## THE NEW ZEALAND MEDICAL JOURNAL Journal of the New Zealand Medical Association



## Has the prevalence and severity of symptoms of asthma changed among children in New Zealand? ISAAC Phase Three

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### Abstract

**Aim** To investigate time trends in prevalence of symptoms of asthma by repeating, during 2001–3 (Phase Three), the International Study of Asthma and Allergies in Childhood (ISAAC) Phase One study that was conducted in New Zealand in 1992–3.

**Methods** ISAAC Phase Three involved repeating the cross-sectional questionnaire survey of two age groups of school children (6–7 years and 13–14 years, children and adolescents respectively) using the same methodology as Phase One. In New Zealand it was conducted in Auckland, Bay of Plenty, Christchurch, Nelson, and Wellington.

**Results** After 9 years, reported asthma ever increased from 24.6% to 30.2% in children and from 24.1% to 32.4% in adolescents (p<0.001). Current wheeze (written questionnaire) significantly decreased in children from 23.6% to 22.2% (p=0.002) and in adolescents from 29.7% to 26.7% (p=0.047), and for the video questionnaire from 18.1% to 11.1% (p<0.001). There was a significant reduction in wheezing limiting speech from 5.0% to 3.7% in children, and 7.9% to 6.2% in adolescents. Little regional variation was found. A higher proportion of children with asthma symptoms now report having ever had asthma.

**Conclusions** The decrease in prevalence and severity of symptoms of asthma is encouraging, but the reasons for these trends are currently unclear. Increases in asthma labelling are likely to be due to greater awareness of asthma. A trend of decreasing prevalence of asthma symptoms, if maintained, has positive implications for lessened burden of disease among asthmatics and lowered cost of treatment.

Asthma has been a national concern in New Zealand since the late 1970s when an asthma mortality epidemic was identified.<sup>1</sup> At the same time, admissions to hospital for asthma increased.<sup>2</sup> Since that time several studies in New Zealand children have shown an increase in asthma symptom prevalence during the period 1969-2000.<sup>3-5</sup>

The International Study of Asthma and Allergies in Childhood (ISAAC) Phase One found a high burden of asthma symptoms in New Zealand children in 1992–3 compared with most other countries,<sup>6</sup> and we hypothesised that the prevalence of asthma symptoms would continue to increase.

ISAAC has completed a worldwide study of the time trends of asthma and allergies in which New Zealand data is included.<sup>7</sup> The time trends in asthma symptoms in the New Zealand ISAAC study are reported in more detail here. New Zealand time trends data for symptoms of rhinoconjunctivitis and eczema will be presented elsewhere.

The objective of this study was to assess recent time trends in asthma symptom prevalence in New Zealand using standardised methodology.

### Methods

The details of the study design and methods for ISAAC Phase Three are described in detail elsewhere.<sup>8</sup> ISAAC Phase Three was conducted in 2001–3 in five centres in New Zealand which had participated in ISAAC Phase One: Auckland, Bay of Plenty, Christchurch, Nelson, and Wellington.

Each centre conducted Phase Three in the same way as Phase One to ensure comparable data. The study centre investigators chose the schools either by new random samples of schools in that area or by going back to the same schools chosen at random in Phase One. The two age groups of children selected were 6–7 and 13–14 year olds, here called children and adolescents respectively.

The older age group completed written questionnaires on asthma, rhinitis, and eczema symptoms at school, and also completed an asthma symptoms video questionnaire. The younger age group took the questionnaire home for parental completion. The key question used for assessing asthma symptom prevalence for both age groups ('current wheeze') was: '*Have you (Has your child) had wheezing or whistling in the chest in the past 12 months?*'.

The severity of asthma symptoms was assessed by three questions that asked about the following symptoms in the past 12 months: number of attacks of wheezing; sleep disturbed due to wheezing; and wheezing severe enough to limit speech to only one or two words at a time between breaths. The video questionnaire showed five scenes of young people with asthma symptoms; wheezing at rest, wheezing with exercise, waking with wheeze, waking with cough, and a severe attack of asthma, and asked if they had experienced these symptoms at any time in their life, if *yes* in the past year, if *yes* one or more times a month.

