjective and self-reported; >10% difference in missing outcome data between groups at 12 months; no information on pre-specified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(mixed age group including people >16 years; intervention group received additional web-based and face-to-face education sessions.)*

Exacerbations-Asthmaexacerbations-NoOfEvents-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(>10% differential rate of missing data between groups at 12 months; subjective self-reported outcome & lack of blinding; No information on pre-specified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(mixed age group including people >16 years; intervention group received additional web-based and face-to-face education sessions.)*

Between-groupdifference-DailyICSdose-MeanNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(lack of blinding and outcomes were subjective and self-reported; >10% difference in missing outcome data between groups at 12 months; no information about prespecified analyses)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Partially applicable *(mixed age group including people >16 years; intervention group received additional web-based and face-to-face education sessions.)*

Between-groupdifference-Symptomfreedays-MeanNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(lack of blinding and outcomes were subjective and self-reported; >10% difference in missing outcome data between groups at 12 months; no information on prespecified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(mixed age group including people >16 years; intervention group received additional web-based and face-to-face education sessions.)*

van den Wijngaart, 2017

Bibliographic Reference	van den Wijngaart, Lara S; Roukema, Jolt; Boehmer, Annemie L M; Brouwer, Marianne L; Hugen, Cindy A C; Niers, Laetitia E M; Sprij, Arwen J; Rikkers-Mutsaerts, Eleonora R V M; Rottier, Bart L; Donders, A Rogier T; Verhaak, Chris M; Pijnenburg, Marielle W; Merkus, Peter J F M; A virtual asthma clinic for children: fewer routine outpatient visits, same asthma control.; The European respiratory journal; 2017; vol. 50 (no. 4)

Study details

Trial name / registration number	NTR 2689
Study location	Netherlands
Study setting	4 general hospitals and 4 tertiary referral centres in the Netherlands
Study dates	No information
Sources of funding	Lung Foundation Netherlands and Dutch Innovation Foundation Health Insurance Companies
Inclusion criteria	Children aged 6-16 years, with a doctor's diagnosis of asthma based on symptoms and a bronchodilator response of forced expiratory volume in 1 s (FEV1) % pred >9%, and/or airway hyperresponsiveness, and/or signs of eosinophilic airways inflammation. All had to have at least one allergy for airborne allergens confirmed by positive skin prick tests and/or blood tests and have computer with internet access
Exclusion criteria	History of admission to the intensive care unit for asthma in the preceding 5 years, difficult-to-treat asthma (defined as uncontrolled or poorly controlled asthma in spite of maintenance treatment with inhaled corticosteroids (ICSs) with at least 800 µg·day–1 regular beclomethasone or equivalent, long-acting bronchodilators and/or montelukast, and/or oral corticosteroids), use of omalizumab, other chronic diseases, and the inability of the parents or children to read and understand Dutch.
Recruitment / selection of participants	No information
Intervention(s)	Virtual asthma clinic including C-ACT monitoring: a web-based portal with a chat and forum module for peers, an information module to enhance knowledge about asthma, and a secure and private module in which the child/parent can log in to consult an individual treatment plan and communicate with the asthma management team. Outpatient visits every 8 months. Digital (c-)ACT completed monthly: If the (C-)ACT score was ⩾20, automatic default messages were emailed with positive and encouraging content. If the (C-)ACT score was <20 feedback to the participants included advice to check their medication use, an individual action plan and a request to contact their asthma team when symptoms persisted. Feedback also sent to the asthma team to prompt contacting the participant within 2 working days to address clinical status
Population subgroups	

Ethnicity	Not reported/unclear
Education Level	Not reported/unclear
Language of Participants	Not reported/unclear
Comparator	Usual care: routine outpatient visits every 4 months, during which patients completed a digital version of the (C-)ACT to assess asthma control. Results of/feedback from (C-)ACT not available to physician or patient.
Number of participants	210
Duration of follow-up	16 months
Indirectness	Intervention includes web-based education as well as C-ACT monitoring
Additional comments	Intention-to-treat analysis

Study arms

Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) (N = 105)
a web-based portal with a chat and forum module for peers, an information module to enhance knowledge about asthma, and a secure and private module in which the child/parent can log in to consult an individual treatment plan and communicate with the asthma management team. Outpatient visits every 8 months. Digital (c-)ACT completed monthly: If the (C-)ACT score was ⩾20, automatic default messages were emailed with positive and encouraging content. If the (C-)ACT score was <20 feedback to the participants included advice to check their medication use, an individual action plan and a request to contact their asthma team when symptoms persisted. Feedback also sent to the asthma team to prompt contacting the participant within 2 working days to address clinical status.

Usual care (N = 105)
Usual care: routine outpatient visits every 4 months, during which patients completed a digital version of the (C-)ACT to assess asthma control. Results of/feedback from (C-)ACT not available to physician or patient.

Characteristics

Arm-level characteristics

Characteristic	Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) (N = 105)	Usual care (N = 105)
% Female Sample size	n = 41 ; % = 39	n = 44 ; % = 41.9
Mean age (SD) Mean (SD)	11.3 (2.9)	11.3 (2.7)
age 6-11 Sample size	n = 59 ; % = 56.2	n = 63 ; % = 60
age 12-16 Sample size	n = 46 ; % = 43.8	n = 42 ; % = 40
Initial ICS dose (ug/day) Mean (SD)	415 (205)	461 (244)
FEV1, % Pred Mean (SD)	94.3 (14.1)	93.6 (14.1)

Characteristic	Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) (N = 105)	Usual care (N = 105)
FENO (ppb) Mean (SD)	27.1 (24.1)	29.5 (26.3)
C-ACT Median (IQR)	22 (20.4 to 23.6)	21.1 (19.1 to 23.1)
ACT Median (IQR)	20.9 (19.1 to 22.7)	20.3 (18.2 to 22.4)
Symptom free days Mean (SD)	26.8 (4.1)	26.2 (4.9)

Outcomes

Study timepoints

- Baseline
- 16 month

Primary and secondary outcomes

Outcome

Mean differences and RRs

Primary and secondary outcomes

Outcome	Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) , Baseline, N = 105	Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) , 16 month, N = 105	Usual care, Baseline, N = 105	Usual care, 16 month, N = 105
Symptoms (symptom free days) Final scores Mean (SD)	26.8 (4.1)	28.5 (1.7)	26.2 (4.9)	27.3 (3.6)
Asthma control (C-ACT score) Range 0 to 27, final scores Mean (SD)	22 (3.2)	23.7 (2.8)	21.1 (4)	22.3 (3.9)
Asthma control (ACT score) Range 5-25, final scores Mean (SD)	20.9 (3.6)	22.1 (2.9)	20.3 (4.2)	21.3 (3.3)
Lung function (FEV1 % predicted) Final scores Mean (SD)	94.3 (14.1)	92.1 (13.5)	96.3 (14.1)	92.3 (14.7)
Asthma exacerbations No of events	n = NR ; % = NR	n = 16 ; % = NR	n = NR ; % = NR	n = 18 ; % = NR

Outcome	Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) , Baseline, N = 105	Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) , 16 month, N = 105	Usual care, Baseline, N = 105	Usual care, 16 month, N = 105
Unscheduled healthcare utilisation (unscheduled visits to outpatient clinic) No of events	n = NR ; % = NR	n = 35 ; % = NR	n = NR ; % = NR	n = 26 ; % = NR
Courses of systemic corticosteroids (delete tbc) No of events	n = NR ; % = NR	n = 11 ; % = NR	n = NR ; % = NR	n = 13 ; % = NR
Unscheduled healthcare utilisation (visits to emergency department) No of events	n = NR ; % = NR	n = 3 ; % = NR	n = NR ; % = NR	n = 2 ; % = NR
Hospital admissions No of events	n = NR ; % = NR	n = 1 ; % = NR	n = NR ; % = NR	n = 2 ; % = NR

Symptoms (symptom free days) - Polarity - Higher values are better
Asthma control (C-ACT score) - Polarity - Higher values are better
Asthma control (ACT score) - Polarity - Higher values are better
Lung function (FEV1 % predicted) - Polarity - Higher values are better
Asthma exacerbations - Polarity - Lower values are better
Unscheduled healthcare utilisation (unscheduled visits to outpatient clinic) - Polarity - Lower values are better
Courses of systemic corticosteroids (delete tbc) - Polarity - Lower values are better
Unscheduled healthcare utilisation (visits to emergency department) - Polarity - Lower values are better
Hospital admissions - Polarity - Lower values are better
Means (final scores) and events at 16 months

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Primaryandsecondaryoutcomes-Symptomfreedays-MeanSD-Virtual asthma clinic including monitoring by C-ACT-Usual care-t16

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Intervention-related deviations from protocol possible due to availability of FEV1 and FENO to treating physicians; no information about protocol, missing data or adherence; outcome based on self-reports (unblinded))*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention included web-based education; outcome based on (C)ACT)*

Primaryandsecondaryoutcomes-C-ACT-MeanSD-Virtual asthma clinic including monitoring by C-ACT-Usual care-t16

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Intervention-related deviations from protocol possible due to availability of FEV1 and FENO to treating physicians; no information about protocol, missing data or adherence; outcome based on self-reports (unblinded))*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention included web-based education)*

Primaryandsecondaryoutcomes-ACTscore-MeanSD-Virtual asthma clinic including monitoring by C-ACT-Usual care-t16

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Intervention-related deviations from protocol possible due to availability of FEV1 and FENO to treating physicians; no information about protocol, missing data or adherence; outcome based on self-reports (unblinded))*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention included web-based education)*

Primaryandsecondaryoutcomes-FEV1%predicted-MeanSD-Virtual asthma clinic including monitoring by C-ACT-Usual care-t16

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Unblinded outcome assessors, no information about missing data, protocol or adherence; intervention-related deviations from protocol possible due to availability of FEV1 and FENO to treating physicians)*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention included web-based education)*

Primaryandsecondaryoutcomes-Asthmaexacerbations-NoOfEvents-Virtual asthma clinic including monitoring by C-ACT-Usual care-t16

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Lack of information about outcome assessment, adherence and pre-specified analyses. Intervention-related deviations from protocol also possible due to availability of FEV1 and FENO to treating physicians in both arms.)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention included web-based education)*

Primaryandsecondaryoutcomes-Coursesofsystemiccorticosteroids-NoOfEvents-Virtual asthma clinic including monitoring by C-ACT-Usual care-t16

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Lack of information about outcome assessment, adherence and pre-specified analyses. Intervention-related deviations from protocol also possible due to availability of FEV1 and FENO to treating physicians in both arms.)*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention included web-based education)*

Primaryandsecondaryoutcomes-Unscheduledvisitstooutpatientclinic-NoOfEvents-Virtual asthma clinic including monitoring by C-ACT-Usual care-t16

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Lack of information about outcome assessment, adherence and pre-specified analyses. Intervention-related deviations from protocol also possible due to availability of FEV1 and FENO to treating physicians in both arms.)*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention included web-based education)*

Primaryandsecondaryoutcomes-Visitstoemergencydepartment-NoOfEvents-Virtual asthma clinic including monitoring by C-ACT-Usual care-t16

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Lack of information about outcome assessment, adherence and pre-specified analyses. Intervention-related deviations from protocol also possible due to availability of FEV1 and FENO to treating physicians in both arms.)*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention included web-based education)*

Primaryandsecondaryoutcomes-Hospitaladmissions-NoOfEvents-Virtual asthma clinic including monitoring by C-ACT-Usual care-t16

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Lack of information about outcome assessment, adherence and pre-specified analyses. Intervention-related deviations from protocol also possible due to availability of FEV1 and FENO to treating physicians in both arms.)*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention included web-based education)*

van der Meer, 2009

Bibliographic Reference	van der Meer, V.; Bakker, M. J.; van den Hout, W. B.; Rabe, K. F.; Sterk, P. J.; Kievit, J.; Assendelft, W. J.; Sont, J. K.; Group, Smashing Study; Internet-based self-management plus education compared with usual care in asthma: a randomized trial; Ann Intern Med; 2009; vol. 151 (no. 2); 110-20

Study details

Other publications associated with this study included in review	van der Meer (2010) and van Gaalen (2013)
Study type	Randomised controlled trial (RCT)
Study location	Netherlands, Leiden and The Hague areaand the Outpatient Clinic of the Department of Pulmonology at the Leiden University Medical Center
Study setting	37 general practices (69 general practitioners) and 1 academic outpatient department
Study dates	Recruitment from September 2005 to September 2006
Sources of funding	Netherlands Organization for Health Re-search and Development, ZonMw, and Netherlands AsthmaFoundation.
Inclusion criteria	physician-diagnosed asthma coded according to the International Classification of Primary Care in the electronic medical record, age 18 to 50 years, prescription of inhaled corticosteroids for at least 3 months in the previous year, no serious comorbid conditions that interfered with asthma treatment, access to the Internet at home, and mastery of the Dutch language.
Exclusion criteria	Patients who were receiving maintenance oral glucocorticosteroid treatment.
Recruitment / selection of participants	Eligible patients were sent an invitation letter followed by 1 reminder letter after 2-4 weeks if they did not respond to the first. This process was continued until 200 patients had entered the study. Randomisation was stratified according to care provider (primary vs subspecialty care) and asthma control at baseline.
Intervention(s)	Internet-based self-management program: including weekly asthma control, monitoring and treatment advice, online and group education, and remote Web communications with a specialized asthma nurse. The Internet-based self-management program consisted of the 4 principal components of asthma self-management and was accessed through the specially de-signed Web site, which allowed monitoring through the Web site (or text message on a mobile telephone), use of an Internet-based treatment plan, online education, and Web communications with a specialized asthma nurse.

