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Traffic related air pollution and development and persistence of asthma and low lung function

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ABSTRACT

Background and aims: Traffic Related Air Pollution (TRAP) exposure is known to exacerbate existing respiratory diseases. We investigated longer term effects of TRAP exposure for individuals with or without existing asthma, and with or without lower lung function.

Methods: Associations between TRAP exposure and asthma (n = 689) and lung function (n = 599) were investigated in the prospective Tasmanian Longitudinal Health Study (TAHS). TRAP exposure at age 45 years was measured using two methods based on residential address: mean annual NO_2 exposure; and distance to nearest major road. Adjusted multinomial logistic regression was used to model the association between exposure to TRAP at 45 years and changes in asthma and lung function, using three follow ups of TAHS (45, 50 and 53 years).

Results: For those who never had asthma by 45, living < 200 m from a major road was associated with increased odds of new asthma that persisted from 50 to 53 years (adjusted Odds Ratio [aOR] 5.20; 95% CI 1.07, 25.4). Asthmatic participants at 45 had an increased risk of persistent asthma up to 53 years if they were living < 200 m from a major road, compared with asthmatic participants living > 200 m from a major road (aOR = 5.21; 95% CI 1.54, 17.6).

Conclusion: For middle aged adults, living < 200 m for a major road (a marker of TRAP exposure) influences both the development and persistence of asthma. These findings have public health implications for asthma prevention strategies in primary and secondary settings.

Abbreviations: TRAP, Traffic Related Air Pollution; TAHS, Tasmanian Longitudinal Health Study; RHINE, Respiratory Health in Northern Europe; ECRHS, European Community Respiratory Health Survey; ESCAPE, European Study of Cohorts for Air Pollution Effects; PM_{10}, particulate matter < 10 μm in diameter; $PM_{2.5}$, particulate matter < 2.5 μm in diameter; COPD, Chronic Obstructive Pulmonary Disease; LUR, Land Use Regression; ATS, American Thoracic Society; ERS, European Respiratory Society; FEV_1, Forced Expiratory Volume in 1 s; FVC, Forced Vital Capacity; DAG, Directed Acyclic Graph; UFP, Ultrafine Particles

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1. Introduction

There is substantial evidence that short term Traffic Related Air Pollution (TRAP) exposure exacerbates existing adult asthma (Guarnieri and Balmes, 2014; Braback and Forsberg, 2009), but evidence is lacking on whether TRAP affects subsequent asthma and lung function for those with or without asthma, as well as for those with or without impaired lung function. Studies of birth cohorts provide evidence for an association between early life TRAP exposure and incidence and persistence of asthma in children (Brandt et al., 2015; Bowatte et al., 2015), but it is not clear whether the same relationship exists in adults. This is a critical knowledge gap. Further investigations on the health effects of air pollution are required to develop better targeted public health preventive strategies and health promotion messages.

A small number of longitudinal studies have investigated the effects of TRAP exposure on the incidence of asthma, but not its persistence (Jacquemin et al., 2015; Jacquemin et al., 2009a; Modig et al., 2009; Young et al., 2014; Paulin and Hansel, 2016). Three longitudinal studies, the Respiratory Health in Northern Europe (RHINE), European Community Respiratory Health Survey (ECRHS) and European Study of Cohorts for Air Pollution Effects (ESCAPE) found that exposure to NO_2 was associated with adult asthma incidence over 9 years. However, a nationwide cohort of US women followed up for three years reported only a modest association with NO_2 exposure and incidence of asthma (Young et al., 2014). Few studies have been conducted on the association between asthma incidence in adults and particulate matter < 10 μm in diameter (PM_{10}), particulate matter < 2.5 μm in diameter ($PM_{2.5}$) or proximity to roads, and their findings have been inconsistent (Jacquemin et al., 2015; Modig et al., 2009; Young et al., 2014; Schindler et al., 2009; Modig et al., 2006). As all of these studies which investigated air pollution exposure and incidence of asthma began as adult cohorts, the potential for misclassification of incident asthma, i.e. the inability to recall early life asthma, may have contributed to the inconsistent findings.

