Prevalence of respiratory symptoms: marked differences within a small geographical area

Marjan H Wieringa, a Joost J Weyler, a Vera J Nelen, b Kristien J Van Hoof, a Frank J Van Bastelaer, a Marc P Van Sprundel a and Paul A Vermeire c

Background Geographical differences in prevalence of respiratory symptoms have been reported between countries in the EC Respiratory Health Survey (ECRHS). The differences between two neighbouring centres in the Antwerp area were surprising. We therefore extended the screening phase of this study to four other areas with different features in this region.

Methods Methods and questionnaires of the first phase of the ECRHS were used to estimate prevalence rates of respiratory symptoms in all areas. Information on some major personal and environmental risk factors was also obtained.

Results Higher prevalence rates of both respiratory symptoms and personal risk factors were recorded in Urban Antwerp, Berendrecht-Zandvliet (harbour area) and Zwijndrecht (industrial area) than in Suburban Antwerp, Essen and Kasterlee (both rural). Neither personal nor environmental risk factors could provide satisfactory explanations for the area differences in symptoms.

Conclusions These large differences between groups of subjects living within a small geographical area prove that estimations of prevalence rates of a whole country based on measurements of prevalence in one specific area should be interpreted very cautiously. Epidemiological research within small geographical areas may thus still prove as informative as comparisons between countries for elucidating causes for different asthma prevalence.

Keywords Respiratory symptoms, asthma, adults, rural, industrial, urban, suburban

Accepted 21 November 1997

Assessment of geographical differences in asthma occurrence is of considerable interest since it could contribute to identification of factors related to asthma occurrence. The EC Respiratory Health Survey (ECRHS) is one of the first large scale studies, performed within several countries across Europe and other continents, using well-standardized methods for assessing geographical variations in prevalence of asthma-related respiratory symptoms. In a first full report of the screening phase of this survey, prevalence rates of asthma symptoms and 'diagnosed asthma' have recently been shown to vary considerably between countries or geographical areas. However, within countries several studies failed to demonstrate marked differences in asthma variables even if the general characteristics of the areas under study had led some authors to expect such differences. A possible limitation of national studies performed within the ECRHS is that the study area almost exclusively involved the population of some major urban centres.

The ECRHS provided us with the first opportunity to determine asthma prevalence rates within the Belgian population. Given the absence of earlier data, we decided to participate in the ECRHS with two areas, where a secondary objective was to investigate whether differences in prevalence could be detected between areas in close proximity. We respectively selected the urban centre of Antwerp and a suburban area at the southern border of the agglomeration. As we identified large and consistent differences in prevalence rates of asthma symptoms between these areas, we decided to extend this study to other areas in the Province of Antwerp with characteristic features.

In this report we present the results of this extensive screening for respiratory symptoms within a rather small geographical area, and report our search for associations with some ecological data of the areas studied.
Methods

Areas
As prescribed in the ECRHS protocol, we had defined two study areas with a total population (all ages) of approximately 150,000 inhabitants. The first area included 13 municipalities at the southern border of Antwerp, a suburban area with residential and rural features. The second area was the busy, densely populated historical urban centre of Antwerp, delineated to the west by the bank of the river Schelde, and on the other sides by the Motorway Ring around the city. Both areas are grouped into the Arrondissement of Antwerp (total population 0.75 million). The mean distance from the centre of the 13 municipalities to the Antwerp city centre is 9 km.

In the population frames obtained from the municipality registers we randomly selected for each area a sample of 4000 subjects of Belgian nationality, aged 20-44 years. They were sent the short postal screening questionnaires during spring, respectively in 1991 for the suburban area and in 1992 for the urban area. In these two areas the same procedure was used for inviting subjects to participate.

After completion of the two Stages of the ECRHS at the end of 1992 and on the basis of the results obtained, we extended our screening in 1993 and 1994 to four other study areas: (1) Berendrecht-Zandvliet, twin villages located in close proximity to the harbour area and its chemical industry 17 km at the north-west of Antwerp centre; (2) Essen, a rural village located at the extreme north of the Province near the Dutch border, at 28 km from Antwerp city; (3) Kasterlee, a rural municipality, located at some 40 km east of Antwerp and distant from any major industry; and (4) Zwijndrecht, a suburban area, 6 km to the west of Antwerp city, which is also located close to the harbour's chemical industry. Total population in each of these four centres ranged between 14,500 and 18,000 inhabitants. Since their overall populations are much smaller than those of the first two Antwerp areas, all subjects aged 20-44 years of Belgian nationality were selected from the municipality registers for being mailed a slightly extended version of the screening questionnaire.

