Topic Brief: Life-span Measurement of Spirometry in Children with Asthma

Date: 2/12/2020
Nomination Number: 0882

Purpose: This document summarizes the information addressing a nomination submitted on 5/6/2019 through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: Asthma is a prevalent chronic condition in children and adults that develops in the setting of various intrinsic and environmental factors. It is treated with a patient tailored action plan that includes trigger avoidance and medication for both symptom control and rescue. A number of cohort studies have found that childhood asthma is a risk factor for abnormal lung growth and function resulting in a proportion of asthmatics developing chronic obstructive lung disease (COPD) in adulthood. This nomination suggests that life cycle spirometry may identify persons with childhood asthma who are at risk for airway remodeling that may lead to COPD and may be amenable to interventions to reduce progression. Current guidelines do not recommend life-span spirometry monitoring for adverse respiratory complications in adulthood.

Program Decision:

Although the nomination met all selection criteria it was not selected for further development as a systematic review due to the small and heterogeneous evidence base and the large number of unpublished studies registered in clinicalTrials.gov.

Key Findings

- We found two systematic reviews relevant to the nomination, but these address only one intervention.
- We identified a small evidence base for the proposed systematic review. Eighteen studies on the use of longitudinal spirometry in children with asthma were identified. Fourteen published studies and 50 studies registered in ClinicalTrials.gov on a variety of interventions to decrease adverse respiratory outcomes were identified.

Background

In 2017 the prevalence of asthma in children less than 18 years old was 8.4% or approximately 6.2 million children compared to 7.7% or approximately 19 million in adults 18 years and older. There has been recent recognition that a subset of patients with childhood asthma develop a non-reversible component due to inflammation induced structural changes.[1] Normal lung function

follows a predictable three phase trajectory starting with growth (from birth to early adulthood), followed by a plateau (several years) and ending with decline due to physiological lung ageing.[2]

Childhood asthma has been associated with low lung function in early adulthood[3] and chronic obstructive pulmonary disease (COPD) due to remodeling of the airways.[4] The NHLBI Childhood Asthma Management Program study found that in children with mild to moderate asthma about 11% went on to have lung function in early adulthood that was equivalent to advanced physiologic stages of COPD.[5] A number of potential prevention and treatment strategies to prevent remodeling have been proposed to include medications (e.g. corticosteroids, biologics), immunotherapy and other behavioral interventions (e.g. smoking cessation) but further research is needed to identify effective interventions.[6, 7 8 9 10 11]

While spirometry is accurate for assessing lung function and guiding treatment in the short-term, longitudinal spirometry from childhood into adulthood to predict the development of outcomes in adulthood, including COPD development has not been established as a standard approach to identify patients with airway remodeling and at risk for COPD. Longitudinal life span monitoring of spirometry in children with asthma could identify patterns of disease in adulthood including a proportion of children who develop an asthma- COPD overlap condition.[12] Lang et. al defined asthma-COPD overlap as current self-reported asthma and a postbronchodilatatory forced expiratory volume in 1 s (FEV1) to forced vital capacity ratio of less than 0.7, without any restrictions regarding smoking.[13]

A systematic review of the literature could assess the predictive value of life-span spirometry monitoring on development of adverse respiratory complications in adulthood, summarize what is known about interventions to prevent COPD and other adult-onset complications, identify research gaps, and suggest future research.

Nomination Summary

The nomination was submitted by the Director of Pediatric Research, the Breathing Institute, Children's Hospital, in Aurora, Colorado. The key questions and PICOTS were developed with his input. The nomination scope was expanded to include a review of the evidence on effective interventions to decrease adverse respiratory outcomes in adulthood including asthma-COPD overlap. If the EPC Program decided to move forward with this nomination CHEST agreed to partner on this topic to develop a practice guideline.

Scope

1. Is periodic, longitudinal life-span, spirometry in children with asthma predictive of adverse respiratory outcomes in adulthood including asthma-COPD overlap?
    a. Does the predictive value vary by stage of asthma, initial measurement of pulmonary function, patient demographics, urban versus rural living, environmental exposures (indoor and outdoor), active or passive smoking, vaping, allergies plus exposure, and history of infections?

2. What is the effectiveness of medications (e.g. corticosteroids, biologics), immunotherapy and other behavioral interventions (e.g. smoking cessation), in decreasing adverse respiratory outcomes in adulthood including asthma-COPD overlap?
    a. Do the interventions effectiveness vary by stage of asthma, initial measurement of pulmonary function, patient demographics, urban versus rural living, environmental exposures (indoor and outdoor), active or passive smoking, vaping, allergies plus exposure, and history of infections?

Contextual Question:

1. What are implementation barriers to periodic spirometry that are especially prominent in primary care (e.g., the cost of a spirometry device, the time needed to perform spirometry and build it into patient/clinic flow, reimbursement policies, clinician education regarding interpretation, and staff who are trained/proficient at performing spirometry)?

Table 1. Questions and PICOTS (population, intervention, comparator, outcome, timing and setting)

Questions	1. Is life-span spirometry in children with asthma predictive of adverse respiratory outcomes in adulthood?	2. What is the effectiveness of medications, immunotherapy, and behavioral interventions in decreasing adverse respiratory outcomes in adulthood?
Population	Children with asthma 0-18 years old	Patients diagnosed with asthma
Interventions	Longitudinal Spirometry into adulthood	Inhaled corticosteroids Leukotriene antagonists Immunotherapy Behavioral therapy
Comparators	Usual care or baseline lung function	Other therapies Usual care Placebo
Outcomes	Respiratory outcomes in adulthood including asthma progression, COPD equivalency, reduced pulmonary function, irreversible respiratory obstruction, ED visits, hospitalizations, mortality, QoL	Respiratory outcomes in adulthood including asthma exacerbations and progression, asthma-COPD overlap, reduced pulmonary function, irreversible respiratory obstruction, ED visits, hospitalizations, mortality, QoL
Timing	Minimum length of follow up of 5 years	Minimum length of follow up of 1 years
Setting	Ambulatory, primary and specialty care	Ambulatory, primary and specialty care

Abbreviations: COPD=chronic obstructive pulmonary disease; ED=emergency department; QoL=quality of life

Assessment Methods

See Appendix A.