In Phase Three the core questions were followed by an additional environmental risk factor questionnaire.<sup>8</sup> Methodology and data from each centre were examined for adherence to protocol, and comparability in methodology between Phases 1 and 3. Ethics Committee approval was obtained for each centre, and centres obtained their own funding.

As in Phase One, the two age groups were analysed separately. Symptom prevalence values in each centre were calculated by dividing the number of positive responses to each question by the number of completed questionnaires for the written and video questionnaires separately. For each centre, the annual change in symptom prevalence was calculated by taking the difference between the Phase One and Phase Three prevalence values and dividing by the number of years between the two surveys.

An estimate of the absolute rate of change per year in asthma symptoms was derived for each centre and also the standard error of the change per year (SE), adjusted for the effect of cluster sampling<sup>9</sup> from which significant changes  $\geq 2$  SE up or down could be derived. The other assessments of change with time were made using a generalised mixed model with a logit link and a binomial error distribution, and modelling the schools as a random effect.

Other factors in the model were gender, ethnicity, school decile, and month of interview as our previous work has shown that a higher (non-statistically significant) rate of positive responses for asthma symptoms were found among adolescents responding in winter months.<sup>10</sup>

### **Results**

The ISAAC Phase Three study was completed to the standards of the ISAAC protocol<sup>8</sup> in all five centres in children and adolescents. However because Wellington had a low response rate (47.2%) in children, this centre was excluded from the analyses for this age group. For the centres included in the analyses, there were 10,873 children (response rate 85.2%) and 13,317 adolescents (response rate 89.2%) (Table 1).

Phase One was conducted in 1992–3 and Phase Three in 2001–3. Thus, the time period between the phases averaged 9 years (range 8–10 years). As for Phase One, Auckland, Wellington, and Christchurch collected the data over 1 year, and in Bay of

Plenty and Nelson over one school term.<sup>6</sup> The later starting times for data collection in two centres were due to delays in obtaining ethical approval where ethics committees originally favoured written consent, but finally approved passive consent so as to be consistent with Phase One methodology.

Centre	6–7 year age group							
	Phase One		Phase Three					
	Year	Ν	Year	Ν	Response			
Auckland	1993	3526	2002	3541	84.6			
Bay of Plenty	1993	2681	2002	2150	79.9			
Nelson	1993	1868	2003	1867	92.0			
Christchurch	1993	3318	2003	3315	86.0			
Total	1993	11393	2003	10873	85.2			
Centre	13–14 year age group							
Auckland	1993	3206	2001	2870	92.3			
Bay of Plenty	1993	2813	2002	1976	76.2			
Wellington	1993	4417	2001	3050	96.9			
Nelson	1993	1838	2003	2305	90.5			
Christchurch	1993	3186	2003	3116	88.2			
Total	1993	15460	2002	13317	89.2			

# Table 1. Phase One year of study and number of participants (N), and Phase Three year of study, number of participants and response rate (%)

Table 2 shows the findings for changes in asthma symptom prevalence between Phase One and Phase Three. When these results were adjusted for gender, ethnicity, school decile, and month of interview, lifetime asthma (asthma ever) significantly increased from 26.3% to 31.9% (p<0.001) in children and 22.8% to 31.3% (p<0.001) in adolescents. However there was a completely different picture for reported symptoms in the last 12 months, which generally did not change or even decreased (Figures 1 and 2).

