



ORCID

Anne K. Ellis  <http://orcid.org/0000-0002-0725-2353>

Mark W. Tenn^{1,2}

Jenny Thiele^{2,3}

Lisa M. Steacy²

Daniel E. Adams²

Anne K. Ellis^{1,2,3} 

¹Department of Biomedical and Molecular Sciences, Queen's University,
Kingston, ON, Canada

²Allergy Research Unit, Kingston General Health Research Institute,
Kingston, ON, Canada

³Department of Medicine, Queen's University, Kingston, ON, Canada

Correspondence

Anne K. Ellis, Division of Allergy and Immunology, Department of
Medicine; Department of Biomedical and Molecular Sciences, Kingston
General Health Research Institute, Kingston, ON, Canada.

Email: ellisa@queensu.ca

REFERENCES

1. Bousquet J, Van CP, Khaltaev N, Aria Workshop Group, World Health Organization. Allergic rhinitis and its impact

on asthma. *J Allergy Clin Immunol.* 2001;108(5 Suppl):S147-S334.

2. Artis D, Spits H. The biology of innate lymphoid cells. *Nature.* 2015;517(7534):293-301.
3. Doherty TA, Scott D, Walford HH, et al. Allergen challenge in allergic rhinitis rapidly induces increased peripheral blood type 2 innate lymphoid cells that express CD84. *J Allergy Clin Immunol.* 2014;133:1203-1205.
4. Lombardi V, Beuraud C, Neukirch C, et al. Circulating innate lymphoid cells are differentially regulated in allergic and nonallergic subjects. *J Allergy Clin Immunol.* 2016;138:305-308.
5. Lao-Araya M, Steveling E, Scadding GW, Durham SR, Shamji MH. Seasonal increases in peripheral innate lymphoid type 2 cells are inhibited by subcutaneous grass pollen immunotherapy. *J Allergy Clin Immunol.* 2014;134:1193-1195.
6. Jochems SP, Piddock K, Rylance J, et al. Novel analysis of immune cells from nasal microbiopsy demonstrates reliable, reproducible data for immune populations, and superior cytokine detection compared to nasal wash. *PLoS One.* 2017;12:e0169805.
7. Karta MR, Rosenthal PS, Beppu A, et al. β 2 integrins rather than β 1 integrins mediate *Alternaria*-induced group 2 innate lymphoid cell trafficking to the lung. *J Allergy Clin Immunol.* 2018;141:329-338.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

DOI: 10.1111/all.13615

Long-term exposure to neighborhood smoke from household heating and risk of respiratory and dermatological prescription medications—Growing Up in New Zealand child cohort study

To the Editor,

Domestic wood-heating has regained popularity in Europe and Northern America due to policies encouraging wood and other biomass burning for energy security and climate change mitigation.¹ Whether these policies are truly low-carbon has been questioned,² and they also have important implications for air quality. Ambient wood-smoke exposure is associated with childhood respiratory diseases³ but investigation of wood-smoke exposure on childhood skin diseases is limited. We aimed to assess childhood exposure to neighborhood environments with wood/coal heated households and the onset of both respiratory and skin diseases.

This analysis included 3461 children (Data S1) from the *Growing Up in New Zealand* cohort study⁴ and used data collected from face-to-face and telephone interviews with their parents during the third trimester of the mother's pregnancy (2008-2010), when the children

were 9 months (2009-2011), 2 years (2011-2012), and 4½ years (2013-2014) old.

We established data linkage with pharmaceutical (Data S2) and perinatal records from New Zealand national datasets. We assessed first-time dispensing for respiratory and/or dermatological medication prescriptions during the cooler season (April to November) (Data S3) in the first 48 months of life as the outcome group (those with no such prescriptions dispensed as the reference group) after excluding same-date episodes that also contained outcomes other than respiratory and/or dermatological (i.e., multiple outcomes).

Based on the smallest statistical area unit (meshblock), we geocoded the children's residential locations to link up with the 2013 New Zealand Index of Deprivation and the density of wood/coal heated households (number per hectare) derived from census

database.⁵ We accounted for residential mobility across the four time points using time-weighted averages of cumulative exposure method.⁶

Multilevel logistic regression was used to assess associations between the exposure variables of wood/coal smoke (either as a continuous or quartile categorical variable) and each binary outcome variables (prescriptions for respiratory medications, or dermatological medications or either respiratory or dermatological medications), with adjustment for child's sex, child's main ethnic group, birth weight, exclusive breastfeeding duration, mother's age at child's birth, household tenure at birth, wood/coal heating of own home, presence of smokers at home, specific household hardship (putting up with feeling cold to save heating costs or being forced to buy cheaper food to afford other things needed), and the meshblock-level NZ Deprivation Index score, as well as the random effects due to clustering in area census units nested within different regional

councils. We conducted sensitivity analyses on the association between exposure and outcome in crude and partly adjusted models, and by using the pharmaceutical records that described prescriptions dispensed during the warmer seasons (December to March).

