



Cohort Profile

Cohort profile: The Childhood Asthma Prevention Study (CAPS)

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Why was the cohort set up?

The Childhood Asthma Prevention Study (CAPS) commenced in 1997 in Sydney, Australia, because of concern about the high and increasing prevalence of childhood asthma.^{1,2} Cross-sectional and ecological studies had shown that exposure to high concentrations of house dust mite (HDM) allergen and being sensitized to HDM were both associated with increased prevalence.^{3–6} Other studies had indicated that children who regularly consumed oily fish containing high

levels of omega-3 fatty acids were less likely to have airway hyper-responsiveness (AHR) and asthma.⁷ Those who regularly consumed oils and spreads containing polyunsaturated fats with a higher proportion of omega-6 fatty acids had an increased prevalence of asthma-like symptoms.⁸

The CAPS investigators determined that a randomized controlled trial was required, both to test the causal hypotheses about these environmental and dietary risk factors, and to evaluate the effectiveness of omega-3 supplementation. We

decided to test the hypothesis that HDM allergen avoidance and omega-3 supplementation, from birth to 5 years of age in high-risk children, would prevent asthma and other manifestations of allergic illness during the first 5 years of life.⁹

CAPS began as a randomized controlled trial (RCT), using a factorial design to test the combined and separate effects of HDM avoidance and omega-3 supplement intervention. Details of the study design and interventions were described in 2001.¹⁰ A secondary aim was to establish a birth cohort of high-risk children to examine the association, over time, between a range of putative risk factors and the incidence of asthma.

Data from the first 5 years of CAPS demonstrated that the study had been successfully established and implemented.^{9,11–13} Based on these initial results and other studies which emphasized the importance of longer-term follow up of trials in primary prevention of allergic disease,¹⁴ follow-up of the cohort was extended beyond 5 years. The participants were re-evaluated at age 8, 3 years after cessation of the intervention, to assess the longer-term effectiveness of the interventions.¹⁵ The age of 8 was chosen as this is the age at which important childhood predictors of adult asthma, including atopy, AHR and obstructive spirometric function, can be reliably measured.^{16,17} Additionally, at age 8, members of the cohort were invited to participate in a subsidiary study examining the childhood determinants of early manifestations of cardiovascular disease. This was initiated because we had successfully acquired information on early life exposures and risk factors relevant to cardiovascular health, including perinatal and postnatal growth, parental smoking, infant and early life nutrition, and socioeconomic data.^{18,19}

The study was further extended through puberty and adolescence (11.5 to 14 years).²⁰ The aims of this period were to examine the relation between puberty and sex-specific changes in respiratory symptoms, lung function, AHR and airway inflammation, and to study the effect of early life and concurrent exposure to environmental risk factors on this relationship. Adolescence is a crucial developmental period during which substantial change is found, with differing prevalences of asthma in males and females.^{21,22} The CAPS study is based at the Woolcock Institute of Medical Research, University of Sydney, Australia.

Who is in the cohort?

CAPS was initially designed as a randomized controlled trial using a factorial design to test the combined and separate effects of HDM avoidance and omega-3 supplementation.¹⁰ Between September 1997 and November 1999, pregnant women whose unborn children were at high risk of developing asthma, because a parent or a sibling had a current diagnosis of asthma or wheezed frequently, were recruited from

the antenatal clinics of six hospitals in Sydney. The selection criteria were: at least one parent or sibling with symptoms of asthma, assessed by screening questionnaire; reasonable fluency in English; a telephone at home; and residence within 30 km of the recruitment centre. Exclusion criteria were: a pet cat at home; the family being on a strict vegetarian diet; a multiple birth; and delivery earlier than 36 weeks' gestation. Details of the recruitment process were published in 2002.¹¹

Of 7171 pregnant women screened, 2095 (29%) were eligible for inclusion. Of these, 616 (29% of those eligible and 9% of those initially screened) were enrolled (Figure 1). The study was powered to detect a 15% absolute reduction in the prevalence of asthma between active and control groups.¹⁰ A survey of 200 eligible non-participants revealed that participating parents had higher levels of tertiary education than non-participants. They did not, however, differ in age, country of birth (Australia versus other), full-time employment or primigravida status.¹¹

How often have they been followed up?

