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Comparison of asthma prevalence in the ISAAC and the ECRHS

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ABSTRACT: International and regional prevalence comparisons are required to test and generate hypotheses regarding the causes of increasing asthma prevalence in various age groups worldwide. The International Study of Asthma and Allergies in Childhood (ISAAC) is the first such study in children and the European Community Respiratory Health Survey (ECRHS) is the first such study in adults.

Therefore, a comparison of the findings of these two surveys was conducted, for the 17 countries in which both surveys were undertaken.

There was a strong correlation between the ISAAC and ECRHS prevalence data, with 64% of the variation at the country level, and 74% of the variation at the centre level, in the prevalence of "wheeze in the last 12 months" in the ECRHS phase I data being explained by the variation in the ISAAC phase I data. There was also generally good agreement in the international patterns observed in the two surveys for self-reported asthma (74% of country level and 36% of centre level variation explained), self-reported asthma before age 14 yrs (64 and 26%), hay fever (61 and 73%) and eczema (41 and 50%).

Thus although there were differences in the absolute levels of prevalence observed in the two surveys, there is good overall agreement between the International Study of Asthma and Allergies in Childhood and European Community Respiratory Health Survey study findings with regard to international prevalence patterns. These findings, therefore, add support to the validity of the two studies, which provide a new picture of global patterns of asthma prevalence from child- to adulthood, and identify some of the key phenomena which future research must address.

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The need for standardized asthma prevalence comparisons has been emphasized by evidence that the prevalence of asthma may be increasing worldwide [1]. Most studies which have determined the prevalence of asthma symptoms using the same methodology in the same community at different times have reported that asthma prevalence has increased in recent decades, and that the size of the increase has, in some cases, been substantial. Although methodological differences between these studies make it difficult to compare the size of the differences in asthma prevalence between countries, the trend of increasing prevalence amongst populations in countries of widely differing lifestyles and ethnic groups is remarkably consistent.

International and regional prevalence comparisons are required to generate and test hypotheses regarding the causes of increasing asthma prevalence worldwide. The International Study of Asthma and Allergies in Childhood (ISAAC) is the first such study in children [2, 3], and the European Community Respiratory Health Survey (ECRHS) is the first such study in adults [4]. Therefore, the findings of these two surveys were compared for the countries and study centres in which both were undertaken.

Methods

The methods of the ISAAC, and ECRHS have been described in detail elsewhere [3, 4], and will only be summarized briefly here. Both studies found a wide variation in asthma symptom prevalence, with particularly high prevalences in English-speaking countries [5–8].

The International Study of Asthma and Allergies in Childhood

The ISAAC involved two phases [3]. Phase I comprised a simple standardized questionnaire that could be used with minimal resources in a large number of countries worldwide. This phase has now been completed [5, 6]. Phase II, which is still in progress, is of similar design to Phase II of the ECRHS (see below), but is being conducted in a smaller number of centres. Thus only Phase I of the ISAAC has been completed and was available for the current analyses. Phase I involved a compulsory survey in 13–14-yr-olds and an optional survey in 6–7-yr-olds. The data for 13–14-yr-olds are focused on here since these involve more centres and are self-reported, and are therefore more comparable with the ECRHS data for 20–44-yr-olds (the data for 6–7-yr-olds were parentally reported). The ISAAC phase I results included data from 463,801 13–14-yr-olds in 155 centres in 56 countries, with an overall response rate of 92% [5, 6].

The European Community Respiratory Health Survey

The ECRHS also involved two phases [4]. In each centre, a representative sample of 3,000 adults, aged 20–44 yrs, completed a phase I screening questionnaire on asthma symptoms and medication use. Individuals answering "yes" to waking with an attack of shortness of breath, an attack of asthma or current asthma medications were defined as "asthmatic". A random subsample of 600 subjects were then studied in more detail in phase II, with skin-prick tests to common allergens, measurement of serum total and specific immunoglobulin E (IgE) levels, bronchial responsiveness to inhaled methacholine, urine electrolyte levels, and an additional questionnaire on asthma symptoms and medical history, occupation and social status, smoking, the home environment, and use of medications and medical services.

The phase I results included data from 138,565 20–44-yr-olds in 48 centres in 22 countries (predominantly in Western Europe), with an overall response rate of 78% [7]. The study found wide variation in asthma symptom prevalence. Symptom prevalence was generally lower in Northern, Central and Southern Europe and higher in the UK, New Zealand, Australia and the USA (*i.e.* in English-speaking countries). All parts of phase II were completed in 34 centres in 15 countries [8], with a further three centres completing all but one part.

