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Residential exposure to livestock farms and lung function in adolescence – The PIAMA birth cohort study

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ABSTRACT

Background: There is a growing interest in the impact of air pollution from livestock farming on respiratory health. Studies in adults suggest adverse effects of livestock farm emissions on lung function, but so far, studies involving children and adolescents are lacking.

Objectives: To study the association of residential proximity to livestock farms and modelled particulate matter $\leq$10 μm (PM_{10}) from livestock farms with lung function in adolescence.

Methods: We performed a cross-sectional study among 715 participants of the Dutch prospective PIAMA (Prevention and Incidence of Asthma and Mite Allergy) birth cohort study. Relationships of different indicators of residential livestock farming exposure (distance to farms, distance-weighted number of farms, cattle, pigs, poultry, horses and goats within 3 km; modelled atmospheric PM_{10} concentrations from livestock farms) with forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) at age 16 were assessed by linear regression taking into account potential confounders. Associations were expressed per interquartile range increase in exposure.

Results: Higher exposure to livestock farming was consistently associated with a lower FEV_1, but not with FVC among participants living in less urbanized municipalities ($<$1500 addresses/km^2, $N = 402$). Shorter distances of homes to livestock farms were associated with a 1.4% (0.2%; 2.7%) lower FEV_1. Larger numbers of farms within 3 km and higher concentrations of PM_{10} from livestock farming were associated with a 1.8% (0.8%, 2.9%) and 0.9% (0.4%,1.5%) lower FEV_1, respectively.

Conclusions: Our findings suggest that higher exposure to livestock farming is associated with a lower FEV_1 in adolescents. Replication and more research on the etiologic agents involved in these associations and the underlying mechanisms is needed.

1. Introduction

There is convincing evidence for adverse long-term effects of air pollution on the lung function of children and adults (Gotschi et al., 2008; Health Effects Institute, 2010; Schultz et al., 2017). Motorized traffic is a major source of air pollution worldwide, and consequently, traffic-related air pollution has been a major focus of the studies to date (Health Effects Institute, 2010; Schultz et al., 2017). Livestock farming is another important source of air pollution. It is associated with emissions of gases such as ammonia, primary particles, including biological components such as endotoxin, as well as secondary particles (formed by atmospheric reactions from gases such as ammonia) (Cambra-Lopez et al., 2010; de Rooij et al., 2017; Schulze et al., 2006; Winkel AM et al., 2015). Ammonia is a respiratory irritant (Loftus et al., 2015). Endotoxin,

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is a pro-inflammatory component of the outer membrane of gram negative bacteria that can cause respiratory health effects (Basinas et al., 2015; Liebers et al., 2008; Hamon et al., 2012).

Studies of the health effects of air pollution from livestock farming are currently scarce, but there is a growing interest in the impact of livestock farm emissions on respiratory health, in particular in the Netherlands, one of the most densely populated countries of the world that also has a very high livestock density (Statistics Netherlands (CBS), 2022a). Several epidemiological studies reported chronic effects including lower lung functions and higher risks of respiratory symptoms, pneumonia, and mortality from chronic lower respiratory tract diseases (COPD) among subjects living close to livestock farms (Borlée et al., 2015, 2017; Radon et al., 2007; Simoes et al., 2022; Freidl et al., 2017; van Kersen et al., 2020; Rasmussen et al., 2017). Also, air pollution from livestock farming has been found to be associated with exacerbations of existing respiratory diseases such as asthma and COPD. In contrast, other studies reported fewer cases of asthma and lower probabilities of dispensing asthma and COPD medication among residents living close to livestock farms (Smit et al., 2014; Post et al., 2021).

At present, only few studies investigated the associations between residential proximity to livestock farming and respiratory health in children or adolescents (Rasmussen et al., 2017; Elliott et al., 2004; Mirabelli et al., 2006; Sigurdarson and Kline, 2006; Pavilonis et al., 2013), who may be more susceptible since their organs are still developing and inhalation dosimetry differs from that of adults (Foos et al., 2008). Higher risks of asthma symptoms and exacerbations have been reported for children and adolescents who live or attend schools close(r) to animal feeding operations (Rasmussen et al., 2017; Mirabelli et al., 2006; Sigurdarson and Kline, 2006; Pavilonis et al., 2013). To the best of our knowledge no study assessed associations between residential proximity to livestock farming and lung function in children. Also, the studies that have been performed in children so far, relied purely on distance as a proxy of exposure.

Therefore, the objective of the current study is to assess associations between residential exposure to livestock farming and lung function measured at age 16 years in the prospective Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) cohort. We used multiple indicators of exposure including distance to livestock farms, numbers of farms and animals in the proximity as well as modelled particulate matter ≤10 μm (PM_{10}) concentrations emitted from livestock farms.

2. Materials and methods

2.1. Study design and population

PIAMA is a population-based prospective birth cohort study that has been described in detail elsewhere (Brunekreef et al., 2002; Wijga et al., 2014). In brief, pregnant women were recruited from communities in the North, West, and Central regions of the Netherlands and their children (N = 3963) have been followed since birth in 1996/97. Information on demographic factors, lifestyle, household and health characteristics has been collected by repeated questionnaires completed by the parents (until age 17) and the participants themselves (from age 11). Medical examinations including spirometry and anthropometry were conducted at several ages in subgroups (more details are provided in the online supplement).

The present study uses lung function measurements that were performed at age 16 in subsets of participants from the northern and central regions of the country. We limited the analysis to lung function measurements performed in 2012–2014 when the participants were about 16 years old as these coincide best with the data on livestock farming exposure, which is for the years 2015 (PM_{10}) and 2016 (distance to livestock farms, numbers of farms and animals). The study sample includes all participants with valid lung function measurements at age 16, information on height and weight at the time of lung function measurement and livestock farming exposure data (valid, geocoded home addresses within the Netherlands). None of these 715 participants lived on a farm. A map of the Netherlands with the home addresses (±100 m random offset for privacy) of the participant is presented in Fig. S1. Ethical approval for the PIAMA study was obtained from the ethical review boards of participating institutes and written informed consent was obtained from participants as well as their parents/legal guardians.

