

Evidence from Australian cohort studies about asthma trajectories and transitions across the life course: a narrative review

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Asthma is a significant global health problem that affects people throughout their lives; the burden is greater among children than for adults. The incidence of asthma began to rise in the 1980s, and now affects 300 million people around the world and contributes to about 1000 deaths each day.¹ The incidence and prevalence of asthma has plateaued in some countries, including Australia, but in others it continues to rise.² Climate change will lead to increased asthma exacerbations and severity.³ In 2023, 2.8 million Australians were living with asthma, which was responsible for 2.5% of the national disease burden; it is the leading cause of disease burden in children under ten years of age.⁴ Further, asthma is frequently associated with other medical conditions, including chronic obstructive pulmonary disease (COPD), ischaemic heart disease, and stroke.⁵

Despite limited breakthroughs in both prevention and treatment, a definitive cure for asthma remains elusive, and the overall prevalence of asthma in Australia has not substantially changed over the past 20 years (12% in 2001, 11% in 2022).⁶

One obstacle that hinders progress to prevention and cure is that not all asthma is the same. Asthma varies in terms of underlying mechanisms, progression, and consequences; “asthma” describes the symptoms and pathophysiology rather than their causes. The term is used to describe episodic difficulty in breathing, usually accompanied by wheeze, caused by narrowed airways and excessive mucus production. We use this term because, unlike many diseases, we do not know the underlying causes of asthma. It is increasingly recognised that asthma has several distinct underlying mechanisms, each characterised by specific molecular signatures (endotypes) that are manifested clinically as different forms of asthma (phenotypes), which can differ by age of onset, severity, treatment response, and other clinical features.⁷

Each asthma endotype/phenotype combination is likely to be associated with a distinct life course trajectory, persisting, resolving, or relapsing over time, depending on factors that influence causation, persistence, progression, and remission throughout life. The key to preventing and curing asthma lies in disentangling the distinct asthma types in order to identify their causes, underlying mechanisms, and long term consequences. We can then determine the best diagnostic tests and predictive biomarkers for different types of asthma. This will facilitate identifying people at risk of asthma, encourage the development of preventive and management approaches, and promote the search for new therapies for all asthma types, with a particular focus on those that are associated with disease persistence, relapse, and progression. Comprehensive understanding of asthma trajectories across the entire lifespan is therefore crucial

Abstract

- Asthma affects more than 300 million people worldwide and is frequently associated with other medical conditions in adults, including chronic obstructive pulmonary disease, ischaemic heart disease, and stroke. Despite the huge burden, there has been little progress toward prevention and cure, possibly related to a one-size-fits-all approach.
- The recent identification of various asthma trajectories over the life course suggests that identifying biomarkers of lifetime transitions could advance progress to prevention and cure. This will require combining data, including for biological samples, from large cohort studies, for analysis using integrated computational biological approaches.
- We summarise key articles on Australian cohort studies that have characterised asthma trajectories across childhood and adulthood in order to inform research focused on curative approaches.
- Five Australian cohorts have provided information on childhood and adulthood asthma trajectories and their relationships with early life factors, later life outcomes, and underlying biological mechanisms. Twelve other cohort studies undertaken in Australia could also contribute valuable information.
- Australian asthma cohort studies have collected a wealth of information across the life course on the drivers, outcomes, and biological mechanisms of asthma. Integrating these resources into harmonised, functionally useful databases will make their data and biospecimens accessible for analysis and research. Australia is well placed for advancing progress in the prevention and cure of asthma.

for effective prevention and management, and for achieving a cure.

Advances in untangling the clinical phenotypes of adult asthma have primarily focused on inflammatory phenotypes. Determining the predominant immune response — eosinophilic, neutrophilic, or paucigranulocytic — has markedly improved precision care for asthma in adults.⁸ It is also known that the prevalence and severity of asthma differ by sex⁹ and age. Sex hormones may protect against asthma, particularly testosterone, the levels of which increase in boys during puberty and decline in mid-adulthood. An inverse relationship between testosterone level and asthma prevalence has been reported, but the precise mechanisms underlying this relationship remain elusive. Differences between people could be related to differences in the growth of airways and lung tissue (dysanaptic growth), which are currently being investigated.¹⁰

The first step to insights into causal, risk, and protective factors for asthma is to characterise asthma trajectories across the life course. Over the past decade, some progress has been made in

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unravelling lifetime asthma trajectories, including in Australian cohort studies. This research is pivotal for identifying people at high risk of asthma and identifying mechanisms underlying asthma in order to guide the development of targeted therapeutic strategies.