Selection of centres and countries for comparison

There were 15 countries in which phase I of both the ISAAC and ECRHS were conducted (see *Appendix*): in these countries, the 66 ISAAC centres included 182,032 13–14-yr-olds and the 39 ECRHS centres 108,171 adults. Of these, 12 countries (Australia, Belgium, Estonia, France, Germany, Ireland, Italy, New Zealand, Spain, Sweden, the UK and the USA) also conducted phase II of the ECRHS. However, there were only 13 centres (Melbourne, Australia; Antwerp, Belgium; Montpellier and Pessac, France; Athens, Greece; Turin and Verona, Italy; Barcelona, Spain; Anglia & Oxford/Cambridge & Ipswich, UK; and Auckland, Christchurch, Hawkes Bay and Wellington, New Zealand) in seven countries in which both of the phase I surveys were conducted, and there were no ECRHS phase II data for two of these centres (Athens and Auckland). Thus the primary analysis was based on countries rather than centres, with all of the centre data being pooled for each country (n=15), although the findings of the analyses by centre (n=13) are also reported.

Measures of symptom prevalence

The analyses involved questions on the prevalence of current wheeze (in the last 12 months) and self-reported history of asthma, rhinitis and eczema from the ISAAC phase I [5, 6] and ECRHS phase I and II [7, 8] questionnaires (table 1). The ECRHS also enquired as to at what age the first asthma attack occurred. Thus, an attempt was also made to estimate the cumulative incidence of asthma at age 14 yrs in the ECRHS, and to compare this with the prevalence of "asthma ever" at age 13–14 yrs in the ISAAC. Both surveys also included questions on waking with cough at night and wheeze after exercise, but the wording was quite different, and was not considered comparable.

Data analysis

For each of the questions, the data were analysed using multiple linear regression with one data point for each country (or centre), weighted by the inverse variance of the prevalence estimate for the country (or centre). The "dependent" variable was the age/sex/smoking-standardized ECRHS adult symptom prevalence in each country (or centre); the "independent" variable was the sex-standardized ISAAC 13–14-yr-old symptom prevalence. Further analyses indicated that the response rates in the ECRHS were not significant predictors of the ECRHS age/sex/smoking-standardized findings and, therefore, for simplicity, this variable was not included in the final models.

Table 1. – Questions included in the International Study of Asthma and Allergies in Childhood (ISAAC) and European Community Respiratory Health Survey (ECHRS)

ISAAC	ECRHS
Phase I	Phase I
Have you had wheezing or whistling in the chest *in the last 12 months*?	Have you had wheezing or whistling in your chest at any time in the last *12 months*?
Have you ever had hay fever?	Do you have any nasal allergies including hay fever?
Phase I	Phase II
Have you had wheezing or whistling in the chest *in the last 12 months*?	Have you had wheezing or whistling in your chest at any time in the last *12 months*?
Have you ever had asthma?	Have you ever had asthma?
	How old were you when you had your first attack of asthma?
Have you ever had hay fever?	Do you have any nasal allergies including hay fever?
Have you ever had eczema?	Have you ever had eczema or any kind of skin allergy?

Results

There was a strong correlation between the ISAAC and ECRHS phase I findings for current wheeze, in both the country and centre analyses, with a high proportion (64 and 74% respectively) of the variation being explained by the ISAAC prevalence findings (table 2 and fig. 1). There was also generally good agreement, in terms of the percentage of variation explained, between the two surveys for self-reported asthma (74 and 36%) (fig. 2), self-reported asthma before age 14 yrs (64 and 26%) (fig. 3), hay fever (61 and 73%) (fig. 4) and eczema (41 and 50%) (fig. 5). All the estimated correlations were statistically significant (table 2) with the exception of asthma by age 14 yrs in the centre analysis (p=0.09).

Although there was a strong correlation between the ISAAC and ECRHS findings, all regression coefficients were significantly <1.0 with the exception of that for hay fever ever (ECRHS phase II *versus* ISAAC phase I) in the country analysis. The regression coefficients were particularly low for asthma by age 14 yrs. The mean prevalence levels for "asthma ever" and asthma by age 14 yrs were lower in the ECRHS data, but the prevalences of wheeze, rhinitis and eczema were higher.