Among 3461 children, 1372 (40%) received respiratory, 2456 (71%) received dermatological, and 2750 (79%) received respiratory or dermatological prescriptions during the cooler season in the first 4 years of life. Among them, there were 8993 respiratory prescriptions (prevalently for allergic-related treatments) including antihistamines (62%) and beta-adrenoceptor agonists (30%); and 25 666 dermatological prescriptions (prevalently in atopic dermatitis treatments) including topical corticosteroids (42%) and barrier creams and emollients (29%). The mean ($\pm$ SD) number of prescriptions dispensed to these children in their first 4 years was 6.6 ($\pm$ 6.1) for respiratory ($n = 1372$), 10.5 ($\pm$ 11.5) for dermatological ($n = 2456$), and

TABLE 1 Multivariable analysis: Exposure to neighborhood ambient wood or coal smoke and the odds of receipt of first-time prescriptions for respiratory, dermatological, and respiratory or dermatological medications during cooler seasons in the first 4 years of life

Independent variables	n	%	Adjusted OR (95% CI)		
			FA ₁ respiratory	FA ₂ dermatological	FA ₃ respiratory or dermatological
Wood or coal smoke 2nd Q ^a (Ref: 1st Q)	865	25	1.08 (0.88, 1.32)	1.04 (0.85, 1.29)	1.15 (0.91, 1.45)
Wood or coal smoke 3rd Q ^a	866	25	1.13 (0.92, 1.38)	1.23 (0.99, 1.52)	1.35 (1.06, 1.71)
Wood or coal smoke 4th Q ^a	865	25	1.27 (1.04, 1.55)	1.38 (1.11, 1.71)	1.48 (1.17, 1.89)
Female (Ref: male)	1686	49	0.68 (0.59, 0.79)	1.06 (0.91, 1.23)	0.91 (0.77, 1.08)
Māori (Ref: European/New Zealander)	793	23	1.19 (0.99, 1.44)	1.47 (1.19, 1.80)	1.42 (1.12, 1.79)
Pacific	332	10	1.06 (0.82, 1.39)	1.21 (0.91, 1.62)	1.30 (0.93, 1.80)
Asian	477	14	1.67 (1.34, 2.07)	1.83 (1.42, 2.37)	1.85 (1.38, 2.50)
Other ethnicities	74	2	1.31 (0.81, 2.12)	0.89 (0.54, 1.46)	1.39 (0.75, 2.58)
Birth weight 2nd T (Ref: 1st T)	1164	34	1.09 (0.92, 1.29)	0.96 (0.80, 1.16)	1.02 (0.82, 1.26)
Birth weight 3rd T	1147	33	0.86 (0.72, 1.03)	0.86 (0.71, 1.03)	0.79 (0.64, 0.97)
Excl. breastfed ≥ 6 M (Ref: <6 M)	776	22	0.87 (0.73, 1.03)	0.96 (0.80, 1.15)	0.99 (0.81, 1.22)
Mother's age 2nd T (Ref: 1st T)	1155	33	0.85 (0.71, 1.02)	0.70 (0.58, 0.85)	0.71 (0.56, 0.88)
Mother's age 3rd T	1153	33	0.85 (0.71, 1.02)	0.62 (0.51, 0.76)	0.65 (0.52, 0.82)
Private rental (Ref: Owner)	1239	36	1.00 (0.85, 1.17)	0.82 (0.69, 0.97)	0.86 (0.71, 1.05)
Public rental	148	4	1.09 (0.76, 1.57)	0.96 (0.63, 1.45)	1.00 (0.62, 1.62)
Other household tenure	76	2	1.63 (1.01, 2.61)	0.66 (0.40, 1.07)	0.73 (0.43, 1.23)
Wood/coal heating at home (Ref: no)	961	28	0.88 (0.75, 1.03)	0.84 (0.71, 0.99)	0.76 (0.63, 0.92)
Number of home smokers ≥ 1 (Ref: 0)	803	23	0.93 (0.78, 1.10)	1.01 (0.83, 1.23)	0.98 (0.79, 1.22)
Household hardship (Ref: no)	1767	51	1.13 (0.98, 1.31)	1.17 (1.00, 1.37)	1.18 (0.99, 1.40)
Area deprivation 2nd T ^a (Ref: 1st T)	1157	33	0.88 (0.74, 1.05)	0.95 (0.79, 1.15)	0.98 (0.79, 1.20)
Area deprivation 3rd T ^a	1153	33	0.92 (0.76, 1.11)	0.95 (0.77, 1.16)	0.94 (0.75, 1.18)
Other model information					
P-value for random intercepts			0.41	0.49	0.54
P-value for linear exposure–response relationship ^b			0.02	0.03	0.003
OR (95%CI) per wood or coal smoke household per ha			1.04 (1.00, 1.09)	1.07 (1.02, 1.12)	1.08 (1.02, 1.14)

Statistically significant odds ratios are shown in bold.

a, area-level variable; b, between the quartiles of wood or coal smoke and the health outcome; 95%CI, 95% confidence intervals; FA, fully adjusted model; ha, hectare; M, month; T, tertile; OR, odds ratios; Ref, reference group; Q, quartile.