# Table 2. Asthma symptoms Phase Three prevalence (%), change per year (%), and standard error (SE, %)

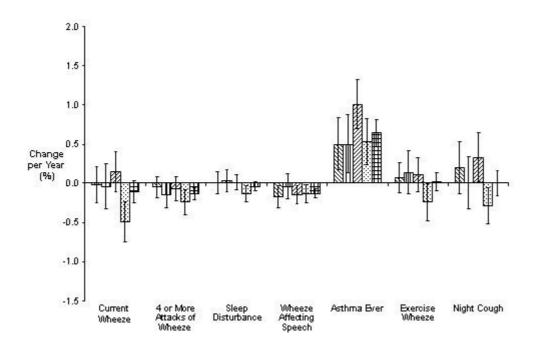
Symptom		Auckland	Bay of Plenty	Wellington	Nelson	Christchurch	Total
		6–7 year age group					
Current wheeze	Phase One	22.5	24.0		18.7	27.2	23.6
	Phase Three	22.4	23.7		20.2	22.3	22.2
	Change per year	-0.02	-0.04		0.15	-0.49*	-0.11
	SE	0.12	0.15		0.13	0.13	0.07
4 or more attacks of	Phase One	7.9	8.2		7.1	10.2	8.5
wheeze	Phase Three	7.4	6.8		6.4	7.8	7.2
	Change per year	-0.05	-0.15		-0.07	-0.24*	-0.13*
	SE	0.07	0.08		0.08	0.08	0.04
Sleep disturbance	Phase One	3.7	3.6		2.2	3.9	3.5
	Phase Three	3.8	3.8		2.4	2.6	3.2
	Change per year	0.01	0.03		0.01	-0.13*	-0.04
	SE	0.07	0.07		0.05	0.05	0.03
Wheeze affecting	Phase One	5.3	4.8		4.6	5.0	5.0
speech	Phase Three	3.8	4.4		3.1	3.6	3.7
	Change per year	-0.17*	-0.04		-0.15*	-0.14*	-0.13*
	SE	0.07	0.08		0.06	0.06	0.03

