National Asthma Council Australia

AUSTRALIAN ASTHMA HANDBOOK

VERSION 2.0

PREVENTION

Primary prevention

Preventive care

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ABBREVIATIONS

CFC	chlorofluorocarbon
COPD	chronic obstructive pulmonary disease
COX	cyclo-oxygenase
DXA	dual-energy X-ray absorptiometry
ED	emergency department
EIB	exercise-induced bronchoconstriction
FEV_1	forced expiratory volume over one second
FEV_6	forced expiratory volume over six seconds
FSANZ	Food Standards Australia and New Zealand
FVC	forced vital capacity
GORD	gastro-oesophageal reflux disease
HFA	formulated with hydrofluroalkane propellant
ICS	inhaled corticosteroid
ICU	intensive care unit
IgE	Immunoglobulin E
IL	interleukin
IU	international units
IV	intravenous
LABA	long-acting beta$_2$-adrenergic receptor agonist
LAMA	long-acting muscarinic antagonist
LTRA	leukotriene receptor antagonist
MBS	Medical Benefits Scheme
NHMRC	National Health and Medical Research Council
NIPPV	non-invasive positive pressure ventilation
NSAIDs	nonsteroidal anti-inflammatory drugs
OCS	oral corticosteroids
OSA	obstructive sleep apnoea
PaCO	carbon dioxide partial pressure on blood gas analysis
PaO	oxygen partial pressure on blood gas analysis
PBS	Pharmaceutical Benefits Scheme
PEF	peak expiratory flow
pMDI	pressurised metered-dose inhaler or 'puffer'
PPE	personal protective equipment
SABA	short-acting beta$_2$ -adrenergic receptor agonist
SAMA	short-acting muscarinic antagonist
SaO_2	oxygen saturation
SpO_2	peripheral capillary oxygen saturation measured by pulse oximetry
TGA	Therapeutic Goods Administration

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DISCLAIMER

Breastfeeding and allergy prevention

Earlier evidence suggested that the risk of asthma might be reduced by prolonged exclusive breastfeeding. The reduction in risk was thought to be greatest in children at high risk of asthma, but small in other children.[75] This evidence was mainly from studies of poor methodological quality.[76]

However, recent studies did not confirm that prolonged exclusive breastfeeding protected against development of asthma,[77] allergic rhinitis,[77] or other allergic disease such as atopic dermatitis (eczema).[78]

Limited evidence from observational or poor quality studies suggests that breastfeeding while solid foods are introduced may help reduce the infant's risk of developing allergies.[79] The Australasian Society of Clinical Immunology and Allergy (ASCIA) current guidelines for *Infant feeding and allergy prevention* recommend breastfeeding for at least 6 months for its range of benefits, with complementary foods introduced at around 6 months (but not before 4 months) while continuing to breastfeed.[79]

Exclusion of allergenic foods from the maternal diet has not been shown to prevent allergies.[79] ASCIA recommends against maternal dietary restrictions while breastfeeding.[79]

ASCIA's guidelines for *Infant feeding and allergy prevention* and *Guide to introducing solid foods* contain practical advice for mothers[4] For updates on ASCIA advice, refer to the ASCIA website (www.allergy.org.au).

▶ Go to: *ASCIA's guidelines for Infant feeding and allergy prevention*

▶ Go to: *ASCIA's guide to introducing solid foods*

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Allergies and exposure to allergens: effects on risk of developing asthma

Note: Although allergic asthma is common, non-allergic asthma also occurs.

Population-based studies have observed a positive association between early life exposure to aeroallergens (house dust mite, mould)[63] or sensitisation to aeroallergens[80] and the development of asthma. However, exposure to allergens may not actually cause asthma.[80]

Allergic rhinitis is a major risk factor for asthma and often precedes it.[81, 82, 83] These associations probably reflect the common allergic causes of both conditions, rather than a causal link.[83]

The combination of sensitisation to aeroallergens and viral infections early in life increases asthma risk.[84]

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Allergen avoidance in children: effects on risk of developing asthma

There is accumulating evidence from systematic reviews of intervention trials that single allergen reduction strategies, such as the use of mattress covers that are impermeable to house dust mite, are not effective in preventing the development of wheezing or asthma in children.[85, 86]

An Australian controlled clinical trial that compared house dust mite avoidance (acaricide and impermeable mattress covers), from birth to 5 years, with simple advice on cleaning, vacuuming, dusting and maintaining adequate ventilation,[87, 88] reported no reduction in the risk of developing asthma at age 11.5 years.[44]

Multimodal allergen avoidance strategies that reduce exposure to both inhalant and food allergens, beginning in late pregnancy or from birth, may reduce the risk of asthma in children under 5 and in children over 5 years.[86] However, these strategies require intensive effort and may not be feasible for many families.

Avoiding exposure to pets does not reduce asthma risk.[89] There is even limited evidence that perinatal exposure to dogs or cats could reduce the risk of allergic disease.[90]

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Restriction diets during pregnancy and lactation: effects on children's risk of developing asthma

Systematic reviews of clinical trials of food allergen avoidance during pregnancy have found no overall reduction in rates of asthma or atopic dermatitis (eczema) in infants.[24, 23] A 2012 Cochrane review concluded that prescription of antigen avoidance diets during pregnancy was unlikely to reduce substantially the risk of asthma or allergies in children with a family history of allergies.[24]

In contrast, two studies have since found that consumption of food allergens during pregnancy was associated with a *lower* risk of allergy and asthma in the offspring.[91, 92]

Restriction diets during pregnancy could also compromise maternal or foetal nutrition.[24]

The Australasian Society of Clinical Immunology and Allergy (ASCIA) allergy information for parents recommends against dietary restrictions during pregnancy or breastfeeding, and recommends that common food allergens (e.g. peanut, egg, fish, soy, cow's milk) should be fed to infants before age 12 months, starting at around 6 months (but not before 4 months).[21]

▶ Go to: *Australasian Society of Clinical Immunology and Allergy's Infant feeding and allergy prevention clinical update*

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Dietary supplementation during pregnancy and in newborns: effects on children's risk of developing asthma

Probiotics and prebiotics

Meta-analyses of clinical trials evaluating probiotics or prebiotics for the prevention of allergies in children have reported possible protection against atopic dermatitis (eczema),[93] but do not show a reduction asthma.