14.0 (± 14.7) for respiratory or dermatological medications ($n = 2750$). The age at first dermatological medication prescription (median=162 days) being earlier than the age at first respiratory medication prescription (465 days) is consistent with the atopic march. Living in the highest density quartile of wood/coal heated households was associated with a 27% [4%-55%], 38% [11%-71%] and 48% [17%-89%] increased odds of receiving first-time prescriptions for respiratory, dermatological, and respiratory or dermatological medications respectively (Table 1). Positive linear exposure-response relationships were detected across all models. Sensitivity analyses showed that the associations between exposure and outcomes were present in all models in the cooler but not in the warmer months (Table 2).

Our findings of an increased odds of young children receiving respiratory medications are consistent with other studies on the effects of wood-smoke exposure.¹ This finding supports using the same modeling approach to assess the rarely reported effects on childhood skin diseases. We could only find four relevant studies on the effects of household wood/coal heating on childhood skin disease (Data S4) but none of these examined exposure to ambient

wood/coal smoke. The less heterogeneous wintertime particulate air pollution in New Zealand (~83% by wood burning) allows us to avoid the need to assess particle mass concentration and compositions from other sources. Therefore, we could apply a simpler approach using the census-based density exposure variable that provides readily interpretable information for policy review (Data S5). In our study, we also took into account wood/coal heating in the child's home, which was counterintuitively associated with a decreased odds of first-time respiratory and/or dermatological prescriptions. However, ground level smoke concentration is very low below the chimney but increases to a maximum at a horizontal distance ($\sim 10 \times$ chimney's height) away from the chimney.⁷ Therefore, wood/coal smoke emitted from neighboring households' chimneys contributes more to indoor infiltration and exposure than that emitted from the chimney in the child's home. The decreased odds we observed here may be related to wood/coal heating being used instead of other less healthy heating methods, for example, unflued gas heating.⁸ Unmeasured residual confounding might still exist (e.g., wood-burner design, seasonal pollination) even though we have adjusted for potential confounders. Nevertheless, we have taken into account both spatial

TABLE 2 Sensitivity analyses: Odds ratios for 2nd, 3rd and 4th quartile of exposure to neighborhood ambient wood or coal smoke in the crude, partly (PA) and fully adjusted (FA) models of receipt of first-time prescriptions for respiratory, dermatological, and respiratory or dermatological medications in the first 4 years of life

	Respiratory Odds ratios (95%CI)	Dermatological Odds ratios (95%CI)	Respiratory or dermatological Odds ratios (95%CI)
Crude (cooler season)	1.08 (0.89, 1.32)	1.12 (0.91, 1.37)	1.23 (0.98, 1.55)
	1.13 (0.93, 1.37)	1.30 (1.05, 1.60)	1.44 (1.14, 1.82)
	1.23 (1.01, 1.15)	1.36 (1.10, 1.69)	1.48 (1.17, 1.88)
	$n = 3461$, $y\% = 40\%$	$n = 3461$, $y\% = 71\%$	$n = 3461$, $y\% = 79\%$
PA ₁ : child variables only (cooler season)	1.08 (0.88, 1.32)	1.08 (0.88, 1.33)	1.19 (0.95, 1.50)
	1.12 (0.92, 1.37)	1.26 (1.02, 1.56)	1.40 (1.10, 1.77)
	1.23 (1.01, 1.50)	1.36 (1.10, 1.69)	1.48 (1.16, 1.87)
	$n = 3461$, $y\% = 40\%$	$n = 3461$, $y\% = 71\%$	$n = 3461$, $y\% = 79\%$
PA ₂ : PA ₁ + maternal variables (cooler season)	1.07 (0.87, 1.30)	1.06 (0.86, 1.30)	1.17 (0.93, 1.47)
	1.12 (0.92, 1.36)	1.24 (1.01, 1.54)	1.38 (1.09, 1.75)
	1.25 (1.02, 1.52)	1.39 (1.12, 1.72)	1.50 (1.18, 1.90)
	$n = 3461$, $y\% = 40\%$	$n = 3461$, $y\% = 71\%$	$n = 3461$, $y\% = 79\%$
PA ₃ : PA ₂ + home environmental variables (cooler season)	1.07 (0.87, 1.30)	1.04 (0.84, 1.28)	1.14 (0.90, 1.44)
	1.11 (0.91, 1.36)	1.22 (0.99, 1.51)	1.34 (1.06, 1.70)
	1.26 (1.03, 1.54)	1.38 (1.11, 1.71)	1.48 (1.17, 1.88)
	$n = 3461$, $y\% = 40\%$	$n = 3461$, $y\% = 71\%$	$n = 3461$, $y\% = 79\%$
FA ₄ : warmer season instead of cooler season	0.97 (0.20, 4.64)	0.92 (0.75, 1.13)	0.94 (0.24, 3.61)
	0.95 (0.20, 4.55)	0.95 (0.78, 1.18)	0.98 (0.25, 3.80)
	0.99 (0.21, 4.68)	0.92 (0.75, 1.13)	1.00 (0.26, 3.81)
	$n = 3184$, $y\% = 22\%$	$n = 3184$, $y\% = 52\%$	$n = 3184$, $y\% = 62\%$