2.2. Livestock farming exposures assessment

We assessed several indicators of livestock farm exposure at the home address at the time of the lung function measurement. For geolocation of the farms, we used the Geographic Information System for Agricultural Holdings (GIAB) database of all agricultural holdings (the location where the farm is registered) for the year 2016. Information on types of animals and annual average numbers of animals per type was linked to the main farm location of each agricultural holding and used to calculate the following exposure indicators: distance to the nearest livestock farm (m), distance-weighted number of farms and distance-weighted number of cattle, pigs, poultry, horses (including ponies), and goats [Σ(n/distance in km)] within a buffer of 3 km of the home address as described previously (de Rooij et al., 2018). These types of animals were chosen based on previous epidemiological studies from the Netherlands and the preponderance of types of animals, and only farms with at least one of the aforementioned types of animals were included.

We also linked geocoded residential addresses with modelled concentrations of PM_{10} originating from livestock farming described in detail elsewhere and in the online supplement (Post et al., 2021). In brief, the Operational Priority Substances (OPS) model is an atmospheric transport and dispersion model for airborne pollutants. It calculates the relation between individual sources and specific receptor points using Gaussian plumes and makes use of trajectories for long-range transport. The OPS model takes into account removal processes of dry and wet deposition and includes chemical conversion to transform primary emitted species into secondary particles. The total concentration at a certain location or grid cell is the sum of the contributions of all individual sources. Livestock-related PM_{10} concentrations were calculated at a 250 m × 250 m resolution with the OPS model (Sauter et al., 2018) using terrain roughness at a 250 m × 250 m resolution, meteorological conditions of 2015 and primary PM_{10} emissions of stable locations in the Netherlands for the year 2015 obtained from the Pollutant Release and Transfer Register (National Institute for Public Health and the Environment (RIVM), 2022a). These emissions were determined by multiplying the number of animals per location with animal-specific and housing type-specific emission factors (Vonk et al., 2016). Emissions from abroad and secondary inorganic aerosols (formed from atmospheric chemical conversions which can partly be attributed to ammonia emissions from livestock farms) were not included in the calculations. Animal category-specific particle size distributions were applied based on measurements (Winkel AM et al., 2015; Lai et al., 2014). PM_{10} concentrations were calculated for the same types of animals as the livestock farming exposure indicators, namely cattle, pigs, poultry, horses (including ponies) and goats. The sum of these animal type specific concentrations is referred to as 'livestock-related PM_{10} exposure'.

2.3. Spirometry

Lung function including forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) was measured between November 2012 and March 2014 by spirometry at age 16 in two research centres (Groningen and Utrecht) as described previously and in the online supplement (Milanzi et al., 2018). In brief, lung function has been measured by experienced technicians with Jaeger Masterscreen pneumotachographs (CareFusion, Yoba Linda, CA, USA) and EasyOne spirometers (ndd Medical Technologies Inc, Zurich, Switzerland), respectively, following the recommendations of the American Thoracic Society (ATS)/European

Respiratory Society (ERS) (Miller et al., 2005). Lung function measures were corrected for differences between spirometers as in previous analyses (Milanzi et al., 2018; Yu et al., 2021).

2.4. Potential confounding variables

We included the same covariates as in previous analyses within this cohort (Milanzi et al., 2018; Yu et al., 2021): age, height and weight at the time of the lung function measurement (all natural-log transformed following the methodology described elsewhere (Raizenne et al., 1996; Hoek et al., 2012)), sex, respiratory infections during the 3 weeks before lung function measurement (yes/no), maternal and paternal allergy (asthma ever, hay fever, and/or allergies to house dust mites or pets, yes/no), parental country of birth (both parents born in the Netherlands, yes/no), high parental education (at least one parent with higher vocational education or university, yes/no), breastfeeding at 12 weeks (yes/no), maternal smoking during pregnancy (yes/no), smoking in the participant's home during the past 12 months (>1x/week, yes/no), active smoking by the participant (>1x/week, yes/no), mould/damp spots in living room and/or participant's bedroom during the past 12 months (yes/no), gas cooking during the past 12 months (yes/no), furry pets in the participant's home during the past 12 months (cat, dog, rodent, yes/no), and average PM_{10} concentration during the 7 days preceding the lung function measurement (from the nearest background monitoring station of the National Air Quality Monitoring Network (National Institute for Public Health and the Environment (RIVM), 2022b)). In addition, we included land-use regression modelled annual average outdoor nitrogen dioxide (NO_2) concentration (Beelen et al., 2013) at the participants home address as a marker of long-term exposure to traffic-related air pollution in the present analysis. Questionnaire-based covariates that can vary over time were obtained from questionnaires completed at age 16 or otherwise at age 14, to coincide as much as possible with the lung function measurement.

2.5. Statistical analysis

We followed the same approach (Raizenne et al., 1996; Hoek et al., 2012) as in previous analyses within the same cohort (Milanzi et al., 2018; Yu et al., 2021) and used linear regression with natural-log transformed absolute lung function values as the dependent variables. We assessed associations with livestock farming exposures one by one and present associations as percent change in lung function (with 95% confidence intervals, CI) calculated from the regression coefficients β as $(e^{\beta}-1)*100\%$. We used natural splines with 6 knots to assess the linearity of exposure-response relationships. Not all relationships were linear (Figs. S2 and S3). Therefore, associations are presented for continuous and categorical exposures. Exposures were categorized using quartiles as cut-offs, except for distance-weighted number of pigs and poultry, for which the median of the non-zero values was used as cut-off because of the many zeros. Associations with continuous exposures were presented for interquartile range (IQR) increase in exposure to facilitate comparison of associations between indicators of exposure.

Associations are presented for minimally (age, height, weight and sex) and fully adjusted (all potential confounders described above) models (complete case analysis). Analyses were performed for the entire study sample and for participants who lived in less urbanized municipalities only (<1500 addresses/km^2 (Statistics Netherlands (CBS), 2022b), N = 402). The analysis within the subgroup that lived in less urbanized municipalities is considered the main analysis as associations within the entire study sample may be biased by urban-rural differences. We assessed the importance of specific animal types with multi-animal type models including (PM_{10} from) all types of animals. Multi collinearity was assessed with variance inflation factors. In sensitivity analyses, we assessed 1) the impact of extreme exposures on associations with continuous exposure variables by excluding participants with the 5% highest exposure values, 2) the independence of associations with livestock farming exposure from PM_{10} from other sources, by additionally adjusting for modelled annual average PM_{10} from sources other than livestock, and 3) the impact of asthmatic participants on our findings by excluding participants with current asthma (the number of asthmatics was too small to allow a separate analysis in asthmatics).