		Auckland	Bay of Plenty	Wellington	Nelson	Christchurch	Total
Asthma ever	Phase One	23.8	25.7		17.6	28.4	24.6
	Phase Three	28.3	30.2		27.7	33.6	30.2
	Change per year	0.50*	0.50*		1.01*	0.53*	0.64*
	SE	0.17	0.19		0.16	0.15	0.09
Exercise wheeze	Phase One	14.8	15.9		13.2	19.2	16.1
	Phase Three	15.4	17.1		14.2	16.8	16.0
	Change per year	0.07	0.14		0.11	-0.24*	0.02
	SE	0.10	0.14		0.11	0.12	0.06
Night cough	Phase One	27.5	28.9		21.1	32.2	28.1
i light tough	Phase Three	29.3	29.0		24.4	29.2	28.4
	Change per year	0.20	0.01		0.33*	-0.29*	0.00
	SE	0.17	0.17		0.16	0.12	0.08
				13–14 year age	graun		
Current wheeze	Phase One	26.5	29.5	31.7	31.0	29.6	29.7
Current wheele	Phase Three	22.5	20.6	32.6	28.0	27.9	26.7
	Change per year	-0.51	-0.98*	0.11	-0.29	-0.17	-0.39*
	SE	0.34	0.21	0.25	0.19	0.23	0.13
4 or more attacks of	Phase One	8.0	9.0	11.1	10.2	9.8	9.7
wheeze	Phase Three	4.9	4.4	7.8	6.6	6.7	6.2
WIICOZC	Change per year	-0.38*	-0.51*	-0.41*	-0.35*	-0.31*	-0.38*
	SE	0.12	0.10	0.13	0.14	0.07	0.06
Sleep disturbance	Phase One	2.7	3.3	3.0	2.6	2.9	2.9
Sleep disturbance	Phase Three	2.9	2.3	3.7	1.7	2.2	2.6
	Change per year	0.02	-0.11	0.08	-0.09	-0.07	-0.05
	SE	0.02	0.07	0.08	0.05	0.07	0.03
Wheeze affecting	Phase One	8.1	7.1	8.3	8.2	7.5	7.9
speech	Phase Three	5.6	4.1	8.1	6.3	6.2	6.2
specen	Change per year	-0.31*	-0.33*	-0.03	-0.19	-0.13	-0.21*
	SE	0.12	0.09	0.14	0.11	0.08	0.05
Asthma ever	Phase One	22.9	22.3	26.4	20.2	25.9	24.1
Asuma ever	Phase Three	27.9	28.3	36.3	20.2 29.4	37.6	32.4
	Change Per Year	0.63*	0.67*	1.24*	0.91*	1.17*	0.93*
	SE	0.26	0.14	0.17	0.15	0.19	0.11
Exercise wheeze	Phase One	36.1	39.4	41.2	43.4	40.3	39.9
Exercise wheeze	Phase Three	32.4	31.6	42.5	41.6	37.8	37.5
	Change per year	-0.45	-0.86*	0.17	-0.17	-0.25	-0.29*
	SE	0.30	0.32	0.31	0.25	0.22	0.14
Night cough	Phase One	29.7	31.3	30.3	26.3	27.4	29.3
Tught cough	Phase Three	30.8	26.9	31.5	20.5	26.8	29.5
	Change per year	0.14	-0.49	0.15	0.13	-0.06	-0.01
	SE	0.26	0.28	0.26	0.28	0.32	0.13
Current wheeze	Phase One	16.3	18.6	19.5	19.1	17.4	18.2
(Video)	Phase Three	11.2	13.4	12.1	11.5	8.8	11.2
(()1000)	Change per year	-0.64*	-0.57*	-0.93*	-0.76*	-0.86*	-0.76*
	SE	0.14	0.15	0.16	0.16	0.11	0.07
Exercise wheeze	Phase One	28.4	28.4	31.1	32.4	32.2	30.4
(video)	Phase Three	15.9	13.5	17.1	15.9	16.2	15.9
(video)	Change per year	-1.56*	-1.66*	-1.75*	-1.64*	-1.60*	-1.64*
	SE	0.23	0.28	0.23	0.32	0.20	0.11
Sleep disturbance	Phase One	11.3	11.4	12.2	10.5	11.3	11.5
(video)	Phase Three	5.1	6.7	5.4	3.9	4.6	5.1
	Change per year	-0.79*	-0.53*	-0.86*	-0.65*	-0.67*	-0.73*
	SE	0.10	0.14	0.08	0.08	0.12	0.05
Night cough (video)	Phase One	20.7	25.2	23.1	23.3	22.5	22.9
ragin cougli (viuco)	Phase Three	20.7	17.2	22.5	23.3 18.4	17.9	19.4
	Change per year	-0.09	-0.88*	-0.08	-0.49*	-0.46	-0.32*
	SE	0.26	0.40	0.22	0.23	0.30	0.13
		0.20	00	0.22	5.25	0.00	5.10

		Auckland	<b>Bay of Plenty</b>	Wellington	Nelson	Christchurch	Total
Severe wheeze	Phase One	11.4	12.8	14.9	11.7	13.2	13.0
(video)	Phase Three	6.3	8.3	6.8	9.4	7.1	7.4
	Change per year	-0.63*	-0.50*	-1.01*	-0.23*	-0.61*	-0.56*
	SE	0.14	0.13	0.14	0.11	0.10	0.06

\*Change  $\geq 2$  standard errors.

Current wheeze reported with the written questionnaire in Phase Three significantly decreased from Phase One in children from 25.7% to 23.5% (p=0.002) and in adolescents from 28.3% to 26.3% (p=0.047). For the video questionnaire, current wheeze significantly decreased from Phase One from 20.5% to 12.4% (p<0.001), and there was a decrease  $\geq$ 2SE for all symptoms in all centres except night cough in Auckland and Wellington where no change was seen (Figure 3).

