e-Appendix

Exposure to Cats and Dogs, and Symptoms of Asthma, Rhinoconjunctivitis and Eczema: an ISAAC Phase Three Study

Symptom definitions

In this article, we focus on "current wheeze" ["Have you (Has your child) had wheezing or whistling in the chest in the past 12 months?"], "asthma ever" ["Have you (Has your child) ever had asthma?"], symptoms of "rhinoconjunctivitis" ["In the past 12 months, have you (has your child) had a problem with sneezing, or a runny, or blocked nose when you (he/she) DID NOT have a cold or the flu?" and "In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?"], and symptoms of "eczema" ["Have you (Has your child) had this itchy rash at any time in the past 12 months?" and "Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?"]. These questions were preceded by the question "Have you (Has your child) ever had an itchy rash coming and going for at least 6 months?" We have also analyzed "symptoms of severe asthma," defined as those with current wheeze who, according to the written questionnaire, in the past 12 months have had four or more attacks of wheeze, or one or more nights of sleep disturbance from wheeze per week, or wheeze affecting speech. Previous ISAAC analyses showed that a combination of these features of more severe wheezing episodes correlated significantly more closely with asthma mortality and hospital admissions than did current wheeze alone.

In the 13- to 14-year-olds, they were also asked to respond to a video questionnaire showing various symptoms of wheeze in children of similar age, and a positive response to the question relating to the scene of the young person wheezing at rest "Has your breathing ever been like this in the past 12 months?" was defined as "current wheeze–video" .

Full details can be found at http://isaac.auckland.ac.nz/.

eTable 1: Association between current cat in the home and current symptoms of asthma, rhinoconjunctivitis, and eczema in children 6 to 7 years old.

Outcome	OR (95% CI)		
	Adjusted* (all children)	Adjusted[†] (children with complete covariate data)	Fully adjusted[‡]
Current wheeze	1.18 (1.12,1.23)	1.11 (1.03,1.18)	1.07 (1.00,1.14)
Current symptoms of severe asthma	1.17 (1.10,1.25)	1.09 (0.99,1.19)	1.05 (0.95,1.15)
Asthma ever	1.10 (1.05,1.16)	1.08 (1.00,1.15)	1.05 (0.98,1.13)
Current symptoms of rhinoconjunctivitis	1.10 (1.04,1.16)	1.08 (1.00,1.16)	1.07 (0.99,1.15)
Current symptoms of severe rhinoconjunctivitis	1.15 (0.97,1.36)	1.11 (0.86,1.44)	1.06 (0.82,1.38)
Hay fever ever	1.05 (0.99,1.11)	1.02 (0.94,1.10)	1.01 (0.94,1.09)
Current symptoms of eczema	1.12 (1.07,1.18)	1.06 (0.99,1.13)	1.05 (0.98,1.12)
Current symptoms of severe eczema	1.43 (1.26,1.63)	1.25 (1.04,1.51)	1.18 (0.98,1.42)
Eczema ever	1.07 (1.02,1.12)	1.03 (0.97,1.09)	1.04 (0.98,1.11)

* Adjusted for sex, region of the world, language, and gross national income per capita (GNI).
[†] Adjusted for sex, region of the world, language, and GNI. Including only centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed.
[‡] Analysis including centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed. Adjusted for sex, region of the world, language, GNI, cooking fuel, maternal education, current maternal and paternal smoking, exercise, television viewing, consumption of fast food, current paracetamol use, older and younger siblings, and truck traffic in street of residence.

eTable 2: Association between dog in the home in the 1st year of life and current symptoms of

asthma, rhinoconjunctivitis, and eczema in children 6 to 7 years old.

Outcome	OR (95% CI)		
	Adjusted* (all children)	Adjusted[†] (children with complete covariate data)	Fully adjusted[‡]
Current wheeze	1.19 (1.14,1.24)	1.07 (1.01,1.14)	1.03 (0.97,1.09)
Current symptoms of severe asthma	1.22 (1.15,1.30)	1.11 (1.02,1.21)	1.05 (0.96,1.14)
Asthma ever	1.08 (1.03,1.14)	1.02 (0.95,1.09)	0.99 (0.93,1.06)
Current symptoms of rhinoconjunctivitis	1.17 (1.11,1.22)	1.09 (1.02,1.17)	1.06 (0.99,1.14)
Current symptoms of severe rhinoconjunctivitis	1.32 (1.15,1.52)	1.23 (0.99,1.52)	1.16 (0.94,1.45)
Hay fever ever	1.07 (1.01,1.13)	1.01 (0.93,1.09)	1.00 (0.92,1.08)
Current symptoms of eczema	1.13 (1.08,1.19)	1.05 (0.99,1.12)	1.04 (0.97,1.10)
Current symptoms of severe eczema	1.47 (1.30,1.65)	1.17 (0.98,1.39)	1.10 (0.92,1.31)
Eczema ever	1.05 (1.01,1.10)	1.00 (0.95,1.06)	1.01 (0.95,1.07)