Recent systematic reviews of clinical trials of probiotic supplementation during pregnancy or in early infancy reported that, overall, there was no statistically significant reduction in children's rates of asthma or wheezing.[26, 94, 28] Included trials varied in the type and duration of probiotic supplementation.

The Australasian Society of Clinical immunology and Allergy advises that '[w]hilst there is moderate evidence that probiotics during pregnancy and breastfeeding may help prevent eczema in early life, recommendations about probiotic supplements cannot currently be made because the optimal species and dose of probiotics that might have an effect is unclear.[93]

A systematic review and meta-analysis of clinical trials evaluating prebiotics (commonly oligosaccharides) added to infant feeds in the prevention of allergy found no significant effect on the rates of asthma development in children.[25] It reported that there was some evidence that a prebiotic supplement added to infant feeds may prevent eczema, but that it was unclear whether the effects of prebiotic differed between children at high risk of allergy and the general population.[25]

Vitamin D

Meta-analysis of the two largest randomised clinical trials of vitamin D supplementation during pregnancy suggests that a daily dose of 4400 IU may reduce the risk of asthma/recurrent wheeze in the first 3 years of life, compared with the dose in standard multivitamin supplements (400 IU).[32] The effect was greatest in those with a circulating 25-hydroxy-vitamin D concentration ≥ 30 ng/mL from study entry to delivery, suggesting that vitamin D levels in early pregnancy may be important.[32]

A systematic review of earlier randomised clinical trials reported a significant inverse association between the prenatal intake of vitamin D and children's risk of developing recurrent wheeze.[31] However, clinical trials have differed in doses and outcomes measured.

Vitamin D supplementation is routinely recommended for pregnant women:[22]

- 1,000 IU (25 microg)/day for those with baseline blood levels 30–49 nmol/L
- 2,000 IU (50 microg)/day for those with baseline blood levels < 30 nmol/L (with retesting at 28 weeks gestation)
- 400 IU as part of a pregnancy multivitamin for women with baseline blood levels above 50 nmol/L.

Fish oil

A systematic review of prospective observational studies and RCTs found that asthma risk is reduced by high fish oil intake in children, including both fish consumption and long-chain omega-3 polyunsaturated fatty acids intake.[95]

However, recent systematic reviews of clinical trials evaluating prenatal long-chain omega-3 polyunsaturated fatty acid supplementation for allergy prevention found that supplementation had no effect on asthma or wheeze in children.[38, 39] Earlier trials reported a reduction in asthma rates in children.[40]

Most studies were designed to measure other allergic outcomes (e.g. atopic dermatitis) and were not powered to detect effects on asthma risk.

The results of randomised clinical trials vary. A clinical trial comparing prenatal supplementation with fish oil (2.7 g of long-chain omega 3 polyunsaturated fatty acids) versus placebo (olive oil) or no intervention reported a significant reduction in the risk of asthma (measured as prescription of asthma medication) at up to age 18–19 years in the fish-oil group compared with the olive oil group, but no difference between groups in lung function or allergic sensitisation at age 18–19 years.[96] In another randomised clinical trial, prenatal supplementation with 2.4 g fish oil per day was associated with a reduction in the rate of wheeze or asthma in children at 3-year follow-up.[41] However, in a study in pregnant women with family history of allergic disease, supplementation with fish oil capsules (800 mg/d docosahexaenoic acid DHA and 100mg/d eicosapentaenoic acid) had no effect on asthma at 3 or 6 years' follow-up, compared with placebo (vegetable oil capsules).[42, 43]

A systematic review of clinical trials evaluating infant supplements found that polyunsaturated fatty acids given as supplements or added to infant formula did not affect rates of asthma at up to age 2 years or at age 2–5 years.[97]

Australasian Society of Clinical Immunology and Allergy advises pregnant women that up to 3 serves of oily fish per week may be beneficial during pregnancy and breastfeeding, based on evidence for a protective effect of omega-3 fatty acids against atopic dermatitis in infants.

▶ Go to: *Australasian Society of Clinical Immunology and Allergy's Infant feeding and allergy prevention clinical update*
Go to: *Royal Australian and New Zealand College of Obstetricians and Gynaecologists' guidance on vitamin and mineral supplementation and pregnancy*

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Vitamins and nutrition: effects on risk of developing asthma

Overall, dietary intake of fruits and vegetables, and a range of vitamins, has been associated with lower rates of asthma or wheeze in systematic reviews of observational studies (mainly cross-sectional studies).[98, 99, 100, 101]

Higher diversity of food during the first year of life has also been associated with lower risk of developing asthma.[65]

Fruits and vegetables

Vegetable intake is inversely associated with risk of current asthma in adults and children.[99] High vegetable consumption is associated with lower rate of wheeze and asthma in adults and children, compared with low vegetable consumption.[100]

High fruit consumption is associated with lower rate of wheeze and asthma in adults and children, compared with low fruit consumption.[100]

While the quality of evidence for a protective effect of fruits and vegetables is generally low, eating plenty of fruits and vegetables can be promoted for its general health benefits.

