Title: Respiratory symptoms in children living near busy roads and their relationship to vehicular traffic: results of an Italian multicenter study (SIDRIA 2)

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Abstract:

Background

Epidemiological studies have provided evidence that exposure to vehicular traffic increases the prevalence of respiratory symptoms and may exacerbate pre-existing asthma in children. Self-reported exposure to road traffic has been questioned as a reliable measurement of exposure to air pollutants.

The aim of this study was to investigate whether there were specific effects of cars and trucks traffic on current asthma symptoms (i.e. wheezing) and cough or phlegm, and to examine the validity of self-reported traffic exposure.

Methods

The survey was conducted in 2002 in 12 centers of Northern, Center and Southern Italy, different in size, climate, latitude and level of urbanization. Standardized questionnaires filled in by parents were used to collect information on health outcomes and exposure to traffic among 33632 6-7 and 13-14 years old children and adolescents. Three questions on traffic exposure were asked: the traffic in the zone of residence, the frequency of truck and of car traffic in the street of residence. The presence of a possible response bias for the self-reported traffic was evaluated using external validation (comparison with objective measurements of traffic flow in the city of Turin) and internal validations (using unconditional and conditional regression models matching by census block, in the cities of Turin, Milan and Rome).

Results

Overall traffic density was weakly associated with asthma symptoms but there was a stronger association with cough or phlegm (high traffic density OR=1.24; 95% CI: 1.04, 1.49). Car and truck traffic were independently associated with cough or phlegm. The strongest associations were found when asthmatic symptoms and cough or phlegm were combined as the final outcome (for high traffic density OR=1.52; 95% CI: 1.17, 1.96). The results of the external validation did not support the existence of a reporting bias for the observed associations, for all the self-reported traffic indicators examined. The internal validations showed contradictory results, but the observed association between traffic density in the zone of residence and respiratory symptoms did not appear explained by an over reporting of traffic by parents of symptomatic subjects.

Conclusions

Children living in zones with intense traffic are at higher risk for respiratory effects.

Background

Vehicular traffic is a major source of outdoor air pollution. Several studies have reported associations between exposure to traffic pollutants in the zone of residence and increased frequency of respiratory tract illnesses [1-10]. A specific role of diesel exhaust from heavy traffic has been suggested in some of these studies [4, 5, 7], and airway inflammation due to exposure to diesel exhaust seems the likely biological mechanism [11, 12]. With respect to the type of respiratory disorder, consistent associations have been found between exposure to traffic fumes and bronchitis symptoms, while the role of these exposures in the etiology of asthma is still unclear [13].

The SIDRIA project - Studi Italiani sui Disturbi Respiratori nell'Infanzia e l'Ambiente [14-16] - is a large multi-center, population-based study conducted in the framework of the International Study of Asthma and Allergies in Childhood (ISAAC) [17]. The findings from SIDRIA-1, conducted in 1994-1995, showed a positive association between indicators of air pollution from heavy vehicular traffic in the street of residence and a wide range of respiratory disorders in children living in highly urbanized areas [18]. However, it was not possible to assess the independent effects of car and truck traffic in that study as the information was not available. A second phase of SIDRIA was conducted in 2002 to evaluate time trends in the prevalence of respiratory disorders in childhood, according to the ISAAC Phase III protocol [19], to confirm the role of several potential risk factors identified in SIDRIA-1 and to explore some new hypotheses.

Self-reported exposure to road traffic has been recently questioned as a reliable measurement of exposure to air pollutants [20-22]. Heinrich et al [20] compared parental report of traffic intensity at the home address with a combination of air pollution measures and GIS based modelled exposure in two different European countries (Germany-Munich and the Netherlands). They found that the degree of agreement between the two methods was relatively low, but the reasons for these discrepancies were not analyzed.

Kuehni et al [21] estimated the association between self-reported exposure to road traffic and respiratory symptoms in preschool children in Leicestershire, UK, and investigated whether the effect could have been caused by reporting bias. The association between traffic exposure and respiratory outcomes was assessed using unconditional logistic regression and conditional regression models (matching by postcode). Matched analysis comparing symptomatic and asymptomatic children living at the same postcode (thus theoretically exposed to similar road traffic) showed odds ratios similar to those observed using the unconditional logistic regression, suggesting that parents of children with respiratory symptoms reported more road traffic than parents of asymptomatic children.

In this paper, based on the data from SIDRIA-2, we present an analysis of the relation between indicators of road traffic pollution and several chronic respiratory symptoms. The main purpose of this analysis was to confirm previous results and to evaluate the possible independent respiratory effects of each type of traffic exposure (truck traffic or car traffic). Since chronic cough may be a manifestation of asthma or it may occur also in otherwise healthy children, we have tried to distinguish the risk factors of asthma symptoms and of symptoms of persistent cough or sputum production (cough or phlegm). A further purpose of the present study was to examine the potential reporting bias due to an over-reporting of traffic intensity by parents of symptomatic children, performing both external and internal validation of the data.

Methods

Population and study design

The SIDRIA-2 study design has been described elsewhere [15, 16, 23] and it will be only summarized here. The survey was conducted in 2002, between January and May, in 12 centers (Bari, Colleferro, Emilia-Romagna, Empoli, Florence, Mantova, Milan, Palermo, Rome, Siena, Turin, Trento) of Northern, Center and Southern Italy, different in size, climate, latitude and level of urbanization. Eight of these centers had already participated in SIDRIA-1 [18]. The protocol of the study was approved by Ethics Committee of the Catholic University in Rome.

The sample included 22442 children (6-7 years old) and 16336 adolescents (13-14 years old) attending respectively the first two grades of the primary school and the last year of the middle school. The primary sampling units were schools, both public and private, weighted for the number of attending subjects. Each center contributed with at least 1000 subjects for each age group.

Data collection

To collect information on the medical history of the children, we used standardized, self administered questionnaires that included also the relevant ISAAC-Phase III questions on asthma, rhinitis and eczema symptoms, and questions on various known or suspected risk factors. For children (6-7 years old), all questionnaires were completed by parents. According to the standard ISAAC protocol [17], the questionnaires for adolescents were filled by adolescents themselves. However, in the SIDRIA study, another questionnaire, including questions on both symptoms and risk factors, was also completed by the adolescents' parents. For reasons of consistency and comparability between age groups, the current analyses are based on the parental questionnaires for both age-groups.

Children with "asthma symptoms" were defined as those reporting in the past 12 months at least one of the following: one or more wheezing episodes, wheeze with exercise, morning chest tightness; or if they reported night dry cough in the last 12 months and had a reporting of lifetime asthma; or those reporting treatment for medically diagnosed asthma or had a hospital admission for asthma in the last 12 months; or if they reported a life time asthma and a positive answer to the question "Is your child still suffering from asthma?".

Children were defined as having "severe asthma" if in the past 12 months at least one of the following were reported: 4 or more wheezing attacks, waking at night with wheezing one or more times a week, an attack severe enough to limit speech to only one or two words at a time between breaths, or a hospital admission for asthma.