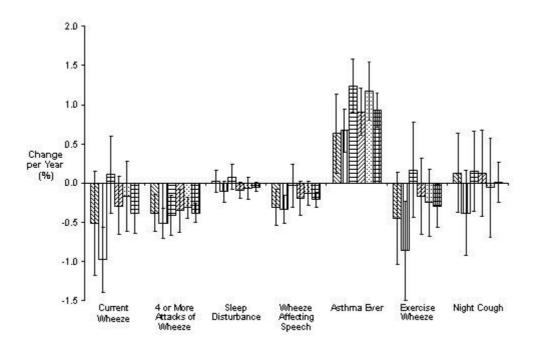


There was a reduction in symptoms of severe asthma in the last 12 months for both age groups: for wheezing limiting speech there was a decrease from 6.4% to 4.7% (p<0.001) in children and a decrease from 8.4% to 6.5% (p<0.001) in adolescents. For 4 or more attacks there was a decrease in adolescents from 7.5% to 4.8% (p<0.001), but the reductions in 4 or more attacks for children, and wheezing disturbing sleep in both age groups were non-significant.

The prevalence of current wheezing in ISAAC Phase Three was more common in boys (50.4%) than girls (49.6%) of the 6–7 year age group (p<0.001), but more

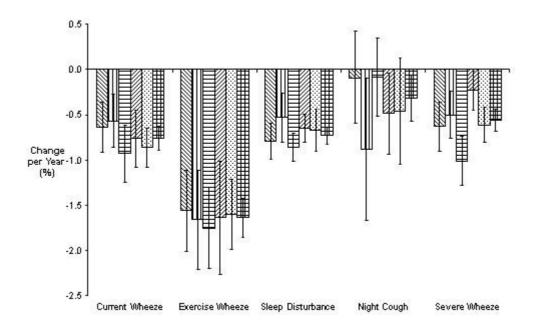
common in girls (52.1%) than boys (47.9%) of the 13–14 year age group (p<0.001), similar to the observations in Phase One.

Among children with current wheeze, reported asthma ever increased from 70.4% to 77.3%, a change of 7.0% (95%CI 6.70–7.26%) and among adolescents from 54.4% to 63.7%, a change of 9.3% (95%CI 9.00–9.65%). However of those with reported asthma ever, the proportion with current wheezing fell from 67.6% to 56.9% and from 67.1% to 52.5% in children and adolescents respectively.



Among children, the relative risk of current wheeze in those with atopy (allergic rhinoconjunctivitis or eczema) was 2.52 (95%CI 2.22–2.87) and among adolescents was 2.13 (95%CI 2.06–2.21). Among those with atopy the proportion with current wheezing did not change between phases (data not shown).

Figure 3. Change per-year in prevalence of symptoms (video questionnaire) for the 13-14 year age group Auckland Bay of Plenty I, Wellington Auckland S, Christchurch S, and Total I + The vertical bars indicate 95% confidence intervals.



### Conclusions

This is the first multicentre study of time trends of the prevalence of asthma symptoms within New Zealand, and the only study examining trends beyond 2000. In contrast with reports of an increase in the prevalence of asthma symptoms from the 1960s to 2000,<sup>4,5,11,12</sup> we found no evidence of any increase in symptoms from 1993 to 2002. In both age groups, there were significant decreases in current wheezing, wheeze limiting speech, and for the adolescent group the video scenes of asthma symptoms. The prevalence of symptoms reported with the video questionnaire were lower than from the written questionnaire, similar to the findings from ISAAC Phase One.<sup>13</sup> The video questionnaire is likely to detect more severe symptoms due to the visual and auditory nature of the signs.

Despite the fact that the prevalence values of most current symptoms including symptoms of severe asthma decreased, reported asthma ever increased in both age groups. This could be due to several factors, including a greater awareness of asthma by parents and adolescents, a greater use of the diagnostic label by doctors, or better asthma control where more children with asthma have gained complete symptom control. Unfortunately information on individual medication use was not collected in this study to explore this further.