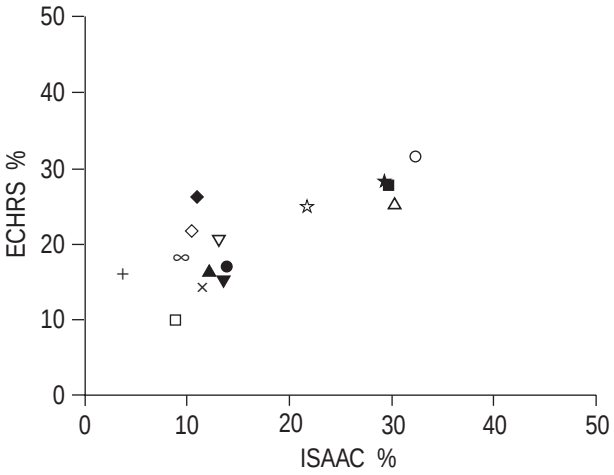

Fig. 1. – Wheeze in last 12 months in European Community Respiratory Health Survey (ECHRS) and International Study of Asthma and Allergies in Childhood (ISAAC) phase I by country (■: Australia; ×: Austria; ▲: Belgium; ◆: Estonia; ▼: France; ●: Germany; +: Greece; ★: Ireland; □: Italy; △: New Zealand; ∞: Portugal; ◇: Spain; ▽: Sweden; ○: UK; ☆: USA.)

Discussion

Evidence from cohort studies suggests that childhood asthma is a risk factor for adult asthma [9]. Thus it would be expected that, if the respective methodologies are valid, there should be a good correlation between findings in children and findings in adults in the same centres or countries. The analyses presented here show generally good agreement between the international prevalence patterns found in the ISAAC and ECRHS. In particular, there was good agreement in the international patterns observed in the two surveys with respect to "wheeze in the last twelve months" (64% of country level variation explained), self-reported asthma (74%), self-reported asthma by age 14 yrs (64%), hay fever (61%) and eczema (41%). There were similar findings at the centre level, except that the percentage of variation explained was relatively lower for self-reported asthma (36%) and self-reported asthma by age 14 yrs (26%). It should be emphasized that problems with translating terms such as "wheeze" could be expected to apply to both children and adults in a particular country, and, therefore, that even finding a perfect correlation between the two sets of study findings would not exclude systematic bias between countries. Nevertheless, these findings are reassuring and, together with the finding of good agreement between the patterns observed with the written and video asthma questionnaires in the ISAAC [5, 6], add support to the validity of the findings of both studies.

Conversely, it should be noted that the good correlation between the two sets of survey findings was, in part, because English-speaking countries showed a high prevalence in both surveys (figs. 1 and 2). A similar pattern was observed with the asthma video questionnaire [5, 6] and this finding is therefore likely to be valid. Nevertheless, if the English-speaking countries were excluded from the present analyses, the correlations observed would have been much weaker, in part simply because the range of variation was less, but also possibly because of translation problems.

Despite the strong correlations between the ISAAC and ECRHS findings, it is striking that the prevalence of "asthma ever" and "asthma by age 14 yrs" was substantially lower in the ECRHS than in the ISAAC. For

Table 2. – Regression of European Community Respiratory Health Survey (ECRHS) phase I* and phase II^{+} against International Study of Asthma and Allergies in Childhood (ISAAC) phase I prevalence data$^{\#}$

	Analysis by country				Analysis by centre			
Symptom	Coef	95% CI	p-value	R^2 %	Coef	95% CI	p-value	R^2 %
Countries/centres n	15				13			
ECRHS phase I *versus* ISAAC phase I								
Wheeze in last 12 months	0.55	0.33–0.77	<0.01	64.2	0.49	0.33–0.66	<0.01	73.7
Hay fever ever	0.66	0.37–0.94	<0.01	61.3	0.60	0.40–0.80	<0.01	72.6
ECRHS phase II *versus* ISAAC phase I								
Wheeze in last 12 months	0.63	0.36–0.91	<0.01	67.6	0.55	0.26–0.84	<0.01	58.6
Asthma by age 14 yrs	0.26	0.14–0.39	<0.01	63.5	0.19	0.00–0.38	0.09	26.3
Asthma ever	0.56	0.35–0.77	<0.01	73.5	0.41	0.07–0.75	0.04	36.2
Hay fever ever	0.74	0.34–1.15	<0.01	56.2	0.53	0.20–0.86	0.01	49.8
Eczema ever	0.51	0.13–0.88	0.02	41.4	0.50	0.19–0.81	0.01	49.5

*: Standardized for age and sex; $^{+}$: standardized for age, sex and smoking; $^{\#}$: standardized for sex. CI: confidence interval.