The prevalence of asthma in both children and adults in Australia is among the highest in the world, more than 8400 per 100000 people (global mean: 3400 per 100000 people).¹¹ In response to the large asthma burden in Australia, numerous researchers have established large, long term cohort studies to study asthma. Consequently, some of the most comprehensive longitudinal studies of asthma in the world have been undertaken here. These internationally significant cohort studies provide a unique opportunity for advancing knowledge of asthma across the life course. With major advances in statistical methodologies, data-driven approaches can be used to develop novel classifications of asthma trajectories. In parallel, novel laboratory and technological techniques are facilitating substantial progress in identifying the factors that underlie or characterise asthma phenotypes and trajectories. To assess the available information on asthma trajectories reported by Australian asthma cohort studies, we performed a narrative review.

We searched PubMed for publications about Australian studies that had characterised asthma trajectories by prospectively collecting information on symptoms at three or more time points during the life course. We included all publications on asthma cohort studies, as well as other possibly relevant cohort studies undertaken in Australia, published by 31 August 2024. We summarise the findings of the included studies narratively.

Australian asthma cohort studies

Five Australian cohort studies have provided insights into asthma trajectories using both traditional manual methods and data-driven techniques to identify trajectories. Together they have identified factors that influence these trajectories and their outcomes (Box 1). Differences between the studies in their research questions, ages at assessment, analysis methods, and ages at outcome assessment mean that their findings in terms of specific trajectories and associations differ. We therefore summarise the findings of each study separately. These methodological differences also add impetus to pursuing harmonisation of the cohort studies to derive more consistent outcomes.

The Tasmanian Longitudinal Health Study (TAHS) is uniquely positioned to provide insights into asthma across the life course with its extensive data collection and long term follow-up spanning both childhood and adulthood. The population-based study followed Tasmanian children born in 1961 from the age of seven years (in 1968), and continues to follow this cohort, now in their seventh decade of life. The study initially enrolled 8583 children (98.8% of children aged seven years attending Tasmanian schools); they were followed up at ages 14, 21, 30, 43, and 53 years, and further assessments will be undertaken.¹²

At each follow-up, comprehensive questionnaires collected information on respiratory health (including asthma), socio-demographic characteristics, lifestyle factors, and medical conditions; clinical evaluations included lung and other respiratory function tests, skin prick tests, and blood sample collection. Using a statistical method to model the natural history of asthma over time, group-based trajectory modelling,

the study authors modelled lifetime asthma trajectories for participants with a history of asthma from age seven to 53 years. They identified five lifetime asthma trajectories, based on age of onset and remission:

- early-onset adolescent remitting (40% of participants who had ever had asthma), which had resolved almost entirely by adolescence;
- early-onset adult remitting (11%), which resolved by adulthood;
- early-onset persistent (9%), which persisted throughout life;
- late-onset remitting (13%), which resolved in later adulthood; and
- late-onset persistent (27%), which persisted indefinitely.¹³

The risk of the early onset persistent trajectory was greatest for children who experienced multiple infections and allergies during early life. Differences in asthma-related genetic markers were also reported for the different trajectories.¹³

One striking finding was that asthma, irrespective of whether it resolved or persisted throughout life, was associated with adverse health outcomes later in life. Most of the asthma trajectories were associated with increased risks of developing other pulmonary and extra-pulmonary medical conditions, including COPD by the age of 53 years. People in the persistent asthma trajectory groups were almost seven times (adult-onset persistent) or nine times (child-onset persistent) as likely to develop COPD as people without asthma. The risk of later COPD was also two to 3.6 times as high for people in the childhood asthma remitting trajectory groups, indicating the need for lifetime monitoring of people with a history of asthma. Both early- and late-onset trajectories were associated with poorer mental health, and late-onset trajectories were also associated with greater risk of cardiovascular disease (Box 2).