* Adjusted for sex, region of the world, language, and gross national income per capita (GNI).
[†] Adjusted for sex, region of the world, language, and GNI. Including only centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed.
[‡] Analysis including centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed. Adjusted for sex, region of the world, language, GNI, cooking fuel, maternal education, current maternal and paternal smoking, exercise, television viewing, consumption of fast food, current paracetamol use, older and younger siblings, and truck traffic in street of residence.

eTable 3: Association between current dog in the home and current symptoms of asthma, rhinoconjunctivitis, and eczema in children 6 to 7 years old.

Outcome	OR (95% CI)		
	Adjusted* (all children)	Adjusted† (children with complete covariate data)	Fully adjusted‡
Current wheeze	1.10 (1.06,1.15)	1.03 (0.97,1.09)	0.98 (0.92,1.04)
Current symptoms of severe asthma	1.11 (1.04,1.17)	1.05 (0.97,1.15)	0.99 (0.91,1.08)
Asthma ever	1.05 (1.01,1.10)	1.01 (0.95,1.08)	0.98 (0.92,1.04)
Current symptoms of rhinoconjunctivitis	1.06 (1.01,1.11)	1.04 (0.98,1.12)	1.03 (0.96,1.10)
Current symptoms of severe rhinoconjunctivitis	1.02 (0.88,1.18)	1.11 (0.89,1.37)	1.08 (0.87,1.34)
Hay fever ever	1.00 (0.95,1.06)	1.01 (0.94,1.08)	1.01 (0.94,1.09)
Current symptoms of eczema	1.03 (0.98,1.07)	1.04 (0.97,1.10)	1.03 (0.97,1.09)
Current symptoms of severe eczema	1.13 (1.00,1.28)	1.03 (0.87,1.22)	0.96 (0.81,1.14)
Eczema ever	1.00 (0.96,1.04)	0.98 (0.93,1.03)	1.00 (0.95,1.06)

* Adjusted for sex, region of the world, language, and gross national income per capita (GNI)
† Adjusted for sex, region of the world, language, and GNI. Including only centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed.
‡ Multivariate analysis including centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed. Adjusted for sex, region of the world, language, GNI, cooking fuel, maternal education, current maternal and paternal smoking, exercise, television viewing, consumption of fast food, current paracetamol use, older and younger siblings, and truck traffic in street of residence.

eTable 4. Association between cat in the home in the 1st year of life and symptoms of asthma, rhinoconjunctivitis, and eczema in children 6 to 7 years old, in centres from affluent and non-affluent countries.

Outcome	OR (95% CI)	
	Adjusted[‡] (centres from affluent countries)	Adjusted[‡] (centres from non-affluent countries)
Current wheeze	1.14 (1.04,1.25)	1.22 (1.08,1.38)
Current symptoms of rhinoconjunctivitis	1.09 (0.98,1.21)	1.10 (0.96,1.27)
Current symptoms of eczema	1.00 (0.91,1.11)	1.22 (1.09,1.37)

[‡] Analysis including centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed. Adjusted for sex, region of the world, language, cooking fuel, maternal education, current maternal and paternal smoking, exercise, television viewing, consumption of fast food, current paracetamol use, older and younger siblings, and truck traffic in street of residence.

eTable 5. Association between current cat in the home and current symptoms of asthma, rhinoconjunctivitis, and eczema in children 13 to 14 years old, in centres from affluent and non-affluent countries.

Outcome	OR (95% CI)	
	Adjusted[‡] (centres from affluent countries)	Adjusted[‡] (centres from non-affluent countries)
Current wheeze	1.11 (0.99,1.26)	1.07 (1.00,1.15)
Current symptoms of rhinoconjunctivitis	1.06 (0.95,1.19)	1.09 (1.02,1.16)
Current symptoms of eczema	1.09 (0.94,1.25)	1.26 (1.16,1.37)

[‡] Analysis including centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed. Adjusted for sex, region of the world, language, cooking fuel, maternal education, current maternal and paternal smoking, exercise, television viewing, consumption of fast food, current paracetamol use, older and younger siblings, and truck traffic in street of residence.

eTable 6. Association between current dog in the home and current symptoms of asthma, rhino conjunctivitis, and eczema in children 13 to 14 years old, in centres from affluent and non-affluent countries.