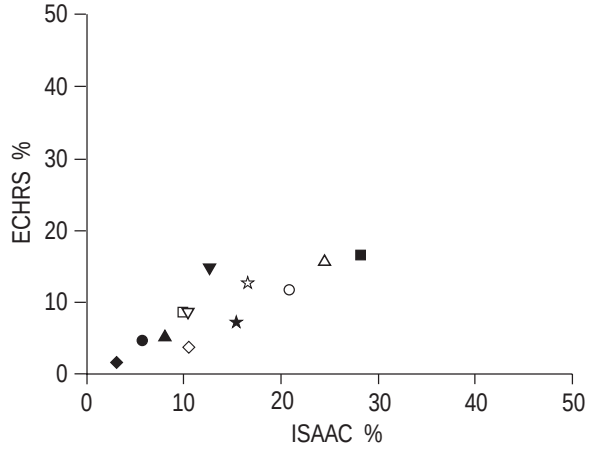

Fig. 2. – Asthma ever in European Community Respiratory Health Survey (ECHRS) phase II and International Study of Asthma and Allergies in Childhood (ISAAC) phase I by country (■: Australia; ▲: Belgium; ◆: Estonia; ▼: France; ●: Germany; ★: Ireland; □: Italy; △: New Zealand; ◇: Spain; ▽: Sweden; ○: UK; ☆: USA.)

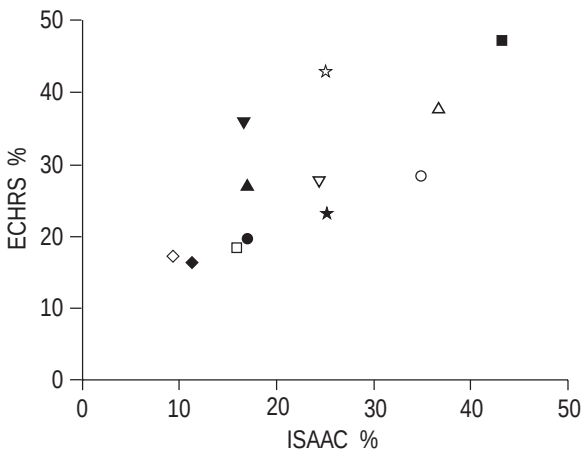

Fig. 4. – Hay fever ever in European Community Respiratory Health Survey (ECHRS) phase II and International Study of Asthma and Allergies in Childhood (ISAAC) phase I by country (■: Australia; ▲: Belgium; ◆: Estonia; ▼: France; ●: Germany; ★: Ireland; □: Italy; △: New Zealand; ◇: Spain; ▽: Sweden; ○: UK; ☆: USA.)

example, the prevalences of "asthma ever" and "asthma by age 14 yrs" in the ECRHS were 10.8 and 5.0% respectively in the UK, whereas the prevalence of "asthma ever" at age 13–14 yrs was 20.8% in the ISAAC. The reasons for this are unclear, but it is possible that the self-reported prevalence of "asthma ever" in adults may be lower because of poor recall in adulthood of childhood conditions [9]. Alternatively, these findings could represent a "cohort effect" (the two surveys have a mean age difference of ~20 yrs) with an increase in reported asthma prevalence over time, either due to changes in diagnostic practice, or a genuine rise in prevalence. A cohort effect on asthma prevalence is plausible since numerous studies in recent years have indicated that the environment encountered during the first years of life may have a large impact on the appearance of asthma and allergies later in life [10, 11]. For example, a recent Swedish study [12] showed a three-fold increase in asthma, hay fever and atopic dermatitis (but not contact dermatitis) among Swedish conscripts born after the 1950s. This cohort effect appears to have occurred in most, if not all, countries in Western Europe, Australasia and the USA. Thus, the good agreement between the ISAAC and ECRHS findings in these countries is consistent with the observation that, although these countries have undergone major changes in environment and lifestyle since the 1950s, they do not appear to have shown major divergences in their respective trends from the time when most of the ECRHS participants were born (the 1960s and 1970s) until the time when the ISAAC participants were born (the early 1980s). This is consistent with studies comparing Estonia and Sweden [13] and former West and East Germany [14], in which the differences in symptoms between these countries were mostly limited to those of <35 yrs of age.

