Human health effects due to proximity to concentrated animal-feeding operations (CAFO)

Project Summary: Outcomes and exposures evaulated in the published literture from 2014 to 2020. updated Annette. BAFM.123

Livestock farming has experienced a significant transformation in the last decades, moving from small, family-owned farms to large farms. To classify those large animal operations, two terms are used: animal feeding operations (AFO) and concentrated animal feeding operations (CAFO). The U.S. Environmental Protection Agency (EPA) defines an AFO as a agricultural enterprise where animals are kept and raised in confined situations. AFOs congregate animals, feed, manure and urine, dead animals, and production operations on a small land area. Likewise, for the EPA, CAFO is a term used for a large concentrated AFO. More precisely, a CAFO is an AFO with more than 1000 animal units confined on site for more than 45 days during the year. The growth and popularity of this type of operations has been accompanied by the concerns due to the potential harmful effects that animal facilities could have on nearby communities. Regarding the swine industry, it has been suggested that facilities that confine animals indoors for feeding might represent a health hazard for surrounding communities because of exposure to odors, emissions and other infectious agents. To understand and estimate the impacts of CAFO on the health of nearby communities, several studies have been carried out in the last years.

Purpose of the Project

In March 2020, the National Pork Board asked our group to provide a summary of the outcome and exposures reported in studies published on the topic of CAFOS and community health since 2014. Our group has performed two systematic reviews that summarize and assess the findings of previous publications approaching the association between animal-feeding operations and the measures of the health of individuals living near animal-feeding operations. In the 2014 review, we reported that 16 publications were relevant to the topic. For this project, we evaluated potentially relevant papers published since 2014.

Brief Summary

We identified 21 additional papers published since 2014. In 2017 was the year in which more studies were published (Figure 1). This growth in relevant papers highlights how much interest in the topic is growing. These "new" studies have been performed mainly in Netherlands, USA, Germany, and Canada and have explored multiple health outcomes (Figure 2). For each study, the reported health outcome measures as well as the measure used to assess exposure to animal feed operations were extracted and grouped into broad outcome and exposure categories respectively. For example if a studie reported asthma as a health outcome, this outcome was categorized into the broader category of lower respiratory diseases. These broad outcomes categories were created based on the affected body system such as digestive, cardiovascular, etc (Table 2). Likewise, if for example the exposure used into the study was distance measured in kilometers to the nearest animal operation, then this exposure was grouped into a broader exposure category called distance (Table 3). We defined a combination as the pair of a broad outcome category and an exposure, for example, lower

respiratory disease (broad outcome category) and distance to the nearest CAFO operation (exposure). In Table 1, the number of combinations in which the broad outcome category was used according to the year. For instance, we can see that for lower respiratory outcomes were the most used and discussed over the last 6 years (Table 1). The studies provided 1636 combinations of exposures and outcomes. For the period between 2014 and 2016 the number of outcomes categories analyzed ranged from 4 to 6. For the period between 2017 and 2019 the number of categories almost doubled (Figure 3).

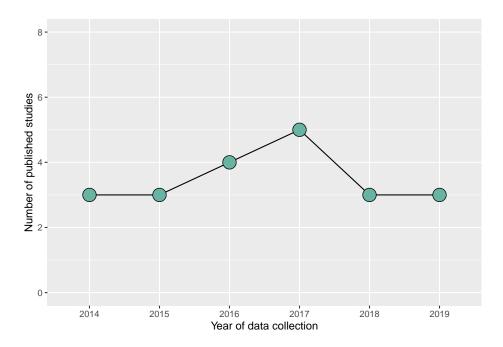


Figure 1: Trendline for the number of studies published since 2014

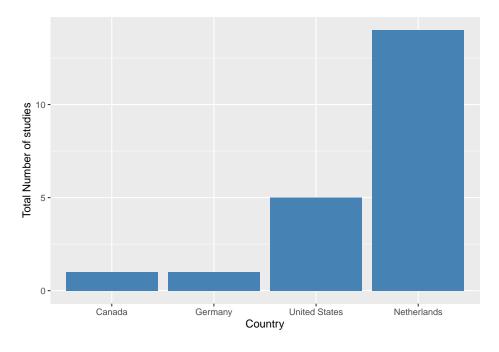


Figure 2: Number of studies published by country since 2014

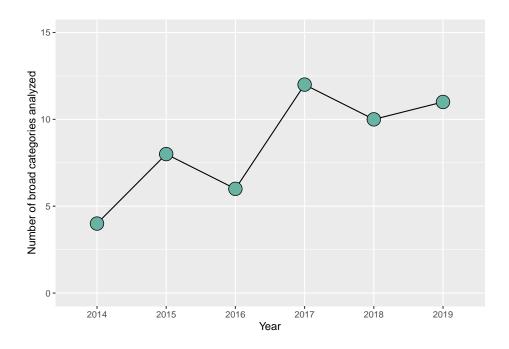


Figure 3: Number of broad outcomes categories analyzed since 2014

From 2014 to 2019, the health outcomes most commonly described are grouped within the broad group of lower respiratory conditions and include symptoms and diseases such as: asthma, chronic obstructive pulmonary disease (COPD), difficulty breathing, wheezing, emphysema, pneumonia, bronchitis, fatigue and cough and reduction of lung function (Figure 4). Other health conditions that have been studies can be grouped in broad outcome categories such as: allergies, upper respiratory, psychological, cardiovascular, neurological and gastrointestinal and infectious. Since 2011 other categories that also have been analyzed include: sleep disorders, osteoarticular, autoimmune, dermatological, blood disorder and metabolic disorders (For more detail about conditions and symptoms presented in each category from 2014 to 2019 see Table 2). This multiplicity in outcomes coincides with the changes that have occurred over the years regarding the focus on particular health outcomes. For example, a few years ago, most research focused on the effects produced in the respiratory system but recently researches have investigated the role played by proximity to facilities with the antimicrobial resistance (AMR).

