Priority	Research questions
Identify, understand and better classify the different forms of asthma, their progression, and effect on airway inflammation and the immune system	1. In adults and children with severe asthma on high dose optimal therapy, can multi-omic analysis in sputum improve classification and indication of possible responders to Ab therapy compared with clinical symptoms, FeNO and eosinophil counts? 2. In adults and children with severe asthma, can non-invasive biomarkers of breath and urine predict responders/non-responders to omalizumab, compared with blood eosinophilia and IgE levels? 3. In adults and children with severe asthma, can urinary doping lab assessment provide signatures of compliance and drug (in) action of triamcinolone or OCS better than FeNO and eosinophil counts?
Assess the effectiveness of patient-professional communication to develop patient-professional partnerships, for example to optimise self-management and adherence	1. In adults and children with asthma, what approaches are being used successfully or could be used to support healthcare professionals to better communicate with patients to achieve better asthma control through effective partnerships that facilitate optimal adherence and self-management? 2. In adults and children with asthma, can using support tools (e.g. different means of communication and models of intervention), in addition to usual care, improve adherence and self-management, resulting in better asthma control? 3. What support tools (e.g. different means of communication and models of intervention) are effective in helping patients and professionals to optimise asthma adherence? 4. How can we develop interventions to optimise patients' engagement with asthma, asthma treatment and the healthcare system? 5. In adults and children with asthma, can a no-blame approach to non-adherence, improve adherence e.g. applying behavioural change theory and ethnically/socially sensitive communication? 6. How can we sustainably support patients and carers to make informed choices about asthma and asthma care? 7. In adults and children with asthma, can developing a better understanding of the psychosocial factors determining outcomes (e.g. depression, emotional stress) improve asthma outcomes compared with usual care?

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Assess the effect of infections in early childhood, the long-term effects of anti-inflammatory treatments, and use of anti-viral drugs and vaccines	1. Can prevention/treatment of viral/bacterial/fungal infections in early childhood impact on the incidence/severity of later asthma, allergies and wheezing illness? 2. Can alteration of the bacterial microbiome (in the gut and/or the lung) in early childhood impact on the incidence/severity of later asthma, allergies and wheezing illness? 3. Can the use of vaccines against viral and/or bacterial infections in childhood or adulthood impact on the frequency and/or severity of asthma attacks? 4. Can the use of anti-viral drugs in childhood or adulthood impact on the frequency and/or severity of asthma attacks? 5. Can administration of long-term anti-inflammatory treatments in childhood reduce the harmful effects of asthma on lung growth to adulthood? 6. Can administration of long-term anti-inflammatory treatments in adulthood reduce the long-term negative impact of asthma on lung function?
Assess impact, adoption and transferability of best practice in regional, national and European asthma programmes, care pathways and asthma clinics	1. What are the most important components of successful large-scale asthma programmes that should be adopted at scale to drive long-term improvement of asthma control? 2. What are the most important components of successful large-scale asthma programmes that should be adopted at scale to drive improvements in patients' QoL, reductions in hospitalisation, asthma mortality, sick leave and disability pension? 3. What motivates people with asthma to self-manage their symptoms effectively? 4. Are national and regional asthma programmes transferable to other regions in Europe, when considering the significant differences in culture, socioeconomic condition, asthma drugs accessibility and national health service structure? 5. Does a national, evidence-based asthma programme improve asthma outcomes in X [country]? 6. Does a digital (m-health) interactive monitoring and self-management decision support system reduce asthma attacks and emergency medical care in people with mild/moderate asthma?