Summary of Literature Findings

- We found no relevant systematic reviews in our search for KQ#1 and one published[14] and one pre-published[15] systematic reviews partially relevant for KQ#2.
- For key question #1 we found no trials and 17 cohort studies of children with asthma followed longitudinally with spirometry into adulthood.[4, 12, 16-30] The search of ClinicalTrials.gov found 3 (1 recruiting and 2 active, not recruiting) observational, longitudinal studies of children with asthma and two specifically followed with spirometry.[31-33]
- For key question #2 we found one trial, 4 cohort, 8 quasi-experimental and one cross-sectional studies for a variety of interventions, including 7 on Omalizumab, a recombinant DNA-derived humanized IgG1k monoclonal antibody. The search of ClinicalTrials.gov identified 36 randomized clinical trials, 7 observational and 7 other study designs, 9 active, not recruiting, 26 recruiting and 15 completed. [34-83] The interventions included 32 behavioral, 10 biologics, 3 immunotherapy and 5 other medications.

Table 2. Literature identified for each Question

Question	Systematic reviews (12/2016-12/2019)	Primary studies (1/2016-12/2019)
Question 1: Is life-span spirometry in children with asthma predictive of adverse respiratory outcomes in adulthood?	Total: 0 • Cochrane: 0 • AHRQ: 0 • VA: 0 • PROSPERO: 0 • Other: 0	Total: 18 • RCT: 0 • Cohort: 18[6, 9-24, 84] Clinicaltrials.gov 3[31-33] • Recruiting: 1 • Active, not yet recruiting: 2
Question 2: What is the effectiveness of medications, immunotherapy, and behavioral interventions in decreasing adverse respiratory outcomes in adulthood?	Total: 2 • Cochrane: 0 • AHRQ: 0 • VA: 0 • PROSPERO: 1[15] • Other: 1[14]	Total: 14 • RCT: 1[85] • Cohort: 4[86-89] • Quasi-experimental: 8[90-97] • Cross-sectional: 1[98] Clinicaltrials.gov: 50 [34-83] • Completed: 15 • Recruiting: 26 • Active, not yet recruiting: 9

See Appendix B for detailed assessments of all EPC selection criteria.

Summary of Selection Criteria Assessment

This nomination meets all selection criteria. For key question one we found no systematic reviews and estimate 18 primary studies about longitudinal life-span, spirometry in children with asthma. For key question two we found 2 systematic reviews that are partially duplicative for primarily monoclonal antibody medication interventions. A systematic review of the evidence base would address the effectiveness of longitudinal monitoring for predicting and interventions to reduce the risk of adverse respiratory outcomes in adulthood, and identify research gaps. An evidence review would be highly impactful and valuable with a partner planning to develop guidance to address known practice variation.

Please see Appendix B for detailed assessments of individual EPC Program selection criteria.

References

1. Jindal SK. Remodeling in asthma and COPD-recent concepts. Lung India. 2016 Jan-Feb;33(1):1-2. doi: 10.4103/0970-2113.173074. PMID: 26933298. https://www.ncbi.nlm.nih.gov/pubmed/26933298 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4748644/

2. Speizer FE, Tager IB. Epidemiology of chronic mucus hypersecretion and obstructive airways disease. Epidemiol Rev. 1979;1:124-42. doi: 10.1093/oxfordjournals.epirev.a036206. PMID: 398264. https://www.ncbi.nlm.nih.gov/pubmed/398264

3. Sears MR, Greene JM, Willan AR, et al. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. N Engl J Med. 2003 Oct 9;349(15):1414-22. doi: 10.1056/NEJMoa022363. PMID: 14534334. https://www.ncbi.nlm.nih.gov/pubmed/14534334

4. Tai A, Tran H, Roberts M, et al. The association between childhood asthma and adult chronic obstructive pulmonary disease. Thorax. 2014 Sep;69(9):805-10. doi: 10.1136/thoraxjnl-2013-204815. PMID: 24646659. https://www.ncbi.nlm.nih.gov/pubmed/24646659