	Patients monitored their asthma weekly by completing an electronic version of the Asthma Control Questionnaire on the Web site and instantly received feedback on the current state of their asthma control along with advice on how to adjust their treatment according to a predefined algorithm and treatment plan. Depending on the scores submitted, patients received 4 types of self-treatment advice. 1) When 4 consecutive Asthma Control Questionnaire scores were 0.5 or less, patients were advised to decrease treatment according to treatment plan. 2) When 2 consecutive scores were greater than 0.5 but less than 1.0, patients were advised to increase treatment according to treatment plan. 3) When 1 score was 1.0 or more but less than 1.5,patients were advised to immediately increase treatment according to treatment plan. 4) Finally, when 1 score was 1.5or more, patients were advised to immediately increase treatment and contact the asthma nurse. Treatment plan: Step numbers (corresponding with recommended steps in the Global Initiative for Asthma guidelines)= Medication 1= rapid-acting β2=agonist as needed (applies to all treatment steps)

	2= low-dose inhaled glucocorticosteroids 3a= low-dose inhaled glucocorticosteroids plus long-acting β2-agonist 3b medium-dose inhaled glucocorticosteroids 3c= high-dose inhaled glucocorticosteroids 4a= medium inhaled glucocorticosteroids plus long-acting β2-agonist 4b= high dose inhaled glucocorticosteroids plus long-acting β2-agonist 4c= contact asthma nurse or other healthcare provider; consider addition of leukotriene modifier 5= contact asthma nurse or other healthcare provider; consider addition of oral glucocorticosterois Advice was no medication changes during the 4 weeks after treatment was stepped up (evaluation period). In addition to weekly assessments, patients could optionally re-port daily symptoms and lung function and were able to contact our asthma nurse though the Web or by telephone. Thus, any acute deterioration warranting a visit to the general practitioner or hospital could be detected. Self-management education consisted of both Web-based and face-to-face, group-based education. Web-based education included asthma information, news, frequently asked questions, and interactive communication with a respiratory nurse specialist. We scheduled 2 group-based education sessions, which lasted 45 to 60 minutes, for patients in the Internet-based self-management group within 6 weeks after entering the trial. Both sessions included exploration of a patient's interests and previous knowledge (negotiating an agenda and patient-centered education), personalized feedback, and empowerment of self-management (self-efficacy and implementing a plan for change)

	All participants were provided basic education about core information on asthma, action of medications, and inhaler technique instructions in a 2-week baseline period before randomisation. They were trained to measure FEV1 daily with a handheld electronic spirometer and to report the highest value of 3 measurements in the morning before taking medication.
Ethnicity	Not reported/unclear
Education Level	Mixed
Language of Participants	Not reported/unclear
Comparator	Usual care: Patients in the usual care group received asthma care according to the Dutch general practice guidelines on asthma management in adults, which recommend a medical review and treatment adjustment every 2 to 4 weeks in unstable asthma and medical review once or twice yearly for patients whose asthma is under control All participants were provided basic education about core information on asthma, action of medications, and inhaler technique instructions in a 2-week baseline period before randomisation. They were trained to measure FEV1 daily with a handheld electronic spirometer and to report the highest value of 3 measurements in the morning before taking medication.
Number of participants	200
Duration of follow-up	12 months
Indirectness	All participants were also provided education; monitoring intervention had multiple components besides the ACT test that were not part of the review protocol.
Additional comments	ITT analysis without imputation

Study arms

Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) (N = 101)

Usual care (N = 99)

Characteristics

Arm-level characteristics

Characteristic	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) (N = 101)	Usual care (N = 99)
% Female Sample size	n = 32 ; % = 32	n = 29 ; % = 29
Mean age (range) Custom value	36 (19-50)	37 (18-50)
Mean asthma duration mean years (range) Custom value	15 (1-47)	18 (0-47)
Smoking status: never (%) Custom value	58%	53%
Former Custom value	30%	33%

Characteristic	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) (N = 101)	Usual care (N = 99)
Current Custom value	12%	14%
Mean predicted FEV1 (%) Mean % (range) Custom value	88 (34-133)	90 (53-118)
Mean daily inhaled corticosteroid dose (µg) mean (range) Custom value	497 (0-1000)	517 (0-2000)
Inhaled long-acting β2-agonist use % Sample size	n = 60 ; % = 59	n = 60 ; % = 60
Asthma quality of life questionnaire mean (range) Custom value	5.73 (3.66-6.94)	5.79 (3.03-7.00)
ACQ score mean (range) Custom value	1.12 (0.07-3.22)	1.11 (0-3.86)
Middle	37%	33%

Characteristic	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) (N = 101)	Usual care (N = 99)
Custom value		
High Custom value	52%	53%
Low Custom value	11%	14%
Symptom-free days (%) (mean, range) Custom value	44.9 (0-100)	44.5 (0-100)

Outcomes

Study timepoints

- 12 month

Dichotomous outcome

Outcome	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education), 12 month, N = 101	Usual care, 12 month, N = 99
Asthma exacerbations number of people	n = 11 ; % = 10.9	n = 10 ; % = 10.1

Outcome	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education), 12 month, N = 101	Usual care, 12 month, N = 99
No of events		

Asthma exacerbations - Polarity - Lower values are better
Exacerbations were defined as deterioration in asthma that required emergency treatment or hospitalization (collected by quarterly questionnaire) or the need for oral steroids for 3 days or more (collected by pharmacy records), as judged by the attending physician, and assessed them over the whole year

Between group comparison

Outcome	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) vs Usual care, 12 month, N2 = 101, N1 = 99
Asthma exacerbations Hazard ratio/95% CI	1.18 (0.51 to 2.74)
ACQ (score 7-0) Mean difference in change from baseline (95%CI) Mean (95% CI)	-0.47 (-0.64 to -0.3)
AQLQ (score 1-7) Mean difference in change from baseline (95%CI) Mean (95% CI)	0.38 (0.2 to 0.56)
FEV1 (L) Mean difference in change from baseline (95%CI) Mean (95% CI)	0.25 (0.03 to 0.46)

Outcome	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) vs Usual care, 12 month, N2 = 101, N1 = 99
Symptom free days (%) Mean difference in change from baseline; control group risk 51.8%; % over 2 weeks; scale from 0-100 Mean (95% CI)	10.9 (0.05 to 21.3)
Daily ICS use (µg) Mean difference in change from baseline; control group: 470µg at 12 months Mean (95% CI)	57 (-38 to 152)

Asthma exacerbations - Polarity - Lower values are better
ACQ (score 7-0) - Polarity - Lower values are better
AQLQ (score 1-7) - Polarity - Higher values are better
FEV1 (L) - Polarity - Higher values are better
Symptom free days - Polarity - Higher values are better
Asthma-related quality of life, as measured by the 32-item Asthma Quality of Life Questionnaire. The minimal important difference is 0.5 on a 7-point scale. Asthma control (minimal important difference is 0.5 on the 7-point Asthma Control Questionnaire scale Prebronchodila-tor FEV1

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Dichotomousoutcome-Asthmaexacerbations-NoOfEvents-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns *(No information about pre-specified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(ntervention group received additional web-based and face-to-face education sessions.)*

Betweengroupcomparison-Asthmaexacerbations-HazardRatioNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns *(No information about prespecified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(intervention group received additional web-based and face-to-face education sessions.)*

Betweengroupcomparison-ACTscore(score6-0)-MeanNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Self-reported outcome and unblinded study (ACQ measurement part of intervention); no information about pre-specified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(intervention group received additional web-based and face-to-face education sessions.)*

Betweengroupcomparison-AQLQ(score1-7)-MeanNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Self-reported outcome and unblinded study (ACQ measurement part of intervention); no information about prespecified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(intervention group received additional web-based and face-to-face education sessions.)*

Betweengroupcomparison-FEV1(L)-MeanNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns *(No information about prespecified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(intervention group received additional web-based and face-to-face education sessions.)*

Betweengroupcomparison-Symptomfreedays-MeanNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Self-reported outcome and unblinded study (ACQ measurement part of intervention); no information about prespecified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(intervention group received additional web-based and face-to-face education sessions.)*

Betweengroupcomparison-DailyICSuse-MeanNineFivePercentCI-Internet-based self-management-Usual care-t12

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns *(Self-reported outcome and unblinded (but not completely subjective an outcome); no information on prespecified outcomes)*
Overall bias and Directness	Overall Directness	Partially applicable *(intervention group received additional web-based and face-to-face education sessions.)*

van Gaalen, 2013

Bibliographic Reference	van Gaalen, JL; Beerthuizen, T; van der Meer, V; van Reisen, P; Redelijkheid, GW; Snoeck-Stroband, JB; Sont, JK; Long-term outcomes of internet-based self-management support in adults with asthma: randomized controlled trial; Journal of medical Internet research; 2013; vol. 15 (no. 9); e188

Study details

Secondary publication of another included study- see primary study for details	See primary study for details: Van der Meer et al (2009) Internet-based self-management plus education compared with usual care in **asthma**: a randomized trial Ann Intern Med; vol. 151 (no. 2); 110-20
Other publications associated with this study included in review	van der Meer (2010)
Ethnicity	Not reported/unclear

Education Level	Mixed
Language of Participants	Not reported/unclear
Duration of follow-up	30 months
Indirectness	Intervention includes education as well as questionnaire-based monitoring.

Study arms

Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) (N = 47)
Internet-based self-management: including weekly asthma control monitoring and treatment advice, online and group education and remote Web communications. Education was provided as web-based portal including interactive communication with a specialized nurse, and 2 face-to-face group based education sessions focussing on self-management. Patients monitored their asthma weekly by completing an electronic version of the ACQ and receiving feedback and 4 types of self- treatment advice on how to adjust their treatment according to a predefined treatment plan: i.4 consecutive ACQ scores of 0.5 or less= decrease treatment according to treatment plan. ii. 2 consecutive scores > 0.5 but < 1.0= increase treatment according to treatment plan. iii. 1 score ≥1.0 but < 1.5 = immediately increase treatment according to treatment plan. iv. 1 score ≥ 1.5= immediately increase treatment and contact the asthma nurse.

Usual care (N = 60)
Usual care: asthma care according to the Dutch general practice guidelines on asthma management in adults, which recommend a medical review and treatment adjustment every 2 to 4 weeks in unstable asthma and medical review once or twice yearly for patients whose asthma is under control.

Outcomes

Study timepoints

- 30 month (van der Meer (2009) study with longer follow-up)

Asthma control

Outcome	Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) vs Usual care, 30 month, N2 = 47, N1 = 60
Quality of life (AQLQ) Asthma quality of life questionnaire, range 1 to 7. Final score Mean (95% CI)	0.29 (0.01 to 0.57)
Asthma control (ACQ) Asthma control questionnaire, range 0 to 7, final score Mean (95% CI)	-0.33 (-0.61 to -0.05)

Quality of life (AQLQ) - Polarity - Higher values are better
Asthma control (ACQ) - Polarity - Lower values are better
Mean differences for ACQ and AQLQ

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Asthmacontrol-AQLQ-MeanNineFivePercentCI-Internet-based self-management-Usual care-t30

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Self-reported subjective outcome and unblinded; post-hoc analysis; investigators likely to know 12 month results before reporting 30 month results; unclear information on missing data as longer follow-up participants were re-recruited.)*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention includes education)*

Asthmacontrol-ACQ-MeanNineFivePercentCI-Internet-based self-management-Usual care-t30

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Self-reported subjective outcome and unblinded; post-hoc analysis; investigators likely to know 12 month results before reporting 30 month results; unclear information on missing data as longer follow-up participants were re-recruited.)*
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention includes education)*

Ye, 2021

Bibliographic Reference	Ye, Ling; Gao, Xiwen; Tu, Chunlin; Du, Chunling; Gu, Wenchao; Hang, Jingqing; Zhao, Lei; Jie, Zhijun; Li, Hailing; Lu, Yueming; Wang, Jin; Jin, Xiaoyan; Hu, Xiao; Wu, Shunquan; Jin, Meiling; Comparative analysis of effectiveness of asthma control test-guided treatment versus usual care in patients with asthma from China.; Respiratory medicine; 2021; vol. 182; 106382

Study details

Trial name / registration number	GSK study ID 201097
Study type	Cluster randomised controlled trial
Study location	China
Study setting	Multicentre, 12 centers in China
Study dates	August 26, 2016 to August 09, 2019
Sources of funding	GSK (China) R&D Limited (GSK study ID 201097).
Inclusion criteria	Men and women aged 18–70 years (both included) with an ACT score <20 at Visit 0, documented clinical history of asthma for ≥6 months, and using ICS alone or ICS/LABA treatment within 1 year prior to or at Visit 0 were included.
Exclusion criteria	A patient was excluded if there was an evidence of life-threatening, severe, and unstable asthma, was a heavy smoker, had a history of alcohol/medication abuse, or respiratory tract infection.
Recruitment / selection of participants	The centres were randomized to either group: ACT-guided treatment group or UC group. There were 6 centres in each group with around 44 patients with asthma per centres. Recruitment method not specified.
Intervention(s)	Patients were required to record PEF, symptoms and medication in a paper diary record card (DRC) every day at morning and evening and completed the ACT at every visit at the clinic. Patients recruited in centres randomized to the ACT-guided treatment group received treatment based on their ACT score: i. ACT score = 25, ≥3 months; treatment adjustment: Step-down treatment ii. ACT score≥20, <25 or ACT score = 25, <3 months; treatment adjustment: No change

	iii. ACT score≤19; treatment adjustment: Step-up treatment The use of ICS/bronchodilators was modified according to the GINA recommendations. ACT scores were used to evaluate asthma control. If asthma was not under control, then treatment was stepped up. If it was controlled after 3 months, then the treatment was stepped down. Investigators did not use any scale; the prescribed the treatment as per GINA guidelines and using their previous experience of treatment of patients with asthma. The ACT was completed prior to any other assessments conducted. The investigators checked the patients' DRC, including symptom score, and evaluated therapeutic compliance.
Ethnicity	Asian
Education Level	Not reported/unclear
Language of Participants	Not reported/unclear
Comparator	Usual care: Patients were required to record PEF, symptoms and medication in a paper diary record card (DRC) every day at morning and evening and completed the ACT at every visit at the clinic. Patients recruited in the centres randomized to the UC group were treated based on the physician's subjective judgment. They completed ACT after the physician's treatment decision. The investigators checked the patients' DRC, including symptom score, and evaluated therapeutic compliance. In the usual care of treatment, the questions included but were not limited to the following: 1. What is the major symptom you have? 2. How do you feel about your symptom in the last 2 weeks?

	3. What kind of tests have you done? 4. What kind of medicines did you take? 5. How do you feel after taking these medicines?
Number of participants	530 randomised; 443 completed the study
Duration of follow-up	24 weeks
Additional comments	ntent-to-Treat population was the primary population of interest and included all patients who signed an informed consent form and underwent >1 post-baseline assessment. In the per protocol (PP) population, only the primary efficacy variables were analysed. It included patients from the ITT population with no major protocol deviations and with ≥80% treatment and diary compliance. The PP population was not analyzed if it comprised >95% or <50% of the ITT population. Safety population was analyzed for the safety assessments and included patients with >1 DRC assessment. A difference of 3 points in the mean ACT scores between the two groups or over time in an individual patient were considered as clinically significant. In the post-hoc subgroup, the difference between ACT-guided treatment and UC group was statistically significant in ACT total score at the 5% level of significance (only for male subgroup). The least squares (LS) mean change from baseline was calculated for ACT total score with 95% confidence interval (CI).