Child: sex, ethnicity, birth weight. *Maternal*: breastfeeding, mother's age. *Home environmental*: smokers, solid fuel heating at home, and household hard-ship. Statistically significant odds ratios are shown in bold.

CI, confidence intervals; FA, fully adjusted model; n , number of children included in the model; PA, partly adjusted model; $y\%$, percentage of children with the outcome.

(meshblock level) and temporal factors (partitioned to cooler season) so that spatial- or temporal-only residual confounding will have been further reduced.

Living in an environment with higher density of wood/coal heated households in the first 4 years is associated with an increased risk of having first-time respiratory and/or dermatological medications (mainly allergy-related), which may indicate the innate immunomodulatory effects of wood-smoke particles.⁹ That the associations were found in the cooler but not the warmer season is consistent with wintertime particulate emissions from residential heating. Our finding that community wood/coal smoke affects skin health of children in an exposure–response relationship is novel and warrants further investigation.

ACKNOWLEDGMENTS

We acknowledge first and foremost the children and the families who are part of the Growing Up in New Zealand study. We acknowledge the numerous government agencies that fund and support Growing Up in New Zealand, in particular, the Social Policy Evaluation and Research Unit (formerly the Families Commission) for their management of the contract on behalf of the Crown, as well as the latest support from the Ministry of Social Development. We also acknowledge the ongoing support from Auckland UniServices and the University of Auckland. We thank all the members of the Growing Up in New Zealand research team for their invaluable work in interviewing participants and managing the data used in this analysis, as well as the members of Growing Up in New Zealand's Kaitiaki Group and Executive Scientific Advisory Board. We also acknowledge the Ministry of Health for technical information support and provision of the national pharmaceutical data. Other funders of the Growing Up in New Zealand study include the Ministry of Business, Innovation and Employment, Ministry of Education, Ministry of Justice, Sport New Zealand, New Zealand Police, Te Puni Kokiri, Housing New Zealand, Ministry for Pacific Peoples, Ministry for Women, Department of Corrections, and Office of the Health and Disability Commissioner.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

HL: hypothesis, data analysis, analytical methods, interpretation, writing manuscript; CC and AW: critical revision, interpretation, editing; MH: acquisition of pharmaceutical data, interpretation, critical comments; AP: statistical concepts and applications, data quality; SM: study design and direction, funding, ethics, overview; CG: study design and supervision, critical revision, interpretation, editing.

ORCID

Cameron C. Grant  <http://orcid.org/0000-0002-4032-7230>

Hak Kan Lai^{1,2}

Carlos A. Camargo Jr^{3,4}

Alistair Woodward⁵

Mark Hobbs^{1,2,6}

Avinesh Pillai^{1,7}

Susan M. Morton^{1,2}

Cameron C. Grant^{1,2,6,8} 

¹Growing Up in New Zealand, School of Population Health, University of Auckland, Auckland, New Zealand

²Centre for Longitudinal Research—He Ara Ki Mua, School of Population Health, University of Auckland, Auckland, New Zealand

³Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts

⁴Department of Emergency Medicine, Massachusetts General Hospital, Boston, Massachusetts

⁵Section of Epidemiology and Biostatistics, School of Population Health, University of Auckland, Auckland, New Zealand

⁶Department of Paediatrics, Child and Youth Health, School of Medicine, University of Auckland, Auckland, New Zealand

⁷Department of Statistics, Faculty of Science, University of Auckland, Auckland, New Zealand

⁸General Paediatrics, Starship Children's Hospital, Auckland, New Zealand

Email: cc.grant@auckland.ac.nz

Correspondence

Cameron C. Grant, Growing Up in New Zealand, University of Auckland, Auckland, New Zealand.