Fish oil

A systematic review of prospective observational studies and RCTs found that high fish oil intake (both fish consumption and long-chain omega-3 polyunsaturated fatty acids intake) was associated with reduced asthma risk reduced in children.[95]

Mediterranean diet

The 'Mediterranean diet' (high in fruits and vegetables, whole grains, oily fish and olive oil, and low in red meat) has been associated with lower rate of asthma or wheeze in systematic review of observational studies.[98]

Fast foods

High intake of fast foods by children has been associated with increased risk of developing asthma in observational studies.[102, 103, 104, 105]

Vitamin D

Pregnancy

There is epidemiological evidence for an association between low vitamin D in pregnancy and increased risk of wheeze and recurrent wheeze or asthma in early childhood[106] and of developing asthma during the first 10 years of life.[65] The quality of evidence varies, but the best available evidence from birth cohort studies reported an inverse association between maternal intake of vitamin D during pregnancy or cord blood level of vitamin D, and childhood wheeze.[106] One systematic review reported a U-shaped relationship between maternal blood 25-hydroxyvitamin D levels and risk of childhood asthma, with the lowest risk at approximately 70 nmol/L.[107]

The results of clinical trials of vitamin D supplementation during pregnancy also suggest a protective effect against wheezing and asthma in early childhood.[32, 31] However, clinical trials have differed in doses and outcomes measured. The findings of one trial suggest that vitamin D levels in early pregnancy may be important.[32]

Intake in childhood

Dietary intake of vitamin D in childhood is associated with lower rate of asthma or wheeze.[98]

Other vitamins

Dietary intake of vitamins C and E have been associated with lower rate of asthma or wheeze.[98]

Systematic review of observational studies shows that low maternal vitamin E intake during pregnancy is associated with increased risk of asthma in offspring up to age 10 years.[65]

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Low birth weight and prematurity: effects on risk of developing asthma

Preterm birth, low birth weight and related perinatal factors are associated with an increased risk of childhood asthma, according to meta-analyses of large datasets from observational studies, including many birth cohort studies.[108, 109, 110, 111]

Preterm birth (gestational age <37 weeks) and younger gestational age at birth are associated with higher risk of preschool wheezing

and of asthma during childhood and adolescence.[108, 110]

Low birth weight (<2.5 kg) is associated with higher risk of wheezing disorders, asthma during childhood and adolescence, and asthma in adulthood.[108, 109, 111] The related variable of weight gain velocity is also linked to asthma risk, with greater infant weight gain associated with risk of preschool wheezing and of asthma during childhood and adolescence.[108, 110]

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Caesarean section: effects on risk of developing asthma

Systematic reviews and meta-analyses of data from observational studies show an association between Caesarean section and a small increase in the child's risk of developing asthma, compared with vaginal delivery.[64, 65, 66]

Some, but not all prospective birth cohort studies have reported an increase in asthma rates among children delivered by caesarean section.[112, 113, 114, 115, 116, 117] Retrospective cohort studies and database studies,[118, 119, 120, 121, 122, 123] case-control studies[124, 125, 126] and population-based cross-sectional studies[127, 128, 129] have reported inconsistent findings for follow-up of various intervals: some found an association between Caesarean section and asthma risk, while others did not.

The mechanism is thought to be due to effects of altered intestinal bacterial flora on the infant's developing immune system.[64, 65, 66]

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Maternal and childhood obesity: effects on risk of developing asthma

Maternal obesity during pregnancy increases the risk of asthma or wheeze in children, based on a meta-analysis of observational studies.[130]

High gestational weight gain was also associated with higher risk of asthma or wheeze.[130]

Childhood overweight or obesity have also been associated with increased risk of developing asthma in some systematic reviews of observational studies.[131, 132, 133]

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Early life viral infections: effects on risk of developing asthma

Early life viral lower respiratory tract infections with respiratory syncytial virus (RSV) or rhinovirus are strongly associated with allergic asthma in childhood.[134, 135, 136, 63]

It is not yet known whether this association is due to inherited risk for both asthma and increased susceptibility to these viruses, or reflects alterations in immune response and lung function caused by the infection.[134] Several genetic polymorphisms have been associated with wheeze following RSV lower respiratory tract infection in full-term infants.[137]

Estimates of attributable risk of asthma due to RSV are 13–22% among children aged 5 years and under, 11–27% among children aged 5–11 years, and 32% among children 12 years and over.[138]

The findings of one study suggested that prophylaxis with palivizumab (humanised IgG_1 monoclonal antibody directed against RSV) in infants may reduce the risk of recurrent wheeze during the first year of life.[12] However, longer-term follow-up found no effect on physician-diagnosed asthma or lung function at 6 years.[139] At present, palivizumab use is mainly restricted to tertiary referral hospitals, where it is used to prevent severe RSV infection in susceptible infants (e.g. premature infants or those with congenital heart disease).

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Traffic air pollution: effects on risk of developing asthma

There is mounting evidence from observational studies for an association between pollution and asthma risk in children. However, it is difficult to control for the influence of confounding factors such as socioeconomic status.