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Develop new treatments for the different types of asthma: treatment-resistant and steroid-resistant asthma, severe asthma, allergic asthma, hyper-responsive asthma	1. In asthma patients with features of fixed airway obstruction, can novel therapies modify structural changes (airway remodelling) and/or improve outcomes (such as lung function, PROs, exercise tolerance, and in the longer term, changes in FEV_1 decline or imaging (HRCT scan)), compared with usual maximal optimised therapy with bronchodilatory effects? 2. In people with uncontrolled asthma associated with poor adherence, can novel technological approaches to problem identification and novel behavioural interventions improve adherence and outcomes such as asthma control, QoL, lung function, PROs, and patient acceptability compared with the usual care? 3. Can novel therapies that modify steroid resistance and make patients responsive to low dose corticosteroid treatment improve outcomes (e.g. reduction in corticosteroid dose and side-effect profile, improve adherence, asthma control, QoL, lung function, PROs, patient acceptability) in people dependent and/or resistant to systemic corticosteroids compared with the usual care? 4. In patients with predominant T2-low asthma, can understanding the pathophysiological mechanisms of asthma in the absence of T2 inflammation and identification of biomarkers to define non-T2 phenotypes and molecular endotypes help understand the patient group better (e.g. patient demographics, asthma control, QoL, lung function including bronchial hyperresponsiveness, and exacerbation profile?
Develop tools for quick, accurate and low cost diagnosis to distinguish asthma from other causes of breathlessness, cough and wheeze	1. In pre-schoolers with breathlessness, cough and wheeze, are specific proteomic, and/or genomic and/or breathomic profiles (analysed with a future simple sensor) better than current predictive scores to forecast asthma at age 8–9 years of age? 2. In adults with breathlessness, cough and wheeze, are specific proteomic and/or genomic and/or breathomic profiles (analysed with a future simple sensor) better for diagnosing asthma versus COPD than the GINA 2016 distinguishing algorithm? 3. In new-borns with a high risk of asthma, can specific proteomic and/or genomic profiles measured in cord blood (as established by a simple measurement device) predict asthma at age 8–9 years? 4. In children and adolescents, can a new questionnaire developed for epidemiological studies better diagnose clinical asthma than the ISAAC questionnaire? 5. In children/adolescents/adults, which diagnostic tests are optimal for ruling in and/or ruling out the diagnosis of asthma in general practice?

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Evaluate the implementation of supported self-management, the educational needs of patients and caregivers, and the challenges faced and training needs of professionals	1. In people with asthma (≥ 5 years), can a multifaceted, whole-systems implementation strategy for supported self-management in routine practice increase ownership of PAAPs (as an implementation outcome), reduce unscheduled care and/or improve asthma control (as a clinical outcome) compared with usual care? 2. Can an intervention that provides education and self-management support for parents of wheezy pre-school children improve parental QoL and/or reduce unscheduled care when compared to usual care? 3. In people with asthma, can an intervention that provides IT-supported self-management (including an interactive PAAP and integration with healthcare records) reduce unscheduled care and/or improve asthma control compared to usual care? 4. In people with asthma from ethnic minorities or different cultural groups, can a culturally tailored intervention that provides education and self-management support reduce unscheduled care and/or improve asthma control compared to usual care? 5. In adults with asthma, does clinical communication with healthcare professionals (e.g. clinician's ability to explain, listen and empathise) can influence adherence to self-management treatment? 6. In adults with asthma, can access to professional support (e.g. routine reviews, telephone or e-mail consultations, tailored information, provision and review of an action plan, lifestyle advice) improve adherence to self-management?
Explore the interaction between asthma, socio-economic and psychological factors, and comorbidities to reduce the risk of severe exacerbations	1. In adults with asthma, can socio-economic and cultural specific interventions (e.g. interventions aimed at those with lower levels of health literacy or ethnic minorities) reduce inequalities in access to asthma services and treatment, reduce frequency of exacerbations and improve quality of life, compared with usual care? 2. In adolescents taking on self-management of their asthma, can digital interventions to address beliefs and behaviours lead to a reduced frequency of exacerbations and improved QoL, when compared with usual care? 3. In adults with asthma, can intervention outcomes (including frequency of exacerbations) be improved by addressing psychological factors (e.g. attention, beliefs and self-management behaviours)? 4. In adults with asthma aged >50 years, what psychological-, socio-economic- or comorbidity-related factors influence how effective an intervention is at reducing frequency of exacerbations?