Furthermore the evidence for longitudinal effects of TRAP exposure on adult lung function are not comparable for different TRAP proxies (NO_2, $PM_{2.5}$, PM_{10} or distance to major roads) and different measures of lung function (FEV_1, FVC or FEV_1/FVC) (Jacquemin et al., 2015; Lubinski et al., 2005; Ackermann-Liebrich et al., 1997). Recent studies provide modest evidence that in individuals with established Chronic Obstructive Pulmonary Disease (COPD) or asthma, longitudinal exposure to TRAP is associated with lung function decline (Carlsen et al., 2015; Lagorio et al., 2006; Qian et al., 2009; Kariisa et al., 2015). To our knowledge, no study has investigated effects of TRAP in subgroups with impaired lung function.

Given the above critical knowledge gaps, we used data from a longitudinal cohort study to investigate associations between adult TRAP exposure and subsequent change in asthma status and lung function over eight years.

2. Methods

2.1. Study population

The study sample comprised of participants of the 45, 50 and 53 year follow ups of the Tasmanian Longitudinal Health Study (TAHS) (Wharton et al., 2006; Gibson et al., 1969; Bowatte et al., 2017a). TAHS is a population based cohort that commenced in 1968, by recruiting (98.7%, n = 8583) of 7 year old children attending schools in the state of Tasmania, Australia. A number of follow-up surveys have been conducted since its inception. The majority of participants (67%) were resurveyed in 2002–05, when their mean age was 45 years. Respondents to this survey who had either participated in past follow up studies and/or reported symptoms of asthma or cough in the 2002–05 survey were invited to participate in a laboratory study in 2005–08 (n = 2387). Of those invited, 1397 (58.6%) participated in a full laboratory visit, including lung function testing and questionnaire. Only a telephone questionnaire or laboratory visit was completed by a further 354 (14.8%).

In 2010–12, when participants were aged around 50 years, those who took part in the 2005–08 laboratory study (n = 1397) were again invited for another laboratory study. Of those invited, 794 (56.8%) performed a full laboratory visit and completed a questionnaire (n = 837) (Bowatte et al., 2017a). In 2012–16, those who participated at the 2002–2005 survey were invited to complete a further survey and laboratory study. Of those, 3609 completed the survey and 2689 performed laboratory testing, including spirometry. The mean (± SD) ages of participants were 44.8 (± 1) (referred to as 45 year follow up), 49.6 (± 0.6) years (referred to as 50 year follow up) and 53.0 (± 1.4) (referred to as 53 year follow up) years, at the 2005–08, 2010–12 and 2012–16 follow ups, respectively. Addresses were geocoded for 705 of 723 (97.5%) participants who completed all three follow ups and who are included in this analysis (Fig. 1).

2.2. TRAP exposure assessment

2.2.1. Living < 200 m from a major road

Distance from each participant's residence to the nearest major road at the 45 year follow up was calculated using ArcGIS 10.1 software (Environmental Systems Research Institute, Redlands, CA). Major roads were defined using public sector mapping agencies (PSMA), Australia transport hierarchy codes 301 and 302. This mainly includes freeways, highways and arterial roads defined as “whose main function is to form the principal avenue of communication for movements: Between capital city and adjoining States and their capital cities; or Between a capital city and key towns; or Between key towns” (The Intergovernmental Committee of Surveying and Mapping, 2006). Participants were categorised into two groups: (i) living < 200 m; and (ii) living > 200 m from a major road. This cut-off was chosen based on the decay observed in levels of major traffic pollutants, given that the sharp decay in pollutant concentrations means that most TRAP components approach background concentrations at approximately 200 m (Karner et al., 2010).

2.3. NO_2 exposure

A satellite based land use regression (LUR) model was used to assign mean annual NO_2 exposures at the 45 year follow up (Knibbs et al., 2014). Briefly, this LUR model predicted mean annual NO_2 levels based on tropospheric NO_2 columns derived from satellite observations in combination with other predictors, such as land use and roads, to estimate ground level NO_2 across Australia. During the study period, 81% of spatial variation in annual NO_2 levels was captured by the model, with a cross-validated prediction error of 19% (Knibbs et al., 2014). An external validation of this LUR model was conducted; it captured 66% of annual NO_2 at a completely independent set of 98 urban background and near-traffic validation sites across Australia. Mean prediction bias in validation study was low (−0.2 ppb) and prediction error comparable to the initial cross-validation results (19% vs 25% in the original and validated results, respectively) (Knibbs et al., 2016). Mean annual residential exposures to outdoor NO_2 were estimated and assigned based on participants' geocoded addresses at 45 years.