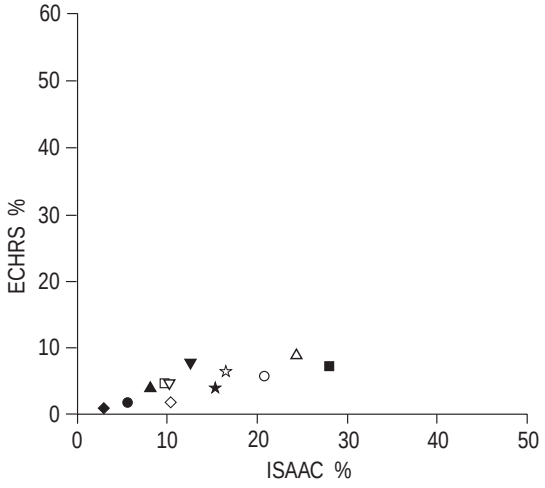

Fig. 3. – Asthma by age 14 yrs in European Community Respiratory Health Survey (ECHRS) phase II and "asthma ever" at age 13–14 yrs in International Study of Asthma and Allergies in Childhood (ISAAC) phase I by country (■: Australia; ▲: Belgium; ◆: Estonia; ▼: France; ●: Germany; ★: Ireland; □: Italy; △: New Zealand; ◇: Spain; ▽: Sweden; ○: UK; ☆: USA.)

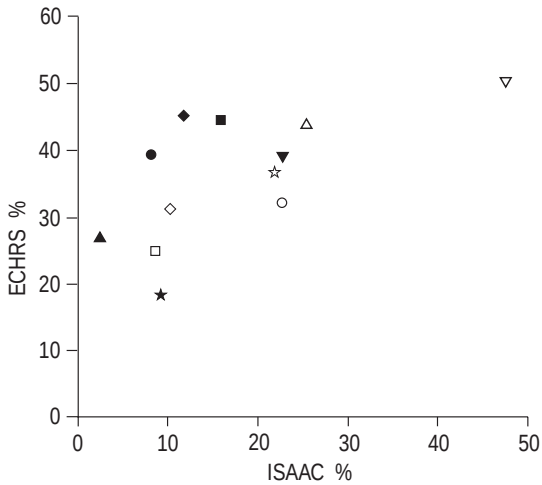

Fig. 5. – Eczema ever in European Community Respiratory Health Survey (ECHRS) phase II and International Study of Asthma and Allergies in Childhood (ISAAC) phase I by country (■: Australia; ▲: Belgium; ◆: Estonia; ▼: France; ●: Germany; ★: Ireland; □: Italy; △: New Zealand; ◇: Spain; ▽: Sweden; ○: UK; ☆: USA.)

Conversely, the prevalence of hay fever was, in general, slightly higher in the ECRHS, even though the question (table 1) focused on current hay fever, whereas the ISAAC question was on having ever had hay fever. The reason for this is unclear, but it may be because the ISAAC was conducted in children below the age of peak prevalence of hay fever.

The ISAAC and ECRHS provide, for the first time, a picture of global patterns of asthma prevalence in childhood and adult life, and enable some preliminary conclusions to be drawn.

First, both studies show a particularly high prevalence of reported asthma symptoms in English-speaking countries, *i.e.* the UK, New Zealand, Australia, the USA and Canada. This appears unlikely to be due entirely to translation problems since similar patterns were observed with the written and video questionnaires in the ISAAC [5, 6].

Secondly, amongst the non-English-speaking European countries, both studies show high asthma prevalence in Western Europe, with lower prevalences in Eastern and Southern Europe. For example, in the ISAAC, there is a clear Northwest/Southeast gradient within Europe, with the highest prevalence in the world being in the UK, and some of the lowest prevalences in Albania and Greece. The West/East gradient was particularly strong with significantly lower prevalence in former East than in former West Germany.

Thirdly, the ISAAC showed that centres in Latin America also had particularly high symptom prevalence. This finding is of particular interest in that the Spanish-speaking centres of Latin America showed higher prevalences than Spain itself, in contrast to the general tendency for more affluent countries to have higher prevalences.