Email: cc.grant@auckland.ac.nz

REFERENCES

1. World Health Organization. *Residential heating with wood and coal: health impacts and policy options in Europe and North America*. WHO Regional Office for Europe. Copenhagen, Denmark: WHO Regional Office for Europe; 2015.
2. Brack D. *Woody Biomass for Power and Heat: Impacts on the Global Climate*. Chatham House, UK: Environment, Energy and Resources Department, The Royal Institute of International Affairs; 2017.
3. Allen RW, Mar T, Koenig J, et al. Changes in lung function and airway inflammation among asthmatic children residing in a woodsmoke-impacted urban area. *Inhalation Toxicol*. 2008;20:423–433.
4. Morton SMB, Atatoa Carr PE, Bandara DK, et al. *Growing Up in New Zealand: A Longitudinal Study of New Zealand Children and Their Families. Report 1: Before We Are Born*. Auckland, New Zealand: Growing Up in New Zealand; 2010. <http://www.growingup.co.nz/en.html>. Accessed Oct 03 2018.
5. Statistics New Zealand. 2013 Census meshblock dataset; 2014. <http://www.stats.govt.nz/Census/2013-census/data-tables/meshblock-dataset.aspx>. Accessed Oct 03 2018.
6. Lai HK, Berry SD, Verbiest MEA, et al. Emergency department visits of young children and long-term exposure to neighbourhood smoke from household heating - The Growing Up in New Zealand child cohort study. *Environ Pollut*. 2017;231:533–540.
7. Bosanquet CH, Pearson JL. The spread of smoke and gases from chimneys. *Trans Farad Soc*. 1936;32:1249–1263.
8. Tin Tin S, Woodward A, Saraf R, Berry SD, Atatoa Carr PE, Morton SMB. Internal living environment and respiratory disease in children:

findings from the Growing Up in New Zealand longitudinal child cohort study. *Environ Health*. 2016;15:120.

9. Lee A, Kinney P, Chillrud S, Jack D. A systematic review of innate immunomodulatory effects of household air pollution secondary to the burning of biomass fuels. *Ann Glob Health*. 2015;81:368-374.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

DOI: 10.1111/all.13618

$\gamma\delta$ T cells amplify *Blomia tropicalis*-induced allergic airway disease

To the Editor,

Allergic asthma is a chronic and heterogeneous immunological disease characterized by airway inflammation, hyper-IgE production, mucus hypersecretion and airway hyperreactivity (AHR). The most studied house dust mites' (HDM) respiratory allergens belong to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* mite species. However, the storage mite *Blomia tropicalis* represents an important allergenic source and sensitization to its allergens is commonly associated with typical clinical manifestations of allergy, including asthma.¹⁻³ Although these mites may coexist in tropical and subtropical regions, *B. tropicalis* is the major allergen in some countries.^{4,5} A limited number of reports have focused on the allergic processes involved in the immune responses triggered by *B. tropicalis*.^{3,6,7} Here, we used allergic asthma murine models and *ex vivo* analysis of *B. tropicalis* allergic subjects to better explore the role of immune cells in allergic responses obtained in the context of *B. tropicalis* exposure.

Mice received *B. tropicalis* allergens exclusively administered intranasally (without adjuvant) for both sensitization and challenge phases (Appendix S1). This model reproduced the major allergic asthma hallmarks, namely enhanced BALF cell counts accompanied by airway eosinophilia and airway hyperresponsiveness (AHR) (Figure 1A and B). We addressed the involvement of IL-4, as a major Th2 cytokine by comparing lung inflammation in IL-4-deficient (IL-4^{-/-}) and wild-type (WT) mice. The lack of IL-4 resulted in the absence of the typical airway eosinophilia and AHR observed in WT mice following *B. tropicalis* sensitization and challenge (Figure S1A and B). These results show that IL-4 is required for *B. tropicalis* allergen-induced asthma in our model.