5. McGeachie MJ. Childhood asthma is a risk factor for the development of chronic obstructive pulmonary disease. Curr Opin Allergy Clin Immunol. 2017 Apr;17(2):104-9. doi: https://dx.doi.org/10.1097/ACI.0000000000000348. PMID: 28118239
6. Melen E, Guerra S. Recent advances in understanding lung function development. F1000Res. 2017;6:726. doi: 10.12688/f1000research.11185.1. PMID: 28620467. https://www.ncbi.nlm.nih.gov/pubmed/28620467
7. Agusti A, Faner R. Lung function trajectories in health and disease. Lancet Respir Med. 2019 Apr;7(4):358-64. doi: 10.1016/S2213-2600(18)30529-0. PMID: 30765254. https://www.ncbi.nlm.nih.gov/pubmed/30765254
8. Nayak AP, Deshpande DA, Penn RB. New targets for resolution of airway remodeling in obstructive lung diseases. F1000Res. 2018;7. doi: 10.12688/f1000research.14581.1. PMID: 29904584. https://www.ncbi.nlm.nih.gov/pubmed/29904584
9. Bergeron C, Tulic MK, Hamid Q. Airway remodelling in asthma: from benchside to clinical practice. Can Respir J. 2010 Jul-Aug;17(4):e85-93. doi: 10.1155/2010/318029. PMID: 20808979. https://www.ncbi.nlm.nih.gov/pubmed/20808979
10. Riccioni G, Di Ilio C, D'Orazio N. Review: Pharmacological treatment of airway remodeling: inhaled corticosteroids or antileukotrienes? Ann Clin Lab Sci. 2004 Spring;34(2):138-42. PMID: 15228224. https://www.ncbi.nlm.nih.gov/pubmed/15228224
11. Hamelmann E, von Mutius E, Bush A, et al. Addressing the risk domain in the long-term management of pediatric asthma. Pediatr Allergy Immunol. 2019 Nov 16. doi: 10.1111/pai.13175. PMID: 31732983. https://www.ncbi.nlm.nih.gov/pubmed/31732983
12. McGeachie MJ, Yates KP, Zhou X, et al. Patterns of Growth and Decline in Lung Function in Persistent Childhood Asthma. N Engl J Med. 2016 May 12;374(19):1842-52. doi: https://dx.doi.org/10.1056/NEJMoa1513737. PMID: 27168434
13. Lange P, Colak Y, Ingebrigtsen TS, et al. Long-term prognosis of asthma, chronic obstructive pulmonary disease, and asthma-chronic obstructive pulmonary disease overlap in the Copenhagen City Heart study: a prospective population-based analysis. Lancet Respir Med. 2016 Jun;4(6):454-62. doi: 10.1016/S2213-2600(16)00098-9. PMID: 27061878. https://www.ncbi.nlm.nih.gov/pubmed/27061878
14. Colombo GL, Di Matteo S, Martinotti C, et al. Omalizumab and long-term quality of life outcomes in patients with moderate-to-severe allergic asthma: a systematic review. Therap. 2019 Jan-Dec;13:1753466619841350. doi: https://dx.doi.org/10.1177/1753466619841350. PMID: 31035904
15. Tan D, Bui, D., Haydn Walters, Perret, J., Lodge, C., Lowe, A., Thomas, P., Matheson, M., Dharmage, S. Inhaled corticosteroids in asthma and risk of chronic obstructive pulmonary disease: a systematic review and meta-analysis of the literature. PROSPERO 2017 CRD42017053543. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017053543. Accessed on Jan 22 2020.
16. Bui DS, Walters HE, Burgess JA, et al. Childhood Respiratory Risk Factor Profiles and Middle-Age Lung Function: A Prospective Cohort Study from the First to Sixth Decade. Ann Am Thorac Soc. 2018 09;15(9):1057-66. doi: https://dx.doi.org/10.1513/AnnalsATS.201806-374OC. PMID: 29894209
17. Owens L, Laing IA, Zhang G, et al. Airway function in infancy is linked to airflow measurements and respiratory symptoms from childhood into adulthood. Pediatr Pulmonol. 2018 08;53(8):1082-8. doi: https://dx.doi.org/10.1002/ppul.24062. PMID: 29806178
18. Belgrave DCM, Granell R, Turner SW, et al. Lung function trajectories from pre-school age to adulthood and their associations with early life factors: a retrospective analysis of three population-based birth cohort studies. Lancet Respir Med. 2018 07;6(7):526-34. doi: https://dx.doi.org/10.1016/S2213-2600(18)30099-7. PMID: 29628377
19. Bui DS, Lodge CJ, Burgess JA, et al. Childhood predictors of lung function trajectories and future COPD risk: a prospective cohort study from the first to the sixth decade of life. Lancet