Using a different data-driven technique, latent class analysis, later TAHS studies identified five combined trajectories of asthma and allergy across the life course from ages seven to 53 years, including people without asthma:

- minimal and least asthma and allergies (49%);
- late-onset hay fever with no asthma (29.5%);
- early-onset remitted asthma and allergies (6.5%);
- late onset asthma and allergies (8.8%); and
- early-onset persistent asthma and allergies (6.2%).¹⁴

The persistent asthma and allergy trajectories were associated with increased risks of COPD by the age of 53 years: 5.3-fold risk for the early-onset trajectory, 3.8-fold risk for the late-onset trajectory. The risks of mental health and cardiovascular disorders in later life were also greater for people with these trajectories, suggesting that inflammation could be a factor in asthma, cardiovascular diseases, and mental health disorders.¹⁴

Further, immunological profiles, including the levels of various interleukins (IL) and tumour necrosis factor (TNF), were developed in TAHS as an approach to elucidating the biological mechanisms of lifetime asthma trajectories. The TAHS findings suggested that deficient IL-10 cytokine responses may contribute to the persistence of asthma from childhood to adulthood, while downregulation of IL-6 and TNF alpha expression was associated with remission.¹⁵

1 Australian cohort studies that have examined asthma trajectories by prospectively collecting information on symptoms at three or more time points during the life course

Study	Analysis method (participants)	Ages assessed	Asthma variables	Trajectories/phenotypes	Risk factors/outcomes
Tasmanian Longitudinal Health Study (TAHS), 2023 ¹³	Group-based trajectory modelling (1506)	7, 13, 18, 32, 43, 50, 53 years	Have you, at any time in your life, suffered from attacks of asthma or wheezy breathing? AND Have you had an attack of asthma in the last 12 months?	Early-onset adolescent remitting (40%) Early-onset adult remitting (11%) Early-onset persistent (9%) Late-onset remitting (13%) Late-onset persistent (27%)	All forms associated with COPD at 53 years except late-onset remitting. Comorbidity greatest for late-onset persistent (increased risk of mental health and cardiovascular conditions).
Tasmanian Longitudinal Health Study (TAHS), 2021 ¹⁴	Latent class analysis (3609)	7, 13, 45, 53 years	Have you, at any time in your life, suffered from attacks of asthma or wheezy breathing? AND Have you had wheezy breathing in the last 12 months?	Minimal or least asthma and allergies (49%) Early onset persistent asthma and allergies (6.2%) Early onset remitted asthma and allergies (6.5%) Late-onset asthma and allergies (8.8%) Late-onset hay fever, no asthma (29.5%)	All groups except late-onset hay fever associated with COPD; association strongest for early onset persistent form (and associated with COPD and lung function deficits). Multimorbidity most frequent for late-onset asthma and allergies form. Early-onset groups associated with pneumonia in childhood.
Melbourne Atopy Cohort Study (MACS), 2014 ¹⁷	Latent class analysis (620)	Every four weeks, 4–64 weeks; 18 months; annually, 2–7 years	0–2 years: cough rattle for more than eight days, wheeze in past four weeks; 3–7 years: at least one reported asthma episode	Never/infrequent wheeze (42.7%) Early transient wheeze (27.5%) Early persistent wheeze (5.7%) Intermediate onset wheeze (20.7%) Late onset wheeze (3.5%)	Lower respiratory tract infection, childcare, and high infant body mass index (corresponding to adult BMI ≥ 25 kg/m ²) linked with early transient wheeze; breastfeeding was protective. Lower respiratory tract infection and sensitisation associated with early persistent wheeze. Lower respiratory tract infection, eczema, and sensitisation associated with intermediate wheeze; family dog, being firstborn were protective. Parental smoking associated with late-onset wheeze; breastfeeding was protective.
Longitudinal Study of Australian Children (LSAC), 2022 ²⁰	Group-based trajectory modelling (3864)	0–1, 2–3, 4–5, 6–7, 8–9, 10–11, 12–13, 14–15 years	Asthma symptoms (wheezing) on questionnaire	Low/no asthma (69%) Transient high asthma (17%) Persistent high asthma (14%)	Exposure to antibiotics in early life, maternal smoking, tobacco smoke in home, poor external environment, cluttered homes, heavy traffic, maternal depression, parental financial hardship, parental stress associated with persistent high asthma and transient high asthma.
Childhood Asthma Prevention Study (CAPS), 2016 ²⁴	Latent transition (370)	Early childhood: 1.5, 3, 5 years. Mid-childhood: 8, 11.5 years	Questions on cough/wheeze/sneezing. Emergency department or hospital admission. Preventers/bronchodilators. Spirometry. Airway hyperresponsiveness. Exhaled nitric oxide.	Early childhood: 1A: Nonatopic, few symptoms (60%/53%/52%) 1B: Atopic, few symptoms (3%/12%/21%) 1C: Nonatopic, asthma and rhinitis symptoms (35%/25%/13%) 1D: Atopic, asthma and rhinitis symptoms (2%/9%/14%) Mid-childhood: 2A: Nonatopic, no respiratory disease (46%/41%) 2B: Atopic, no respiratory disease (23%/33%) 2C: Nonatopic, asthma symptoms, no airway hyperreactivity or airway inflammation (12%/8%) 2D: Atopic asthma (19%/19%)	Maternal smoking during pregnancy: reduced risk of phenotypes 1B/2B at 5 and 11.5 years; greater risk of 1C at 1.5 years. Breastfed six months or longer: greater risk of 1B at 1.5 years. Children with eczema: greater risk of 1B, 1D, 2B, 2D. Children with older siblings: reduced risk of 1B at 5 years. of 2D at 8 years; greater risk of 1C at 1.5 years. Children with tertiary educated parents: reduced risk of 1C at 1.5 years.