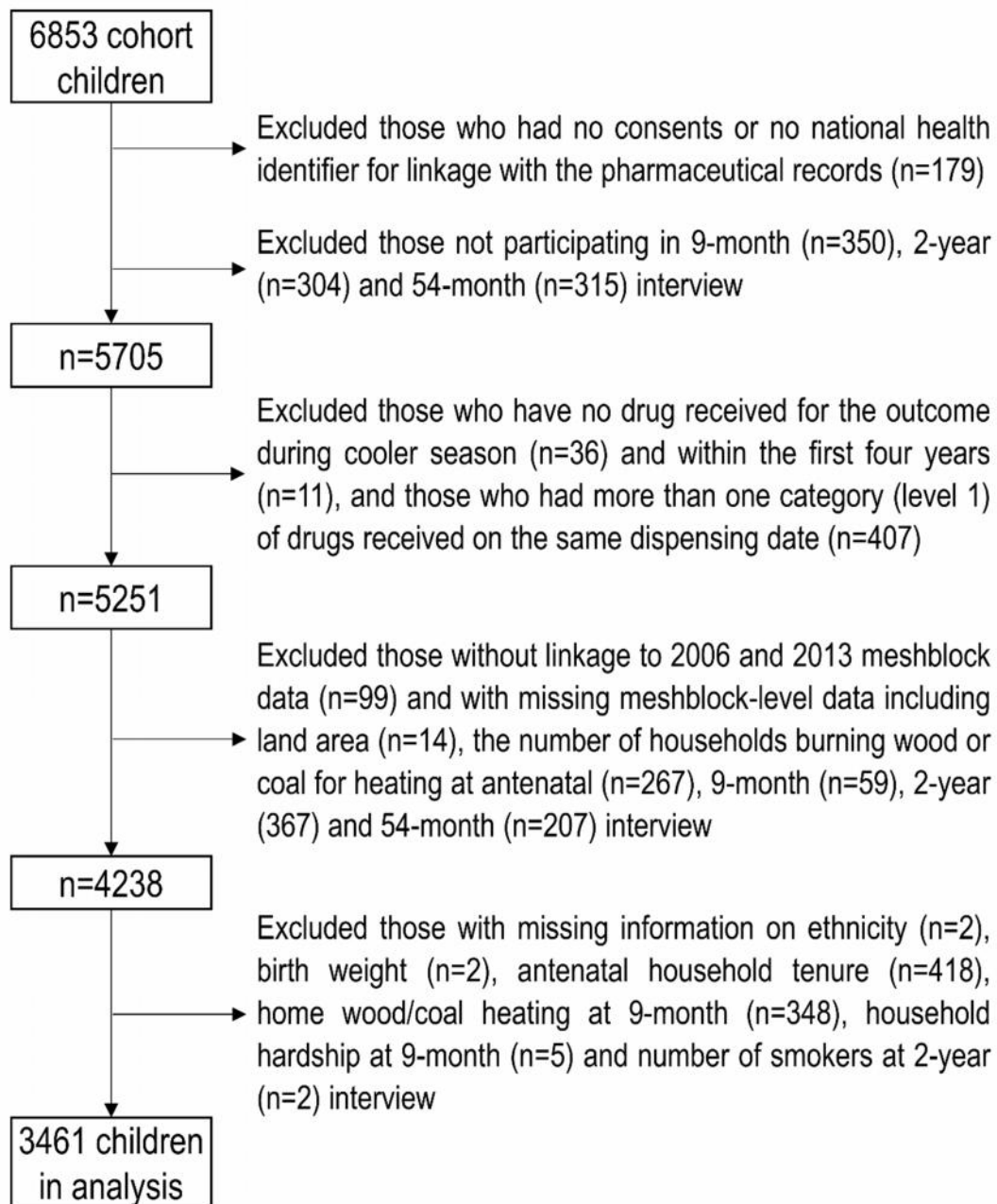
Distinct immune cells, such as iNKT cells and $\gamma\delta$ T cells, may be capable to secrete IL-4 and favour asthmatic inflammatory Th2-cytokine-dependent responses.^{8,9} As previously described, iNKT cells can be divided into three major subsets, iNKT1 (IFN- γ and IL-4 producers), iNKT2 (IL-4 producers) and iNKT17 (IL-17 producers). These subsets were present in the lung of *B. tropicalis*-treated mice

(Figure S2A). No major differences were observed concerning their ability to secrete IL-4, IL-13 or IFN- γ but the frequency of IL-17-producing iNKT cells was enhanced when compared to controls (Figure S2A). However, this enhanced frequency was not critical for airway inflammation since iNKT cell-deficient mice presented similar airway eosinophilia than WT mice (Figure S2B).

Concerning $\gamma\delta$ T cells, including the V γ 1.1⁺ (hereafter mentioned as V γ 1⁺) $\gamma\delta$ T-cell subset, we found that their number were higher in the lung of *B. tropicalis*-treated than in NaCl-treated mice (Figure S3). It is noteworthy that airway eosinophilia and AHR were significantly reduced in *B. tropicalis*-sensitized and *B. tropicalis*-challenged TCR δ ^{-/-} mice when compared to WT controls (Figure 1C, 1D). Further, IgE levels in the serum, Mucin-5 mRNA expression and mucus deposition in the lung were also impaired in TCR δ ^{-/-} compared to WT mice (Figure S4). Previous reports have shown that the influence of $\gamma\delta$ T cells on allergic responses may be complex.⁹ Here, we focused our analysis on V γ 1⁺ and V γ 1⁻ $\gamma\delta$ T-cell subsets (Figure S5A). Among $\gamma\delta$ T cells, IL-4 and IL-13 were mainly produced by the V γ 1⁺ $\gamma\delta$ T-cell subset in the lungs of the asthmatic mice (Figure S5B and C). Of note, the frequency of IL-4⁺ and IL-13⁺ among gated V γ 1⁺ $\gamma\delta$ T cells from *B. tropicalis*-treated mice was higher than in controls (Figure S5B). These cells also secreted higher levels of IFN- γ and IL-17 in asthmatic mice (Figure S5B). In contrast, the percentage of IL-4⁺, IL-13⁺, IL-17⁺ and IFN- γ ⁺ among gated V γ 1⁻ subset was similar in mice treated with *B. tropicalis* and controls (Figure S5B and C). These findings indicating that cytokine-producing V γ 1⁺ $\gamma\delta$ T cells may be critical for this inflammatory allergic response.