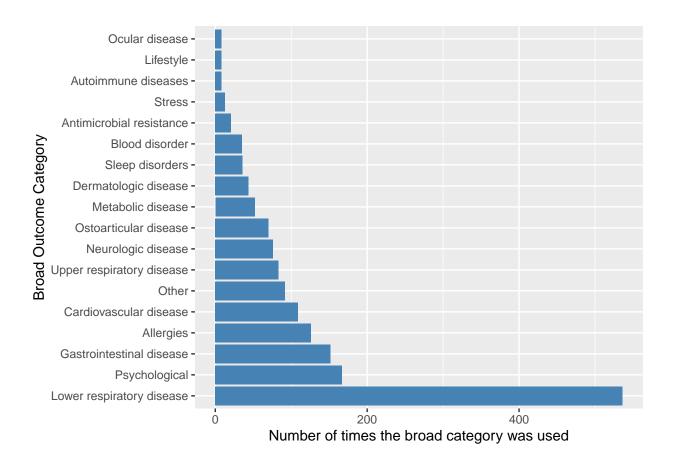


Figure 4: Number of times the broad outcome category was used in the studies published since 2014

From 2014 to date, 1637 different outcome / exposure combinations were identified in 21 relevant publications. Although there are multiple ways to establish and measure exposition to animal feeding operations, these can be grouped in broader categories which include: emissions, animal and farm density, distance to the nearest CAFO, odors and type of CAFO (swine, poultry, cattle etc.)(Figure 5). For the emission category the measure included dust emissions, ammonia (NH3) and particulate matter (PM10). To sum up, it is possible to appreciate a growth in the number of studies published during the last seven years as well as a growing trend to explore more health outcomes in these studies.

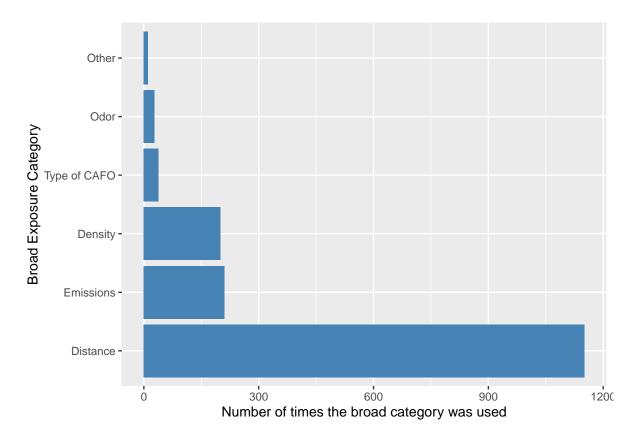


Figure 5: Number of times the broad exposure category was used in the studies published since 2014

Material and methods

Study designs eligible

Eligible studies for this update were all types of observational studies reporting any health outcome or measures of the resistance of resident (colonized) bacterial populations measured directly on human subjects. Eligible studies must include more than one unit of measurement of exposure (e.g., more than one farm per exposure group) to be included because of concerns about confounding. Additionally, studies where the unit of measurement of the outcome was a population aggregate were excluded. The populations of interest were humans living in communities near and not near animal-feeding operations that might reasonably be described as industrial. This criterion excludes studies that assess the impact of occupational exposure to livestock. Production systems that appeared to be grass-based, nomadic, or confined smallholder operations were not relevant to the update. Studies and outcomes that related to environment such as air, water, and soil or built environment were not eligible. Animal models of human disease were not eligible because it is unclear how an animal model of human disease would accurately reproduce short- and long-term effects of exposure to AFOs.

Information sources and search

The MEDLINE® databases was searched. Eligible studies reported exposure to an AFO and an individual-level human health outcome. Two reviewers performed study selection and data extraction. The syntax used in the latest systematic review was used here limiting the time from 2014 to 2020. The strategy comprised two concepts animal feeding operations and community health. Studies that only reported animal health outcomes were excluded.

Study selection

763 studies were obtained and uploaded into online systematic review software (DistillerSR®, Ottawa, ON, Canada). During Level 1 screening, the following question to assess the relevance of citation abstracts and titles was used:

1. Does the title and/or abstract describe primary research reporting the association between livestock (intensive- not pastoral) and human interactions (direct or indirect) and measures of human health measured on humans?

Citations were excluded if the reviewer answered "no" to this question. 50 studies passed Level 1 and progressed to Level 2. The following questions to assess each article retained after the full-text evaluation were used:

- 1. Does the study use a unit of analysis at the individual human level in the community (but not occupational, such as farm worker)?
- 2. Does the study include more than one unit of measurement of exposure?

The study was excluded if the reviewer answered "no" to either question. If the reviewer answered "yes" to both questions, the study progressed to the data extraction. Finally, 21 studies passed Level 2 and passed to the extraction of information.

Data collection process

For each of the 21 studies, the reviewer extracted the study year, the study population's location (country), the reported health outcome measures as well as the measure used to assess the exposure to animal feeding operations. Subsequently, these outcomes and exposures were categorized into broad categories in order to summarize and get some descriptive information.

Table 1: Number of times broad category was combinated by years

	2014	2015	2016	2017	2018	2019
Allergies	12	23	12	37	0	42
Antimicrobial resistance	21	0	0	0	0	0
Autoimmune diseases	0	0	0	0	8	0
Blood disorder	0	0	0	17	0	18
Cardiovascular disease	0	0	0	65	8	36
Dermatologic disease	0	0	6	22	16	0
Gastrointestinal disease	3	7	12	71	41	18
Lifestyle	0	0	0	0	8	0
Lower respiratory disease	24	127	48	201	22	114
Metabolic disease	0	0	0	34	0	18
Neurologic disease	0	3	0	55	0	18
Ocular disease	0	0	0	0	8	0
Ostoarticular disease	0	0	0	34	0	36
Other	0	0	70	0	22	0
Psychological	0	2	0	71	40	54
Sleep disorders	0	1	0	17	0	18
Stress	0	13	0	0	0	0
Upper respiratory disease	0	1	21	37	6	18