Outcome	OR (95% CI)	
	Adjusted[‡] (centres from affluent countries)	Adjusted[‡] (centres from non-affluent countries)
Current wheeze	1.11 (1.01,1.22)	1.09 (1.01,1.17)
Current symptoms of rhinoconjunctivitis	1.11 (1.02,1.21)	1.09 (0.97,1.11)
Current symptoms of eczema	1.09 (0.98,1.22)	1.20 (1.10,1.30)

[‡] Analysis including centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed. Adjusted for sex, region of the world, language, cooking fuel, maternal education, current maternal and paternal smoking, exercise, television viewing, consumption of fast food, current paracetamol use, older and younger siblings, and truck traffic in street of residence.

eTable 7: Association between cat in the home in the 1st year of life and symptoms of asthma, rhino conjunctivitis, and eczema in children 6 to 7 years old, in affluent and non-affluent countries.

Outcome	OR (95% CI)		
	Adjusted* (all children)	Adjusted[†] (children with complete covariate data)	Fully adjusted[‡]
Current wheeze AFFLUENT	1.11 (1.03,1.20)	1.13 (1.04,1.24)	1.14 (1.04,1.25)
Current wheeze NON AFFLUENT	1.46 (1.36,1.56)	1.29 (1.14,1.45)	1.22 (1.08,1.38)
Current symptoms of rhinoconjunctivitis AFFLUENT	1.09 (1.00,1.20)	1.07 (0.97,1.19)	1.09 (0.98,1.21)
Current symptoms of rhinoconjunctivitis NON AFFLUENT	1.26 (1.17,1.36)	1.14 (0.99,1.30)	1.10 (0.96,1.27)
Current symptoms of eczema AFFLUENT	1.03 (0.96,1.13)	0.99 (0.90,1.09)	1.00 (0.91,1.11)
Current symptoms of eczema NON AFFLUENT	1.36 (1.27,1.46)	1.26 (1.12,1.41)	1.22 (1.09,1.37)

* Adjusted for sex, region of the world, language, and gross national income per capita (GNI).
[†] Adjusted for sex, region of the world, language, and GNI. Including only centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates EXCEPT SIBLINGS have been removed.
[‡] Analysis including centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed. Adjusted for sex, region of the world, language, GNI, cooking fuel, maternal education, current maternal and paternal smoking, exercise, television viewing, consumption of fast food, current paracetamol use, and truck traffic in street of residence.

eTable 8: Association between cat in the home in the 1st year of life and symptoms of asthma, rhino conjunctivitis, and eczema in children 6 to 7 years old in affluent and non-affluent countries, ignoring questions on younger and older siblings.

Outcome	OR (95% CI)		
	Adjusted* (all children)	Adjusted[†] (children with complete covariate data)	Fully adjusted[‡]
Current wheeze AFFLUENT	1.11 (1.03,1.20)	1.12 (1.03,1.22)	1.13 (1.03,1.23)
Current wheeze NON AFFLUENT	1.46 (1.36,1.56)	1.37 (1.26,1.50)	1.30 (1.19,1.42)
Current symptoms of rhinoconjunctivitis AFFLUENT	1.09 (1.00,1.20)	1.08 (0.98,1.19)	1.10 (0.99,1.21)
Current symptoms of rhinoconjunctivitis NON AFFLUENT	1.26 (1.17,1.36)	1.15 (1.05,1.27)	1.10 (1.00,1.22)
Current symptoms of eczema AFFLUENT	1.03 (0.96,1.13)	0.99 (0.90,1.08)	1.00 (0.91,1.10)
Current symptoms of eczema NON AFFLUENT	1.36 (1.27,1.46)	1.32 (1.20,1.44)	1.28 (1.17,1.41)

* Adjusted for sex, region of the world, language, and gross national income per capita (GNI).
[†] Adjusted for sex, region of the world, language, and GNI. Including only centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates EXCEPT SIBLINGS have been removed.
[‡] Analysis including centres with at least 70% data available for all covariates. All children who had a missing value for any of the covariates have been removed. Adjusted for sex, region of the world, language, GNI, cooking fuel, maternal education, current maternal and paternal smoking, exercise, television viewing, consumption of fast food, current paracetamol use, and truck traffic in street of residence.