Children were defined as having “cough or phlegm” if they reported cough or phlegm for at least 4 days a week (in the absence of a cold) for one or more months a year.

Questions on traffic included a parental subjective evaluation of traffic density in the zone of residence (“absent”, “low”, “moderate” or “high”) and of the daily frequency of passing cars and trucks in the street of residence (“never or seldom”, “sometimes”, “frequently”, “continuously”). The exact wording is reported in the Appendix 1 (Table 1).

Data analyses

Odds ratio (OR) and 95% confidence intervals (95% CI) were estimated with multiple logistic regression analyses. The basic analyses were for “asthma symptoms” and “cough or phlegm”, but we also conducted multinomial logistic regression analyses comparing: i) those with asthma symptoms without cough or phlegm; ii) those with cough or phlegm without asthma symptoms; and iii) those with the combination of the two conditions, with the remaining subjects, negative for both symptoms. For “cough or phlegm”, the analyses focused on the possible independent effect of cars and trucks transit in the street of residence. In some of the analyses, in order to obtain sufficient numbers in each category, car transit was recoded into three categories (“absent/sometimes”, “frequently” and “continuously”) and truck transit was also recoded into three categories (“absent”, “sometimes” and “frequently/continuously”).

Potential confounding factors included in the multiple logistic regression models were: sex, age, parental asthma or allergy (rhinitis or eczema), parental education (higher educational level between parents as a proxy of socioeconomic status – SES), passive smoke at home (at least one smoker -mother, father or others- in the household), indoor mould/dampness, floor of the apartment, change of residence and study area. The effect of cluster sampling by school was considered and each regression model was adjusted for autocorrelation within schools. In order to explore the role of potential effect modifiers, we performed subgroup analyses for different factors (age, gender, latitude, parental education, smoking, parental asthma or allergies, level of urbanization, indoor mould/dampness, floor of the apartment, change of residence), in each case considering the associations of truck traffic exposure (frequent or continuous vs never) and the investigated respiratory symptoms. Statistical significance of the interaction terms were evaluated. All analyses were conducted using STATA 9 (Stata Corporation, College Station, Texas).

Data validation

External validation. In the city of Turin objective data on traffic flows were obtained from the local company of public transportation (5T S.C.R.L), that measures hourly traffic mostly in street segments with medium-high volume of traffic. The address of each subject included in the survey was geocoded and linked to objective data on traffic using a Geographical Information System (GIS). We excluded 204 subjects (out of 3453) attending a school in the municipality but resident outside the city of Turin, for which objective traffic information and geocoding was not available. For each segment of street we calculated average daily vehicle count in work hours (h.07-19) weighted by the number of observations available; this information was linked to the subject using a computer based GIS, excluding subjects living in internal civic numbers. We positively matched 887 subjects out of 3249 (328 street segments out of 1067). All GIS analyses were performed with the ArcGis software version 9 (ESRI, Redlands, CA). We analyzed the frequency distribution for some characteristics of the subjects, including reported traffic, separately for children linked with objective traffic count and for non-linked subjects. We performed the Kruskal-Wallis test to assess the differences between median traffic counts and calculated robust confidence intervals for Hodges-Lehmann median differences. The same analysis was performed for subjects with and without a reporting of current respiratory symptoms, separately for asthmatic symptoms and cough or phlegm (ANOVA test).

Internal validation. In the 3 metropolitan areas of Turin, Milan and Rome (N=10285), we matched the children by census block. The assumption is that within this small area (f.i., in Turin a census block covers a mean of 250 subjects - [24]) the true exposure to road traffic in an urban context would be similar; therefore, if the association between traffic exposure and symptoms is true, it should disappear when the comparisons are stratified by census block (matched analysis, using conditional logistic regression). For this analysis, only data from census blocks where at least one symptomatic and one asymptomatic subject were living could be used; therefore, a varying number of census block was included in the analysis for each of the respiratory symptoms examined. To further investigate the possibility of a reporting bias, in the subgroup of subjects that could be matched by census block we performed a further unconditional logistic regression analysis after attributing to symptomatic subjects the mean traffic exposure reported by parents of asymptomatic subjects; in this way, we theoretically excluded the possibility of a bias due to over-reporting of traffic by parents of symptomatic subjects. In these analyses, reported life time asthma was also included as an endpoint .

Results

The parental questionnaire was completed for 20016 6-7 years old (response rate 89.2%) and for 13616 13-14 years old (response rate 83.3%). Table 1 shows the combined prevalence of asthma symptoms and cough or phlegm. Overall, 13.5% of children (95% CI: 13.2%, 13.9%) were reported to have asthma symptoms, and 6.8% (95% CI: 6.6%, 7.1%) to have cough or phlegm. For 2.9% (95% CI: 2.7%, 3.0%) of the subjects, cough or phlegm and asthma symptoms were concomitant. The frequency of each traffic indicator is presented in Table 2 of the appendix.

The prevalences of respiratory symptoms in the various subgroups are shown in Table 2. Respiratory symptoms were more frequent if a parental history of asthma or allergies was reported, among subjects exposed to passive tobacco smoke and in the presence of moulds/dampness in the child's bedroom. The prevalence of respiratory symptoms increased inversely with parental education, and directly with urbanization level.

Table 3 shows the associations of traffic indicators with asthma symptoms and with cough or phlegm. Reported high traffic density, continuous car transit and continuous truck transit in the street of residence were weakly associated with asthma symptoms. There were stronger associations of reported high traffic density, continuous car transit and continuous truck transit with cough or phlegm. The associations were generally stronger for truck transit than for car transit.

For comparison with the literature, we present the results of the associations for different asthma symptoms in Table 3 of the appendix. In the same table, we also report the associations separately for light and severe asthma symptoms, and for symptoms of cough or phlegm of different duration (1-2 months a year and 3 or more months a year). Light and severe asthmatic symptoms, as well as symptoms of cough or phlegm of different persistence, did not show a clear pattern with traffic indicators; only for truck traffic the data suggest a trend for stronger associations in subjects with more severe symptoms.

The relationship between these traffic indicators and the respiratory outcomes was explored in detail (Table 4) evaluating the associations with asthma symptoms without cough or phlegm, cough or phlegm without asthma and the combination of the two conditions. Asthma symptoms, when alone, were only weakly associated with high traffic density, continuous car and continuous truck transit. Traffic exposure indicators were more strongly associated with cough or phlegm, and particularly when accompanied by asthma symptoms. For this last condition (asthma with cough or phlegm) there were strong and significant associations for all the indicators.

The analyses of the independent and joint effects of truck traffic and car traffic on the risk of cough or phlegm are shown in Table 5. In some categories the numbers are relatively small and the effect estimates are therefore unstable. The table confirms an independent effect of truck transit on cough or phlegm (OR=1.50; 95% CI: 0.93, 2.43), and also shows a similar association for car transit (OR=1.30; 95% CI: 0.94, 1.81).