Study arms

Symptom/control questionnaires (ACT-guided treatment) (N = 242)
Asthma control test (ACT) guided treatment

Usual care (N = 265)

Characteristics

Arm-level characteristics

Characteristic	Symptom/control questionnaires (ACT-guided treatment) (N = 242)	Usual care (N = 265)
% Female Sample size	n = 115 ; % = 47.5	n = 135 ; % = 49.3
Mean age (SD) Mean (SD)	48 (12.81)	48 (13.43)
Ethnicity Han nationality Sample size	n = 237 ; % = 97.9	n = 261 ; % = 98.5
Smoking history: never smoking Sample size	n = 208 ; % = 86	n = 227 ; % = 85.7
Smoking Sample size	n = 1 ; % = 0.4	n = 0 ; % = 0
Quit smoking Sample size	n = 33 ; % = 13.6	n = 38 ; % = 14.3
Asthma severity: Mild Sample size	n = 117 ; % = 48.3	n = 159 ; % = 60

Characteristic	Symptom/control questionnaires (ACT-guided treatment) (N = 242)	Usual care (N = 265)
Moderate Sample size	n = 104 ; % = 43	n = 75 ; % = 28.3
Severe Sample size	n = 21 ; % = 8.7	n = 31 ; % = 11.7
ICS medication time (months) Mean (SD)	19.3 (29.1)	25 (40.33)
Asthma exacerbation history Sample size	n = 37 ; % = 15.3	n = 56 ; % = 21.1
At least one concurrent medication Sample size	n = 131 ; % = 54.1	n = 167 ; % = 63

Outcomes

Study timepoints

- Baseline
- 24 week

Dichotomous outcomes

Outcome	Symptom/control questionnaires (ACT-guided treatment), Baseline, N = 242	Symptom/control questionnaires (ACT-guided treatment), 24 week, N = 242	Usual care, Baseline, N = 265	Usual care, 24 week, N = 265
Asthma exacerbations (moderate/severe exacerbations not defined, patients per arm) (n (%)) assessed by the physician at each scheduled visit by reviewing the DRC, as well as by asking specific questions related to adverse events. 10 exacerbations events in each group No of events	n = NR ; % = NR	n = 8 ; % = 3.3	n = NR ; % = NR	n = 10 ; % = 3.8

Asthma exacerbations (moderate/severe exacerbations not defined, patients per arm) - Polarity - Lower values are better
ITT population; assessed by the physician at each scheduled visit by reviewing the DRC, as well as by asking specific questions related to adverse events

Continuous outcomes - contrast

Outcome	Symptom/control questionnaires (ACT-guided treatment) vs Usual care, Baseline, N2 = 263, N1 = 241	Symptom/control questionnaires (ACT-guided treatment) vs Usual care, 24 week, N2 = 263, N1 = 241
Asthma control (ACT score) Change score, range 5 to 25 Mean (95% CI)	NR (NR to NR)	1.3 (0.5 to 2.1)
Lung Function (FEV1) (% (not reported whether L or %	NR (NR to NR)	1.85 (1.57 to 5.28)

Outcome	Symptom/control questionnaires (ACT-guided treatment) vs Usual care, Baseline, N2 = 263, N1 = 241	Symptom/control questionnaires (ACT-guided treatment) vs Usual care, 24 week, N2 = 263, N1 = 241
predicted)) Change score Mean (95% CI)		
Quality of life (AQLQ (s) score) Change score, symptom domain, range 1-7 Mean (95% CI)	NR (NR to NR)	0.3 (0 to 0.6)

Asthma control (ACT score) - Polarity - Higher values are better
Lung Function (FEV1) - Polarity - Higher values are better
Quality of life (AQLQ (s) score) - Polarity - Higher values are better
percentage of patients who had an ACT score ≥20 or an improvement of >3 points in the ACT total score in >1 post-baseline assessment during the 24-week treatment period.
AQLQ and FEV1 mean differences calculated from arm-based change scores. Entered as contrast data as variability data only available for the difference between arms (see Fig 2 in paper). Error noted in paper for lower CI for FEV1 - must be a negative number not a positive number

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Exacerbations-Moderate/severeexacerbations-NoOfEvents-ACT-guided treatment-Usual care-t24

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Exacerbations recorded by patients record card (unblinded); no information about pre-specified analyses in protocol.)*
Overall bias and Directness	Overall Directness	Partially applicable *(Unclear if definition of outcome matched protocol)*

AsthmacontroltestLSmeanchangefrombaselineinACTscore-MeanNineFivePercentCI-ACT-guided treatment-Usual care-t24

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Subjective outcome and assessors aware of intervention; no information about prespecified analyses)*
Overall bias and Directness	Overall Directness	Directly applicable

Continuousoutcomes-contrast-AQLQ(s)score(range1-7)-MeanNineFivePercentCI-ACT-guided treatment-Usual care-t24

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Subjective outcome and assessors aware of intervention; no information about prespecified analyses)*
Overall bias and Directness	Overall Directness	Directly applicable

Continuousoutcomes-contrast-FEV1-MeanNineFivePercentCI-ACT-guided treatment-Usual care-t24

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns *(No information about prespecified analyses)*
Overall bias and Directness	Overall Directness	Directly applicable

Zhang, 2020

Bibliographic Reference	Zhang, Jing; Yin, Chengchen; Li, Hongfang; Wei, Weipeng; Gong, Yuansha; Tang, Fushan; Application of Once-Monthly Self-Reported ACT Questionnaire in Management of Adherence to Inhalers in Outpatients with Asthma.; Patient preference and adherence; 2020; vol. 14; 1027-1036

Study details

Study type	Randomised controlled trial (RCT)
Study location	China
Study setting	Clinic of respiratory medicine in central hospital in northwestern China
Study dates	Recruitment from February 2016 to July 2019
Sources of funding	Key Discipline of Zunyi Medical University
Inclusion criteria	Patients with asthma; diagnosed according to the diagnostic criteria for bronchial asthma prevention and treatment guidelines developed by the Asthma workgroup of the Chinese Medical Association Respiratory Diseases Branch. All patients were older than 18 years of age, and were able to understand and complete the ACT and Test of adherence to inhalers (TAI) questionnaire. The participants included both newly diagnosed patients and patients with already existing asthma. And the different kinds of patients were equally randomized into the observation and control group. Patients with asthma exacerbation were included when they started inhaled treatment after their severe acute symptoms were controlled

	by intravenous or oral glucocorticoid and/or bronchodilators. Severe patients account for about 10% of the total number of participant asthma patients and the number of severe patients in the two groups was roughly equal.
Exclusion criteria	difficult to understand the content of the test questionnaire; respiratory infection within 1 month; combined with other lung diseases or chronic heart, liver and kidney diseases; pregnant women.
Intervention(s)	Participants received the treatment of the control group plus they took the self-reported ACT questionnaire at the end of each months after starting treatment and were asked to bring ACT results to physicians or pharmacists at the next visit or to send the results to physicians or pharmacists through Wechat or email immediately after the questionnaire was finished. The patients' asthma control was tested in five levels from influence of asthma to daily activities, the frequency of asthma attacks, the frequency of nighttime asthma, the frequency of use of reliever (rescue) medicine and the general self-assessment in the past 4 weeks with scores of the five problems were added to calculate the total ACT score. The ACT score interpretation criteria: 25 for complete asthma control; 20–24 for partial to good asthma control; 19 and less for poor asthma control. Participants were guided by physicians and pharmacists on the significance of ACT and how to complete the ACT questionnaire on the first day of the study. The guidance of physicians and pharmacists in performing ACT usually means that the respiratory physicians explained to the patients the significance of ACT and the knowledge related to disease and symptom control in ACT and that the pharmacists explained to patients the relevant knowledge of inhalation therapy in ACT. In summary: Day 0: Pulmonary function measurement, inhaler technique training, ACT training. Month 1-6: standardized inhaler therapy, ACT in the end of every month

Ethnicity	Asian
Education Level	Not reported/unclear
Language of Participants	Non-English Assumed due to all participant Chinese residing in China.
Comparator	The patients were treated with standardized medication of combination of inhaled corticosteroids (ICS) and long-acting β2 receptor agonists (LABA) for asthma control and health education (involving inhaler technique training helpful for patients to use the inhalers correctly) Day 0: pulmonary function measurement, inhaler technique training Month 1-6: standardized inhaler therapy
Number of participants	627
Duration of follow-up	6 months
Indirectness	Unclear what adjustments to treatment were made as a result of ACT. Intervention aimed to improve self-management.
Additional comments	Not specified

Study arms

Symptom/control questionnaires (ACT monitoring with results sent to physician) (N = 315)
Observational group

Control group (N = 312)

Characteristics

Study-level characteristics

Characteristic	Study (N = 627)
% Female Sample size	n = 332 ; % = 53
Mean age (SD) Range: 19-68 years Mean (SD)	42.7 (11.8)

Arm-level characteristics

Characteristic	Symptom/control questionnaires (ACT monitoring with results sent to physician) (N = 315)	Control group (N = 312)
FEV1 % predicted Mean (SD)	56.05 (13.49)	56.12 (13.02)
PEF % predicted Mean (SD)	63.42 (6.72)	63.15 (7.34)

Outcomes

Study timepoints

- Baseline
- 6 month

Lung function

Outcome	Symptom/control questionnaires (ACT monitoring with results sent to physician), Baseline, N = 315	Symptom/control questionnaires (ACT monitoring with results sent to physician), 6 month, N = 315	Control group, Baseline, N = 312	Control group, 6 month, N = 312
Lung function (FEV1 % predicted) Improvement/change score after treatment Mean (SD)	56.05 (13.49)	36.72 (7.64)	56.12 (13.02)	19.94 (3.49)
Lung function (PEF % predicted) Improvement/change score after treatment Mean (SD)	63.42 (6.72)	41.69 (5.78)	63.15 (7.34)	23.85 (2.64)

Lung function (FEV1 % predicted) - Polarity - Higher values are better
Lung function (PEF % predicted) - Polarity - Higher values are better
the quark4 lung function meter manufactured by COSMED Company in Italy to measure and compare the lung function [FEV1 (forced expiratory volume in one second), PEF (peak expiratory flow), both indexes were recorded as percent predicted ones] of the two groups of patients before and after 6 months of treatment.

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Lungfunction-FEV1%predicted-MeanSD-Observational group-Control group-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Some concerns about lack of information about randomisation and pre-specified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(unclear what adjustments to treatment were made; intervention was using the ACT aiming to improve adherence/self-management which in turn may improve clinical outcomes)*

Lungfunction-PEF%predicted-MeanSD-Observational group-Control group-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Lack of details over randomisation and pre-specified analyses)*
Overall bias and Directness	Overall Directness	Partially applicable *(unclear what adjustments to treatment were made; intervention was using the ACT aiming to improve adherence/self-management which in turn may improve clinical outcomes)*

Appendix E Forest plots

Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) vs usual care (by pharmacists) in adults

Figure 2: Asthma exacerbations (severe exacerbations, final scores, lower is better, FUP:6 months)

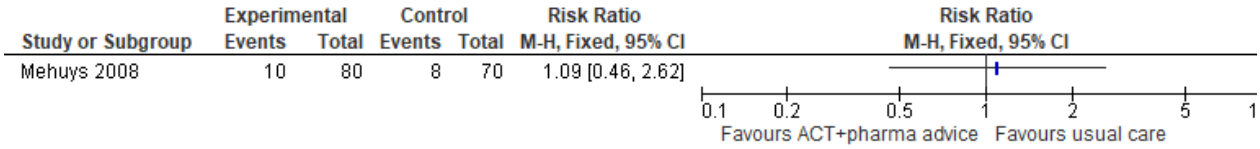


Figure 3: Unscheduled health utilisation) emergency department visits or hospitalisation, final scores, lower is better, FUP: 6 months)

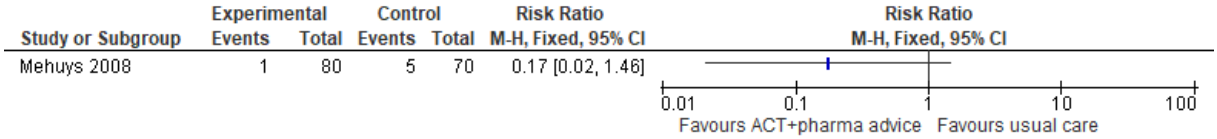


Figure 4: Asthma control (ACT score, range 0 to 25, final scores, higher is better, FUP: 6 months)

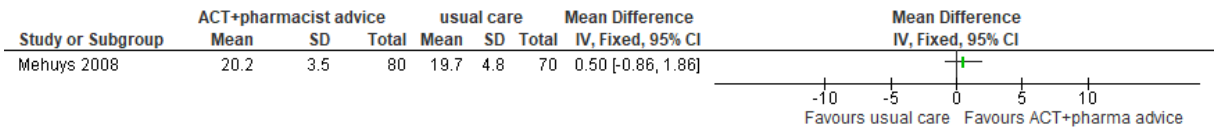


Figure 5: Quality of life (AQLQ, scale 0 to 7, final scores, higher is better, FUP: 6 months)

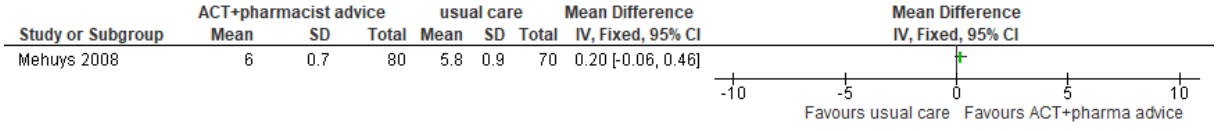


Figure 6: Lung function (morning PEF, % predicted, final scores, higher is better, FUP: 6 months)