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Evaluate the role of lung function testing and new ways of measuring airway inflammation in monitoring asthma	1. Which lung function test is best to evaluate and monitor obstructive airways disease and guide treatment in preschool children with recurrent wheeze? 2. How do measures of airways resistance in preschool children with recurrent wheeze correlate with spirometric abnormalities when they are older? 3. Do young asthmatic children (under 5 years of age) with small airways dysfunction, as measured by multiple breath washout technique, respond differently to standard ICS compared to those children without small airways dysfunction? 4. In people with asthma, how the identification of inflammatory subtypes of asthma through (multi)-omics techniques be we translated to clinical practice? 5. Do exhaled biomarkers allow non-invasive inflammometry of patients with asthma, enabling therapy-based stratification? 6. Which functional parameters (e.g. FeNO, FEV_1, eosinophilic inflammation) should be monitored to optimise long-term outcomes in people with asthma? 7. Which diagnostic tests are optimal for ruling in and / or ruling out the diagnosis of asthma in adults and children with suspected asthma in general practice / primary care?
Identify biomarkers for exacerbations and understand the interactions between biomarkers, risk and comorbidities	To prospectively define an exacerbation in patients with asthma experiencing an exacerbation, can any biomarker (obtained immediately/in point of care nature) provide a measurement that discriminates patients with asthma symptoms from patients with an exacerbation? 1. Can combining patient characteristics with easily obtainable real-time biomarkers (e.g. from exhaled breath) provide a clinical prediction model that reliably identifies patients at risk of exacerbations in primary care settings better than the current assessment of future risk of patients with asthma in primary care? 2. Can a (preferably non-invasive) real-time measurement (such as exhaled biomarker profiling) provide a measurement based on biomarkers to identify patients with exacerbator-prone phenotype? 3. Can assessing sets of biomarkers in patients with recurrent exacerbations of asthma treated in secondary care predict responsiveness to specific biologicals in reducing exacerbations compared with the current state-of-the-art tests? 4. Can a combination set of biomarkers (including circulating eosinophils and exhaled biomarker profile) enable physicians to understand the effect of comorbidities in people with asthma (such as rhinosinusitis, polyposis obstructive sleep apnoea, respiratory infections, obesity and depression) to provide more personalised treatment (the 'one pill' approach versus providing treatment for each condition i.e. a 'multi-pill' approach)?

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Understand the increase in asthma (both childhood asthma and different types of asthma, such as allergic and hyper-responsive asthma) to help develop primary and secondary prevention strategies	1. Does the lung microbiome have functional effects on the development of allergy and asthma that can be modulated to prevent disease onset and progression (e.g. in children born in a sterile environment through C-section)? 2. Do infections reveal a predisposition to develop asthma or are they causally related to asthma? 3. Does exposure to allergens affect the rate of asthma, severity of asthma, asthma control and response to treatment? 4. What effect do lifestyle factors (such as smoking and diet) have on the development and progression of asthma in children and adults?
Assess the efficacy of existing and new drugs on different asthma phenotypes	1. Recognising that within the asthma population, patients are poorly controlled for different reasons; can we further develop our understanding of these reasons and find a means (perhaps novel biomarkers, combined with clinical features) that enable identification of the drivers of poor control in individual patients. 2. Can the novel biomarkers, combined with clinical characteristics, enable the research and development of novel therapies that target the different drivers of poor control, enable the identification of the most appropriate patients for clinical studies, and the assessment of the efficacy of novel therapies against usual care? 3. Asthma-COPD overlap syndrome represent some of the least well-controlled asthma patients: can we develop an improved understanding of this syndrome to enable identification of patients, and to develop clinical end-points that demonstrate the benefit of new therapeutic opportunities versus the usual care? 4. Recognising that adherence to asthma medication is poor, particularly in mild / moderate asthmatics, can we benefit from the advances in electronics to develop aids that provide feedback to the patient with the objectives of supporting and monitoring adherence? 5. Can asthma control be improved and hospitalisations reduced by treating patients holistically, including adequate treatment of co-morbidities, changes are made to lifestyle through education, increased activity and improved nutrition?