Spatial assignment of exposure measures to home addresses was performed using ArcGis 10. Statistical analyses were conducted using SAS 9.4 except for the exposure-response analysis with splines, which were performed with R-Studio Version 4.1.2.

3. Results

3.1. Population characteristics

Characteristics of the study population are presented in Table 1 and were similar for the subgroup of participants who lived in less urbanized municipalities and the entire study sample. Participants were on average 16.4 years old. Parental level of education was generally high, but tended to be lower for the less urbanized subsample. Nine percent of the participants had asthma. Compared to the full PIAMA cohort, children of highly educated parents were overrepresented in the current study sample, but differences with the full cohort were small otherwise (Table S1). On average, participants were living for 12 years at their current address (Table 1). Of the entire sample, only 15 participants had changed address in the previous year.

3.2. Livestock farming exposure

The median distance to the nearest livestock farm was 673 m for the subsample living in less urbanized municipalities (Table 2) and 807 m for the entire study sample (Table S2). All participants from less urbanized municipalities and 99% of the entire sample had a livestock farm within 3 km of their home. On most of these farms cattle and/or horses were present, followed by goats, pigs and poultry. Model predicted animal type-specific PM_{10} concentrations at the home addresses were highest for poultry, followed by cattle and pigs.

Correlations between exposure variables are presented in Fig. S4. Correlations with the distance of the participant's home to the nearest livestock farm were low to moderate and negative for all other livestock farming exposure indicators ($r = -0.08$ to -0.60). Correlation with the number of farms was high for the number of cattle ($r = 0.92$) and low to moderate for numbers of other types of animals ($r = 0.08$ to 0.63). Total PM_{10} from livestock farming was highly correlated with PM_{10} from poultry and pigs ($r = 0.99$ and 0.89, respectively). Correlations between animal type-specific PM_{10} concentrations ranged from 0.34 to 0.86.

3.3. Lung function and livestock farming

Fully adjusted estimates of associations between livestock farm exposure proxies and lung function tended to be slightly larger than minimally adjusted estimates (Tables 3 and S3). Associations were largely limited to participants who lived in less urbanized municipalities, and were more consistent for FEV_1 than for FVC. Among those who lived in less urbanized municipalities, living closer to livestock farms and larger numbers of farms was associated with a lower FEV_1 [−1.4% (95% CI -2.7 to −0.2%) and −1.8% (−2.9 to −0.8%), respectively per IQR]. Negative associations with FEV_1 were observed for all types of animals and were strongest for horses [−1.4% (2.3% to −0.5%), Table 3].

Also for PM_{10} minimally and fully adjusted associations with lung function were generally similar, more pronounced among those who lived in less urbanized municipalities and limited to FEV_1 (Tables 4 and S4). In models with continuous PM_{10} exposure, higher concentrations of both total livestock farming PM_{10} and animal-specific PM_{10} for all included animal species were associated with lower FEV_1. Associations per interquartile range increase in PM_{10} exposure ranged from −0.4%

Table 1

Characteristics of the study populations – potential confounders, urbanization and occupancy, lung function and asthma.

Characteristic	Less urbanized municipalities [a]		Entire study sample	
	n (%)	N	n (%)	N
Potential confounders				
Female sex, n (%)	203 (51)	402	378 (53)	715
Age (years), mean ± SD	16.4 ± 0.2	402	16.4 ± 0.2	715
Height (cm), mean ± SD	176.0 ± 8.8	402	175.5 ± 8.7	715
Weight (kg), mean ± SD	64.4 ± 9.9	402	64.2 ± 10.2	715
Parental allergy				
Allergic mother, n (%)	122 (30)	402	231 (32)	715
Allergic father, n (%)	132 (33)	402	240 (34)	714
Dutch nationality, n (%)	371 (93)	397	647 (92)	700
Parental education				
Low/intermediate, n (%)	174 (43)	402	265 (37)	715
High, n (%)	228 (57)	402	450 (63)	715
Maternal smoking during pregnancy, n (%)	65 (16)	400	93 (13)	709
Breastfeeding >12 weeks, n (%)	192 (51)	380	394 (58)	679
Active smoking, n (%)	35 (9)	384	50 (7)	683
Second-hand smoke at home, n (%)	28 (7)	386	45 (7)	684
Use of gas for cooking, n (%)	292 (76)	386	533 (78)	683
Mould/damp spots in bedroom/living room, n (%)	41 (11)	381	70 (10)	678
Furry pets (cat, dog and/or rodent) at home, n (%)	239 (61)	391	406 (58)	699
Annual avg. NO_2 at home address (μg/m^3), mean ± SD	18.0 ± 4.6	402	20.6 ± 5.4	715
Short term exposure to PM_{10} (μg/m^3), mean ± SD	18.6 ± 7.2	399	18.6 ± 7.0	704
Annual avg. PM_{10} from other sources at home address (μg/m^3), mean ± SD	16.4 ± 2.1	402	17.0 ± 2.2	715
Urbanization and occupancy				
Degree of urbanization (home address) [b]				
Extremely urbanized (≥2500 addresses/km^2), n (%)	–	–	45 (6)	715
Strongly urbanized (1500-2000 addresses/km^2), n (%)	–	–	268 (37)	715
Moderately urbanized (1000-1500 addresses/km^2), n (%)	151 (38)	402	151 (21)	715
Hardly urbanized (500-1000 addresses/km^2), n (%)	183 (36)	402	183 (26)	715
Not urbanized (<500 addresses/km^2), n (%)	68 (17)	402	68 (10)	715
Occupancy (years), mean ± SD [b]	12.0 ± 4.9	402	11.9 ± 4.9	715
Lung function and asthma				
FEV_1 (L), mean ± SD	4.0 ± 0.7	402	3.9 ± 3.7	715
FVC (L), mean ± SD	4.8 ± 0.9	402	4.7 ± 0.9	715
FEV_1 (% predicted), mean ± SD [c]	97.5 ± 10.3	402	97.0 ± 10.4	715
FVC (%predicted) , mean ± SD [c]	100.8 ± 9.5	402	100.4 ± 9.8	715
Recent cold/respiratory infection, n (%)	159 (39)	402	300 (42)	715
Current asthma, n (%) [d]	36 (9)	388	59 (9)	685

[a] Less than 1500 addresses/km.^{2}.

[b] Home address at the time of lung function measurement.

[c] Calculated with the Global Lung Initiative reference equations (Quanjer et al., 2012).

[d] Two out of three: asthma ever diagnosed, wheeze in past 12 months, asthma medication prescribed in past 12 months.