The enhanced frequency of IL-4-producing V γ 1⁺ $\gamma\delta$ T cells in the lung of *B. tropicalis*-treated mice (Figure S5B) led us to the question whether airway eosinophilia and AHR could be restored by transferring fully competent V γ 1⁺ $\gamma\delta$ T cells to *B. tropicalis*-sensitized and *B. tropicalis*-challenged TCR δ ^{-/-} mice. This was the case since the adoptive transfer of 25 000 V γ 1⁺ $\gamma\delta$ T cells from WT mice one hour before the first challenge restored airway inflammation, particularly for airway eosinophilia, and AHR in TCR δ ^{-/-} mice (Figure 1E and F). In contrast, adoptive transfer of V γ 1⁺ $\gamma\delta$ T cells from IL-4^{-/-} mice had no effect (Figure 1E and F). The failure to develop an effective AHR

1 **Supplementary material 1: Attrition flow diagram describing the number of children**
2 **included in this data analysis**



3
4

Supplementary material 2: Using pharmaceutical records to define outcomes

Using each child's unique National Health Index (NHI) number, we established linkage between the *Growing Up in New Zealand* data and regional and national datasets, including perinatal records and the New Zealand Ministry of Health Pharmaceutical Collection. The Pharmaceutical Collection includes records of all subsidized medications dispensed to the cohort children from community pharmacies. In New Zealand, more than 20,000 medicines and medical devices are currently subsidized by the government (www.pharmac.govt.nz/medicines). Prescriptions for children under six years old are fully subsidized (1). The Pharmaceutical Collection does not include medications dispensed from hospital pharmacies during emergency department or inpatient visits or given directly by a doctor in emergency circumstances on a physicians' supply order. Our earlier study has applied these data to describe community antibiotic prescriptions dispensed to the cohort (2).

Both respiratory and dermatological outcomes in this analysis are defined based on broad drug classification level-1 categories in the Pharmaceutical Collection. Level-2 classifications of respiratory medication prescriptions in our data included antihistamines, beta-adrenoceptor agonists, inhaled corticosteroids, nasal preparations, anticholinergic agents, and inhaled long-acting beta-adrenoceptor agonists. Level-2 classifications of prescriptions for dermatological medications included topical corticosteroids, barrier creams and emollients, topical anti-bacterials and antifungals, psoriasis and eczema preparations, parasitocidal preparations, antipruritic preparations, scalp preparations, minor skin infection preparations, anti-acne preparations, disinfecting and cleansing agents, and other skin preparations.

Caution in interpretations: The prescription outcomes we defined in this study could represent a mix of several treatments or preparations rather than a specific disease. Besides, acute or asymptomatic events that required emergency room visits or hospital admissions were not captured. Nevertheless, pharmaceutical data in New Zealand has full coverage across the country (3) with high quality necessary for epidemiological research (4).

References:

1. Ministry of Health. Prescription charges. 2017. www.health.govt.nz/your-health/conditions-and-treatments/treatments-and-surgery/medications/prescription-charges (accessed on 20 July 2017).
2. Hobbs MR, Grant CC, Ritchie SR, Chelimo C, Morton SMB, Berry S, Thomas MG. Antibiotic consumption by New Zealand children: exposure is near universal by the age of 5 years. *Journal of Antimicrobial Chemotherapy* 2017;72:1832-1840.
3. Ministry of Health. Pharmaceutical Collection. www.health.govt.nz/nz-health-statistics/national-collections-and-surveys/collections/pharmaceutical-collection. Accessed on 28 November 2017.
4. Hallas J, Hellfritsch M, Rix M, Olesen M, Reilev M, Pottegård A. Odense Pharmacoepidemiological Database: A Review of Use and Content. *Basic Clin Pharmacol Toxicol*. 2017;120(5):419-425.

Supplementary material 3: Justifications for the partition of cooler and warmer seasons

Sources of ambient temperature data for the four cities in New Zealand with the largest populations:

City	Population	Source of temperature data
Auckland	1,495,000	http://www.myweather2.com/City-Town/New-Zealand/Auckland/climate-profile.aspx
Wellington	405,000	http://www.myweather2.com/City-Town/New-Zealand/Wellington/climate-profile.aspx
Christchurch	389,700	http://www.myweather2.com/City-Town/New-Zealand/Christchurch/climate-profile.aspx
Hamilton	230,000	http://www.myweather2.com/City-Town/New-Zealand/Hamilton/climate-profile.aspx

	Average minimum temperature (°C)				
	Auckland	Wellington	Christchurch	Hamilton	Population-weighted average
January	16	14	12	16	15.1
February	16	14	12	16	15.1
March	15	13	9	14	13.7
April	13	12	7	12	11.8
May	11	10	4	10	9.7
June	9	8	1	8	7.5
July	8	7	1	7	6.7
August	8	7	3	7	7.0
September	10	9	5	9	9.0
October	12	10	6	11	10.7
November	13	11	8	12	11.8
December	15	13	10	15	13.9
<i>Population</i>	<i>1,495,000</i>	<i>405,000</i>	<i>389,700</i>	<i>230,000</i>	
<i>Weighting</i>	<i>0.59</i>	<i>0.16</i>	<i>0.15</i>	<i>0.09</i>	

Reference:

"Subnational Population Estimates: At 30 June 2016 (provisional)". Statistics New Zealand. 21 October 2016. Accessed on 16 August 2017.