Respir Med. 2018 07;6(7):535-44. doi: https://dx.doi.org/10.1016/S2213-2600(18)30100-0. PMID: 29628376
20. Fuchs O, Bahmer T, Weckmann M, et al. The all age asthma cohort (ALLIANCE) - from early beginnings to chronic disease: a longitudinal cohort study. BMC polm. 2018 Aug 20;18(1):140. doi: https://dx.doi.org/10.1186/s12890-018-0705-6. PMID: 30126401
21. Schramm D, Reuter M, Grabenhenrich LB, et al. What does lung function tell us about respiratory multimorbidity in childhood and early adulthood? Results from the MAS birth cohort study. Pediatr Allergy Immunol. 2018 08;29(5):481-9. doi: https://dx.doi.org/10.1111/pai.12901. PMID: 29604118
22. Bui DS, Burgess JA, Lowe AJ, et al. Childhood Lung Function Predicts Adult Chronic Obstructive Pulmonary Disease and Asthma-Chronic Obstructive Pulmonary Disease Overlap Syndrome. Am J Respir Crit Care Med. 2017 07 01;196(1):39-46. doi: https://dx.doi.org/10.1164/rccm.201606-1272OC. PMID: 28146643
23. Berry CE, Billheimer D, Jenkins IC, et al. A Distinct Low Lung Function Trajectory from Childhood to the Fourth Decade of Life. Am J Respir Crit Care Med. 2016 09 01;194(5):607-12. doi: https://dx.doi.org/10.1164/rccm.201604-0753OC. PMID: 27585385
24. Hancox RJ, Gray AR, Poulton R, et al. The Effect of Cigarette Smoking on Lung Function in Young Adults with Asthma. Am J Respir Crit Care Med. 2016 08 01;194(3):276-84. doi: https://dx.doi.org/10.1164/rccm.201512-2492OC. PMID: 26866532
25. Backman K, Piippo-Savolainen E, Ollikainen H, et al. Long-term effects of pneumococcal colonization during early childhood wheezing. Pediatr Int. 2016 Sep;58(9):831-5. doi: https://dx.doi.org/10.1111/ped.12939. PMID: 26833958
26. Siroux V, Boudier A, Dolgopoloff M, et al. Forced midexpiratory flow between 25% and 75% of forced vital capacity is associated with long-term persistence of asthma and poor asthma outcomes. J Allergy Clin Immunol. 2016 06;137(6):1709-16.e6. doi: https://dx.doi.org/10.1016/j.jaci.2015.10.029. PMID: 26688518
27. Tagiyeva N, Devereux G, Fielding S, et al. Outcomes of Childhood Asthma and Wheezy Bronchitis. A 50-Year Cohort Study. Am J Respir Crit Care Med. 2016 Jan 01;193(1):23-30. doi: https://dx.doi.org/10.1164/rccm.201505-0870OC. PMID: 26351837
28. Strunk RC, Colvin R, Bacharier LB, et al. Airway Obstruction Worsens in Young Adults with Asthma Who Become Obese. J Allergy Clin Immunol Pract. 2015 Sep-Oct;3(5):765-71.e2. doi: https://dx.doi.org/10.1016/j.jaip.2015.05.009. PMID: 26164807
29. Yavuz ST, Civelek E, Comert S, et al. Development of rhinitis may be an indicator for the persistence of childhood asthma. Int J Pediatr Otorhinolaryngol. 2014 May;78(5):843-9. doi: https://dx.doi.org/10.1016/j.ijporl.2014.02.026. PMID: 24655470
30. Harmsen L, Ulrik CS, Porsbjerg C, et al. Airway hyperresponsiveness and development of lung function in adolescence and adulthood. Respir Med. 2014 May;108(5):752-7. doi: https://dx.doi.org/10.1016/j.rmed.2014.01.009. PMID: 24512967
31. Wessex Asthma Cohort of Difficult Asthma (WATCH) ClinicalTrials.gov Identifier: NCT03996590. U.S. National Library of Medicine; 2019. https://clinicaltrials.gov/ct2/show/NCT03996590. Accessed on Jan 15 2019.
32. Project Viva: a Longitudinal Study of Health for the Next Generation ClinicalTrials.gov Identifier: NCT02820402. U.S. National Library of Medicine; 2016. https://clinicaltrials.gov/ct2/show/NCT02820402. Accessed on Jan 15 2019.
33. Observational Study of Obstructive Lung Disease (NOVELTY) (NOVELTY) ClinicalTrials.gov Identifier: NCT02760329. U.S. National Library of Medicine; 2016. https://clinicaltrials.gov/ct2/show/NCT02760329. Accessed on Jan 15 2019.
34. University GW, Rho I. Community Healthcare for Asthma Management and Prevention of Symptoms. https://ClinicalTrials.gov/show/NCT02454192; 2010.
35. University of Turin I. Vitamin D Deficiency and Asthma Exacerbation. https://ClinicalTrials.gov/show/NCT02661191; 2012.

36. Institutet K. The Safety and Efficacy of Intralymphatic Immunotherapy in Pollen Allergic Adolescents and Young Adults With Asthma. https://ClinicalTrials.gov/show/NCT03394508; 2013.
37. Missouri Breaks Industries Research I, Research S. Factors Influencing Pediatric Asthma. https://ClinicalTrials.gov/show/NCT03302962; 2013.
38. University L. The Mixed Phenotype of Asthma and COPD: the Overlap Syndrome. https://ClinicalTrials.gov/show/NCT03817333; 2014.
39. Chicago UoIa, Center EFH, Center RUM. Asthma Action at Erie Trial. https://ClinicalTrials.gov/show/NCT02481986; 2015.
40. Hospital SCs, Hospital MMBCs, Center H. Text2Breathe: Enhance Parent Communication to Reduce Pediatric Asthma Disparities. https://ClinicalTrials.gov/show/NCT03032159; 2015.
41. Roche H-L. Longitudinal Cohort Study in Participants With Severe Asthma to Assess Biomarkers. https://ClinicalTrials.gov/show/NCT02537691; 2015.
42. S.A RME. Study for Evaluating Life Quality in Patients With Rhinoconjunctivitis. https://ClinicalTrials.gov/show/NCT02488447; 2015.
43. Sanofi, Pharmaceuticals R. Evaluation of Dupilumab in Patients With Persistent Asthma (Liberty Asthma Quest). https://ClinicalTrials.gov/show/NCT02414854; 2015.
44. Stephen J. Teach M, MPH, Institute P-COR, Institute CsR. Breathe With Ease: A Unique Approach to Managing Stress (BEAMS). https://ClinicalTrials.gov/show/NCT02374138; 2015.
45. System HFH. Teen Asthma Control Encouraging a Healthier Lifestyle. https://ClinicalTrials.gov/show/NCT02575326; 2015.
46. University of North Carolina CH, Institute P-COR. Using Question Prompt Lists During Pediatric Asthma Visits to Increase Adolescent Involvement. https://ClinicalTrials.gov/show/NCT02498834; 2015.
47. Health NJ, Permanente K. The Breathe Well Program for Adults With Asthma. https://ClinicalTrials.gov/show/NCT02761837; 2016.
48. Medicine AECo, National Heart L, Institute B. Childhood Asthma Perception Study. https://ClinicalTrials.gov/show/NCT02702687; 2016.
49. University Hospital G. Effect of Mepolizumab on Decrease of Systemic Corticosteroids in Patients With Severe Eosinophilic Asthma. https://ClinicalTrials.gov/show/NCT03453021; 2016.
50. Allergy NIo, Diseases I, Consortium I-CA, et al. A Trial of Mepolizumab Adjunctive Therapy for the Prevention of Asthma Exacerbations in Urban Children. https://ClinicalTrials.gov/show/NCT03292588; 2017.
51. AstraZeneca, Amgen. Study to Evaluate Tezepelumab in Adults & Adolescents With Severe Uncontrolled Asthma. https://ClinicalTrials.gov/show/NCT03347279; 2017.
52. Brigham, Hospital Ws, Institute P-COR, et al. Patient Empowered Strategy to Reduce Asthma Morbidity in Highly Impacted Populations; PeRson EmPowered Asthma RElief. https://ClinicalTrials.gov/show/NCT02995733; 2017.
53. Center MM, National Heart L, Institute B. Promoting Asthma Guidelines and Management Through Technology-Based Intervention and Care Coordination. https://ClinicalTrials.gov/show/NCT03066596; 2017.
54. Glasgow NG, Clyde. Pulmonary Rehabilitation for Uncontrolled Asthma Associated With Elevated BMI. https://ClinicalTrials.gov/show/NCT03630432; 2017.
55. Glassberg M, Miami Uo. Allogeneic Human Cells (hMSC) Via Intravenous Delivery in Patients With Mild Asthma. https://ClinicalTrials.gov/show/NCT03137199; 2017.
56. GlaxoSmithKline, IMS Q. Prevalence of Severe Asthma in Spanish Hospitals. https://ClinicalTrials.gov/show/NCT03137043; 2017.
57. Health NJ, Arizona Uo. An Asthma Collaboration to Reduce Childhood Asthma Disparities on the Navajo Nation. https://ClinicalTrials.gov/show/NCT03377647; 2017.
58. Hospital A. Mepolizumab: Real World Evidence Study for the Treatment of Severe Eosinophilic Asthma in Greece. https://ClinicalTrials.gov/show/NCT04084613; 2017.