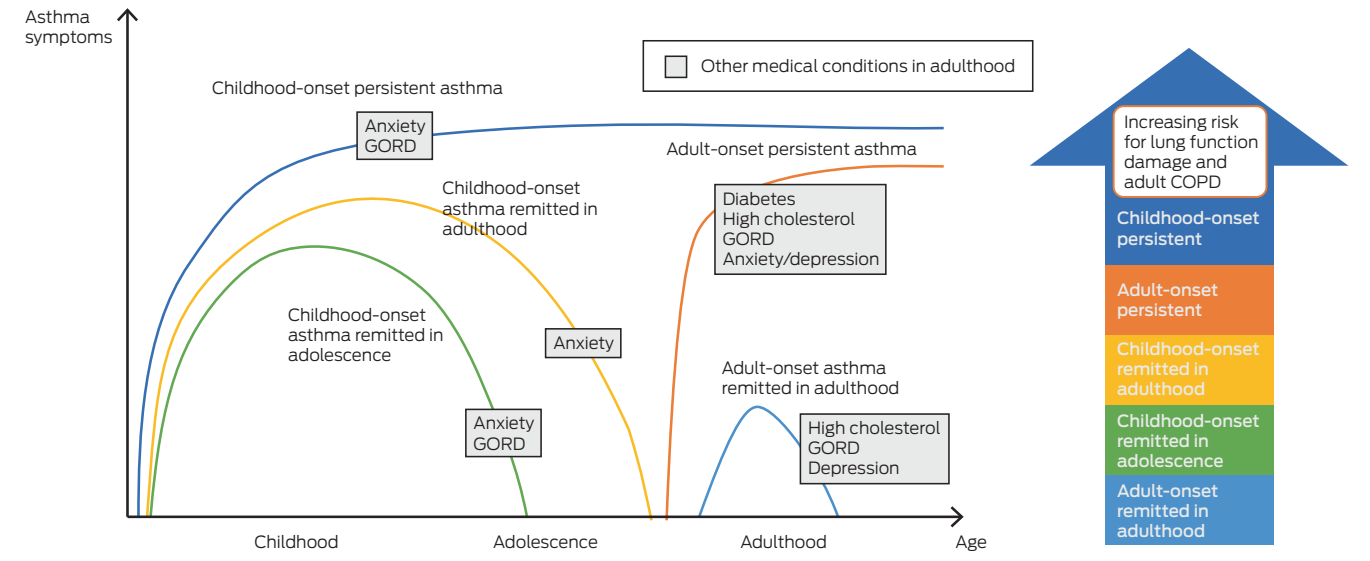
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Study	Analysis method (participants)	Ages assessed	Asthma variables	Trajectories/phenotypes	Risk factors/outcomes
Western Australian Pregnancy Cohort (Raine), 2023 ²⁶	Manual asthma classification (864)	6, 14, 22 years	Doctor diagnosis of asthma ever AND asthma medication use or wheezing in past twelve months	Early onset-transient) (only at 6 years) (39%) Late-onset adult (only at 14, 22 years) (15%) Persistent (at both times) (26%)	Prenatal bisphenol A associated with persistent asthma in men. Prenatal monobenzyol phthalate associated with transient asthma; persistent asthma less likely. Prenatal monoisobutyl and monoisodecyl phthalate associated with adult asthma