(−0.9 to −0.0%) for PM_{10} from horses to −1.9% (−3.2 to −0.6%) for PM_{10} from goats for participants living in less urbanized areas (Table 4).

3.4. Multi-animal type models

In models with all animal types, associations with FEV_1 attenuated (Fig. 1) and confidence intervals became wider, but the negative associations of numbers of horses and goats with FEV_1 remained (marginally) statistically significant ($p < 0.1$ and 0.05, respectively). Associations with animal-specific PM_{10} were no longer statistically significant in models with PM_{10} from all animal types, but estimates for PM_{10} from poultry and horses were very similar in single- and multi-animal models. Variance inflation factors went up to 3.6 and 4.2 in models with numbers of animals and animal-specific PM_{10}, respectively, indicating that there are some, but no serious multi-collinearity issues in models with multiple animal types.

3.5. Sensitivity analyses

The negative associations with FEV_1 remained statistically significant, except for numbers of poultry and horses when we excluded participants with the highest 5% exposure values (Fig. S5). Associations of livestock farming PM_{10} with FEV_1 attenuated after adjustment for total PM_{10} from other sources, but remained statistically significant for total livestock PM_{10} and PM_{10} from poultry (Fig. 2). Associations remained largely unchanged when we restricted the analysis to participants without asthma (Fig. S6).

4. Discussion

This paper describes the associations of several livestock farm exposure indicators with lung function at age 16 in the PIAMA birth cohort. We found that living closer to livestock farms and larger numbers of livestock farms and animals as well as higher concentrations

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[1] Adjusted for sex, and ln-transformed age, height and weight, breastfeeding, respiratory infections during the 3 weeks preceding the lung function measurement, maternal and paternal allergy, parental country of birth, high parental education, breastfeeding at 12 weeks, maternal smoking during pregnancy; smoking, mould/damp spots, gas cooking, and furry pets in the participant's home, annual average NO_2 concentration at the home address, average concentration of PM_{10} during the seven days preceding the lung function measurement. Expressed per IQR increase in exposure. IQRs for the less urbanized study sample (from Table 2) were used in all analyses.

[2] [2]Multi-exposure models included distance-weighted numbers of animals and animal-specific PM_{10}, respectively, for all animals. Associations with numbers of animals and animal-type specific PM_{10} were assessed in separate models.

Table 2
Distributions of the residential livestock farm exposure proxies for the home addresses of participants living in less urbanized municipalities[a].

Exposure	>0, n (%) [b]	P25	Median	P75	IQR
Distance of home to the nearest livestock farm (m)	402 (100)	422	673	1005	583.0
Distance-weighed number of farms/animals within 3 km					
Farms [Σ(number of farms/km)]	402 (100)	8.2	12.9	23.0	14.8
Cattle [Σ(number of animals/km)]	400 (100)	634.2	1262.6	2199.8	1565.6
Pigs [Σ(number of animals/km)]	252 (63)	0	147.7	2361.5	2361.5
Poultry [Σ(number of animals/km)]	242 (60)	0	8020.6	51,636.7	51,636.7
Horses [Σ(number of animals/km)]	395 (98)	15.5	37.9	64.3	48.8
Goats [Σ(number of animals/km)]	311 (77)	0.5	5.4	65.0	64.5
Modelled PM_{10} from livestock farming					
Total [μg/m^3] [c]	402 (100)	0.1414	0.1835	0.3215	0.1801
Cattle [μg/m^3]	402 (100)	0.0117	0.0146	0.0187	0.0070
Pigs [μg/m^3]	402 (100)	0.0090	0.0166	0.0503	0.0413
Poultry [μg/m^3]	402 (100)	0.1166	0.1519	0.2472	0.1306
Horses [μg/m^3]	402 (100)	0.0009	0.0014	0.0017	0.0008
Goats [μg/m^3]	402 (100)	0.0001	0.0002	0.0006	0.0005

P25 = 25th percentile, P75 = 75th percentile, IQR = interquartile range.

[a] Defined as municipalities with less than 1500 addresses/km.^{2}.

[b] Number and percentage of participants with at least one livestock farm/ animal as specified within 3 km of their home or $PM_{10} > 0$ μg/m^3.

[c] Total PM_{10} from all specific animals included in this analysis, i.e. cattle, pigs, poultry, horses and goats.

of PM_{10} from livestock farming were associated with a lower FEV_1 at age 16 among participants living in less urbanized municipalities.

To the best of our knowledge, no other study assessed the association between long-term residential livestock farming exposure and lung function in children or adolescents. Two studies assessed these associations in adults. In a study from the Netherlands, FEV_1, but not FVC tended to be lower in participants with larger numbers of farms within 1 km of their homes (Borlée et al., 2017). In a study from Germany, FEV_1 was lower among subjects with more than 12 stables compared to no stables within 500 m of their homes (Radon et al., 2007). Moreover, a recent review of studies assessing the respiratory health effects of low levels of endotoxin also provided stronger evidence for associations between endotoxin exposure and FEV_1, than for associations between endotoxin exposure and FVC (Farokhi et al., 2018). The observed associations between livestock farming exposure and FEV_1 in our study and other studies and in particular the presence of associations with FEV_1 in the absence of associations with FVC suggest that livestock farming exposure increases airway obstruction, but does not affect lung volume.

Our findings are consistent with findings from earlier studies from the US that assessed the respiratory health effects of living or attending school in proximity to livestock farming in children and adolescents of different ages up to the age of 17 years. These studies observed that living or attending school in proximity to industrial food animal production was associated with higher prevalence of wheeze and physician-diagnosed asthma, exacerbations of asthma and prescriptions of asthma medication (Rasmussen et al., 2017; Mirabelli et al., 2006; Sigurdarson and Kline, 2006; Pavilonis et al., 2013). However, evidence regarding the respiratory health effects of livestock farming is not unequivocal. Two Dutch studies reported lower prevalence of asthma and asthma-medication dispensing in children living close to livestock farms (Smit et al., 2014; Post et al., 2021). Similarly, a study from the Alpine area found that specific farm types, namely traditional farms with cows, were associated with lower prevalence of asthma (Illi et al., 2012). Comparisons between these studies and the present study are hampered by differences with regard to the health outcome (asthma versus lung function) and differences in study design and methods.