Further analyses were performed to explore the possible effect modifiers of the association with frequent or continuous truck transit (Figure 1). Higher risks were observed for females for asthma symptoms (OR=1.34; 95% CI: 1.17, 1.53) and cough or phlegm (OR=1.62; 95% CI: 1.33, 1.98) than for males (OR=1.08; 95% CI: 0.94,1.24; and OR=1.35; 95% CI: 1.14, 1.60 respectively). The pattern was present for both age groups. Cough or phlegm were more associated with truck transit in the Northern areas of the Country (OR=1.75; 95% CI: 1.47, 2.08) than in the Central and in the Southern areas (OR=1.37; 95% CI: 1.10, 1.71 and OR=1.09; 95% CI: 0.78, 1.51). Asthma symptoms were more associated with truck transit in the urban or rural areas (OR=1.31; 95% CI: 1.16, 1.47) than in the metropolitan areas (i.e. municipalities with more than 500.000 inhabitants) (OR=1.03; 95% CI: 0.87, 1.21). For both symptoms, higher associations (not statistically significant) were observed for the lowest level of parental education (13 years or less) than for the highest levels (high school/University). Asthma symptoms were more associated with truck transit when parental asthma or allergies were not reported. Age, smoking, presence of mould stain, change of residence and floor level did not act as effect modifiers. Comparable results were observed for the indicator of continuous car traffic (Figure 1 appendix).

Results of the external validation

The subgroup of subjects linked with traffic data had a consistent and significantly higher exposure to all the reported traffic indicators ($p<0.0001$, Tab 4 appendix). This was an expected result, given the fact that objective traffic data are available mostly for streets with high traffic intensity. In this subgroup, a lower prevalence of asthmatic symptoms was observed.

All traffic indicators from questionnaire predicted the daily median number of vehicles passing in work hours: for lorry frequency “never or seldom”=8549 (95% CI: 6500, 9073), "sometimes"=10626 (95% CI: 9580, 11525), "frequently"=14359 (95% CI: 12848, 15834), "always or nearly always"=19120 (95% CI: 16817, 22618); the same was observed for the three categories of traffic density in the zone: "absent\low"=8459 (95% CI: 5332, 9073), "intermediate"=10109 (95% CI: 8857, 10692), "high"=17745 (95% CI: 15814, 18722) and for car frequency: "never\sometime"=7378 (95% CI: 5042, 9566), "frequently"=9840 (95% CI: 8914, 10692), "always or nearly always"=15277 (95% CI: 13664, 16873). The Kruskal-Wallis test for median traffic count by categories of each traffic question was always highly significant ($p<0.0001$). The same analysis was performed separately for subjects with and without a reporting of current respiratory symptoms. Figure 2 reports the results of this analysis for subjects with and without symptoms of cough or phlegm; at the ANOVA test there were no differences between the two groups of symptomatic and asymptomatic subjects in the daily median number of vehicles passing in the road of residence. F.i., the p-value for the interaction were $p=0.3997$ for traffic density in the area of residence; $p= 0.2659$ for truck transit and $p=0.9149$ for car transit. Similar results were obtained when we analysed separately the subjects with and without a reporting of asthmatic symptoms (data not shown).

Results of the internal validation

In the overall sample recruited in the cities of Turin, Milan and Rome, we obtained valid addresses for 88.8% out of 10285 subjects, leaving N=9034 subjects that were included in the following analysis (whole sample). Tables 5 and 6-appendix report the descriptive characteristics of the whole sample and of the subgroup of subjects matched by census block for cough or phlegm, for which only 2446 subjects could be included (498 census blocks out of 4210). This subgroup differed from the whole sample in a lower level of parental education, a higher prevalence of younger children and a lower exposure to traffic in the zone of residence and of car traffic in the street of residence. The higher prevalence of symptomatic subjects is due to the procedure of matching.

In the whole sample, significant associations were observed for symptoms of cough or phlegm for all the three indicators of exposure, while no significant associations were present for current asthma symptoms or lifetime asthma (Figure 3-first column).

Figure 3 (second column) shows the associations between traffic indicators and respiratory symptoms using unconditional logistic regression in the subgroup of subjects matched for cough or phlegm: a similar pattern compared with those of the whole sample (first column) was found for symptoms of cough or phlegm, while higher risks were present for asthma symptoms and particularly for lifetime asthma. The results of the conditional regression analysis (Figure 3-third column) differed according to the traffic indicator examined. When traffic density in the zone of residence was considered, no association was still present, for all the endpoints. When the two indicators of the traffic in the street of residence were considered, the ORs for lifetime asthma reduced and were not statistically significant, the ORs for current asthma symptoms reduced or remained stable and not statistically significant, while those for cough or phlegm remained positive and statistically significant.

The results of the unconditional logistic regression analysis in which, for each census block, we attributed to symptomatic subjects the mean traffic exposure reported by parents of asymptomatic subjects are reported in Figure 4 (second column). For all the outcomes and all the traffic indicators (except for the comparison between cough or phlegm and truck traffic) the associations remained stable and the point estimates were often higher than those observed using original data (Figure 4-first column).

Discussion

This study confirms our previously-reported associations between frequency and density of traffic in the street of residence and current respiratory symptoms in children [18]. For all indicators of traffic density and frequency, an increase in symptoms by level of exposure was observed. The strongest associations were for cough or phlegm and truck traffic, although an independent effect of continuous car traffic was found. Traffic fume exposure was weakly associated with asthma symptoms, but the association was stronger if asthma was accompanied by cough or phlegm.

The results of the external validation did not support the existence of a reporting bias for the observed associations, for all the self-reported traffic indicators examined. The internal validations showed contradictory results, but the observed association between traffic density in the zone of residence and respiratory symptoms did not appear explained by an over reporting of traffic by parents of symptomatic subjects. The statistical methods applied for the internal data validation appear to have limitations, and studies that specifically address the issue of response bias are warranted.

Interpretation of the results

Few published studies have analyzed the effects of traffic in relationship to combinations of respiratory outcome such as asthma symptoms and persistent cough or phlegm. A positive association of air pollution with bronchitis symptoms, but not with asthma, has been reported in some studies [3, 6]. Other studies found both associations; e.g. Kim et al. [25] found a significant increase in the risk of bronchitic symptoms and asthma in relation to higher level of traffic related to pollution in a US area with relatively clean air [25]. However, the findings of different studies should be compared with caution, because the definition of asthma adopted may be different and it can often include symptoms that may be related to bronchitis rather than to asthma [26]. In fact we have found an increased risk of asthma symptoms in children exposed to car and truck traffic fumes, essentially restricted to those who also reported cough or phlegm. There are two possible explanations for these findings. Firstly, it is possible that these children only had chronic bronchitis and did not have asthma symptoms, i.e. that they were “misdiagnosed” by our asthma symptom questionnaire [27]. The second, and perhaps more likely explanation, is that these children experienced an increased risk for a form of asthma that also involved persistent cough and phlegm.