COPD = chronic obstructive pulmonary disease. ♦

2 Conceptual diagram of lifetime asthma trajectories and related medical conditions during adulthood, based on findings of the Tasmanian Longitudinal Health Study¹³



COPD = Chronic obstructive pulmonary disease; GORD = gastro-oesophageal reflux disease. ♦

The Melbourne Atopy Cohort Study (MACS)¹⁶ focused exclusively on childhood, providing insights into childhood trajectories of wheeze, the hallmark symptom of asthma. Initiated in the 1990s, MACS is a birth cohort study that enrolled 620 children prior to their birth; they were frequently followed up every four weeks until 18 months after birth, then annually until seven years of age, and again at twelve, 18, and 25 years of age. Originally designed to investigate the role of infant formula in allergic disease in children at high risk of asthma, MACS has evolved into one of the first cohort studies focused on factors that influence asthma and allergic disease, amassing extensive questionnaire, clinical assessment, and biospecimen data.¹⁶

The MACS investigation of wheeze trajectories from birth to seven years using latent class analysis was among the first in the world. Five distinct wheeze trajectories were identified: never/infrequent (42.7%); early transient wheeze (27.5%); early persistent wheeze (5.7%); intermediate-onset wheeze (20.7%); and late-onset wheeze (3.5%). These findings indicated that specific early life factors could initiate each trajectory. Early transient wheeze was related to frequent viral lower respiratory tract infections during early childhood. Early persistent wheeze

appeared to be driven by lower respiratory tract infections and reactivity to allergens, wherein two distinct respiratory system insults contributed to asthma development (two-hit hypothesis). The intermediate-onset wheeze trajectory was associated with childhood allergies, including eczema and sensitisation to food and aeroallergens, while the late-onset wheeze trajectory was associated with exposure to parental smoking.¹⁷ Importantly, all persistent wheezing trajectories included reduced lung function by 18 years of age,¹⁸ underscoring the long term impact of early wheeze trajectories on respiratory health.

The Longitudinal Study of Australian Children birth cohort also contributed to knowledge of factors driving lifetime asthma and wheeze trajectories.¹⁹⁻²² This cohort study, conducted in partnership with the Australian Department of Social Services, the Australian Institute of Family Studies, and the Australian Bureau of Statistics, commenced in March 2003 with 5107 children and has collected data every two years. In the eight waves of data collected to date (from birth to 15 years) and using group-based trajectory modelling, this cohort study has identified three trajectories: low/no asthma, transient high asthma, and persistent high asthma. Poor housing,²⁰ exposure to heavy traffic,²¹ and psychosocial stressors²² contributed to the

transient and persistent asthma trajectories, indicating the role of environmental and social factors in asthma development and its persistence throughout childhood.

The Childhood Asthma Prevention Study, initially established as a randomised controlled trial of interventions for reducing asthma incidence, has evolved into an observational cohort study.²³ Data from birth to 11.5 years were used to model the natural transitions of asthma, related symptoms, and allergy through childhood using latent transition analysis.²⁴ The study findings support the characterisation of distinct asthma trajectories with unique causes and natural histories.

The Raine study is a longitudinal birth cohort study in Perth, Western Australia,²⁵ that recruited 2900 pregnant women during 1989–1991 and followed their 2868 offspring eighteen times over 34 years. Four longitudinal asthma trajectories²⁶ were manually defined according to data collected at six, 14, and 22 years of age: no asthma, early-onset asthma only (at age six years), late-onset asthma only (at age 14 or 22 years), and persistent asthma (at both the early and late timepoints). Higher prenatal in utero exposure to environmental plastic-related toxins was associated with certain asthma trajectories: exposure to bisphenol A with persistent asthma in men, and to phthalates with adult-onset asthma in men.²⁶

Other studies that have collected asthma-relevant data in Australia

Several other cohort studies have collected data and biospecimens in Australia that could contribute to asthma prevention and potential cures (Box 3):