Fourthly, in the ISAAC, the rest of the world outside of the Americas and Western Europe generally showed relatively low asthma prevalence. In particular, prevalence was low in developing countries such as China and Taiwan. Conversely, there were several more affluent Asian countries (Singapore, Japan and Hong Kong) which showed relatively high asthma prevalences. Perhaps the most striking contrast was between Hong Kong and Guangzhou, which are close geographically and involve the same language and predominant ethnic group; Hong Kong (the more affluent city) had a 12-month prevalence of wheeze of 10.1% compared with 2.0% in Guangzhou (the less affluent city).

These striking findings appear to be inconsistent with some "established" theories of asthma causation, *e.g.* they are inconsistent with a major role of air pollution in international patterns of asthma prevalence [5]. Conversely, they are generally consistent with some more recently proposed theories of asthma causation, including a possible protective role of some infant infections [15]. Certainly, these findings identify the key phenomena which future research, and future theories of asthma causation, must address and be able to explain.

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Appendix – Countries and centres included in the joint analysis of responders to the ECHRS and the 13–14-yr-old responders to the ISAAC

			ECHRS	
Country	Centre	ISAAC phase I	Phase I	Phase II*
Australia	Adelaide	3030	-	-
	Melbourne	2759	3220	669
	Perth	3650	-	-
	Sydney	2839	-	-
Austria	Salzburg	3371	-	-
	Urfahr-Umgebung	1515	-	-
	Vienna	-	2131	-
Belgium	Antwerp	1515	2964/3076**	1122
Estonia	Narva	1424	-	-
	Tallinn	3560	-	-
	Tartu	-	2460	431
France	Bordeaux/Pessac	3302	2936	544
	Grenoble	-	2804	473
	Marseille	3494	-	-
	Montpellier	3384	3736	456
	Nancy	-	1263	-
	Paris	-	3113	652
	Strasbourg	5403	-	-
	West Marne	2961	-	-
Germany	Erfurt	-	3272	731
	Greifswald	3169	-	-
	Hamburg	-	3312	1252
	Münster	4003	-	-
Greece	Athens	2561	3324	-
Ireland	Dublin	-	2408	454
	Ireland*	3157	-	-
	Kilkenny-Wexford	-	1724	-
Italy	Ascoli Piceno	1130	-	-
	Cosenza	1068	-	-
	Cremona	1201	-	-
	Emilia-Romagna	3961	-	-
	Empoli	1046	-	-
	Florence	1171	-	-
	Frosinone	1147	-	-
	Milan	3373	-	-
	Pavia	-	816	310
	Rome	3323	-	-
	Siena	1181	-	-
	Trent	4426	-	-
	Turin	1242	2505	244
	Verona	2208	2713	340
New Zealand	Auckland	3206	2941	-
	Bay of Plenty	2813	-	-
	Christchurch	3191	3024	457
	Hawkes Bay	3550	2979	316
	Nelson	1839	-	-
	Wellington	4424	3033	481
Portugal	Coimbra	-	1764	-
	Funchal	3532	-	-
	Lisbon	3030	-	-
	Portimão	1058	-	-
	Porto	3131	2086	-
Spain	Albacete	-	3391	435
	Barcelona	3031	2731	393
	Bilbao	3212	-	-
	Cadiz	3270	-	-
	Cartagena	3017	-	-
	Castellón	3094	-	-
	Galdakao	-	3037	486
	Huelva	-	2244	271
	Oviedo	-	2918	357
	Pamplona	3040	-	-
	Seville	-	2148	-
	Valencia	3179	-	-

	Valladolid	3178	-	-
Sweden	Gothenburg	-	2885	682
	Linköping	3377	-	-
	Umea	-	3292	552
	Uppsala	3075	3146	622
UK				
England	Anglia and Oxford	2324	-	-
	Cambridge	-	2595	277
	Ipswich	-	3390	448
	North-East/Yorkshire	3709	-	-
	North Thames	2220	-	-
	North-West	3029	-	-
	Norwich	-	3148	473
	South Thames	2297	-	-
	South and West	2707	-	-
	Sunderland	2092	-	-
	Surrey/Sussex	2114	-	-
	Trent	2207	-	-
	West Midlands	2219	-	-
Scotland	Dundee	-	4275	-
	Scotland*	4444	-	-
Wales	Caerphilly	-	2384	381
	Wales*	2351	-	-
USA	Chicago	1422/3756**	-	-
	Portland	-	2982	723
	Seattle	230	-	-
Total		182032	108171	13032

*: National random sample; **: values from two different centres given.