Livestock farms emit a complex mixture of gases and particles, including bioaerosols (Cambra-Lopez et al., 2010; Seedorf et al., 1998). It is currently unclear which pollutants are responsible for the adverse effects of livestock farming exposure on respiratory health. We observed associations with PM_{10} emitted from livestock farming. However, PM_{10} mass concentrations are also an indicator of other farm-related emissions such as endotoxin that can be transported with particulate matter (de Rooij et al., 2019). The evidence on the etiologic role of specific agents or PM_{10} constituents in the respiratory health effects of livestock farming is currently limited, but endotoxin, tended to be associated with FVC in a study of adults living in livestock-dense areas of the Netherlands (de Rooij et al., 2019). In contrast to our study, no association between PM_{10} and lung function has been found in that study, and associations with endotoxin were found for FVC, but not for FEV_1. Unfortunately, no information on PM_{10} composition was available for our study area to assess the role of endotoxin in the observed associations with livestock farming. Also, the role of specific animals remains unclear. Mutually adjusted models with numbers of animals suggest that goats and horses may be important. Associations between numbers of goats and asthma have been reported in Dutch adults previously (Borlée et al., 2015; Smit et al., 2014). However, evidence from adult studies is not unequivocal with different studies suggesting roles for other types of animals including pigs, cattle, poultry and sheep in respiratory health (Borlée et al., 2015; Smit et al., 2014; Post et al., 2021).

A potential limitation is the cross-sectional design of the study. However, exposure is likely representative for longer-term exposure as occupancy was on average 12 years. Another potential limitation is that exposure was defined based on the home address only, which might induce some exposure measurement error as the participants spend significant amounts of their time at other locations. This exposure measurement error is likely non-differential as exposure estimates were derived in the same way for all participants regardless of their lung function. Moreover, there might be some exposure misclassification due to the fact that we used farm locations to calculate distance-weighted numbers of animals and stable locations to estimate PM_{10}. These locations may differ from the actual locations of the animals such as stables and pastures. There is a slight mismatch in timing of the lung function measurements (performed in 2012–2014) and the exposure data, which relate to farm locations from 2016, emissions and meteorology from 2015. During this period, no major changes in locations occurred (Statistics Netherlands (CBS), 2022a). We assessed the sensitivity of the spatial patterns of PM_{10} concentrations to differences in meteorology and emissions between the years 2012–2015 and found spatial patterns to be robust against differences in meteorology and emissions (more details are provided in the online supplement). Other misclassifications regarding PM_{10} modelling may occur due to for instance uncertainty in emission characteristics or uncertainty in the dispersion modelling itself. Our study was limited to two regions of the country and may not be generalizable to other parts of the country or other countries with different types, management practices and intensities of livestock farming. We were unable to assess whether asthmatics are differentially susceptible to livestock farming exposure as our study sample included too few asthmatics.

5. Conclusion

Our study adds to the growing body of evidence on the adverse effects of livestock farming exposures on the respiratory health and

Table 3

Minimally [a] and fully adjusted [b] associations[c] of the residential livestock farm exposure proxies with FEV_1 and FVC at age 16 for participants who live in less urbanized municipalities. [d]