For all areas involved, the population density, expressed as number of inhabitants per km2, was calculated from data obtained from the statistical year book of 1993 of the province of Antwerp. Air pollution data (sulphur dioxide [SO2], nitrogen dioxide [NO2], particulate matter [PM] and ozone) were obtained from the Official Flemish network for Atmospheric Pollution Monitoring (VMM) (Table 1). Data on SO2 were available from 1991 till 1995, in all areas; but for the other pollutants, data were missing in some areas or for some years.

Questionnaire
The postal screening questionnaire (ECRHS), published previously, collected some personal information (gender, age) and further asked about respiratory symptoms (wheezing, nocturnal chest tightness, breathlessness, dyspnoea or cough, and asthma attacks occurring in the last 12 months), as well as the presence of nasal allergy and the present use of asthma medicines. To prevent any bias resulting from a prior diagnosis by a physician or from public awareness of an increased occurrence of asthma, the word 'asthma' was only used in the questions about acute symptoms and medication at the end of the questionnaire, and nowhere else, not even in the accompanying letter. Translation into Dutch had been carried out according to the ECRHS protocol which included a back translation from Dutch to English.

In the slightly extended version of the screening questionnaire used in the four areas in 1993-1994, two symptom questions from the extensive Stage II questionnaire were added; the non-specific but sensitive question about having 'ever having had trouble with your breathing' and the more specific question about 'ever having had asthma' to estimate the cumulative incidence. Nine questions used in Stage II concerning important determinants for respiratory symptoms were also added at the end of this extended screening questionnaire; they enquired about family history of asthma, smoking of the mother during pregnancy or childhood, personal smoking, having had a severe respiratory infection before the age of 5, age of completing full time education, present occupation and the occurrence of respiratory symptoms at work.

Response
In all areas two reminders were sent to the initial non-responders. In the urban and suburban areas respectively 2964 (74%) and 3076 (76%) subjects returned the questionnaire. In the other areas the response rates were also approximately 75%, with 2638 (75%), 2686 (77%) and 2774 (74%) participants responding in respectively Kasterlee, Essen and Berendrecht-Zandvliet. The response rate in Zwijndrecht was slightly lower (66%), with 1994 questionnaires returned. In total 16,132 subjects participated in this survey, approximately as many males as females (50.9% males).

In the first two areas, a random sample of the responders to Stage I was invited for Stage II, including an extended interview questionnaire, lung function and allergy testing. The response to the extended questionnaire was 70% in the suburban area and 65% in the urban area.

Statistical analysis
All data were analysed by gender. Prevalence rates were calculated by dividing the number of positive answers by the total number of responders to the particular question. Subsequently the adjusted associations between asthma variables and area of residence were calculated using a logistic regression model. For the urban and suburban area the questions about risk factors were missing in the screening questionnaire, therefore we used Stage II data on these risk factors in the analysis. To deal with the missing data for the risk factors in the two areas, a model was used including an indicator variable (dummy) for the presence of data for the risk factor and a product variable for the risk factor and the indicator variable. The statistical packages Statistica (Stat Soft, Inc., Tulsa, USA) and EGRET (SERC, CYTEL, Seattle, USA) were used for the analysis.

Results
Table 1 shows prevalence rates of all respiratory symptoms and risk factors within each area. Urban Antwerp had the highest and Essen the lowest prevalence rates for most of the symptoms.

In both rural areas males tended to have higher prevalence rates than females, while in the other areas the trend was
and the lowest in Berendrecht-Zandvliet and Kasterlee (10 µg/m³). Respectively.

Urban Antwerp and Zwijndrecht (30 and 25 |µg/m³ respectively) were found, from the lowest in Kasterlee to the highest in Urban Antwerp, had median values in all areas. In nearly all areas, males more often reported 'ever asthma' than females; in Urban Antwerp the frequency, as based on data from Stage II, was nearly twice as high as in Kasterlee. Opposite. Reporting of nocturnal coughing was higher in females in all areas. For smoking, Zwijndrecht had the lowest levels. The ECRHS Stage II data for the Antwerp centres indicated lower rates for maternal smoking during pregnancy than in the other areas, and also less frequently a low level of education.