59. Hospital B. REPLACE: Can Exercise Replace Inhaled Corticosteroid Treatment in Asthma? A RCT. https://ClinicalTrials.gov/show/NCT03290898; 2017.
60. Hospital C-JF. National Mobile Asthma Management System-E Project. https://ClinicalTrials.gov/show/NCT02917174; 2017.
61. Hospital UoSPG, Paulo UoS, University SCF, et al. Integrated Primary Care for Chronic Lung Disease: PACK Brazil. https://ClinicalTrials.gov/show/NCT02786030; 2017.
62. Stefania La Grutta M, Biomedica IplRelI. Study and Development of Application Models of "Therapeutic Education to the Patient" (TEP) in Asthmatic Children. https://ClinicalTrials.gov/show/NCT02636920; 2017.
63. Thessaloniki AUO, Ltd ASCS, BULGARIA NAOGPI. Combined Bio- and Neuro-Feedback vs. Varenicline Use for Smoking Cessation. https://ClinicalTrials.gov/show/NCT02991781; 2017.
64. University of California D. Home Visits to Optimize Medical and Educational Success Among Sacramento Schoolchildren With Asthma. https://ClinicalTrials.gov/show/NCT03335046; 2017.
65. Allergy NIo, Diseases I, Consortium I-CA. Cockroach Immunotherapy in Children and Adolescents. https://ClinicalTrials.gov/show/NCT03541187; 2018.
66. AstraZeneca. Description/Characterisation of Asthmatics Eligible for Biologic Therapy Referral in Prim. and Sec. Care in Europe. https://ClinicalTrials.gov/show/NCT03629782; 2018.
67. AstraZeneca, Parexel, LLC M. Observational Study of Characteristics, Treatment and Outcomes With Severe Asthma in the United States (CHRONICLE). https://ClinicalTrials.gov/show/NCT03373045; 2018.
68. Calgary Uo, Solutions AIH, Association CD. Enhancing Community Health Through Patient Navigation, Advocacy and Social Support. https://ClinicalTrials.gov/show/NCT03077386; 2018.
69. GlaxoSmithKline. A Safety and Efficacy Study of Mepolizumab in Subjects With Severe Asthma. https://ClinicalTrials.gov/show/NCT03562195; 2018.
70. Hospital HUC, Foundation of Ida Montin TfoF. Comparison of Biologicals in Treatment of Severe Asthma. https://ClinicalTrials.gov/show/NCT04158050; 2018.
71. Hospital RI, Health SoRIDo, District PPS, et al. Rhode Island Asthma Integrated Response Program. https://ClinicalTrials.gov/show/NCT03583814; 2018.
72. London QMUo. Self-management Intervention to Improve Adolescents' Asthma Control. https://ClinicalTrials.gov/show/NCT03536416; 2018.
73. Pharmaceuticals N, Novartis. Systemic Corticosteroids Avoidance Study in Severe Asthma Patients. https://ClinicalTrials.gov/show/NCT03629249; 2018.
74. Philadelphia CsHo, Pennsylvania Uo, Education-Plus I, et al. West Philadelphia Controls Asthma. https://ClinicalTrials.gov/show/NCT03514485; 2018.
75. University of California SF, Pediatrics AAo. Implementing Pathways to Improve Pediatric Asthma Care. https://ClinicalTrials.gov/show/NCT03736603; 2018.
76. University VC, National Heart L, Institute B. RVA Breathes: A Richmond City Collaboration to Reduce Pediatric Asthma Disparities. https://ClinicalTrials.gov/show/NCT03297645; 2018.
77. University WS, National Heart L, Institute B. Translating an Efficacious Illness Management Intervention for Youth With Asthma. https://ClinicalTrials.gov/show/NCT03317977; 2018.
78. AstraZeneca, Amgen. Study to Evaluate Tezepelumab in Adults With Severe Uncontrolled Asthma. https://ClinicalTrials.gov/show/NCT03927157; 2019.
79. Institute ACsHR. Implementing a Guidelines-Based M-Health Intervention for High Risk Asthma Patients. https://ClinicalTrials.gov/show/NCT03842033; 2019.
80. Pennsylvania Uo, National Heart L, Institute B. Clinic Navigation and Home Visits to Improve Guideline-based Care and Outcomes in Low Income Minority Adults With Asthma. https://ClinicalTrials.gov/show/NCT04023422; 2019.