2.4. Lung function

Pre-bronchodilator spirometry was performed using the EasyOne™ Ultrasonic Spirometer (Ndd, Medizintechnik, AG, Switzerland) according to American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines (Miller et al., 2005). Global Lung Initiative 2012 (GLI 2012) reference values were used to derive z-scores (Quanjer et al., 2012) for lung function variables. The z-scores were expressed as

standard deviations (SD) and described the deviations from the mean predicted value. z-Scores of lung function represent the deviation from the age-, sex-, height- and race-adjusted population mean in SD units.

2.5. Definitions of lung function

For analytical purposes, z-scores of FEV_1, FVC and FEV_1/FVC were each categorised into two groups, normal or low, based on the lower 10% (z-score ≤ − 1.28) of the sample in the three follow ups. For example, participants with $zFEV_1$ score < −1.28 were categorised as "low FEV_1" and participants with $zFEV_1$ > −1.28 as "normal FEV_1". Similarly, using the −1.28 cut-off, zFVC and $zFEV_1$/FVC were categorised into "normal FVC", "low FVC", "normal FEV_1/FVC" and low "FEV_1/FVC".

We defined the TAHS 45 year follow up study as the "baseline". Participants who had normal FEV_1 (z ≥ −1.28) at baseline were categorised into three groups based on their FEV_1 at subsequent follow ups (50 and 53 years):

i) normal FEV_1 at all three follow ups ("persistently normal FEV_1");
ii) normal FEV_1 at baseline and low FEV_1 at any subsequent follow up ("normal FEV_1 45, low FEV_1 50 or 53"); and
iii) normal FEV_1 at baseline and low FEV_1 at both subsequent follow ups ("normal FEV_1 45, low FEV_1 50 and 53").

Participants who had low FEV_1 at baseline (z < −1.28) were categorised into three groups based on FEV_1 at subsequent follow ups:

i) low FEV_1 at baseline and normal FEV_1 at both subsequent follow ups ("low FEV_1 45, normal FEV_1 50 and 53");
ii) low FEV_1 at baseline and low FEV_1 at any subsequent follow up ("low FEV_1 45, low FEV_1 50 or 53"); and
iii) low FEV_1 at all three follow ups ("persistently low FEV_1").

Participants were categorised into similar groups for FVC and FEV_1/FVC.

2.6. Definitions of asthma

"Current asthma at 45, 50 and 53 years" was defined as any episode of asthma or use of asthma medication during the last 12 months. Based on current asthma status at baseline (45 years), we grouped participants into two categories: i) no current asthma; or ii) current asthma at baseline. The "no current asthma at baseline" group was further categorised into three sub-groups based on subsequent asthma at 50 and 53 years:

i) no asthma at any follow up ("no asthma");
ii) no asthma at baseline and asthma at any subsequent follow up ("no asthma 45, asthma at 50 or 53"); and
iii) no asthma at baseline and asthma at both subsequent follow ups ("no asthma 45, asthma at 50 and 53").

Similarly, the group with current asthma at baseline was further categorised into three sub-groups based on subsequent asthma status at 50 and 53 years:

i) current asthma at baseline and no asthma at both subsequent follow ups ("asthma 45, no asthma 50 and 53");
ii) current asthma at baseline and asthma at either subsequent follow up ("asthma 45, asthma 50 or 53"); and
iii) current asthma at all three time points ("persistent asthma").

"Ever asthma before 45 years" was defined as participants who reported ever having asthma, but not current asthma at age 45 years. "Asthma ever before 45" was defined as participants who reported ever having asthma before 45 years and who reported (parent reported) ever asthma at 7 and 14 years, but not current asthma at 45 years. "No asthma" was defined as participants who never reported having asthma at 7, 14 (parental report of asthma), 45, 50 and 53 years.