Large differences in population density (range 236–4902 inhabitants/km²). Table 1) were found, from the lowest in Kasterlee to the highest in Urban Antwerp, but these densities did not seem to be related to symptom prevalences in the areas. For SO₂, the highest annual median values were recorded in Urban Antwerp and Zwijndrecht (30 and 25 µg/m³ respectively) and the lowest in Berendrecht-Zandvliet and Kasterlee (10 µg/m³). A slight decline in SO₂ was seen in most areas from 1991 to 1995. Ozone levels available for 1995 in Kasterlee, Berendrecht-Zandvliet and Urban Antwerp, had median values of 35; 25; 15 µg/m³, and peak values of 245; 220; 270 µg/m³ respectively. Annual median (peak) NOₓ levels were slightly higher in Urban than Suburban Antwerp (45 (225) and 40 (200) µg/m³ resp.). Peak value of PM in Suburban Antwerp was almost twice as high as in Urban Antwerp (1250 and 780 µg/m³), while the median values were similar (55 (1760) µg/m³).

Table 2 shows the associations between respiratory symptoms and area of residence, adjusted for age, familial asthma, mother smoking during childhood and pregnancy, having had a severe respiratory infection before the age of 5, education level and smoking. For each outcome variable the area with the lowest prevalence was taken as reference area. This Table demonstrates that Urban Antwerp, Berendrecht-Zandvliet and Zwijndrecht overall still had higher symptom rates than Suburban Antwerp, Kasterlee and Essen.

### Table 1 Prevalence of respiratory symptoms in the last 12 months and risk factors per area and gender (%)

<table>
<thead>
<tr>
<th>Symptom/risk factor</th>
<th>Suburban Antwerp</th>
<th>Urban Antwerp</th>
<th>Kasterlee</th>
<th>Essen</th>
<th>Berendrecht-Zandvliet</th>
<th>Zwijndrecht</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>Trouble breathing²</td>
<td>21.5b</td>
<td>26.6b</td>
<td>36.0b</td>
<td>28.2b</td>
<td>17.5b</td>
<td>15.9b</td>
</tr>
<tr>
<td>Asthma attack</td>
<td>1.20b</td>
<td>1.34b</td>
<td>2.50b</td>
<td>2.70</td>
<td>1.53b</td>
<td>1.29b</td>
</tr>
<tr>
<td>Asthma medication</td>
<td>2.20</td>
<td>2.49</td>
<td>2.94</td>
<td>3.70</td>
<td>2.83b</td>
<td>2.42b</td>
</tr>
<tr>
<td>Nasal allergy</td>
<td>20.2</td>
<td>21.5</td>
<td>25.2</td>
<td>25.3</td>
<td>17.7b</td>
<td>19.4</td>
</tr>
<tr>
<td>Ever asthma³</td>
<td>3.09b</td>
<td>5.05b</td>
<td>8.33b</td>
<td>4.80b</td>
<td>4.58b</td>
<td>3.25b</td>
</tr>
<tr>
<td>Familiar asthma⁴</td>
<td>10.4b</td>
<td>12.1b</td>
<td>12.8b</td>
<td>15.9b</td>
<td>11.8b</td>
<td>11.5b</td>
</tr>
<tr>
<td>M. smoking child,⁵</td>
<td>24.5b</td>
<td>19.7b</td>
<td>26.8b</td>
<td>31.1b</td>
<td>16.0b</td>
<td>17.9</td>
</tr>
<tr>
<td>M. smoking preg.⁶</td>
<td>5.39b</td>
<td>3.79b</td>
<td>7.66b</td>
<td>8.71b</td>
<td>9.28b</td>
<td>8.79b</td>
</tr>
<tr>
<td>Severe resp. inf. &lt;5y⁷</td>
<td>7.47b</td>
<td>10.2b</td>
<td>12.4b</td>
<td>9.80b</td>
<td>6.10b</td>
<td>4.96b</td>
</tr>
<tr>
<td>Low education level⁸</td>
<td>36.1b</td>
<td>42.4b</td>
<td>35.9b</td>
<td>39.9b</td>
<td>34.6b</td>
<td>57.2</td>
</tr>
<tr>
<td>Smoking heavy</td>
<td>10.4b</td>
<td>5.68b</td>
<td>14.4b</td>
<td>8.45b</td>
<td>7.60b</td>
<td>7.86b</td>
</tr>
<tr>
<td>Light</td>
<td>23.2b</td>
<td>19.7b</td>
<td>30.1b</td>
<td>25.3b</td>
<td>24.5b</td>
<td>20.9</td>
</tr>
<tr>
<td>Ex</td>
<td>19.1b</td>
<td>25.4b</td>
<td>19.1b</td>
<td>22.3b</td>
<td>22.9b</td>
<td>22.4</td>
</tr>
<tr>
<td>Never</td>
<td>47.3b</td>
<td>49.2b</td>
<td>36.4b</td>
<td>43.9b</td>
<td>45.0b</td>
<td>48.9</td>
</tr>
<tr>
<td>Smoking</td>
<td>33.6b</td>
<td>25.4b</td>
<td>44.3b</td>
<td>33.8b</td>
<td>32.1b</td>
<td>28.7</td>
</tr>
</tbody>
</table>