Table 2: Health outcomes grouped into broad categories

Broad Category	Outcome variable	Reference
Allergies	Allergic conjunctivitis	Hooiveld et al. 2016
Allergies	Allergic rhinitis	Dijk et al. 2017
Allergies	Allergic rhinitis	Smit et al. 2014
Allergies	Allergic rhinitis/Hay fever	Baliatsas et al. 2017
Allergies	Allergic rhinitis/Hay fever	Baliatsas et al. 2019
Allergies	Allergic rhinitisa	Dijk et al. 2017
Allergies	Current allergies	Schultz et al. 2019
Allergies	Hay fever	Hooiveld et al. 2016
Allergies	Lung Allergies	Schultz et al. 2019
Allergies	Nasal allergies	Borlee et al. 2015
Allergies	Nasal Allergies	Schultz et al. 2019
Allergies	Nasal or Lung Allergies & Current allergies	Schultz et al. 2019
Antimicrobial resistance	Methicillin resistant Staphylococcus aureus nasal carriage	Schinasi et al. 2014
Autoimmune diseases	Chronic/long-term diseases: autoimmune diseases	Star et al. 2018
Blood disorder	Anemia	Baliatsas et al. 2017
Blood disorder	Anemia	Baliatsas et al. 2019
Cardiovascular disease	Atherosclerosis	Baliatsas et al. 2017
Cardiovascular disease	Chronic/long-term diseases of the cardiovascular system	Star et al. 2018
Cardiovascular disease	Coronary heart disease	Baliatsas et al. 2017
Cardiovascular disease	Heart disease (risk) cluster	Baliatsas et al. 2019
Cardiovascular disease	Heart failure	Baliatsas et al. 2017 Baliatsas et al. 2017
Cardiovascular disease	Hypertension	Baliatsas et al. 2017 Baliatsas et al. 2017
Cardiovascular disease	Hypertension	Baliatsas et al. 2019
Dermatologic disease	Atopic eczema	Hooiveld et al. 2016
Dermatologic disease	Chronic/long-term diseases of the skin	Star et al. 2018
Dermatologic disease Dermatologic disease	Constitutional eczema	Dijk et al. 2017
Dermatologic disease Dermatologic disease	Infections of the skin	Star et al. 2018
Dermatologic disease		
Gastrointestinal disease	Vertiginous syndrome	Dijk et al. 2017 Levallois et al. 2014
	Acute children gastroenteritis	
Gastrointestinal disease	Campylobacter	Poulsen et al. 2018
Gastrointestinal disease	Chronic enteritis	Hooiveld et al. 2016
Gastrointestinal disease	Chronic enteritis/ulcerative colitis	Dijk et al. 2017
Gastrointestinal disease	Chronic/long-term diseases of the GI-tract	Star et al. 2018
Gastrointestinal disease	Clostridium difficile colonization	Zomer et al. 2017
Gastrointestinal disease	Diarrhoea	Hooiveld et al. 2015
Gastrointestinal disease	E. coli	Poulsen et al. 2018
Gastrointestinal disease	Gastro-intestinal infections	Dijk et al. 2017
Gastrointestinal disease	Gastro-oesophageal reflux disease	Baliatsas et al. 2017
Gastrointestinal disease	Gastro-oesophageal reflux disease	Baliatsas et al. 2019
Gastrointestinal disease	Gastroenteritis presumed infection	Hooiveld et al. 2016
Gastrointestinal disease	Gastrointestinal infection	Hooiveld et al. 2016
Gastrointestinal disease	Gastrointestinal symptoms	Hooiveld et al. 2015
Gastrointestinal disease	Infections of the GI-tract	Star et al. 2018
Gastrointestinal disease	Infectious Diarrhea	Poulsen et al. 2018
Gastrointestinal disease	inflammatory bowel disease	Kalkowska et al. 201
Gastrointestinal disease	Inflammatory bowel disease (IBD) and Total infections	Star et al. 2018
Gastrointestinal disease	Nauseous	Hooiveld et al. 2015
Gastrointestinal disease	Non-Specific Diarrhea	Poulsen et al. 2018
Gastrointestinal disease	Obstipation	Hooiveld et al. 2015
Gastrointestinal disease	Reflux/gastric acid	Hooiveld et al. 2015

