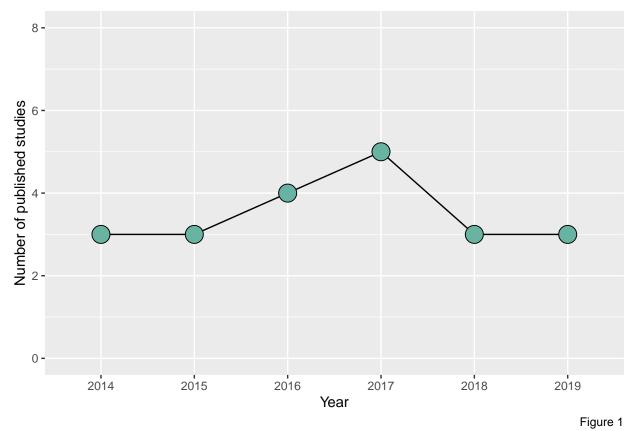
Human health effects due to proximity to concentrated animal-feeding operations (CAFO)

Updated outcomes/exposures from 2014 to 2019

Livestock farming has experienced a significant transformation in the last decades, moving from small, family-owned farms to large farms. In order to define and classify those large animal operations, two terms have been adopted: animal feeding operations (AFO) and concentrated animal feeding operations (CAFO). The U.S. Environmental Protection Agency (EPA) define AFOs as 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 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 exposition to odors, emissions and other harmful agents.

In order to understand and estimate the possible deleterious impacts of CAFO over the health of nearby communities, several studies have been carried out in the last years. Our group has performed two systematic reviews whose goal was to 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. Although there were 16 papers relevant to the topic before 2014, we found 21 additional papers published since then. 2017 was the year in which more studies were published (Figure 1). This shows how much the topic has growing. These "new" studies have been performed mainly in Netherlands, USA, Germany and Canada and have explored multiple health outcomes (Figure 2).

In order to summarize and organize the multiple outcomes analized in the studies, the reported outcomes were grouped in broad categories based on the affected body system such as digestive, cardiovascular, etc (Table 2). Whereas for the period of time between 2014 and 2016 the number of outcomes categories analyzed ranged from 4 to 6, for the period of time between 2017 and 2019 the number of categories almost doubled (Figure 3). We defined a combination as the pair of a broad category and a exposure, for example, lower respiratory problem (broad category) and distance to the nearest CAFO operation (exposure). In the table 1, it is possible to observe the number of combinations in which the broad 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).



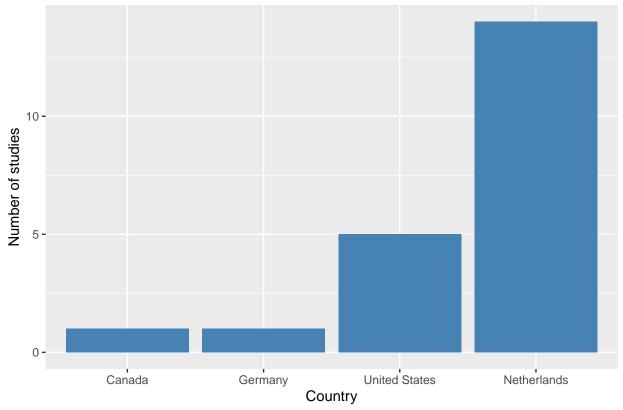


Figure 2

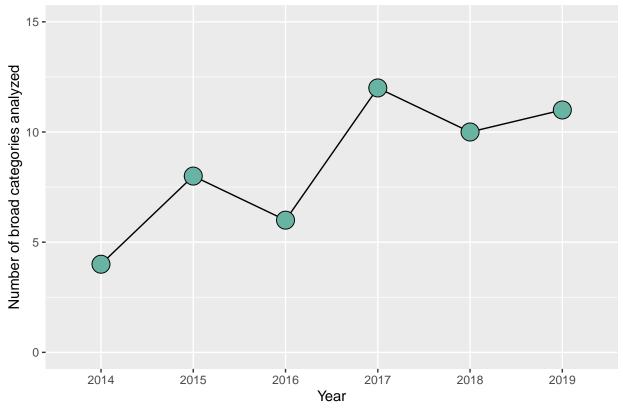


Figure 3

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).

From 2014 to date, 1637 different outcome / exposure combinations were identified in 20 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.