In the 1980s several studies in the UK concluded that asthma was being significantly under diagnosed. At the same time, concerns about rising asthma prevalence, increased hospital admissions for asthma and asthma mortality resulted in a push for increased recognition and treatment of asthma in developed countries. The findings

presented above suggest that the trends established in the 1980s to increase the diagnosis of asthma in those with symptoms of asthma has continued into the new millennium so that fewer children with wheeze are not diagnosed with asthma.

There may be an increase in the labelling of asthma within preschool children who have viral-induced wheeze which has a good prognosis and which does not progress to the classical asthma phenotype in school age children or mislabelling of asthma earlier in life. There is no evidence that preventative treatment of asthma symptoms in preschool children improves the prognosis of asthma.<sup>14,15</sup>

There was no evidence that the relationship between asthma and atopic disease is changing—the proportion of children with current wheeze reporting other atopic disease did not change between phases. The higher prevalence of current wheeze among boys in the younger age group and among adolescent girls is consistent with earlier reports.<sup>13</sup>

The strengths of this study are the inclusion of several New Zealand centres, three in the North Island and two in the South Island, and the ability to make valid comparisons with the rest of the world due to the standardised methodology used. The numbers of subjects and response rates of the centres included in the analyses are high, and centres completed rigorous data and methodology checks. The time interval (8–10 years) was similar to previous New Zealand studies where increases over time have been found.<sup>3–5,16</sup>

The 6–7 year age group in Wellington was excluded from the analyses to avoid possible bias due to a low response rate. In the Bay of Plenty, lower participation rates were found for both age groups compared with other centres for Phase Three, and a slightly lower response rate for the 6–7 year age group for Phase One, but within the allowable range. In general, most centres reported less enthusiasm from schools to participate in the Phase Three study than was experienced in Phase One because of curriculum pressures (especially for the secondary schools), the change to a four term year, as well as difficulties in interpreting the Privacy Act. These factors may have contributed to the lower response rate (85%, 89% in children and adolescents respectively) than that achieved in Phase One (91%, 93%).

There are limitations of the study which should be considered. Symptom prevalence has been examined at two time points only, so estimates of mean yearly changes during the time period of the study cannot be interpreted with confidence as a consistent linear change. There is the possibility of recall bias for wheezing ever and asthma ever. This may be worse for adolescents who may not recall events in early life. Also a diagnosis of asthma may have been made and later retracted, but still reported by parents or adolescents as 'asthma ever'.

There was a real concern that the study would not be able to be completed in two centres due to ethics committees favouring active written consent, rather than the passive consent used in Phase One. In the event, approval for passive consent was granted, but the commencement of the study was delayed in those centres. Active consent is very likely to result in lower response rates and importantly the Phase One protocol would not have been duplicated.<sup>17</sup>

In December 2006 the New Zealand National Ethics Advisory Committee developed guidelines on conducting observational studies in an ethical manner that are intended

to facilitate high quality studies, protect the interests of participants, and underpin public assurance of good study conduct.<sup>18</sup> These guidelines allow passive consent to be the model of choice for observational studies such as ISAAC.

Possible reasons for the observed decrease in symptom prevalence after a period of increase include a decrease in intensity of an aggravating environmental factor or a protective environmental/management factor. There may also be improved management of individuals with asthma. For example, a growing number of studies suggest that ingestion of antioxidants may be associated with fewer asthma symptoms,<sup>19,20</sup> and health messages from education programmes targeted at the prevention of heart disease may have also influenced the prevalence of asthma. However, there is currently no evidence that New Zealand children are in fact eating more healthily; rather there is increased concern about unhealthy diets.

Obesity is linked with wheezing,<sup>21</sup> but evidence points to an increase in obesity in New Zealand children,<sup>22</sup> rather than a decrease which might accompany a decrease in reported asthma symptoms. Could there be an increase in prevalence which is eventually limited by the genetic potential for asthma in the population? Or a cohort effect where a historical event has increased prevalence within a group born during a given period, and that exposure has now stopped? Could the increase, and now decrease be influenced by perception of symptoms due to a decrease in awareness programmes?