- the Barwon Infant Study (BIS) has followed a birth cohort of more than 1000 infant–mother pairs since 2010, providing rich datasets and biospecimens;²⁸
- the Melbourne Epidemiological Study of Childhood Asthma (MESCA) has tracked children since 1964;²⁹
- the Generation Victoria (Gen V) study at the Murdoch Children's Research Institute began in 2021 and is following 120 000 children;³⁰
- the HealthNuts study recruited 5276 one-year-old children in 2007 and recently completed its 15-year follow-up assessments;³¹
- the Perth Infant Asthma Follow-up study followed 253 children from birth to 24 years and gathered comprehensive data on airway responsiveness and lung function as early life predictors of asthma;³² and
- the Busselton Health study began in 1966, and has regularly surveyed both child and adults in cohorts from the Busselton region of Western Australia.³³

An important planned nested cohort study is the Airway Epithelium Respiratory Illnesses and Allergy (AERIAL) study in Western Australia, which aims to collect information on the airway epithelium for 400 children from in utero to five years of age.³⁴

Additionally, Australia plays a key role in the largest international multi-generation study of asthma that includes a parent study (European Community Respiratory Health Survey)³⁵ and an offspring study examining pre-conception risk factors (Respiratory Health in Northern Europe Spain and Australia, RHINESSA).³⁶ These cohort studies are valuable resources that

can improve knowledge about asthma and outcomes across the life course.

Discussion

We have reviewed the major findings of Australian cohort studies regarding asthma trajectories and the potential of these resources for advancing the Cure Asthma initiative. Given some differences in findings about the definition and characterisation of asthma trajectories, their determinants, and associated outcomes, predicting which people with asthma will experience persistent disease or develop adverse pulmonary and extra-pulmonary conditions remains difficult. Further large scale research will be needed to identify people at risk of asthma before its onset to enable targeted interventions for preventing its development.

Major gaps in our knowledge of lifetime asthma trajectories remain, as some studies investigated early life while others investigated later life. Given the limited time periods covered by each study, a whole of life picture is not yet possible.

Biospecimens collected during Australian cohort studies offer a unique opportunity to explore the biological mechanisms and biomarkers underlying asthma trajectories. Determining predictive biomarkers and novel drug targets would pave the way to much needed breakthroughs in drug discovery. Given the far-reaching effects of asthma across the life course, our ultimate goals are prevention and cure. We must reduce the asthma burden and its effects on lung function and other conditions in adults, including COPD, even for people for whom symptomatic asthma has resolved.

Early interventions to prevent these long term complications is essential. A notable example of how knowledge of lifetime lung health trajectories could influence clinical practice is the recent development of a free online lung function tracker tool,³⁷ designed to assist clinicians with monitoring changes in lung function over time. Integrating asthma-specific risk prediction algorithms into this tool would improve its clinical usefulness for preventing and managing asthma, providing a more personalised approach to managing this complex and widespread disease.

Limitations

Merging and harmonising the findings of the large cohort studies is difficult, also because of the complex ethics and data governance frameworks for each study. These aspects need to be carefully considered when establishing cohort studies, as has been done for similar European projects, such as LifeCycle.³⁸

Conclusion

We are fortunate to have access to extensive longitudinal Australian cohort study data about people with asthma, including data collected for large international asthma cohort studies. It would be opportune to build on these unique research resources. It is essential to integrate their rich data as complementary, harmonised, and functionally useful databases, making the vast volume of data and biospecimens collected over many years accessible and usable. Using novel statistical and artificial intelligence techniques to interrogate the combined cohort datasets will enable us to comprehensively identify lifetime asthma trajectories and advance our knowledge about asthma phenotypes and endotypes, their biomarkers, and their underlying mechanisms and causes, opening the door to drug