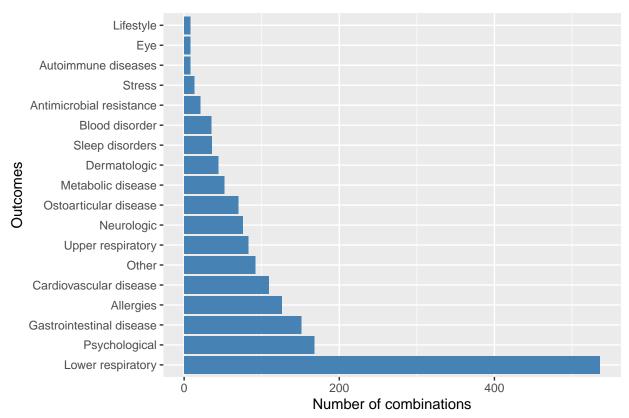


Figure 4

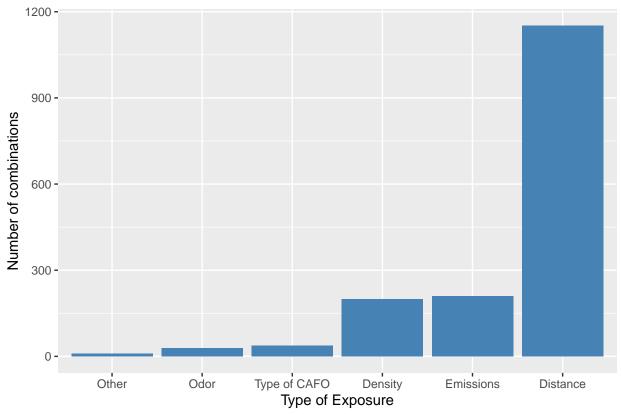


Figure 5

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, 20 studies passed Level 2 and passed to the extraction of information.

Data collection process

For each of the 20 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	0	0	6	22	16	0
Eye	0	0	0	0	8	0
Gastrointestinal disease	3	7	12	71	40	18
Lifestyle	0	0	0	0	8	0
Lower respiratory	24	127	48	201	22	114
Metabolic disease	0	0	0	34	0	18
Neurologic	0	3	0	55	0	18
Ostoarticular disease	0	0	0	34	0	36
Other	0	0	70	0	22	0
Psychological	0	2	0	71	41	54
Sleep disorders	0	1	0	17	0	18
Stress	0	13	0	0	0	0
Upper respiratory	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
Cardiovascular disease	Hypertension	Baliatsas et al. 2017
Cardiovascular disease	Hypertension	Baliatsas et al. 2019
Dermatologic	Atopic eczema	Hooiveld et al. 2016
Dermatologic	Chronic/long-term diseases of the skin	Star et al. 2018
Dermatologic	Constitutional eczema	Dijk et al. 2017
Dermatologic	Infections of the skin	Star et al. 2018
Dermatologic	Vertiginous syndrome	Dijk et al. 2017
Eye	Infections of the eye	Star et al. 2018
Gastrointestinal disease	Acute children gastroenteritis	Levallois et al. 2014
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	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	GERD	Baliatsas et al. 2017
Gastrointestinal disease	GERD	Baliatsas et al. 2019
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. 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
	, -	