Several previous questionnaire-based studies and surveys that used objective traffic counts as exposure metrics, have suggested that heavy traffic powered by diesel engines is more harmful for respiratory health than light traffic powered by gasoline engines [13, 26]. When we analyzed the effects of car and truck traffic separately on cough or phlegm, we found a stronger association with heavy traffic exposure (Table 4), consistent with the findings from other studies [4, 7, 9]. In the study conducted by Janssen and coworkers [7], chronic respiratory symptoms were positively associated with high truck traffic and with air pollutants related to truck traffic counts [7]. In a cross-sectional study conducted on a sample of 1242 children (7-12 years old) [9], respiratory symptoms were more prevalent among children attending schools located close (<100 m) to highways, particularly if the highway had a high truck traffic density.

We found significant associations of car traffic with cough or phlegm, although these were generally weaker than the associations for truck traffic (Tables 4 and 5). These findings could indicate that car traffic may also represent a source of pollutants increasing the risk of chronic cough or phlegm. However, these findings could also be related to the very high, and still increasing, number of cars powered by diesel engines at present circulating in Italy [28], and does not necessarily indicate that other types of car fume exposure also increase the risk of respiratory symptoms. Children exposed to both, continuous car traffic and frequent or continuous truck transit, showed the highest risk of cough or phlegm (Table 5). This is consistent with the hypothesis that truck and car traffic involve similar exposures (e.g. diesel fumes).

With respect to exposure to heavy traffic and related respiratory outcomes, we found stronger associations in females, for both age groups. An increased susceptibility of girls to air pollution has been reported by several investigators [4, 9, 10, 25] and was partially observed also in SIDRIA-1 [18]. A higher pollutant-to-lung volume ratio that results from larger airways relative to lung size in girls than in boys and enhanced cholinergic irritability could be considered as possible explanations

[29, 30]. A gradient in the geographical distribution of the ORs for truck exposure and cough or phlegm is present in our data. This trend is consistent with the hypothesis that geo-climatic factors characterizing the Northern regions do favor accumulation of atmospheric pollutants. We do not have a direct interpretation for the strong association (although not statically significant) between truck frequency and cough or phlegm in children of less educated parents, but it should be noted that the same type of effect modification by socioeconomic status has been seen in other studies of air pollution, regarding short term [31, 32] and long term effects [33].

In contrast with the findings of the previous phase of SIDRIA, for symptoms of cough or phlegm we did not observe stronger associations among subjects living in metropolitan areas compared to those living in less urbanized areas; on the contrary, stronger associations were observed for asthma symptoms among urban-rural areas. A possible interpretation may be the presence of higher contrasts in pollution levels in urban-rural areas than in metropolitan areas.

Strengths and limitations

The main strength of the present study is that it was based on a large random general population sample with a high response rate (86.7%). The information on symptoms of asthma and cough or phlegm included items derived from standardized validated questionnaires, that have been used in previous epidemiological studies in this population [34] and internationally [17].

The main weakness of our study is that it relies for both symptoms and exposure on self-reported information. In this study, the validity of information on traffic exposure was deeply evaluated in order to examine the existence of a possible reporting bias due to an over-reporting of traffic intensity by parents of symptomatic children, suggested by some authors [21].

In the subgroup of children for which objective measurements of traffic in the segment of street of residence were available in the city of Turin, we observed that the daily median count of vehicles was well predicted by the categories of traffic indicators reported by parents, without systematic differences between symptomatic and asymptomatic children. A similar finding was observed in the same city in the first phase of the SIDRIA study [18]. These results do not support the existence of a reporting bias for the observed associations, for each of the traffic indicators and each of the respiratory symptoms examined. The major limitations of this external validation are that it was possible in a single centre and it was based on a selected group of highly exposed subjects that could be linked with an objective measure.

Applying a method comparable to that used by Kuehni et al [21] where 7-digit postal code was used as a variable of matching, we observed that the associations between reported traffic (trucks or cars) in the street of residence and symptoms of cough or phlegm did not disappear in the conditional logistic regression where subjects were matched by census block (Fig.3). On the contrary, any associations disappeared when the reported traffic in the zone or residence (that is, an area based indicator) was examined in the conditional analysis, for each of the respiratory symptoms. These results could imply that parents of subjects with symptoms of cough or phlegm could over-report the traffic in the street of residence (but not the traffic density in the zone of residence). However, another plausible explanation for these findings is the presence of a residual variability in the type of roads within the same census block. Actually, subjects that live in the same census block share the same traffic intensity of the area (zone), not necessarily of the street, in which they live.

The main limitation of these procedures of matching (according to which at least one symptomatic and one asymptomatic subject have to be present in each census block or in each street) is the small number of subjects included in the analyses. Furthermore, the results suggest that the subjects included in the subgroup analyses can be strongly selected, i.e. no more representative of the whole population.

To further investigate the existence of a possible reporting bias, in the subgroup of subjects that could be matched by census block we performed an unconditional logistic regression analysis after attributing to symptomatic subjects the mean traffic exposure reported by parents of asymptomatic subjects; in this way, we theoretically excluded the possibility of a bias due to over-reporting of traffic by parents of symptomatic subjects. The results of this analysis (Fig.4) could imply the existence of an over-reporting of truck traffic (but not of car traffic and of traffic in the zone of residence) by parents of subjects with cough or phlegm (but not with current or lifetime asthma). However, we think that these results should be interpreted cautiously, due to the previously discussed limitations of the procedure of matching.

Kuehni et al [21] reported that parents of children with more severe respiratory problems (i.e. asthma diagnosis and bronchodilator use) are particularly prone to overestimate traffic exposure, given that they have "received the broadest media coverage with regard to air pollution". However, in the total sample included in the SIDRIA study, we consistently found the strongest associations with traffic indicators for symptoms of cough or phlegm rather than for asthma symptoms; furthermore, severe and light asthmatic symptoms did not show a different association with traffic indicators. The validation analyses consistently did not show evidence of an over-reporting of traffic by parents of children for which current or lifetime asthma was reported. Therefore, if a reporting bias is present, this should be related mainly to the presence of symptoms like cough or phlegm. Although not impossible, it seems unlikely that parents of children suffering for cough or phlegm are more prone to over-report traffic exposure while parents of children suffering for asthma are not.

The study of Piro et al [22] suggested that subjects with a chronic diseases tend to report more air pollution problems in area of living. In our study (Fig 1), parental asthma or allergy did not act as modifiers of the association between cough or phlegm and truck traffic; for asthma symptoms, the association was stronger among parents that did not report asthma or allergies. Other studies have found that the association between exposure to traffic and asthma are higher among children with no reported family history [35, 36] or maternal history of asthma [37]. These findings are reassuring with regards to the possibility of a reporting bias due to an over-reporting of traffic information among parents suffering from asthma or allergic disorders.