	Minimally adjusted (N = 402)						Fully adjusted (N = 343)					
	FEV_1			FVC			FEV_1			FVC		
	% diff.	(95% CI)	p-value	(95% CI)	% diff.	p-value	% diff.	(95% CI)	p-value	% diff.	(95% CI)	p-value
Distance to nearest farm (m)												
>1005	Ref			Ref			Ref			Ref		
673–1005	−0.3	(-3.2; 2.7)	0.829	0.7	(-1.8; 3.1)	0.597	−0.8	(-3.9; 2.5)	0.644	−0.0	(-2.7; 2.7)	0.981
422–673	−1.8	(-4.6; 1.2)	0.237	−0.3	(-2.7; 2.2)	0.822	−2.6	(-5.7; 0.6)	0.105	−0.1	(-2.8; 2.6)	0.928
≤422	−2.2	(-5.1; 0.7)	0.137	1.8	(-0.7; 4.3)	0.164	−3.6	(-6.7; −0.3)	0.031	1.0	(-1.8; 3.8)	0.503
per IQR (cont. in -m)	−1.0	(-2.1; 0.1)	0.081	0.5	(-0.5; 1.4)	0.343	−1.4	(-2.7; −0.2)	0.025	0.4	(-0.7; 1.5)	0.481
Farms [Σ(number of farms/km)]												
≤8.2	Ref			Ref			Ref			Ref		
8.2–12.9	−1.6	(-4.4; 1.3)	0.287	−1.5	(-3.9; 0.9)	0.223	−2.9	(-5.9; 0.2)	0.064	−2.2	(-4.8; 0.4)	0.099
12.9–23.0	−2.5	(-5.3; 0.5)	0.098	−1.0	(-3.4; 1.5)	0.421	−3.4	(-6.4; −0.3)	0.035	−1.8	(-4.4; 0.9)	0.202
>23.0	−4.1	(-6.9; −1.2)	0.006	−1.2	(-3.6; 1.3)	0.356	−4.8	(-7.8; −1.6)	0.004	−1.2	(-3.9; 1.5)	0.383
per IQR (cont.)	−1.3	(-2.3; −0.3)	0.008	−0.4	(-1.2; 0.4)	0.306	−1.8	(-2.9; −0.8)	0.001	−0.6	(-1.5; 0.3)	0.191
Cattle [Σ(number of animals/km)]												
≤634.2	Ref			Ref			Ref			Ref		
634.2–1262.6	−1.2	(-4.1; 1.7)	0.409	−0.6	(-3.0; 1.9)	0.645	−2.0	(-5.1; 1.1)	0.205	−1.6	(-4.2; 1.1)	0.251
1262.6–2199.8	−2.3	(-5.2; 0.6)	0.124	−1.0	(-3.4; 1.5)	0.417	−2.0	(-5.1; 1.2)	0.220	−1.2	(-3.9; 1.5)	0.372
>2199.8	−3.3	(-6.2; −0.4)	0.025	−1.4	(-3.8; 1.1)	0.278	−4.0	(-7.0; −0.9)	0.013	−1.7	(-4.3; 1.0)	0.214
per IQR (cont.)	−0.4	(-0.8; −0.0)	0.035	−0.2	(-0.5; 0.1)	0.215	−0.6	(-1.0; −0.1)	0.010	−0.3	(-0.7; 0.1)	0.113
Pigs [Σ(number of animals/km)]												
0	Ref			Ref			Ref			Ref		
0–1607.6	−1.6	(-4.1; 0.9)	0.198	−0.9	(-3.0; 1.2)	0.378	−2.2	(-4.8; 0.6)	0.119	−1.3	(-3.6; 1.1)	0.295
>1607.6	−4.5	(-6.9; −2.1)	<0.001	−1.3	(-3.3; 0.8)	0.234	−4.4	(-7.1; −1.6)	0.003	−1.3	(-3.7; 1.1)	0.279
per IQR (cont.)	−0.7	(-1.0; −0.3)	0.001	−0.2	(-0.5; 0.1)	0.245	−0.8	(-1.3; −0.4)	<0.001	−0.3	(-0.7; 0.0)	0.084
Poultry [Σ(number of animals/km)]												
0	Ref			Ref			Ref			Ref		
0–26,569.1	−0.8	(-3.3; 1.8)	0.554	−0.4	(-2.5; 1.8)	0.724	0.1	(-2.6; 2.9)	0.944	0.1	(-2.2; 2.4)	0.938
>26,569.1	−2.7	(-5.1; −0.2)	0.038	−1.2	(-3.3; 0.9)	0.258	−2.6	(-5.2; 0.2)	0.065	−1.1	(-3.4; 1.2)	0.353
per IQR (cont.)	−0.3	(-0.6; −0.1)	0.015	−0.2	(-0.4; 0.0)	0.107	−0.6	(-1.0; −0.3)	0.001	−0.3	(-0.6; −0.0)	0.044
Horses [Σ(number of animals/km)]												
≤15.5	Ref			Ref			Ref			Ref		
15.5–37.9	0.6	(-2.4; 3.6)	0.704	0.3	(-2.2; 2.8)	0.828	0.1	(-3.1; 3.4)	0.960	0.2	(-2.5; 3.0)	0.888
37.9–64.3	−0.8	(-3.7; 2.2)	0.590	−1.5	(-3.9; 0.9)	0.218	−1.5	(-4.6; 1.7)	0.351	−1.7	(-4.3; 1.0)	0.214
>64.3	−3.0	(-5.8; −0.1)	0.046	−1.9	(-4.3; 0.5)	0.129	−4.0	(-7.1; −0.8)	0.015	−2.7	(-5.3; 0.1)	0.057
per IQR (cont.)	−0.9	(-1.7; −0.2)	0.020	−0.5	(-1.2; 0.1)	0.100	−1.4	(-2.3; −0.5)	0.004	−0.8	(-1.6; −0.1)	0.036
Goats [Σ(number of animals/km)]												
≤0.5	Ref			Ref			Ref			Ref		
0.5–5.4	−1.6	(-4.4; 1.4)	0.289	0.5	(-1.9; 3.0)	0.667	−2.0	(-5.1; 1.2)	0.226	−0.5	(-3.2; 2.2)	0.707
5.4–65.0	−0.8	(-3.7; 2.1)	0.570	0.3	(-2.1; 2.7)	0.824	−2.0	(-5.1; 1.1)	0.202	−1.2	(-3.8; 1.5)	0.393
>65.0	−4.6	(-7.4; −1.7)	0.002	−1.5	(-3.9; 1.0)	0.239	−5.3	(-8.4; −2.2)	0.001	−2.1	(-4.8; 0.6)	0.132
per IQR (cont.)	−0.3	(-0.4; −0.1)	0.000	−0.1	(-0.2; 0.0)	0.091	−0.3	(-0.4; −0.1)	<0.001	−0.1	(-0.2; 0.0)	0.124

[a] Adjusted for sex, and ln-transformed age, height and weight.

[b] Adjusted for sex, and ln-transformed age, height and weight, breastfeeding, respiratory infections during the 3 weeks preceding the lung function measurement, maternal and paternal allergy, parental country of birth, high parental education, breastfeeding at 12 weeks, maternal smoking during pregnancy; smoking, mould/damp spots, gas cooking, and furry pets in the participant's home, annual average NO_2 concentration at the home address, average concentration of PM_{10} during the seven days preceding the lung function measurement.

[c] Quartiles were used as cut-offs except for pigs and poultry, where the median of all non-zero values was used as cut-off. Quartiles, medians and IQRs for the less urbanized study sample (from Table 2) were used in all analyses. To facilitate comparison of associations between exposure indicators, largest differences (corresponding to lowest exposures) were used as the reference for distance to farms and inverse distance (-m) was used in analyses with distance as a continuous variable.

[d] Defined as municipalities with less than 1500 addresses/km.^{2}.

suggests that higher residential livestock farming exposure is associated with a lower FEV_1 in adolescents. Replication and more research on the etiologic agents involved in these associations and the underlying mechanisms is needed.

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Author contributions

Pauline Kiss and Ulrike Gehring designed the study. Pauline Kiss and Ulrike Gehring performed the formal analysis, and Pauline Kiss wrote the initial manuscript under the supervision of Ulrike Gehring. Lidwien A.M. Smit, Myrna M.T. de Rooij, Lenny Hogerwerf, Hendrika A.M. Sterk and Ulrike Gehring contributed to the methodology, and Jolanda Boer, Gerard H. Koppelman, Roel Vermeulen, Judith M Vonk, Roel Vermeulen and Ulrike Gehring secured funding. All authors (i) provided substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work, (ii) reviewed a the mansuscript, (iii) approved the final version, and (iv) agreed to be

Table 4

Minimally [a] and fully adjusted [b] associations[c] of modelled total PM_{10} from livestock farming and modelled animal type-specific PM_{10} with FEV_1 and FVC at age 16 for participants who live in less urbanized municipalities.[d]