2.7. Statistical analysis

We investigated TRAP exposure at age 45 years (mean annual NO_2 exposure or living < 200 m from a major road) and change in asthma status from ages 45 to 53 years defined as a three-level variable, as described above. To investigate associations with TRAP exposure for current asthmatics at age 45 and never asthmatics by age 45, we used multinomial logistic regression models. To account for potential recall bias of asthma retrospectively reported by never asthmatics, a sensitivity analysis was performed after removing participants whose parents reported ever asthma when their child was 7 or 14 years old. Another sensitivity analysis was performed after removing participants who reported asthma between ages 45 and 53 years, but not current asthma at ages 45, 50 or 53 years to investigate the effects of TRAP exposure on current asthma. We also performed a sensitivity analysis by excluding people who had changed addresses during 45, 50 and 53 follow-ups.

The association between TRAP and lung function change was non-linear. The association between TRAP exposure at age 45 years and subsequent change in lung function categories as a three level variable was analysed for participants with low lung function (i.e. low FEV_1) and normal lung function (i.e. normal FEV_1) using multinomial logistic regression models. The modifying effect of baseline asthma on the association between TRAP exposure and lung function was investigated by adding a binary variable of current asthma at age 45 years as an interaction term in the multinomial models.

NO_2 exposure was fitted as a continuous variable and living < 200 m as a categorical variable in all models. Results for living < 200 m from a major road were reported as Odds Ratios (ORs) and 95% Confidence Intervals (CIs). The results for NO_2 exposure were scaled to an interquartile range increase (IQR) in mean annual NO_2 at age 45 years, which in this sample was 2.4 ppb. A Directed Acyclic Graph (DAG) drawn in DAGitty software (Textor et al., 2011) was used to select possible confounders. Socio-economic status (defined using education), smoking status, type of cooking, type of heating and rural or urban location (using accessibility/remoteness index of Australia 2006) were included in all models. To investigate the effect of area level socioeconomic status on asthma, we included Relative Socio-Economic Advantage and Disadvantage (IRSAD) of the Socio-Economic Indexes for Areas (SEIFA), developed by the Australian Bureau of Statistics, as a confounder in a separate sensitivity analysis (Pink, 2013). STATA version 13.1 (Stata corporation, College Station, Texas, USA) was used to perform all statistical analyses.

3. Results

Of the participants with relevant information, 689 had complete information on asthma outcomes at 45, 50 and 53 years, and geocoded address at 45 years, of these 599 completed spirometry at three follow ups (Fig. 1). For participants who attended all three follow ups, current smoking and use of wood/coal for heating decreased between age 45 to 53 years (Table 1), but there was no change in the prevalence of asthma (Table 2). Altogether, 24 (3.5%) participants had new onset asthma from 50 to 53 years, 91 (13.2%) had persistent asthma from 45 to 53, and 452 (65.3%) had no asthma (Table 2). There was a modest correlation between distance to nearest major roads and NO_2 ($r = -0.45$). The mean difference between NO_2 exposure in participants living < 200 m (mean 6.6 [± 3.4] ppb) versus > 200 m (mean 4.8 [± 2.2] ppb) from a major road was statistically significant, with the participants living < 200 m from a major road having a higher NO_2 exposure (*t*-test, p < 0.0001).

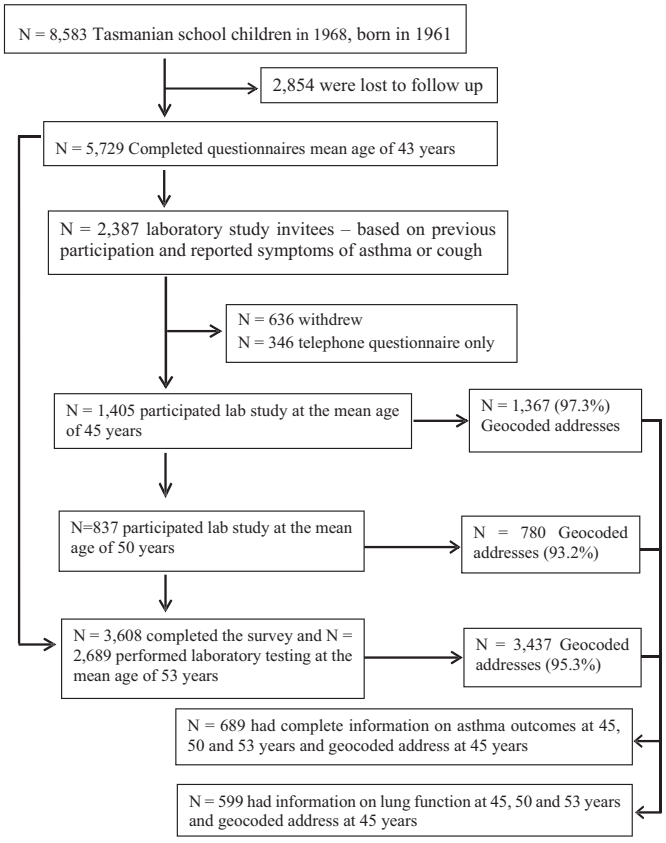

Fig. 1. Tasmanian Longitudinal Health Study flow diagram.