Participants have been assessed on 42 occasions between 36 weeks of gestation and age 14 years. Assessments were performed on the mother at 36 weeks of gestation and on the child at ages 1, 3, 6, 9, and 12 months, every 3 months until aged 5 years, every 6 months until aged 7.5, at ages 8, 9 and 11, and then every 3 months until age 14. A detailed schedule of the data collection times and instruments used is shown in Table 1. During the first 5 years, the study team performed home visits at 36 weeks gestation, then at 1 month after birth, at 3 months, then every 3 months until 12 months, then every 6 months until age 5. A series of interviewer-administered questionnaires were conducted with the participant's parents or guardians. In addition, anthropometric measurements were performed and a home environmental assessment, including dust collection, made. Telephoned interview questionnaires were administered to parents between the 6-monthly home visits from ages 1 to 5. Clinical examinations were performed by study nurses, blinded to treatment group allocation, at ages 1.5, 3, and 5 years at one of two Sydney hospitals (Westmead and Liverpool).

Regular phone calls were made at 6-week intervals to promote adherence to the protocol and to ensure an adequate supply of the goods used in the interventions. Using a 3-day weighed food record and a food frequency questionnaire, respectively, the children's dietary intake was measured at 18 months and 3 years. Between 18 months and 3 years, whole blood was collected from some parents and most participants for DNA extraction and analysis.

After the cessation of the intervention at age 5, telephoned interviewer-administered questionnaires were conducted every 6 months from ages 5 to 8. At age 8, another blinded clinical assessment was performed at