The possibility of important residual confounding in our results is low, as we adjusted for several known or suspected risk factors for respiratory symptoms; however, we lacked some outdoor and indoor information, like ventilation characteristics of the house. Indeed, in Italy different times of windows' opening have been reported between North and Central Italy [38], even if the magnitude of the effect was small on indoor air pollutants concentrations.

Our questionnaire was focused on traffic pollution in the street and zone of residence, but did not collect information about other exposures such as those close to the schools. The absence of these details could have led to a small random misclassification of the exposures in the participants, while it seems unlikely as an explanation of the observed positive associations.

For reasons of consistency and comparability between age groups, we based the analyses on the parental questionnaires for both age-groups. However, in a sensitivity analysis we examined the associations between traffic indicators and respiratory symptoms including the answers on symptoms given by adolescents (Table 7 appendix). The results for the outcome of cough or phlegm were substantially unchanged.

Conclusions

Although the specific set of airborne toxicants that facilitate and promote respiratory effects are still not known, our findings add further evidence to support a causal effect of exposure to traffic road pollution on respiratory illnesses in childhood. The limitations of the validation methods applied indicate the need of studies that specifically address the issue of response bias, in order to verify its existence and to correctly quantify it.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

EM assisted in the planning of the study, data collection, data management and analyses and drafted the manuscript. GB was involved in statistical analyses, interpretation of the results, and helped drafting the manuscript. CG was national coordinator of the study, conceived the study and participated in its design and conduction and in the manuscript preparation. NP contributed to data analyses, interpretation of the results, and critical review of the manuscript. FF, LB, ECh, GG, PS, VDO, LA, CG and GC were local coordinator and were involved in the conception and design of the study, acquisition of local data, interpretation of the results, and critical review of the manuscript. RC was involved in statistical analyses and performed the GIS analyses. AB and GV participated in the study design, statistical analyses, and revision of the manuscript. MB, RP and LA, as respiratory specialists, were involved in medical data collection, interpretation of the results and revision of the paper. EC, as air quality specialist, contributed to exposure assessment and critical review of the manuscript. All of the authors have read and approved the final version of the manuscript.

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Figure legends

Figure 1: Associations between exposure to truck transit and respiratory symptoms, by several characteristics. The figure reports the associations (OR and 95% CI) between exposure to truck transit (frequent/continuous *vs* never) and asthma symptoms and cough or phlegm, by different factors (age, gender, latitude, level of urbanization, parental education, indoor mould/dampness, change of residence, floor of the apartment, passive smoke at home, parental asthma or allergies). All ORs were adjusted for potential confounder, excluding the stratification factor. Statistical significance (p values) of the interaction terms are reported. SIDRIA 2.

Figure 2: Box Plot of the daily number of vehicles by categories of traffic indicators. The figure reports the daily number of vehicles by traffic in the zone of residence (upper), truck transit in the street of residence (intermediate) and car transit in the street of residence (lower), by presence (1) or absence (0) of symptoms of cough or phlegm. SIDRIA 2 Torino

Figure 3: Associations (unconditional and conditional logistic regression) between self-reported traffic indicators and respiratory symptoms. Results (OR and 95% CI) are reported for the whole sample (first column) and the subgroup of subjects that could be matched by census block (unconditional logistic regression: second column; conditional regression: third column). SIDRIA 2 Roma, Torino and Milano.

Figure 4: Associations (unconditional logistic regression, OR and 95% CI) between self-reported traffic indicators and respiratory symptoms. Results are reported for the subgroup of subjects that could be matched by census block using original data on reported traffic (first column) and assigning to cases in each census block the average traffic reported by controls (second column*). SIDRIA 2 Roma, Torino and Milano.

Tables

Table 1. Prevalence of respiratory outcomes investigated in a sample of Italian schoolchildren.

		Asthma symptoms		
		YES n (%)	**NO** n (%)	**TOTAL**
Cough or phlegm	**YES** n (%)	961 (2.9%)	1337 (4.0%)	2298 (6.8%)
	NO n (%)	3591 (10.7%)	27743 (82.5%)	31334 (93.2%)
	TOTAL	4552 (13.5%)	29080 (86.5%)	33632 (100%)

Table 2. Prevalence (%) of current respiratory symptoms by various subgroups (N=33632)

	Asthma symptoms % (n)	Cough or phlegm % (n)
Total	13.5 (4552)	6.8 (2298)
Age		
6-7 year olds	13.7 (2736)	8.4 (1687)
13-14 year olds	13.3 (1816)	4.5 (611)
Gender		
male	14.6 (2531)	7.4 (1275)
female	12.4 (2012)	6.3 (1019)
Parental asthma or allergies		
yes	17.6 (2376)	8.9 (1202)
no	10.8 (2176)	5.4 (1096)
Urbanization level		
<10,000 inhabitants	11.2 (623)	5.3 (295)
10-100,000 inhabitants	13.2 (1246)	5.6 (534)
100-500,000 inhabitants	14.8 (973)	7.1 (468)
>500,000 inhabitants	14.2 (1710)	8.3 (1001)
Exposure to passive smoke		
yes	14.8 (2509)	7.4 (1254)
no	12.2 (2019)	6.2 (1030)
Presence of mould/dampness		
yes	17.4 (631)	8.7 (314)
no	12.9 (3598)	6.5 (1807)
missing	*14.8 (323)*	*8.1 (177)*
Parental education		
primary school	15.1 (207)	7.8 (107)
secondary school	14.2 (1420)	7.4 (734)
high school	13.3 (2031)	6.5 (990)
university	12.7 (853)	6.6 (443)
Floor level of apartment		
Ground	13.5 (1273)	6.2 (585)
1st-2nd floor	13.9 (1962)	6.6 (933)
3rd floor or more	12.9 (1231)	7.7 (738)
Change of residence		
Yes	12.6 (2182)	6.3 (1099)
No	14.5 (2174)	7.4 (1109)

Table 3. Associations between traffic indicators and asthma symptoms and cough or phlegm

	Asthma symptoms				Cough or phlegm			
	n cases	(%)	OR*	95% CI	n cases	(%)	OR*	95% CI
Traffic density								
Absent	564	12.5	1.00		270	6.0	1.00	
Low	1228	12.6	1.04	0.93-1.16	558	5.7	0.94	0.80-1.10
Moderate	1375	13.8	1.13	1.01-1.26	689	6.9	1.04	0.89-1.22
High	795	14.6	1.17	1.03-1.33	475	8.7	1.24	1.04-1.49
Frequency cars transit								
Never	309	12.7	1.00		142	5.9	1.00	
Sometimes	1147	12.1	0.95	0.83-1.10	517	5.5	0.90	0.74-1.10
Frequently	1399	13.6	1.06	0.93-1.22	679	6.6	1.02	0.84-1.26
Continuously	1108	14.9	1.16	1.00-1.33	656	8.8	1.32	1.08-1.63
Frequency trucks transit								
Never	1412	12.3	1.00		652	5.7	1.00	
Sometimes	1644	13.6	1.10	1.02-1.19	812	6.7	1.14	1.02-1.26
Frequently	682	14.5	1.16	1.05-1.29	399	8.5	1.41	1.23-1.61
Continuously	211	15.7	1.27	1.08-1.50	132	9.8	1.67	1.36-2.06

* All ORs were adjusted for study centre, age, sex, parental asthma or allergies, parental education, passive smoke at home, indoor moulds, floor level of the apartment and change of residence.