3.1. TRAP exposure at age 45 and changes to asthma between 45 and 53 years

3.1.1. Participants with no current asthma at baseline

For those with no current asthma at baseline, living < 200 m from a major road was associated with new asthma that persisted to ages 50 to 53 years (adjusted Odds Ratio [aOR] 5.20; 95% CI 1.07, 25.4) (Table 3). A sensitivity analysis that removed participants with parent reported childhood asthma (asthma ever before 45) showed a similar trend (aOR 6.20; 95% CI 0.94, 41.0) (Table S1). NO_2 exposure at baseline was associated with new current asthma at ages 50 or 53 years (aOR 1.37 95% CI 1.00, 1.88) (Table 3). In our sensitivity analysis, there were a substantial number of participants who incorrectly recalled past asthma status. Of the participants who reported asthma never before age 45 years, 16% were found to have parental reports of early asthma.

3.1.2. Participants with current asthma at baseline

Living < 200 m from a major road at baseline was associated with persistent current asthma between 45 and 53 years (aOR 5.21; 95% CI 1.54, 17.6) and current asthma at 50 or 53 years (aOR 4.34; 95% CI 1.12, 16.8), but not with NO_2 exposure (Table 3). Only 14 participants reported asthma between 45 and 53 years, but not current asthma at 45, 50 and/or 53 years (Table S2). A sensitivity analysis that removed these participants showed similar associations (Table S2).

Of the participants who had geocoded addresses at 45 and 50 years, 53 (8.2%) moved, and additional 101 (14.7%) by the 53 year follow-up. Similar associations were observed after removing participants who changed their residential addresses between 45 and 53 or 45 and 53 years (Table S3). An additional sensitivity analysis including IRSAD as a confounder showed similar associations for both of our exposure variables, NO_2 exposure or living < 200 m from a major road, and change of asthma status (Table S4).

3.2. TRAP exposure at age 45 years and change of lung function between 45 and 53 years

There were no associations either between NO_2 exposure or living < 200 m from a major road and any lung function outcomes (Table 4, Tables S5 & S6).

We did not observe any significant interactions between the effects of proxies for TRAP (NO_2 or living < 200 m from a major road) and baseline asthma on subsequent lung function change (results not shown).

4. Discussion

This cohort study has shown that exposure to TRAP was associated with both persistent and new onset asthma in adults. Living < 200 m from a major road at baseline (45 years of age) was associated with increased odds of new asthma in participants who reported never having asthma before 45 years. The association remained the same when participants whose parents reported childhood asthma were excluded from this group. Living < 200 m from a major road at baseline was associated with persistent asthma between ages 45 and 53 years. We also noted a modest association between NO_2 exposure at baseline and incidence of asthma by 50 or 53 years.

In our study, the majority of the significant associations were with living < 200 m from a major road. These results were not observed using more sophisticated modelled NO_2 concentrations. The literature indicates that freshly emitted pollutants and suspended particles follow strong spatial gradients proximal to major roads. For most pollutants, an approximately exponential decay occurs to background level concentrations within approximately 300 to 500 m (Zhu et al., 2002). We selected our threshold distance of 200 m from a major road based on

Table 1
Study characteristics of those who participated in 45, 50 and 53 year follow ups and had geocoded addresses at 45 years (N = 689).