Broad Category	Outcome variable	Reference
Gastrointestinal disease	Salmonella	Poulsen et al. 2018
Gastrointestinal disease	Stomach ache (pain in belly)	Hooiveld et al. 2015
Gastrointestinal disease	Stomach complaints	Hooiveld et al. 2015
Lifestyle	Lifestyle: weight and diet	Star et al. 2018
Lower respiratory	Asthma	Dijk et al. 2017
Lower respiratory	Asthma	Hooiveld et al. 2016
Lower respiratory	Asthma	Smit et al. 2014
Lower respiratory	Asthma Emergency Department Visits	Rasmussen et al. 2017
Lower respiratory	Asthma Episode in last 12 months	Schultz et al. 2019
Lower respiratory	Asthma Hospitalizations	Rasmussen et al. 2017
Lower respiratory	Asthma medication in last 12 months	Schultz et al. 2019
Lower respiratory	Asthma symptoms /Limitation of activities	Loftus et al. 2015
Lower respiratory	Asthma symptoms /Nighttime waking	Loftus et al. 2015
Lower respiratory	Asthma symptoms /Shortness of breath	Loftus et al. 2015
Lower respiratory	Asthma symptoms /Symptoms worse in morning	Loftus et al. 2015
Lower respiratory	Asthma symptoms /Use of short-acting "relief" medication	Loftus et al. 2015
Lower respiratory	Asthma symptoms /Wheezing	Loftus et al. 2015
Lower respiratory	Chronic bronchitis/bronchiectasis	Dijk et al. 2017
Lower respiratory	Chronic/long-term diseases of the airways	Star et al. 2018
Lower respiratory	Cold/flu	Hooiveld et al. 2015
Lower respiratory	Community-acquired pneumonia (CAP)	Kalkowska et al. 2018
Lower respiratory	COPD	Borlee et al. 2015
Lower respiratory	COPD	Hooiveld et al. 2016
Lower respiratory	COPD	Smit et al. 2014
Lower respiratory	Cough	Hooiveld et al. 2015
Lower respiratory	Current asthma	Borlee et al. 2015
Lower respiratory	Current asthma	Schultz et al. 2019
Lower respiratory	Doctor Diagniosed Asthma	Schultz et al. 2019
Lower respiratory	Emphysema /COPD	Dijk et al. 2017
Lower respiratory	Emphysema/COPD	Dijk et al. 2017 Dijk et al. 2017
Lower respiratory	Exacerbations in Asthma	Dijk et al. 2017 Dijk et al. 2017
Lower respiratory	Exacerbations in COPD	Dijk et al. 2017 Dijk et al. 2017
Lower respiratory	Fatigue	Hooiveld et al. 2015
Lower respiratory	FEV1 evening (ml)	Kersen et al. 2020
Lower respiratory	FEV1 morning (ml) / forced expiratory volume	Kersen et al. 2020
Lower respiratory	FEV1%	Loftus et al. 2015
Lower respiratory	FEV1% predicted	Schultz et al. 2019
Lower respiratory	FEV1/FVC ratio	Schultz et al. 2019 Schultz et al. 2019
Lower respiratory	Infections of the airways	Star et al. 2018
Lower respiratory	Influenza	Hooiveld et al. 2016
Lower respiratory	Lower respiratory tract infections	Dijk et al. 2017
Lower respiratory		Baliatsas et al. 2017
- *	Lung cancer	
Lower respiratory	Lung cancer New Asthrop OCS (and continuation) Orderel	Baliatsas et al. 2019
Lower respiratory	New Asthma OCS (oral corticosteroid) Ordersl	Rasmussen et al. 2017
Lower respiratory	PEF evening (1/min)	Kersen et al. 2020
Lower respiratory	PEF morning (l/min) / peak expiratory flow	Kersen et al. 2020
Lower respiratory	pneumonia Programia	Freidl et al. 2017
Lower respiratory	Preumonia	Baliatsas et al. 2017
Lower respiratory	Pneumonia	Baliatsas et al. 2019
Lower respiratory	Pneumonia	Dijk et al. 2017
Lower respiratory	Pneumonia	Hooiveld et al. 2016
Lower respiratory	Respiratory symptoms	Baliatsas et al. 2017

Broad Category	Outcome variable	Reference
Lower respiratory	Respiratory symptoms	Baliatsas et al. 2019
Lower respiratory	Respiratory symptoms	Dijk et al. 2017
Lower respiratory	Respiratory symptoms	Hooiveld et al. 2015
Lower respiratory	Shortness of breath/difficulty breathing	Hooiveld et al. 2015
Lower respiratory	Wheezing or whistling on chest in last 12 months / COPD	Borlee et al. 2015
Lower respiratory	Wheezing or whistling on chest in last 12 months / Current asthma	Borlee et al. 2015
Lower respiratory	Wheezing or whistling on chest in last 12 months /Nasal allergies	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	Dizziness	Hooiveld et al. 2015
Neurologic	Dizziness/Vertigo	Baliatsas et al. 2017
Neurologic	Dizziness/Vertigo	Baliatsas et al. 2019
Neurologic	Headache	Hooiveld et al. 2015
Neurologic	Neurological symptoms	Hooiveld et al. 2015
Neurologic	Vertiginous syndrome	Dijk et al. 2017
Neurologic	Vertigo/dizziness	Dijk et al. 2017
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	All contacts (primary health care visits)	Dijk et al. 2016
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
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 patients/Acute somatic symptoms: symptoms of the GI-tract	Star et al. 2018
Psychological	IBD patients/Total acute somatic symptoms/ MUPS	Star et al. 2018
Psychological Psychological	IBD patients/Total infections	Star et al. 2018
Psychological Psychological	Memory/Concentration problem	Baliatsas et al. 2019
Psychological Psychological	Memory/Concentration problems	Baliatsas et al. 2017
Psychological Psychological	Memory/Concentration problems	Baliatsas et al. 2019
Psychological Psychological	Sadness	Hooiveld et al. 2015
Sleep disorders	Sleep problems	Baliatsas et al. 2017
Sleep disorders Sleep disorders	Sleep problems	Baliatsas et al. 2017 Baliatsas et al. 2019
Sleep disorders	Sleeping problems	Hooiveld et al. 2015
Stress	Odour annoyance	Hooiveld et al. 2015
Stress	Stress related symptoms	Hooiveld et al. 2015
Upper respiratory	Acute URI	Hooiveld et al. 2016

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

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