Table 4. Associations between traffic indicators and asthma symptoms with or without cough or phlegm.

	Asthma symptoms WITHOUT cough or phlegm				Cough or phlegm WITHOUT asthma symptoms				Asthma symptoms WITH cough or phlegm			
	n cases	(%)	OR*	95% CI	n cases	(%)	OR*	95% CI	n cases	(%)	OR*	95% CI
Traffic density												
Absent	465	10.3	1.00		171	3.8	1.00		99	2.2	1.00	
Low	996	10.2	1.00	0.89-1.13	326	3.4	0.83	0.69-1.00	232	2.4	1.12	0.88-1.42
Moderate	1083	10.9	1.08	0.95-1.22	397	4.0	0.92	0.75-1.11	292	2.9	1.27	1.02-1.57
High	601	11.0	1.13	0.99-1.28	281	5.2	1.14	0.92-1.41	194	3.6	1.52	1.17-1.96
Frequency cars transit												
Never	254	10.5	1.00		87	3.6	1.00		55	2.3	1.00	
Sometimes	938	9.9	0.93	0.80-1.07	308	3.3	0.91	0.72-1.15	209	2.2	0.97	0.71-1.34
Frequently	1129	11.0	1.03	0.89-1.19	409	4.0	1.07	0.83-1.36	270	2.6	1.10	0.80-1.52
Continuously	823	11.0	1.07	0.92-1.25	371	5.0	1.30	1.02-1.67	285	3.8	1.53	1.11-2.10
Frequency trucks transit												
Never	1158	10.1	1.00		398	3.5	1.00		254	2.2	1.00	
Sometimes	1299	10.8	1.07	0.98-1.17	467	3.9	1.10	0.95-1.26	345	2.9	1.27	1.09-1.48
Frequently	525	11.1	1.13	1.01-1.26	242	5.1	1.44	1.23-1.69	157	3.3	1.51	1.21-1.87
Continuously	150	11.2	1.21	1.01-1.46	71	5.3	1.47	1.13-1.93	61	4.5	2.11	1.58-2.81

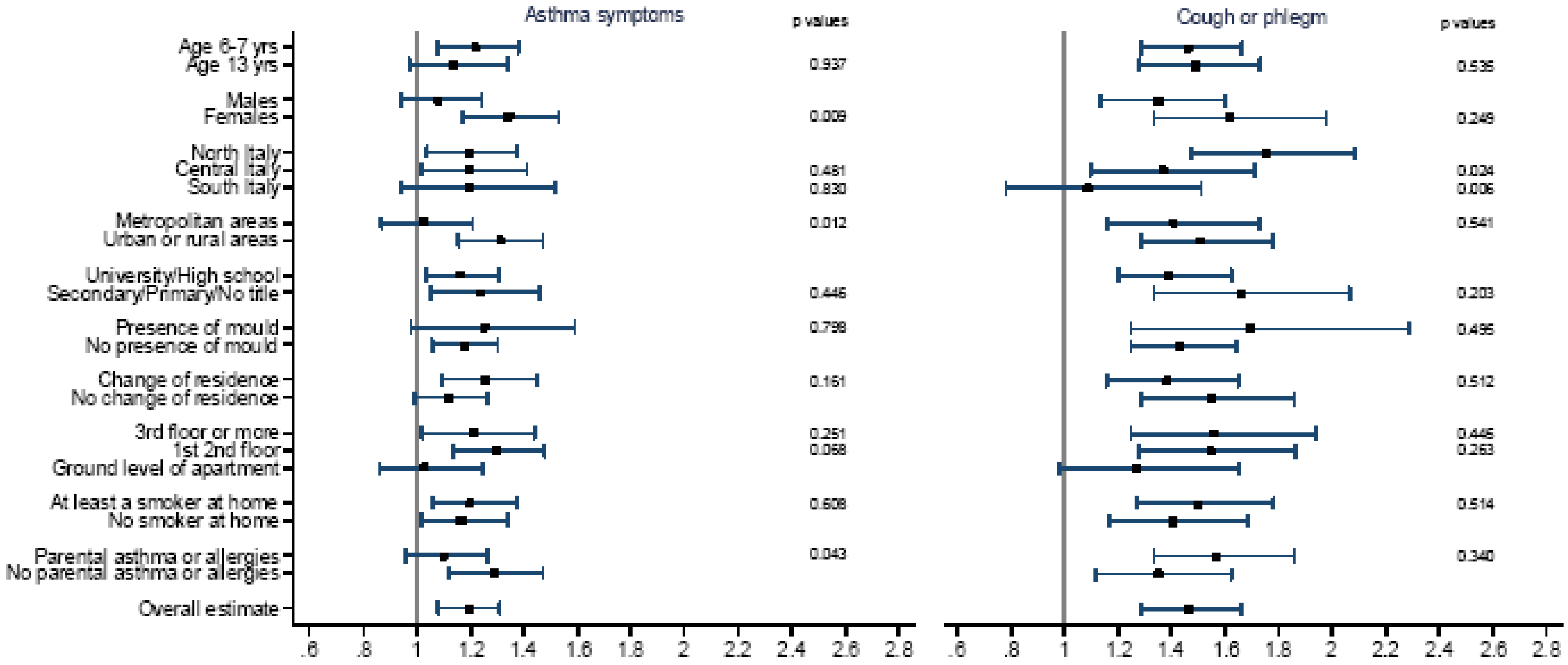
* All ORs were adjusted for study centre, age, sex, parental asthma or allergies, parental education, passive smoke at home, indoor moulds, floor level of the apartment and change of residence.

Table 5. Associations between combined exposure to truck and car transit and cough or phlegm.

			Trucks transit		
			Never	**Sometimes**	**Freq/continuously**
Cars transit	**Never/ sometimes**	*n cases (%)*	*426 (5.3)*	*211 (5.9)*	*19 (8.2)*
		OR* (95% CI)	**1.00**	**1.12 (0.95-1.32)**	**1.50 (0.93-2.43)**
	Frequently	*n cases (%)*	*168 (6.3)*	*370 (6.4)*	*140 (7.7)*
		OR* (95% CI)	**1.09 (0.90-1.33)**	**1.12 (0.96-1.30)**	**1.42 (1.15-1.75)**
	Continuously	*n cases (%)*	*56 (7.8)*	*228 (8.4)*	*372 (9.3)*
		OR* (95% CI)	**1.30 (0.94-1.81)**	**1.42 (1.19-1.70)**	**1.60 (1.36-1.87)**

*All ORs were adjusted for presence of current asthma symptoms, study centre, age, sex, parental asthma or allergies, parental education, passive smoke at home, indoor moulds, floor level of the apartment and change of residence.