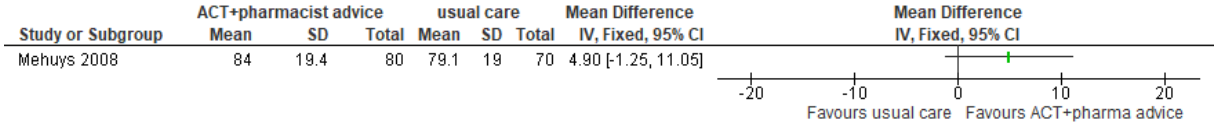
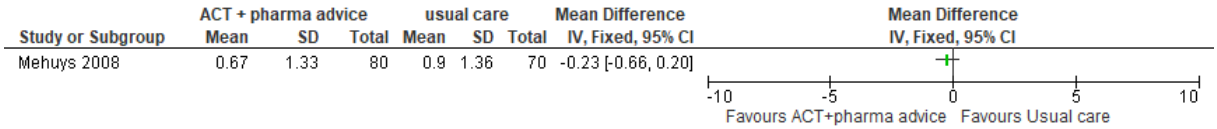


Figure 7: Reliever/rescue medication use (puff/day; mean over previous 14 days, final scores, lower is better, FUP: 6 months)



Symptom/control questionnaires (ACT-guided treatment) vs usual care (physician's judgment) in adults

Figure 8: Asthma exacerbations (moderate/severe exacerbations, final scores, lower is better, FUP:24 weeks)

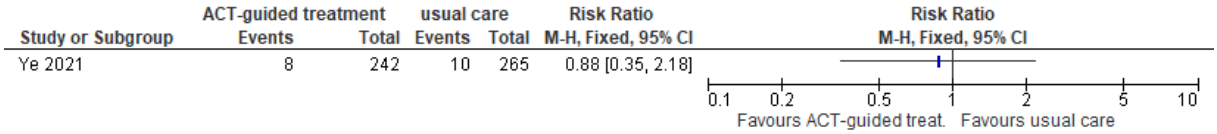


Figure 9: Asthma control (ACT score, range 5 to 25, change scores, higher is better, FUP: 24 weeks)

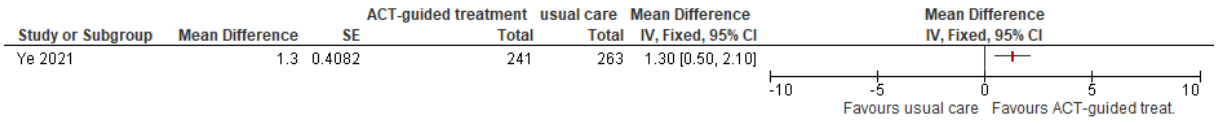


Figure 10: Lung function (FEV1, % change score, higher is better, FUP: 24 weeks)

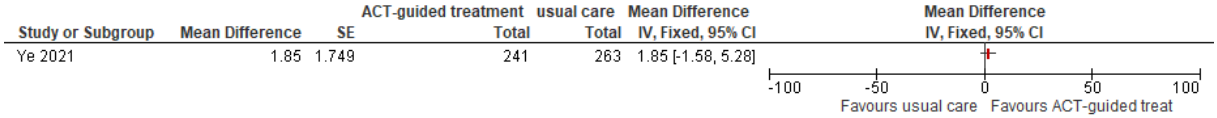
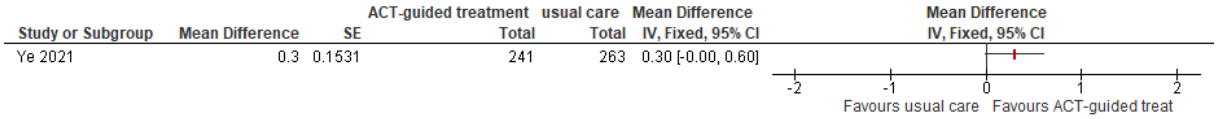


Figure 11: Quality of life (AQLQ symptom domain, range 1 to 7, change score, higher is better, FUP: 24 weeks)



Symptom/control questionnaires (ACT monitoring with results sent to physician) vs usual care (ICS/LABA & education) in adults

Figure 12: Lung function (FEV1 % predicted, change score, higher is better, FUP: 6 months)

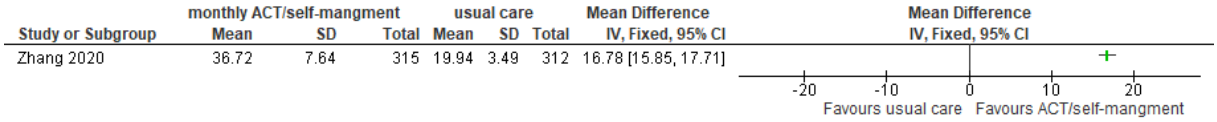
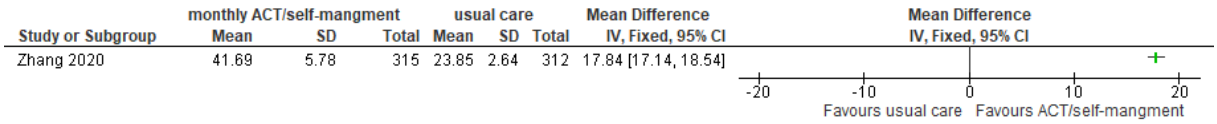


Figure 13: Lung function (PEF % predicted, change score, higher is better, FUP: 6 months)



Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) vs usual care (Dutch guidelines) in adults

Figure 14: Asthma exacerbations (final scores, lower is better, FUP: 12 months)

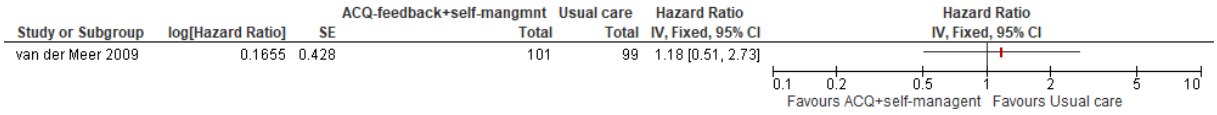


Figure 15: Asthma control (ACQ, range 0 to 7, lower is better change scores, FUP: 12 months)

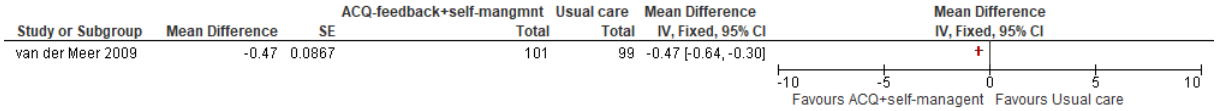


Figure 16: Asthma control (ACQ, range 0 to 7, lower is better, change scores, FUP: 30 months)

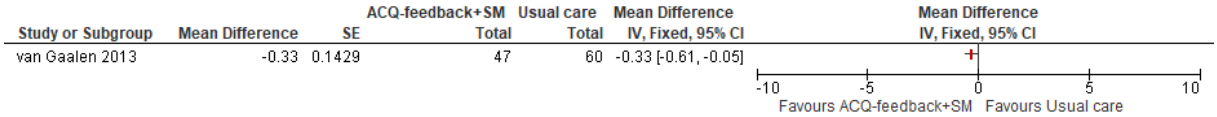


Figure 17: Quality of life (AQLQ, range 1 to 7, change score, higher is better, FUP: 12 months)

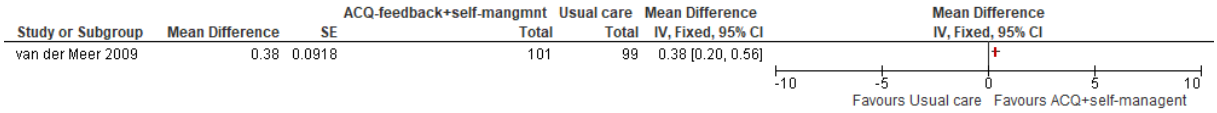


Figure 18: Quality of life (AQLQ, range 1 to 7, change score, higher is better, FUP: 30 months)

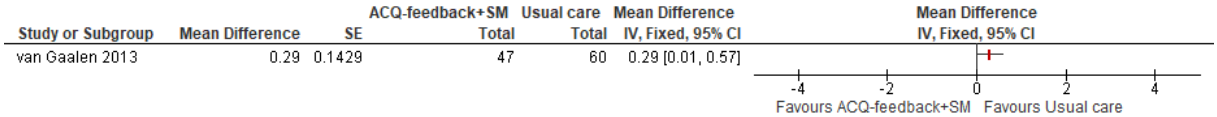


Figure 19: Lung function (FEV1, L, change scores, higher is better, FUP:12 months)

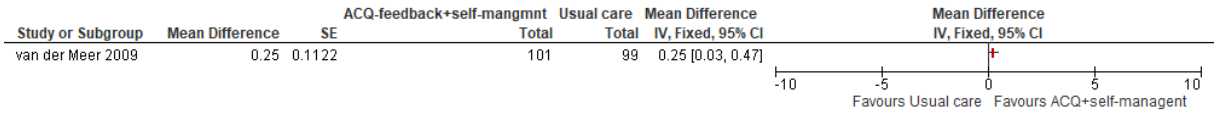


Figure 20: Symptoms (symptom-free days, %change scores, higher is better, FUP: 12 months)

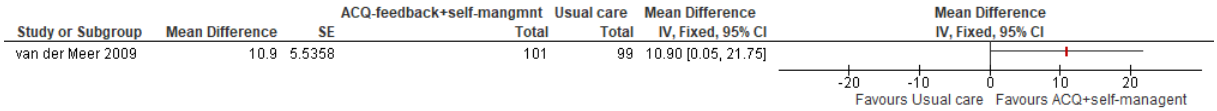
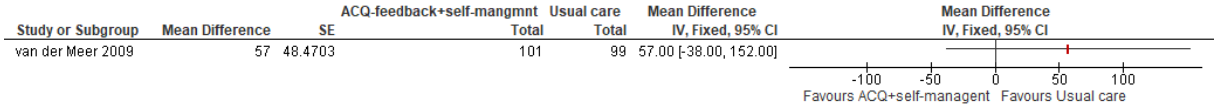


Figure 21: Dose of regular asthma therapy/preventer medication (daily ICS use, mcg, change scores, FUP: 12 months)



Symptom scores or diaries (symptom questions with feedback to support self-management) vs Control-Qs +feedback in adults

Figure 22: Unscheduled healthcare utilisation (number of emergency room visits, change score, lower is better, FUP: 12 months)

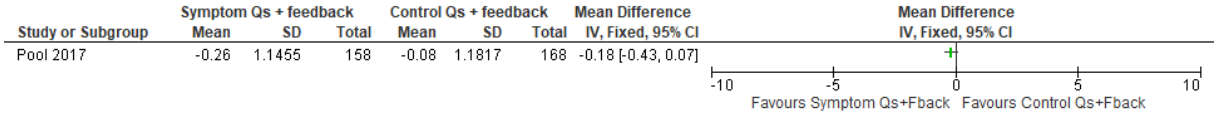


Figure 23: Unscheduled healthcare utilisation (number of outpatient visits, change score, lower is better, FUP: 12 months)

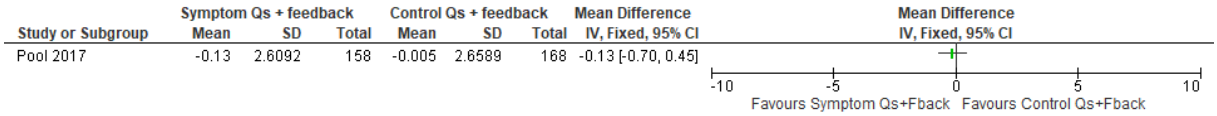


Figure 24: Asthma control (ACT score, range 5 to 25, change score, higher is better, FUP:12 months)

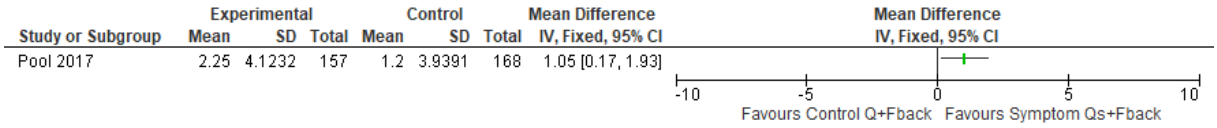


Figure 25: Dose of regular asthma therapy / preventer medication (number of asthma medications, change score, lower is better, FUP:12 months)

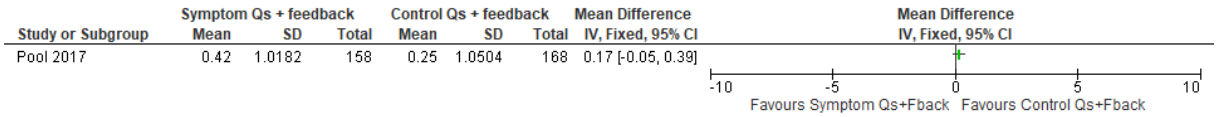
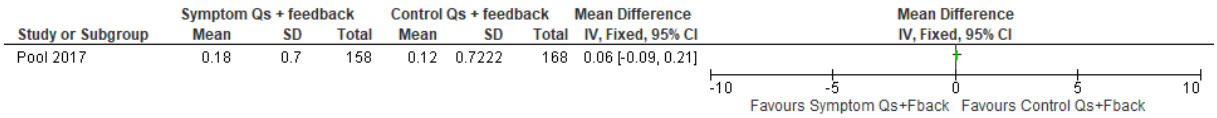


Figure 26: Dose of regular asthma therapy / preventer medication (number of asthma controller medications, change score, lower is better, FUP: 12 months)



Symptom/control questionnaires (ACQ monitoring with feedback to self-management, plus education) vs usual care (Dutch guidelines) in children and young people

Figure 27: Asthma exacerbations (final score, lower is better, FUP: 12 months)

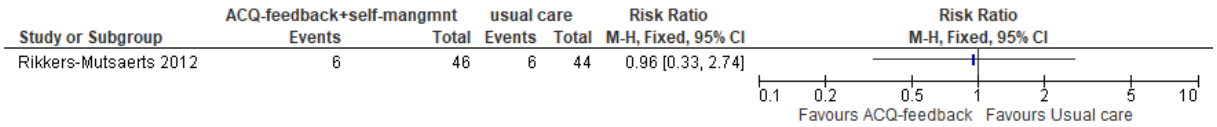


Figure 28: Asthma control (ACQ, range 0 to 7, change scores, lower is better, FUP: 12 months)

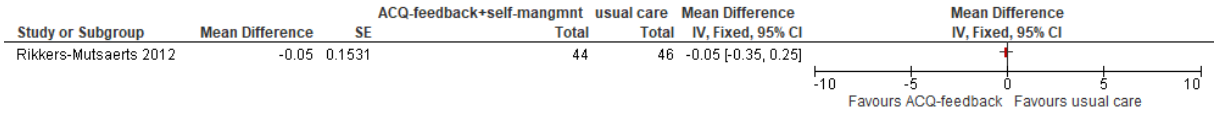


Figure 29: Quality of life (paediatric asthma-QOL-q, range 1 to 7, change score, higher is better, FUP: 12 months)