² Occurring ever in the past.
³ Data from Stage II (smaller numbers).
⁴ Asthma of father, mother, brother or sister.
⁵ Mother smoking in childhood or before birth.
⁶ Mother smoking during pregnancy.
⁷ Severe respiratory infection before the age of 5.
⁸ Age completing full-time education lower or equal than 18.
Table 2 Adjusted odds ratios (95% confidence intervals) for area of residence, including urban and suburban Antwerp Stage II data for the risk factors

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Suburban Antwerp</th>
<th>Urban Antwerp</th>
<th>Kasterlee (rural)</th>
<th>Essen (rural)</th>
<th>Berendrecht-Zandvliet (harbour)</th>
<th>Zwijndrecht (industrial)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>trouble breathing</td>
<td>ref</td>
<td>1.15</td>
<td>1.74</td>
<td>2.34</td>
<td>0.74-1.78</td>
<td>1.43-2.13</td>
</tr>
<tr>
<td>wheezing/whistling</td>
<td>ref</td>
<td>1.58</td>
<td>1.72</td>
<td>2.33</td>
<td>0.91-2.73</td>
<td>1.30-2.27</td>
</tr>
<tr>
<td>+ breathlessness</td>
<td>ref</td>
<td>1.99</td>
<td>1.77</td>
<td>2.84</td>
<td>1.34</td>
<td>1.14</td>
</tr>
<tr>
<td>+ without a cold</td>
<td>1.35</td>
<td>1.43</td>
<td>2.40</td>
<td>3.10</td>
<td>ref</td>
<td>1.23</td>
</tr>
<tr>
<td>nocturnal tightness</td>
<td>ref</td>
<td>1.58</td>
<td>1.72</td>
<td>2.33</td>
<td>1.01</td>
<td>1.14</td>
</tr>
<tr>
<td>nocturnal dyspnoea</td>
<td>ref</td>
<td>1.34</td>
<td>2.68</td>
<td>1.72</td>
<td>0.91-2.73</td>
<td>1.30-2.27</td>
</tr>
<tr>
<td>nocturnal coughing</td>
<td>ref</td>
<td>0.98-1.87</td>
<td>1.36</td>
<td>1.64</td>
<td>1.90</td>
<td>1.16</td>
</tr>
<tr>
<td>asthma attack</td>
<td>1.27</td>
<td>1.48</td>
<td>3.03</td>
<td>2.31</td>
<td>1.30</td>
<td>1.19</td>
</tr>
<tr>
<td>asthma medication</td>
<td>0.50</td>
<td>0.33-4.89</td>
<td>0.49-4.46</td>
<td>1.13-8.13</td>
<td>0.95-5.62</td>
<td>0.62-2.75</td>
</tr>
<tr>
<td>nasal allergy</td>
<td>0.14-1.77</td>
<td>1.00-5.43</td>
<td>1.05-5.02</td>
<td>0.90-4.42</td>
<td>0.72-2.11</td>
<td>0.75-2.46</td>
</tr>
<tr>
<td>ever asthma</td>
<td>1.07</td>
<td>1.07-5.43</td>
<td>1.29</td>
<td>2.07</td>
<td>1.49</td>
<td>1.06</td>
</tr>
</tbody>
</table>