In systematic reviews and meta-analyses:

- prenatal exposure to air pollution (including nitrogen dioxide, particulate matter) was associated with increased risk of wheezing and asthma in children[140]
- early life exposure to air pollution (nitrogen dioxide, ozone, volatile organic compounds, and particulate matter) was associated with increased risk of allergic asthma in children[63]
- childhood exposure to traffic pollution including black carbon (soot from vehicle emissions), nitrogen dioxide, fine particulate matter, carbon monoxide and particulate matter, were associated with increased risk of asthma.[141, 142]

The role of traffic-related air pollution in the development of adult-onset asthma is less conclusive than in childhood asthma due to

fewer studies and heterogeneity among studies.[143]

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Indoor air pollution: effects on risk of developing asthma

Epidemiological studies have consistently reported an association between early life exposure to indoor dampness and mould (particularly visible mould and mould odour)[144] and increased risk of developing asthma or wheeze.[144, 145, 146, 147] However, it is difficult to control for the influence of confounding factors such as socioeconomic status.

Exposure to fumes from polyvinyl chloride products (PVC) surface materials is associated with increased risk of asthma in children, while exposure to heated PVC fumes (mainly in the workplace) is associated with increased risk of asthma in adults.[148]

The use of gas stoves or ovens in the home has also been associated with development of asthma in children.[149]

Various indoor pollutants have also been associated with increased risk of adult-onset asthma. These include airborne substances used in the home (e.g. cleaning sprays)[150] and many airborne substances encountered in workplaces.

▶ Go to: *Work-related asthma*

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Infant feeding and asthma prevention

Recommendations

Recommend breastfeeding where possible for its health benefits, but do not advise prolonged exclusive breastfeeding (as recommended in the past for allergy prevention). Instead, recommend the introduction of a variety of solid foods at around 6 months (but not before 4 months), while continuing to breastfeed.

Note: Prolonged exclusive breastfeeding does not prevent asthma in children. Delayed introduction of commonly allergenic foods increases the risk of developing food allergy.

▶ **Go to:** *ASCIA's guidelines on infant feeding and allergy prevention*

▶ **Go to:** *ASCIA's guide to introducing solid foods*

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- ASCIA 2016[1]

Last reviewed version 2.0

For infants at high risk of asthma (e.g. family history of asthma and allergies), do not recommend the use of hydrolysed formula or soy formula in preference to breast milk, or in preference to standard formula where breastfeeding is not possible.

Note: Hydrolysed formula and soy formula are not effective in asthma prevention.

How this recommendation was developed

Evidence-based recommendation

Based on literature search and formulated by multidisciplinary working group

Key evidence considered:

- Boyle et al. 2016[2]

Last reviewed version 2.0

Do not recommend dietary restrictions for breastfeeding women to prevent asthma in their children.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- ASCIA 2016[1]

Last reviewed version 2.0

Do not routinely recommend dietary supplements (e.g. prebiotics/probiotics, vitamins, fish oil) as an asthma-prevention strategy for breastfeeding women or for infants.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- ASCIA 2016[1]

Last reviewed version 2.0

More information

Safety of asthma medicines while breastfeeding

Australian product information identifies some medicines that are known to pass into breast milk (e.g. adrenaline, aminophylline, prednisolone, sodium cromoglycate, terbutaline).[3]

The concentration of active ingredient in breast milk is likely to be low for several common asthma medicines (e.g. beclomethasone dipropionate, budesonide, fluticasone propionate, combination fluticasone propionate/salmeterol, nedocromil, ipratropium bromide).[3]

For some asthma medicines (e.g. formoterol, omalizumab, montelukast), or test substances (e.g. mannitol, used in bronchial provocation [challenge] testing), it is not known whether or not the active ingredient is excreted into breast milk, so caution is recommended.[3]

Australian product information identifies only a small number of asthma medicines that are not recommended for breastfeeding women (e.g. adrenaline, aminophylline, hydrocortisone for injection, prednisolone), and recommends that caution is needed when others (e.g. omalizumab, montelukast) are given to breastfeeding women.[3]

Information about the safety of medicines during lactation (included in product information for each medicine) emphasises the need to balance the potential benefits of asthma treatment with the possible risks to the infant.[3]

Note: Product information provided by pharmaceutical manufacturers and registered with the Therapeutic Goods Administration is written and approved when the medicine is first marketed, but is not routinely updated as new evidence becomes available. When product information includes a caution or contraindication for breastfeeding, health professionals should check current evidence before advising the woman about her choices, so that mothers do not stop breastfeeding unnecessarily, based on incomplete information.

Up to date information is available from the following sources:

- The Drugs and Lactation Database (LactMed), compiled by the US National Library of Medicine, provides comprehensive current information on the safety of medicines during breastfeeding
- The National Prescribing Service (NPS) Medicines Line provides information for the public about medicines and safety: 1300 MEDICINE (1300 633 424)
- Telephone information services about the safety of medicines while breastfeeding are also available for health professionals and breastfeeding women in some areas of Australia.

Table. Local pregnancy and breastfeeding safety information services

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/71

▶ Go to: Therapeutic Goods Administration database of product information (including lactation safety codes for each medicine)
Go to: The US National Library of Medicine's Drugs and Lactation Database (LactMed)

Systemic corticosteroids and breast milk

Peak plasma level of systemic corticosteroid occurs at approximately 2 hours post dose, so peak milk level will also occur around this time. Therefore, the infant's exposure to corticosteroids in breast milk can be further reduced by breastfeeding the infant just before each daily dose and avoiding feeding again until at least 4 hours after the dose.[4, 5]

If high-dose corticosteroids need to be used for longer than 10 days, the infant should be monitored for growth and development.[4, 5]

The US National Library of Medicine's Drugs and Lactation Database (LactMed) states that: *limited information indicates that maternal doses of prednisolone up to 50 mg produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants. With high maternal doses, avoiding breastfeeding for 4 hours after a dose should markedly decrease the dose received by the infant. However, this [manoeuvre] is probably not necessary in most cases.*

▶ Go to: The US National Library of Medicine's Drugs and Lactation Database (LactMed)