Lower respiratory disease Lower respiratory	Broad Category	Outcome variable	Reference
Gastrointestinal disease Lifestyle Lower respiratory disease Lower respiratory diseases Lower respirat	Gastrointestinal disease	Salmonella	Poulsen et al. 2018
Lifestyle Lifestyle: weight and diet State tal. 2018 Lower respiratory disease Lower respiratory diseases Lower respiratory disea	Gastrointestinal disease	Stomach ache (pain in belly)	Hooiveld et al. 2015
Lower respiratory disease Lower respiratory	Gastrointestinal disease	Stomach complaints	Hooiveld et al. 2015
Lower respiratory disease Lower respiratory	Lifestyle	Lifestyle: weight and diet	Star et al. 2018
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma	Dijk et al. 2017
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma	Hooiveld et al. 2016
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma	Smit et al. 2014
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma Emergency Department Visits	Rasmussen et al. 2017
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma Episode in last 12 months	Schultz et al. 2019
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma Hospitalizations	Rasmussen et al. 2017
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma medication in last 12 months	Schultz et al. 2019
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma symptoms /Limitation of activities	Loftus et al. 2015
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma symptoms /Nighttime waking	Loftus et al. 2015
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma symptoms /Shortness of breath	Loftus et al. 2015
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma symptoms /Symptoms worse in morning	Loftus et al. 2015
Lower respiratory disease Lower respiratory	Lower respiratory disease	Asthma symptoms /Use of short-acting "relief" medication	Loftus et al. 2015
Lower respiratory disease Lower respiratory disease Chronic obstructive pulmonary disease (COPD) Smit et al. 2014 Lower respiratory disease Cold/flu Lower respiratory disease Lower respiratory di	Lower respiratory disease	Asthma symptoms /Wheezing	Loftus et al. 2015
Lower respiratory disease Lower respiratory	Lower respiratory disease	Chronic bronchitis/bronchiectasis	Dijk et al. 2017
	Lower respiratory disease	Chronic obstructive pulmonary disease (COPD)	Borlee et al. 2015
	Lower respiratory disease	Chronic obstructive pulmonary disease (COPD)	Hooiveld et al. 2016
	Lower respiratory disease	Chronic obstructive pulmonary disease (COPD)	Smit et al. 2014
Lower respiratory disease Lower respiratory	Lower respiratory disease		Star et al. 2018
Lower respiratory disease Lower respiratory	Lower respiratory disease	Cold/flu	Hooiveld et al. 2015
Lower respiratory disease Lower respiratory	Lower respiratory disease	Community-acquired pneumonia (CAP)	Kalkowska et al. 2018
Lower respiratory disease FEV1 evening (ml) FEV1 morning (ml) / forced expiratory volume FEV1/ predicted Lower respiratory disease FEV1// Protatio Lower respiratory disease PEF evening (l/min) Kersen et al. 2017 Rasmussen et al. 2017 Lower respiratory disease Lower respiratory disease PEF morning (l/min) / peak expiratory flow Rersen et al. 2020 PEF morning (l/min) Rersen et al. 2017 Rasmussen et al. 2017 R	Lower respiratory disease	Cough	Hooiveld et al. 2015
Lower respiratory disease Lower respiratory	Lower respiratory disease	Current asthma	Borlee et al. 2015
Lower respiratory diseaseEmphysema / COPDDijk et al. 2017Lower respiratory diseaseExacerbations in AsthmaDijk et al. 2017Lower respiratory diseaseExacerbations in AsthmaDijk et al. 2017Lower respiratory diseaseExacerbations in COPDDijk et al. 2017Lower respiratory diseaseFatigueHooiveld et al. 2015Lower respiratory diseaseFEV1 evening (ml)Kersen et al. 2020Lower respiratory diseaseFEV1 morning (ml) / forced expiratory volumeKersen et al. 2020Lower respiratory diseaseFEV1% predictedSchultz et al. 2019Lower respiratory diseaseFEV1/FVC ratioSchultz et al. 2019Lower respiratory diseaseInfluenzaHooiveld et al. 2016Lower respiratory diseaseLower respiratory diseaseLower respiratory diseaseLower respiratory diseaseLower respiratory diseaseLung cancerBaliatsas et al. 2017Lower respiratory diseaseLung cancerBaliatsas et al. 2017Lower respiratory diseaseNew Asthma OCS (oral corticosteroid) OrderslRasmussen et al. 2017Lower respiratory diseasePEF evening (l/min)Kersen et al. 2020Lower respiratory diseasePeF morning (l/min) / peak expiratory flowKersen et al. 2017Lower respiratory diseasePneumoniaBaliatsas et al. 2017Lower respira	Lower respiratory disease	Current asthma	Schultz et al. 2019
Lower respiratory disease	Lower respiratory disease	Doctor Diagniosed Asthma	Schultz et al. 2019
Lower respiratory disease PEF morning (l/min) Kersen et al. 2017 Lower respiratory disease Pneumonia Paliatsas et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017	Lower respiratory disease	Emphysema /COPD	Dijk et al. 2017
Lower respiratory disease Lung cancer Lower respiratory disease Preumonia Baliatsas et al. 2017 Lower respiratory disease Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2016	Lower respiratory disease	Emphysema/COPD	Dijk et al. 2017
Lower respiratory disease Fatigue Hooiveld et al. 2015 Lower respiratory disease FEV1 evening (ml) Kersen et al. 2020 Lower respiratory disease FEV1 morning (ml) / forced expiratory volume Kersen et al. 2020 Lower respiratory disease FEV1% Loftus et al. 2015 Lower respiratory disease FEV1% predicted Schultz et al. 2019 Lower respiratory disease FEV1/FVC ratio Schultz et al. 2019 Lower respiratory disease Infections of the airways Star et al. 2018 Lower respiratory disease Lower respiratory tract infections Dijk et al. 2017 Lower respiratory disease Lung cancer Baliatsas et al. 2017 Lower respiratory disease Lung cancer Baliatsas et al. 2019 Lower respiratory disease New Asthma OCS (oral corticosteroid) Ordersl Rasmussen et al. 2017 Lower respiratory disease PEF morning (l/min) Kersen et al. 2020 Lower respiratory disease PEF morning (l/min) / peak expiratory flow Kersen et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017	Lower respiratory disease	Exacerbations in Asthma	Dijk et al. 2017
Lower respiratory diseaseFEV1 evening (ml)Kersen et al. 2020Lower respiratory diseaseFEV1 morning (ml) / forced expiratory volumeKersen et al. 2020Lower respiratory diseaseFEV1%Loftus et al. 2015Lower respiratory diseaseFEV1% predictedSchultz et al. 2019Lower respiratory diseaseFEV1/FVC ratioSchultz et al. 2019Lower respiratory diseaseInfections of the airwaysStar et al. 2018Lower respiratory diseaseLower respiratory tract infectionsDijk et al. 2017Lower respiratory diseaseLung cancerBaliatsas et al. 2017Lower respiratory diseaseLung cancerBaliatsas et al. 2019Lower respiratory diseaseNew Asthma OCS (oral corticosteroid) OrderslRasmussen et al. 2017Lower respiratory diseasePEF evening (l/min)Kersen et al. 2020Lower respiratory diseasePEF morning (l/min) / peak expiratory flowKersen et al. 2017Lower respiratory diseasePneumoniaFreidl et al. 2017Lower respiratory diseasePneumoniaBaliatsas et al. 2019Lower respiratory diseasePneumoniaBaliatsas et al. 2017Lower respiratory diseasePneumoniaDijk et al. 2017Lower respiratory diseasePneumoniaDijk et al. 2017Lower respiratory diseasePneumoniaPneumoniaLower respiratory diseasePneumoniaPneumonia	Lower respiratory disease	Exacerbations in COPD	Dijk et al. 2017
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Lower respiratory disease	Fatigue	Hooiveld et al. 2015
Lower respiratory disease FEV1% predicted Schultz et al. 2019 Lower respiratory disease FEV1/FVC ratio Schultz et al. 2019 Lower respiratory disease Infections of the airways Star et al. 2018 Lower respiratory disease Influenza Hooiveld et al. 2016 Lower respiratory disease Lower respiratory tract infections Dijk et al. 2017 Lower respiratory disease Lung cancer Baliatsas et al. 2017 Lower respiratory disease Lung cancer Baliatsas et al. 2019 Lower respiratory disease New Asthma OCS (oral corticosteroid) Ordersl Rasmussen et al. 2017 Lower respiratory disease PEF evening (l/min) Kersen et al. 2020 Lower respiratory disease PEF morning (l/min) / peak expiratory flow Kersen et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017	Lower respiratory disease	FEV1 evening (ml)	Kersen et al. 2020
Lower respiratory disease PEF evening (l/min) Rersen et al. 2017 Lower respiratory disease Lower respiratory disease PeF morning (l/min) / peak expiratory flow Lower respiratory disease Pneumonia Peridl et al. 2017 Lower respiratory disease Pneumonia Pneumonia Paliatsas et al. 2019 Lower respiratory disease Pneumonia			
Lower respiratory disease	Lower respiratory disease	FEV1%	Loftus et al. 2015
Lower respiratory disease Pneumonia Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Hooiveld et al. 2016	Lower respiratory disease	FEV1% predicted	Schultz et al. 2019
Lower respiratory disease	Lower respiratory disease	FEV1/FVC ratio	Schultz et al. 2019
Lower respiratory disease Lower respiratory tract infections Dijk et al. 2017 Lower respiratory disease Lung cancer Baliatsas et al. 2019 Lower respiratory disease New Asthma OCS (oral corticosteroid) Ordersl Rasmussen et al. 2017 Lower respiratory disease PEF evening (l/min) Kersen et al. 2020 Lower respiratory disease PEF morning (l/min) / peak expiratory flow Kersen et al. 2020 Lower respiratory disease Pneumonia Freidl et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2019 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Pneumonia Dijk et al. 2017 Hooiveld et al. 2016	Lower respiratory disease	Infections of the airways	Star et al. 2018
Lower respiratory disease Lung cancer Baliatsas et al. 2017 Lower respiratory disease Lung cancer Baliatsas et al. 2019 Lower respiratory disease New Asthma OCS (oral corticosteroid) Ordersl Rasmussen et al. 2017 Lower respiratory disease PEF evening (l/min) Kersen et al. 2020 Lower respiratory disease PEF morning (l/min) / peak expiratory flow Kersen et al. 2020 Lower respiratory disease Pneumonia Freidl et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2019 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Hooiveld et al. 2016	Lower respiratory disease	Influenza	Hooiveld et al. 2016
Lower respiratory disease Lung cancer New Asthma OCS (oral corticosteroid) Ordersl Rasmussen et al. 2019 Respiratory disease PEF evening (l/min) Rersen et al. 2020 Lower respiratory disease Lower respiratory disease PEF morning (l/min) / peak expiratory flow Rersen et al. 2020 Rersen et al. 2020 Rersen et al. 2020 Rersen et al. 2017 Rersen et al. 2017 Rersen et al. 2017 Preidl et al. 2017 Representation disease Pneumonia Pneumonia Pneumonia Pneumonia Dijk et al. 2017 Rersen et al. 2017	Lower respiratory disease	Lower respiratory tract infections	Dijk et al. 2017
Lower respiratory disease Pneumonia Lower respiratory disease Pneumonia Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Hooiveld et al. 2016	Lower respiratory disease	Lung cancer	Baliatsas et al. 2017
Lower respiratory disease PEF evening (l/min) Kersen et al. 2020 Lower respiratory disease PEF morning (l/min) / peak expiratory flow Kersen et al. 2020 Lower respiratory disease pneumonia Freidl et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Hooiveld et al. 2016	Lower respiratory disease	Lung cancer	Baliatsas et al. 2019
Lower respiratory disease Preumonia Pneumonia Baliatsas et al. 2017 Baliatsas et al. 2019 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Hooiveld et al. 2016			Rasmussen et al. 2017
Lower respiratory disease pneumonia Freidl et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2019 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Hooiveld et al. 2016			
Lower respiratory disease Pneumonia Baliatsas et al. 2017 Lower respiratory disease Pneumonia Baliatsas et al. 2019 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Hooiveld et al. 2016	Lower respiratory disease	PEF morning (l/min) / peak expiratory flow	
Lower respiratory disease Pneumonia Baliatsas et al. 2019 Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Hooiveld et al. 2016	- ,		
Lower respiratory disease Pneumonia Dijk et al. 2017 Lower respiratory disease Pneumonia Hooiveld et al. 2016			Baliatsas et al. 2017
Lower respiratory disease Pneumonia Hooiveld et al. 2016			
	Lower respiratory disease		
Lower respiratory disease Respiratory symptoms Baliatsas et al. 2017			
	Lower respiratory disease	Respiratory symptoms	Baliatsas et al. 2017