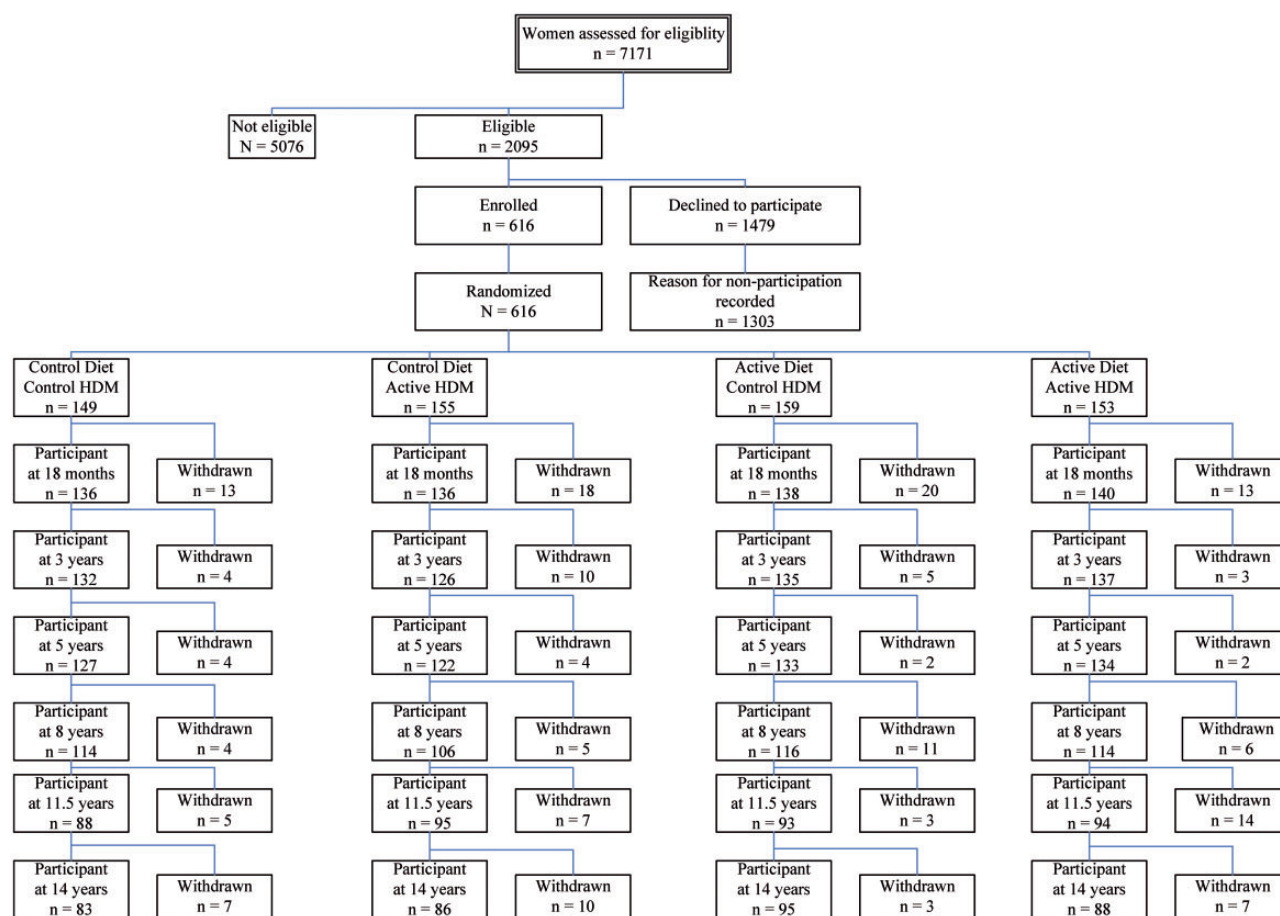


Figure 1. Flowchart for CAPS to age 14 years. Participants at each period were those who completed at least a questionnaire at the major clinical assessment. Participants were considered withdrawn if they had formally withdrawn from the study at or before the assessment.

hospital and a home visit was conducted. Both assessments were similar to those conducted up to age 5 and, for the first time, included AHR. At around age 9, another dietary intake measurement was taken via a telephoned interviewer-administered 24-h recall questionnaire.²³

From age 11 onwards, participants were contacted every 3 months to provide information about puberty and growth. At 3-monthly intervals from around the child's 11th birthday, the parents were contacted by phone or short-message service (SMS) to measure the child's height, using a provided wall-mounted stadiometer, with the results sent back via a web-based data collection tool, SMS or phone. Annually, from around age 11, the children were asked to complete a questionnaire to assess pubertal stage. These included Tanner pubertal stages diagrams^{24–26} and the Pubertal Development Scale.^{27,28} These were administered as a paper questionnaire, either mailed or via a web-based data collection system. This was the first age at which participants were asked to self-complete a questionnaire. At ages 11.5 and 14, another clinical assessment was performed at the hospitals and various interviewer-administered questionnaires were asked of the parents.

Throughout the follow-up period, where a participant was unable to attend a clinical assessment (despite attempts to re-schedule), questionnaires were administered by telephone. If at any time a participant declined to participate but did not formally withdraw, they were re-contacted to participate in the next scheduled assessment. Participants could withdraw at any time and, if so, contact was ceased. During the clinical assessments, not all participants were able to perform all procedures on the day of testing. If so, they were invited to repeat the measurement at a future date. Additionally, not all participants were willing, during clinical assessments, to have blood collected or skin prick tests performed. The number of participants who completed tests is shown in Table 2. Hence, the total number of participants completing questionnaires at the clinical assessment is greater than the number who provided other clinical measurements at that assessment.

Loss to follow-up

Of the 616 participants recruited at birth, the number participating in the major clinical assessments, as determined

Table 1. CAPS questionnaire and measurement data collection schedule

	Months (m)			Years (y)											
	1 m before birth	1 m	3, 6, 9, 12 m	1.5 y	2, 2.5 y	3 y	3.5–4.5 ^a y	5 y	5.5–7.5 ^a y	8 y	9 y	11, 11.25 y	11.5 y	11.75–13.75 ^b y	14 y >14.25 ^b y
Questionnaire															
Home environment	X	X	X	X	X	X	X	X	X	X			X		X
Family history, pregnancy and perinatal	X														
Symptoms and illness	X	X	X	X	X	X	X	X	X						
Diet	X	X	X	X	X	X	X	X							
Clinical				X		X		X		X					X
Ethnicity (4.5 years only)				X			X								
Puberty (annually)											X (11 y)			X (12, 13 y)	X (14, 15, 16 y)
Measurement															
Dust collection	X	X	X	X	X	X	X	X	X				X		X
Anthropometric	X	X	X	X	X	X	X	X	X	X			X		X
Dietary intake				X		X				X					
Physical examination				X	X	X		X		X			X		X
Blood collection				X	X	X		X		X			X		X
Skin prick test				X		X		X		X			X		X
Forced oscillation technique						X		X		X			X		X
Spirometry								X		X			X		X
Methacholine challenge										X			X		X
Exhaled nitric oxide										X			X		X
Cardiovascular										X			X		X
Urine													X	X [*] (12.5 y)	X
DNA						X									X

^a6-monthly measurements.^bQuarterly measurements.