\* Adjusted for age, familial asthma, mother smoking in childhood or before birth, mother smoking during pregnancy, severe respiratory infection before the age of 5, smoking and education level

\* Occurring ever in the past.
Discussion

In this extensive survey we found surprisingly large differences in prevalence of respiratory symptoms for both males and females between six different areas within a relatively close distance (maximal spread of 40 km). Higher rates were found in Urban Antwerp, Berendrecht-Zandvliet (harbour area) and Zwijndrecht (industrial area) than in southern Suburban Antwerp, Essen and Kasterlee (both rural), and there was a similar trend for a number of personal risk factors.

Large differences in reporting of respiratory symptoms were also recorded in the ECRHS. However, differences between centres within a given country tended to be small, in contrast with rather large differences in the Antwerp area. Notably, the symptom prevalence rates in Urban Antwerp, Berendrecht-Zandvliet and Zwijndrecht were close to the median values of the ECRHS, whereas those in Suburban Antwerp and the rural villages were mostly below the values of the ECRHS.

Although the surveys were made over a 4-year span, i.e. between 1991 and 1994, little or no publicity had been given to the results of the first surveys performed in Urban and Suburban Antwerp. Somewhat greater awareness for respiratory symptoms in the areas where higher prevalence was recorded cannot be excluded, especially in Berendrecht-Zandvliet, but a similar increased awareness would have been expected in Essen, which is exposed to the predominating southwesterly winds carrying exhausts from the chemical industry of the harbour area. Seasonal differences are unlikely to affect results of the ECRHS questionnaire, as was shown previously; in addition most of our surveys were carried out in approximately the same seasons, i.e. spring and early summer. The method of sampling was not identical in all areas: in both Antwerp areas only a random sample of the population (1/10 of all registered young adults) were questioned, whereas all young adults were questioned in the other areas; however, we do not expect it caused major bias in the area differences. Finally, the screening questionnaire was somewhat longer in the other areas than in both Antwerp areas, but the initial block of questions of the ECRHS screening was kept unchanged and it was still listed in the initial part of the later version.

Several studies have reported higher prevalence or mortality rates of asthma in urban areas, but it still remains unclear what factors could be responsible for this difference. Since in our combined surveys, including a total of 16,132 subjects, prevalence of several personal and environmental risk factors has been recorded, we have investigated the effects of these factors on the associations between symptoms and areas by adjusting for them. Some bias in this adjustment could have resulted from the use of data of Phase II for the Antwerp centres, if this phase had selected more subjects with more symptoms and more risk factors. However, we expect such a bias in the adjustment to be negligible. The use of Phase II data in adjusting associations between area and symptoms when Phase I data were lacking can therefore be justified.

The main personal risk factor for asthma in most Western countries is atopy and allergy to house dust mite (HDM). We recently reported that also in Urban and Suburban Antwerp HDM is the most prevalent allergen. House dust mite allergy accounted for most of the difference in a prior diagnosis of asthma between the areas, whereas different reporting of recent asthma symptoms could only poorly be explained by this or any other allergy. Since we did not perform allergy testing in the four other areas, we cannot further assess to what extent allergy could account for the differences in asthma symptoms between the six areas of this report.

Between these areas reporting of other personal risk factors was different: this was especially the case for family occurrence of asthma, mother's smoking and severe respiratory infections during childhood, as well as for smoking of the respondents. However, after adjustment it appears that differences in symptoms between areas cannot be explained by differences in the personal risk factors that were considered.

Other personal risk factors to be considered relate to socioeconomic status (SES), although their role remains controversial. In our study we used the age of leaving school as a proxy variable for SES, but this proxy factor hardly explained the symptom differences. Some recently reviewed studies suggest that changes in diet introduced during the last decades in Essen could be responsible for the increase in asthma and rhinitis. We did not collect information about this factor, but differences between the areas seem quite unlikely in this homogeneous Flemish population.