Supplementary material 4: Literature review on the effects of wood/coal smoke on children skin

PubMed search terms: (children OR child OR childhood) AND (skin OR eczema OR "atopic dermatitis" OR dermal) AND (wood OR coal) AND (heating OR burning OR combustion OR stove)

We identified only four relevant studies when we searched the PubMed database in June 2018 using the above search terms. Two studies in Germany investigated the effects of wood/coal heating on eczema in children. Both studies found no association between the indoor wood/coal used for heating the home and the odds of atopic dermatitis (1) and eczema (2). A cross-sectional study in Belarus also did not find any associations between exposure to indoor wood/coal heating at home and the odds of atopic eczema and recurrent itchy rash in the past 12 months among children living in both urban and rural areas (3). The one published study to date that has shown an association between childhood exposure to indoor wood-stove heating and the presence of physician-diagnosed atopic dermatitis was conducted in Finland, but the association was only evident among children living on farms (OR 1.44, $p=0.049$) and not among children living in other rural or in urban settings (4).

References:

1. von Mutius E, Illi S, Nicolai T, Martinez FD. Relation of indoor heating with asthma, allergic sensitisation, and bronchial responsiveness: survey of children in south Bavaria. *BMJ*. 1996;312(7044):1448-50.
2. Duhme H, Weiland SK, Rudolph P, Wienke A, Kramer A, Keil U. Asthma and allergies among children in West and East Germany: a comparison between Münster and Greifswald using the ISAAC phase I protocol. *International Study of Asthma and Allergies in Childhood*. *Eur Respir J*. 1998;11(4):840-7.
3. Shpakou A, Brożek G, Stryzhak A, Neviartovich T, Zejda J. Allergic diseases and respiratory symptoms in urban and rural children in Grodno Region (Belarus). *Pediatr Allergy Immunol*. 2012;23(4):339-46.
4. Kilpeläinen M, Koskenvuo M, Helenius H, Terho E. Wood stove heating, asthma and allergies. *Respir Med*. 2001;95(11):911-6.

Supplementary material 5: Current policies on wood/coal smoke emissions

Wood burners are still promoted by the government for household heating in some developed countries, including Denmark, Germany, Norway, the United Kingdom and North America (1). In London, where the government has provided incentives for new wood burners, the annual increase, from 2009 to 2011, in particulate matter concentration due to domestic wood burning for heating in wintertime was estimated to be at least six times more than the annual decrease in particulate concentration due to road traffic emission control schemes (2). Wood/coal burning has now become an increasing source of fine particulate emissions globally (3) and could have exceeded the particulate emissions from road transport (4).

In New Zealand, the regulation on wood smoke emissions, stated in the Resource Management Regulations 2004 (The National Environmental Standards for Air Quality – Section 22-23) (5), is that "the discharge of particles to air from a woodburner installed after 1 September 2005 in a building on a property with an allotment size of less than 2 hectares is prohibited". However, exemption is given to households with woodburners that satisfy specific standards including wood smoke discharge being less than 1.5 g of particles for each kilogram of dry wood burnt. Under the New Zealand National Environmental Standards for PM₁₀ of 50 microgram per cubic meter, to dilute 1.5 g of particles requires 30,000 m³ of fresh clean air, which is a volume of air that is 10 times above the height of a single storey house on a typical suburban land area of 800 m². A review of the current regulation on wood/coal smoke emissions would appear necessary given the rapid increases in population density in some urban areas of New Zealand in recent years.

References:

1. World Health Organization. Residential heating with wood and coal: health impacts and policy options in Europe and North America. 2015. WHO Regional Office for Europe, Copenhagen, Denmark.
2. Fuller GW, Tremper AH, Baker TD, Yttri KE, Butterfield D. Contribution of wood burning to PM₁₀ in London. *Atmospheric Environment* 2014;87:87-94.
3. Sigsgaard T, Forsberg B, Annesi-Maesano I, Blomberg A, Bolling A, Boman C, et al.. Health impacts of anthropogenic biomass burning in the developed world. *Eur Respir J* 2015; 46: 1577-1588.
4. Robinson DL. Wood burning stoves produce PM_{2.5} particles in amounts similar to traffic and increase global warming. *BMJ* 2015; 351:h3738.
5. New Zealand Government. Resource Management (National Environmental Standards for Air Quality) Regulations 2004 (SR 2004/309). (<http://www.legislation.govt.nz/regulation/public/2004/0309/latest/DLM286835.html>) Wellington, New Zealand. 2004.