Broad Catogory	Outcome variable	Reference
Broad Category		
Lower respiratory disease	Respiratory symptoms	Baliatsas et al. 2019
Lower respiratory disease	Respiratory symptoms	Dijk et al. 2017
Lower respiratory disease	Respiratory symptoms	Hooiveld et al. 2015
Lower respiratory disease	Shortness of breath/difficulty breathing	Hooiveld et al. 2015
Lower respiratory disease	Wheezing or whistling on chest in last 12 months	Borlee et al. 2015
Metabolic disease	Diabetes mellitus	Baliatsas et al. 2017
Metabolic disease	Diabetes mellitus	Baliatsas et al. 2019
Metabolic disease	Hyperlipidemia	Baliatsas et al. 2017
Neurologic disease	Dizziness	Hooiveld et al. 2015
Neurologic disease	Dizziness/Vertigo	Baliatsas et al. 2017
Neurologic disease	Dizziness/Vertigo	Baliatsas et al. 2019
Neurologic disease	Headache	Hooiveld et al. 2015
Neurologic disease	Neurological symptoms	Hooiveld et al. 2015
Neurologic disease	Vertiginous syndrome	Dijk et al. 2017
Neurologic disease	Vertigo/dizziness	Dijk et al. 2017
Ocular disease	Infections of the eye	Star et al. 2018
Ostoarticular disease	Osteoporosis	Baliatsas et al. 2017
Ostoarticular disease	Osteoporosis	Baliatsas et al. 2019
Ostoarticular disease	Rheumatoid arthritis	Baliatsas et al. 2017
Ostoarticular disease	Rheumatoid arthritis	Baliatsas et al. 2019
Other	Contacts for acute respiratory infections	Dijk et al. 2016
Other	Contacts for respiratory diagnoses	Dijk et al. 2016
Other	Contacts for respiratory symptoms	Dijk et al. 2016
Other	Diagnosis /Other infectious disease	Hooiveld et al. 2016
Other	Infections of the urinary tract	Star et al. 2018
Other	Lower back pain	Kalkowska et al. 2018
Other	Neoplasms: cancer	Star et al. 2018
Other	Other infectious disease	Hooiveld et al. 2016
Other	Primary health care visits	Dijk et al. 2016
Psychological	Acute psychological and social disorders	Star et al. 2018
Psychological	Acute psychological and social problems	Star et al. 2018
Psychological	Anxiety	Baliatsas et al. 2017
Psychological	Anxiety	Baliatsas et al. 2019
Psychological	Anxiety and depression	Star et al. 2018
Psychological	Anxiousness	Hooiveld et al. 2015
Psychological	Depression	Baliatsas et al. 2017
Psychological	Depression	Baliatsas et al. 2019
Psychological	Depression	Dijk et al. 2017
Psychological	IBD and Acute somatic symptoms of the GI-tract	Star et al. 2018
Psychological	IBD and Medically unexplained physical symptoms	Star et al. 2018
Psychological	IBD and Total acute somatic symptoms	Star et al. 2018
Psychological	Memory/Concentration problem	Baliatsas et al. 2019
Psychological Psychological	Memory/Concentration problems	Baliatsas et al. 2017
Psychological Psychological	Memory/Concentration problems Sadness	Baliatsas et al. 2019
Psychological		Hooiveld et al. 2015
Sleep disorders	Sleep problems	Baliatsas et al. 2017
Sleep disorders Sleep disorders	Sleep problems Sleeping problems	Baliatsas et al. 2019 Hooiveld et al. 2015
Stress	Odour annoyance	Hooiveld et al. 2015
Stress	Stress related symptoms	Hooiveld et al. 2015
Upper respiratory disease	Acute URI	Hooiveld et al. 2016
Upper respiratory disease	Acute URI (upper respiratory infection)	Hooiveld et al. 2016
opportion primory disease	Tiouse of a (apper respiratory infection)	11001VCIQ Ct al. 2010