Table 2. The number of participants in CAPS at the major data collection times who were enrolled in the study, those withdrawn and those who completed questionnaires and the other major measurements

	Collection time (years)					
	1.5	3	5	8	11.5	14
	<i>n</i>	<i>n</i>	<i>n</i>	<i>n</i>	<i>n</i>	<i>n</i>
Enrolled in study	552	530	518	492	463	436
Withdrawn from study ^a	64	22	12	26	29	27
Completed:						
Questionnaires	550	530	516	450	370	352
Anthropometric measures	536	516	468	449	292	196
Blood tests	374	409	396	316	257	178
Skin prick tests	535	522	488	402	292	195
Dietary intake measures	424	456		222 ^b		
Spirometry			381	418	283	190
Methacholine challenge				357	269	179
Exhaled nitric oxide				397	290	191
Cardiovascular assessment				405		193
Urine sample					277	183

^aThe number withdrawn from the study is the number of participants who withdrew before or at the assessment period.

^bDietary intake was measured at around 9 years of age.

by completion of the clinical questionnaire, were: 550/616 (89%) at age 1.5 years, 530/616 (86%) at 3, 516/616 (84%) at 5, 450/616 (73%) at 8, 370/616 (60%) at 11.5 and 352/616 (57%) at 14 (Table 2). The loss to follow-up was minimal in the first 5 years ($n = 100$), with the greatest loss occurring in the first 12 to 18 months. Common reasons for early withdrawal were that the participants had moved residence and did not leave any forwarding address or telephone number, had moved out of the study area or were withdrawn for medical reasons.¹¹ The number of withdrawals was similar in each of the randomized groups (see Figure 1). Differences between those who participated at the major clinical assessments at ages 5, 8, 11.5 and 14 years, and those who did not, are described in Table 3. The results show that, compared with non-responders at these assessments, respondent mothers were older, more highly educated, more likely to be in full-time employment, more likely to have breastfed for 6 or more months and less likely to have smoked during pregnancy. Respondent fathers were also older, more highly educated and more likely to be in full-time employment than non-respondent fathers.

What has been measured?

The administered questionnaires collected information on family characteristics, pregnancy and perinatal details, the indoor home environment, diet, symptoms, illnesses, health care use, vaccinations, medication use and puberty stages as described in Table 4. Other measurements included house dust mite allergen concentrations in the bed and/or other sites

at home, anthropometric measures, dietary intake, physical examination for wheeze and eczema, allergen skin prick tests, spirometric lung function, methacholine challenge tests, forced oscillometry, exhaled nitric oxide (FENO) and blood tests for total and specific IgE, lipids, inflammatory markers, sex hormones and DNA.^{15,20} Both targeted gene and genome-wide analyses have been conducted on subsets of the cohort.^{29–33} In addition, when the participants were aged 14, telomere length was estimated on these specimens and further specimens were collected.³⁴ Blood pressure, carotid ultrasound, pulse-wave velocity, and pulse-wave analysis were also conducted,^{18,19} as described in Table 5. We assessed the cytokine (interleukin-5, IL-13, IL-10 and gamma-interferon) concentration in the supernatant of peripheral blood mononuclear cells (PBMCs) collected at ages 18 months and 3, 5 and 8 years and stimulated *in vitro* with HDM extract, an indicator of specific Th2-like and Th1-like responsiveness.³⁵ All measurements and assessments were performed by the study team except the cardiovascular measurements taken at ages 8 and 14, which were performed by cardiovascular researchers. When the children were aged 13–15, data linkage between CAPS data and academic performance data from the Australian National Assessment Program Literacy and Numeracy (NAPLAN) test was performed.³⁶

What has the study found? Key findings and publications

To date, there have been 63 peer-reviewed publications reporting CAPS results. With respect to our principal aim,

Table 3. Comparison of participants who participated and those who did not participate in the clinical assessments of CAPS at ages 5, 8, 11.5 and 14 years