81. Philadelphia CsHo, Health NIo, National Heart L, et al. The Tailored Adherence Incentives for Childhood Asthma Medications (TAICAM) Trial. https://ClinicalTrials.gov/show/NCT03907410; 2019.
82. University D, Health NIo, Research NIoN. Peer i-Coaching for Activated Self-Management Optimization in Adolescents and Young Adults With Chronic Conditions. https://ClinicalTrials.gov/show/NCT03938324; 2019.
83. University of California SF, National Heart L, Institute B. Pulmonary Specialist-Health Coach Consult Model Pilot. https://ClinicalTrials.gov/show/NCT03695276; 2019.
84. Hallberg J, Thunqvist P, Schultz ES, et al. Asthma phenotypes and lung function up to 16 years of age-the BAMSE cohort. Allergy. 2015 Jun;70(6):667-73. doi: 10.1111/all.12598. PMID: 25703776. https://www.ncbi.nlm.nih.gov/pubmed/25703776
85. Hamelmann E, Bateman ED, Vogelberg C, et al. Tiotropium add-on therapy in adolescents with moderate asthma: A 1-year randomized controlled trial. J Allergy Clin Immunol. 2016 Aug;138(2):441-50 e8. doi: 10.1016/j.jaci.2016.01.011. PMID: 26960245. https://www.ncbi.nlm.nih.gov/pubmed/26960245
86. Sadatsafavi M, Lynd LD, De Vera MA, et al. One-year outcomes of inhaled controller therapies added to systemic corticosteroids after asthma-related hospital discharge. Respir Med. 2015 Mar;109(3):320-8. doi: 10.1016/j.rmed.2014.12.014. PMID: 25596136. https://www.ncbi.nlm.nih.gov/pubmed/25596136
87. Abu-Kishk I, Polakow-Farkash S, Elizur A. Long-term outcome after pediatric intensive care unit asthma admissions. Allergy Asthma Proc. 2016 Nov;37(6):169-75. doi: 10.2500/aap.2016.37.4008. PMID: 27931294. https://www.ncbi.nlm.nih.gov/pubmed/27931294
88. Chanoine S, Dumas O, Benmerad M, et al. Long-term benefits of inhaled corticosteroids in asthma: the propensity score method. Pharmacoepidemiol Drug Saf. 2015 Mar;24(3):246-55. doi: 10.1002/pds.3639. PMID: 24966014. https://www.ncbi.nlm.nih.gov/pubmed/24966014
89. Devillier P, Wahn U, Zielen S, et al. Grass pollen sublingual immunotherapy tablets provide long-term relief of grass pollen-associated allergic rhinitis and reduce the risk of asthma: findings from a retrospective, real-world database subanalysis. Expert Rev Clin Immunol. 2017 Dec;13(12):1199-206. doi: 10.1080/1744666X.2017.1398082. PMID: 29072507. https://www.ncbi.nlm.nih.gov/pubmed/29072507
90. Folque MM, Lozano J, Riggioni C, et al. 'Real-life' experience in asthmatic children treated with omalizumab up to six-years follow-up. Allergol Immunopathol (Madr). 2019 Jul - Aug;47(4):336-41. doi: 10.1016/j.aller.2018.09.009. PMID: 30509559. https://www.ncbi.nlm.nih.gov/pubmed/30509559
91. Yorgancioglu A, Oner Erkekol F, Mungan D, et al. Long-Term Omalizumab Treatment: A Multicenter, Real-Life, 5-Year Trial. Int Arch Allergy Immunol. 2018;176(3-4):225-33. doi: 10.1159/000488349. PMID: 29772578. https://www.ncbi.nlm.nih.gov/pubmed/29772578
92. Saji J, Yamamoto T, Arai M, et al. Efficacy of long-term omalizumab therapy in patients with severe asthma. Respir Investig. 2017 Mar;55(2):114-20. doi: 10.1016/j.resinv.2016.11.002. PMID: 28274526. https://www.ncbi.nlm.nih.gov/pubmed/28274526
93. Odajima H, Ebisawa M, Nagakura T, et al. Long-term safety, efficacy, pharmacokinetics and pharmacodynamics of omalizumab in children with severe uncontrolled asthma. Allergol Int. 2017 Jan;66(1):106-15. doi: 10.1016/j.alit.2016.06.004. PMID: 27507228. https://www.ncbi.nlm.nih.gov/pubmed/27507228
94. Bagnasco D, Caminati M, Menzella F, et al. One year of mepolizumab. Efficacy and safety in real-life in Italy. Pulm Pharmacol Ther. 2019 Oct;58:101836. doi: 10.1016/j.pupt.2019.101836. PMID: 31473366. https://www.ncbi.nlm.nih.gov/pubmed/31473366
95. Polosa R, Morjaria JB, Caponnetto P, et al. Persisting long term benefits of smoking abstinence and reduction in asthmatic smokers who have switched to electronic cigarettes. Discov Med. 2016 Feb;21(114):99-108. PMID: 27011045. https://www.ncbi.nlm.nih.gov/pubmed/27011045

96. Detoraki A, Di Capua L, Varricchi G, et al. Omalizumab in patients with eosinophilic granulomatosis with polyangiitis: a 36-month follow-up study. J Asthma. 2016;53(2):201-6. doi: 10.3109/02770903.2015.1081700. PMID: 26377630. https://www.ncbi.nlm.nih.gov/pubmed/26377630
97. Jahnz-Rozyk K, Lis J, Warchol M, et al. Clinical and economic impact of a one-year treatment with omalizumab in patients with severe allergic asthma within a drug programme in Poland. BMC Pulm Med. 2018 Mar 16;18(1):48. doi: 10.1186/s12890-018-0610-z. PMID: 29548318. https://www.ncbi.nlm.nih.gov/pubmed/29548318
98. Boulet LP, Boulay ME, Milot J, et al. Longitudinal comparison of outcomes in patients with smoking-related asthma-COPD overlap and in non-smoking asthmatics with incomplete reversibility of airway obstruction. Int J Chron Obstruct Pulmon Dis. 2019;14:493-8. doi: 10.2147/COPD.S192003. PMID: 30880939. https://www.ncbi.nlm.nih.gov/pubmed/30880939

Author
David W. Niebuhr

Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Acknowledgements
Robyn A. Paynter, Research Librarian at Scientific Resource Center, VA Portland Health Care System, Portland, Oregon

This report was developed by staff at the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. No statement in this article should be construed as an official position of the Agency for Healthcare Research and Quality or of the U.S. Department of Health and Human Services.