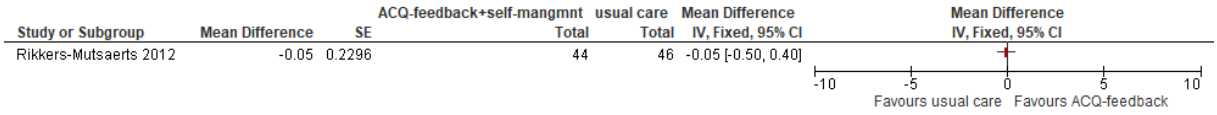


Figure 30: Dose of regular asthma therapy / preventer medication (daily ICS dose, mcg, change scores, lower is better, FUP: 12 months)

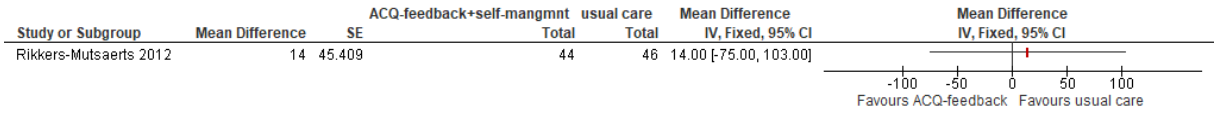
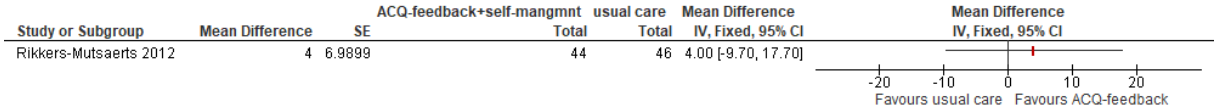


Figure 31: Symptoms (symptom free days, change score, higher is better, FUP: 12 months)



Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) vs usual care in children and young people

Figure 32: Unscheduled healthcare utilisation (visits to emergency department; lower is better, FUP: 16 months)

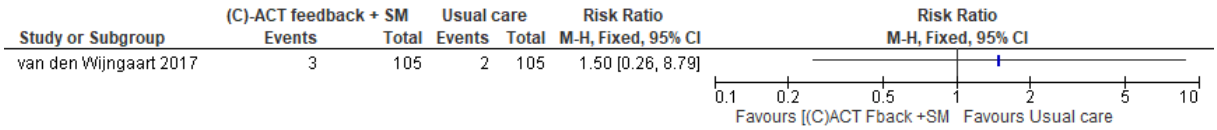


Figure 33: Unscheduled healthcare utilisation (hospital admissions; lower is better, FUP: 16 months)

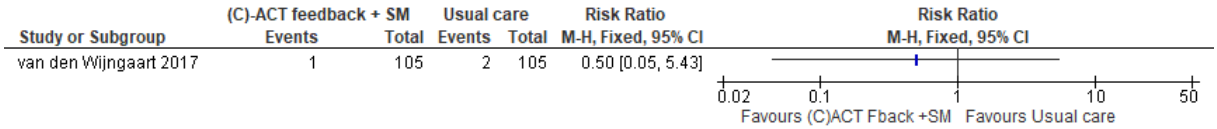


Figure 34: Unscheduled healthcare utilisation (unscheduled visits to outpatients; lower is better, FUP: 16 months)

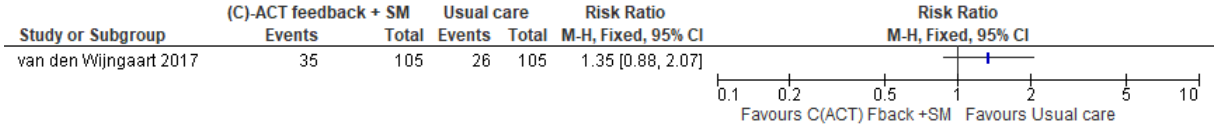


Figure 35: Asthma exacerbations (final score, lower is better, FUP: 16 months)

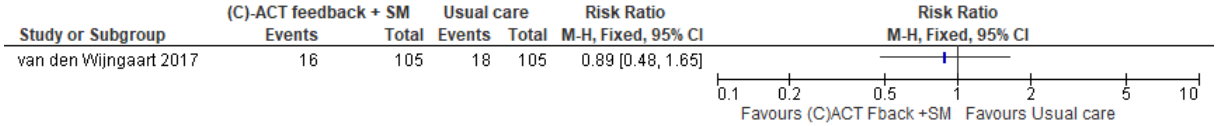


Figure 36: Asthma control (ACT, range 5-25, final score, higher is better, FUP: 16 months)

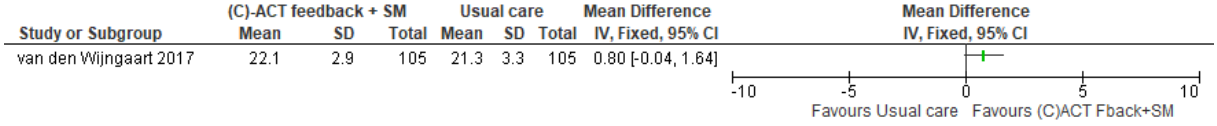


Figure 37: Asthma control (C-ACT, range 0-27, final score, higher is better, FUP: 16 months)

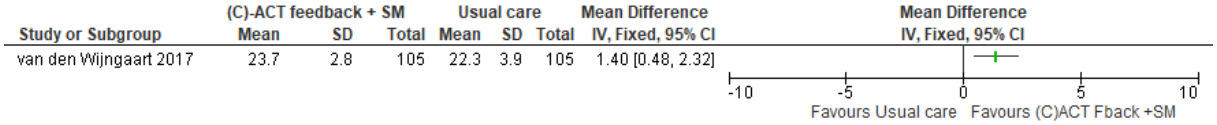


Figure 38: Lung function (FEV1 % predicted, higher is better, final score, FUP: 16 months)

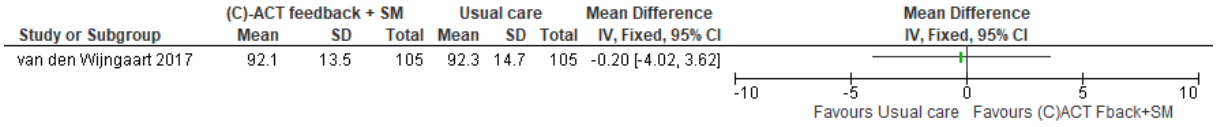
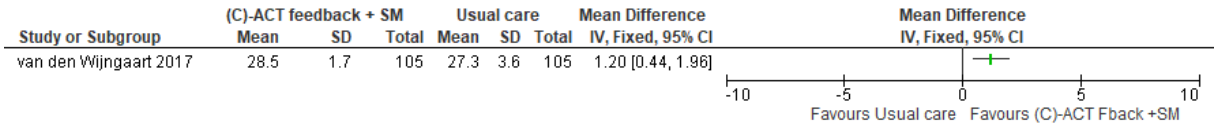


Figure 39: Symptoms (symptom free days, final score, higher is better, FUP: 16 months)



Appendix F GRADE tables

Table 12: Clinical evidence profile: Symptom/control questionnaires (ACT monitoring with pharmacist advice based on ACT score, plus education) vs usual care (by pharmacists) in adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACT-score & pharmacist advice	usual care (by pharmacists) in adults	Relative (95% CI)	Absolute (95% CI)		
Asthma exacerbations (severe exacerbations, final score, lower is better, FUP 6 Mo)												
1	randomised trials	serious[a]	not serious	serious[b]	very serious[c]	none	10/80 (12.5%)	8/70 (11.4%)	RR 1.09 (0.46 to 2.62)	**10 more per 1,000** (from 62 fewer to 185 more)	⨁◯◯◯ Very low	CRITICAL
Unscheduled healthcare utlisation (emergency department visits or hospitalisation, final scores, lower is better, FUP 6 Mo)												
1	randomised trials	serious[d]	not serious	serious[b]	very serious[c]	none	1/80 (1.3%)	5/70 (7.1%)	RR 0.17 (0.02 to 1.46)	**59 fewer per 1,000** (from 70 fewer to 33 more)	⨁◯◯◯ Very low	CRITICAL
Asthma control (ACT score, range 0 to 25, final score, higher is better, FUP 6 mo)												
1	randomised trials	very serious[e]	not serious	serious[b]	not serious[f]	none	80	70	-	MD **0.5 higher** (0.86 lower to 1.86 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (asthma-QoL questionnaire, scale 0 to 7, final score, higher is better, FUP 6 Mo)												
1	randomised trials	very serious[e]	not serious	serious[b]	not serious[f]	none	80	70	-	MD **0.2 higher** (0.06 lower to 0.46 higher)	⨁◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACT-score & pharmacist advice	usual care (by pharmacists) in adults	Relative (95% CI)	Absolute (95% CI)		
Lung function (morning PEF, % predicted, final score, higher is better, FUP 6 Mo); at 6 months)												
1	randomised trials	serious[g]	not serious	serious[b]	serious[h]	none	80	70	-	MD **4.9 higher** (1.25 lower to 11.05 higher)	⨁◯◯◯ Very low	CRITICAL
Reliever/rescue medication use (puff/day; mean over previous 14 days, final score, lower is better, FUP 6 Mo)												
1	randomised trials	very serious[e]	not serious	serious[b]	not serious[f]	none	80	70	-	MD **0.23 lower** (0.66 lower to 0.2 higher)	⨁◯◯◯ Very low	CRITICAL

a. Downgraded by one increment due to some concerns about risk of bias (no info about prespecified analyses)

b. Downgraded by one increment for intervention indirectness (intervention group received education as well and questionnaire monitoring)

c. Downgraded by two increments for imprecision because the confidence interval crosses both MIDs (0.8-1.25)

d. Downgraded by one increment due to some concerns about risk of bias (no info about prespecified analyses and no information about outcome assessment)

e. Downgraded by two increments because study at high risk of bias (self-reported outcome and unblinded: no information in prespecified analyses and unclear why ITT analysis presented for primary outcomes and per-protocol analysis for secondary outcomes)

f. Published MIDs: ACT=3; AQLQ=0.5; reliever/rescue medication=0.81 puffs/day

g. Downgraded by one increment due to some concerns about risk of bias (no information about prespecified analyses and unclear why PP used for secondary outcomes but ITT for primary outcomes)

h. Downgraded by one increment for imprecision because the confidence interval crosses one MID (calculated as baseline SD of control and intervention groups /2=9.05)

Table 13: Clinical evidence profile: Symptom/control questionnaires (ACT-guided treatment) vs usual care (physician's judgment) in adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACT-guided treatment	usual care (physician's judgment) in adults	Relative (95% CI)	Absolute (95% CI)		
Asthma exacerbations (moderate/severe exacerbations, final score, lower is better, FUP 24 weeks)												
1	randomised trials	very serious[a]	not serious	serious[b]	very serious[c]	none	8/242 (3.3%)	10/265 (3.8%)	RR 0.88 (0.35 to 2.18)	**5 fewer per 1,000** (from 25 fewer to 45 more)	⨁◯◯◯ Very low	CRITICAL
Asthma control (LS mean change in ACT score, change score, higher is better, FUP 24 weeks)												
1	randomised trials	very serious[d]	not serious	not serious	not serious[e]	none	241	263	-	MD **1.3 higher** (0.5 higher to 2.1 higher)	⨁⨁◯◯ Low	CRITICAL
Lung function (FEV1 (% change score; higher is better, FUP 24 weeks)												
1	randomised trials	serious[f]	not serious	not serious	not serious[g]	none	241	263	-	MD **1.85 higher** (1.58 lower to 5.28 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (AQLQ symptom domain, range 1-7; change score; higher is better, FUP 24 weeks)												
1	randomised trials	very serious[d]	not serious	not serious	serious[h]	none	241	263	-	MD **0.3 higher** (0 to 0.6 higher)	⨁◯◯◯ Very low	CRITICAL

a. Downgraded by two increments due to concerns about risk of bias (exacerbations determined by patients record card and unblinded; no information about pre-specified analyses in protocol.)

b. Downgraded by one increment for outcome indirectness (not defined and so not clear whether meets protocol definition)

c. Downgraded by two increments for imprecision because the confidence interval crossed both MIDs (MIDs for dichotomous outcomes: 0.8 and 1.25)

d. Subjective outcome and assessors aware of intervention; no information about prespecified analyses

e. Published MID for ACT=3

f. Downgraded by one increment due to some concerns about risk of bias (no information about prespecified analyses)

g. MID= Follow-up SD/2=9.8 (baseline SDs not available)

h. Downgraded by one increment for imprecision because confidence interval crosses one MID (published MID for AQLQ=0.5)

Table 14: Clinical evidence profile: Symptom/control questionnaires (ACT monitoring with results sent to physician) vs usual care (ICS/LABA & education) in adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACT self-management	usual care (ICS/LABA & education) in adults	Relative (95% CI)	Absolute (95% CI)		
Lung function (FEV1 % predicted, change score, higher is better, 6 mo FUP)												
1	randomised trials	very serious[a]	not serious	serious[b]	not serious[c]	none	315	312	-	MD **16.78 higher** (15.85 higher to 17.71 higher)	⨁◯◯◯ Very low	CRITICAL
Lung function (PEF % predicted, change score, higher is better, 6 Mo FUP)												
1	randomised trials	very serious[a]	not serious	serious[b]	not serious[c]	none	315	312	-	MD **17.84 higher** (17.14 higher to 18.54 higher)	⨁◯◯◯ Very low	CRITICAL

a. Downgraded by two increments because the study is at high risk of bias (no details about randomisation and pre-specified analyses)

b. Downgraded by one increment for intervention indirectness (unclear what adjustments to treatment and/or self-management made in response to ACT monitoring, though results were sent to physician)

c. MID calculated using baseline SD (of intervention + control groups/2)/2; FEV1: 6.63; PEF: 3.52