Participants	Original	Participated in the major clinical assessment							
		5 years		8 years		11.5 years		14 years	
		No	Yes	No	Yes	No	Yes	No	Yes
Child characteristics									
Gender									
Male	312 (51%)	55 (55%)	257 (50%)	84 (51%)	228 (51%)	125 (51%)	187 (51%)	126 (48%)	186 (53%)
Female	304 (49%)	45 (45%)	259 (50%)	82 (49%)	222 (49%)	121 (49%)	183 (49%)	138 (52%)	166 (47%)
HDM intervention group									
Control	309 (50%)	49 (49%)	260 (50%)	79 (48%)	230 (51%)	128 (52%)	181 (49%)	131 (50%)	178 (51%)
Active	307 (50%)	51 (51%)	256 (50%)	87 (52%)	220 (49%)	118 (48%)	189 (51%)	133 (50%)	174 (49%)
Diet intervention group									
Control	303 (49%)	54 (54%)	249 (48%)	83 (50%)	220 (49%)	120 (49%)	183 (49%)	134 (51%)	169 (48%)
Active	313 (51%)	46 (46%)	267 (52%)	83 (50%)	230 (51%)	126 (51%)	187 (51%)	130 (49%)	183 (52%)
Breastfeeding $\geq$ 6 months	227 (39%)	15* (23%)	212* (41%)	41* (32%)	186* (41%)	67* (32%)	160* (43%)	70* (31%)	157* (45%)
Child has older siblings	422 (69%)	70 (70%)	352 (68%)	116 (70%)	306 (68%)	179 (73%)	243 (66%)	193* (73%)	229* (65%)
Parent characteristics at child's birth									
Age (years) (mean ($\pm$ SD))									
Mother	28.4 (5.3)	26.2* (5.6)	28.9* (5.2)	27.0* (5.6)	29.0* (5.1)	27.6* (5.6)	29.0* (5.1)	27.9* (5.7)	28.8* (5.0)
Father	30.8 (6.1)	28.8* (6.8)	31.1* (5.9)	29.5* (6.4)	31.2* (5.9)	30.2* (6.3)	31.2* (5.9)	30.4 (6.2)	31.0 (6.0)
Australian born									
Mother	457 (74%)	82 (82%)	375 (73%)	127 (77%)	330 (73%)	185 (75%)	272 (74%)	192 (73%)	265 (75%)
Father	421 (69%)	69 (70%)	352 (69%)	111 (67%)	310 (69%)	166 (68%)	255 (69%)	172 (65%)	249 (71%)
Tertiary educated									
Mother	276 (45%)	32* (32%)	244* (47%)	53* (32%)	223* (50%)	85* (35%)	191* (52%)	92* (35%)	184* (52%)
Father	265 (44%)	34 (35%)	231 (45%)	54* (33%)	211* (47%)	90* (37%)	175* (48%)	98* (38%)	167* (48%)
Full-time employment									
Mother	278 (45%)	43 (43%)	235 (46%)	71 (43%)	207 (46%)	95* (39%)	183* (50%)	104* (39%)	174* (49%)
Father	518 (84%)	77 (78%)	441 (86%)	132 (80%)	386 (86%)	195* (80%)	323* (87%)	207* (79%)	311* (88%)
Mother smoked during pregnancy									
Primigravida	150 (24%)	31 (31%)	119 (23%)	44 (27%)	106 (24%)	72* (29%)	78* (21%)	76* (29%)	74* (21%)
	199 (33%)	28 (30%)	171 (33%)	51 (32%)	148 (33%)	68 (28%)	131 (35%)	72* (28%)	127* (36%)

*Indicates a significant difference (emboldened) ($P < 0.05$) between those who participated and those who did not, based on a chi-square test for categorical variables or a t-test for age.