Hospital admissions relate mostly to more severe asthma, and from 1993 to 2002 there was no change in hospital admissions due to asthma among children (3.6 per 1000) but among adolescents admissions nearly halved (2.4 to 1.3 per 1000) (New Zealand Health Information Service). Decreased severity of asthma is often attributed to wider use of inhaled corticosteroids (ICS). Data on dispensing of ICS were available only for the whole age group (6-17 years) from 1993 to 2001 and showed that total adjusted amount of ICS was stable during this period.<sup>23</sup> There are no data available by centre and age group, or on usage by individuals.

Long acting  $\beta$ -agonists usage is unlikely to have had an impact on asthma prevalence reported from symptoms because since their funding in 1997 they were accessible only to the few children on high dose ICS  $\geq$ 800 µgBDP equivalents/day. While the increased use of effective treatment, especially ICS, may be important in reducing the severity of episodes, it is unlikely to explain the decrease in mild wheeze symptoms.<sup>24</sup>

From 1993 to 2002 the number of tonnes of tobacco released in New Zealand was stable (767.0, 771.2 respectively), but the number of cigarettes sold fell from 3.5 to 2.7 million (NZ Customs Service, New Zealand Overseas Trade Statistics 2007); the number of cigarette equivalents sold as tobacco is not measured. While it is tempting to speculate that a reduction in cigarette smoking may have resulted in a reduction in asthma symptoms, this is implausible as there was an increase in prevalence of asthma symptoms seen in earlier decades at the same time as cigarette smoking was falling. There has also been an increased attendance at childcare facilities, which has been associated with a reduced risk of developing asthma.<sup>25</sup>

It is also highly unlikely that any genetic influences, sensitisation to environmental allergens and respiratory syncytial virus infection in early life changed over that period, and thus these potential explanations remain highly speculative.

The prevalence of symptoms of asthma remains high by international standards, with New Zealand ranked in the top five countries among ISAAC Phase Three time trend centres,<sup>7,26</sup> with levels similar to the levels in Australia, the United Kingdom, Ireland, Canada, and the United States. The prevalence of current symptoms has decreased not only in New Zealand but also in Australia, the United Kingdom, and parts of Western Europe.<sup>24,26,27</sup> However symptom prevalence has increased in other parts of the world, including Latin America and parts of Europe, and especially in low prevalence centres so that the differences between the English-speaking countries and the rest of the world have lessened.

To summarise, the prevalence of asthma symptoms in New Zealand is mainly decreasing which is good news. The explanation for this trend is unknown, but it is likely to be due to a combination of factors, including changes in unknown environmental causes of current asthma symptoms, or changes in asthma awareness or asthma treatment.

A trend of decreasing prevalence of asthma symptoms, if maintained, has positive implications for lessened burden of disease among asthmatics and lowered cost of treatment.

#### Competing interests: None known.

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**Acknowledgements:** We thank the New Zealand funding bodies: the Health Research Council of New Zealand, the Asthma and Respiratory Foundation of New Zealand, the Child Health Research Foundation, the Hawke's Bay Medical Research Foundation, the Waikato Medical Research Foundation, Glaxo Wellcome New Zealand, the NZ Lottery Board, and Astra Zeneca New Zealand.

In addition:

- We are grateful to the children and parents who cooperated and participated in this study.
- The coordination and assistance by the school staff is sincerely appreciated.

• We appreciate the work of the Phase Three field workers in New Zealand who were: Tania Slater, Pip Hall, and Ben Harding (Wellington); Paula Masterton and Beryl Slade (Christchurch); Philippa Ellwood, Tadd Clayton, and Nancy Williams (Auckland); Mereana White and Paiheke McGarvey (Bay of Plenty); and Robyn Liddell (Nelson).

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