Broad Category	Outcome variable	Reference
Upper respiratory disease	Laryngitis/tracheitis acute	Hooiveld et al. 2016
Upper respiratory disease	Nasal colonization of Enterobacteriaceae	Kock et al. 2016
Upper respiratory disease	Nasal colonization of non-fermenters	Kock et al. 2016
Upper respiratory disease	Nasal colonization of S. aureus	Kock et al. 2016
Upper respiratory disease	Sinusitis acute/chronic	Hooiveld et al. 2016
Upper respiratory disease	Sore throat	Hooiveld et al. 2015
Upper respiratory disease	Upper respiratory infections	Kalkowska et al. 2018
Upper respiratory disease	Upper respiratory tract infections	Baliatsas et al. 2017
Upper respiratory disease	Upper respiratory tract infections	Baliatsas et al. 2019
Upper respiratory disease	Upper respiratory tract infections	Dijk et al. 2017

Table 3: Exposures grouped into broad categories

Broad Category	Outcome variable	Reference
Density	CAFO density region	Hooiveld et al. 2016
Density	Cattle density	Levallois et al. 2014
Density	Livestock density	Dijk et al. 2017
Density	Livestock farm density	Baliatsas et al. 2019
Density	Number of animals in 500 m radius Cattle	Hooiveld et al. 2015
Density	Number of animals in 500 m radius Pigs	Hooiveld et al. 2015
Density	Number of animals in 500 m radius Poultry	Hooiveld et al. 2015
Density	Number of animals within 1000m of the residence Goats	Freidl et al. 2017
Density	Number of animals within 1000m of the residence Poultry	Freidl et al. 2017
Density	Number of cattle within 500 m	Dijk et al. 2017
Density	Number of farm animals within 1000 m	Zomer et al. 2017
Density	Number of farms	Zomer et al. 2017
Density	Number of farms (any type) within 1000m of residence	Freidl et al. 2017
Density	Number of livestock farms in 1000 m	Borlee et al. 2015
Density	One or more farms within 100 m	Dijk et al. 2017
Density	One or more farms within 500 m	Dijk et al. 2016
Density	One or more farms within 500 m	Dijk et al. 2017
Density	One or more farms within 500 m	Smit et al. 2014
Density	One or more farms within 500 m (ref no farms)	Dijk et al. 2016
Density	Permitted farrowing swine per square mile	Schinasi et al. 2014
Density	Permitted non-farrowing swine per square mile	Schinasi et al. 2014
Density	Permitted swine per square mile of block group	Schinasi et al. 2014
Density	Poultry density	Levallois et al. 2014
Density	Residence in area with livestock density	Kock et al. 2016
Density	Swine density	Levallois et al. 2014
Distance	Distance in meters from patient to nearest Farm	Zomer et al. 2017
Distance	Distance residence and closest farm with minimum number of (250 poultry)	Freidl et al. 2017
Distance	Distance residence and closest farm with minimum number of (50 goats)	Freidl et al. 2017
Distance	Distance to general practice	Dijk et al. 2016
Distance	Distance to nearest farm	Smit et al. 2014
Distance	Distance to nearest farm Cattle	Dijk et al. 2017
Distance	Distance to nearest farm Minks	Dijk et al. 2017
Distance	Distance to nearest farm Poultry	Dijk et al. 2017
Distance	Distance to nearest farm Sheep	Dijk et al. 2017
Distance	Distance to nearest farm Swine	Dijk et al. 2017
Distance	Distance to nearest farm with poultry	Dijk et al. 2017
Distance	Distance to nearest farm with swine	Dijk et al. 2017