Prenatal and childhood exposure to tobacco smoke

Tobacco smoking by pregnant women damages children's respiratory health. It also increases the risk of stillbirth, spontaneous abortion, reduced foetal growth, preterm birth, low birth weight, placental abruption, sudden infant death, cleft palate, cleft lip and childhood cancers.[6]

Risk of developing asthma

Prenatal exposure to tobacco smoke and exposure during infancy increase the risk of wheezing during early childhood.[7]

▶ See: *Primary prevention of asthma*

Effects on children's asthma

Evidence from an Australian cohort study suggests that children with asthma whose mothers smoked during pregnancy benefit less from treatment with inhaled corticosteroids, and show less improvement in airway hyperresponsiveness over time, than those with asthma but no intrauterine exposure to smoke.[8]

Breastfeeding and allergy prevention

Earlier evidence suggested that the risk of asthma might be reduced by prolonged exclusive breastfeeding. The reduction in risk was thought to be greatest in children at high risk of asthma, but small in other children.[9] This evidence was mainly from studies of poor methodological quality.[10]

However, recent studies did not confirm that prolonged exclusive breastfeeding protected against development of asthma,[11] allergic rhinitis,[11] or other allergic disease such as atopic dermatitis (eczema).[12]

Limited evidence from observational or poor quality studies suggests that breastfeeding while solid foods are introduced may help reduce the infant's risk of developing allergies.[1] The Australasian Society of Clinical Immunology and Allergy (ASCIA) current guidelines for *Infant feeding and allergy prevention* recommend breastfeeding for at least 6 months for its range of benefits, with complementary foods introduced at around 6 months (but not before 4 months) while continuing to breastfeed.[1]

Exclusion of allergenic foods from the maternal diet has not been shown to prevent allergies.[1] ASCIA recommends against maternal dietary restrictions while breastfeeding.[1]

ASCIA's guidelines for *Infant feeding and allergy prevention* and *Guide to introducing solid foods* contain practical advice for mothers[13] For updates on ASCIA advice, refer to the ASCIA website (www.allergy.org.au).

▶ Go to: *ASCIA's guidelines for Infant feeding and allergy prevention*

▶ Go to: *ASCIA's guide to introducing solid foods*

Last reviewed version 2.0

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Asthma prevention in children at risk of developing asthma

Recommendations

Advise parents/carers to ensure babies and children are not exposed to cigarette smoke.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- ASCIA 2009[1]
- RACGP 2014[2]

Last reviewed version 2.0

If a family already has pets, it is not necessary to remove them to reduce a child's risk of developing asthma, unless the child develops clinical evidence of pet allergy and this is confirmed by skin-prick or allergen-specific IgE testing.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- ASCIA[3]

Last reviewed version 2.0

In children without demonstrated specific hypersensitivities, do not routinely recommend allergen avoidance measures for the purpose of reducing the child's risk of developing asthma.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Do not recommend single allergen avoidance measures (e.g. house dust mite-impermeable mattress covers) for the purpose of reducing the child's risk of developing asthma.

How this recommendation was developed

Evidence-based recommendation

Based on literature search and formulated by multidisciplinary working group

Key evidence considered:

- Arroyave et al. 2014[4]
- Maas et al. 2009[5]
- Gehring et al. 2012[6]

Last reviewed version 2.0

Advise parents/carers that damp, mouldy home environments may increase asthma risk in children and should be avoided if possible (e.g. by ventilation and mould removal), but that there is not clear evidence that anti-mould strategies will prevent asthma.

Note: Exposure to potentially harmful fumes from chemicals in cleaning products (e.g. chlorine bleach) should also be avoided.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Quansah et al. 2012[7]
- Tischer et al. 2011[8]
- Dotterud et al. 2013[9]

Last reviewed version 2.0

Advise parents/carers that children's risk of developing asthma may be increased by various types of indoor and outdoor pollution (e.g. unflued gas heaters, traffic pollution).

How this recommendation was developed

Evidence-based recommendation

Based on literature search and formulated by multidisciplinary working group.

Key evidence considered:

- Khreis et al. 2017[10]
- Quansah et al 2012[7]
- Gasana et al. 2012[11]
- Tischer et al. 2011[8]
- Patelarou et al. 2015[12]
- Jaakkola & Knight. 2008[13]
- Ponsonby et al. 2000[14]

Last reviewed version 2.0

Advise parents/carers to avoid unnecessary paracetamol use, but to give children paracetamol at recommended doses when indicated and according to current guidelines for managing fever or pain.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Cheelo et al. 2015[15]
- Heintze et al. 2013[16]

- Etminan et al. 2009[17]
- Wickens et al. 2011[18]
- Bakkeheim et al. 2011[19]
- Amberbi, et al. 2011[20]
- Kreiner-Møller et al. 2012[21]
- Lowe et al. 2010[22]
- Kurukulaaratchy et al. 2012[23]
- Koniman et al. 2007[24]
- Rusconi et al. 2011[25]
- Kuschnir et al. 2007[26]
- Vlaski, et al. 2007[27]
- Foliaki et al. 2008[28]
- Garcia et al. 2008[29]
- Del-Rio-Navarro et al. 2008[30]
- Del-Rio-Navarro et al. 2006[31]
- Beasley et al. 2011[32]
- Beasley et al. 2008[33]
- Karimi et al. 2006[34]
- Barragán Meijueiro et al. 2006[35]
- Sharma & Banga 2007[36]
- Wong et al. 2007[37]
- Cohet et al. 2004[38]
- Rodriguez-Martinez et al. 2008[39]

Last reviewed version 2.0

Prescribe antibiotics, proton pump inhibitors or antacids for children as indicated and where a clinical benefit is likely, but avoid unnecessary use.