Appendix A: Methods

We assessed nomination for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Absence of Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years 1/01/2016 to 12/13/2019 on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
  - AHRQ Evidence Reports https://www.ahrq.gov/research/findings/evidence-based-reports/index.html
  - EHC Program https://effectivehealthcare.ahrq.gov/
- US Department of Veterans Affairs Products publications
  - Evidence Synthesis Program https://www.hsrd.research.va.gov/publications/esp/
  - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program https://www.healthquality.va.gov/
- Cochrane Systematic Reviews https://www.cochranelibrary.com/
- PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
- PubMed https://www.ncbi.nlm.nih.gov/pubmed/
- Health System Evidence https://www.healthsystemsevidence.org/
- PDQ Evidence https://www.pdq-evidence.org/

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a limited literature search in Ovid MEDLINE for the last four years from 01/01/2016 to 12/13/2019. We reviewed all studies identified titles and abstracts for inclusion. We classified identified studies by question and study design to estimate the size and scope of a potential evidence review.

Search strategy

Key Question #1

Ovid MEDLINE(R) ALL 1946 to December 13, 2019
Date searched: December 16, 2019
Librarian conducting search**:** Robin Paynter, MLIS
1 Asthma/ (122750)
2 asthma*.ti,ab,kf. (155048)
3 or/1-2 (173684)
4 respiratory function tests/ or spirometry/ or bronchospirometry/ (63507)

5 (spirometr* or bronchospirometr* or ((airflow or airway or lung or pulmonary or respirat*) adj2 (function or test*))).ti,ab,kf. (93553)
6 or/4-5 (124952)
7 Longitudinal Studies/ or Follow-up Studies/ or Prospective Studies/ or (cohort or follow-up or longitudinal or prospective or prospectively).ti,ab. (2362444)
8 (COPD or (chronic adj2 (airway or obstruct* or pulmon* or respirat*)) or follow-up or (life adj (long or span or time)) or lifelong or lifespan or lifetime or "long term" or longitudinal* or periodic* or prospective or predict* or "time series").ti,ab,kf. (3661444)
9 or/7-8 (4299541)
10 (adolescent/ or child/ or child, preschool/) and (adult/ or middle aged/ or young adult/) (1545231)
11 (((adolescen* or child* or juvenile or pediatr* or preschool or pre-school or school-age or teen* or youth*) adj5 (adult* or middle-aged)) or decade).ti,ab,kf. (273558)
12 or/10-11 (1738890)
13 and/3,6,9,12 (1993)
14 limit 13 to yr="2016 -Current" (292)
15 ((evidence or systematic) adj3 (review or synthesis)).ti,ab. or review.ti. or (review or systematic review).pt. (2786804)
16 and/14-15 (61)
17 and/3,6-8,12 (759)
18 limit 17 to yr="2016 -Current" (194)
19 18 not (comment or editorial or letter).pt. (191)

ClinicalTrials.gov
Date searched: December 30, 2019
33 studies found for: ((adolescent OR child OR childhood OR children OR juvenile OR pediatric OR paediatric OR preschool OR pre-school OR school-age OR teenage OR youth) AND (adult OR adulthood OR middle-aged OR geriatric) OR decade OR decades) AND (spirometry OR bronchospirometry OR function OR test) AND AREA[ConditionSearch] (asthma AND (COPD OR chronic airway OR chronic obstructive OR chronic pulmonary OR chronic respiratory OR follow-up OR life long OR life span OR life time lifelong OR lifespan OR lifetime OR long term OR longitudinal OR periodic OR predictive OR prospective OR retrospective OR time series)) AND AREA[StudyFirstPostDate] EXPAND[Term] RANGE[01/01/2014, 12/30/2019]