Table 15: Clinical evidence summary: Symptom/control questionnaires (ACQ monitoring with feedback to support self-management, plus education) vs usual care (Dutch guidelines) in adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACQ-feedback + self-management	usual care (Dutch guidelines) in adults	Relative (95% CI)	Absolute (95% CI)		
Asthma exacerbations, final score, lower is better, FUP 12 Mo)												
1	randomised trials	serious[a]	not serious	serious[b]	very serious[c]	none	11/101 (10.9%)	10/99 (10.1%)	HR 1.18 (0.51 to 2.73)	**17 more per 1,000** (from 48 fewer to 151 more)	⨁◯◯◯ Very low	CRITICAL
Asthma control (ACQ, range 0 to 7, lower is better, FUP 12 Mo)												
1	randomised trials	very serious[d]	not serious	serious[b]	serious[e]	none	101	99	-	MD **0.47 lower** (0.64 lower to 0.3 lower)	⨁◯◯◯ Very low	CRITICAL
Asthma control (ACQ, range 0 to 7, final score, lower is better, FUP 30 Mo												
1	randomised trials	very serious[f]	not serious	serious[b]	serious[e]	none	47	60	-	MD **0.33 lower** (0.61 lower to 0.05 lower)	⨁◯◯◯ Very low	CRITICAL
Quality of life (AQLQ , range 1 to 7, change score, higher is better, FUP 12 Mo)												
1	randomised trials	serious[d]	not serious	serious[b]	serious[e]	none	101	99	-	MD **0.38 higher** (0.2 higher to 0.56 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (AQLQ, range 1 to 7, final score, higher is better, FUP 30 Mo)												
1	randomised trials	very serious[f]	not serious	serious[b]	serious[e]	none	47	60	-	MD **0.29 higher** (0.01 higher to 0.57 higher)	⨁◯◯◯ Very low	CRITICAL
Lung function (FEV1, L, change score, higher is better, FUP 12 Mo)												
1	randomised trials	serious[a]	not serious	serious[b]	serious[e]	none	101	99	-	MD **0.25 higher** (0.03 higher to 0.47 higher)	⨁◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACQ-feedback + self-management	usual care (Dutch guidelines) in adults	Relative (95% CI)	Absolute (95% CI)		
Symptoms (symptom-free days, %, change score, higher is better, FUP 12 Mo)												
1	randomised trials	very serious[d]	not serious	serious[b]	serious[g]	none	101	99	-	MD **10.9 higher** (0.05 higher to 21.75 higher)	⨁◯◯◯ Very low	CRITICAL
Dose of regular asthma therapy / preventer medication (daily ICS use, mcg, change score, FUP 12 Mo)												
1	randomised trials	serious[h]	not serious	serious[b]	not serious[i]	none	101	99	-	MD **57 higher** (38 lower to 152 higher)	⨁⨁◯◯ Low	CRITICAL

a. Downgraded by one increment due to some concerns about risk of bias (no information about prespecified analyses)

b. Downgraded by one increment for intervention indirectness (intervention group received additional web-based and face-to-face education sessions)

c. Downgraded by two increments for imprecision because the confidence interval crosses both MIDs (0.8 to 1.25)

d. Downgraded by two increments because study at high risk of bias (self-reported outcome and unblinded study (ACQ measurement part of intervention); no information about pre-specified analyses)

e. Downgraded by one increment for imprecision because the confidence interval crosses one MID (published MIDs: ACQ=0.5; AQLQ=0.5; FEV1=0.23L))

f. Downgraded by two increments because study at high risk of bias (self-reported subjective outcome and unblinded; post-hoc analysis; investigators likely to know 12 month results before reporting 30 month results; unclear information on missing data as longer follow-up participants were re-recruited)

g. Downgraded by one increment for imprecision because the confidence interval crosses one MID (SD calculated from 95%CI/2=19.55)

h. Downgraded by one increment due to some concerns about risk of bias [self-reported outcome and unblinded (but not completely subjective an outcome); no information on prespecified outcomes]

i. MID: SD from 95%CI/2=171.35

Table 16: Clinical evidence summary: Symptom scores or diaries (symptom questions with feedback to support self-management) vs control questions and feedback in adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Symptom-Qs + feedback +self-management	Control-Qs +feedback	Relative (95% CI)	Absolute (95% CI)		
Unscheduled healthcare utlisation (number of emergency room visits, change score, lower is better, FUP 12 Mo)												
1	randomised trials	not serious	not serious	serious[a]	not serious[b]	none	158	168	-	MD **0.18 lower** (0.43 lower to 0.07 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Unscheduled healthcare utilisation (number of outpatient visits, change score, lower is better, FUP 12 Mo)												
1	randomised trials	not serious	not serious	serious[a]	not serious[b]	none	158	168	-	MD **0.13 lower** (0.7 lower to 0.45 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Asthma control (ACT, range 5 to 25, change score, higher is better, FUP 12 Mo)												
1	randomised trials	not serious	not serious	serious[a]	not serious[c]	none	157	168	-	MD **1.05 higher** (0.17 higher to 1.93 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Dose of regular asthma therapy / preventer medication (number of asthma medications, change score, lower is better, FUP 12 Mo)												
1	randomised trials	not serious	not serious	very serious[d]	not serious[b]	none	158	168	-	MD **0.17 higher** (0.05 lower to 0.39 higher)	⨁⨁◯◯ Low	CRITICAL
Dose of regular asthma therapy / preventer medication (number of asthma controller medications, change score, lower is better, FUP 12 Mo)												
1	randomised trials	not serious	not serious	very serious[d]	not serious[b]	none	158	168	-	MD **0.06 higher** (0.09 lower to 0.21 higher)	⨁⨁◯◯ Low	CRITICAL

a. Downgraded by 1 increment due to indirectness of intervention (use of non-validated asthma symptom questionnaire. Only 7/11 Q are directly about asthma symptoms)

b. MIDs= SD/2 of the intervention and control group; SDs were calculated using the baseline mean (95% CI) of the intervention and control group to get the standard error and then convert it to SD; MIDs: ED visits: 0.98; outpatient visits: 1.99; asthma medications: 1.0; asthma controller medications: 0.78

c. Published MID for ACT=3

d. Downgraded by 2 increments due to indirectness of intervention (use of non-validated asthma symptom questionnaire. Only 7/11 Q are directly about asthma symptoms) and outcome [not identical to dose of regular asthma therapy / preventer medication (ICS dose)]

Table 17: Clinical evidence profile: Symptom/control questionnaires (ACQ monitoring with feedback to self-management, plus education) compared to usual care (Dutch guidelines) in children and young people

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACQ-feedback + self-management	usual care (Dutch guidelines) in CYP	Relative (95% CI)	Absolute (95% CI)		
Asthma exacerbations (lower is better, FUP 12 Mo)												
1	randomised trials	very serious[a]	not serious	very serious[b]	very serious[c]	none	6/46 (13.0%)	6/44 (13.6%)	**RR 0.96** (0.33 to 2.74)	**5 fewer per 1,000** (from 91 fewer to 237 more)	⨁◯◯◯ Very low	CRITICAL
Asthma control (ACQ, change score, lower is better, FUP 12 Mo)												
1	randomised trials	very serious[a]	not serious	very serious[b]	not serious[d]	none	44	46	-	MD **0.05 lower** (0.35 lower to 0.25 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (paediatric asthma-QOL-q, change score, higher is better, FUP 12 Mo)												
1	randomised trials	very serious[a]	not serious	very serious[b]	not serious[d]	none	44	46	-	MD **0.05 lower** (0.5 lower to 0.4 higher)	⨁◯◯◯ Very low	CRITICAL
Dose of regular asthma therapy / preventer medication (daily ICS dose, change score, lower is better, FUP 12 Mo)												
1	randomised trials	very serious[a]	not serious	very serious[b]	serious[g]	none	44	46	-	MD **14 mcg higher** (75 lower to 103 higher)	⨁◯◯◯ Very low	CRITICAL
Symptoms (symptom free days, change score, higher is better, FUP 12 Mo)												
1	randomised trials	very serious[a]	not serious	very serious[b]	serious[h]	none	44	46	-	MD **4 higher** (9.7 lower to 17.7 higher)	⨁◯◯◯ Very low	CRITICAL

a. Downgraded by two increments because study at high risk of bias (>10% differential rate of missing data between groups at 12 months; subjective self-reported outcome & lack of blinding; No information on pre-specified analyses)

b. Downgraded by two increments for indirectness for population (mixed age group including people >16 years) and intervention (intervention group received additional web-based and face-to-face education sessions).

c. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs (MID for dichotomous outcomes: 0.8 and 1.25)

d. Based on MID for ACQ& pediatric QoL in children and young people: 0.5 for both measures

e. Downgraded by one increment for imprecision because the confidence interval crossed one MID (MID calculated using 95%CI of mean difference=215.34; MID=SD/2=107.7)

f. Downgraded by 1 increment as the confidence interval crossed one MID (MID calculated using 95% CI of the mean difference by calculating the standard error and converting to SD; MID:SD/2= 16.7)

Table 18: Clinical evidence summary Symptom/control questionnaires (C-ACT monitoring with feedback to support self-management, plus education) vs usual care in children and young people

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	C-ACT-feedback + self-management	usual care	Relative (95% CI)	Absolute (95% CI)		
Unscheduled healthcare utilisation (visits to emergency department, final score, lower is better, FUP 16 Mo)												
1	randomised trials	very serious[a]	not serious	serious[b]	very serious[c]	none	3/105 (2.9%)	2/105 (1.9%)	RR 1.50 (0.26 to 8.79)	**10 more per 1,000** (from 14 fewer to 148 more)	⨁◯◯◯ Very low	CRITICAL
Unscheduled healthcare utilisation (hospital admissions, final score, lower is better, FUP 16 Mo)												
1	randomised trials	very serious[a]	not serious	serious[b]	very serious[c]	none	1/105 (1.0%)	2/105 (1.9%)	RR 0.50 (0.05 to 5.43)	**10 fewer per 1,000** (from 18 fewer to 84 more)	⨁◯◯◯ Very low	CRITICAL
Unscheduled healthcare utilisation (unscheduled visits to outpatients, final score, lower is better, FUP 16 Mo)												
1	randomised trials	very serious[a]	not serious	serious[b]	serious[d]	none	35/105 (33.3%)	26/105 (24.8%)	RR 1.35 (0.88 to 2.07)	**87 more per 1,000** (from 30 fewer to 265 more)	⨁◯◯◯ Very low	CRITICAL
Asthma exacerbations (final score, lower is better, FUP 16 Mo)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	C-ACT-feedback + self-management	usual care	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious[a]	not serious	serious[b]	very serious[c]	none	16/105 (15.2%)	18/105 (17.1%)	RR 0.89 (0.48 to 1.65)	**19 fewer per 1,000** (from 89 fewer to 111 more)	⨁◯◯◯ Very low	CRITICAL
Asthma control (ACT, range 5 to 25, final score; higher is better, FUP 16 Mo)												
1	randomised trials	very serious[e]	not serious	serious[b]	not serious[f]	none	105	105	-	MD **0.8 higher** (0.04 lower to 1.64 higher)	⨁◯◯◯ Very low	CRITICAL
Asthma control (C-ACT, range 0 to 27, final score; higher is better, FUP 16 Mo)												
1	randomised trials	very serious[e]	not serious	serious[b]	serious[g]	none	105	105	-	MD **1.4 higher** (0.48 higher to 2.32 higher)	⨁◯◯◯ Very low	CRITICAL
Lung function (FEV1, % predicted, final score; FUP 16 Mo)												
1	randomised trials	very serious[h]	not serious	serious[b]	not serious[i]	none	105	105	-	MD **0.2 lower** (4.02 lower to 3.62 higher)	⨁◯◯◯ Very low	CRITICAL
Symptoms (symptom free days, final score; higher is better, FUP 16 Mo)												
1	randomised trials	very serious[e]	not serious	very serious[j]	not serious[i]	none	105	105	-	MD **1.2 higher** (0.44 higher to 1.96 higher)	⨁◯◯◯ Very low	CRITICAL

a. Downgraded by 2 increments as the evidence was at very high risk of bias (due to lack of information about outcome assessment, adherence, and pre-specified analyses. Intervention-related deviations from protocol also possible due to availability of FEV1 and FENO to treating physicians in both arms)

b. Downgraded by one increment for intervention indirectness because intervention included web-based education as well as C-ACT monitoring

c. Downgraded by 2 increments for imprecision because the confidence interval crossed both MIDs (MIDs for dichotomous outcomes: 0.8 and 1.25)

d. Downgraded by one increment because the confidence interval crossed one MID (MIDs for dichotomous outcomes: 0.8 and 1.25)

e. Intervention-related deviations from protocol possible due to availability of FEV1 and FENO to treating physicians; no information about protocol, missing data or adherence; outcome based on self-reports (unblinded)

f. Published MID for ACT=3

g. Downgraded by one increment for imprecision because confidence interval crosses one MID (published MID for C-ACT=2)