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Heintze et al. 2013[16]
- Mitre et al. 2018[40]

Last reviewed version 2.0

In children with atopic dermatitis or allergic rhinitis, manage according to current guidelines (including with antihistamines, if indicated) but do not prescribe or recommend long-term antihistamine treatment specifically for the purpose of reducing the child's risk of developing asthma.

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Early Treatment of the Atopic Child Study Group. 1998[41]

Last reviewed version 2.0

Consider specific allergen immunotherapy in children with allergic rhinitis who have a history of proven, clinically important sensitisation to a particular allergen that cannot feasibly be avoided and for which for specific allergen immunotherapy is available.

Note: Specific allergen immunotherapy is indicated for the management of allergy, not prevention of asthma. However, early treatment before the onset of asthma may reduce the risk of asthma symptoms and asthma medication requirements.

Note: Make sure parents understand that treatment must be long term (3–5 years), and understand the cost and risks of the treatment.

Note: TGA-approved indications for commercially available preparations vary according to age group.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Kristiansen et al. 2017[42]
- Valovirta et al. 2018[43]
- Jacobsen et al. 2007[44]
- Novembre et al. 2004[45]

Last reviewed version 2.0

More information

Smoking: effects on risk of developing asthma

Exposure to tobacco smoke toxins *in utero* or in infancy has been associated with increased risk of wheezing and asthma in children.[46, 47]

Maternal smoking during pregnancy is associated with an almost twofold increase in asthma in infants aged 2 years or less.[47]

Several large systematic reviews and meta-analyses of prospective cohort studies have reported that maternal smoking during pregnancy and exposure to tobacco smoke in infancy are associated with large increases in the risk of wheezing in the first 2 years of life.[47, 48]

A meta-analysis of observational studies (mainly cross-sectional studies) found that exposure to environmental tobacco smoke was associated with an increase in childhood asthma,[49] but this association was weaker than that between exposure to environmental tobacco smoke and wheezing.

Epigenetic effects may modify the effects of environmental risk factors, including exposure to tobacco smoke, on development of asthma.[50] However, a longitudinal cohort study[51] found no association between smoking by grandparents (including during pregnancy with the mothers of the study cohort) early wheezing or asthma at age 7 in grandchildren.

Last reviewed version 2.0

Pets: effects on risk of developing asthma

Some studies have identified perinatal exposure to pets (dogs or cats) as a potentially protective factor against allergic disease, but results are inconsistent between studies.[52]

This effect appears to genotype dependent. A recent large prospective study found that exposure to pets (especially cats) from birth reduced the risk of childhood asthma, pneumonia, and bronchiolitis in genetically susceptible children.[53]

Last reviewed version 2.0

Allergies and exposure to allergens: effects on risk of developing asthma

Note: Although allergic asthma is common, non-allergic asthma also occurs.

Population-based studies have observed a positive association between early life exposure to aeroallergens (house dust mite, mould)[54] or sensitisation to aeroallergens[55] and the development of asthma. However, exposure to allergens may not actually cause asthma.[55]

Allergic rhinitis is a major risk factor for asthma and often precedes it.[56, 57, 58] These associations probably reflect the common allergic causes of both conditions, rather than a causal link.[58]

The combination of sensitisation to aeroallergens and viral infections early in life increases asthma risk.[59]

Last reviewed version 2.0

Allergen avoidance in children: effects on risk of developing asthma

There is accumulating evidence from systematic reviews of intervention trials that single allergen reduction strategies, such as the use of mattress covers that are impermeable to house dust mite, are not effective in preventing the development of wheezing or asthma in children.[4, 5]

An Australian controlled clinical trial that compared house dust mite avoidance (acaricide and impermeable mattress covers), from birth to 5 years, with simple advice on cleaning, vacuuming, dusting and maintaining adequate ventilation,[60, 61] reported no reduction in the risk of developing asthma at age 11.5 years.[62]

Multimodal allergen avoidance strategies that reduce exposure to both inhalant and food allergens, beginning in late pregnancy or from birth, may reduce the risk of asthma in children under 5 and in children over 5 years.[5] However, these strategies require intensive effort and may not be feasible for many families.

Avoiding exposure to pets does not reduce asthma risk.[63] There is even limited evidence that perinatal exposure to dogs or cats could reduce the risk of allergic disease.[52]

Last reviewed version 2.0

Traffic air pollution: effects on risk of developing asthma

There is mounting evidence from observational studies for an association between pollution and asthma risk in children. However, it is difficult to control for the influence of confounding factors such as socioeconomic status.

In systematic reviews and meta-analyses:

- prenatal exposure to air pollution (including nitrogen dioxide, particulate matter) was associated with increased risk of wheezing and asthma in children[64]
- early life exposure to air pollution (nitrogen dioxide, ozone, volatile organic compounds, and particulate matter) was associated with increased risk of allergic asthma in children[54]
- childhood exposure to traffic pollution including black carbon (soot from vehicle emissions), nitrogen dioxide, fine particulate matter, carbon monoxide and particulate matter, were associated with increased risk of asthma.[10, 11]

The role of traffic-related air pollution in the development of adult-onset asthma is less conclusive than in childhood asthma due to fewer studies and heterogeneity among studies.[65]

Last reviewed version 2.0

Indoor air pollution: effects on risk of developing asthma

Epidemiological studies have consistently reported an association between early life exposure to indoor dampness and mould (particularly visible mould and mould odour)[7] and increased risk of developing asthma or wheeze.[7, 66, 67, 8] However, it is difficult to control for the influence of confounding factors such as socioeconomic status.