Table 4. Details of the main CAPS questionnaires

Questionnaire	Information collected
Home environment	Housing details (house type, age, building material, building foundations), number of home occupants, cooking power source, visible mould, pet ownership, child's bedroom details (temperature, humidity, number of occupants, heating source, cooling source, flooring type, rugs or mats, visible mould), child's bed details (type and age of bed, blanket, pillow, mattress, cover), exposure to tobacco smoke
Family history, pregnancy and perinatal data questionnaire	Mother and father (age, date of birth, country of birth, indigenous status, highest level of education, employment status, history of asthma, eczema, or hayfever) Pregnancy information (asthma diagnosed during pregnancy, medication use, vitamin/supplement use, smoking status, foods avoided during pregnancy, gestational diabetes, pre-eclampsia, hypertension) Perinatal information (gravidity, parity, gestational age, labour complications, cord blood taken, Apgar score, resuscitation required, admission to neonatal intensive care or special care nursery, time of birth, birthweight, birth length, head circumference, meconium aspiration, hyaline membrane disease, other neonatal complications)
Symptoms and illness questionnaire	Symptoms (sleep disturbed by coughing, wheeze, itchy rash, runny nose, flexural dermatitis), doctor-diagnosed (eczema, allergic rhinitis/hay fever, pneumonia, whooping cough, bronchiolitis, bronchitis, croup, asthma), significant medical or surgical problems, immunizations given, antibiotic use
Diet	Details of breastfeeding, use of infant formula, use of cow's milk or other milk substitutes and introduction of solid food; vitamin/dietary supplement use and type; consumption of milk and solid foods (asked of mothers if breastfeeding and of children if started solid foods); use of study capsules, spreads and oils
Clinical	Details and history of symptoms: cough (ever or past 12/18 months, longest episode, episode lasted a week or more, during sleep, during physical activity, without a cold), wheeze (ever or past 12/18 months, episode for a week or more, longest episode, without a cold, caused difficulty breathing, health care use for wheeze, during sleep, during physical activity), rhinitis (ever or previous 12/18 months, episode for a week or more, longest episode, frequency of episode), eczema (itchy rash ever or previous 12 months); food allergy (asked up to 3 years: status and type of reaction); food avoidance (asked up to 3 years: type and on whose advice); doctor diagnosis and visited a GP, specialist, emergency department or hospital admission for eczema, allergic rhinitis, pneumonia, bronchiolitis, whooping cough, bronchitis, cough, asthma (from 8 years: diabetes or heart problems); medication (use, type, duration and frequency); snoring (at 5 years: ever and frequency; from 8 years: ever, frequency, loudness, stop breathing, struggle breathing during sleep, fall asleep at school, while watching television or during the daytime); television viewing (asked from 8 years: days per week, hours per day on weekday and weekend); parental health (parent or grandparent experienced a heart attack or stroke); childcare attendance and type (asked up to 5 years)
Ethnicity	Child's maternal and paternal grandparents' country of birth
Puberty	Tanner stages, puberty development scale, date of menarche (girls)

we found that the interventions were successful in reducing HDM allergen concentration in dust collected from beds and in increasing the ratio of omega-3 to omega-6 fatty acids detected in plasma at age 5.^{9,37} However, neither HDM avoidance nor omega-3 fatty acid supplementation, as implemented from birth to age 5, reduced the prevalence of asthma, atopy or other atopic disorders at age 5, nor at the longer-term follow up ages 8 and 11.5.^{9,15,20}

The CAPS study has reported a number of analyses of the association between risk factors of asthma and allergic disease and the incidence of these diseases. We have found the following.

- Birthweight below the first tertile was associated with a greater risk of current asthma and poorer lung function at age 8 years.³⁸
- Longer duration of breastfeeding (>6 months) was associated with an increased risk of allergic sensitization at ages 5 and 8.^{39,40}

- Early childhood eczema, but not early life wheeze or rhinitis, predicted subsequent development of allergen sensitization by age 5.⁴¹
- Owning a pet cat or dog before age 5 was associated with a reduced risk of being atopic at age 5.⁴²
- Exposure to low and high, but not intermediate, levels of HDM allergen was associated with a lower prevalence of HDM atopy and asthma at age 5.⁴³
- At age 8, exposure to vehicular traffic, quantified as the weighted road density at the child's residential address, was positively associated with HDM sensitization and rhinitis.⁴⁴
- The presence of HDM-specific interleukin-5 responses at ages 3, 5, and 8 was associated with the presence of asthma and atopy at age 8.⁴⁵

We have reported a number of findings about the early life predictors and manifestations of cardiovascular disease. Key findings at age 8 include the following.