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Develop tools to assess asthma self-management and asthma inhaler technique in primary care settings	1. In asthma patients (of all severities), can asthma outcomes be improved by objective measurement of adherence and real-time feedback? 2. In asthma patients (of all severities), can adherence over time be objectively measured and reported to both the patient and healthcare professional? 3. In asthma patients (of all severities), can the use of a real-time symptom score (generated from ongoing active and passive data collection related to symptoms) result in fewer asthma exacerbations? 4. In asthma patients (of all severities), does stepping up/down medication based on SABA2 use as a proxy measure of asthma control, result in fewer asthma exacerbations (and is there economic benefit), as compared to following usual care guidelines for stepping up/down medication? 5. In asthma patients of all severities, can the use of a real-time inhaler technique feedback (e.g. from sensors on the inhaler device and/or video analysis) when compared to standard inhaler technique review by a healthcare professional once a year, result in fewer asthma exacerbations, an increase in patients stepping down medication, amount of SABA2 used/as proxy of asthma control and behavioural propensities? 6. In asthma patients of all severities, can the use of a real-time inhaler use monitoring (e.g. from sensors on the inhaler device) when compared to no monitoring, improve adherence to medication?
Investigate the impact of environmental factors on asthma and exacerbations, such as air quality (indoor and outdoor), climate, allergens and microorganisms and UV radiation	1. What are the mechanisms linking total (outdoor and indoor) pollution to the development and progression of asthma? 2. How do certain types of farming (livestock farming in western countries), proximity to animals from a young age (keeping a dog or keeping animals such as chickens in the home in non-western cultures) and other lifestyles protect children from developing allergy and asthma? 3. What is the role of the lung microbiome in shaping the evolution of severe asthma across the lifecourse? 4. What are the molecular and cellular mechanisms of asthma exacerbations linked to infection, air pollution or other environmental factors? 5. What are the environmental drivers of airway wall remodelling in asthma and can it be prevented and reversed? 6. What are the most effective means of preventing occupational asthma, and how can they be delivered?

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Understand the impact of exposure to substances known to trigger asthma, and the impact of strategies that regulate and control this exposure	1. Can using a temperature controlled laminar flow device above a child's bed for 12 months, compared with not using one, reduce the number of children requiring at least one hospital admission/emergency attendance in the following 12 months in children aged 4-17 years diagnosed with allergic asthma, on regular ICS (BTS Step 2 or above), multi-sensitised to house dust mite (HDM)/cat/dog allergen and with recent hospital admission or emergency attendance with exacerbation? 2. Can mite proof encasings, compared with poly cotton encasings, reduce the number of children requiring at least one hospital admission/emergency attendance in the following 12 months in children aged 4-17 years diagnosed with allergic asthma, on regular ICS (BTS Step 3 or above), mono-sensitised to HDM, living in a non-smoking home and with recent emergency hospital admission or emergency attendance with exacerbation? 3. Can counselling the primary caregiver (and providing pharmacotherapy) to make the household smoke-free reduce the number of children requiring at least one hospital admission/emergency attendance in the following 12 months in children aged 4–17 years, diagnosed with asthma, on regular ICS (BTS Step 3 or above), ETS in the home, and with recent emergency department attendance or hospital admission with asthma exacerbation? 4. In adults with mild-to-moderate asthma with polyp, sinusitis and allergic rhinitis, can regular treatment with anti-IGE treatment, compared with regular treatment, reduce exacerbations, symptoms, inflammation markers (eNO), BHR, steroid use/dose and improve QoL, with improvements present at 6-12 month and 3 year follow-up? 5. In patients with asthma with history of smoking with <12 % reversibility, can asthma control be improved (ACT score, fewer exacerbations, better QoL, need for prn relief) if receiving regular treatment with ICS/LABA or ICS + LABA+ LAMA? 6. In patients with asthma with history of smoking, can SC treatment change exacerbation rates, dose of steroids, BHR, airways inflammatory markers in 6-12 months (treatment with asthma will be the same ICS/LABA in group with SC treatment and no SC treatment)?

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