	Minimally adjusted (N = 402)						Fully adjusted (N = 343)					
	FEV_1			FVC			FEV_1			FVC		
	% diff.	(95% CI)	p-value	% diff.	(95% CI)	p-value	% diff.	(95% CI)	p-value	% diff.	(95% CI)	p-value
Total PM_{10} from livestock farming [μg/m^3]												
≤0.141	Ref			Ref			Ref			Ref		
0.141–0.184	2.5	(-0.4; 5.6)	0.095	1.4	(-1.1; 3.9)	0.271	2.7	(-0.5; 6.0)	0.103	1.5	(-1.2; 4.3)	0.282
0.184–0.322	−0.9	(-3.8; 2.1)	0.554	0.4	(-2.0; 2.9)	0.733	−0.4	(-3.6; 3.0)	0.829	0.7	(-2.2; 3.6)	0.649
>0.322	−3.2	(-6.0; −0.2)	0.037	−0.9	(-3.4; 1.6)	0.473	−3.7	(-7.1; −0.2)	0.041	−1.0	(-4.0; 2.1)	0.534
per IQR (cont.)	−0.6	(-1.0; −0.2)	0.008	−0.2	(-0.6; 0.1)	0.191	−0.9	(-1.5; −0.4)	0.001	−0.4	(-0.8; 0.1)	0.103
PM_{10} from cattle [μg/m^3]												
≤0.012	Ref			Ref			Ref			Ref		
0.012–0.015	−2.4	(-5.2; 0.5)	0.109	−1.4	(-3.7; 1.1)	0.272	−0.6	(-3.7; 2.6)	0.709	−1.0	(-3.7; 1.7)	0.454
0.015–0.019	−1.4	(-4.2; 1.6)	0.359	−0.7	(-3.1; 1.8)	0.586	0.7	(-2.6; 4.1)	0.694	0.6	(-2.2; 3.5)	0.691
>0.019	−4.8	(-7.6; −1.9)	0.001	−2.1	(-4.5; 0.4)	0.097	−4.1	(-7.2; −0.9)	0.014	−1.6	(-4.3; 1.2)	0.258
per IQR (cont.)	−0.9	(-1.7; −0.0)	0.041	−0.3	(-1.0; 0.3)	0.324	−1.0	(-1.9; −0.1)	0.027	−0.5	(-1.2; 0.3)	0.245
PM_{10} from pigs [μg/m^3]												
≤0.009	Ref			Ref			Ref			Ref		
0.009–0.017	0.2	(-2.7; 3.2)	0.877	0.2	(-2.3; 2.7)	0.890	1.1	(-2.0; 4.4)	0.477	1.0	(-1.6; 3.8)	0.452
0.017–0.050	−0.3	(-3.2; 2.7)	0.824	0.1	(-2.4; 2.6)	0.939	0.7	(-2.8; 4.3)	0.696	0.7	(-2.3; 3.8)	0.643
>0.050	−4.3	(-7.2; −1.4)	0.004	−1.0	(-3.5; 1.5)	0.424	−4.1	(-7.6; −0.4)	0.032	−0.6	(-3.7; 2.7)	0.728
per IQR (cont.)	−0.9	(-1.8; −0.0)	0.040	−0.1	(-0.8; 0.7)	0.802	−1.3	(-2.3; −0.2)	0.016	−0.3	(-1.2; 0.6)	0.536
PM_{10} from poultry [μg/m^3]												
≤0.117	Ref			Ref			Ref			Ref		
0.117–0.152	1.7	(-1.2; 4.8)	0.250	0.6	(-1.9; 3.1)	0.661	2.2	(-0.9; 5.5)	0.171	1.0	(-1.6; 3.8)	0.445
0.152–0.247	−0.5	(-3.4; 2.5)	0.759	1.3	(-1.1; 3.9)	0.296	0.5	(-2.7; 3.8)	0.767	2.1	(-0.7; 5.0)	0.144
>0.247	−3.1	(-6.0; −0.2)	0.040	−1.0	(-3.5; 1.5)	0.427	−3.0	(-6.4; 0.6)	0.100	−0.6	(-3.6; 2.5)	0.717
per IQR (cont.)	−0.5	(-0.8; −0.1)	0.008	−0.2	(-0.5; 0.1)	0.163	−0.8	(-1.2; −0.3)	0.001	−0.3	(-0.7; 0.0)	0.089
PM_{10} from horses [μg/m^3]												
≤0.0009	Ref			Ref			Ref			Ref		
0.0009–0.0014	−2.1	(-4.9; 0.8)	0.159	−0.9	(-3.3; 1.6)	0.466	−2.2	(-5.2; 1.0)	0.179	−1.1	(-3.7; 1.6)	0.418
0.0014–0.0017	−4.6	(-7.4; −1.7)	0.002	−1.9	(-4.4; 0.5)	0.122	−4.3	(-7.4; −1.1)	0.009	−1.9	(-4.6; 0.9)	0.179
>0.0017	−4.2	(-6.9; −1.3)	0.005	−2.0	(-4.4; 0.4)	0.106	−3.5	(-6.6; −0.3)	0.033	−1.7	(-4.4; 1.0)	0.215
per IQR (cont.)	−0.4	(-0.8; 0.0)	0.063	−0.2	(-0.6; 0.2)	0.261	−0.4	(-0.9; −0.0)	0.048	−0.2	(-0.5; 0.2)	0.419
PM_{10} from goats [μg/m^3]												
≤0.0001	Ref			Ref			Ref			Ref		
0.0001–0.0002	−1.2	(-4.0; 1.8)	0.434	−1.1	(-3.5; 1.4)	0.379	0.6	(-2.5; 3.9)	0.700	−0.1	(-2.8; 2.7)	0.943
0.0002–0.0006	−2.1	(-4.9; 0.8)	0.148	−0.7	(-3.1; 1.8)	0.580	−1.4	(-5.0; 2.3)	0.443	−0.8	(-3.9; 2.4)	0.609
>0.0006	−5.4	(-8.2; −2.5)	<0.001	−2.4	(-4.8; 0.1)	0.065	−5.5	(-9.2; −1.6)	0.006	−2.4	(-5.7; 1.0)	0.165
per IQR (cont.)	−2.0	(-3.1; −0.9)	<0.001	−0.5	(-1.4; 0.5)	0.336	−1.9	(-3.2; −0.6)	0.005	−0.3	(-1.4; 0.9)	0.627

[a] Adjusted for sex, and ln-transformed age, height and weight.

[b] Adjusted for sex, and ln-transformed age, height and weight, breastfeeding, respiratory infections during the 3 weeks preceding the lung function measurement, maternal and paternal allergy, parental country of birth, high parental education, breastfeeding at 12 weeks, maternal smoking during pregnancy; smoking, mould/damp spots, gas cooking, and furry pets in the participant's home, annual average NO_2 concentration at the home address, average concentration of PM_{10} during the seven days preceding the lung function measurement.

[c] Quartiles were used as cut-offs except for pigs and poultry, where the median of all non-zero values was used as cut-off. Quartiles, medians and IQRs for the less urbanized study sample (from Table 2) were used in all analyses. To facilitate comparison of associations between exposure indicators, largest differences (corresponding to lowest exposures) were used as the reference for distance to farms and inverse distance (-m) was used in analyses with distance as a continuous variable.