Table 5. Details of CAPS assessment tools and measurements

Assessment tool/ Measurement	Details
Dust collection	Dust collected from child's bed (or parents' bed if child slept there >2 h/day), and child's play area. House dust mite allergen was extracted from dust samples
Anthropometric measurements	Birth to 12 months: weight, length, head circumference; 12 months onwards: weight and height, with height measured quarterly from 11 years; 8 years: waist and hip circumference; 11.5 and 14 years: body fat and trunk fat by bioelectrical impedance analysis; mother's and father's height and weight (when child aged 8 years only)
Dietary intake	18 months: 3-day weighed food record; 3 years: food frequency questionnaire; 9 years: 24-h dietary recall
Physical examination	Audible wheeze, presence of nasal crusting or discharge, presence of flexural eczema
Blood collection	Total immunoglobulin E (IgE); specific IgE (at 8 years only: alternaria, cat, rye-grass, house dust mite); fatty acids: plasma omega-3, omega-6 and various fatty acids; lipids: cholesterol (total, high-density lipoprotein, low-density lipoprotein) and triglycerides; cytokines: house dust mite stimulated: IL 4 (18 months only), IL 5, IL 10, IL 13 (3, 5 and 8 years), interferon-gamma; hormones: estradiol (girls at 11.5 years only), testosterone (boys at 11.5 and 14 years), insulin-like growth factor 1 (11.5 and 14 years)
Skin prick test	Allergens tested include: egg, cow's milk, salmon, tuna, peanut, house dust mite, cat, dog, cockroach, ryegrass, aspergillus, alternaria, and grass-mix
Forced oscillation technique	Respiratory reactance (Xrs) and respiratory resistance (Rrs)
Spirometry	Forced expiratory volume in 1 s (FEV ₁) and forced vital capacity (FVC)
Methacholine challenge	Dose-response ratio, and airway hyper-responsiveness measured by PD ₂₀ FEV ₁
Exhaled nitric oxide	Measure of airway inflammation
Cardiovascular measures	Blood pressure, carotid intima media thickness, augmentation index, carotid artery distensibility, carotid pulse pressure, brachial pulse wave velocity, non-fasting blood sample for: total cholesterol, high-density lipoprotein cholesterol, triglycerides, apolipoproteins A1 and B, high-sensitivity C-reactive protein, asymmetric dimethylarginine
Overnight urine sample	Gonadotropins, follicle-stimulating hormone
DNA	Single nucleotide polymorphisms (SNPs) at 3 years: IL13, IL14, intergenic, PHF11, CTLA4, filaggrin and CD14; telomere length at 3 and 14 years

- Compared with boys, girls—independent of height—had lower carotid extra-medial thickness⁴⁶ and greater arterial wave augmentation.⁴⁷
- Greater carotid intima medial thickness was associated with lower high-density lipoprotein (HDL) cholesterol, higher levels of asymmetric dimethylarginine (ADMA), and higher systolic blood pressure.¹⁸
- Excessive weight gain in infancy was associated with greater carotid intima medial thickness⁴⁸ and carotid extra-medial thickness.⁴⁹
- Maternal smoking in pregnancy was associated with significantly lower HDL cholesterol.⁵⁰
- Consuming a large amount of dairy food at age 18 months was associated with lower blood pressure at age 8.⁵¹
- Omega-3 supplementation during the first 5 years of life did not improve arterial structure and function at age 8;¹⁹ it did, however, reverse the inverse association between impaired fetal growth and arterial wall thickness.⁵²
- Lower spirometric lung volumes were associated with increased vascular stiffness.⁵³

- The presence of asthma and of airway inflammation was not associated with alterations in systemic ADMA or L-arginine levels.⁵⁴
- Shorter telomere length in early childhood was associated with arterial wall thickness.³⁴
- Carotid extra-medial thickness, but not carotid intima-media thickness, was associated with local arterial stiffness.⁵⁵
- At age 14, the augmentation index was higher in girls than boys and was closely associated with change in height between ages 8 and 14.⁵⁶

The dietary intake data have been used to characterize the diet of Australian children and to assess the impact of diet components on weight gain and the development of obesity. We have reported the following.

- Distribution of types of food, nutrients and portion sizes,⁵⁷ meat intake⁵⁸ and the intake of energy-dense, nutrient-poor foods⁵⁹ among children aged 18 months were described.
- Higher intakes of protein and meat at age 18 months were positively associated with greater adiposity at age

8,⁶⁰ and high intakes of meat and carbohydrates were associated with high body mass index from birth to age 11.5 years in boys.⁶¹

- Adequate dairy consumption at age 9 was associated with diets of higher nutritional quality, but also with higher intakes of energy,²³ and energy consumed in liquid form contributed more to the development of obesity.⁶²

Genomic data from participants with asthma in the cohort have contributed to multi-centre (Australian and international) genome-wide association studies (GWAS), as part of the Australian Asthma Genetics Consortium to identify new risk loci for asthma and allergic disease in children.^{29–33}

Advanced statistical techniques have been applied to the longitudinally collected data, with repeated measures to provide new insights into asthma, allergic disease and obesity. Finite mixture models have been used to explore the heterogeneity in asthma, atopy and growth by defining latent subgroups, often called classes or phenotypes.