Variable		45 year follow up (N_1 = 1367)	50 year follow up (N_2 = 780)	53 year follow up (N_3 = 3431)
Male sex n (%)		338 (49.1)	338 (49.1)	338 (49.1)
Education	Grade 1–12 n (%)	277 (40.3)	277 (40.3)	277 (40.3)
	Trade/apprenticeship/university degree or higher n (%)	410 (59.7)	410 (59.7)	410 (59.7)
Smoking status	Never smoked n (%)	316 (46.0)	309 (44.9)	324 (46.0)
	Past but not current n (%)	213 (31.0)	259 (37.6)	276 (39.1)
	Current n (%)	158 (23.0)	121 (17.6)	105 (14.9)
Type of cooking	Gas n (%)	153 (22.4)	193 (28.5)	174 (26.2)
	Electric n (%)	529 (77.6)	485 (71.5)	492 (73.8)
Type of heating	Wood/coal n (%)	320 (46.7)	236 (34.8)	261 (38.3)
	Gas room heater n (%)	60 (8.8)	46 (6.8)	49 (7.2)
	Other n (%)	305 (44.5)	397 (58.5)	372 (54.5)
TRAP exposure	NO_2 (ppb) (mean [SD])	5.3 [2.7]	4.7 [2.6]	3.4 [2.3]
	Living < 200 m from a major road n (%)	191 (27.7)	187 (28.8)	187 (27.8)

N_1, N_2 and N_3 – total number of participants with geocoded addresses at 45, 50 and 53 year follow ups, respectively.

Table 2
Asthma (N = 689) and preBD FEV_1 (z-scores) (N = 599) for those who participated in the 45, 50 and 53 year follow ups.

Outcome	45 year follow up n (%)	50 year follow up n (%)	53 year follow up n (%)	Status of current asthma at 45 years	45, 50 and 53 year follow ups n (%)	
Current asthma	157 (22.8)	168 (24.4)	154 (22.4)	No current asthma at 45 years	No asthma	452 (65.3)
					No asthma 45, asthma 50 or 53	58 (8.4)
					No asthma 45, asthma 50 and 53	24 (3.5)
				Current asthma at 45 years	Asthma 45, no asthma 50 and 53	32 (4.6)
					Asthma 45, asthma 50 or 53	34 (4.9)
					Persistent asthma	91 (13.2)
Low preBD FEV_1	95 (15.9)	100 (16.7)	86 (14.4)	Normal FEV_1 at 45 years	Persistently normal FEV_1	467 (78.0)
					Normal FEV_1 45, low FEV_1 50 or 53	23 (3.8)
					Normal FEV_1 45, low FEV_1 50 and 53	14 (2.3)
				Low FEV_1 at 45 years	Low FEV_1 45, normal FEV_1 50 and 53	14 (2.3)
					Low FEV_1 45, low FEV_1 50 or 53	27 (4.5)
					Persistently low FEV_1	54 (9.0)

Table 3
The association between NO_2 exposure and living < 200 m from a major road at 45 years and change in asthma status from 45 to 53 years after removing participants who reported ever asthma before 45 years.

	Asthma	Unadjusted			Adjusted[a]		
		OR	95% CI	p	OR	95% CI	p
< 200 m	No asthma	(Reference category)			(Reference category)		
	No asthma 45, asthma 50 or 53	1.48	0.67, 3.24	0.33	1.60	0.71, 3.60	0.26
	No asthma 45, asthma 50 and 53	4.33	0.95, 19.7	0.06	5.20	1.07, 25.4	0.04
	Asthma 45, no asthma 50 and 53	(Reference category)			(Reference category)		
	Asthma 45, asthma 50 or 53	2.58	0.78, 8.53	0.12	4.34	1.12, 16.8	0.03
	Persistent asthma	3.07	1.08, 8.74	0.04	5.21	1.54, 17.6	0.01
NO_2	No asthma	(Reference category)			(Reference category)		
	No asthma 45, asthma 50 or 53	1.25	0.94, 1.65	0.13	1.37	1.00, 1.88	0.05
	No asthma 45, asthma 50 and 53	1.00	0.47, 2.13	0.99	1.32	0.60, 2.90	0.49
	Asthma 45, no asthma 50 and 53	(Reference category)			(Reference category)		
	Asthma 45, asthma 50 or 53	0.96	0.68, 1.35	0.81	1.31	0.84, 2.05	0.23
	Persistent asthma	0.88	0.66, 1.19	0.42	1.12	0.76, 1.64	0.57

[a] Adjusted for education, smoking status, rural/urban location, type of cooking and type of heating. ORs given per IQR increase in mean annual NO_2 exposure (i.e. 2.4 ppb).

previous studies (Brugge et al., 2007; Dadvand et al., 2014), and were informed by the Special Report of the Health Effects Institute (HEI Panel on the Health Effects of Traffic-Related Air Pollution, 2010). NO_2 is considered a useful proxy of combustion sources, especially related to TRAP.