Broad Category	Outcome variable	Reference
Distance	Distance to the nearest farm	Baliatsas et al. 2017
Distance	Distance to the nearest farm	Baliatsas et al. 2019
Distance	Distance to the nearest farm	Borlee et al. 2015
Distance	Distance to the nearest farm	Dijk et al. 2016
Distance	Distance to the nearest farm	Dijk et al. 2017
Distance	Live within 1 mile of a CAFO	Schinasi et al. 2014
Distance	Living within 500 meter of all animals farms	Star et al. 2018
Distance	Living within 500 meter of no animals farms	Star et al. 2018
Distance	Living within 500 meter of pigs farms	Star et al. 2018
Distance	Living within 500 meter of poultry farms	Star et al. 2018
Distance	Poultry operation Activity quantile	Poulsen et al. 2018
Distance	Presence of any type of farm within a certain distance of residence	Freidl et al. 2017
Distance	Presence of cattle farm animals within 1000 m	Baliatsas et al. 2017
Distance	Presence of cattle farm animals within 1000 m	Baliatsas et al. 2019
Distance	Presence of cattle farm animals within 500 m	Baliatsas et al. 2017
Distance	Presence of cattle farm animals within 500 m	Baliatsas et al. 2019
Distance	Presence of cattle within 500 m	Dijk et al. 2017
Distance	Presence of farm -intervals of residence (1000m)	Freidl et al. 2017
Distance	Presence of farm -intervals of residence (1500m)	Freidl et al. 2017
Distance	Presence of farm -intervals of residence (2000m)	Freidl et al. 2017
Distance	Presence of farm -intervals of residence (2000m)	Freidl et al. 2017
Distance	Presence of farm animals in 1000 m	Borlee et al. 2015
Distance	Presence of farm animals in 500 m	Borlee et al. 2015
Distance	Presence of farm animals in 500 m	Smit et al. 2014
Distance	Presence of farm animals within 500 m Cattle	Dijk et al. 2016
Distance	Presence of farm animals within 500 m Goats	Dijk et al. 2016 Dijk et al. 2016
Distance Distance	Presence of farm animals within 500 m Minks	Dijk et al. 2016 Dijk et al. 2016
Distance Distance	Presence of farm animals within 500 m Poultry	
Distance Distance		Dijk et al. 2016
	Presence of farm animals within 500 m Sheep Presence of farm animals within 500 m Swine	Dijk et al. 2016
Distance		Dijk et al. 2016
Distance	Presence of farm animals within 500 n	Smit et al. 2014
Distance	Presence of goats farm animals within 1000 m	Baliatsas et al. 2017
Distance	Presence of goats farm animals within 1000 m	Baliatsas et al. 2019
Distance	Presence of goats farm animals within 500 m	Baliatsas et al. 2017
Distance	Presence of livestock farms	Borlee et al. 2015
Distance	Presence of livestock within 500 m Poultry	Dijk et al. 2017
Distance	Presence of livestock within 500 m Swine	Dijk et al. 2017
Distance	Presence of mink farm animals within 1000 m	Baliatsas et al. 2017
Distance	Presence of mink farm animals within 1000 m	Baliatsas et al. 2019
Distance	Presence of mink farm animals within 500 m	Baliatsas et al. 2017
Distance	Presence of mink farm animals within 500 m	Baliatsas et al. 2019
Distance	Presence of pig farm animals within 1000 m	Baliatsas et al. 2017
Distance	Presence of pig farm animals within 1000 m	Baliatsas et al. 2019
Distance	Presence of pig farm animals within 500 m	Baliatsas et al. 2017
Distance	Presence of pig farm animals within 500 m	Baliatsas et al. 2019
Distance	Presence of poultry farm animals within 1000 m	Baliatsas et al. 2017
Distance	Presence of poultry farm animals within 1000 m	Baliatsas et al. 2019
Distance	Presence of poultry farm animals within 500 m	Baliatsas et al. 2017
Distance	Presence of poultry farm animals within 500 m	Baliatsas et al. 2019
Distance	Proximity to industrial food animal production	Rasmussen et al. 20
Distance	Residential distance to farms of one or more livestock categories (Km)	Kalkowska et al. 20
Distance	Residential distance to the nearest CAFO	Schultz et al. 2019

Broad Category	Outcome variable	Reference
Emissions	Distance to the nearest farm	Loftus et al. 2015
Emissions	Distance weighted PM10 emission from farms within 500 m	Dijk et al. 2016
Emissions	Lag 0 NH3	Kersen et al. 2020
Emissions	Lag 0 PM10	Kersen et al. 2020
Emissions	Lag 1 NH3	Kersen et al. 2020
Emissions	Lag 1 PM10	Kersen et al. 2020
Emissions	Lag 2 NH3	Kersen et al. 2020
Emissions	Lag 2 PM10	Kersen et al. 2020
Emissions	Log-weighted ammonia (NH3) emission	Baliatsas et al. 2017
Emissions	Log-weighted ammonia (NH3) emission	Baliatsas et al. 2019
Emissions	Log-weighted fine dust emission	Baliatsas et al. 2017
Emissions	Log-weighted fine dust emission	Baliatsas et al. 2019
Emissions	Modelled fine dust emission from farms	Borlee et al. 2015
Emissions	PM 10 emission from within 500 m	Smit et al. 2014
Emissions	PM10 Emission from farms within 500 m	Dijk et al. 2017
Emissions	Weekly ammonia exposure	Loftus et al. 2015
Odor	Ever have contact with horses	Schinasi et al. 2014
Odor	Ever have contact with pigs, chickens, cows, or turkeys	Schinasi et al. 2014
Odor	Ever have contact with uncooked meat products at work or at home	Schinasi et al. 2014
Odor	Ever smell odor from a farm with animals when at home	Schinasi et al. 2014
Odor	Reporting odour annoyance in neighbourhood	Hooiveld et al. 2015
Other	Live in a rural area	Schinasi et al. 2014
Other	Living within 1500m of Q-fever positive farm	Freidl et al. 2017
Other	Living within 2000m of Q-fever positive farm	Freidl et al. 2017
Other	Serostatus for Coxiella burnetii	Freidl et al. 2017
Other	Serostatus for Coxiella burnetii (Q-fever)	Freidl et al. 2017
Type of CAFO	Type of CAFO (ALL)	Hooiveld et al. 2016
Type of CAFO	Type of CAFO (Goat only)	Hooiveld et al. 2016
Type of CAFO	Type of CAFO (Poultry only)	Hooiveld et al. 2016
Type of CAFO	Type of CAFO (Swine only)	Hooiveld et al. 2016