Exposure to fumes from polyvinyl chloride products (PVC) surface materials is associated with increased risk of asthma in children, while exposure to heated PVC fumes (mainly in the workplace) is associated with increased risk of asthma in adults.[13]

The use of gas stoves or ovens in the home has also been associated with development of asthma in children.[68]

Various indoor pollutants have also been associated with increased risk of adult-onset asthma. These include airborne substances used in the home (e.g. cleaning sprays)[69] and many airborne substances encountered in workplaces.

▶ Go to: *Work-related asthma*

Last reviewed version 2.0

Paracetamol: effects on risk of developing asthma

Prenatal and childhood paracetamol use has been associated with increased asthma risk in several observational studies. However, causality has not been demonstrated. The effect is small, and the association may be due to confounding by indication.

Health professionals can advise pregnant women that there is some evidence from around the world that paracetamol use in pregnancy might increase the baby's risk of wheezing or asthma, but that paracetamol is still considered the best option for pain relief in pregnant women.[70]

Prenatal exposure

Meta-analyses of observational studies (mainly prospective cohorts) show that paracetamol use during pregnancy is associated with increases in the risk of wheeze in early childhood and of childhood asthma at age 5 or older.[46, 15, 71, 72, 17] However, this finding must be interpreted with caution because of heterogeneity among studies and the fact that some studies did not control for maternal respiratory tract infections.

Early life exposure

Several systematic reviews have reported an association between paracetamol use in infancy and development of asthma.[16, 71, 17] However, many of the included studies were of low quality and the association may be due to confounding.

A meta-analysis of observational studies found that increasing frequency of use of paracetamol during infancy was associated with a small increase in the risk of childhood asthma, but the effect was reduced to very small after adjusting for respiratory tract infections.[15] A recent systematic review of systematic reviews (overview)[46] concluded that there was no significant association between paracetamol use during infancy and childhood asthma, after adjustment for lower respiratory tract infections.

Last reviewed version 2.0

Proton pump inhibitors and H2 receptor antagonists

Associations between acid-suppressive medicines and allergic disease have been reported in observational studies.

The use of acid-suppressive medication during pregnancy has been associated with increased risk of asthma and allergy in the offspring.[73, 74, 75, 76]

A retrospective study of a large cohort of US children reported that children prescribed H_2 receptor antagonists or proton pump inhibitors during the first 6 months of infancy had a significant increases in the risk of subsequent asthma.[40]

Last reviewed version 2.0

Antihistamines in children with allergies: effects on risk of developing asthma

Long-term antihistamine treatment has been investigated as a strategy for preventing the development of asthma in children with allergies.

In a single multi-country, double-blind, randomised, placebo-controlled trial in children aged 1–2 years with atopic dermatitis,[77] 18 months' treatment with cetirizine (0.25mg/kg twice daily) did not reduce the risk of developing asthma, compared with placebo. However, in the subgroup of children sensitised to grass pollen or house dust mite, cetirizine treatment was associated with a reduction in the rate of new asthma diagnoses, compared with placebo.[77]

Last reviewed version 2.0

Specific allergen immunotherapy (desensitisation): effects on risk of developing asthma

Note: Specific allergen immunotherapy is prescribed for allergic rhinitis, not for asthma prevention.

Few randomised controlled trials have been designed to evaluate specific allergen immunotherapy in children with allergic rhinitis who do not have asthma. Each of the available studies has reported a reduction in the onset of asthma.

A systematic review found that specific allergen immunotherapy in children with allergic rhinitis was associated with a short-term reduction in the risk developing asthma.[42] However, this benefit was not maintained long term. Overall, immunotherapy did not reduce the risk of developing a first allergic disease over the short term.[42]

A recent randomised controlled trial evaluated 3 years' treatment with SQ grass sublingual immunotherapy in children aged 5–12 years with a clinically relevant history of grass pollen allergic rhinoconjunctivitis and no medical history or signs of asthma at baseline. At follow-up 2 years after finishing treatment, immunotherapy did not affect time to onset of asthma diagnosis (defined by reversible airflow limitation).[78] However, immunotherapy reduced the risk of experiencing asthma symptoms or using asthma medication at the end of 3 years' treatment, during the 2-year posttreatment follow-up, and during the entire 5-year trial period.[78]

Last reviewed version 2.0

Maternal and childhood obesity: effects on risk of developing asthma

Maternal obesity during pregnancy increases the risk of asthma or wheeze in children, based on a meta-analysis of observational studies.[79]

High gestational weight gain was also associated with higher risk of asthma or wheeze.[79]

Childhood overweight or obesity have also been associated with increased risk of developing asthma in some systematic reviews of

observational studies.[80, 81, 82]

Last reviewed version 2.0

Aetiology of exercise-induced bronchoconstriction

Both genetics and environment may contribute to exercise-induced bronchoconstriction.[83]

Exercise-induced bronchoconstriction occurs when a person's ventilatory rate is high and their airways must heat and humidify a large volume of air in a short time. Dehydration of the airway leads to release of inflammatory mediators within the airway and contraction of airway smooth muscle.[83] Dry air is one risk factor.[83]

Exercise-induced bronchoconstriction in athletes who do not have chronic asthma may have different pathogenesis and presentation than exercise-induced bronchoconstriction in people with asthma.[83] Elite athletes often report onset of exercise-induced bronchoconstriction after age 20 years and after many years of high-level training.[84]

In elite athletes, exercise-induced bronchoconstriction is probably due to chronic injury to airway epithelium associated with long-term frequent prolonged high ventilation rates in the presence of environmental exposure to cold air, dry air, and airborne pollutants such as ozone, particulate matter:

- The high prevalence of exercise-induced bronchoconstriction in ice-rink athletes has been linked to inhalation of cold dry air in combination with airborne pollutants from fossil-fuelled ice resurfacing machines
- Exercise-induced bronchoconstriction in skiers and other winter athletes has been linked to injury of airway epithelium due to conditioning large volumes of cold dry air[85, 86, 87]
- The high prevalence of asthma and exercise-induced bronchoconstriction reported among competitive swimmers has been associated with exposure to chlorine in indoor swimming pools[85, 88, 89]
- The increased prevalence of exercise-induced bronchoconstriction among distance runners, compared with the general population, has been attributed to exposure to high levels of airborne allergens and ozone[83, 85]
- Certain airborne viruses inhaled during exercise may also contribute to exercise-induced bronchoconstriction.[83]

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Asthma prevention in adults

Recommendations

Advise people who work with airborne sensitisers or irritants that many airborne substances can damage respiratory health and may cause asthma.

▶ **See:** *Work-related asthma*

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

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If a patient who is exposed to occupational sensitisers or irritants develops new-onset rhinitis and/or respiratory symptoms, offer urgent referral to a specialist (e.g. respiratory physician, occupational physician or allergist) with experience in investigating and managing work-related asthma.

▶ **See:** *Work-related asthma*

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

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Warn sportspeople, particularly elite athletes, that training while exposed to airborne pollutants or cold, dry air may increase the risk of developing asthma.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to named source(s):

- Parsons et al. 2013[1]
- Weiler et al. 2010[2]
- Anderson et al. 2008[3]
- Sue-Chu et al. 2010[4]
- Bougault et al. 2010[5]
- Bougault et al. 2009[6]

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More information

Prevention of work-related asthma within the workplace

Work-related asthma is potentially preventable. Preventive measures focus on controlling workers' exposure to respiratory irritants and sensitisers at the workplace, and must be undertaken by employers.

An Australian report has recommended that employers should minimise exposure to sensitisers and irritants for all workers in high-risk workplaces.[7] Actions by employers should be guided by occupational health and safety authorities and specialists with expertise in work-related asthma.

Prevention strategies currently in use include:

- elimination of the substance from the workplace (e.g. substituting the substance, remote control handling)
- reducing exposure (e.g safety procedures, training)
- isolating the substance (e.g. changed work processes, segregation of areas)
- ventilation
- wearing personal respirators, protective clothing and masks.

The most effective strategy is to eliminate or minimise exposures at the source or in the environment.[8, 9]

Avoiding the use of powdered latex gloves (e.g. substituting with low-protein, powder-free natural rubber latex gloves or latex-free gloves) reduces natural rubber latex aeroallergens, natural rubber latex sensitisation and natural rubber latex asthma in healthcare workers.[8]

There is limited evidence that the use of respirators is effective in preventing occupational asthma.[8] Most studies have measured effects of respirators on exposure, not asthma incidence. Limited evidence suggests that the risk of developing asthma among workers using hexahydrophthalic anhydride in epoxy resin manufacture may be reduced by wearing respirators. A combination of information and training, exhaust ventilation, and wearing of respirators while handling of powdered bread improvers may reduce the risk of symptomatic sensitisation to flour and fungal amylase in bakers. Small studies suggest that respirators can reduce exposure to isocyanates among spray painters if they are well designed, fitted and maintained, and workers are trained to use them correctly.

If a face mask is recommended to minimise exposure to a particular sensitiser or irritant, the employer should select the appropriate type, and provide the worker with education and training to use it properly. Personal protection should be part of a comprehensive control program – not the sole strategy for reducing exposure.

If an employee develops work-related asthma, this should be considered as a warning that other workers may be at risk and that control measures at the workplace should be reviewed.

Aetiology of exercise-induced bronchoconstriction

Both genetics and environment may contribute to exercise-induced bronchoconstriction.[10]

Exercise-induced bronchoconstriction occurs when a person's ventilatory rate is high and their airways must heat and humidify a large volume of air in a short time. Dehydration of the airway leads to release of inflammatory mediators within the airway and contraction of airway smooth muscle.[10] Dry air is one risk factor.[10]

Exercise-induced bronchoconstriction in athletes who do not have chronic asthma may have different pathogenesis and presentation than exercise-induced bronchoconstriction in people with asthma.[10] Elite athletes often report onset of exercise-induced bronchoconstriction after age 20 years and after many years of high-level training.[11]

In elite athletes, exercise-induced bronchoconstriction is probably due to chronic injury to airway epithelium associated with long-term frequent prolonged high ventilation rates in the presence of environmental exposure to cold air, dry air, and airborne pollutants such as ozone, particulate matter:

- The high prevalence of exercise-induced bronchoconstriction in ice-rink athletes has been linked to inhalation of cold dry air in combination with airborne pollutants from fossil-fuelled ice resurfacing machines
- Exercise-induced bronchoconstriction in skiers and other winter athletes has been linked to injury of airway epithelium due to conditioning large volumes of cold dry air[12, 13, 14]
- The high prevalence of asthma and exercise-induced bronchoconstriction reported among competitive swimmers has been associated with exposure to chlorine in indoor swimming pools[12, 15, 16]
- The increased prevalence of exercise-induced bronchoconstriction among distance runners, compared with the general population, has been attributed to exposure to high levels of airborne allergens and ozone[10, 12]
- Certain airborne viruses inhaled during exercise may also contribute to exercise-induced bronchoconstriction.[10]

References

1. Parsons, J P, Hallstrand, TS, Mastronarde, J G, *et al*. An official American Thoracic Society clinical practice guideline: exercise-