Even though distance to a major road is a relatively crude measure of TRAP, it may better capture the mixture of other important pollutants such as volatile organic compounds (VOCs), black carbon, fine and ultrafine particles (UFP). Moreover, like most LUR models, ours was not capable of distinguishing aged NO_2 from freshly-produced NO_2. In contrast, distance to major roads may better reflect freshly-produced pollutants, including NO_2, in the pollutant mixture that links with reactive compounds to cause adverse health effects. Freshly emitted UFP closer to major roads may differ in chemical composition and reactivity from UFP that have undergone atmospheric transformation (condensation, evaporation, and dilution) during wind transportation, due to altered particle composition and size distribution (Sioutas et al., 2005).

Previous epidemiological studies investigating the effect of NO_2 on the incidence of asthma have reported heterogeneous results. While two studies found long term exposure to NO_2 was associated with asthma incidence in adults (Modig et al., 2009; Jacquemin et al., 2009b), another reported that NO_2 exposure was associated with asthma incidence only in atopic subjects (Modig et al., 2006). A recent publication from the ESCAPE study, which pooled six European cohorts, found a borderline association between NO_2 and incidence of asthma (OR = 1.10; 95% CI 0.99, 1.21; per 10 $\mu g/m^3$) (Jacquemin et al., 2015). Another recent nationwide study of US women reported that TRAP exposure, measured by both $PM_{2.5}$ and NO_2, was associated with asthma

Table 4
The association between living < 200 m from a major road at 45 years and change in FEV_1 from 45 to 53 years.

	Lung function	Unadjusted			Adjusted[a]		
		OR	95% CI	p	OR	95% CI	p
< 200 m	Normal FEV_1	(Base outcome)			(Base outcome)		
	Normal FEV_1 45, low FEV_1 50 or 53	1.27	0.51, 3.15	0.61	1.25	0.50, 3.14	0.64
	Normal FEV_1 45, low FEV_1 50 and 53	2.17	0.74, 6.38	0.16	1.97	0.65, 6.00	0.23
	Low FEV_1 45 normal FEV_1 50 and 53	(Base outcome)			(Base outcome)		
	Low FEV_1 45 low FEV_1 50 or 53	0.90	0.23, 3.49	0.88	1.09	0.26, 4.56	0.91
	Persistently low FEV_1	0.90	0.26, 3.08	0.87	0.99	0.26, 3.69	0.98
NO_2	Normal FEV_1	(Base outcome)			(Base outcome)		
	Normal FEV_1 45, low FEV_1 50 or 53	1.02	0.71, 1.45	0.94	0.94	0.63, 1.40	0.76
	Normal FEV_1 45, low FEV_1 50 and 53	1.32	0.98, 1.79	0.07	1.18	0.82, 1.69	0.38
	Low FEV_1 45, normal FEV_1 50 and 53	(Base outcome)			(Base outcome)		
	Low FEV_1 45, low FEV_1 50 or 53	1.68	0.75, 3.72	0.20	2.14	0.83, 5.49	0.11
	Persistently low FEV_1	1.25	0.58, 2.70	0.58	1.45	0.59, 3.61	0.42

[a] Adjusted for education, smoking status, rural/urban location, gas cooking and gas heating.

incidence; IQR increase in $PM_{2.5}$ (3.6 μg/m^3): OR 1.20 95% CI 0.99, 1.46 and NO_2 (5.8 ppb): OR 1.12 95% CI 0.96, 1.30 (Young et al., 2014). Our results related to NO_2 exposure at baseline and incidence of asthma by 50 or 53 years showed a modest association that agreed with the results of ESCAPE study and the nationwide study of US women (Jacquemin et al., 2015; Young et al., 2014). Although there was a positive association, we did not see any significant associations related to NO_2 exposure and persistent asthma. This may have been related to the small numbers in the persistent asthma group. Both magnitude and length of exposure are important parameters in the relationship between air pollution exposure and adverse lung health outcomes. Although not adequately studied in animal or human studies, it can be hypothesised that the longer the exposure to TRAP the higher the incidence of asthma. The previous studies investigating NO_2 exposure and incidence of asthma used different exposure lengths, two reported incidence for less than four years of exposure (Young et al., 2014; Modig et al., 2006) and three for exposure periods between 7 and 10 years (Modig et al., 2009; Young et al., 2014; Jacquemin et al., 2009b). However, these studies did not show any clear link between length of exposure and magnitude of the effect estimates related to incidence of asthma. In the current study, we reported incidence for a mean follow up age of 8.4 years this length of time might be enough to detect asthma incidence, however a longer time frame would detect more incidence cases.