3 Australian cohort studies that could provide valuable information on asthma across the life course

Study	Start year	Age at start, in years (enrollees)	Age at follow-up	Wheeze/asthma definition	Lung function assessed	Biological samples
Melbourne Epidemiological Study of Childhood Asthma (MESCA) ²⁹	1964	7	10,14,21,28,35,42	Reported presence of asthma or wheezing episodes or bronchitis.	At all follow-ups.	None.
Busselton Health studies ³³	1966	Various (20 000)	Various	Standard asthma questions.	Spirometry: forced oscillation technique.	None.
Tasmanian Longitudinal Health Study (TAHS) ¹²	1967	7 (8583)	13, 21, 32, 43, 53, 63 years	Standard asthma questions.	Spirometry: 7, 13, 21, 32, 43, 53, 63 years. Complex lung function: 53 years. Forced oscillation technique: 63 years.	Blood: 7, 43, 53, 63 years.
Perth Infant Asthma Follow-up (PIAF) ³²	1987	0 (253)	1, 6, 12 months; 6, 12, 18, 24 years	Reported physician diagnosis; reported wheeze.	Airway responsiveness to histamine: 1, 6, 12 months (rapid tidal volume VmaxFRC), and 6, 11, 18 years (spirometry).	Blood: 6, 12, 18, 24 years.
Western Australian Pregnancy Cohort (Raine) ²⁵	1989	Mothers: preconception; mean one year prior to birth (2868)	1, 2, 3, 5, 14, 17, 18, 20, 22, 25, 27, 28 years	ISAAC questions.	Forced oscillation technique, spirometry, airway hyperresponsiveness: infant/child (5 years), adolescence (13 years), young adult (22 years).	Cord serum, placenta, plasma (childhood, adolescence, young adult).
Melbourne Atopy Cohort Study (MACS) ¹⁶	1990	0 (620)	Every four weeks, 4–64 weeks; 18 months; annually, 2–7 years	MACS respiratory questions; ISAAC questions (from 12 years).	Spirometry: 12, 18, 25 years.	Cord blood/serum. Newborn screening cards. Blood: 18, 25 years. Milk at birth, 5 days, 3 months.
European Community Respiratory Health Study (ECRHS) ³⁵	1993	20–44 (876)	60–84 years	ISAAC questions.	Spirometry: all follow-ups.	Blood: all follow-ups.
Childhood Asthma Prevention Study (CAPS) ²³	1997	0 (616)	36 weeks' gestation; 1, 3 months; every three months to 5 years; every six months to 7.5 years; 8, 9, 11 years; every three months to 14 years	Various: Survey questions on wheeze and asthma; airway hyperreactivity at 8 years.	Forced oscillation technique: 3, 5, 8, 11.5, 14 years. Spirometry: 5, 8, 11.5, 14 years.	Blood: at birth (cord), 1.5, 3, 5, 8, 11.5, 14 years.
Longitudinal Study of Australian Children (LSAC) ²⁰	2003	0 (5107)	0–1, 2–3, 4–5, 6–7, 8–9, 10–11, 12–13, 14–15 years	Survey questions on wheeze and asthma: reported physician diagnosis; wheezing symptoms.	Spirometry: 11–12 years.	Blood: 11–12 years.
HealthNuts ³¹	2007	1 (5278)	1, 4, 6, 10, 15 years	ISAAC questions.	Spirometry: 6, 10, 15 years.	Newborn screening cards at birth. Blood: 1, 4, 6, 10, 15 years.
Barwon Infant study (BIS) ²⁸	2010	0 (1074)	28 weeks' gestation; birth; 1, 3, 6, 9, 12, 18 months; 2, 4, 9 years	ISAAC questions.	Multiple breath washout: 4 weeks, 4 years. ? Spirometry: 9 years.	Blood: maternal (28 weeks); cord; 6 months; 1, 4, 9 years.
Respiratory Health in Northern Europe (RHINESSA) ³⁶	2014	18–53 (245)	28–63 years	ISAAC questions.	Spirometry: both follow-ups.	Blood at both follow-ups.

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3 Continued

Study	Start year	Age at start, in years (enrollees)	Age at follow-up	Wheeze/asthma definition	Lung function assessed	Biological samples
Generation Victoria (GenV) ³⁰	2021	0 (120 000)	1.5 years	Parent reported (not yet clear).	None yet.	Neonatal blood. Parent, infant saliva. Infant two-year stool. Breast milk.

ISAAC = International Study of Asthma and Allergies in Children.²⁷ VmaxFRC = maximal forced expiratory flow at functional residual capacity. * Australian components. ◆

discovery and development. The challenge remains to develop creative approaches for translating discoveries into precision interventions that prevent and cure asthma.

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