Figure 1


Asthma symptoms
p values
Age 6-7 yrs
Age 13 yrs
Males
Females
North Italy
Central Italy
South Italy
Metropolitan areas
Urban or rural areas
University/High school
Secondary/Primary/No title
Presence of mould
No presence of mould
Change of residence
No change of residence
3rd floor or more
1st 2nd floor
Ground level of apartment
At least a smoker at home
No smoker at home
Parental asthma or allergies
No parental asthma or allergies
Overall estimate
0.937
0.009
0.481
0.830
0.012
0.446
0.798
0.161
0.251
0.058
0.608
0.043
Cough or phlegm
p values
0.535
0.249
0.024
0.006
0.541
0.203
0.495
0.512
0.445
0.263
0.514
0.340
.6
.8
1
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1.6
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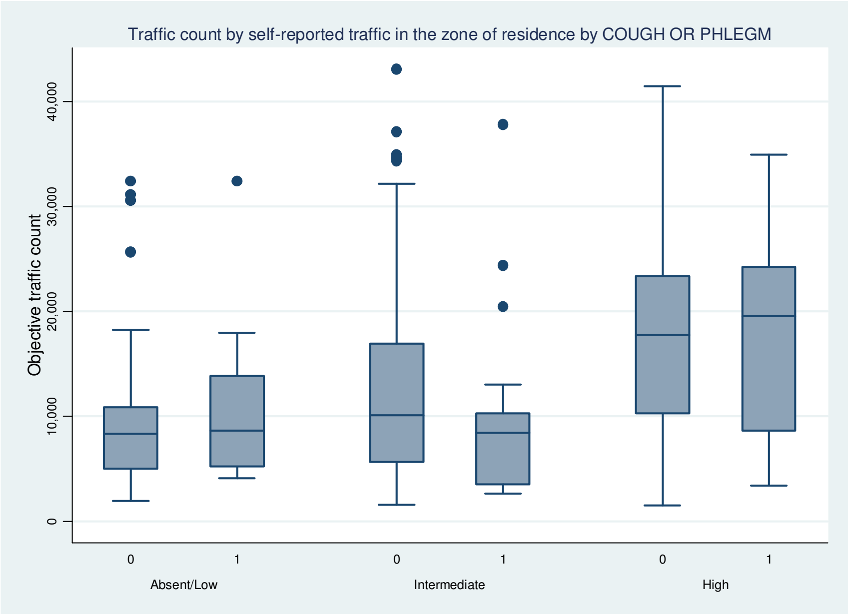
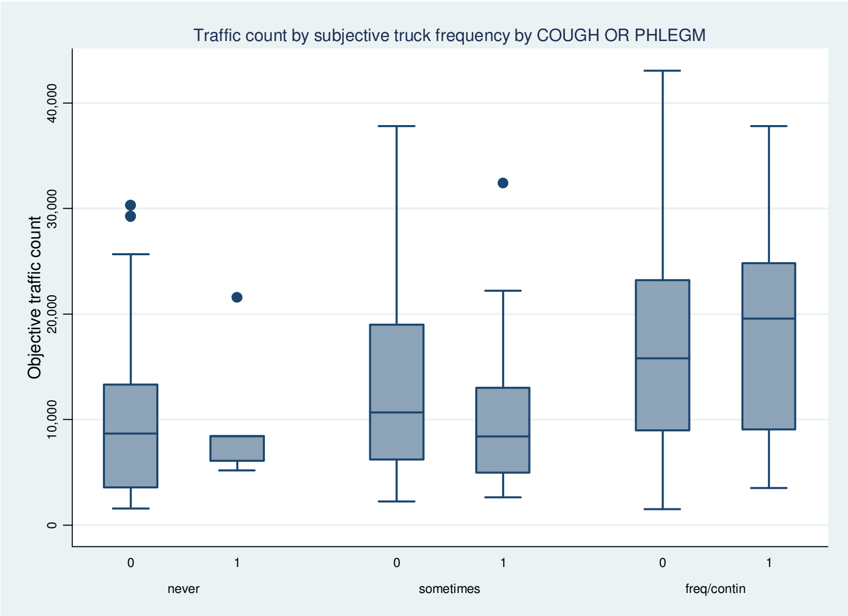
2
2.2
2.4
2.6
2.8


Traffic count by self-reported traffic in the zone of residence by COUGH OR PHLEGM
Objective traffic count
0
10,000
20,000
30,000
40,000
0
1
0
1
0
1
Absent/Low
Intermediate
High


Traffic count by subjective truck frequency by COUGH OR PHLEGM
Objective traffic count
0
10,000
20,000
30,000
40,000
0
1
0
1
0
1
never
sometimes
freq/contin