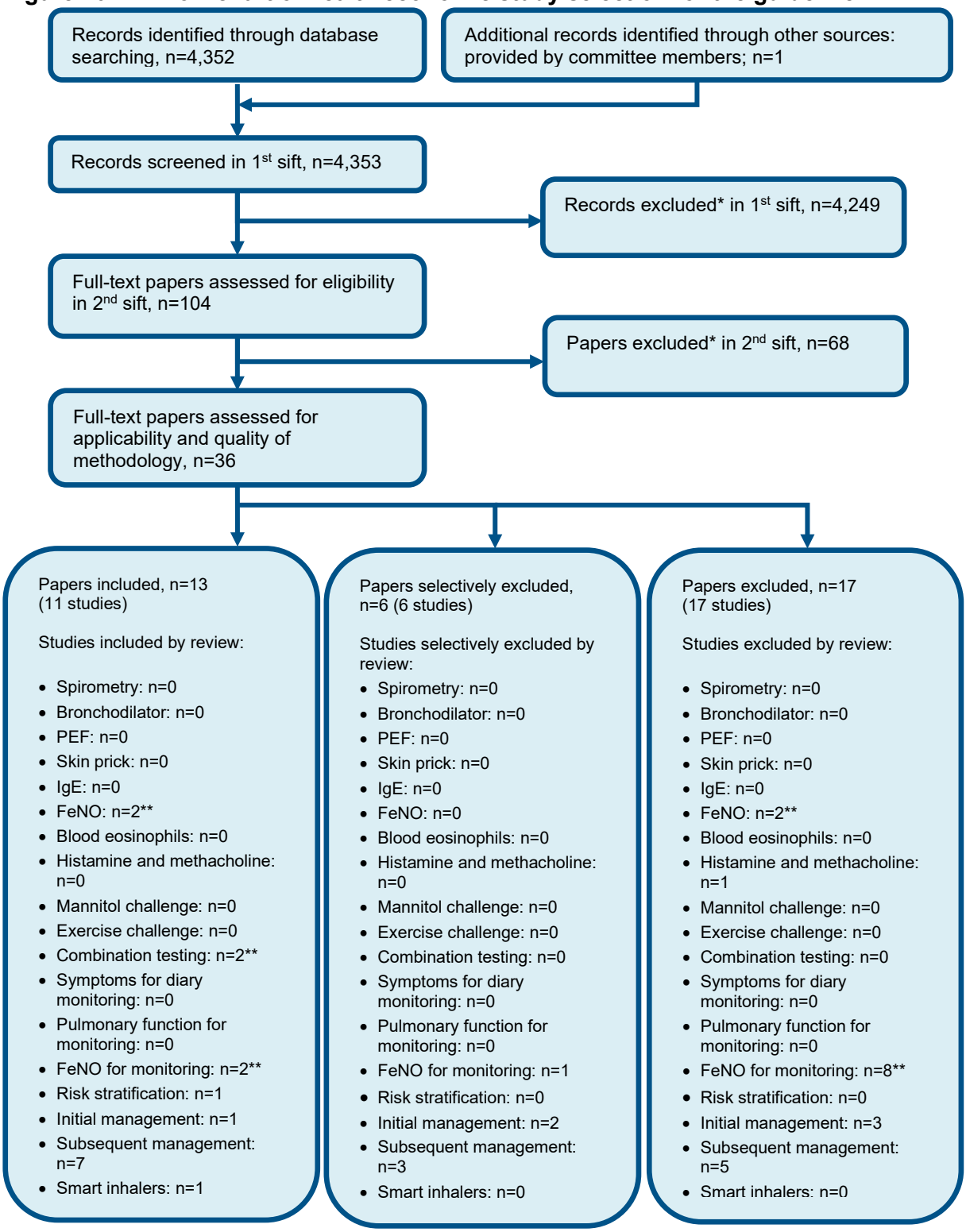
h. Unblinded outcome assessors, no information about missing data, protocol or adherence; intervention-related deviations from protocol possible due to availability of FEV1 and FENO to treating physicians

i. MID for FEV1 % predicted calculated using baseline SD/2= 7.05; for symptom free days: 2.25

j. Downgraded by two increments for intervention indirectness (intervention included web-based education as well as C-ACT monitoring) and outcome indirectness (based on C-ACT)

Appendix G Economic evidence study selection

Figure 40: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language
** Includes studies that are in multiple reviews

Appendix H Economic evidence tables

None.

Appendix I Excluded studies

I.1 Clinical studies

Table 19: Studies excluded from the clinical review

Study	Reason for exclusion
Ahmed, Sara, Ernst, Pierre, Bartlett, Susan J et al. (2016) The Effectiveness of Web-Based Asthma Self-Management System, My Asthma Portal (MAP): A Pilot Randomized Controlled Trial. Journal of medical Internet research 18(12): e313	- Study does not contain an intervention relevant to this review protocol *Intervention is multi-component digital intervention which includes self-monitoring of symptoms (and eg exercise and medication adherence) plus education (which is linked to nurse management system). Multiple self-monitoring inputs (not just symptom monitoring) determine subsequent management*
Amorha, Kosisochi C; Okonta, Mathew J; Ukwe, Chinwe V (2021) Impact of pharmacist-led educational interventions on asthma control and adherence: single-blind, randomised clinical trial. International journal of clinical pharmacy 43(3): 689-697	- Study does not contain an intervention relevant to this review protocol *Multi-component intervention includes instruction on how to complete a symptoms/peak flow diary. But not clear that management was based on this (only one patient completed it for short period)*
Arga, M., Sahbaz, H., Bakirtas, A. et al. (2014) Does self-monitoring by means of symptom diaries improve asthma control in children?. Journal of Asthma 51(3): 299-305	- Study design not relevant to this review protocol *Observational study. Symptom diary/no symptom diary groups not allocated or randomised.*
Arikan Ayyildiz, Z., Isik, S., Caglayan-Sozmen, S. et al. (2014) Effect of asthma education programme on asthma control in children with uncontrolled asthma. Allergy: European Journal of Allergy and Clinical Immunology 69(suppl99): 441	- Conference abstract
Arikan-Ayyildiz, Zeynep, Isik, Sakine, Caglayan-Sozmen, Sule et al. (2016) Efficacy of asthma education program on asthma control in children with uncontrolled asthma. The Turkish journal of pediatrics 58(4): 383-388	- Study does not contain an intervention relevant to this review protocol *Intervention education only*

Study	Reason for exclusion
Banasiak, Nancy Cantey (2018) Implementation of the Asthma Control Test in Primary Care to Improve Patient Outcomes. Journal of pediatric health care : official publication of National Association of Pediatric Nurse Associates & Practitioners 32(6): 591-599	- Study design not relevant to this review protocol *Not an RCT. Implementation study with pre/post assessment.*
Beerthuizen, Thijs, Rijssenbeek-Nouwens, Lucia H, van Koppen, Sophia M et al. (2020) Internet-Based Self-Management Support After High-Altitude Climate Treatment for Severe Asthma: Randomized Controlled Trial. Journal of medical Internet research 22(7): e13145	- Population not relevant to this review protocol *Study in patients with severe asthma*
Beerthuizen, Thijs, Voorend-van Bergen, Sandra, van den Hout, Wilbert B et al. (2016) Cost-effectiveness of FENO-based and web-based monitoring in paediatric asthma management: a randomised controlled trial. Thorax 71(7): 607-13	- Comparator in study does not match that specified in this review protocol *Same study as Voorend-van Bergen (2015) which is excluded. control group also uses a different frequency and format of ACT.*
Bergen, S.V., Beerthuizen, T., Van Den Hout, W. et al. (2015) Cost-effectiveness of FeNO-and web-based monitoring in pediatric asthma management. European Respiratory Journal 46(suppl59)	- Conference abstract
Bernholm, Katrine Feldballe, Homoe, Anne-Sophie, Meteran, Howraman et al. (2018) F eNO-based asthma management results in faster improvement of airway hyperresponsiveness. ERJ open research 4(4)	- Comparator in study does not match that specified in this review protocol *Arms: treatment based on FENO Vs treatment based on ACQ. No usual care comparator*
Bodajko-Grochowska, A., Emeryk, A., Markut-Miotla, E. et al. (2017) Asthma Control Test (ACT) or Asthma Control Questionnaire (ACQ)?-validity and responsiveness in children. European Respiratory Journal 50(supplement61)	- Conference abstract
Bruzzese, J., George, M.R., Liu, J. et al. (2018) The preliminary impact of a web-based intervention for adolescents with uncontrolled asthma: Results from a randomized pilot trial. American Journal of Respiratory and Critical Care Medicine 197(meetingabstracts)	- Conference abstract

Study	Reason for exclusion
Cano Fuentes, G, Dastis Bendala, C, Morales Barroso, I et al. (2014) A randomised clinical trial to evaluate the effectiveness of an educational intervention developed for adult asthmatics in a primary care centre. Atencion primaria / Sociedad Espanola de Medicina de Familia y Comunitaria 46(3): 117-139	- Study not reported in English *Article in Spanish*
Chen, Jianli and Chen, Yongmin (2021) A nurse-led hierarchical management model for the out-of-hospital management of children with bronchial asthma: a prospective randomized controlled study. American journal of translational research 13(6): 6488-6497	- Study does not contain an intervention relevant to this review protocol
Cowden, John D, Wilkerson-Amendell, Sharon, Weathers, Laura et al. (2015) The talking card: Randomized controlled trial of a novel audio-recording tool for asthma control. Allergy and asthma proceedings 36(5): e86-91	- Study does not contain an intervention relevant to this review protocol *Intervention is not symptom diary/questionnaire*
Dardouri, Maha, Sahli, Jihene, Ajmi, Thouraya et al. (2020) Effect of Family Empowerment Education on Pulmonary Function and Quality of Life of Children With Asthma and Their Parents in Tunisia: A Randomized Controlled Trial. Journal of pediatric nursing 54: e9-e16	- Study does not contain an intervention relevant to this review protocol
Dokbua, S, Dilokthornsakul, P, Chaiyakunapruk, N et al. (2018) Effects of an Asthma Self-Management Support Service Provided by Community Pharmacists: A Systematic Review and Meta-Analysis. Journal of managed care & specialty pharmacy 24(11): 1184-1196	- Systematic review used as source of primary studies *systematic review. Any potentially included studies before 2012 cut-off*
Farouk, R.A., Abdel-Latif, G.A.-R., Dwedar, I.A. et al. (2023) Validation of asthma management approach according to risk factors. Egyptian Journal of Chest Diseases and Tuberculosis 72(1): 16-24	- Study does not contain an intervention relevant to this review protocol *and incorrect study design: cohort study*
Fedele, David A, Janicke, David M, McQuaid, Elizabeth L et al. (2018) A Behavioral Family Intervention for Children with Overweight and Asthma. Clinical practice in pediatric psychology 6(3): 259-269	- Study does not contain an intervention relevant to this review protocol

Study	Reason for exclusion
Federman, A., O'Conor, R., Mindlis, I. et al. (2018) A comprehensive self-management support program improves asthma control and quality of life among older adults: Results of a randomized controlled trial. American Journal of Respiratory and Critical Care Medicine 197(meetingabstracts)	- Conference abstract
Federman, Alex D, O'Conor, Rachel, Mindlis, Irina et al. (2019) Effect of a Self-management Support Intervention on Asthma Outcomes in Older Adults: The SAMBA Study Randomized Clinical Trial. JAMA internal medicine 179(8): 1113-1121	- Study does not contain an intervention relevant to this review protocol
Fornell, L.L., Escriche, X.F., Alvarez, S.A. et al. (2014) Can we improve the follow up of asthmatic patients with asthma educational program (PAMA)?. European Respiratory Journal 44(suppl58)	- Conference abstract
Gao, Guozhen, Liao, Yaoji, Mo, Lulu et al. (2020) A randomized controlled trial of a nurse-led education pathway for asthmatic children from outpatient to home. International journal of nursing practice 26(3): e12823	- Study does not contain an intervention relevant to this review protocol *Multi-component education intervention that includes asthma diary.*
George, Maureen, Bruzzese, Jean-Marie, Lynn S Sommers, Marilyn et al. (2021) Group-randomized trial of tailored brief shared decision-making to improve asthma control in urban black adults. Journal of advanced nursing 77(3): 1501-1517	- Study does not contain an intervention relevant to this review protocol
Gladanac, B., Chen, K., McNab, S. et al. (2021) Interactive digital technology can improve paediatric asthma control. Respirology 26(suppl2): 126	- Conference abstract
Grammatopoulou, Eirini Pt PhD, Skordilis, Emmanouil K PhD, Haniotou, Aikaterini Md Fccp et al. (2017) The effect of a holistic self-management plan on asthma control. Physiotherapy theory and practice 33(8): 622-633	- Study does not contain an intervention relevant to this review protocol *Multi-component self-management (eg action plan, education) intervention including instructions on symptoms and PEF monitoring. Not clear that management changed as a result of symptoms monitoring*

Study	Reason for exclusion
Guendelman, S, Meade, K, Chen, YQ et al. (2004) Asthma control and hospitalizations among inner-city children: results of a randomized trial. Telemedicine journal and e-health 10suppl2: S-6	- Conference abstract
Hemati, Z., Shakerian, B., Shirani, F. et al. (2017) Effect of the orem self-care model on quality of life in adolescents with asthma. Journal of Comprehensive Pediatrics 8(2): e59343	- Study does not contain an intervention relevant to this review protocol
Hepworth, C., Lilley, A., Gait, L. et al. (2019) A multidisciplinary community-based complex intervention on children with asthma. European Respiratory Journal 54(supplement63)	- Conference abstract
Holley, S., Knibb, R., Latter, S. et al. (2018) Self-efficacy, asthma control and quality of life in adolescents with asthma taking part in an intervention study. Clinical and Translational Allergy 8(supplement2)	- Conference abstract
Holmes, Lucy C, Orom, Heather, Lehman, Heather K et al. (2022) A pilot school-based health center intervention to improve asthma chronic care in high-poverty schools. The Journal of asthma : official journal of the Association for the Care of Asthma 59(3): 523-535	- Study does not contain an intervention relevant to this review protocol
Honkoop, P.J., Loymans, R..J.B., Termeer, E. et al. (2014) Targeting different levels of asthma control by symptom and biomarker driven strategies: A cluster randomised trial in primary care. American Journal of Respiratory and Critical Care Medicine 189(meetingabstracts)	- Conference abstract
Honkoop, Persijn J, Loijmans, Rik J B, Termeer, Evelien H et al. (2015) Symptom- and fraction of exhaled nitric oxide-driven strategies for asthma control: A cluster-randomized trial in primary care. The Journal of allergy and clinical immunology 135(3): 682-8e11	- Comparator in study does not match that specified in this review protocol
Horner, Sharon D and Brown, Adama (2014) Evaluating the effect of an asthma self-management intervention for rural families. The	- Study does not contain an intervention relevant to this review protocol

Study	Reason for exclusion
Journal of asthma : official journal of the Association for the Care of Asthma 51(2): 168-77	
Hui, Chi Yan, Walton, Robert, McKinstry, Brian et al. (2017) The use of mobile applications to support self-management for people with asthma: a systematic review of controlled studies to identify features associated with clinical effectiveness and adherence. Journal of the American Medical Informatics Association : JAMIA 24(3): 619-632	- Systematic review used as source of primary studies
Iamlaor, U. and Taneepanichskul, S. (2021) Effectiveness of asthma self-care program through mobile Line application (SALA) on lung function among asthma patients in Angthong Hospital: A randomized control trial. Journal of the Medical Association of Thailand 104(2): 264-270	- Study does not contain an intervention relevant to this review protocol
Janssens, T. and Harver, A. (2014) Effect of resistive load training on asthma trigger identification. American Journal of Respiratory and Critical Care Medicine 189(meetingabstracts)	- Conference abstract
Jin, H.J., Nam, Y.H., Kim, S. et al. (2019) Clinical efficacy of information and communication technology based monitoring of asthma: A prospective, randomized controlled, multicenter study. Allergy: European Journal of Allergy and Clinical Immunology 74(supplement106): 396	- Conference abstract
Khdour, M.R.; Hallak, H.O.; Elayyan, S.O. (2020) Pharmaceutical care for adult asthma patients: A controlled intervention one year follow up study. International Journal of Clinical Pharmacy 42(1): 222	- Conference abstract
Kim, M.-A., Ye, Y.-M., Park, J.-W. et al. (2014) A computerized asthma-specific quality of life: A novel tool for reflecting asthma control and predicting exacerbation on behalf of the premier researchers aiming new era in asthma and allergic diseases (PRANA) study group. International Archives of Allergy and Immunology 163(1): 36-42	- Study design not relevant to this review protocol