References

- [1] Kersen W van, Oldenwening M, Aalders B, Bloemsma LD, Borlée F, Heederik D, et al. Acute respiratory effects of livestock-related air pollution in a panel of copd patients. Environment International 2020;136:105426.
- [2] Baliatsas C, Smit LA, Dückers ML, Dijk CE van, Heederik D, Yzermans CJ. Patients with overlapping diagnoses of asthma and copd: Is livestock exposure a risk factor for comorbidity and coexisting symptoms and infections? BMC Pulmonary Medicine 2019;19:105.
- [3] Schultz AA, Peppard P, Gangnon RE, Malecki KM. Residential proximity to concentrated animal feeding operations and allergic and respiratory disease. Environment International 2019;130:104911.
- [4] Kalkowska DA, Boender GJ, Smit LA, Baliatsas C, Yzermans J, Heederik DJ, et al. Associations between pneumonia and residential distance to livestock farms over a five-year period in a large population-based study. PloS One 2018;13.
- [5] Star BJ van der, Dijk CE van, Zock J-P, Smit LA, Baliatsas C, Heederik DJ, et al. Healthcare utilisation prior to the diagnosis of inflammatory bowel diseases and the influence of livestock exposure: A longitudinal case-control study. PloS One 2018;13.
- [6] Poulsen MN, Pollak J, Sills DL, Casey JA, Rasmussen SG, Nachman KE, et al. Residential proximity to high-density poultry operations associated with campylobacteriosis and infectious diarrhea. International

- Journal of Hygiene and Environmental Health 2018;221:323-33.
- [7] Dijk CE van, Zock J-P, Baliatsas C, Smit LA, Borlée F, Spreeuwenberg P, et al. Health conditions in rural areas with high livestock density: Analysis of seven consecutive years. Environmental Pollution 2017;222:374–82.
- [8] Rasmussen SG, Casey JA, Bandeen-Roche K, Schwartz BS. Proximity to industrial food animal production and asthma exacerbations in pennsylvania, 2005–2012. International Journal of Environmental Research and Public Health 2017;14:362.
- [9] Zomer TP, Duijkeren E van, Wielders C, Veenman C, Hengeveld P, Van Der Hoek W, et al. Prevalence and risk factors for colonization of clostridium difficile among adults living near livestock farms in the netherlands. Epidemiology & Infection 2017;145:2745–9.
- [10] Baliatsas C, Borlée F, Dijk CE van, Star B van der, Zock J-P, Smit LA, et al. Comorbidity and coexisting symptoms and infections presented in general practice by copd patients: Does livestock density in the residential environment play a role? International Journal of Hygiene and Environmental Health 2017;220:704–10.
- [11] Freidl GS, Spruijt IT, Borlée F, Smit LA, Gageldonk-Lafeber AB van, Heederik DJ, et al. Livestock-associated risk factors for pneumonia in an area of intensive animal farming in the netherlands. PloS One 2017;12.
- [12] Dijk CE van, Garcia-Aymerich J, Carsin A-E, Smit LA, Borlée F, Heederik DJ, et al. Risk of exacerbations in copd and asthma patients living in the neighbourhood of livestock farms: Observational study using longitudinal data. International Journal of Hygiene and Environmental Health 2016;219:278–87.
- [13] Hooiveld M, Smit LA, Sman-de Beer F van der, Wouters IM, Dijk CE van, Spreeuwenberg P, et al. Doctor-diagnosed health problems in a region with a high density of concentrated animal feeding operations: A cross-sectional study. Environmental Health 2016;15:24.
- [14] Köck R, Werner P, Friedrich A, Fegeler C, Becker K, Bindewald O, et al. Persistence of nasal colonization with human pathogenic bacteria and associated antimicrobial resistance in the german general population. New Microbes and New Infections 2016:9:24–34.
- [15] Borlée F, Yzermans CJ, Dijk CE van, Heederik D, Smit LA. Increased respiratory symptoms in copd patients living in the vicinity of livestock farms. European Respiratory Journal 2015;46:1605–14.
- [16] Loftus C, Yost M, Sampson P, Torres E, Arias G, Vasquez VB, et al. Ambient ammonia exposures in an agricultural community and pediatric asthma morbidity. Epidemiology (Cambridge, Mass) 2015;26:794.
- [17] Hooiveld M, Dijk CE van, Sman-de Beer F van der, Smit LA, Vogelaar M, Wouters IM, et al. Odour annoyance in the neighbourhood of livestock farming–perceived health and health care seeking behaviour. Annals of Agricultural and Environmental Medicine 2015;22.
- [18] Schinasi L, Wing S, Augustino KL, Ramsey KM, Nobles DL, Richardson DB, et al. A case control study of environmental and occupational exposures associated with methicillin resistant staphylococcus aureus nasal carriage in patients admitted to a rural tertiary care hospital in a high density swine region. Environmental Health 2014;13:54.
- [19] Smit LA, Hooiveld M, Sman-de Beer F van der, Opstal-van Winden AW, Beekhuizen J, Wouters IM, et al. Air pollution from livestock farms, and asthma, allergic rhinitis and copd among neighbouring residents. Occupational and Environmental Medicine 2014;71:134–40.
- [20] Levallois P, Chevalier P, Gingras S, Déry P, Payment P, Michel P, et al. Risk of infectious gastroenteritis in young children living in québec rural areas with intensive animal farming: Results of a case–control study (2004–2007). Zoonoses and Public Health 2014;61:28–38.
- [21] Dijk CE van, Smit LA, Hooiveld M, Zock J-P, Wouters IM, Heederik DJ, et al. Associations between proximity to livestock farms, primary health care visits and self-reported symptoms. BMC Family Practice 2016;17:22.