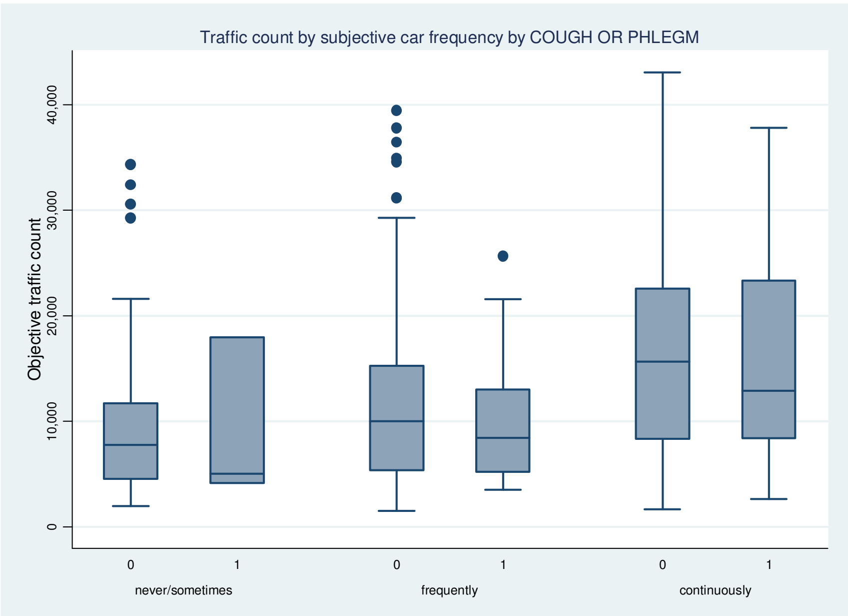
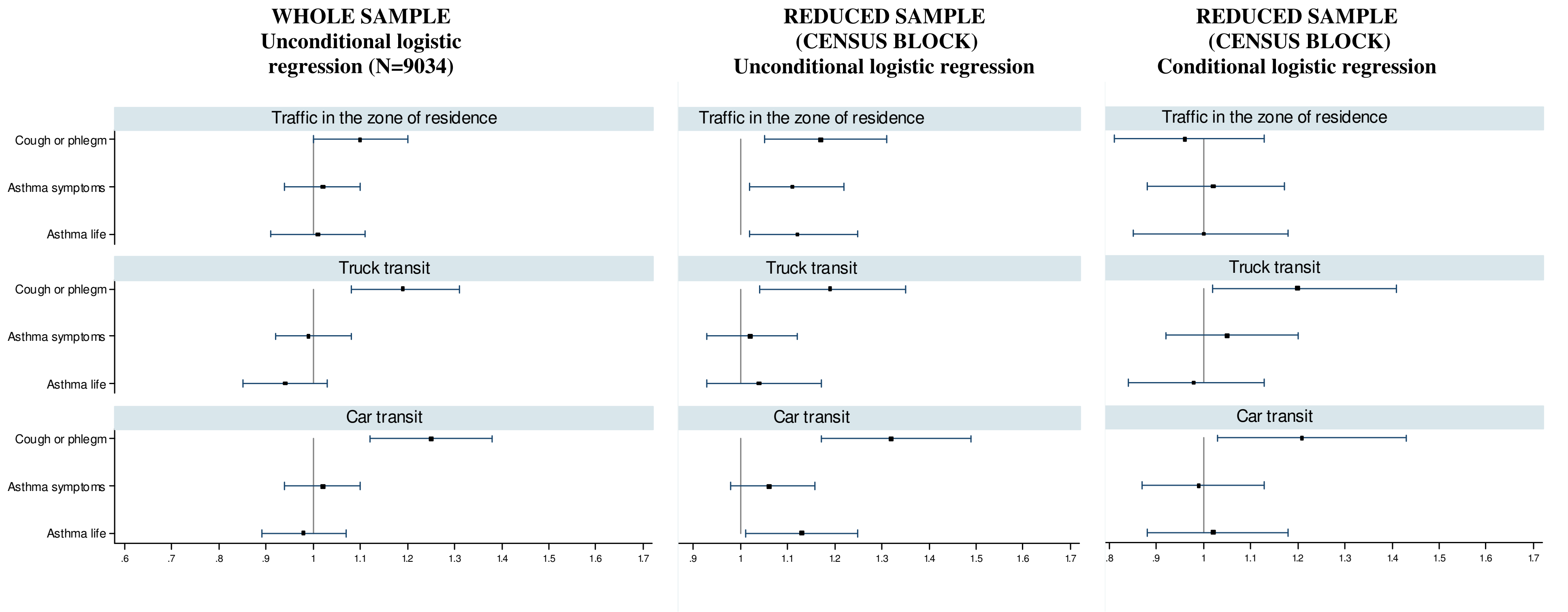

Traffic count by subjective car frequency by COUGH OR PHLEGM
Objective traffic count
0
10,000
20,000
30,000
40,000
0
1
0
1
0
1
never/sometimes
frequently
continuously

Figure 2

Figure 3

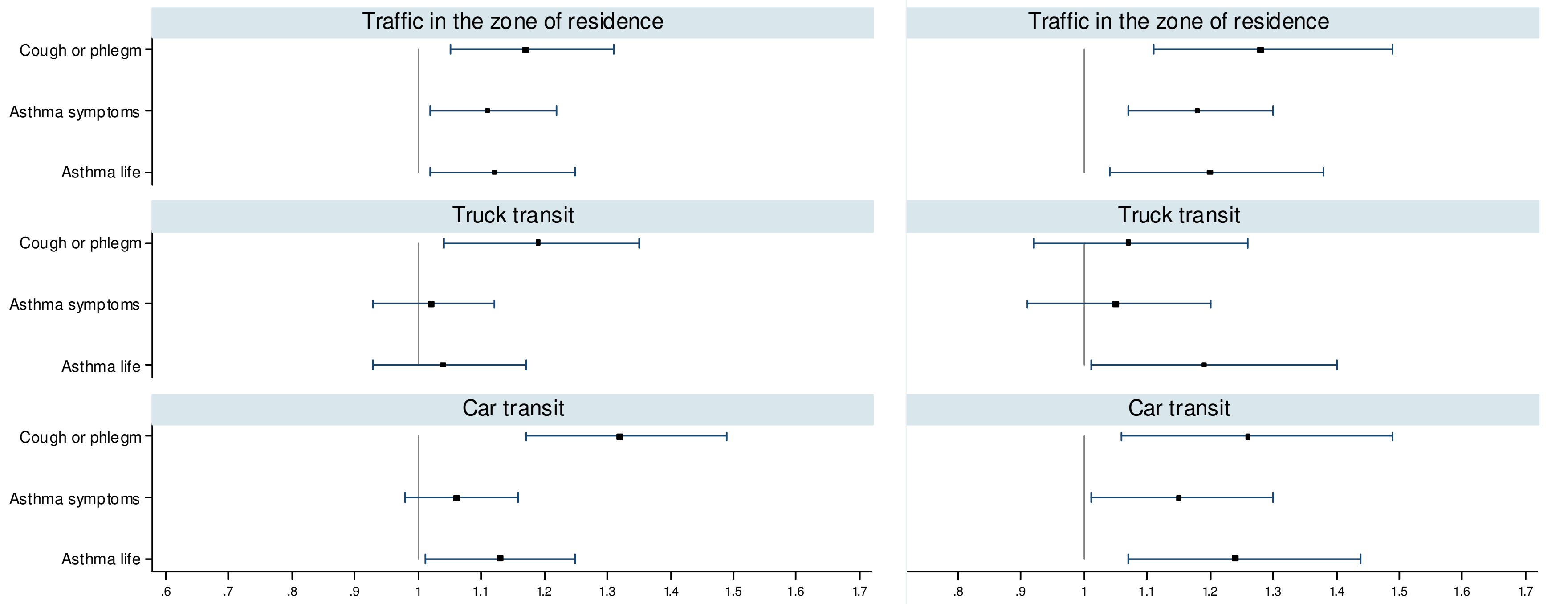


WHOLE SAMPLE
Unconditional logistic regression (N=9034)
REDUCED SAMPLE (CENSUS BLOCK)
Unconditional logistic regression
REDUCED SAMPLE (CENSUS BLOCK)
Conditional logistic regression
Traffic in the zone of residence
Truck transit
Car transit
Cough or phlegm
Asthma symptoms
Asthma life
.6
.7
.8
.9
1
1.1
1.2
1.3
1.4
1.5
1.6
1.7

Figure 4

REDUCED SAMPLE (CENSUS BLOCK) Unconditional logistic regression

REDUCED SAMPLE (CENSUS BLOCK)* Unconditional logistic regression



Additional files provided with this submission:

Additional file 1: migliore_appendix ms13_02.doc, 329K
http://www.ehjournal.net/imedia/1670024997255096/supp1.doc