[d] Defined as municipalities with less than 1500 addresses/km.^{2}.

accountable for all aspects of the work.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Myrna MT de Rooij reports a relationship with NCOH (Netherlands Center for One Health) that includes: travel reimbursement. Gerard H. Koppelman reports a relationship with Netherlands Lung Foundation that includes: funding grants. Gerard H. Koppelman reports a relationship with ZonMw that includes: funding grants. Gerard H. Koppelman reports a relationship with Teva The Netherlands that includes: funding grants. Gerard H. Koppelman reports a relationship with GSK that includes: consulting or advisory and funding grants. Gerard H. Koppelman reports a relationship with Vertex that includes: funding grants. Gerard H. Koppelman reports a relationship with Ubbo Emmius foundation that includes: funding grants. Gerard H. Koppelman reports a relationship with European Union (H2020) that includes: funding grants. Gerard H. Koppelman reports a relationship with Pure IMS that includes: consulting or advisory. Gerard H. Koppelman reports a relationship with Sanofi that includes: consulting or advisory. Gerard H. Koppelman reports a relationship with Astra Zeneka that includes: consulting or advisory. Lidwien AM Smit reports a relationship with Ministry of Health, Welfare and Sport of the Netherlands that includes: funding grants. Lenny Hogerwerf reports a relationship with Ministry of Health, Welfare and Sport of the Netherlands that includes: funding grants. Lidwien AM Smit reports a relationship with Ministry of Agriculture, Nature and Food Quality of The Netherlands that includes: funding grants.

Data availability

Data requests can be sent to the first author. Requests and conditions under which it is possible to share data will be assessed on a case-by-case basis by the PIAMA steering committee.

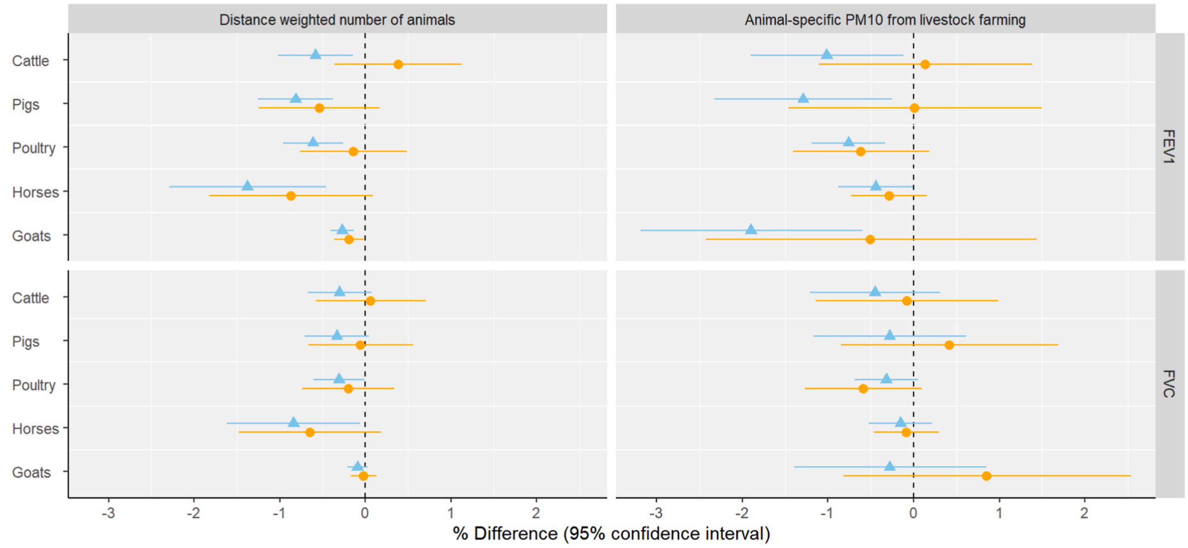

Fig. 1. Comparison of association estimates [1] from single exposure (light blue triangles) and multi exposure models [2] (orange dots) with continuous exposure variables for participants living in less urbanized municipalities. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

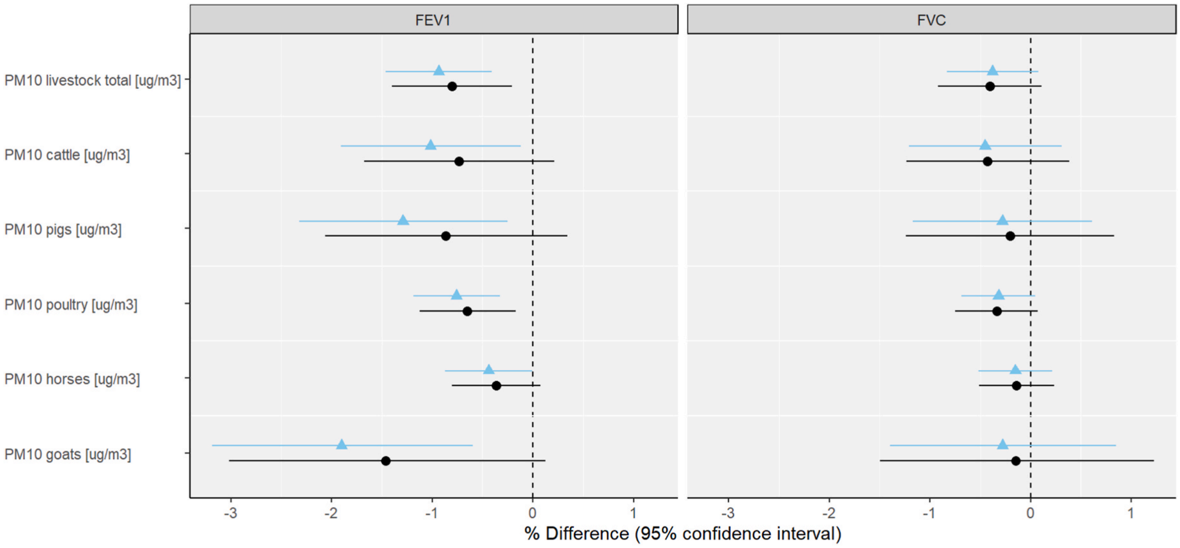

Fig. 2. Association estimates [1] for PM_{10} from livestock (continuous) from fully adjusted models (light blue triangles) and models with additional adjustment for non-livestock PM_{10} (black dots) for participants living in less urbanized municipalities. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.115134.

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