- A latent class analysis of allergen skin prick tests performed at ages 1.5 to 8 years revealed four phenotypes: late mixed inhalant sensitization; mixed food and inhalant sensitization; HDM monosensitized; and no atopy.⁶³ All three atopy phenotypes were associated with asthma, eczema and rhinitis, but the strongest association, particularly for asthma, was with the mixed food and inhalant sensitization phenotype, implying that food sensitization in early life might be of greater significance for subsequent risk of asthma than previously thought.
- Growth mixture models have been applied to body mass index (BMI) data collected from birth to age 11.5 and identified three BMI growth trajectories, differing qualitatively between boys and girls;⁶¹ growth mixture models applied to height collected from ages 11–14 showed that girls with asthma at age 8 had a higher probability of belonging to a later growth trajectory.⁶⁴
- A latent transition analysis model was applied to data from age 0–11.5 years to incorporate the longitudinal patterns of several manifestations of asthma into a single model, to simultaneously define phenotypes and examine their transitions over time.⁶⁵ It provided quantitative support for the view that asthma is a heterogeneous entity, and that some children with wheeze and other respiratory symptoms in early life progress to asthma in mid-childhood, whereas others become asymptomatic.

What are the study's main strengths and weaknesses?

The major strengths of this study are:

- i. an existing, well-motivated cohort of participants with good retention rates during the first 5–8 years of life;
- ii. the detailed characterization of early life constitutive and environmental risk factors for asthma and allergic disease, which has extended from the antenatal period to age 14 years, and which is accompanied by equally detailed characterization of allergic and respiratory outcomes, including objective measurements during this period;
- iii. use of the strongest possible study design, an RCT to test HDM avoidance and dietary fatty acid intervention, both of which were successfully implemented from birth to age 5 years, giving a unique opportunity to assess the long-term outcome of these interventions;
- iv. the high-risk nature of the cohort, which represents the population most likely to be the target for future interventions to reduce asthma and allergic disease;
- v. use of the participants, and of their accompanying early life details, to study other childhood diseases including obesity and cardiovascular disease; and
- vi. a long-serving, multidisciplinary and committed research team, many of whom have been involved in CAPS since its inception or soon after, allowing a strong engagement with the participants and a greater understanding of the resultant data.

The main weakness of CAPS, as for most long-term cohort studies, is attrition as the participants grow older. As the participants have entered and moved through adolescence, they have become less interested in participating in clinical examinations. This has resulted in 32% (196/616) of the original sample completing clinical testing at 14 years. A by-product of this attrition is that the remaining sample in CAPS is from a higher socioeconomic background (Table 3) than those who have withdrawn.

Can I get hold of the data? Where can I find out more?

The CAPS study team are interested in collaborating with others. Researchers interested in collaborating with CAPS researchers or wishing to access CAPS data are encouraged to contact our Chief Investigator, Dr Brett Toelle [brett.toelle@sydney.edu.au]. For approval from the Chief Investigator, researchers will be asked to write a short proposal describing the aims of their project and specifying what data would be required.

Profile in a nutshell

- CAPS was established as a randomized controlled trial to test the effectiveness of a house dust mite avoidance intervention and an omega-3 supplement intervention for the primary prevention of asthma; it is now a well-established birth cohort for studying the natural development of asthma.
- Pregnant women ($n = 616$), whose unborn children were at risk of developing asthma, were recruited from hospitals in Sydney, Australia, between 1997 and 1999.
- On 42 separate occasions from 36 weeks of gestation to age 14 years, data have been collected using questionnaires and other clinical measurements and assessments; 352 subjects remain eligible for future follow-up.
- Information collected and tests performed have included: family history, pregnancy and perinatal details, environmental exposures, dietary intake, child's symptoms and illnesses, anthropometric measures, DNA, skin prick tests, spirometry, airway hyper-responsiveness, exhaled nitric oxide, lipids, fatty acids, cytokines, pubertal stages, hormones and cardiovascular function.
- More than 63 peer-reviewed articles have been published. Researchers interested in collaborating can contact Chief Investigator Dr Brett Toelle [brett.toelle@sydney.edu.au].

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