Key Question #2
MEDLINE ALL (Ovid) searched on January 21, 2020

Concept	
1 asthma/ or asthma, aspirin-induced/ or asthma, exercise-induced/ or asthma, occupational/ or status asthmaticus/ (125694 2 asthma*.ti,kf. (99665 3 or/1-2 (137746	Lines 1-3 Asthma
4 exp Anti-Asthmatic Agents/ or exp Bronchodilator Agents/ or exp Adrenal Cortex Hormones/ or exp Leukotriene Antagonists/ or exp Biological Products/ or exp Immunotherapy/ or exp Behavior Therapy/ or Smoking Cessation/ or Tobacco Smoke Pollution/ (1464377 5 (((antiasthma* or anti-asthma* or bronchodilat* or broncho-dilat* or bronchial-dilat*) adj2 (agent or agents or drug or drugs or pharma*)) or leukotriene* or biologic* or immunotherap* or immuno-therap* or (behavio?r* adj2 therap*) or smoking or smoke).ti,ab,kf. (1196458 6 or/4-5 (2510448	Lines 4-6 Pharm Non-pharm interventions
7 Disease Progression/ or Clinical Deterioration/ or Pulmonary Disease, Chronic Obstructive/ or Respiratory Insufficiency/ or Emergency Service, Hospital/ or Hospitalization/ or Mortality/ or "Cause of Death"/ or Mortality, Premature/ or "Quality of Life"/ (640893 8 (((asthma* or disease) adj2 progress*) or "chronic obstructive" or COPD or (respiratory adj1 insufficien*) or (emergency adj1 (department* or room*)) or hospital* or mortality or QoL or "quality of life").ti,ab,kf. (2229175 9 or/7-8 (2485495 10 and/3,6,9 (10292	Lines 7-9 Outcomes
11 10 and ((("5" or "6" or "7" or "8" or "9" or "10" or five or fifth or six or sixth or seven or seventh or eight or eighth or nine or ninth or ten or tenth or year or years) adj5 year*) or followup or follow-up or decade* or lifecourse or lifespan or lifetime or long-term or longitud*).ti. (506	Line 11 follow-up time period
12 11 not ((exp Animals/ not Humans/) or (animal model* or cat or cats or dog or dogs or mice or mouse or rat or rats).ti.) (506 13 limit 12 to english language (459 14 (controlled clinical trial or randomized controlled trial).pt. (587658 15 trial.ti. or ((control adj2 group*) or controlled or random* or trial).ab. (2056222 16 or/14-15 (2208511 17 13 and 16 (184	Line 12 **Human Limit** Line 13 **English Limit** Lines 14-15 **RCT CCT Limit**
18 limit 17 to yr="2015 -Current" (45) 19 (meta-analysis or systematic review).pt. (180810 20 (meta-analy* or metaanaly* or ((evidence or systematic) adj3 (review or synthesis))).ti,ab,kf. (285769 21 or/19-20 (307530 22 13 and 21 (16	Line 18 Date limit 5 YR Lines 19-20 **SR, MA Limit**
23 limit 22 to yr="2017 -Current" (3 24 Follow-Up Studies/ or Longitudinal Studies/ or Prospective Studies/ or Retrospective Studies/ (1816852 25 (followup or follow-up or longitudinal* or prospectiv* or retrospectiv*).ti,ab,kf. (2173189 26 or/24-25 (2804025) 27 13 and 26 (286) 28 limit 27 to yr="2015 -Current" (83) 29 or/18,23,28 (104) 30 13 not 29 (355) 31 (comment or editorial or letter).pt. (1802747) 32 30 not 31 (352) 33 limit 32 to yr="2015 -Current" (24)	Line 23 Date Limit=3 YR Lines 24-25 **Follow-up Longitudinal Prospective Retrospective Limit** Line 28 Date Limit=5 YR Lines 30-32 **OTHER Limit** Line 33 Date Limit=5 YR
Systematic Review, Meta-analysis (last 3 years)	N=3 (see results below)
RCT,CCT	N=45 (see results below)
Follow-up, Longitudinal, Prospective, Retrospective	N=83 (see EndNote Library)

Concept	
Other	N=352 (See EndNote Library)
ClinicalTrials.gov N=167 https://clinicaltrials.gov/ct2/results?cond=Asthma&term=progression+OR+COPD+OR+chronic+obstructive+OR+respiractory+insufficiency+OR+emergency+department+OR+hospitalization+OR+mortality+OR+quality+of+life&type=&rslt=&recrs=a&recrs=f&recrs=d&recrs=g&recrs=h&recrs=e&age_v=&gndr=&intr=corticosteroid+OR+leukotriene+OR+biologic+OR+immunotherapy+OR+immuno-therapy+OR+behavioral+OR+smoking+OR+smoke&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=01%2F01%2F2015&sfpd_e=01%2F21%2F2020&lupd_s=&lupd_e=&sort=	

Value

We assessed the nomination for value. We considered whether or not the clinical, consumer, or policymaking context had the potential to respond with evidence-based change; and if a partner organization would use this evidence review to influence practice.

Appendix B. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, spirometry is widely available in the U.S.
1b. Is the nomination a request for an evidence report?	Yes.
1c. Is the focus on effectiveness or comparative effectiveness?	Yes, on effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, it is biologically plausible that childhood asthma is associated with COPD in adulthood. The use of longitudinal spirometry to predict progression to COPD in children with asthma is reasonable to consider.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Asthma is prevalent in children and approximately 11% with mild to moderate asthma develop lung function in early adulthood equivalent to advanced COPD.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, both asthma and COPD are associated with significant morbidity, mortality, and disability.
2c. Incorporates issues around both clinical benefits and potential clinical harms	No, the nomination focuses on benefits of longitudinal spirometry in asthmatics in childhood. Harms were not mentioned.
2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, asthma and COPD are associated with high direct (emergency care and hospitalization) and indirect (school and work absenteeism and disability) costs.
3. Desirability of a New Evidence Review/Absence of Duplication	
3. A recent high-quality systematic review or other evidence review is not available on this topic	While we found two reviews relevant to key question 2 they focused only on monoclonal antibodies. We found no systematic reviews addressing key question 1. .
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes, guidelines recommend periodic spirometry in children with asthma to guide therapy in the short-term but not longitudinal lifespan spirometry to guide therapy aimed at preventing adult-onset outcomes, such as development of COPD.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes, longitudinal lifespan spirometry of children with asthma is not standard of care.

Selection Criteria	Assessment
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	Size/scope of review: • Total of studies: • 18 cohort studies across KQ #1 • 14 studies across KQ #2; • Estimate of systematic review size: small *ClinicalTrials.gov*. • KQ#1: 3 studies from 01/01/2014 to 12/30/2019 with 1 recruiting, 2 active not recruiting • KQ#2: 50 studies from 01/01/2015 to 01/21/2020 with 26 recruiting, 9 active not recruiting and 15 completed.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	There are well-known U.S. and international groups developing guidelines on asthma management that are potentially influential. In addition federal agencies, such as the CDC, are interested in improving asthma care and improving outcomes to include COPD.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	Yes, a partner (CHEST) has committed to using this proposed review to develop a practice guideline on the topic to promote practice change.

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; CDC=Centers for Disease Control and Prevention; COPD=Chronic Obstructive Pulmonary Disease; KQ=key question; NHLBI=National Heart, Lung and Blood Institute, NAEPP=National Asthma Education and Prevention Program;