We have previously shown that current TRAP exposure was associated with current asthma in this cohort using both a cross-sectional and a repeated measures analysis in middle age adults (Bowatte et al., 2017a; Bowatte et al., 2017b). The current analysis provides evidence that TRAP exposure at age 45 years in this cohort is associated with both the incidence and persistence of asthma. Although we investigated TRAP exposure at age 45 years and its relationship to subsequent asthma and lung function, it is possible that the effects found are related to the cumulative exposure of TRAP over a longer period of time.

One of the major limitations of previous studies is the lack of prospective data regarding previous asthma, especially during childhood. All these studies determined “ever having asthma” at the time of the study (i.e. adulthood), which required participants to recall previous asthma. There is evidence that retrospective, self-reported childhood asthma is unreliable, especially for asthma in early childhood (Burgess et al., 2006). One of the major strengths of our study is that we have captured asthma status throughout the life course, including childhood at ages 7 and 14 years.

4.1. Strengths & limitations

TAHS is a longitudinal cohort study with a special emphasis on respiratory health. The cohort has been well characterised with objective measures, including lung function. Validated questionnaires have been used to collect information regarding respiratory health and other confounding variables.

However, there are also some limitations to our study. We used living < 200 m from a major road at 45 years as a proxy of TRAP. Distance to major road from the residential address is an indicator for the complex mix of TRAP (Karner et al., 2010) and there was a modest correlation between distance to major roads and mean annual NO_2 at the home address in TAHS ($r = -0.45$). Distance to major roads represents a simple proxy for TRAP and may account for the complex mixture of traffic related pollutants. However, distance to major roads may not capture exposure to traffic related pollutants accurately as the measure has limited information on traffic volume, composition of exhaust, climatic factors (wind patterns, rain fall and humidity), land use characteristics, topography and other influential factors (Brauer, 2010). NO_2 exposure in this study was derived from a national LUR model that has predicted annual NO_2 exposure with relatively low error (19%). One of the major strengths of this model is that it uses a single, Australia-wide model for all participants regardless of location (Knibbs et al., 2014). Given that TRAP is a complex mixture of pollutants of which NO_2 is but one component, our findings cannot be ascribed only to NO_2. Both proxies of TRAP used in the current analysis have their own advantages and disadvantages, and these have been discussed elsewhere (Brauer, 2010).

In this sample about 25% of the participants moved to a new residential address between 45 and 53 years. However, in the sensitivity analysis, after removing partcipants moved between follow ups showed simillar associations. In the current analysis, we categorised low lung function by considering the lower 10% of the population and did not see significant associations with TRAP exposure and lower lung function. We did not use a 5% cut off as the numbers were too small (data not shown). Since we have used 10% as the cut off, instead of the more commonly used 5%, there is a possibility for misclassification of outcomes but this is likely to be non-differential which may have pushed the estimates towards null. As such, our findings are more likely to underestimate the magnitude of the true effect.

In conclusion, our analysis provides evidence that TRAP exposure is associated with both the incidence and persistence of asthma in middle age adults. Additionally, our study provides evidence that recall of asthma by adults can introduce significant bias to the results obtained. This highlights the importance of future research using large well characterised cohorts with detailed data on previous asthma to further understand the association between TRAP exposure and incidence of asthma in adults. A better understanding of the effects of environmental exposures, such as TRAP, on asthma and lung function can be used to inform guidelines and planning policies aimed at preserving lung function and preventing the long term damage which may lead to Chronic Obstructive Pulmonary Disease.

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Appendix A. Supplementary data: Traffic related air pollution and development and persistence of asthma and low lung function

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