Effect of outdoor air pollution is also to be considered when seeking an explanation for our areas' differences in asthma occurrence. Population density could be a rough index for the degree of urbanization and thus for the degree of environmental air pollution; although there were large differences in density of population between areas, we do not expect that they could account for the differences in respiratory symptoms. Parameters of air pollution usually considered include NO\textsubscript{x}, ozone, SO\textsubscript{2}, as well as suspended particles, especially those with diameter less than 10\textmu m, mostly attributed to vehicle exhausts, especially from diesel vehicles. A recent report summarizes the association between environmental pollution and asthma occurrence and concludes that 'as regards initiation of asthma most available evidence does not support a causal role of non-biological air pollution'. This conclusion is supported by the study of Devereux et al. who failed to find differences in asthma prevalence between two English areas with marked differences in air pollution.

In our study the urban city centre of Antwerp and the chemical industry in the harbour area were also presumed to have a higher degree of air pollution, and in fact we recorded a much larger difference in symptom prevalence in these areas versus the suburban and rural areas than was recorded in the English study. We therefore attempted to collect data to confirm differences in air pollution. Unfortunately the air pollution monitoring system in our region is quite incomplete. Data are often only collected at one point per area, which was not necessarily representative for the whole area; as an example the sampling station for the suburban area was located quite near a highway. Still we estimate that collected levels could at least have provided an indication for the severity of pollution within each area.

For NO\textsubscript{x} we only had data for two areas, without any indication that there were more asthma symptoms in the area with higher average levels for NO\textsubscript{x} pollution. For SO\textsubscript{2} a clear association was also lacking, since high symptom prevalence rates in Urban Antwerp indeed corresponded to the highest mean and peak levels, but on the other hand high prevalence rates in Berendrecht-Zandvliet corresponded with the lowest levels of
SO₂. Data on ozone concentrations were available in three of our
areas and none showed an association with symptoms. Unfortu-
nately PM₁₀ had not been measured at the time of our study,
but data on PM in two areas again failed to show any indication
for an association with respiratory symptom rates. Our fragment-
ary findings obviously do not exclude air pollution as a cause for
area differences, but surely fail to support it. Recent studies suggest
that pollutants could act indirectly by decreasing the threshold
of allergen exposure to cause bronchoconstriction, but we
have no data to support this interesting hypothesis.

Occupational exposure could also be considered as a cause of
symptom differences between subjects and areas. Available
evidence here is quite indirect and speculative. A higher degree
of occupational exposure could explain why in rural areas
more males tended to report respiratory symptoms than females. Symptom differences between the areas seemed to be
larger in females, possibly indicating that in them 'true' area
differences are less confounded by occupational exposure.

At this stage we obviously failed to provide robust plausible
explanations for the marked differences in asthma symptom
prevalence between the various areas in and around Antwerp,
this also applied for HDM allergy, which was only assessed in
Urban and Suburban Antwerp. We therefore need to proceed
further, for example by documentation and adjustment for per-
sonal factors, by more adequate measurements of air pollution
and by considering additional risk factors.

In conclusion, surprisingly large differences in respiratory
symptom prevalence rates were found in young adults living in
a small geographical area. Therefore, estimations of prevalence
rates of a whole country based on measurements of prevalence
in one specific area, as done in some large international preval-
ence studies, should be interpreted very cautiously. Our results
confirm that epidemiological investigations in the field of asthma
should not be limited to large urban populations of different
countries or continents, since studies in relatively small areas
may prove as informative for elucidating causes for different
asthma prevalence.

Acknowledgements
This study was supported by Grant # HH/06/43 of the Impulse
Programme ‘Health Hazards’ of the Belgian Science Policy
Office and by a grant of the Nationaal Fonds voor Geneeskundig
Wetenschappelijk Onderzoek. Full support was also given by
Dr B Standaert, Director of the Provincial Institute of Hygiene
and Dr M Udberg, Director of the Flemish Lung and
Tuberculosis Association (VRGT). The authors also gratefully
acknowledge the invaluable technical help of Mrs L Claus,
L Thys, C Van den Heuvel, R Claes, G Van de Vyver as well as
Mr M Willemen and J Geldhof. Part of the results presented are
from a national analysis of data collected from the ECRHS;
any final international comparison may use a different form of
analysis. The authors are greatly indebted to Prof. P Burney,
C Luczynska, S Chinn and D Jarvis for providing the full
support of the ECRHS during the survey.

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