Study	Reason for exclusion
Kim, Mi-Ae, Ye, Young-Min, Park, Jung-Won et al. (2014) A computerized asthma-specific quality of life: a novel tool for reflecting asthma control and predicting exacerbation. International archives of allergy and immunology 163(1): 36-42	- Duplicate reference
Kuipers, Esther, Wensing, Michel, de Smet, Peter et al. (2017) Self-management research of asthma and good drug use (SMARAGD study): a pilot trial. International journal of clinical pharmacy 39(4): 888-896	- Study design not relevant to this review protocol *Study not randomised*
Lim, Angelina S, Stewart, Kay, Abramson, Michael J et al. (2014) Multidisciplinary Approach to Management of Maternal Asthma (MAMMA): a randomized controlled trial. Chest 145(5): 1046-1054	- Study does not contain an intervention relevant to this review protocol *Multi-component intervention*
Ljungberg, H.; Carleborg, A.; Nordlund, B. (2019) Clinical effect on asthma control using a novel digital selfmanagement solution: A physician blinded randomized controlled crossover trial. European Respiratory Journal 54(supplement63)	- Conference abstract
Ljungberg, Henrik, Carleborg, Anna, Gerber, Hilmar et al. (2019) Clinical effect on uncontrolled asthma using a novel digital automated self-management solution: a physician-blinded randomised controlled crossover trial. The European respiratory journal 54(5)	- Study does not contain an intervention relevant to this review protocol *Multi-component digital intervention - electronic symptom monitoring and bluetooth spirometer combined*
Lu, L, Lin, RJ, Guan, RZ et al. (2019) Influence of five-in-one management mode on disease prevention and control of school children with asthma. Zhonghua ER ke za zhi = chinese journal of pediatrics 57(11): 870-875	- Study not reported in English
Lu, Mei, Ownby, Dennis R, Zoratti, Edward et al. (2014) Improving efficiency and reducing costs: Design of an adaptive, seamless, and enriched pragmatic efficacy trial of an online asthma management program. Contemporary clinical trials 38(1): 19-27	- Study does not contain an intervention relevant to this review protocol

Study	Reason for exclusion
Lv, Shaoxia, Ye, Xiaohong, Wang, Zhijiang et al. (2019) A randomized controlled trial of a mobile application-assisted nurse-led model used to improve treatment outcomes in children with asthma. Journal of advanced nursing 75(11): 3058-3067	- Study does not contain an intervention relevant to this review protocol *Multi-component digital intervention including 'health diary', that did communicate with healthcare team. Not clear that health diary included symptom assessment or that care was altered as a result of health diary alone*
Manfrin, A.; Thomas, T.; Krska, J. (2016) Symptom control and adherence are major issues for asthmatic patients: Can they be improved and are they linked?. Pharmacoepidemiology and Drug Safety 25(supplement2): 18-19	- Conference abstract
Manfrin, Andrea; Thomas, Trudy; Krska, Janet (2015) Randomised evaluation of the Italian medicines use review provided by community pharmacists using asthma as a model (RE I-MUR). BMC health services research 15: 171	- Secondary publication of an included study that does not provide any additional relevant information
Manfrin, Andrea, Tinelli, Michela, Thomas, Trudy et al. (2017) A cluster randomised control trial to evaluate the effectiveness and cost-effectiveness of the Italian medicines use review (I-MUR) for asthma patients. BMC health services research 17(1): 300	- Data not reported in an extractable format or a format that can be analysed *ACT is a study outcome but not clear in paper if the ACT is considered part of intervention. Can exclude due to no usable outcomes as ACT scores (measuring asthma control) were reported as median (IQR) which we can't meta-analyse. Comparator not usual care.*
Martin, S.H., De Heredia, J.H.P., Gomez, M. et al. (2017) "App" for uncontrolled moderate-severe asthma patients follow-up. European Respiratory Journal 50(supplement61)	- Conference abstract
Mcdonald, V., Clark, V., Wark, P. et al. (2017) Multidimensional assessment and targeted therapy of severe asthma: A randomised controlled trial (RCT). European Respiratory Journal 50(supplement61)	- Conference abstract
McDonald, V.M., Clark, V.L., Wark, P.A.B. et al. (2017) Multidimensional assessment and targeted therapy of severe persistent asthma: A randomised controlled trial. Respirology 22(supplement2): 66	- Conference abstract

Study	Reason for exclusion
Montalbano, Laura, Ferrante, Giuliana, Cilluffo, Giovanna et al. (2019) Targeting quality of life in asthmatic children: The MyTEP pilot randomized trial. Respiratory medicine 153: 14-19	- Comparator in study does not match that specified in this review protocol *MyTEP includes monitoring of symptoms and c-ACT completion as part of a multi-component intervention (eg incl bluetooth spirometer). Also comparator group includes receipt of a health app so judged to be not usual care.*
Nemanic, Tiva, Sarc, Irena, Skrgat, Sabina et al. (2019) Telemonitoring in asthma control: a randomized controlled trial. The Journal of asthma : official journal of the Association for the Care of Asthma 56(7): 782-790	- Study does not contain an intervention relevant to this review protocol
Perron, G., Garcia, M., Carbonnel, F. et al. (2019) The Childhood Asthma Control Test improves the therapeutic adaptations recommended for asthmatics aged 6 to 11 years in primary practice. A Randomized comparative prospective study. Presse Medicale 48(9): e257-e266	- Study not reported in English
Rank, Matthew A, Bertram, Susan, Wollan, Peter et al. (2014) Comparing the Asthma APGAR system and the Asthma Control Test TM in a multicenter primary care sample. Mayo Clinic proceedings 89(7): 917-25	- Study design not relevant to this review protocol
Ravandi, Bahareh, Thompson, Lindsey R, Barry, Frances et al. (2022) Use of a validated asthma questionnaire to increase inhaled corticosteroid prescribing in the pediatric emergency department. The Journal of asthma : official journal of the Association for the Care of Asthma 59(2): 378-385	- Study design not relevant to this review protocol
Real, Francis J, Beck, Andrew F, DeBlasio, Dominick et al. (2019) Dose Matters: A Smartphone Application to Improve Asthma Control Among Patients at an Urban Pediatric Primary Care Clinic. Games for health journal 8(5): 357-365	- Study does not contain an intervention relevant to this review protocol
Reece, E.R.; Burnette, A.F.; Lewis-Land, C.J. (2017) Pilot study of asthmawin mobile iphone app in the management of asthma. Journal of Allergy and Clinical Immunology 139(2supplement1): ab382	- Conference abstract

Study	Reason for exclusion
Rhee, Hyekyun; Love, Tanzy; Mammen, Jennifer (2019) Comparing Asthma Control Questionnaire (ACQ) and National Asthma Education and Prevention Program (NAEPP) asthma control criteria. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology 122(1): 58-64	- Study design not relevant to this review protocol
Rijssenbeek-Nouwens, L.H., Beerthuizen, T., Snoeck-Stroband, J.B. et al. (2019) eHealth self-management support after high-altitude climate treatment (HACT) of severe asthma: A randomised controlled trial. European Respiratory Journal 54(supplement63)	- Conference abstract
Ryan, D, Price, D, Musgrave, SD et al. (2012) Clinical and cost effectiveness of mobile phone supported self monitoring of asthma: multicentre randomised controlled trial. BMJ (online) 344(7854)	- Comparator in study does not match that specified in this review protocol *Multi-component digital intervention including symptom records, drug use and peak flow monitoring. Links to nurse to FUP when in amber or red zones. Comparator was paper version of same monitoring instructions so the trial is only really testing the electronic nature of the monitoring.*
Serhal, Sarah, Mitchell, Bernadette, Krass, Ines et al. (2022) Rethinking the gold standard - The feasibility of randomized controlled trials within health services effectiveness research. Research in social & administrative pharmacy : RSAP 18(9): 3656-3668	- Study design not relevant to this review protocol
Shanmugam, S, Varughese, J, Nair, MAS et al. (2012) Pharmaceutical care for asthma patients: a Developing Country's Experience. Journal of research in pharmacy practice 1(2): 66-71	- Study does not contain an intervention relevant to this review protocol *Multi-component intervention: asthma care diary which consists of mainly pictorial representation of asthma, an information leaflet for patients, small briefing on asthma, pictorial representation of the five steps in asthma management, how to use peak flow meter, inhalation techniques for selected inhalation devices, asthma management plan, and asthma symptoms log sheet. Simple provision of a symptom log sheet does not infer that care was modified as a result of it being completed and used by healthcare team.Poor reporting, FUP 29 days so only potential outcome in protocol is PEF*

Study	Reason for exclusion
Shdaifat, Mu'min Billah M; Khasawneh, Rawand A; Alefan, Qais (2022) Clinical and economic impact of telemedicine in the management of pediatric asthma in Jordan: a pharmacist-led intervention. The Journal of asthma : official journal of the Association for the Care of Asthma 59(7): 1452-1462	- Study design not relevant to this review protocol
Snoeck-Stroband, J.B., Beerthuizen, T., Rijssenbeek-Nouwens, L. et al. (2017) Web-based self-management support after pulmonary rehabilitation of difficult to treat asthma: A randomised controlled trial. European Respiratory Journal 50(supplement61)	- Conference abstract
Tinelli, Michela; White, John; Manfrin, Andrea (2018) Novel pharmacist-led intervention secures the minimally important difference (MID) in Asthma Control Test (ACT) score: better outcomes for patients and the healthcare provider. BMJ open respiratory research 5(1): e000322	- Data not reported in an extractable format or a format that can be analysed *Another analysis of Manfrin et al (2017) which is excluded. ACT outcomes also not extractable and able to meta-analyse.*
Van Bragt, S., Van Den Bemt, L., Vaessen-Verberne, A. et al. (2014) Effectiveness of individualized self management support for children with asthma in Dutch outpatient clinics, preliminary results of a randomized controlled trial. European Respiratory Journal 44(suppl58)	- Conference abstract
Van Bragt, D., van den Bemt, L. Kievits, Regien et al (2015) PELICAN: a cluster-randomized controlled trial in Dutch general practices to assess a self-management support intervention based on individual goals for children with asthma. The Journal of asthma: official journal of the Association for the Care of Asthma; vol. 52 (no. 2); 211-9	- Data not reported in an extractable format or a format that can be analysed
Van Den Wijngaart, L.S., Kievit, W., Roukema, J. et al. (2016) The virtual asthma clinic for children: A cost-effectiveness analysis. Pediatric Pulmonology 51(supplement43): 65	- Conference abstract

Study	Reason for exclusion
Van der Meer, V., van Stel, HF., Bakker, M.J. et al (2010) Weekly self-monitoring and treatment adjustment benefit patients with partly controlled and uncontrolled asthma: an analysis of the SMASHING study. Respiratory research, vol 11.	- Secondary publication of an included study that does not provide any additional relevant information
van Dijk, Bas C P, Svedsater, Henrik, Heddini, Andreas et al. (2020) Relationship between the Asthma Control Test (ACT) and other outcomes: a targeted literature review. BMC pulmonary medicine 20(1): 79	- Systematic review used as source of primary studies
Van Vliet, D, Van Horck, M, Van De Kant, K et al. (2014) Electronic monitoring of symptoms and lung function to assess asthma control in children. Annals of allergy, asthma and immunology 113(3): 257-262	- Study design not relevant to this review protocol *Not randomised*
Velychko, V.I.; Venher, Y.I.; Lahoda, D.O. (2020) A responsible patient: from theory to practice on a model of a patient with bronchial asthma. Wiadomosci lekarskie (Warsaw, Poland : 1960) 73(3): 444-448	- Study does not contain an intervention relevant to this review protocol *Multi-component intervention in 2 arms (asthma school education plus self-monitoring including symptom; medication plus self-monitoring including symptoms) with additional control arm. Not clear that care altered according to self-monitoring of symptoms.*
Voorend-van Bergen, S, Vaessen-Verberne, A A, de Jongste, J C et al. (2015) Asthma control questionnaires in the management of asthma in children: A review. Pediatric pulmonology 50(2): 202-8	- Study design not relevant to this review protocol *Narrative review - useful background only*
Voorend-van Bergen, Sandra, Vaessen-Verberne, Anja A, Brackel, Hein J et al. (2015) Monitoring strategies in children with asthma: a randomised controlled trial. Thorax 70(6): 543-50	- Comparator in study does not match that specified in this review protocol *Treatment adjusted according to 1) ACT monthly web-based Vs 2) ACT 4 monthly clinic - based*
Wang, KY, Chian, CF, Lai, HR et al. (2010) Clinical pharmacist counseling improves outcomes for Taiwanese asthma patients. Pharmacy world & science : PWS 32(6): 721-729	- Study does not contain an intervention relevant to this review protocol *Multi=component intervention - only includes vague mention of instruction on the format to record symptoms in a diary.*

Study	Reason for exclusion
Wen, Tzu-Ning, Lin, Hsueh-Chun, Yeh, Kuo-Wei et al. (2022) Effectiveness of eAsthmaCare on Symptoms, Childhood Asthma Control Test, and Lung Function among Asthmatic Children. Journal of medical systems 46(11): 71	- Study does not contain an intervention relevant to this review protocol *Multi-component intervention of eAsthma-care (website self-management intervention, which enabled web-based self-learning) and which includes self-monitoring of symptoms and home PEFR monitoring and does interact with HCPs.Care (by researchers) altered according to symptoms and lung function monitoring, not symptoms alone. Alterations in care based on these in control group also a potential issue.*
Wong, Lai-Yan, Chua, Siew-Siang, Husin, Abdul-Rahman et al. (2017) A pharmacy management service for adults with asthma: a cluster randomised controlled trial. Family practice 34(5): 564-573	- Study does not contain an intervention relevant to this review protocol
Yadav, Anita and Thapa, Parbati (2019) Pharmacist Led Intervention on Inhalation Technique among Asthmatic Patients for Improving Quality of Life in a Private Hospital of Nepal. Pulmonary medicine 2019: 8217901	- Study does not contain an intervention relevant to this review protocol

I.2 Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2006 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

None.